Enantioselective Synthesis of (—)-Maoecrystal V by Enantiodetermining C—H Functionalization

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Supporting Information. Part 1

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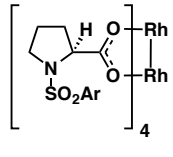
Synthesis

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 temperature was 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 (EMD, Geduran, no. 1.11567.9026) as the stationary phase. Proton nuclear magnetic resonance spectra were recorded at 400, 500, and 600 MHz on Varian Unity Inova. Carbon nuclear magnetic resonance spectra were recorded at 100 MHz, 125 MHz, and 150 MHz on Varian Unity Inova, and Varian Unity Inova spectrometers. All chemical shifts were reported in δ units relative to tetramethylsilane. Optical rotations were measured on a Rudolph Autopol III polarimeter. High resolution mass spectral data were obtained by the Mass Spectrometry laboratory at the University of California, Santa Barbara.

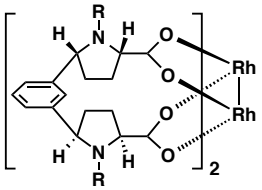
Part A. Enantioseletive synthesis of dihydrobenzofuran precursors.

a. Catalytic approach.



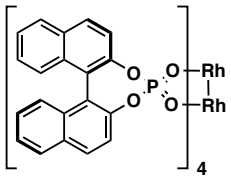
Ar = *p*-$C_{12}H_{25}C_6H_4$

Rh_2(*S*-DOSP)$_4$

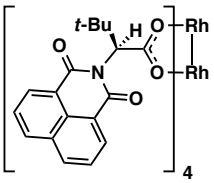


R = SO_2-2,4,6-tri-*i*-PrC_6H_2

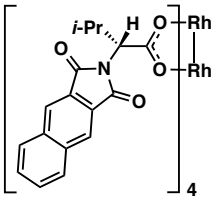
Rh_2(*S*-biTISP)$_2$



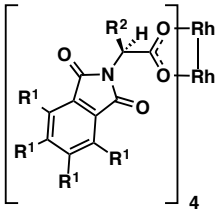
Rh_2(R-BNP)$_4$



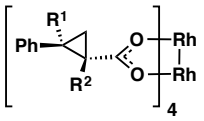
Rh_2(*S*-NTTL)$_4$



Rh_2(*R*-BPTV)$_4$

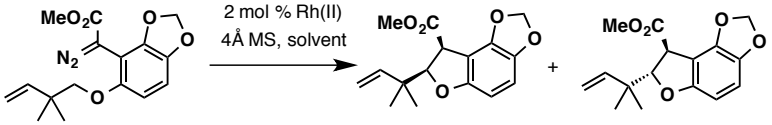


R^1 = H, R^2 = *t*-Bu	**Rh_2(*S*-PTTL)$_4$**
R^1 = H, R^2 = adamantyl	**Rh_2(*S*-PTAD)$_4$**
R^1 = H, R^2 = *i*-Pr	**Rh_2(*S*-PTV)$_4$**
R^1 = Cl, R^2 = *t*-Bu	**Rh_2(*S*-TCPTTL)$_4$**
R^1 = Cl, R^2 = adamantyl	**Rh_2(*S*-TCPTAD)$_4$**



R^1 = Ph, R^2 = 4-BrPh	**Rh_2(*R*-BTPCP)$_4$**
R^1 = H, R^2 = Ph	**Rh_2(*R*-DPCP)$_4$**

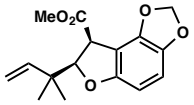
Scheme S1. Rhodium catalysts and their structures (for Tables 1 and 2).



9 *cis*-**10** *trans*-**10**

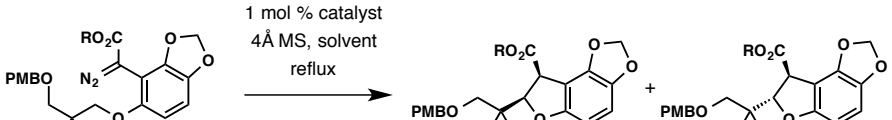
General procedure for CH-cyclization of 9 (Table 1): A mixture of diazo compound **9** (0.05 mmol, 1 equiv), 4 Å molecular sieves (~0.5 g, 0.10 g/0.01 mmol of the diazo compound) and the solvent (2 mL) was degassed by bubbling argon for about 10 min. Under argon atmosphere, a solution of catalyst in degassed solvent (0.5 mL) was added dropwise over 0.5 min to the above mixture. The resulting mixture was then stirred at the designated temperature for 2-3 h. The solvent was then removed under vacuum and the residue was purified by flash chromatography.

Note: The absolute configuration of chiral centers in the products was not determined.



cis-**10**

Dihydrobenzofuran *cis*-10 (entry 1): Purified by flash chromatography (SiO_2, 10% ethyl acetate in hexanes). Ee: 70% (Chiralcel® AD-H, 0.5% *i*-PrOH in hexane, flow rate = 1.0 mL/min, detection at λ=210 nm, t_R=12.3 min, minor; 13.3 min, major). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 6.64 (dd, *J*=8.3, 0.6 Hz, 1H), 6.32 (dd, *J*=8.3, 0.6 Hz, 1H), 6.05 (dd, *J*=17.8, 10.6 Hz, 1H), 5.90 (dd, *J*=8.8, 1.4 Hz, 2H), 5.07-4.99 (m, 2H), 4.48 (d, *J*=8.0 Hz, 1H), 4.09-4.02 (m, 1H), 3.56 (s, 3H), 1.25 (s, 3H), 1.22 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 170.4 (C), 156.3 (C), 143.2 (C), 142.3 (C), 141.8 (CH), 112.4 (CH_2), 109.0 (C), 107.7 (CH), 101.5 (CH_2), 100.6 (CH), 93.5 (CH), 51.6 (CH_3), 47.0 (CH), 39.8 (C), 26.9 (CH_3), 22.6 (CH_3). IR (neat): 2952, 1735, 1457, 1435, 1231, 1204, 1163, 1067, 1050, 1009 cm^{-1}. HRMS-APCI (*m/z*): $[M+H]^+$ calcd. for $C_{16}H_{21}O_5$, 291.1227; found, 291.1225.

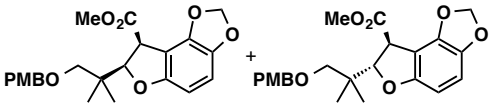


11 *cis*-**12** *trans*-**12**

General procedure for CH-cyclization of 11 (Table 2): Diazo ester **11** (13.6 μmol/mL in hexanes, 2.5 mL, 15.0 mg, 33.9 μmol, 1.0 equiv) was transferred into a vial. The solvent was removed by rotary evaporation and replaced with 2.5 mL of the appropriate solvent. Similarly, the rhodium catalyst (1 mg/mL in CH_2Cl_2, 0.339 μmol, 1 mol %) was transferred to a 10 mL round-bottomed flask. The solvent was removed by rotary evaporation and replaced with 1.0 mL of the appropriate solvent. To the solution of the catalyst was added activated, powdered 4 Å molecular sieves (50 mg), and the solution was heated to reflux. The solution of the diazo compound **11** was then added dropwise over 2 h to the catalyst solution at reflux. The mixture was stirred for an extra 30 min, and cooled. The reaction mixture was filtered through Celite® to remove the molecular sieves and rinsed with the reaction solvent. The filtrate was concentrated and analyzed by ^{1}H NMR spectroscopy to determine the dr. The crude product was purified by flash column

chromatography (using a Pasteur pipet as a column, eluting with 15% ethyl acetate in hexanes). The product was isolated as a mixture of *cis* and *trans* isomers.

Note: The absolute configuration of chiral centers in the products was not determined.

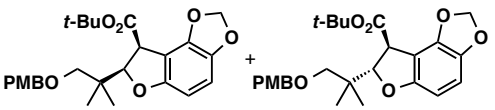


cis-**12a** *trans*-**12a**

Dihydrobenzofuran 12a (R = Me):

Characterization data is reported on the mixture. The data for *trans*-**12a** was compared to the published data, and the other compound was tentatively assigned to be *cis*-**12a.**

^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): d 7.25 (d, *J*=9.4 Hz, 2H, *cis*), 7.19 (d, *J*=8.6 Hz, 2H, *trans*), 6.89-6.84 (overlap), 6.63 (d, *J*=8.2 Hz, 1H, *cis*), 6.61 (d, *J*=8.3 Hz, 1H, *trans*), 6.29 (d, *J*=8.2 Hz, 1H, *cis*), 6.21 (d, *J*=8.3 Hz, 1H, *trans*), 5.93 (d, *J*=1.4 Hz, 1H, *trans*), 5.91 (d, *J*=1.4 Hz, 1H, *cis*), 5.89 (d, *J*=1.4 Hz, 1H, *cis*), 5.86 (d, *J*=1.4 Hz, 1H, *trans*), 4.99 (d, 1H, *J*=7.1 Hz, 1H, *trans*), 4.75 (d, 1H, *J*=8.0 Hz, 1H, *cis*), 4.47 (s, 2H, *cis*), 4.40-4.36 (overlap), 4.32 (d, *J*=11.8 Hz, 1H, *trans*), 4.04 (d, *J*=8.0 Hz, 1H, *cis*), 3.80 (s, overlap), 3.72 (s, 3H, *trans*), 3.65 (s, 3H, *cis*), 3.43 (d, *J*=8.9 Hz, 1H, *cis*), 3.32-3.36 (overlap), 1.09 (s, 3H, *cis*), 1.01 (s, 3H, *cis*), 0.97 (s, 3H, *trans*), 0.96 (s, 3H, *trans*). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 172.1 (*trans*), 171.4 (*cis*), 159.0 (*trans*), 158.9 (*cis*), 156.4 (overlap), 143.4 (*trans*), 143.2 (*cis*), 142.1 (*cis*), 141.8 (*trans*), 130.7 (*cis*), 130.5 (*trans*), 128.9 (*cis*), 128.8 (*trans*), 113.6 (*trans*), 113.6 (*cis*), 109.1 (*cis*), 107.8 (*trans*), 107.6 (*cis*), 107.4 (*trans*), 101.4 (overlap), 100.6 (*cis*), 99.8 (*trans*), 91.0 (*trans*), 90.5 (*cis*), 76.9 (*cis*), 75.9 (*trans*), 72.9 (*cis*), 72.9 (*trans*), 55.3 (overlap), 52.5 (*trans*), 52.2 (*cis*), 46.7 (*trans*), 46.5 (*cis*), 38.8 (*trans*), 37.9 (*cis*), 20.6 (*cis*), 20.5 (*trans*), 20.3 (*trans*), 20.3 (*cis*). IR (film): 2953, 2878, 1737, 1456, 1231 cm^{-1}. HRMS-NSI (*m/z*): $[M]^+$ calcd for $C_{23}H_{26}O_7$ 414.1673; found 414.1675. HPLC analysis: Chiralcel® OD-H, 1% *i*-PrOH in hexanes, flow rate = 1.0 mL/min, detection at λ=210 nm, *cis*-**12a:** t_R=18.3 min, 20.1 min; *trans*-**12a:** t_R=11.5 min, 23.9 min.



cis-**12b** *trans*-**12b**

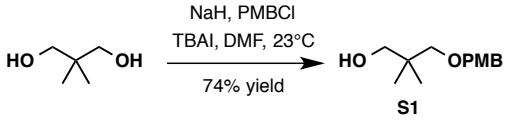
Dihydrobenzofuran 12b (R = *t*-Bu):

Characterization data is reported on the mixture. The *cis*-**12b** and *trans*-**12b** assignments in the ^{1}H NMR are made tentatively by comparison to the ^{1}H NMR spectra of **12a**, which has the same general pattern.

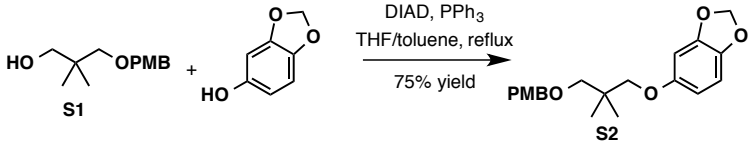
^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 7.25 (d, *J*=8.7 Hz, 2H, *cis*), 7.20 (d, *J*=8.7 Hz, 2H, *trans*), 6.89-6.84 (overlap), 6.62 (dd, *J*=8.3, 0.4 Hz, 1H, *cis*), 6.60 (dd, *J*=8.3, 0.7 Hz, 1H, *trans*), 6.27 (dd, *J*=8.3, 0.6 Hz, 1H, *cis*) 6.19 (d, *J*=8.3 Hz, 1H, *trans*), 5.92 (d, *J*=1.5 Hz, 1H, *trans*), 5.90 (d, *J*=1.4 Hz, 1H, *cis*), 5.88 (overlap), 4.96 (d, *J*=7.1 Hz, 1H, *trans*), 4.72 (d, *J*=8.2 Hz, 1H, *cis*), 4.47 (s, 2H, *cis*), 4.42 (d, *J*=11.9 Hz, 1H, *trans*), 4.36 (d, *J*=11.9 Hz, 1H, *trans*), 4.26 (d, *J*=7.1 Hz, 1H, *trans*), 3.96 (d, *J*=8.2 Hz, 1H, *cis*), 3.80 (s, overlap), 3.45 (d, *J*=8.9 Hz, 1H, *cis*) 3.34 (d, *J*=8.9 Hz, 1H, *cis*), 3.32 (d, *J*=9.0 Hz, 1H, *trans*) 3.27 (d, *J*=9.0 Hz, 1H, *trans*), 1.46 (s, 9H, *trans*), 1.41 (s, 9H,

cis), 1.15 (s, 3H, *cis*), 1.09 (s, 3H, *cis*), 0.96 (s, 3H, *trans*), 0.94 (s, 3H, *trans*). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 170.6, 170.4, 159.0, 158.9, 156.4, 156.4, 143.5, 143.1, 141.9, 141.8, 130.8, 130.7, 128.9, 128.8, 113.7, 113.6, 110.2, 108.0, 107.7, 107.5, 101.4, 101.2, 100.5, 99.7, 90.8, 90.4, 81.7, 81.7, 77.2, 75.9, 72.9, 55.3, 48.3, 48.0, 38.8, 38.1, 27.9, 27.8, 21.0, 20.7, 20.6, 19.9. IR (film): 2973, 2932, 1729, 1457, 1232 cm^{-1}. HRMS (NSI) *m/z:* $[M+Na]^+$ calcd for $C_{26}H_{32}O_7Na$ 479.2040; found 479.2042. HPLC analysis (peaks were not separated completely to baseline, ee values are approximate): SS-WHELK column, 0.3 % *i*-PrOH in hexanes flow rate = 0.8 mL/min, dection at λ=210 nm, ***cis*-12b:** t_R=28.3 min, 32.4 min; ***trans*-12b:** t_R= 30.6 min, 36.6 min.

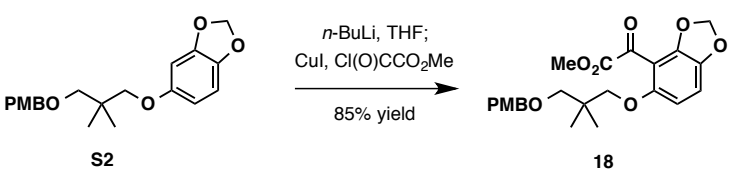
b. Transannular cyclization approach.



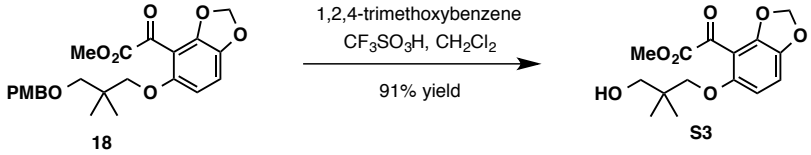
Alcohol S1. Sodium hydride (60% dispersion in mineral oil, 3.84 g, 96.0 mmol) was added portion-wise to a solution of 2,2-dimethyl-1,3-propanediol (8.32 g, 79.9 mmol) in DMF (80 mL) at 0 °C. The resulting mixture was stirred for 30 min, then *n*-Bu_4NI (2.96 g, 8.01 mmol) and *p*-methoxybenzyl chloride (10.8 mL, 79.7 mmol) were added. After stirring for an additional 1 h at 0 °C, the reaction mixture was allowed to warm to 23 °C and stirred overnight. The resultant suspension was quenched with a saturated aqueous NH_4Cl solution and extracted with ethyl acetate. 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 (25-35% ethyl acetate in hexanes) to afford the alcohol **S1** (13.3 g, 59.3 mmol, 74%). ^{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).



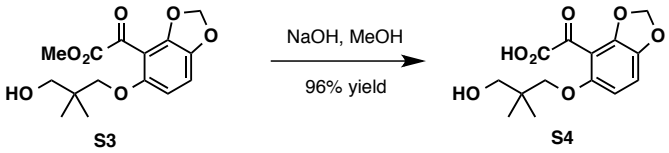
Ether S2. Diisopropyl azodicarboxylate (10 mL, 51.0 mmol) was added dropwise to a solution of sesamol (8.20 g, 59.4 mmol), alcohol **S1** (10.2 g, 46.0 mmol) and Ph_3P (13.2 g, 50.0 mmol) in THF (120 mL) and toluene (10 mL) at 0 °C. The resulting mixture was then heated at reflux for 18 h. After cooling, 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 ether **S2** (11.4 g, 33.1 mmol, 75%). ^{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, *J*=8.5, 2.5 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).



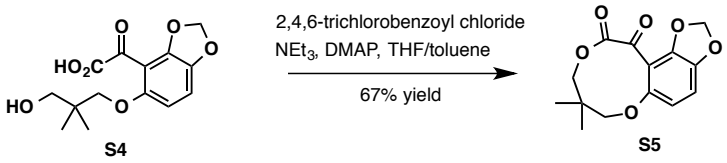
α-Keto ester 18. *n*-Butyllithium (16.7 mL, 2.5 M in hexanes, 41.4 mmol) was added dropwise to a solution of substrate **S2** (11.4 g, 33.1 mmol) in THF (120 mL) at 0 °C and the resulting dark-yellow solution was stirred at room temperature for 2 h. Then the reaction mixture was cooled to 0 °C and CuI (3.45 g, 18.2 mmol) was added. The reaction was stirred for 1 h at 23 °C then resultant dark-brown solution was cooled to -78 °C and methyl chlorooxoacetate (3.8 mL, 41.4 mmol) was added and the reaction mixture was allowed to stir at 23 °C for 3 h. The reaction mixture then was quenched with a saturated aqueous NH_4Cl solution and extracted with ethyl acetate. 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 (25% ethyl acetate in hexanes) to deliver α-keto ester **18** (12.1 g, 28.2 mmol, 85%). ^{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).



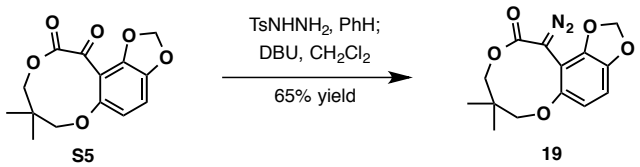
Alcohol S3. Modified Jung's procedure was used[1]. Triflic acid (10 μL, 0.116 mmol) was added to a solution of substrate **18** (0.100 g, 0.232 mmol) and 1,2,4-trimethoxybenzene (0.117 g, 0.697 mmol) in CH_2Cl_2 (10 mL). After stirring for 20 min, the resultant yellow solution was quenched with triethylamine (0.10 mL), and washed with 1M aqueous solution of HCl and water sequentially. The organic phase was dried over Na_2SO_4, concentrated and the residue was purified by column chromatography on silica gel (50% ethyl acetate in hexanes) to deliver alcohol **S3** (65.6 mg, 0.211 mmol, 91%). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 6.87 (d, *J*=8.6 Hz, 1H), 6.36 (d, *J*=8.6 Hz, 1H), 6.02 (s, 2H), 3.89 (s, 3H), 3.72 (s, 2H), 3.42 (s, 2H), 2.33 (s, 1H), 0.94 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 183.6, 164.0, 154.0, 149.6, 142.5, 113.0, 108.8, 103.9, 102.9, 76.4, 68.9, 53.0, 36.6, 21.7. HRMS-ESI (*m*/*z*): $[M]^+$ calcd for $C_{15}H_{18}O_7Na$, 310.1053; found, 310.1056.



Acid S4. A precooled 1 M methanolic solution of sodium hydroxide (10 mL) was added to a solution of alcohol **S3** (0.175 g, 0.565 mmol) in MeOH (1 mL) at 0 °C. After stirring overnight, methanol was evaporated under reduced pressure until dryness. The crude mixture was dissolved in water (20 mL) and extracted with diethyl ether. The aqueous phase was then acidified by addition of 1M aqueous solution of HCl to PH=3 and extracted with ethyl acetate. The combined organic phase was dried over Na_2SO_4 and concentrated to afford product **S4** (0.160 g, 0.541 mmol, 96%). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.96 (br. s, 2H), 6.87 (d, *J*=8.6 Hz, 1H), 6.34 (d, *J*=8.6 Hz, 1H), 6.04 (s, 2H), 3.77-3.63 (m, 2H), 3.56 (s, 2H), 0.96 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 184.7, 165.8, 153.7, 149.6, 142.8, 113.0, 108.7, 103.8, 102.9, 75.8, 68.4, 36.3, 21.6. HRMS-ESI (*m*/*z*): $[M-H+2Na]^+$ calcd for $C_{14}H_{15}O_7Na_2$, 341.0613; found, 341.0611.

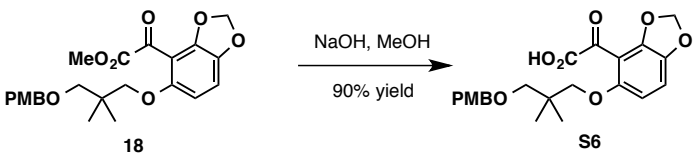


Macrolactone S5. Triethylamine (0.12 mL, 0.865 μmol) was added to a mixture of substrate **S4** (0.160 g, 0.540 mmol) and 2,4,6-trichlorobenzoyl chloride (0.210 g, 0.865 mmol) in THF (10 mL) and the reaction was stirred for 2 h at 23 °C. The resulting white precipitate was filtered, the filtrate was diluted with toluene (40 mL) and heated at reflux. A solution of DMAP (106 mg, 0.865 mmol) in toluene (10 mL) was then added dropwise over 1 h. After additional 30 min, the reaction mixture was cooled, concentrated, and the residue was purified by column chromatography on silica gel (50% ethyl acetate in hexanes) to afford product **S5** (0.101 g, 0.363 mmol, 67%). ^{1}H NMR (500 MHz, DMSO-D_6, 80°C) δ (ppm): 7.17 (d, *J*=8.5 Hz, 1H), 6.78 (d, *J*=8.5 Hz, 1H), 6.17 (s, 2H), 4.35 (brs, 2H), 4.14 (s, 2H), 0.95 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ (ppm): 183.9, 163.8, 155.3, 149.0, 144.0, 113.5, 112.1, 110.0, 103.3, 82.3, 73.8, 35.8, 24.3. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{14}H_{14}O_6Na$, 301.0688; found, 301.0686.



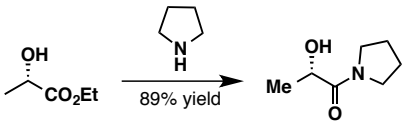
Diazomacrolactone 19. A mixture of substrate **S5** (40 mg, 0.143 mmol) and $TsNHNH_2$ (27 mg, 0.143 mmol) in benzene (5 mL) was heated to reflux for 2 h, during that time water was collected in a Dean-Stark apparatus. After cooling, the solvent was removed under reduced pressure and the residue was directly submitted to the next step without purification.
DBU (43 mg, 0.286 mmol) was added to the above crude hydrazone solution in CH_2Cl_2 (5 mL) at 23 °C. After stirring for 5 h, the solvent was removed and the residue was purified by column chromatography on silica gel (25% ethyl acetate in hexanes) to deliver product **19** (27.1 mg, 93.4 μmol, 65%). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 6.69 (d, *J*=8.4 Hz, 1H), 6.51 (d, *J*=8.4 Hz, 1H), 6.00 (s, 2H), 3.93 (br. s, 4H), 1.03 (brs, *J*=6.3 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 168.2, 153.2, 144.3, 143.1, 112.5, 107.6, 103.1, 102.2, 82.2, 82.3, 74.3, 38.7, 24.0. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{14}H_{14}N_2O_5Na$, 313.0800; found, 313.0803.

c. Chiral auxiliary approach



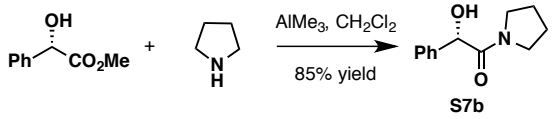
α-Keto acid S6. A precooled 1M methanolic solution of sodium hydroxide (100 mL) was added to a solution of α-keto ester **18** (3.65 g, 8.48 mmol) in MeOH (10 mL) at 0 °C. The resultant solution was stirred for 1 h before MeOH was evaporated under reduced pressure. The crude mixture was dissolved in water (150 mL) and extracted with diethyl ether. The

aqueous phase was acidified by addition of 1M aqueous solution of HCl and extracted with ethyl acetate. The combined organic phase was washed with brine, dried over Na_2SO_4 and concentrated. The product was precipitated with hexanes and the resulting solid was filtered off to afford product **S6** (3.18 g, 7.64 mmol, 90%). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.20 (d, *J*=8.7 Hz, 2H), 6.84 (d, *J*=8.7 Hz, 2H), 6.69 (d, *J*=8.5 Hz, 1H), 6.47 (d, *J*=2.5 Hz, 1H), 6.31 (dd, *J*=8.5, 2.5 Hz, 1H), 5.90 (s, 2H), 4.43 (s, 2H), 3.80 (s, 3H), 3.66 (s, 2H), 3.29 (s, 2H), 1.00 (s, 6H). ^{13}C NMR (126 MHz, CD_3OD) δ (ppm): 185.7, 165.5, 159.2, 154.0, 149.2, 142.4, 130.6, 128.9, 113.2, 112.4, 108.6, 103.0, 102.7, 75.0, 74.9, 72.5, 54.2, 35.7, 21.1. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{22}H_{24}O_8Na$, 439.1369; found, 439.1365.



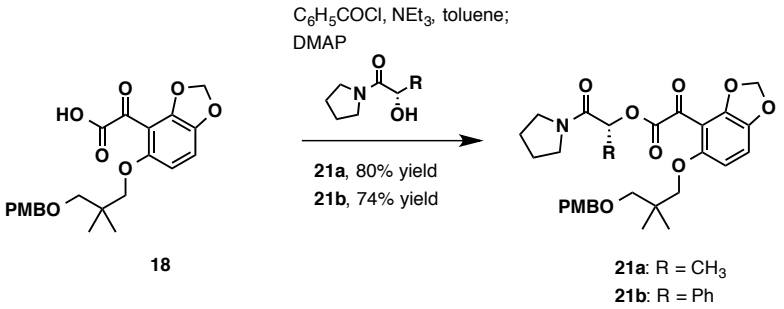
S7a

Lactic acid amide S7a[2]**.** A mixture of pyrolidine (7.2 mL, 87.7 mmol) and (*S*)-ethyl lactate (9.2 mL, 80.2 mmol) was stirred at 23 °C for 3 days. The solvent was removed and the residue was distilled under vacuum to afford **S7a** (11.2 g, 78.1 mmol, 89%). $[\alpha]_D^{23}$ -45.5° (*c* 1.5, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 4.23 (q, *J*=6.6 Hz, 1H), 3.82 (brs, 1H), 3.57-3.46 (m, 1H), 3.46-3.34 (m, 2H), 3.34-3.22 (m, 1H), 2.01-1.75 (m, 4H), 1.27 (d, *J*=6.6 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 173.4, 65.4, 46.2, 45.9, 26.0, 23.8, 20.5. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_7H_{13}O_2Na$, 166.0844; found, 166.0821.

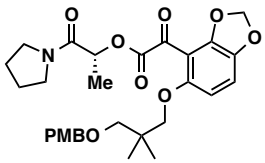


S7b

Mandelic acid amide S7b[3]**.** $AlMe_3$ (0.64 mL, 6.68 mmol) was added dropwise to a stirred solution of pyrrolidine (0.470 g, 6.62 mmol) in CH_2Cl_2 (15 mL) at 23 °C. After the resultant colorless solution was stirred for 20 min, a solution of (*S*)-methyl 2-hydroxy-2-phenylacetate (1.00 g, 6.02 mmol) in CH_2Cl_2 (5.0 mL) was added dropwise. After stirring for additional 2 h, the reaction mixture was poured into 1 M aqueous solution of HCl (100 mL) and extracted with CH_2Cl_2. The combined organic phase was washed with brine, dried over Na_2SO_4 and concentrated to afford the pure mandelic acid amide **S7b** (1.05 g, 5.17 mmol, 85%). $[\alpha]_D^{23}$ +79.1° (*c* 2.5, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.46–7.28 (m, 5H), 5.04 (s, 1H), 4.71 (brs, 1H), 3.68–3.56 (m, 1H), 3.54–3.43 (m, 1H), 3.43–3.32 (m, 1H), 2.93–2.77 (m, 1H), 1.95–1.67 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 170.6, 139.0, 128.8, 128.4, 127.7, 72.6, 46.5, 45.8, 25.8, 23.7. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{12}H_{15}NO_2Na$, 228.1000; found, 228.0990.

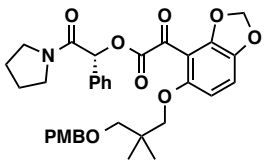


General procedure for esterification of α-keto acid 18. Benzoyl chloride (0.82 mL, 7.06 mmol) was added dropwise to a mixture of α-keto acid **18** (2.70 g, 6.49 mmol) and NEt_3 (1.1 mL, 7.91 mmol) in toluene (50 mL) at 23 °C and the resultant slurry was stirred for 30 min. Then the corresponding chiral amide (7.10 mmol) and DMAP (0.930 g, 7.62 mmol) were added sequentially. After stirring for 2 h, the reaction was poured into 0.5 M aqueous solution of HCl (100 mL) and extracted with ethyl acetate. The combined organic phase was washed with a saturated solution of sodium bicarbonate and water, dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel (10% ethyl acetate in dichloromethane) to deliver a corresponding product.



21a

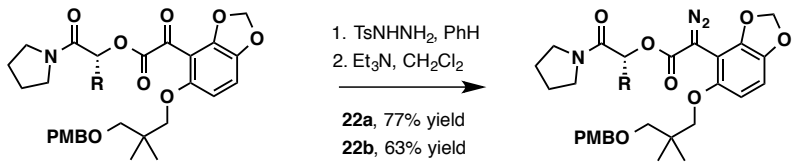
Lactamide 21a: (2.87 g, 5.30 mmol, 80%). $[\alpha]_D^{23}$ +17.9° (*c* 0.5, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.19 (d, *J*=8.7 Hz, 2H), 6.94-6.78 (m, 3H), 6.35 (d, *J*=8.7 Hz, 1H), 6.05 (d, *J*=1.3 Hz, 1H), 6.03 (d, *J*=1.3 Hz, 1H), 5.46 (q, *J*=6.7 Hz, 1H), 4.39 (s, 2H), 3.80 (s, 3H), 3.78-3.72 (m, 2H), 3.68-3.60 (m, 1H), 3.56-3.38 (m, 3H), 3.26 (d, *J*=8.9 Hz, 1H), 3.23 (d, *J*=8.9 Hz, 1H), 2.00-1.91 (m, 2H), 1.90-1.79 (m, 2H), 1.51 (d, *J*=6.7 Hz, 3H), 0.97 (s, 3H), 0.97 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ (ppm): 183.0, 167.4, 162.6, 159.2, 154.4, 149.4, 142.4, 130.9, 129.1, 113.8, 112.8, 109.0, 103.9, 102.8, 75.6, 75.5, 73.0, 70.6, 55.4, 46.5, 46.3, 36.4, 26.4, 24.0, 22.26, 22.25, 16.8. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{29}H_{35}NO_9Na$, 564.2210; found, 564.2195.



21b

Mandelamide 21b: (2.90 g, 4.81 mmol, 74%): $[\alpha]_D^{23}$ +19.3° (*c* 1.5, MeOH). ^1H NMR (500 MHz, $CDCl_3$); δ (ppm): 7.54–7.46 (m, 2H), 7.39–7.32 (m, 3H), 7.16 (d, *J*=8.6 Hz, 2H), 6.86–6.78 (m, 3H), 6.34 (s, 1H), 6.31 (d, *J*=8.7 Hz, 1H), 5.98 (d, *J*=1.3 Hz, 1H), 5.91 (d, *J*=1.3 Hz, 1H), 4.35 (s, 2H), 3.78 (s, 3H), 3.70 (d, *J*=8.9 Hz, 1H), 3.63 (d, *J*=8.9 Hz, 1H), 3.62–3.51 (m, 2H), 3.46–3.38 (m, 1H), 3.32–3.25 (m, 1H), 3.21 (d, *J*=9.0 Hz, 1H), 3.18 (d,

J=9.0 Hz, 1H), 1.93–1.70 (m, 4H), 0.92 (s, 3H), 0.91 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$); δ (ppm): 182.5, 165.2, 162.3, 159.0, 154.3, 149.3, 142.2, 133.4, 130.8, 129.2, 128.0, 128.8, 128.2, 113.6, 112.6, 108.8, 103.6, 102.6, 75.4, 75.3, 75.3, 72.8, 55.2, 46.5, 46.0, 36.2, 26.2, 23.7, 22.1. HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{34}H_{37}NO_9Na$, 626.2366; found, 626.2352.

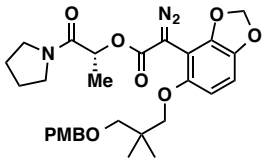


21

22a: R = CH_3
22b: R = Ph

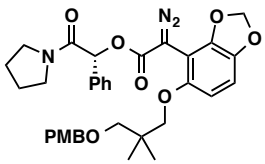
General procedure for the preparation of α-diazo esters 22. A mixture of lactamide **21a** or mandelamide **21b** (1.35 mmol) and $TsNHNH_2$ (0.251 g, 1.35 mmol) in benzene (20 mL) was heated at reflux for 2 h, during which water was collected in a Dean-Stark apparatus. After cooling, the solvent was removed and the residue was directly submitted to next step without purification.

Triethylamine (0.50 mL, 3.59 mmol) was added to the above crude hydrazone solution in CH_2Cl_2 (30 mL) at 23 °C. The reaction mixture was stirred overnight, concentrated, and the residue was purified by column chromatography on silica gel (from 25% ethyl acetate in hexanes to 50% ethyl acetate in dichloromethane) to afford the corresponding diazo ester compounds.



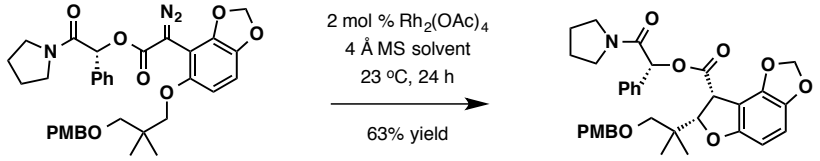
22a

Diazoester 22a: (0.575 g, 1.07 mmol, 77%). $[\alpha]_D^{23}$ +33.1° (*c* 1.5, MeOH). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.20 (d, *J*=8.7 Hz, 2H), 6.82 (d, *J*=8.7 Hz, 2H), 6.70 (d, *J*=8.5 Hz, 1H), 6.31 (d, *J*=8.5 Hz, 1H), 5.96 (s, 2H), 5.39 (q, *J*=6.7 Hz, 1H), 4.41 (s, 2H), 3.78 (s, 3H), 3.74–3.68 (m, 2H), 3.66–3.59 (m, 1H), 3.55–3.47 (m, 1H), 3.46–3.41 (m, 1H), 3.41–3.34 (m, 1H), 3.30 (s, 2H), 1.98–1.88 (m, 2H), 1.86–1.78 (m, 2H), 1.45 (d, *J*=6.7 Hz, 3H), 1.01 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 168.5, 159.1, 152.1, 147.1, 142.0, 131.0, 129.1, 113.8, 108.0, 103.3, 101.7, 97.4, 75.9, 74.9, 73.0, 69.0, 55.4, 46.3, 46.2, 36.3, 26.4, 24.1, 22.4, 22.4, 16.9. HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{29}H_{35}N_3O_8Na$, 576.2322; found, 576.2316.



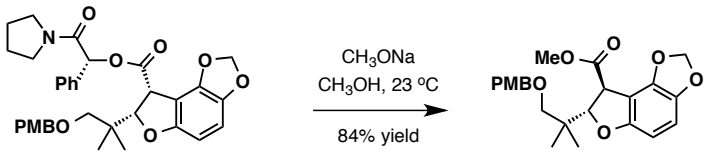
22b

Diazoester 22b: (0.523 g, 0.850 mmol, 63 %). $[\alpha]_D^{23}$ +62.2° (*c* 1.5, MeOH). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.52–7.44 (m, 2H), 7.40–7.32 (m, 3H), 7.18 (d, *J*=8.6 Hz, 2H), 6.80 (d, *J*=8.6 Hz, 2H), 6.68 (d, *J*=8.5 Hz, 1H), 6.30 (d, *J*=8.5 Hz, 1H), 6.21 (s, 1H), 5.93 (s, 1H), 5.82 (brs, 1H), 4.39 (s, 2H), 3.77 (s, 3H), 3.73–3.62 (m, 3H), 3.61–3.51 (m, 1H), 3.45–3.35 (m, 1H), 3.29 (s, 2H), 3.27–3.16 (m, 1H), 1.96–1.69 (m, 4H), 1.01 (s, 3H), 1.00 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 166.5, 159.1, 152.1, 147.0, 142.0, 134.5, 131.1, 129.1, 129.1, 128.9, 128.5, 113.7, 107.9, 103.3, 101.7, 97.5, 75.9, 76.0, 74.7, 73.0, 55.4, 46.4, 46.0, 36.3, 26.3, 23.9, 22.4, 22.4. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{34}H_{37}N_3O_8Na$, 638.2478; found, 638.2454.



22b 23b

Dihydrobenzofuran 23b. The freshly prepared diazoester **22b** (7.30 g, 11.9 mmol) was dissolved in CH_2Cl_2 (250 mL). 4Å Molecular sieves (13 g) were added. Rhodium acetate (105 mg, 0.238 mmol) was added and the reaction mixture was stirred at 23 °C for 24 h. The reaction mixture was filtered through a short pad of Celite and concentrated. The residue was purified by column chromatography on silica gel (25% ethyl acetate in hexanes). Only fractions containing pure major diastereomer were collected to afford **23 b** (4.4 g, 7.5 mmol, 63%). $[\alpha]_D^{23}$ +46.1° (*c* 1.0, MeOH). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.46–7.39 (m, 2H), 7.34–7.29 (m, 3H), 7.08 (d, *J*=8.7 Hz, 2H), 6.75 (d, *J*=8.7 Hz, 2H), 6.51 (dd, *J*=8.3, 0.6 Hz, 1H), 6.11 (d, *J*=8.3 Hz, 1H), 6.00 (s, 1H), 5.68 (d, *J*=1.5 Hz, 1H), 5.64 (d, *J*=1.5 Hz, 1H), 5.04 (d, *J*=6.2 Hz, 1H), 4.50 (d, *J*=6.2 Hz, 1H), 4.27 (d, *J*=11.8 Hz, 1H), 4.20 (d, *J*=11.8 Hz, 1H), 3.72 (s, 3H), 3.56–3.43 (m, 2H), 3.35–3.27 (m, 1H), 3.24 (s, 2H), 3.12–3.00 (m, 1H), 1.88–1.61 (m, 4H), 0.93 (s, 3H), 0.92 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 171.4, 165.9, 158.9, 156.7, 143.7, 141.8, 133.7, 130.8, 129.2, 128.9, 128.7, 113.6, 107.9, 107.0, 101.2, 99.6, 90.8, 75.8, 75.2, 72.8, 55.2, 46.5, 46.2, 45.8, 39.2, 26.1, 23.8, 21.0, 20.2. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{34}H_{37}NO_8Na$, 610.2417; found, 610.2425.

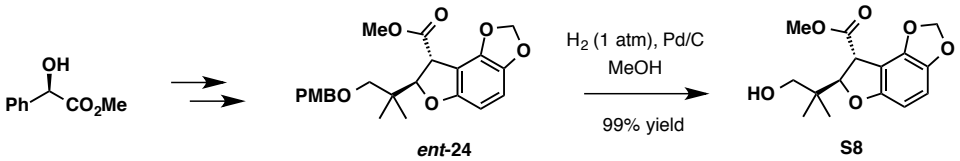


23b 24

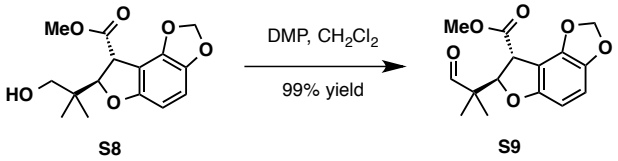
Dihydrobenzofuran 24. A freshly prepared solution of sodium methoxide (2.00 g, 37.5 mmol) in methanol (20 mL) was added to a solution of compound **23b** (4.40 g, 7.50 mmol) in MeOH (100 mL) at 0 °C. After stirring for 5 min at the same temperature, the reaction mixture was poured into 1 M aqueous solution of HCl (200 mL), extracted with ethyl acetate. The combined organic phase was washed with water, dried over Na_2SO_4 and concentrated. The residue was purified by column chromatography on silica gel (10% ethyl acetate in hexanes) to afford **24** (2.90 g, 6.64 mmol, 88%). Ee: 84% (Chiralcel® OD-H; 1% *i*-PrOH in

hexanes; flow rate = 1.0 mL/min; detection at 215 nm; t_1=17.9 min (minor); t_2=33.9 min (major)). $[\alpha]_D^{23}$ +13.6° (*c* 1.0, MeOH). ^{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).

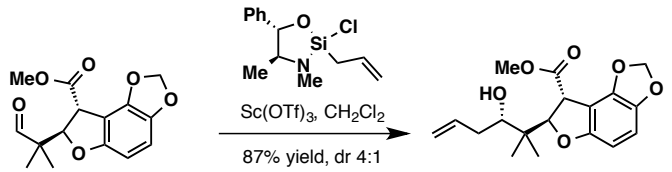
d. Determination of the absolute configuration of dihydrobenzofuran *ent*-24.



Alcohol S8. 10% Palladium on activated carbon (8.5 mg, 7.99 μmol) was added to a solution of substrate ***ent*-24** (0.118 g, 0.285 mmol) in methanol (7 mL). The resultant solution was connected to a hydrogen balloon and stirred overnight. The reaction was filtered through a short pad of Celite and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (50% ethyl acetate in hexanes) to afford **S8** (79.0 mg, 0.269 mmol, 99%). $[\alpha]_D^{23}$ -31.8° (*c* 1.5, CH_3OH). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 6.63 (d, *J*=8.3, 1H), 6.23 (d, *J*=8.3 Hz, 1H), 5.96 (d, *J*=1.4 Hz, 1H), 5.90 (d, *J*=1.4 Hz, 1H), 4.98 (d, *J*=7.2 Hz, 1H), 4.28 (d, *J*=7.2 Hz, 1H), 3.79 (s, 3H), 3.55 (s, 2H), 2.10 (s, 1H), 0.96 (s, 3H), 0.92 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 172.4, 156.2, 143.8, 142.3, 108.3, 106.9, 101.7, 100.1, 91.5, 70.0, 53.0, 46.8, 39.5, 19.8, 19.2. HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{15}H_{18}O_6Na$, 317.1001; found, 317.1008.

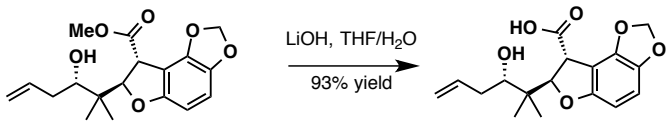


Aldehyde S9. Dess-Martin periodinane (0.193 g, 0.455 mmol) was added to a solution of substrate **S8** (79.0 mg, 0.269 mmol) in CH_2Cl_2 (7.0 mL) at 0 °C. After stirring for 2 h at 0 °C, the reaction mixture was quenched with a saturated aqueous $NaHCO_3$ and $Na_2S_2O_3$ solution and extracted with 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 (25% ethyl acetate in hexanes) to deliver product **S9** (78.0 mg, 0.267 mmol, 99%). $[\alpha]_D^{23}$ -18.6° (*c* 1.5, MeOH). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 9.59 (s, 1H), 6.62 (d, *J*=8.3, 1H), 6.22 (d, *J*=8.3 Hz, 1H), 5.95 (d, *J*=1.4 Hz, 1H), 5.90 (d, *J*=1.4 Hz, 1H), 5.17 (d, *J*=6.7 Hz, 1H), 4.16 (d, *J*=6.7 Hz, 1H), 3.80 (s, 3H), 1.14 (s, 3H), 1.13 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 203.6, 171.4, 155.9, 143.8, 142.5, 108.5, 106.3, 101.8, 100.3, 89.0, 53.0, 50.2, 47.1, 18.0, 17.1. HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{15}H_{16}O_6Na$, 315.0845; found, 315.0854.



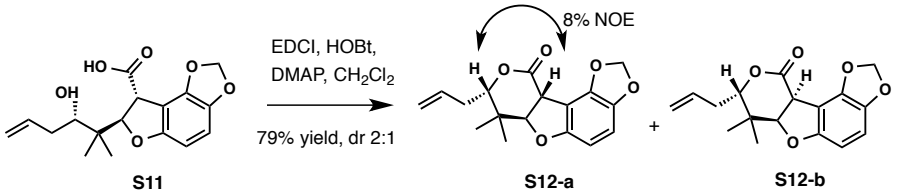
S9 **S10**

Alcohol S10. A solution of the (*S*,*S*)-Leighton reagent[4] (0.132 g, 0.493 mmol) in CH_2Cl_2 (2 mL) and $Sc(OTf)_2$ (24.3 mg, 49.3 μmol) were sequentially added to a solution of substrate **S9** (72.0 mg, 0.247 mmol) in CH_2Cl_2 (5 mL) at 0 °C. The reaction mixture was stirred for 2 h before *n*-Bu_4NF (1.0 M solution in THF, 0.6 mL, 0.600 mmol) was added. The resulting mixture was stirred for additional 30 min at 23 °C. Then the reaction was poured into water (20 mL) and extracted with ethyl acetate. The combined organic phase was washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography (25% ethyl acetate in hexanes) to deliver product **S10** as mixture of diastereomers (d.r 4:1, 72.0 mg, 0.216 mmol, 87%). The pure major diastereomer was separated by preparative HPLC (Chiralcel® OD-H; 1% *i*-PrOH in hexanes; flow rate = 1.0 ml/min; detection at 210 nm; t_1=24.4 min; t_2=42.6 min). ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 6.60 (d, *J*=8.2 Hz, 1H), 6.21 (d, *J*=8.2 Hz, 1H), 5.93 (d, *J*=1.3 Hz, 1H), 5.91-5.80 (m, 2H), 5.20-5.12 (m, 2H), 5.05 (d, *J*=7.2 Hz, 1H), 4.33 (d, *J*=7.2 Hz, 1H), 3.76 (s, 3H), 3.59 (dd, *J*=10.5, 2.1 Hz, 1H), 2.44-2.34 (m, 1H), 2.25 (br. s, 1H), 2.16-2.06 (m, 1H), 1.01 (s, 3H), 0.85 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ (ppm): 172.4, 156.2, 143.5, 142.0, 135.9, 118.1, 108.0, 106.9, 101.5, 99.9, 91.8, 74.7, 52.8, 46.8, 41.5, 36.2, 18.8, 17.7. HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{18}H_{22}O_6Na$, 357.1314; found, 357.1305.



S10 **S11**

Acid S11. Lithium hydroxide (5.0 mg, 0.202 mmol) was added to a stirred solution of substrate **S10** (13.5 mg, 40.4 μmol) in THF (1 mL) and water (1 mL) at 0 °C. After stirring at 0 °C for 2 h, the reaction mixture was diluted with water, acidified to pH=3 by addition of 1 M aqueous solution of HCl, and extracted with ethyl acetate. The combined organic phase was dried over Na_2SO_4 and concentrated to deliver product **S11** (12.0 mg, 37.5 μmol, 93%). ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 6.63 (d, *J*=8.3 Hz, 1H), 6.23 (d, *J*=8.3 Hz, 1H), 5.95 (d, *J*=1.2 Hz, 1H), 5.90 (d, *J*=1.2 Hz, 1H), 5.89-5.81 (m, 1H), 5.23-5.13 (m, 2H), 5.08 (d, *J*=6.7 Hz, 1H), 4.38 (d, *J*=6.6 Hz, 1H), 3.63 (dd, *J*=10.5, 1.9 Hz, 1H), 2.45-2.37 (m, 1H), 2.20-2.08 (m, 1H), 1.04 (s, 3H), 0.87 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ (ppm): 176.64, 156.41, 143.82, 142.24, 135.79, 118.68, 108.45, 106.45, 101.78, 100.09, 91.58, 74.95, 46.79, 41.74, 36.39, 18.94, 18.04. HRMS-ESI (*m*/*z*): $[M+Na]^+$ calcd for $C_{17}H_{20}O_6Na$, 343.1158; found, 343.1149.

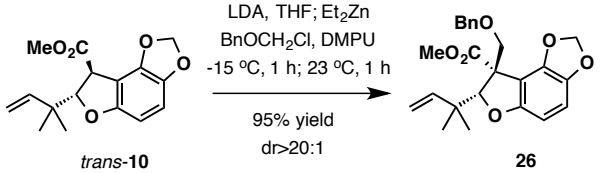


Lactone S12. *N*-(3-Dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride (9.5 mg, 48.8 μmol), 1-hydroxybenzotriazole (6.7 mg, 48.8 μmol) and 4-dimethylaminopyridine (1.0 mg, 8.20 μmol) were added sequentially to a solution of acid **S11** (12.0 mg, 37.5 μmol) in CH_2Cl_2 (2 mL) at 23 °C. After stirring for 1 h, the reaction mixture was diluted with CH_2Cl_2 (20 mL), washed with 1M aqueous solution of HCl, a saturated aqueous solution of sodium bicarbonate and water. The organic phase was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography (10% ethyl acetate in hexanes) to deliver **S12-a** and **S12-b** separately.

S12-a (6.0 mg, 19.9 μmol, 53%): $[\alpha]_D^{23}$ +17.4° (*c* 0.21, $CHCl_3$). ^{1}H NMR (500 MHz, C_6D_6) δ (ppm): 6.48 (dd, *J*=8.2, 0.8 Hz, 1H), 6.23 (d, *J*=8.2 Hz, 1H), 5.78 (dddd, *J*=17.0, 10.3, 7.8, 5.9 Hz, 1H), 5.43 (s, 2H), 5.07-4.97 (m, 2H), 3.82 (d, *J*=14.7 Hz, 1H), 3.50 (d, *J*=14.7 Hz, 1H), 3.41 (dd, *J*=10.0, 3.1 Hz, 1H), 2.15-2.06 (m, 1H), 1.86-1.79 (m, 1H), 0.71 (s, 3H), 0.67 (s, 3H). ^{13}C NMR (126 MHz, C_6D_6) δ (ppm): 167.4, 157.0, 144.8, 143.7, 134.3, 117.2, 107.5, 105.5, 101.7, 101.4, 90.5, 85.8, 45.4, 35.6, 33.3, 21.8, 18.6. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{17}H_{18}O_5Na$, 325.1052; found, 325.1062.

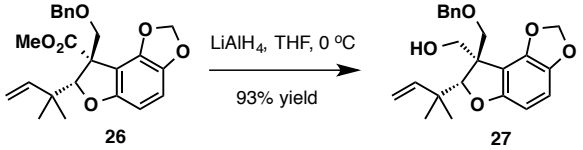
S12-b (3.0 mg, 9.95 μmol, 26%): $[\alpha]_D^{23}$ -99.2° (*c* 0.5 , $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 6.63 (dd, *J*=8.3, 0.7 Hz, 1H), 6.23 (d, *J*=8.3 Hz, 1H), 6.00 (d, *J*=1.3 Hz, 1H), 5.95 (d, *J*=1.3 Hz, 1H), 5.93-5.83 (m, 1H), 5.17-5.07 (m, 2H), 4.59 (d, *J*=8.8 Hz, 1H), 4.43 (d, *J*=8.8 Hz, 1H), 4.40 (dd, *J*=9.6, 3.3 Hz, 1H), 2.44-2.30 (m, 2H), 1.20 (s, 3H), 1.05 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ (ppm): 167.4, 155.7, 144.5, 142.9, 133.8, 117.9, 108.3, 105.4, 102.0, 100.0, 88.6, 80.4, 44.3, 36.9, 33.8, 21.9, 17.9. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{17}H_{18}O_5Na$, 325.1052; found, 325.1062.

Part B. Synthesis of maoecrystal ZG.



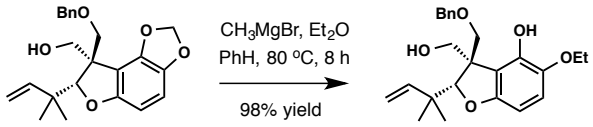
Ester 26. A solution of *n*-BuLi (4.0 mL, 2.24 M in hexanes, 8.96 mmol) was added dropwise to a solution of *i*-Pr_2NH (1.4 mL, 9.99 mmol) in THF (10 mL) at -78 °C. After stirring at the same temperature for 10 min, a solution of **10** (1.16 g, 4.00 mmol) in THF (10 mL) was added. After stirring for further 15 min, a solution of $ZnEt_2$ (10 mL, 1.0 M in heptane, 10.0 mmol) was added and the mixture was stirred for 5 min at -78 °C. Then dry DMPU (6.6 mL) was added and followed by BOMCl (Sigma-Aldrich, Inc., ~60% purity, 2.3 mL, 9.92 mmol). The mixture was then stirred at -15 °C for 1 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 (eluent: 20% ethyl acetate in hexanes) to afford ester **26** (1.56 g, 3.80 mmol, 95%, dr >20:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.34–7.25 (m, 3H), 7.24–7.19 (m, 2H), 6.64 (d, *J*=8.2 Hz, 1H), 6.27 (d, *J*=8.2 Hz, 1H), 5.97 (dd, *J*=17.4, 11.1 Hz, 1H), 5.86 (d, *J*=1.5 Hz, 1H), 5.80 (d, *J*=1.5 Hz, 1H), 5.00–4.92 (m, 2H), 4.66 (s, 1H), 4.55 (d, *J*=12.5 Hz, 1H), 4.52 (d, *J*=12.5 Hz, 1H), 4.07 (d, *J*=9.7 Hz, 1H), 3.87 (d, *J*=9.7 Hz, 1H), 3.52 (s, 3H), 1.15 (s, 3H), 1.11 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 170.7, 155.7, 142.9, 142.03, 141.98, 138.0, 128.2, 127.7, 127.6, 111.9, 111.7, 107.6, 101.4, 100.1, 93.0, 73.3, 70.5, 58.0, 51.5, 40.4, 26.7, 22.8. HRMS-ESI (*m*/z): $[M+Na]^+$ calcd for $C_{24}H_{26}O_6Na$, 433.1627; found, 433.1614.



26 **27**

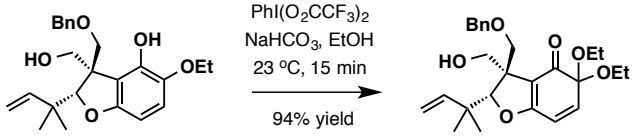
Alcohol 27. Lithium aluminum hydride (0.300 g, 7.91 mmol) was added to a solution of **26** (1.60 g, 3.90 mmol) in THF (39 mL) at 0 °C. After stirring for 2 h, the reaction was carefully quenched by adding 0.30 mL of water. After stirring for 5 min at 0 °C, 0.30 mL of aqueous NaOH (15% w/w) solution was added and the mixture was stirred for 5 min. Water (0.90 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 (eluent: 25% of ethyl acetate in hexanes) to afford **27** (1.39 g, 3.63 mmol, 93%). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.37–7.25 (m, 5H), 6.61 (d, *J*=8.2 Hz, 1H), 6.26 (d, *J*=8.2 Hz, 1H), 6.15 (dd, *J*=17.7, 10.8 Hz, 1H), 5.90 (d, *J*=1.4 Hz, 1H), 5.83 (d, *J*=1.4 Hz, 1H), 5.11 (dd, *J*=17.7, 1.3 Hz, 1H), 5.02 (dd, *J*=10.8, 1.3 Hz, 1H), 4.57 (s, 2H), 4.55 (s, 1H), 3.92 (dd, *J*=11.7, 7.6 Hz, 1H), 3.89–3.83 (m, 2H), 3.80 (d, *J*=9.4 Hz, 1H), 2.20 (*virt.* t, *J*=6.5 Hz, 1H), 1.19 (s, 3H), 1.17 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 155.1, 144.0, 142.9, 141.7, 138.1, 128.2, 127.6, 127.5, 112.9, 111.9, 107.4, 101.0, 100.4, 93.2, 73.4, 71.3, 62.7, 56.1, 40.9, 26.3, 25.1. HRMS-ESI (*m*/z): $[M+Na]^+$ calcd for $C_{23}H_{26}O_5Na$, 405.1678; found, 405.1661.



27 **28**

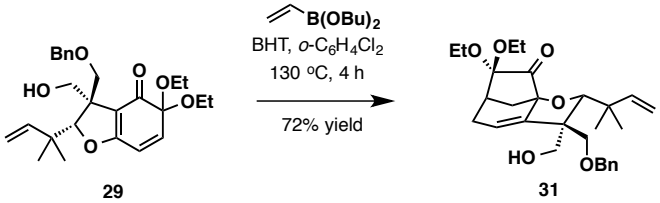
Alcohol 28. Methylmagnesium bromide (3.1 mL, 3.0 M in Et_2O, 9.30 mmol) was added dropwise to a solution of **27** (0.700 g, 1.83 mmol) in benzene (18 mL) at room temperature. The reaction flask was sealed and heated to 80 °C for 8 h. After cooling, the reaction was acidified by careful addition of 1 M aqueous solution of HCl at 0 °C. The mixture was extracted with ethyl acetate and the combined organic layer was washed with brine twice, dried over Na_2SO_4. After concentration, the residue was purified by column chromatography on silica gel (eluent: 25% ethyl acetate in hexanes) to afford **28** (0.717 g, 1.80 mmol, 98%). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 8.61 (s, 1H), 7.44–7.28 (m, 5H), 6.68 (d, *J*=8.5 Hz, 1H), 6.25 (dd, *J*=8.5, 0.7 Hz, 1H), 6.17 (dd, *J*=17.7, 10.8 Hz, 1H), 5.10 (d, *J*=17.7 Hz,

1H), 5.02 (d, *J*=10.8 Hz, 1H), 4.65 (d, *J*=12.1 Hz, 1H), 4.61 (d, *J*=12.1 Hz, 1H), 4.23 (s, 1H), 4.06-3.96 (m, 3H), 3.86 (dd, *J*=11.7, 6.2 Hz, 1H), 3.83 (d, *J*=9.1 Hz, 1H), 3.73 (d, *J*=9.1 Hz, 1H), 2.69 (*virt.* t, *J*=6.3 Hz, 1H), 1.41 (t, *J*=6.9 Hz, 3H), 1.19 (s, 3H), 1.14 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 154.0, 144.1, 143.6, 141.4, 137.1, 128.5, 127.9, 127.7, 115.7, 114.4, 111.8, 99.1, 93.3, 73.7, 71.4, 65.5, 60.7, 56.6, 41.1, 25.7, 25.6, 15.1. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{24}H_{30}O_5Na$, 421.1991; found, 421.1990.



28 **29**

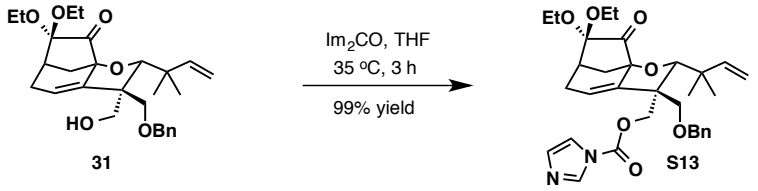
***Ortho*-quinone ketal 29.** Iodobenzene bis(trifluoroacetate) (0.918 g, 2.13 mmol) was added to a mixture of the substrate **28** (0.710 g, 1.78 mmol) and $NaHCO_3$ (0.299 g, 3.56 mmol) in EtOH (36 ml) at 0 °C. The mixture was stirred for 15 min at 23 °C. Then the solvent was removed by evaporation and the residue was purified by column chromatography on silica gel (eluent: 10-15% ethyl acetate in hexanes) to afford the quinone **29** (0.738 g, 1.67 mmol, 94%). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.37-7.23 (m, 5H), 6.55 (d, *J*=10.2 Hz, 1H), 6.38 (d, *J*=10.2 Hz, 1H), 5.87 (dd, *J*=17.6, 10.9 Hz, 1H), 5.07 (d, *J*=17.6 Hz, 1H), 5.02 (d, *J*=10.9 Hz, 1H), 4.82 (s, 1H), 4.69 (dd, *J*=11.0, 1.9 Hz, 1H), 4.58 (d, *J*=12.1 Hz, 1H), 4.51 (d, *J*=12.1 Hz, 1H), 3.99 (t, *J*=11.0 Hz, 1H), 3.88 (dd, *J*=11.0, 1.9 Hz, 1H), 3.73 (d, *J*=9.3 Hz, 1H), 3.71-3.54 (m, 5H), 1.21 (t, *J*=7.0 Hz, 3H), 1.15 (t, *J*=7.0 Hz, 3H), 1.14 (s, 3H), 1.10 (s, 3H).^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 191.5, 171.5, 143.8, 142.5, 138.3, 128.3, 127.48, 127.47, 118.7, 114.8, 113.2, 97.7, 93.3, 73.3, 70.7, 62.2, 58.61, 58.55, 55.9, 41.3, 26.5, 24.0, 15.5, 15.4. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{26}H_{34}O_6Na$, 465.2253; found, 465.2252.



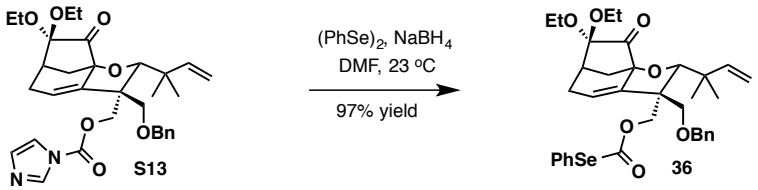
29 **31**

Alcohol 31. A solution of the substrate **29** (0.738 g, 1.67 mmol), 2,6-di-tertbutyl-4-methylphenol (0.615 g, 3.34 mmol), and vinylboronic acid dibutyl ester (1.10 g, 5.00 mmol) in 1,2-dichlorobenzene (50 mL) was heated at 120 °C for 12 h, then 130 °C for 4 h. After cooling, the solvent was removed by evaporation and the residue was purified by column chromatography on silica gel (eluent: 5% ethyl acetate in dichloromethane) to afford the title compound **31** (0.597 g, 1.20 mmol, 72%) as a single isomer. ^{1}H NMR (500 MHz, C_6H_6) δ (ppm): 7.21-7.09 (m, 4H), 7.05 (t, *J*=7.1 Hz, 1H), 6.33 (dd, *J*=17.8, 10.8 Hz, 1H), 5.66 (t, *J*=3.2 Hz, 1H), 4.95 (d, *J*=17.8 Hz, 1H), 4.84 (d, *J*=10.8 Hz, 1H), 4.52 (s, 1H), 4.16 (d, *J*=12.2 Hz, 1H), 4.12 (d, *J*=12.2 Hz, 1H), 3.81 (dd, *J*=11.4, 4.3 Hz, 1H), 3.67-3.49 (m, 5H), 3.42 (d, *J*=9.0 Hz, 1H), 3.28 (dq, *J*=9.2, 7.0 Hz, 1H), 2.49 (dd, *J*=10.2, 5.0 Hz, 1H), 2.37 (*virt.* t, *J*=5.0 Hz, 1H), 2.16 (dd, *J*=18.4, 3.1 Hz, 1H), 2.01 (*virt.* t, *J*=6.5 Hz 1H), 1.92 (ddd, *J*=18.4, 5.3, 3.4 Hz, 1H), 1.53 (d, *J*=10.2 Hz, 1H), 1.32 (s, 3H), 1.14 (s, 3H), 0.98 (t, *J*=7.0 Hz, 3H), 0.94 (t, *J*=7.0 Hz, 3H). ^{13}C NMR (126

MHz, C_6H_6) δ (ppm): 202.8, 145.9, 145.2, 138.8, 128.5, 127.7, 127.6, 120.1, 111.5, 101.8, 90.7, 85.6, 73.4, 73.3, 64.1, 58.5, 58.3, 54.5, 40.7, 37.3, 33.1, 28.3, 28.2, 24.8, 15.4, 15.3. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{28}H_{38}O_6Na$, 493.2566; found, 493.2549.

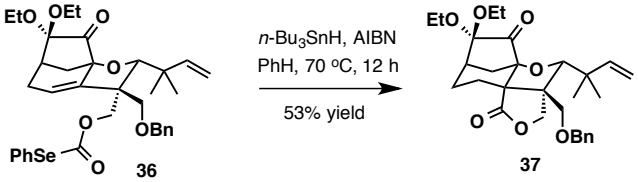


Ester S13. A solution of substrate **31** (0.620 g, 1.32 mmol) and carbonyldiimidazole (1.07 g, 6.60 mmol) in THF (22 mL) was heated at 35 °C for 3 h. After cooling, silica gel was added until no CO_2 bubbling was observed. The solvent then was removed and the residue was purified by column chromatography on silica gel (eluent: 25-30% ethyl acetate in hexanes) to deliver product **S13** (0.739 g, 1.31 mmol, 99%). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.98 (s, 1H), 7.31-7.19 (m, 6H), 7.03 (s, 1H), 6.09 (dd, *J*=17.6, 10.8 Hz, 1H), 5.64 (*virt.* t, *J*=3.5 Hz, 1H), 4.97 (d, *J*=17.6 Hz, 1H), 4.87 (d, *J*=10.8 Hz, 1H), 4.56 (d, *J*=10.9 Hz, 1H), 4.43 (s, 2H), 4.37 (d, *J*=10.9 Hz, 1H), 4.35 (s, 1H), 3.75-3.48 (m, 5H), 3.41 (d, *J*=9.2 Hz, 1H), 2.65 (*virt.* t, *J*=4.9 Hz, 1H), 2.45 (dd, *J*=10.5, 5.0 Hz, 1H), 2.31 (ddd, *J*=18.7, 3.6, 1.5 Hz, 1H), 2.23 (ddd, *J* = 18.7, 4.8, 3.3 Hz, 1H), 1.61 (d, *J*=10.5 Hz, 1H), 1.22 (t, *J*=7.1 Hz, 3H), 1.21 (s, 3H), 1.18 (s, 3H), 1.15 (t, *J*=7.0 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 203.1, 148.0, 143.6, 143.5, 137.5, 136.7, 130.5, 128.1, 127.5, 127.4, 121.1, 116.8, 111.2, 101.2, 90.4, 85.0, 73.2, 71.7, 68.0, 58.5, 58.0, 51.9, 40.2, 36.7, 32.6, 28.1, 27.2, 25.1, 15.14, 15.11. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{32}H_{40}O_7N_2Na$, 587.2733; found, 587.2706.

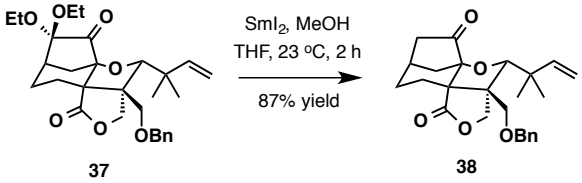


Selenocarbonate 36. Sodium borohydride (0.218 g, 5.74 mmol) was added to a solution of PhSeSePh (2.00 g, 6.40 mmol) in DMF (25 mL) at 23 °C. After stirring for 10 min, the resulting solution was transferred via cannula to a flask containing substrate **S13** (0.720 g, 1.28 mmol). After stirring for 3 h, the reaction mixture was diluted with 50% ethyl acetate in hexanes, quenched with water, and extracted with ethyl acetate. 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 (eluent: 5-10% ethyl acetate in hexanes) to deliver product **36** (0.805 g, 1.23 mmol, 97%). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.60-7.54 (m, 2H), 7.42-7.24 (m, 8H), 6.07 (dd, *J*=17.7, 10.9 Hz, 1H), 5.48 (*virt.* t, *J*=3.3 Hz, 1H), 5.05 (dd, *J*=17.7, 1.4 Hz, 1H), 4.96 (dd, *J*=10.9, 1.3 Hz, 1H), 4.49-4.41 (m, 3H), 4.34 (s, 1H), 4.25 (d, *J*=10.9 Hz, 1H), 3.75-3.50 (m, 4H), 3.47 (d, *J*=9.2 Hz, 1H), 3.34 (d, *J*=9.2 Hz, 1H), 2.71-2.59 (m, 1H), 2.41 (dd, *J*=10.5, 5.0 Hz, 1H), 2.34-2.20 (m, 2H), 1.65 (dd, *J*=10.5, 1.0 Hz, 1H), 1.23 (t, *J*=7.1 Hz, 3H), 1.18 (s, 3H), 1.17 (t, *J*=7.1 Hz, 3H), 1.14 (s, 3H).^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 203.2, 166.1, 143.6, 143.5, 138.1, 135.8, 129.2, 129.1, 128.2, 127.31, 127.30, 125.7, 121.0, 111.5, 101.4, 90.6, 85.1, 73.1, 71.5, 68.0,

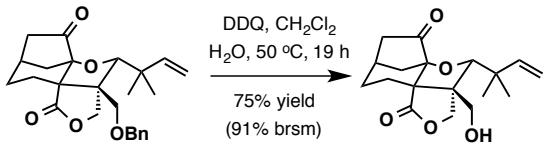
58.5, 58.0, 52.3, 40.3, 36.8, 32.7, 28.1, 27.0, 25.2, 15.2, 15.2. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{35}H_{42}O_7SeNa$, 677.1993; found, 677.1966.



Lactone 37. Azobisisobutyronitrile (AIBN, 0.180 g, 1.10 mmol) and tributyltin hydride (0.550 g, 1.89 mmol) were added sequentially to a degassed solution of the substrate **36** (0.350 g, 0.535 mmol) in benzene (27 mL). The reaction mixture was heated at 70 °C for 12 h. After cooling, the solvent was removed and the residue was purified by column chromatography on silica gel (eluent: 65–85% dichloromethane in hexane) to deliver product **37** (0.141 g, 0.283 mmol, 53%). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.38–7.30 (m, 2H), 7.32–7.25 (m, 1H), 7.27–7.21 (m, 2H), 5.98 (dd, *J*=17.6, 10.9 Hz, 1H), 5.09 (dd, *J*=17.6, 1.3 Hz, 1H), 5.03 (dd, *J*=10.9, 1.3 Hz, 1H), 4.72 (d, *J*=10.0 Hz, 1H), 4.49 (s, 1H), 4.45 (d, *J*=11.8 Hz, 1H), 4.41 (d, *J*=11.8 Hz, 1H), 4.19 (d, *J*=10.0 Hz, 1H), 3.76–3.50 (m, 4H), 3.44 (d, *J*=9.7 Hz, 1H), 3.41 (d, *J*=9.7 Hz, 1H), 3.36 (dd, *J*=11.9, 1.4 Hz, 1H), 2.68–2.64 (m, 1H), 2.33–2.24 (m, 1H), 2.10 (dd, *J* = 11.9, 4.4 Hz, 1H), 1.86 (dd, *J* = 13.5, 5.6 Hz, 1H), 1.78–1.66 (m, 2H), 1.23 (t, *J*=7.1 Hz, 3H), 1.17 (t, *J*=7.1 Hz, 3H), 1.14 (s, 3H), 1.11 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 213.0, 176.7, 143.2, 137.6, 128.4, 127.7, 127.3, 112.1, 99.2, 89.7, 88.7, 73.4, 71.6, 66.8, 58.1, 57.9, 56.8, 54.4, 40.4, 37.9, 27.9, 25.6, 22.0, 15.3, 15.1. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{29}H_{38}O_7Na$, 521.2515; found, 521.2496.

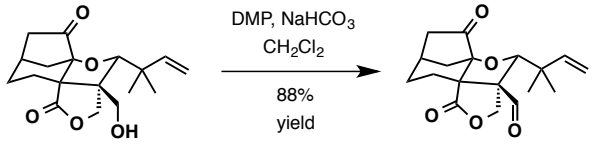


Ketone 38. A solution of SmI_2 (2.9 mL, 0.1 M in THF, 0.290 mmol) was added to a solution of substrate **37** (29.1 mg, 58.6 μmol) in THF (0.60 mL) and MeOH (60 μL). After stirring at 23 °C for 2 h, the reaction mixture was diluted with hexanes, quenched with a saturated aqueous $NaHCO_3$ solution, and extracted with 10% ethyl acetate in hexanes. The combined organic phase was washed with a saturated aqueous $Na_2S_2O_3$ solution, brine, dried over Na_2SO_4, concentrated and the residue was purified by column chromatography on silica gel (eluent: 10% ethyl acetate in hexanes) to deliver the product **38** (21.0 mg, 51.2 μmol, 87%). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.38–7.31 (m, 2H), 7.33–7.26 (m, 1H), 7.27–7.21 (m, 2H), 5.98 (dd, *J*=17.6, 10.9 Hz, 1H), 5.09 (dd, *J*=17.6, 1.3 Hz, 1H), 5.04 (dd, *J*=10.9, 1.3 Hz, 1H), 4.69 (d, *J*=9.9 Hz, 1H), 4.45 (d, *J*=11.9 Hz, 1H), 4.42 (s, 1H), 4.40 (d, *J*=11.9 Hz, 1H), 4.23 (d, *J*=9.9 Hz, 1H), 3.43 (d, *J*=9.8 Hz, 1H), 3.42 (ddd, *J*=11.5, 4.5, 1.5 Hz, 1H), 3.36 (d, *J*=9.8 Hz, 1H), 2.73–2.67 (m, 1H), 2.47–2.39 (m, 1H), 2.36 (ddd, *J*=18.9, 7.3, 1.2 Hz, 1H), 2.02 (dd, *J*=18.9, 4.3 Hz, 1H), 1.96–1.83 (m, 2H), 1.64–1.51 (m, 2H), 1.14 (s, 3H), 1.12 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 218.8, 176.3, 143.1, 137.4, 128.4, 127.8, 127.5, 112.2, 89.3, 88.9, 73.3, 71.0, 66.4, 56.2, 54.4, 42.3, 40.3, 32.8, 28.6, 25.9, 24.4. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{25}H_{30}O_5Na$, 433.1991; found, 433.1973.



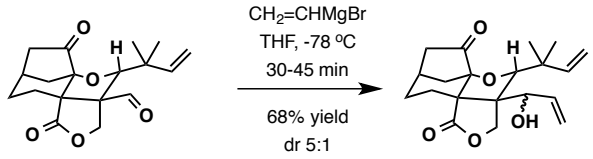
38 39

Alcohol 39. 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (DDQ, 0.106 g, 0.467 mmol) was added to a solution of the substrate (19.2 mg, 46.8 μmol) in CH_2Cl_2 (2 mL) and H_2O (0.2 mL) at 23 °C. The flask was sealed and heated at 50 °C (oil bath temperature) for 19 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 (eluent: 15-30% ethyl acetate in hexanes) to deliver the product (11.2 mg, 35.0 μmol, 75%), together with recovered starting material **38** (3.4 mg, 8.28 μmol, 18%). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 6.00 (dd, *J*=17.7, 10.9 Hz, 1H), 5.14 (dd, *J*=17.7, 1.2 Hz, 1H), 5.10 (dd, *J*=10.9, 1.2 Hz, 1H), 4.71 (d, *J*=10.0 Hz, 1H), 4.43 (s, 1H), 4.22 (d, *J*=10.0 Hz, 1H), 3.69 (dd, *J*=11.1, 4.5 Hz, 1H), 3.58 (dd, *J*=11.1, 4.5 Hz, 1H), 3.44 (ddd, *J*=11.7, 4.4, 1.5 Hz, 1H), 2.76-2.71 (m, 1H), 2.51-2.41 (m, 1H), 2.39 (ddd, *J*=18.9, 7.3, 1.2 Hz, 1H), 2.10 (dd, *J*=18.9, 4.3 Hz, 1H), 1.96 (dd, *J*=13.6, 5.2 Hz, 1H), 1.90 (dd, *J*=11.7, 4.5 Hz, 1H), 1.76-1.62 (m, 2H), 1.42 (t, *J*=4.5 Hz, 1H), 1.18 (s, 3H), 1.13 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ(ppm): 219.0, 176.4, 143.1, 112.5, 89.3, 88.7, 66.1, 63.8, 56.3, 55.1, 42.4, 40.3, 32.8, 28.6, 25.9, 24.2. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{18}H_{24}O_5Na$, 343.1521; found, 343.1506.



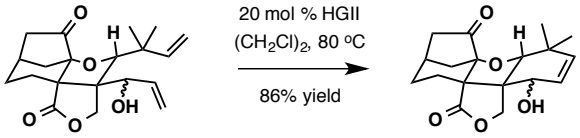
39 40

Aldehyde 40. Sodium bicarbonate (21.2 mg, 0.252 mmmol) and Dess-Martin periodinane (26.7 mg, 63.0 μmol) were added sequentially to a solution of alcohol **39** (10.1 mg, 31.5 μmol) in CH_2Cl_2 (1.5 mL) at 23 °C. After stirring for 1 h, the reaction mixture was diluted with CH_2Cl_2, quenched with a saturated aqueous solution of $NaHCO_3$ and $Na_2S_2O_3$, 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 (eluent: 20% ethyl acetate in hexanes) to deliver **40** (8.8 mg, 27.6 μmol, 88%). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 9.56 (s, 1H), 5.91 (dd, *J*=17.7, 10.9 Hz, 1H), 5.40 (s, 1H), 5.13 (dd, *J*=17.7, 1.0 Hz, 1H), 5.11 (dd, *J*=10.9, 1.0 Hz, 1H), 4.62 (d, *J*=10.3 Hz, 1H), 4.44 (d, *J*=10.3 Hz, 1H), 3.45 (ddd, *J*=11.8, 4.2, 1.5 Hz, 1H), 2.81-2.74 (m, 1H), 2.44 (dd, *J*=7.4, 1.3 Hz, 1H), 2.43-2.35 (m, 1H), 2.07 (dd, *J*=18.9, 4.2 Hz, 1H), 2.02 (dd, *J*=11.8, 3.9 Hz, 1H), 1.93-1.86 (m, 1H), 1.68-1.61 (m, 1H), 1.41 (ddd, *J*=14.6, 12.7, 5.3 Hz, 1H), 1.17 (s, 3H), 1.16 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 218.9, 200.0, 173.8, 142.2, 113.6, 89.0, 86.9, 65.4, 64.1, 60.8, 42.8, 40.0, 32.5, 28.4, 25.5, 24.1. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{18}H_{22}O_5Na$, 341.1365; found, 341.1358.



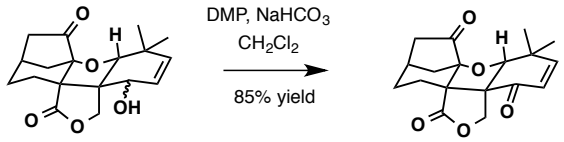
40 **41**

Allylic alohol 41. Vinylmagnesium bromide (0.60 mL, 0.88 M in THF, 0.528 mmol) was added to a solution of the substrate (26.4 mg, 82.9 μmol) in THF (4 mL) at -78 °C. After stirring for 30-45 min, the reaction mixture was quenched with saturated aqueous NH_4Cl, 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 (eluent: 15-25% ethyl acetate in hexanes) to deliver **41** (19.4 mg, 56.4 μmol, 68%, dr = 5:1). Major isomer: ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 5.97 (dd, *J*=17.8, 10.8 Hz, 1H), 5.68 (ddd, *J*=16.9, 9.9, 8.5 Hz, 1H), 5.40 (d, *J*=16.9 Hz, 1H), 5.29 (d, *J*=9.9 Hz, 1H), 5.06 (dd, *J*=17.8, 1.3 Hz, 1H), 5.04 (dd, *J*=10.8, 1.3 Hz, 1H), 4.56 (d, *J*=9.5 Hz, 1H), 4.52 (d, *J*=9.5 Hz, 1H), 4.42 (s, 1H), 4.23 (dd, *J*=8.5, 2.1 Hz, 1H), 3.44 (ddd, *J*=11.7, 4.3, 1.5 Hz, 1H), 2.74-2.69 (m, 1H), 2.47-2.41 (m, 1H), 2.39 (dd, *J*=18.9, 7.3 Hz, 1H), 2.12 (dd, *J*=18.9, 4.3 Hz, 1H), 2.06 (dd, *J*=15.1, 4.5 Hz, 1H), 1.95 (ddd, *J*=15.1, 13.0, 5.3 Hz, 1H), 1.88 (dd, *J*=11.7, 4.2 Hz, 1H), 1.69-1.62 (m, 1H), 1.35 (d, *J*=2.1 Hz, 1H), 1.12 (s, 3H), 1.09 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 219.6, 176.4, 144.2, 137.4, 119.5, 111.5, 89.1, 87.6, 73.2, 63.5, 58.1, 57.0, 42.3, 41.2, 32.9, 28.6, 26.19, 26.18. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{20}H_{26}O_5Na$, 369.1678; found, 369.1672.



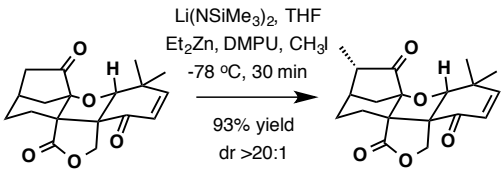
41 **42**

Cyclohexenol 42. A solution of Hoveyda-Grubbs second generation catalyst (6.3 mg, 10.1 μmol) in degassed $ClCH_2CH_2Cl$ (2.5 mL) was added to substrate **41** (17.4 mg, 50.2 μmol). The flask was sealed, and the mixture was heated at 80 °C for 3 h. After cooling, the solvent was removed and the residue was purified by column chromatography on silica gel (eluent: 15-25% ethyl acetate in hexanes) to deliver **42** (13.7 mg, 43.0 μmol, 86%). Major isomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 5.56 (dd, *J*=10.0, 2.1 Hz, 1H), 5.33 (dd, *J*=10.0, 1.3 Hz, 1H), 5.02 (s, 1H), 4.62 (d, *J*=10.5 Hz, 1H), 4.48-4.43 (m, 1H), 4.28 (d, *J*=10.5 Hz, 1H), 3.23 (ddd, *J*=11.8, 4.5, 1.6 Hz, 1H), 2.92-2.81 (m, 1H), 2.76-2.70 (m, 1H), 2.45 (ddd, *J*=18.8, 7.3, 1.6 Hz, 1H), 2.21-2.09 (m, 2H), 1.96 (dd, *J*=11.8, 4.1 Hz, 1H), 1.85-1.76 (m, 2H), 1.65-1.58 (m, 1H) 1.26 (s, 3H), 1.22 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 217.4, 176.7, 139.9, 129.0, 91.8, 85.4, 70.5, 64.3, 56.7, 54.9, 43.9, 37.4, 34.4, 31.8, 28.6, 26.4, 24.2, 19.0. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{18}H_{22}O_5Na$, 341.1365; found 341.1371.



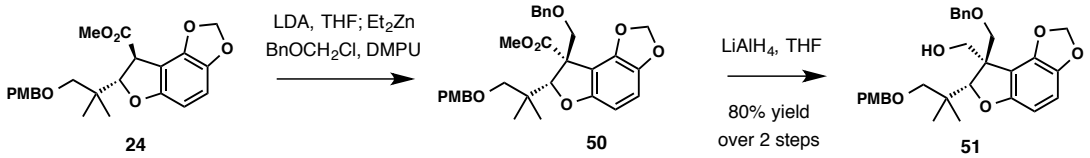
42 **43**

Enone 43. Sodium bicarbonate (44.6 mg, 0.531 mmmol) and Dess-Martin periodinane (56.0 mg, 0.132 mmol) were added sequentially to a solution of substrate **42** (13.7 mg, 43.0 μmol) in CH_2Cl_2 (2.5 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 column chromatography on silica gel (15-25% ethyl acetate in hexanes) to deliver **43** (11.6 mg, 36.7 μmol, 85%). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 6.64 (d, *J*=10.1 Hz, 1H), 5.84 (d, *J*=10.1 Hz, 1H), 5.41 (s, 1H), 4.71 (d, *J*=10.4 Hz, 1H), 3.78 (d, *J*=10.4 Hz, 1H), 3.18 (ddd, *J*=11.9, 4.5, 1.5 Hz, 1H), 2.89-2.78 (m, 1H), 2.77-2.71 (m, 1H), 2.44 (ddd, *J*=18.9, 7.2, 1.5 Hz, 1H), 2.34-2.26 (m, 2H), 2.15 (dd, *J*=18.9, 4.5 Hz, 1H), 1.96 (dd, *J*=11.9, 4.1 Hz, 1H), 1.67-1.61 (m, 1H), 1.39 (s, 3H), 1.37 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 215.5, 195.2, 175.4, 157.3, 127.4, 92.1, 82.9, 67.6, 58.6, 58.1, 43.5, 39.6, 34.3, 31.0, 28.5, 26.3, 23.8, 18.3. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{18}H_{20}O_5Na$, 339.1208; found, 339.1209.



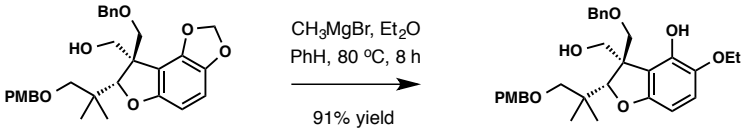
Maoecrystal ZG (2). A solution of $LiN(SiMe_3)_2$ (1.0 M in toluene, 0.15 mL, 0.150 mmol) was added to a solution of the substrate **43** (6.5 mg, 20.5 μmol) in THF (1.5 mL) at -78 °C. After stirring at that temperature for 15 min, a solution of $ZnEt_2$ (1.0 M in heptane, 0.15 mL, 0.150 mmol) was added and the mixture was stirred for 5 min at -78 °C. Then dry DMPU (0.30 mL) was added followed by iodomethane (20 μL, 0.321 mmol). After stirring at -78 °C for 30 min, the reaction was quenched with a saturated aqueous NH_4Cl 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 (eluent: 25% ethyl acetate in hexanes) to deliver racemic **2** (6.3 mg, 19.1 μmol, 93%). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 6.64 (d, *J*=10.1 Hz, 1H), 5.83 (d, *J*=10.1 Hz, 1H), 5.26 (s, 1H), 4.71 (d, *J*=10.4 Hz, 1H), 3.78 (d, *J*=10.4 Hz, 1H), 3.13 (ddd, *J*=12.3, 3.6, 1.4 Hz, 1H), 2.87-2.78 (m, 1H), 2.37-2.27 (m, 3H), 2.13 (qd, *J*=7.5, 3.6 Hz, 1H), 2.06 (dd, *J*=12.3, 4.4 Hz, 1H), 1.70-1.63 (m, 1H), 1.40 (s, 3H), 1.37 (s, 3H), 1.20 (d, *J*=7.5 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ (ppm): 217.9, 195.3, 175.6, 157.3, 127.4, 93.1, 82.9, 67.6, 58.5, 57.9, 46.3, 39.6, 35.6, 31.0, 30.7, 26.9, 23.9, 18.4, 16.7. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{19}H_{22}O_5Na$, 353.1365; found 353.1372.

Part C. Enantioselective synthesis of (-)-maoecrystal V



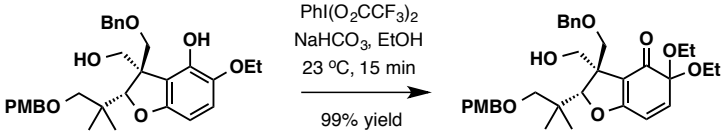
Ester 50. A solution of *n*-BuLi (2.7 mL, 2.4 M in hexanes, 6.48 mmol) was added dropwise to a solution of *i*-Pr_2NH (1.0 mL, 7.15 mmol) in THF (15 mL) at -78 °C. After stirring at the same temperature for 20 min, a solution of **24** (1.90 g, 4.35 mmol) in THF (20 mL) was added. After stirring for further 20 min, Et_2Zn (0.43 mL, 4.20 mmol) was added and the solution was stirred for 10 min at -78 °C. Then dry DMPU (7.0 mL) was added followed by $BnOCH_2Cl$ (Sigma-Aldrich, Inc., ~60% purity, 2.0 mL, 8.63 mmol). The mixture was then stirred at 0 °C for 0.5 h and 23 °C for 2 h. The reaction was quenched with a saturated aqueous NH_4Cl solution at 0 °C, and extracted with ethyl acetate. 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 (10% ethyl acetate in hexanes) to afford ester **50** (2.02 g).

Alcohol 51. Lithium aluminum hydride (0.330 g, 8.68 mmol) was added to a solution of **50** (2.02 g) in THF (50 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 0.5 mL of water at 0 °C. After stirring for 5 min at 0 °C, 5 mL of aqueous solution of NaOH (15% w/w) was added and the mixture was stirred for 10 min. The white solid was filtered off, the filtrate was concentrated and the residue was purified by column chromatography on silica gel (15% of ethyl acetate in hexanes) to afford **51** (1.76 g, 3.47 mmol, 80% yield over two steps). $[\alpha]_D^{23}$ -15.9° (*c* 1.0, MeOH). ^{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, *J*=11.4, 7.1 Hz, 1H), 3.93 (dd, *J*=11.4, 6.0 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).



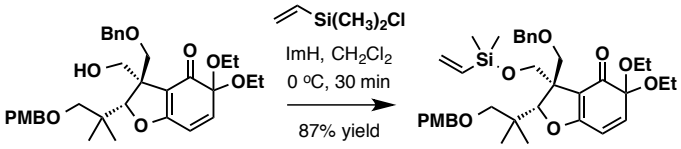
51 52

Alcohol 52. Methylmagnesium bromide (6.7 mL, 3.0 M in Et_2O, 19.8 mmol) was added dropwise to a solution of **51** (2.00 g, 3.95 mmol) in benzene (40 mL) at room temperature. The reaction mixture was refluxed for 6 h. After cooling, the reaction was carefully poured into 200 ml of 1 M aqueous solution of HCl. The mixture was extracted with ethyl acetate 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 **52** (1.88 g, 3.60 mmol, 91%). $[\alpha]_D^{23}$ +24.0° (*c* 1.0, $CHCl_3$). ^{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 (br. s, 1H), 1.41 (t, *J*=7.0 Hz, 3H), 1.10 (s, 3H), 1.08 (s, 3H).



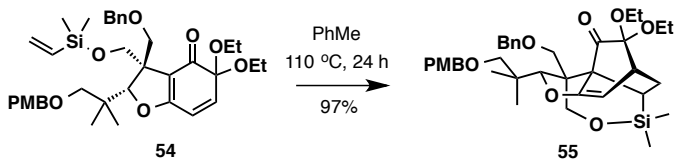
52 53

***Ortho*-quinone 53.** Iodobenzene bis(trifluoroacetate) (1.67 g, 3.89 mmol) was added to a mixture of the substrate **52** (1.85 g, 3.54 mmol) and $NaHCO_3$ (0.710 g, 8.45 mmol) in EtOH (35 mL) at 23 °C. The mixture was stirred for 15 min. The solvent was removed by evaporation and the residue was purified by column chromatography on silica gel (25% ethyl acetate in hexanes) to afford quinone **53** (1.98 g, 3.50 mmol, 99%). $[\alpha]_D^{23}$ +2.3° (*c* 1.0, MeOH). ^{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 (br. s, 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).



53 54

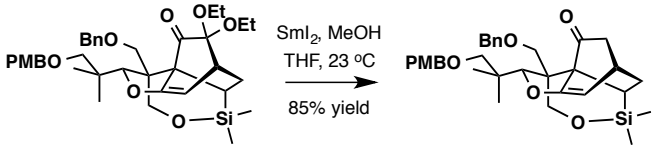
Vinylsilane 54. Chlorodimethylvinylsilane (0.95 mL, 6.89 mmol) was added to a solution of the substrate **53** (1.95 g, 3.44 mmol) and imidazole (0.930 g, 13.8 mmol) in CH_2Cl_2 (35 mL) at 23 °C. The reaction mixture was stirred for 5 h, poured into water (100 mL), and extracted with CH_2Cl_2. The combined 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 **54** (1.96 g, 3.01 mmol, 87%). $[\alpha]_D^{23}$ +25.6° (*c* 1.0, MeOH). ^{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, *J*=19.8, 14.9 Hz, 1H), 5.99 (dd, *J*=14.9, 4.4 Hz, 1H), 5.73 (dd, *J*=19.8, 4.4 Hz, 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, *J*=9.3, 7.1 Hz, 1H), 3.47 (dq, *J*=9.3, 7.1 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).



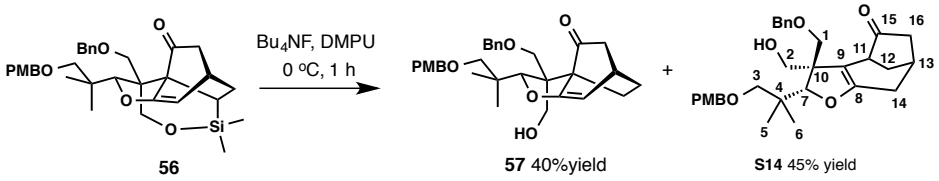
54 55

Enol ether 55. A solution of the substrate **54** (1.92 g, 2.95 mmol) and 2,6-di-tertbutyl-4-methylphenol (65.0 mg, 0.295 mmol) in toluene (60 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

55 (1.86 g, 2.86 mmol, 97%) as a single isomer. $[\alpha]_D^{23}$ 6.4° (*c* 1.0, MeOH). ^{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, *J*=9.5, 7.5 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, *J*=11.6, 10.3, 3.8 Hz, 1H), 1.57 (*virt.* t, *J*=9.6 Hz, 1H), 1.34 (ddd, *J*=11.4, 9.3, 2.0 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).



Ketone 56. A solution of SmI_2 (0.1 M in THF, 65 mL, 6.50 mmol) was added to a solution of **55** (0.840 g, 1.29 mmol) in THF (17 mL) and MeOH (1.7 mL). After stirring at for 2 h 23 °C, the reaction mixture was quenched with a saturated aqueous $NaHCO_3$ and $Na_2S_2O_3$ solution, and extracted with ethyl acetate. The combined organic phase was washed with brine, a saturated aqueous solution of $Na_2S_2O_3$, 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 **56** (0.56 g, 1.10 mmol, 85%). $[\alpha]_D^{23}$ 0.0° (*c* 1.0, MeOH). ^{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, *J*=17.4, 1.9 Hz, 1H), 2.10–2.00 (m, 1H), 1.87 (ddd, *J*=11.5, 10.5, 3.6 Hz, 1H), 1.57–1.51 (m, 1H), 1.42 (dd, *J*=10.2, 8.2 Hz, 1H), 1.02 (s, 6H), 0.15 (s, 3H), 0.07 (s, 1H).

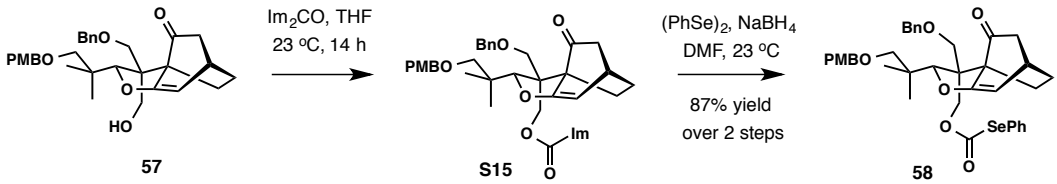


Alcohol 57. A solution of *n*-Bu_4NF (4.45 mL, 1.0 M in THF, 4.45 mmol) (*n*-Bu_4NF must be fresh, the usage of aged *n*-Bu_4NF causes a significant decrease in the yield of compound **57**) was added to a solution of the substrate (0.500 g, 0.890 mmol) in DMPU (23 mL) at 0 °C. After stirring at the same temperature for 1 h, the reaction mixture was poured into a saturated aqueous $NaHCO_3$ solution (100 mL) 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 (pre-neutralized with 1% NEt_3 in hexanes, eluent: gradient from 15% to 35% ethyl acetate in hexanes) to deliver the product **57** (0.180 g, 0.356 mmol, 40%) and two byproducts (0.200 g, 0.395 mmol, 45%),

one of which transformed into the other, **S14**, even upon standing in a freezer within a few days.

57: $[\alpha]_D^{23}$ -57.0° (*c* 1.0, $CHCl_3$). ^1H 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, *J*=11.4, 6.2 Hz, 1H), 3.85 (dd, *J*=11.4, 5.2 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 (br. s, 1H), 2.91–2.86 (m, 1H), 2.28 (ddd, *J*=13.1, 11.9, 3.6 Hz, 1H), 2.16–2.05 (m, 1H), 1.97 (ddd, *J*=13.3, 10.0, 5.6 Hz, 1H), 1.82–1.74 (m, 1H), 1.72–1.64 (m, 1H), 1.03 (s, 6H).

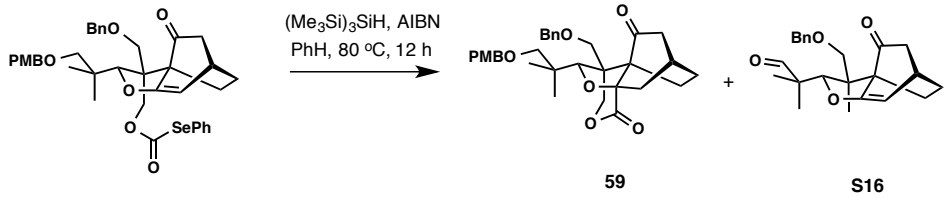
S14: $[\alpha]_D^{23}$ -98.4° (*c* 1.5, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$) δ (ppm): 7.36 (d, *J*=7.3 Hz, 2H, *Ar*), 7.33 (t, *J*=7.3 Hz, 2H, *Ar*), 7.28 (t, *J*=7.3 Hz, 1H, *Ar*), 7.19 (d, *J*=8.6 Hz, 2H, *Ar*), 6.85 (d, *J*=8.6 Hz, 2H, *Ar*), 4.61 (d, *J*=11.5 Hz, 1H, CH_2Ph), 4.46 (d, *J*=11.5 Hz, 1H, CH_2Ph), 4.34 (s, 2H, $CH_2C_6H_4OCH_3$), 4.16 (s, 1H, *H-7*), 3.85 (dd, *J*=11.5, 5.4 Hz, 1H, *H-2*), 3.80 (s, 3H, $C_6H_4OCH_3$), 3.73 (dd, *J*=11.5, 7.2 Hz, 1H, *H-2*), 3.60 (d, *J*=9.1 Hz, 1H, *H-1*), 3.57 (d, *J*=9.1 Hz, 1H, *H-1*), 3.27 (d, *J*=9.1 Hz, 1H, *H-3*), 3.25 (d, *J*=9.1 Hz, 1H, *H-3*), 3.05 (d, *J*= 4.3 Hz, 1H, *H-11*), 2.85 (t, *J*=6.3 Hz, 1H, *OH*), 2.69 (m, 1H, *H-13*), 2.57 (dd, *J*=17.1, 4.5 Hz, 1H, *H-14*), 2.33 (dd, *J*=18.4, 7.3 Hz, 1H, *H-16*), 2.16 (dd, *J*=18.5, 3.3 Hz, 1H, *H-16*), 2.00 (d, *J*=17.1 Hz, 1H, *H-14*), 1.96–1.88 (m, 1H, *H-12*), 1.65 (dd, *J*=11.5, 3.2 Hz, 1H, *H-12*), 1.07 (s, 3H, *H-5*), 1.04 (s, 3H, *H-6*). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 211.7, 159.0, 152.2, 138.2, 130.4, 129.0, 128.3, 127.9, 127.6, 113.7, 110.8, 91.1, 77.3, 73.9, 73.4, 72.8, 63.0, 55.6, 55.2, 43.1, 42.9, 38.6, 34.1, 31.4, 29.9, 22.6, 21.7. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{31}H_{38}O_6Na$, 529.2566; found, 529.2570.



Ketone S15. A solution of **57** (0.370 g, 0.731 mmol) and carbonyldiimidazole (1.20 g, 7.31 mmol) in THF (20 mL) was stirred at room temperature for 14 h. The reaction mixture was poured into water (100 mL), the product was extracted with ethyl acetate, the combined organic phase was washed with water, dried over Na_2SO_4 and concentrated to provide crude **S15** (0.440 g), which was used directly without further purification.

Selenocarbonate 58. Sodium borohydride (0.140 g, 3.66 mmol) was added to a solution of PhSeSePh (1.14 g, 3.66 mmol) in DMF (20 mL) at 23 °C. After stirring for 10 min, the resulting solution was transferred via cannula to a flask containing the above substrate **S15** (0.440 g). After stirring for 3 h, the reaction mixture poured into a saturated aqueous $NaHCO_3$ solution (100 ml), and extracted with ethyl acetate. 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: 15% ethyl acetate in hexanes) to deliver **58** (0.438 g, 0.636 mmol, 87%). $[\alpha]_D^{23}$ -21.9° (*c* 1, $CHCl_3$). ^1H 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),

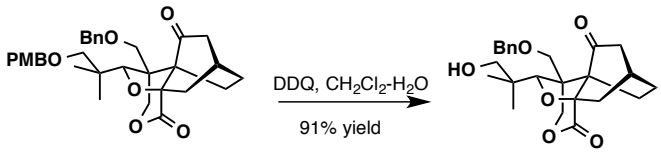
4.42–4.34 (m, 3H), 4.23 (s, 1H), 3.80 (s, 3H), 3.65 (d, *J*=8.9 Hz, 1H), 3.27 (d, *J*=8.9 Hz, 1H), 3.15 (d, *J*=8.9 Hz, 1H), 2.90–2.83 (m, 1H), 2.16–2.02 (m, 2H), 1.88–1.72 (m, 3H), 1.64–1.57 (m, 1H), 1.00 (s, 3H), 0.99 (s, 3H).



58 **59** 40% yield **S16** 22% NMR yield

Lactone 59. A degassed solution of AIBN (12.0 mg, 72.5 μmol) and tris(trimethylsilyl)silane (72 mg, 0.290 mmol) in benzene (5 mL) was added to a solution of **58** (100 mg, 0.145 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 **59** (31.0 mg, 58 μmol, 40%) and **S16** (ca. 5.0 mg was isolated due to its instability on silica gel column, 9%). $[\alpha]_D^{23}$ -6.3° (*c* 1.0, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 7.33 (t, *J*=7.3 Hz, 2H), 7.28 (d, *J*=7.3 Hz, 1H), 7.23–7.18 (m, 4H), 6.87 (d, *J*=8.6 Hz, 2H), 4.60 (d, *J*=11.9 Hz, 1H), 4.57 (d, *J*=9.3 Hz, 1H), 4.49 (dd, *J*=11.9, 1.1 Hz, 1H), 4.45 (d, *J*=11.8 Hz, 1H), 4.38–4.30 (m, 4H), 3.81 (s, 3H), 3.49 (d, *J*=9.3 Hz, 1H), 3.17 (d, *J*=9.2 Hz, 1H), 3.07 (d, *J*=9.2 Hz, 1H), 3.01 (ddd, *J*=14.4, 4.3, 2.8 Hz, 1H), 2.42–2.31 (m, 2H), 2.31–2.26 (m, 1H), 2.03–1.96 (m, 2H), 1.72–1.66 (m, 1H), 1.64–1.53 (m, 2H), 0.98 (s, 3H), 0.95 (s, 3H).

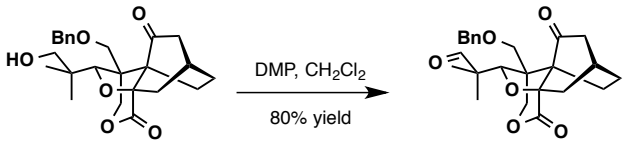
S16. ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 9.76 (s, 1H), 7.34–7.29 (m, 2H), 7.28–7.30 (m, 3H), 5.31 (d, *J*=7.0 Hz, 1H), 4.51 (d, *J*=11.8 Hz, 1H), 4.41 (d, *J*=11.8 Hz, 1H), 4.37 (d, *J*=8.1 Hz, 1H), 4.19 (s, 1H), 3.61 (d, *J*=8.1 Hz, 1H), 2.89 (*virt.* dt, *J*=7.0, 2.8 Hz, 1H), 2.10 (*virt.* dt, *J*=17.5, 3.0 Hz, 1H), 2.05 (dd, *J*=17.4, 2.3 Hz, 1H), 1.86–1.79 (m, 2H), 1.79–1.79–1.71 (m, 1H), 1.65–1.58 (m, 1H), 1.20 (s, 3H), 1.11 (s, 3H), 1.06 (s, 3H). HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{23}H_{28}O_4Na$, 391.1885; found, 391.1903. $[\alpha]_D^{23}$ was not recorded due to its instability.



59 **S17**

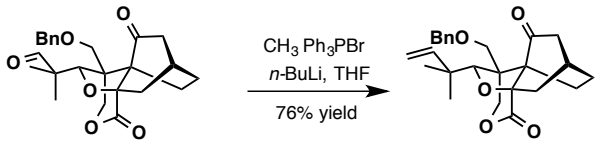
Alcohol S17. DDQ (25 mg, 0.112 mmol) was added to a solution of the substrate **59** (30.0 mg, 56.0 μmol) in CH_2Cl_2 (2.5 mL) and H_2O (0.2 mL) at 23 °C. After stirring for 1 h, the reaction mixture was diluted with CH_2Cl_2, quenched with a saturated aqueous $NaHCO_3$ solution, and extracted with CH_2Cl_2. 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 **S17** (21.0 mg, 50.7 μmol, 91%). $[\alpha]_D^{23}$ -8.1° (*c* 1.0, $CHCl_3$). ^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, *J*=12.1, 1.1 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, *J*=14.5, 4.3, 2.8 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).



S17 **S18**

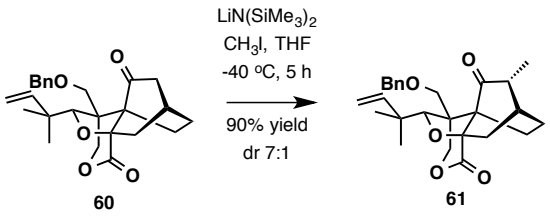
Aldehyde S18. Sodium bicarbonate (0.103 g, 1.23 mmol) and Dess-Martin periodinane (0.140 g, 0.328 mmol) were added sequentially to a solution of alcohol **S17** (85.0 mg, 0.205 mmol) in CH_2Cl_2 (10 mL) at 23 °C. After stirring for 1 h, the reaction mixture was diluted with CH_2Cl_2, quenched with a 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 (15% ethyl acetate in hexanes) to deliver the product **S18** (67.5 mg, 0.163 mmol, 80%). $[\alpha]_D^{23}$ -13.4° (*c* 1.0, $CHCl_3$). ^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, *J*=14.5, 4.3, 2.4 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).



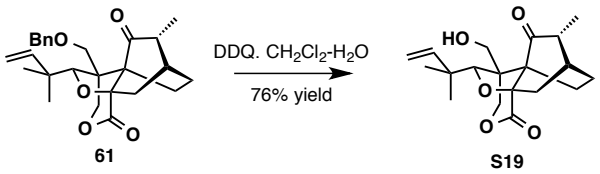
S18 **60**

Alkene 60. A solution of *n*-BuLi (2.25 M in hexanes, 0.35 mL, 0.764 mmol) was added to a suspension of CH_3PPh_3Br (0.311 g, 0.974 mmol) in THF (5 mL) at 0 °C. After stirring at the same temperature for 15 min, 4 ml of the resulting yellow solution was transferred to a solution of aldehyde **S18** (44 mg, 0.107 mmol) in THF (2 mL) at 0 °C. After stirring for 10 min, the reaction was quenched with a saturated aqueous NH_4Cl solution and extracted with ethyl acetate. 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 (15% ethyl acetate in hexanes) to deliver the product **60** (33.5 mg, 81.7 μmol, 76%). $[\alpha]_D^{23}$ -15.5° (*c* 0.5, $CHCl_3$). ^1H 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, *J*=17.6, 10.8 Hz, 1H), 5.07 (dd, *J*=17.6, 0.9 Hz, 1H), 5.04 (d, *J*=10.8 Hz, 1H), 4.51 (d, *J*=9.3 Hz, 1H), 4.51 (d, *J*=11.7 Hz, 1H), 4.46 (d, *J*=11.7 Hz, 1H), 4.37 (dd, *J*=11.7, 1.5 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, *J*=14.4, 4.5, 2.6 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).

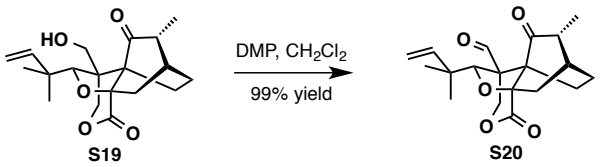


Alkene 61. A solution of $LiN(SiMe_3)_2$ (1.0 M in toluene, 0.353 mL, 0.353 mmol) was added to a solution of the substrate (29.0 mg, 70.7 μmol) in THF (6 mL) at -78 °C. After stirring at that temperature for 15 min, iodomethane (26 μL, 0.424 mmol) was added. The reaction mixture was stirred at -78 °C for 1 h, then at -40 °C for 4 h. The reaction was quenched with a saturated aqueous NH_4Cl solution at -40 °C and extracted with ethyl acetate. 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 (15% ethyl acetate in hexanes) to deliver **61** as an inseparable mixture of diastereomers (27 mg, 63.7 μmol, 90%, dr = 7:1). $[\alpha]_D^{23}$ -18.5° (*c* 0.5, $CHCl_3$). **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, *J*=17.6, 10.8 Hz, 1H), 5.07 (dd, *J*=17.6, 1.2 Hz, 1H), 5.04 (dd, *J*=10.8, 1.2 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, *J*=14.4, 4.7 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).

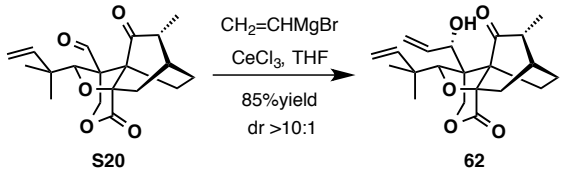


Alcohol S19. DDQ (0.133 g, 0.589 mmol) was added to a solution of the substrate (25.0 mg, 58.9 μmol, dr = 7:1) in CH_2Cl_2 (2 mL) and H_2O (0.2 mL). The flask was sealed and heated at 50 °C for 12 h. After cooling, the reaction mixture was diluted with CH_2Cl_2, quenched with a saturated aqueous $NaHCO_3$ 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 (15% ethyl acetate in hexanes) to deliver the product **S19** as a single diastereomer (15 mg, 44.9 μmol, 76%), together with recovered starting material **61** as a mixture of the diastereomers (5 mg, 11.2 μmol, dr = 10:1, 20%). $[\alpha]_D^{23}$ -36.7° (*c* 0.5, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$); δ (ppm): 6.03 (dd, *J*=17.6, 10.8 Hz, 1H), 5.10 (dd, *J*=17.6, 1.0 Hz, 1H), 5.06 (dd, *J*=10.8, 1.0 Hz, 1H), 4.51 (d, *J*=11.8 Hz, 1H), 4.09 (d, *J*=1.5 Hz, 1H), 4.01 (dd, *J*=11.8, 1.5 Hz, 1H), 3.95 (dd, *J*=12.1, 8.3 Hz, 1H), 3.58 (dd, *J*=12.1, 4.6 Hz, 1H), 3.30 (dd, *J*=8.3, 4.6 Hz, 1H), 3.14 (dd, *J*=14.6, 4.6 Hz, 1H), 2.40–2.34 (m, 1H), 2.13–2.09 (m, 1H), 1.98–1.85 (m, 2H), 1.74 (ddd, *J*=14.8, 10.9, 7.9 Hz, 1H), 1.67 (*virt.* dt, *J*=14.6, 1.8 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,

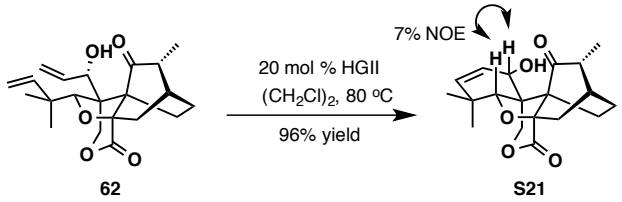
$CDCl_3$); δ (ppm): 217.7, 169.7, 143.0, 112.3, 87.7, 82.1, 67.8, 61.2, 58.1, 48.9, 48.7, 40.4, 35.1, 32.7, 25.7, 25.0, 19.3, 18.2, 15.5. HRMS-ESI (*m/z*): $[M+Na]^+$ calcd for $C_{19}H_{26}O_5Na$, 357.1678; found, 357.1669.



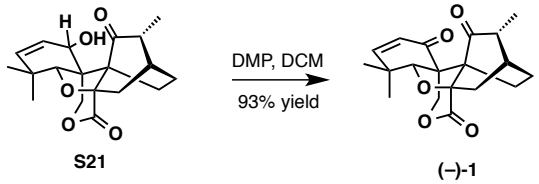
Aldehyde S20. Sodium bicarbonate (23 mg, 0.26 mmol) and Dess-Martin periodinane (38 mg, 89.8 μmol) were added sequentially to a solution of alcohol **S19** (10.0 mg, 29.9 μmol) in CH_2Cl_2 (1.5 mL) at 23 °C. After stirring for 2 h, the reaction mixture was diluted with CH_2Cl_2, quenched with a saturated 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 **S20** (9.9 mg, 29.8 μmol, 99%). $[\alpha]_D^{23}$ -59.8° (*c* 0.5, $CHCl_3$). ^1H NMR (600 MHz, $CDCl_3$); δ (ppm): 10.23 (s, 1H), 5.99 (dd, *J*=17.4, 10.8 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, *J*=12.1, 1.3 Hz, 1H), 3.07 (dd, *J*=14.8, 4.4 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*=14.8, 2.0 Hz, 1H), 1.66 (ddd, *J*=14.5, 11.0, 7.4 Hz, 1H), 1.61-1.57 (m, 1H), 1.19 (d, *J*=7.4 Hz, 3H), 1.14 (s, 3H), 1.12 (s, 3H).



Allylic alohol 62. A suspension of dry $CeCl_3$ (67.0 mg, 0.27 mmol)[5] in THF (1 mL) was stirred at 23 °C for 2 h. Vinylmagnesium bromide (0.29 mL, 0.94 M in THF, 0.27 mmol) was added to the above suspension at -78 °C. After stirring at the same temperature for 1 h, a solution of **S20** (12.0 mg, 30.0 μmol) in THF (2 mL) was added. After stirring for further 1 h at -78 °C, the reaction mixture was quenched with a saturated aqueous $NaHCO_3$ solution, and extracted with ethyl acetate. 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 (15% ethyl acetate in hexanes) to deliver the product **62** as a single isomer (11 mg, 30.6 μmol, 85%). The configuration of the allylic hydroxyl was determined by 1D NOE NMR experiment after the next step. $[\alpha]_D^{23}$ -40.2° (*c* 0.5, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$); δ (ppm): 6.21 (dd, *J*=17.6, 10.8 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, *J*=10.8, 1.3 Hz, 1H), 4.63 (d, *J*=11.8 Hz, 1H), 4.46 (d, *J*=1.9 Hz, 1H), 4.07 (dd, *J*=11.8, 1.9 Hz, 1H), 3.83 (dd, *J*=11.9, 6.7 Hz, 1H), 3.15 (dd, *J*=14.4, 4.7 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).

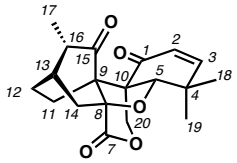


Cyclohexenol S21. Hoveyda-Grubbs second generation catalyst (3.0 mg, 4.78 μmol) was added to substrate **62** (9.0 mg, 25.0 μmol) in degassed 1,2-dichloroethane (1 ml). The flask was sealed, and the mixture was heated at 80 °C for 2 h. After cooling, the solvent was removed and the residue was purified by column chromatography on silica gel (25% ethyl acetate in hexanes) to deliver **S21** (8.0 mg, 24.1 μmol, 96%). $[\alpha]_D^{23}$ -17.1° (*c* 0.5, $CHCl_3$). ^1H NMR (500 MHz, $CDCl_3$); δ (ppm): 6.07 (br. s, 1H), 5.48 (dd, *J*=10.2, 2.3 Hz, 1H), 5.41 (dd, *J*=10.2, 1.5 Hz, 1H), 4.67 (d, *J*=12.6 Hz, 1H), 4.52 (dd, *J*=12.6, 1.6 Hz, 1H), 4.11 (d, *J*=1.6 Hz, 1H), 3.23 (dd, *J*=14.4, 4.8 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 (1). Sodium bicarbonate (32.5 mg, 0.387 mmol) and Dess-Martin periodinane (41.0 mg, 96.7 μmol) were added sequentially to a solution of substrate **S21** (10.7 mg, 32.2 μmol) in CH_2Cl_2 (2 mL) at 23 °C. After stirring for 1 h, the reaction mixture was diluted with CH_2Cl_2, quenched with a saturated aqueous $NaHCO_3$ 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 (20% ethyl acetate in hexanes) to deliver (-)-maoecrystal V (10.0 mg, 30.3 μmol, 93%). $[\alpha]_D^{23}$ -101.1° (*c* 0.35, CH_3OH), [lit.[6] $[\alpha]_D^{23}$ -92.9° (*c* 0.70, CH_3OH)]. ^1H 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, *J*=12.2, 1.2 Hz, 1H), 3.19 (dd, *J*=14.6, 4.7 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 (151 MHz, **$CDCl_3$**) δ (ppm): 211.5, 194.8, 169.0, 156.7, 127.0, 84.9, 84.1, 69.2, 56.5, 51.9, 48.2, 38.2, 34.5, 32.6, 30.6, 18.54, 18.51, 18.0, 15.1. Data for racemic material: ^1H 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) calcd for $C_{19}H_{22}O_5Na$ [M+Na] 353.1365, found 353.1360.

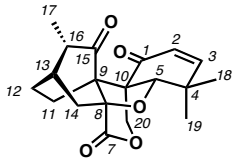
Table S1. Comparison of ^{1}H NMR Data of Synthetic and Reported Maoecrystal V (d_5-Pyridine)



1

position	synthetic **1** (600 MHz)	reported for natural **1** (400 MHz)[6]
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)

Table S2. 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)[6]
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

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