Angewandte Chemie
Eine Zeitschrift der Gesellschaft Deutscher Chemiker

Supporting Information

69451 Weinheim, Germany

Supporting Information for:

Catalytic Enantioselective Synthesis of Tetrasubstituted Tertiary Ethers. Ready Access to Fully-substituted α-Hydroxyketones, esters, and acids.

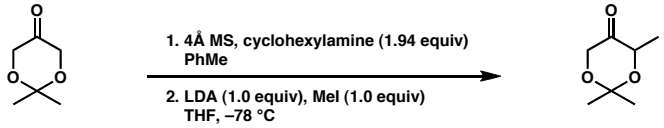
Masaki Seto, Jennifer L. Roizen, and Brian M. Stoltz

The Arnold and Mabel Beckman Laboratories of Chemical Synthesis
Division of Chemistry and Chemical Engineering
California Institute of Technology
Pasadena, CA 91125, USA

Table of Contents:

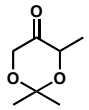
Materials and Methods. Unless otherwise stated, reactions were performed in flame-dried glassware under an argon atmosphere using dry, deoxygenated solvents. Solvents were dried by passage through an activated alumina column under argon. Tetrabutylammonium triphenyldifluorosilicate (TBAT) was purchased from Sigma-Aldrich Chemical Company and azeotropically dried five times from acetonitrile prior to use. Trimethylsilyl chloride (TMSCl) and triethyl amine (TEA) were distilled from sodium hydride immediately prior to use. Sodium iodide was dried by heating at 90 °C (2 torr) for 12 h. Bis(3,5,3',5'-dimethoxydibenzylideneacetone)palladium(0) ($Pd(dmdba)_2$) was purchased from Sigma-Aldrich Chemical Company and stored in a glove box prior to use. (*S*)-*t*-Bu-PHOX was prepared by known methods.[1] Cyclohexylamine, alkyl halides, triethylsilyl chloride and diallyl carbonate were used without further purification. Molecular sieves were purchased from Aldrich as activated 5 μm powder and stored in a 120 °C drying oven until immediately prior to use unless otherwise noted. Reaction temperatures were controlled by an IKAmag temperature modulator. Thin-layer chromatography (TLC) was performed using E. Merck silica gel 60 F254 precoated plates (0.25 mm) and visualized by UV fluorescence quenching, anisaldehyde, or CAM staining. Florisil® (100-200 mesh) and ICN Silica gel (particle size 0.032-0.063 mm) were used for flash chromatography. Chiral HPLC analysis was performed with an Agilent 1100 Series HPLC utilizing chiralpak AD or chiralcel OD-H columns (4.6 mm x 25 cm) obtained from Daicel Chemical Industries, Ltd. with visualization at 254 nm or 220 nm. Chiral GC anaylsis was performed with an Agilent 6850 GC utilizing a G-TA (30 m x 0.25cm) column (1.0 mL/min carrier gas flow). Optical rotations were measured with a Jasco P-1010 polarimeter at 589 nm. ^{1}H and ^{13}C NMR spectra were recorded on a Varian Mercury 300 NMR spectrometer (at 300 MHz and 75 MHz respectively), and are reported relative to Me_4Si (δ 0.0). Data for ^{1}H NMR spectra are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Data for ^{13}C NMR spectra are reported in terms of chemical shift relative to Me_4Si (δ 0.0). IR spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer and are reported in wavenumbers (cm^{-1}). High resolution mass spectra were obtained from the Caltech Mass Spectral Facility.

Representative Procedure for the Synthesis of 2,2-Dimethyl-1,3-dioxan-5-ones.

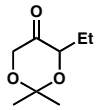


2,2,4-Trimethyl-1,3-dioxan-5-one.
To a solution of 2,2-dimethyl-1,3-dioxan-5-one (5.0 g, 38.4 mmol, 1.0 equiv)[2] in toluene (125 mL, 0.3 M) were added 4Å molecular sieves (5.0 g) and cyclohexylamine (8.50 mL, 74.3 mmol, 1.94 equiv) at room temperature (ca. 25 °C). The mixture was stirred for 14 h, then the molecular sieves were removed by filtration. The filtrate was concentrated under reduced pressure to give crude imine (7.95 g).
Lithium diisopropylamine was prepared in a separate flask by dropwise addition of *n*-BuLi (2.50 M in hexanes, 15.4 mL, 38.5 mmol, 1.0 equiv) via syringe to a solution of

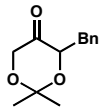
diisopropylamine (5.40 mL, 38.5 mmol, 1.0 equiv) in THF (60 mL, 0.64 M) at –78 °C. The mixture was stirred at 0 °C for 10 min, and then cooled to –78 °C. A solution of the imine (7.95 g) in THF (40.0 mL) was added dropwise via syringe to the resulting LDA solution at –78 °C. The reaction mixture was warmed to –35 °C, and stirred for 2 h, after which point it was re-cooled to –78 °C, and MeI (2.39 mL, 38.4 mmol, 1.0 equiv) was added. The reaction was warmed to room temperature (ca. 25 °C) over 3 h. Saturated aq NH_4Cl (60 mL) was added to the reaction mixture and the mixture was stirred at room temperature overnight. The mixture was extracted with Et_2O (3 x 50 mL). The combined organic layers were washed with brine (30 mL), dried over $MgSO_4$, and filtered. Solvent was removed under reduced pressure and the residue was purified by flash chromatography (20% Et_2O in pentane on silica gel) to give 2,2,4-trimethyl-1,3-dioxane-5-one (3.93 g, 71% yield) as a pale orange oil.



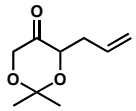
4-Methyl-2,2-dimethyl-1,3-dioxan-5-one (**SI 1a**).[3] 71% yield. Pale orange oil; R_f 0.72 (20% EtOAc in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.37 (qd, *J* = 6.9, 1.5 Hz, 1H), 4.28 (dd, *J* = 17.1, 1.5 Hz, 1H), 4.01 (d, *J* = 17.1 Hz, 1 H), 1.47 (s, 3H), 1.43 (s, 3H), 1.31 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 210.2, 101.0, 71.1, 66.6, 24.1, 23.9, 14.3; IR (Neat Film NaCl) 2994, 2944, 1745, 1376, 1227, 1101 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_7H_{12}O_3$ [M]$^+$: 144.0786, found 144.0786.



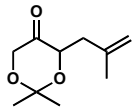
4-Ethyl-2,2-dimethyl-1,3-dioxan-5-one (**SI 1g**).[3] 72% yield. Colorless oil; R_f 0.58 (20% Et_2O in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.27 (dd, *J* = 17.0, 1.5 Hz, 1H), 4.17-4.13 (m, 1H), 3.98 (d, *J* = 17.0 Hz, 1H), 1.97-1.83 (m, 1H), 1.66-1.51 (m, 1H), 1.46 (s, 3H), 1.44 (s, 3H), 0.98 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.9, 100.9, 76.0, 66.9, 24.2, 23.7, 22.0, 9.7; IR (Neat Film NaCl) 2986, 2940, 2881, 1749, 1376, 1225, 1165, 1115, 1077, 1011, 867 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_8H_{14}O_3$ [M]$^+$: 158.0943, found 158.0939.



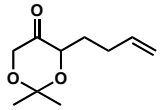
4-Benzyl-2,2-dimethyl-1,3-dioxan-5-one (**SI 1h**).[4] 73% yield. Yellow oil; R_f 0.54 (20% Et_2O in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31-7.16 (m, 5H), 4.46 (ddd, *J* = 9.3, 3.3, 1.8 Hz, 1H), 4.26 (dd, *J* = 17.1, 1.8 Hz, 1H), 4.01 (d, *J* = 17.1 Hz, 1H), 3.24 (dd, *J* = 15.0, 3.3 Hz, 1H), 2.79 (dd, *J* = 15.0, 9.3 Hz, 1H), 1.43 (s, 3H), 1.34 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.1, 137.9, 129.4, 128.4, 126.6, 101.2, 75.8, 66.8, 34.6, 24.1, 23.7; IR (Neat Film NaCl) 3030, 2988, 2938, 2884, 1747, 1498, 1454, 1375, 1252, 1223, 1173, 1101, 1062, 748, 700 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{13}H_{16}O_3$ [M]$^+$: 220.1100, found 220.1092.



4-Allyl-2,2-dimethyl-1,3-dioxan-5-one (**SI 1i**).[3a, 5] 65% yield. Colorless oil; R_f 0.43 (10% EtOAc in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.92-5.78 (m, 1H), 5.20-5.08 (m, 2H), 4.33-4.24 (m, 2H), 4.01 (d, *J* = 16.8 Hz, 1H), 2.69-2.60 (m, 1H), 2.38-2.27 (m, 1H), 1.47 (s, 3H), 1.45 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.2, 133.6, 117.7, 101.1, 74.6, 66.8, 32.9, 24.1, 23.8; IR (Neat Film NaCl) 2989, 1749, 1376, 1254, 1224, 1177, 1162, 1103 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_9H_{14}O_3$ [M]$^+$: 170.0943, found 170.0951.

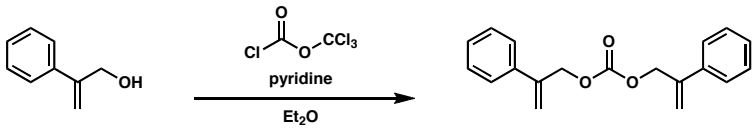


2,2-Dimethyl-4-(2-methylallyl)-1,3-dioxan-5-one (**SI 1c**). 66% yield. Pale orange oil; R_f 0.56 (20% Et_2O in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.83 (s, 1H), 4.81 (s, 1H), 4.42 (ddd, *J* = 9.6, 3.0, 1.2 Hz, 1H), 4.29 (dd, *J* = 17.1, 1.8 Hz, 1H), 4.01 (d, *J* = 17.1 Hz, 1H), 2.69 (app. dd, *J* = 15.6, 3.0 Hz, 1H), 2.20 (dd, *J* = 15.8, 9.6 Hz, 1H), 1.77 (s, 3H), 1.48 (s, 3H), 1.44 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.5, 141.6, 112.5, 101.1, 73.8, 66.7, 36.2, 24.1, 23.8, 23.0; IR (Neat Film NaCl) 3079, 2988, 2940, 1748, 1650, 1426, 1374, 1223, 1175, 1106, 1076, 1048, 1016, 899, 833 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{10}H_{16}O_3$ [M]$^+$: 184.1100, found 184.1101.



4-(But-3-enyl)-2,2-dimethyl-1,3-dioxan-5-one (**SI 1d**).[6] 53% yield. Colorless oil; R_f 0.38 (20% Et_2O in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.85-5.72 (m, 1H), 5.09-4.98 (m, 2H), 4.29-4.21 (m, 2H), 3.98 (d, *J* = 16.8 Hz, 1H), 2.30-2.08 (m, 2H), 2.03-1.92 (m, 1H), 1.70-1.58 (m, 1H), 1.45 (s, 3H), 1.44 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 210.0, 137.7, 115.8, 101.0, 73.8, 66.8, 29.3, 27.6, 24.1, 23.9; IR (Neat Film NaCl) 2988, 2938, 2884, 1748, 1642, 1434, 1376, 1251, 1225, 1175, 1103, 1071, 916, 864 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{10}H_{16}O_3$ [M]$^+$: 184.1100, found 184.1131.

Synthesis of Bis(2-phenylallyl) carbonate (**SI 2**)**.**

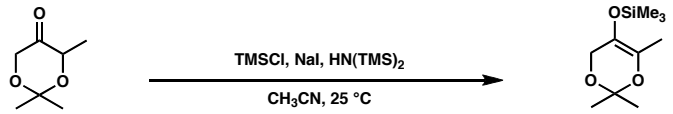


To a solution of 2-phenylallyl alcohol[7] (2.0 g, 14.9 mmol, 1.0 equiv) and pyridine (1.2 mL, 14.9 mmol, 1.0 equiv) in Et_2O (11 mL, 1.35 M) was added dropwise diphosgene (0.45 mL, 3.73 mmol, 0.25 equiv) via syringe at 0 °C over 20 min. The mixture was stirred at room temperature (ca. 25 °C) for 20 h. The white solid was removed by filtration, and the filter cake was washed with Et_2O. The filtrate was washed with aqueous $CuSO_4$ (5mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash chromatography (10% EtOAc in hexanes on silica gel) to give carbonate (1.26 g, 57% yield) as a colorless oil. R_f 0.61 (10% EtOAc in hexanes);

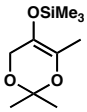
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44-7.23 (m, 10H), 5.55 (s, 2H), 5.38 (s, 2H), 5.04 (s, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.1, 142.2, 138.0, 128.7, 128.4, 126.2, 115.9, 69.4; IR (Neat Film NaCl) 3058, 1747, 1496, 1448, 1395, 1254, 970, 912, 778, 706 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{19}H_{18}O_3$ [M]$^+$: 294.1256, found 294.1250.

Synthesis of Silyl Enol Ethers

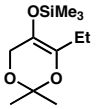
Representative Procedure for the Synthesis of Trimethylsilyl Enol Ethers.



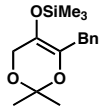
2,2,4-Trimethyl-5-trimethylsilyloxy-1,3-diox-4-ene (**SI 3a**).
To a solution of 2,2,2-trimethyl-1,3-dioxan-5-one (1.0 g, 6.94 mmol, 1.0 equiv), hexamethyldisilazane (1.75 mL, 13.4 mmol, 1.9 equiv), and sodium iodide (1.17 g, 7.81 mmol, 1.1 equiv) in acetonitrile (10.0 mL, 0.7 M) was added TMSCl (1.0 mL, 7.82 mmol, 1.1 equiv) at room temperature (ca. 25 °C). After the mixture was stirred at room temperature for 16 h, pentane (20 mL) was added to the mixture. The mixture was stirred at room temperature for 2 min, and then the pentane was decanted. After additional pentane extractions (5 x 10 mL), the combined pentane layer was washed with water (3 x 30 mL) and brine (30 mL), dried over Na_2SO_4, concentrated under reduced pressure. The residue was purified by flash chromatography (2% Et_2O in pentane on Florisil®) to give 2,2,4-Trimethyl-5-trimethylsilyloxy-1,3-diox-4-ene (0.481 g, 32% yield) as a colorless oil.



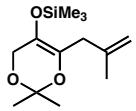
2,2,4-Trimethyl-5-trimethylsilyloxy-1,3-diox-4-ene (**SI 3a**). 32% yield. Colorless oil; R_f 0.25 (10% Et_2O in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.04 (q, *J* = 1.8 Hz, 2H), 1.76 (t, *J* = 1.8 Hz, 3H), 1.45 (s, 6H), 0.20 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 134.9, 125.5, 98.3, 61.1, 24.2, 14.2, 0.8; IR (Neat Film NaCl) 2995, 2958, 2939, 1384, 1370, 1276, 1254, 1224, 1151, 1120, 1072, 893, 846 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_7H_{11}O_3$ [M-C_3H_9Si]$^+$: 143.0708, found 143.0718.



2,2-Dimethyl-4-ethyl-5-trimethylsilyloxy-1,3-diox-4-ene (**SI 3g**). 35% yield. Colorless oil; R_f 0.52 (20% Et_2O in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.03 (app. t, *J* = 1.2 Hz, 2H), 2.16 (q, *J* = 7.4 Hz, 2H), 1.43 (s, 6H), 1.00 (t, *J* = 7.4 Hz, 3H), 0.18 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.5, 124.7, 98.1, 61.1, 24.2, 20.8, 11.1, 0.7; IR (Neat Film NaCl) 2964, 1384, 1369, 1276, 1254, 1223, 1199, 1148, 1122, 1079, 1035, 894, 867, 844, 752 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_8H_{13}O_3$ [M-C_3H_9Si]$^+$: 157.0865, found 157.0749.

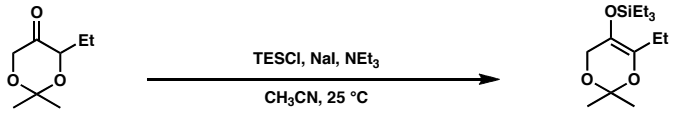


2,2-Dimethyl-4-benzyl-5-trimethylsilyloxy-1,3-diox-4-ene (**SI 3h**).16% yield. Colorless oil; R_f 0.44 (10% EtOAc in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32-7.12 (m, 5H), 4.09 (t, *J* = 1.2 Hz, 2H), 3.47 (app. s, 2H), 1.35 (s, 6H), 0.17 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.9, 136.9, 128.9, 128.3, 126.4, 126.2, 98.4, 61.1, 34.0, 24.1, 0.9; IR (Neat Film NaCl) 3029, 2994, 2957, 2837, 1748, 1603, 1495, 1454, 1382, 1370, 1276, 1253, 1230, 1199, 1144, 1093, 888, 845 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{16}H_{24}O_3Si$ [M]$^+$: 292.1495, found 292.1482.

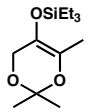


2,2-dimethyl-4-(2-methylallyl)-5-trimethylsilyloxy-1,3-diox-4-ene (**SI 3c**). 32% yield. Colorless oil; R_f 0.46 (50% EtOAc in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.779 (s, 1H), 4.775 (s, 1H), 4.07 (t, *J* = 1.1 Hz, 2H), 2.86 (s, 2H), 1.73 (s, 3H), 1.44 (s, 6H), 0.18 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.5, 136.0, 126.6, 111.7, 98.3, 61.1, 36.2, 24.2, 22.7, 0.8; IR (Neat Film NaCl) 3077, 2994, 2902, 2838, 1749, 1653, 1454, 1382, 1370, 1276, 1253, 1229, 1198, 1146, 1096, 891, 846 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{13}H_{24}O_3Si$ [M]$^+$: 256.1495, found 256.1500.

Representative Procedure for the Synthesis of Triethylsilyl Enol Ethers.

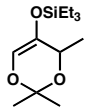


4-Ethyl-2,2-dimethyl-5-triethylsilyloxy-1,3-diox-4-ene (**SI 4g**).
To a solution of 4-ethyl-2,2-dimethyl-1,3-dioxane-5-one (0.50 g, 3.16 mmol, 1.0 equiv), Et_3N (0.71 mL, 5.09 mmol, 1.6 equiv) and NaI (0.62 g, 4.14 mmol, 1.3 equiv) in acetonitrile (5.0 mL, 0.63 M) was added TESCl (0.69 mL, 4.11 mmol, 1.3 equiv) at room temperature (ca. 25 °C). After the mixture was stirred for 20 h, pentane (10 mL) was added. The mixture was stirred at room temperature for 2 min, and then pentane was decanted. After additional pentane extractions (5 x 10 mL), the combined pentane layers were washed with water (20 mL) and brine (20 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash chromatography (1% Et_2O in petroleum ether on silica gel) to give triethylsilyl enol ether **4b** (0.659 g, 77% yield) and 4-Ethyl-2,2-dimethyl-5-triethylsilyloxy-1,3-diox-5-ene (70.6 mg, 8% yield).

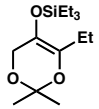


4-Methyl-2,2-dimethyl-5-triethylsilyloxy-1,3-diox-4-ene (**4a**). 77% yield. Colorless oil; R_f 0.50 (10% Et_2O in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.04 (q, *J* = 1.9 Hz, 2H), 1.77 (t, *J* = 1.9 Hz, 3H), 1.43 (s, 6H), 0.98 (t, *J* = 8.1 Hz, 9H), 0.65 (q, *J* = 8.1 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 134.4, 125.6, 98.2, 61.2, 24.3, 14.0, 6.9, 5.5; IR (Neat Film

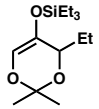
NaCl) 2995, 2956, 2915, 2878, 1459, 1383, 1369, 1276, 1221, 1198, 1150, 1120, 1071, 1002, 873, 850, 729 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{13}H_{26}O_3Si$ $[M]^+$: 258.1651, found 258.1642.



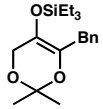
Triethyl(2,2,4-trimethyl-4*H*-1,3-dioxin-5-yloxy)silane (SI 5a). 6% yield. Colorless oil; R_f 0.55 (10% Et_2O in hexanes); ^1H NMR (300 MHz, $CDCl_3$) δ 6.10 (d, *J* = 1.5 Hz), 4.23 (qd, *J* = 6.6, 1.5 Hz), 1.47 (s, 3H), 1.44 (s, 3H), 1.32 (d, *J* = 6.6 Hz, 3H), 0.98 (t, *J* = 7.8 Hz, 9H), 0.71-0.63 (m, 6H).



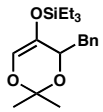
4-Ethyl-2,2-dimethyl-5-triethylsilyloxy-1,3-diox-4-ene (SI 4g). 77% yield. Colorless oil; R_f 0.53 (5% Et_2O in toluene); ^1H NMR (300 MHz, $CDCl_3$) δ 4.04 (t, *J* = 1.2 Hz, 2H), 2.19 (qt, *J* = 7.5, 1.2 Hz, 2H), 1.43 (s, 6H), 1.02-0.96 (m, 12H), 0.65 (q, *J* =7.8 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.0, 124.8, 98.0, 61.1, 24.3, 20.7, 11.1, 6.9, 5.5; IR (Neat Film NaCl) 2958, 2878, 1383, 1369, 1276, 1221, 1198, 1147, 1121, 1079, 1012, 857, 745, 730 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_8H_{13}O_3Si$ $[M-C_6H_{15}]^+$: 185.0634, found 185.0639.



4-Ethyl-2,2-dimethyl-5-triethylsilyloxy-1,3-diox-5-ene (SI 5g). 8% yield. Colorless oil; R_f 0.57 (5% Et_2O in toluene); ^1H NMR (300 MHz, $CDCl_3$) δ 6.14 (d, *J* = 1.5 Hz, 1H), 4.08 (ddd, *J* = 6.6, 3.6, 1.5 Hz, 1H), 1.87-1.72 (m, 1H), 1.69-1.55 (m, 1H), 1.46 (s, 3H), 1.43 (s, 3H), 1.01-0.92 (m, 12H), 0.70-0.62 (m, 6H).

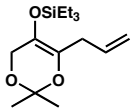


4-Benzyl-2,2-dimethyl-5-triethylsilyloxy-1,3-diox-4-ene (SI 4h). 78% yield. Colorless oil; R_f 0.41 (10% Et_2O in hexanes); ^1H NMR (300 MHz, $CDCl_3$) δ 7.31-7.12 (m, 5H), 4.10 (t, *J* = 1.2 Hz, 2H), 3.49 (s, 2H), 1.33 (s, 6H), 0.98 (t, *J* = 8.1 Hz, 9H), 0.66 (q, *J* = 8.1 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.0, 136.5, 128.9, 128.3, 126.5, 126.1, 98.3, 61.2, 33.8, 24.1, 6.9, 5.7; IR (Neat Film NaCl) 2956, 2877, 1454, 1382, 1370, 1276, 1226, 1198, 1145, 1093, 1016, 867, 746, 729, 731, 696 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{19}H_{30}O_3Si$ $[M]^+$: 334.1964, found 334.1978.

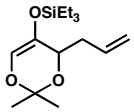


Triethyl(4-benzyl-2,2-dimethyl-4*H*-1,3-dioxin-5-yloxy)silane (SI 5h). 10% yield. Pale yellow oil; R_f 0.50 (10% Et_2O in hexanes); ^1H NMR (300 MHz, $CDCl_3$) δ 7.33-7.15 (m,

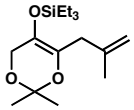
5H), 6.13 (d, *J* = 1.2Hz, 1H), 4.31 (ddd, *J* = 8.4, 3.0, 1.2 Hz, 1H), 3.16 (dd, *J* = 14.4, 3.0 Hz, 1H), 2.80 (dd, *J* = 14.3, 8.4 Hz, 1H), 1.43 (s, 3H), 1.42 (s, 3H), 1.01 (t, *J* = 7.8 Hz, 9H), 0.69 (q, *J* = 7.8 Hz, 6H).



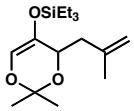
4-Allyl-2,2-dimethyl-5-triethylsilyloxy-1,3-diox-4-ene (**SI 4i**). 69% yield. Colorless oil; R_f 0.58 (10% EtOAc in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.87-5.73 (m, 1H), 5.15-5.01 (m, 2H), 4.06 (t, *J* = 1.2 Hz, 2H), 2.96-2.91 (m, 2H), 1.44 (s, 6H), 0.99 (t, *J* = 8.1 Hz, 9H), 0.66 (q, *J* = 8.1 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.8, 134.4, 126.0, 116.2, 98.3, 61.1, 32.1, 24.3, 6.9, 5.6; IR (Neat Film NaCl) 2995, 2957, 2913, 2879, 1639, 1458, 1414, 1382, 1370, 1278, 1241, 1196, 1147, 1084, 1016, 970, 909, 871, 851, 746, 731 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{15}H_{28}O_3Si$ [M]$^+$: 284.1808, found 284.1836.



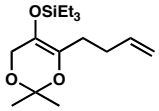
(4-Allyl-2,2-dimethyl-4*H*-1,3-dioxin-5-yloxy)triethylsilane (SI 5i). 10% yield. Pale yellow oil; R_f 0.65 (10% EtOAc in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.14 (d, *J* = 1.2 Hz, 1H), 5.97-5.83 (m, 1H), 5.16-5.04 (m, 2H), 4.16 (ddd, *J* = 7.2, 3.3, 1.2 Hz, 1H), 2.61-2.49 (m, 1H), 2.40-2.27 (m, 1H), 1.46 (s, 3H), 1.43 (s, 3H), 0.98 (t, *J* = 7.8 Hz, 9H), 0.67 (q, *J* = 7.8 Hz, 6H).



2,2-Dimethyl-6-(2-methylallyl)-4*H*-1,3-dioxin-5-yloxy)triethylsilane (SI 4c). 46% yield. Colorless oil; R_f 0.19 (10% Et_2O in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.78 (s, 2H), 4.08 (t, *J* = 1.1 Hz, 2H), 2.89 (s, 2H), 1.74 (s, 3H), 1.43 (s, 6H), 0.98 (t, *J* = 8.1 Hz, 9H), 0.65 (q, *J* = 8.1 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.5, 135.6, 126.7, 111.7, 98.3, 61.1, 36.0, 24.3, 22.7, 6.9, 5.6; IR (Neat Film NaCl) 2956, 2913, 2878, 1382, 1369, 1276, 1225, 1198, 1146, 1095, 1010, 851, 730 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{13}H_{26}O_3Si$ [M –H_2]$^+$ 297.1886, found 297.1851.



(2,2-dimethyl-4-(2-methylallyl)-4*H*-1,3-dioxin-5-yloxy)triethylsilane (SI 5c). 15% yield. Colorless oil; R_f 0.27 (10% Et_2O in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.13 (d, *J* = 1.5 Hz, 1H), 4.82 (s, 1H), 4.80 (s, 1H), 4.25 (ddd, *J* = 9.0, 2.7, 1.5 Hz, 1H), 2.61-2.53 (m, 1H), 2.20 (dd, *J* = 14.7, 9.0 Hz, 1H), 1.79 (s, 3H), 1.46 (s, 3H), 1.43 (s, 3H), 0.98 (t, *J* = 7.8 Hz, 9H), 0.67 (q, *J* = 7.8 Hz, 6H).



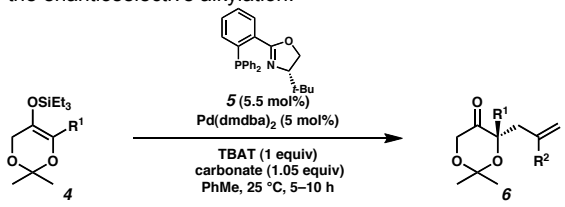
(6-(but-3-enyl)-2,2-dimethyl-4*H*-1,3-dioxin-5-yloxy)triethylsilane (SI 4d). 66% yield. Colorless oil; R_f 0.58 (10% Et_2O in hexanes); ^1H NMR (300 MHz, $CDCl_3$) δ 5.90-5.77 (m, 1H), 5.07-5.0 (m, 1H), 5.0-4.93 (m, 1H), 4.05 (s, 2H), 2.30-2.13 (m, 4H), 1.43 (s, 6H), 0.98 (t, *J* = 7.8 Hz, 9H), 0.65 (q, *J* = 7.8 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.5, 137.2, 125.7, 114.8, 98.2, 61.1, 30.9, 27.0, 24.3, 6.9, 5.6; IR (Neat Film NaCl) 2995, 2957, 2914, 2878, 2838, 1383, 1369, 1277, 1223, 1198, 1147, 1085, 1006, 857, 745, 730 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{16}H_{30}O_3Si$ $[M]^+$: 298.1964, found 298.1967.

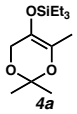
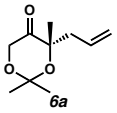
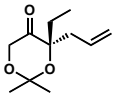
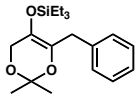
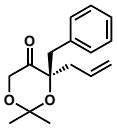
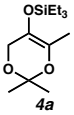
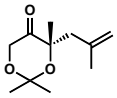
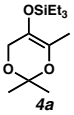
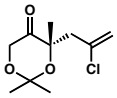
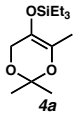
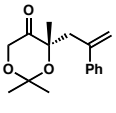
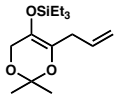
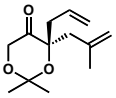
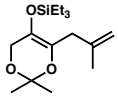
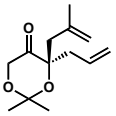
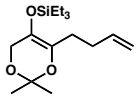
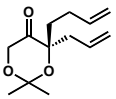
Asymmetric Alkylation Reaction

Representative Procedure for the Asymmetric Alkylation Reaction of Triethylsilyl Enol Ethers.

(*R*)-4-Allyl-2,2,4-trimethyl-1,3-dioxan-5-one (6a).
A 100 mL round-bottom flask was flame dried under vacuum and back-filled with argon. $Pd(dmdba)_2$ (20.3 mg, 0.025 mmol, 0.05 equiv), (*S*)-*t*-Bu-PHOX (10.6 mg, 0.027 mmol, 0.055 equiv), and TBAT (270 mg, 0.50 mmol, 1.0 equiv) were added to the flask. The system was evacuated under vacuum and back-filled with argon (3 x). Toluene (15 mL, 0.033 M) was added by syringe and the mixture was stirred at room temperature (ca. 25 °C) for 30 min. Diallyl carbonate (75.2 μL, 0.52 mmol, 1.05 equiv) and silyl ether **4a** (108 mg, 0.50 mmol, 1.0 equiv) were added. When the reaction was complete by TLC (after ca. 9 h), the reaction mixture was loaded onto a silica gel column and eluted with 2% Et_2O in petroleum ether to give tetrasubstituted **6a** (78.8 mg, 86% yield, 87% ee).

Table SI 1. Substrate scope for the enantioselective alkylation.[a]



Entry	Substrate	Product	Yield [%][b]	*ee* [%][c]
1			86	87
2			79	93
3			85	86
4[d]			73	82
5[e]			59	92
6[f]			73	94
7[d]			93	88
8			88	85
9			83	92

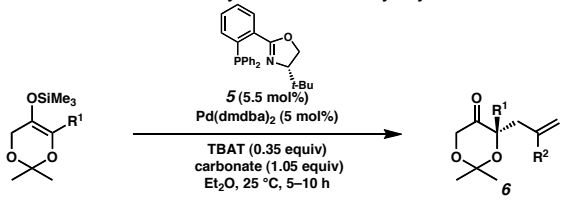
[a] Reactions were performed with silyl enol ether (0.5 mmol) and diallyl carbonate (1.05 equiv) in PhMe (0.033 M) unless stated otherwise. [b] Isolated yields. [c] Measured by chiral GC or HPLC. [d] Employed dimethallyl carbonate (1.05 equiv). [e] Employed dichloroallyl carbonate (1.05 equiv) at 35°C. [f] Employed diphenylallyl carbonate (1.05 equiv).

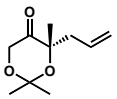
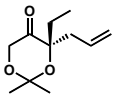
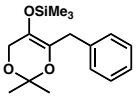
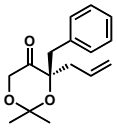
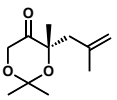
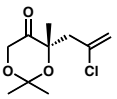
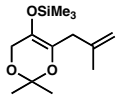
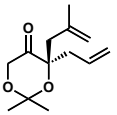
Representative Procedure for the Asymmetric Alkylation Reaction of Trimethylsilyl Enol Ethers.

(*R*)-4-Allyl-2,2,4-trimethyl-1,3-dioxan-5-one (6a).

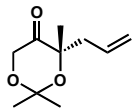
A 100 mL round-bottom flask was flame-dried under vacuum and back-filled with argon. $Pd(dmdba)_2$ (20.3 mg, 0.025 mmol, 0.05 equiv), (*S*)-*t*-Bu-PHOX (10.6 mg, 0.027 mmol, 0.055 equiv), and TBAT (94.3 mg, 0.18 mmol, 0.35 equiv) were added to the flask. The system was evacuated under vacuum and back-filled with argon (x 3). Et_2O (30 mL) was added by syringe, and the mixture was stirred at room temperature (ca. 28 °C) for 30 min. Diallyl carbonate (75.2 μL, 0.52 mmol, 1.05 equiv) and silyl ether **4d** (108 mg, 0.50 mmol, 1.0 equiv) were added. When the reaction was complete by TLC (after ca. 5 h), the reaction mixture was filtered through silica gel, and chased with Et_2O. The filtrate was evaporated under reduced pressure (~60 mmHg), the residue was purified by flash chromatography (2% Et_2O in petroleum ether on silica gel) to give tetrasubstituted **6a** (76.2 mg, 83% yield, 90% ee).

Table SI 2. Substrate scope for the enantioselective alkylation of trimethylsilyl enol ethers.[a]

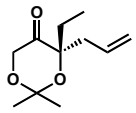


Entry	Substrate	Product	Yield [%][b]	*ee* [%][c]
1			83	90
2			79	93
3			84	85
4[d]			59	89
5[e]			28	91
6			86	85

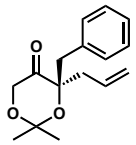
[a] Reactions were performed with substrate (0.5 mmol) in Et_2O (0.0167 M) with diallyl carbonate (1.05 equiv) unless stated otherwise. [b] Isolated yields. [c] Measured by chiral GC or HPLC. [d] Employed dimethallyl carbonate (1.05 equiv). [e] Employed dichloroallyl carbonate (1.05 equiv) at 35 °C.



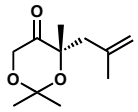
(*S*)-4-allyl-4-methyl-2,2-dimethyl-1,3-dioxan-5-one (6a). Colorless oil; R_f 0.22 (20% Et_2O in hexanes); ^1H NMR (300 MHz, $CDCl_3$) δ 5.90-5.76 (m, 1H), 5.13-5.04 (m, 2H), 4.21 (s, 2H), 2.57-2.50 (m, 1H), 2.45-2.37 (m, 1H), 1.49 (s, 3H), 1.48 (s, 3H), 1.39 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 210.9, 132.6, 119.0, 100.1, 82.2, 67.1, 43.6, 26.9, 26.7, 24.4; IR (Neat Film NaCl) 3079, 2989, 2942, 1742, 1641, 1429, 1382, 1373, 1229, 1203, 1180, 1161, 1143, 1080, 1007, 919 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{10}H_{18}O_3$ $[M]^+$: 184.1100, found 184.1096; $[\alpha]_D^{23.0}$ –68.6° (*c* 0.510, CH_2Cl_2, 90% ee); $[\alpha]_D^{27.5}$ –60.3° (*c* 0.845, CH_2Cl_2, 87% ee).



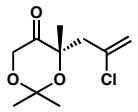
(*S*)-4-allyl-4-ethyl-2,2-dimethyl-1,3-dioxan-5-one (Table 2, entry 2). Colorless oil; R_f 0.48 (20% Et_2O in hexanes); ^1H NMR (300 MHz, $CDCl_3$) δ 5.89-5.70 (m, 1H), 5.14-5.02 (m, 2H), 4.17 (s, 2H), 2.60-2.39 (m, 2H), 1.91-1.64 (m, 2H), 1.49 (s, 3H), 1.48 (s, 3H), 0.88 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 210.8, 132.6, 118.9, 100.0, 85.2, 67.5, 41.4, 29.9, 27.0, 26.7, 7.7; IR (Neat Film NaCl) 3079, 2984, 2941, 2884, 1737, 1428, 1382, 1372, 1231, 1200, 1172, 1150, 1086, 1009, 918 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{11}H_{18}O_3$ $[M]^+$: 198.1256, found 198.1258; $[\alpha]_D^{24.4}$ –0.20° (*c* 0.575, CH_2Cl_2, 93% ee).



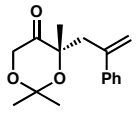
(*R*)-4-allyl-4-benzyl-2,2-dimethyl-1,3-dioxan-5-one (Table 2, entry 3). Colorless oil; R_f 0.44 (20% Et_2O in hexanes); ^1H NMR (300 MHz, $CDCl_3$) δ 7.29-7.18 (m, 5H), 5.97-5.83 (m, 1H), 5.17-5.10 (m, 2H), 4.05 (d, *J* = 18.0 Hz, 1H), 3.87 (d, *J* = 18.0 Hz, 1H), 3.08 (d, *J* = 13.5 Hz, 1H), 2.93 (d, *J* = 13.5 Hz, 1H), 2.63-2.45 (m, 2H), 1.50 (s, 3H), 1.27 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 210.0, 136.2, 132.4, 131.3, 128.0, 126.8, 119.3, 99.9, 85.5, 67.7, 43.2, 43.1, 27.7, 25.6; IR (Neat Film NaCl) 3077, 3031, 2990, 2939, 1736, 1496, 1454, 1426, 1382, 1372, 1231, 1196, 1102, 1052, 918 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{16}H_{20}O_3$ $[M]^+$: 260.1412, found 260.1417; $[\alpha]_D^{23.3}$ +21.4° (*c* 0.825, CH_2Cl_2, 86% ee); $[\alpha]_D^{24.2}$ +22.2° (*c* 1.055, CH_2Cl_2, 85% ee).



(*S*)-2,2,4-trimethyl-4-(2-methylallyl)-1,3-dioxan-5-one (Table 2, entry 4). Colorless oil; R_f 0.46 (20% Et_2O in hexanes); ^1H NMR (300 MHz, $CDCl_3$) δ 4.88 (s, 1H), 4.72 (s, 1H), 4.27 (d, *J* = 17.9 Hz, 1H), 4.19 (d, *J* = 17.9 Hz, 1H), 2.50 (d, *J* = 13.7 Hz, 1H), 2.39 (d, *J* = 13.7 Hz, 1H), 1.81 (s, 3H), 1.51 (s, 3H), 1.48 (s, 3H), 1.43 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 211.1, 141.5, 115.4, 100.0, 83.0, 67.3, 46.8, 27.0, 26.6, 25.0, 24.6; IR (Neat Film NaCl) 2987, 2943, 2919, 1742, 1645, 1440, 1382, 1373, 1230, 1200, 1159, 1106, 1010, 896 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{11}H_{18}O_3$ $[M]^+$: 198.1256, found 198.1263; $[\alpha]_D^{26.5}$ –87.7° (*c* 0.735, CH_2Cl_2, 89% ee).

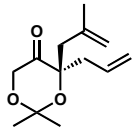


(*S*)-4-(2-chloroallyl)-2,2,4-trimethyl-1,3-dioxan-5-one (Table 2, entry 5). Colorless oil; R_f 0.50 (20% Et_2O in hexanes); ^1H NMR (300 MHz, $CDCl_3$) δ 5.30 (d, *J* = 1.2 Hz, 1H), 5.22 (d, *J* = 0.6 Hz, 1H), 4.37 (d, *J* = 17.7 Hz, 1H), 4.21 (d, *J* = 17.9 Hz, 1H), 2.91 (d, *J* = 14.4 Hz, 1H), 2.73 (d, *J* = 14.4 Hz, 1H), 1.55 (s, 3H), 1.51 (s, 3H), 1.47 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.9, 137.1, 117.0, 100.5, 81.3, 67.1, 48.1, 27.4, 26.2, 25.1; IR (Neat Film NaCl) 2991, 2941, 2897, 1744, 1633, 1425, 1383, 1374, 1229, 1203, 1182, 1158, 1106, 1060, 1011, 891 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{16}H_{20}O_3$ $[M–CH_3]^+$: 203.0475, found 203.0484; $[\alpha]_D^{20.7}$ –89.7° (*c* 1.030, $CHCl_3$, 93% ee).

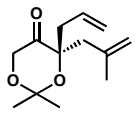


(*S*)-2,2,4-trimethyl-4-(2-phenylallyl)-1,3-dioxan-5-one (Table 2, entry 6). Colorless oil; R_f 0.23 (5% Et_2O in toluene); ^1H NMR (300 MHz, $CDCl_3$) δ 7.40-7.19 (m, 5H), 5.33 (d, *J* = 1.5 Hz, 1H), 5.13 (s, 1H), 4.08 (d, *J* = 17.7 Hz, 1H), 3.95 (d, *J* = 17.7 Hz, 1H), 2.98 (s, 2H), 1.39 (s, 3H), 1.38 (s, 3H), 1.19 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 210.8, 144.5, 142.3, 128.1, 127.4, 127.0, 117.9, 99.9, 82.7, 67.3, 44.9, 26.5, 25.5; IR (Neat Film NaCl)

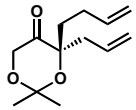
2988, 2940, 1742, 1626, 1495, 1444, 1382, 1372, 1229, 1198, 1158, 1117, 1010, 905, 778, 699 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{16}H_{20}O_3$ $[M]^+$: 260.1412, found 260.1417; $[\alpha]_D^{23.1}$ –45.9° (*c* 0.940, CH_2Cl_2, 94% ee).



(*R*)-4-allyl-2,2-dimethyl-4-(2-methylallyl)-1,3-dioxan-5-one (6e). Colorless oil; R_f 0.55 (20% Et_2O in hexanes); ^1H NMR (300 MHz, $CDCl_3$) δ 5.84 (dddd, *J* = 17.2, 10.2, 7.1, 7.1 Hz, 1H), 5.16-5.05 (m, 2H), 4.89 (ddd, *J* = 3.6, 1.5, 1.5 Hz, 1H), 4.74 (dd, *J* = 2.4, 0.9 Hz, 1H), 4.23 (d, *J* = 17.9 Hz, 1H), 4.15 (d, *J* = 17.9 Hz, 1H), 2.56-2.52 (m, 1H), 2.48-2.46 (dd, *J* = 4.8, 0.9 Hz, 2H), 1.81 (t, *J* = 1.2 Hz, 3H), 1.51 (s, 3H), 1.50 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 210.2, 141.4, 132.6, 119.1, 115.7, 99.9, 85.5, 67.9, 44.8, 42.5, 27.3, 26.3, 24.9; IR (Neat Film NaCl) 3078, 2986, 2944, 2919, 1740, 1642, 1427, 1383, 1372, 1231, 1197, 1159, 1001, 901 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{13}H_{20}O_3$ $[M]^+$: 224.1412, found 224.1410; $[\alpha]_D^{23.3}$ +20.5° (*c* 0.515, CH_2Cl_2, 85% ee).



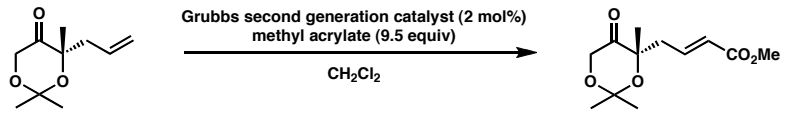
(*S*)-4-allyl-2,2-dimethyl-4-(2-methylallyl)-1,3-dioxan-5-one (Table 2, entry 8). Colorless oil; R_f 0.55 (20% Et_2O in hexanes); $[\alpha]_D^{26.6}$ –21.9° (*c* 0.620, CH_2Cl_2, 88% ee).



(*S*)-4-allyl-4-(but-3-enyl)-2,2-dimethyl-1,3-dioxan-5-one (6f). Colorless oil; R_f 0.33 (10% Et_2O in hexanes); ^1H NMR (300 MHz, $CDCl_3$) δ 5.86-5.70 (m, 2H), 5.11-4.92 (m, 4H), 4.19 (d, *J* = 18.0 Hz, 2H), 4.15 (d, *J* = 18.0 Hz, 2H), 2.60-2.45 (m, 2H), 2.27-1.95 (m, 2H), 1.93-1.69 (m, 2H), 1.51 (s, 3H), 1.48 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 210.5, 138.2, 132.4, 119.1, 115.0, 100.1, 84.5, 67.4, 41.9, 36.1, 27.7, 27.3, 26.5; IR (Neat Film NaCl) 3079, 2987, 2941, 1738 1642, 1427, 1382 1372, 1232, 1209, 1168, 1148, 1098, 998, 915 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{13}H_{20}O_3$ $[M]^+$: 224.1412, found 224.1416; $[\alpha]_D^{20.2}$ +7.04° (*c* 1.030, CH_2Cl_2, 92% ee).

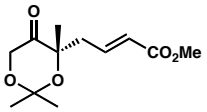
Synthesis of of α,β-Unsaturated Esters by Cross Metathesis.

Representative Procedure for the Synthesis of α,β-Unsaturated Esters.

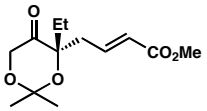


(*S,E*)-methyl-4-(2,2,4-trimethyl-5-oxo-1,3-dioxan-4-yl)but-2-enoate (6b). To a solution of terminal olefin **6a** (30.0 mg, 0.163 mmol, 1 equiv) and methyl acrylate (0.14 mL, 1.55 mmol, 9.5 equiv) in CH_2Cl_2 (1.6 mL, 0.1 M) was added Grubbs second generation catalyst (2.8 mg, 0.0033 mmol, 0.02 equiv) at room temperature (ca. 25°C).

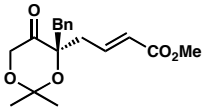
The mixture was stirred at 37 °C for 40 h. Ethyl vinyl ether (0.5 mL) was added, and it was stirred at 37 °C for 10 min. The mixture was filtered through silica gel with Et_2O/petroleum ether (1:2). After the filtrate was evaporated under reduced pressure (~60 mmHg), the residue was purified by flash column chromatography (10% Et_2O in petroleum ether on silica gel) to give α,β-unsaturated **6b** (32.8 mg, 83% yield).



(*S,E*)-methyl 4-(2,2,4-trimethyl-5-oxo-1,3-dioxan-4-yl)but-2-enoate (6b). 83% yield. Colorless oil; R_f 0.23 (20% Et_2O in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.92 (dt, *J* = 15.6, 7.8 Hz, 1H), 5.87 (dt, *J* = 15.6, 1.3 Hz, 1H), 4.23 (s, 2H), 3.73 (s, 3H), 2.71-2.63 (m, 1H), 2.54-2.47 (m, 1H), 1.50 (s, 3H), 1.45 (s, 3H), 1.43 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 210.1, 166.7, 143.1, 124.7, 100.5, 81.5, 66.8, 51.7, 41.3, 27.5, 26.2, 24.5; IR (Neat Film NaCl) 2992, 2951, 1727, 1659, 1437, 1374, 1338, 1274, 1231, 1197, 1180, 1155, 1117, 1008, 990 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{12}H_{19}O_5$ $[M+H]^+$: 243.1232, found 243.1224; $[\alpha]_D^{24.8}$ –49.7° (*c* 0.715, CH_2Cl_2, 90% ee).



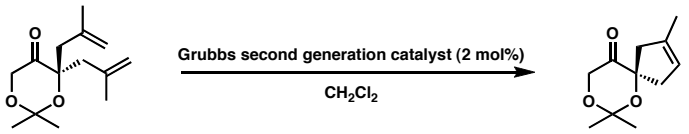
(*S,E*)-methyl 4-(4-ethyl-2,2-dimethyl-5-oxo-1,3-dioxan-4-yl)but-2-enoate (SI 6g). 89% yield. Colorless oil; R_f 0.19 (20% Et_2O in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.92 (dt, *J* = 15.6, 7.6 Hz, 1H), 5.88 (dt, *J* = 15.6, 1.5 Hz, 1H), 4.21 (s, 2H), 3.74 (s, 3H), 2.71-2.53 (m, 2H), 1.92-1.78 (m, 2H), 1.51 (s, 3H), 1.49 (s, 3H), 0.90 (t, *J* = 7.4 H, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 210.0, 166.7, 143.3, 124.6, 100.2, 84.6, 67.3, 51.7, 39.2, 30.4, 27.3, 26.4, 7.8; IR (Neat Film NaCl) 2985, 1726, 1658, 1435, 1383, 1373, 1271, 1232, 1196, 1177, 1084, 1033, 1013 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{13}H_{21}O_5$ $[M+H]^+$: 257.1389, found 257.1385; $[\alpha]_D^{24.9}$ –3.14° (*c* 0.655, CH_2Cl_2, 94% ee).



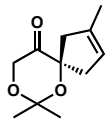
(*S,E*)-methyl 4-(4-benzyl-2,2-dimethyl-5-oxo-1,3-dioxan-4-yl)but-2-enoate (SI 6h). 75% yield. Colorless oil; R_f 0.19 (20% Et_2O in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31-7.13 (m, 5H), 7.00 (ddd, *J* = 15.6, 8.1, 7.2 Hz, 1H), 5.89 (dt, *J* = 15.9, 1.5 Hz, 1H), 4.06 (d, *J* = 18.0 Hz, 1H), 3.86 (d, *J* = 18.0 Hz, 1H), 3.74 (s, 3H), 3.06 (d, *J* = 13.5 Hz, 1H), 2.94 (d, *J* = 13.5 Hz, 1H), 2.72 (ddd, *J*= 14.4, 6.9, 1.2 Hz, 1H), 2.58 (ddd, *J* = 14.4, 8.1, 1.2 Hz, 1H), 1.48 (s, 3H), 1.32 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.3, 166.7, 142.9, 135.5, 131.1, 128.1, 127.1, 124.9, 100.3, 84.8, 67.5, 51.8, 43.8, 40.8, 27.0, 26.3; IR (Neat Film NaCl) 2992, 2950, 1725, 1658, 1435, 1385, 1374, 1271, 1234, 1198, 1171, 1114, 1098, 1054, 988, 702 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{18}H_{22}O_5$ $[M]^+$: 318.1467, found 318.1469; $[\alpha]_D^{27.1}$ +14.9° (*c* 0.550, CH_2Cl_2, 85% ee).

Synthesis of Spiro Compounds by Ring-Closing Metathesis.

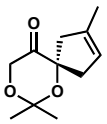
Representative Procedure for the Synthesis of Spiro Compounds 6c and 6d.



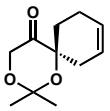
(*R*)-2,7,7-trimethyl-6,8-dioxaspiro[4.5]dec-2-en-10-one (6c).
To a solution of diene **6h** (60 mg, 0.268 mmol, 1.0 equiv) in CH_2Cl_2 (10 mL) was added Grubbs second generation catalyst (4.6 mg, 0.0054 mmol, 0.02 equiv) at room temperature. After the mixture was stirred at 35 °C for 40 h, it was concentrated under reduced pressure. The residue was purified by flash chromatography (2% Et_2O in petroleum ether on silica gel) to give the cyclopentene **6c** (51.4 mg, 98% yield) as a colorless oil.



(*R*)-2,7,7-trimethyl-6,8-dioxaspiro[4.5]dec-2-en-10-one (6d). 95% yield. Colorless oil; R_f 0.37 (20% Et_2O in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.22-5.20 (m, 1H), 4.31 (s, 2H), 2.91-2.52 (m, 4H), 1.73-1.71 (m, 3H), 1.49 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 210.1, 137.1, 120.8, 100.2, 88.3, 66.8, 48.5, 45.0, 27.0, 26.8, 16.5; IR (Neat Film NaCl) 2991, 2941, 1740, 1426, 1382, 1372, 1231, 1199, 1152, 1098, 1058, 988, 846 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{11}H_{16}O_3$ $[M]^+$: 196.1100, found 196.1095; $[\alpha]_D^{23.1}$ +19.2° (*c* 0.725, CH_2Cl_2, 85% ee).

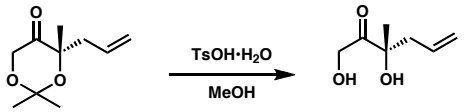


(*S*)-2,7,7-trimethyl-6,8-dioxaspiro[4.5]dec-2-en-10-one (SI 6c). 87% yield. Colorless oil; R_f 0.37 (20% Et_2O in hexanes); $[\alpha]_D^{24.0}$ –20.4° (*c* 0.885, CH_2Cl_2, 88% ee).

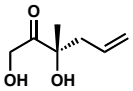


(*S*)-2,2-dimethyl-1,3-dioxaspiro[5.5]undec-8-en-5-one (6d). 90% yield. Colorless oil; R_f 0.24 (10% Et_2O in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.80-5.70 (m, 1H), 5.67-5.58 (m, 1H), 4.27 (s, 2H), 2.60-2.47 (m, 1H), 2.38-2.18 (m, 2H), 2.17-1.81 (m, 3H), 1.51 (s, 3H), 1.47 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 211.1, 126.4, 122.8, 100.5, 79.9, 66.6, 33.5, 29.9, 27.7, 26.3, 21.8; IR (Neat Film NaCl) 3030, 2991, 2938, 2911, 1739, 1429, 1382, 1372, 1259, 1230, 1200, 1155, 1099, 1062, 999, 886, 836, 778, 651 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{11}H_{16}O_3$ $[M]^+$: 196.1100, found 196.1139; $[\alpha]_D^{20.2}$ –20.9° (*c* 1.045, CH_2Cl_2, 92% ee).

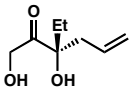
Acetonide Cleavage: Representative Procedure for the Synthesis of Diol 7.



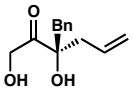
(*S*)-1,3-dihydroxy-3-methylhex-5-en-2-one (Table 3, entry 1**)**.
To a solution of acetonide **6a** (80.5 mg, 0.44 mmol, 1.0 equiv) in MeOH (4.4 mL, 0.1 M) was added *p*-toluenesulfonic acid monohydrate (8.3 mg, 0.044 mmol, 0.1 equiv) at room temperature (ca. 25 °C). After the mixture was stirred for 3.5 h, Et_3N (0.2 mL) was added. The mixture was concentrated under reduced pressure. The residue was purified by flash chromatography (30% EtOAc in hexanes on silica gel) to give diol **7a** (57.4 mg, 90% yield) as a colorless oil.



(*S*)-1,3-dihydroxy-3-methylhex-5-en-2-one (Table 3, entry 1). 90% yield. Colorless oil; R_f 0.21 (33% EtOAc in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.79-5.65 (m, 1H), 5.23-5.14 (m, 2H), 4.55 (dd, *J* = 20.0, 5.1 Hz, 1H), 4.46 (dd, *J* = 20.0, 5.1 Hz, 1H), 2.92 (t, *J* = 5.1 Hz, 1H), 2.74 (s, 1H), 2.57-2.50 (m, 1H), 2.42-2.35 (m, 1H), 1.39 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 214.1, 131.5, 120.8, 78.2, 65.3, 44.5, 25.6; IR (Neat Film NaCl) 3413, 2980, 1721, 1641, 1414, 1370, 1169, 1019, 923 cm^{-1}; HRMS (ES+) *m*/*z* calc'd for $C_7H_{13}O_3$ $[M+H]^+$: 145.0865, found 145.0850; $[\alpha]_D^{23.5}$ –14.2° (*c* 0.810, CH_2Cl_2, 90% ee).

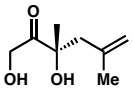


(*S*)-1,3-dihydroxy-3-ethylhex-5-en-2-one (Table 3, entry 2**)**. 97% yield; Colorless oil; R_f 0.32 (33% EtOAc in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.76-5.62 (m, 1H), 5.20-5.12 (m, 2H), 4.47 (dd, *J* = 19.8, 4.8 Hz, 1H), 4.40 (dd, *J* = 19.8, 4.8 Hz, 1H), 2.94 (t, *J* = 4.8 Hz, 1H), 2.84 (s, 1H), 2.53-2.38 (m, 2H), 1.86-1.64 (m, 2H), 0.86 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 214.1, 131.6, 120.5, 81.1, 66.2, 43.6, 32.2, 7.7; IR (Neat Film NaCl) 3436, 2976, 1717, 1641, 1414, 1272, 1158, 1111, 1042, 922 cm^{-1}; HRMS (EI+) *m*/*z* calc'd for $C_8H_{14}O_3$ $[M]^+$: 158.0943, found 158.0948; $[\alpha]_D^{24.0}$ –0.37° (*c* 0.715, CH_2Cl_2, 93% ee).

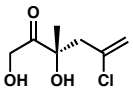


(*S*)-1,3-dihydroxy-3-benzylhex-5-en-2-one (Table 3, entry 3). 91% yield. colorless oil; R_f 0.50 (33% EtOAc in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35-7.24 (m, 3H), 7.13 (dd, *J* = 7.4, 1.9 Hz, 2H), 5.81-5.67 (m, 1H), 5.23-5.14 (m, 2H), 4.41 (dd, *J* = 20.1, 4.8 Hz, 1H), 4.07 (dd, *J* = 20.1, 4.8 Hz, 1H), 3.14 (d, *J* = 13.8 Hz, 1H), 2.92-2.86 (m, 2H), 2.65 (dd, *J* = 13.8, 7.4 Hz, 1H), 2.51 (s, 1H), 2.45-2.38 (dd, *J* = 14.1, 7.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 214.5, 134.8, 131.5, 130.3, 128.9, 127.6, 120.8, 81.4, 67.2, 45.2, 43.7; IR (Neat Film NaCl) 3436, 3079, 3030, 2917, 1717, 1640, 1496, 1454, 1429, 1412, 1259, 1098, 1043, 978, 924, 759, 703 cm^{-1}; HRMS (EI+) *m*/*z* calc'd for $C_{13}H_{16}O_3$

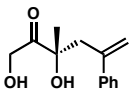
$[M]^+$: 220.1100, found 220.1069; $[\alpha]_D^{23.3}$ +16.1° (*c* 0.690 CH_2Cl_2, 86% ee).



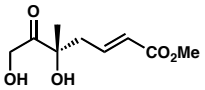
(*S*)-1,3-dihydroxy-3,5-dimethylhex-5-en-2-one (Table 3, entry 4). 97% yield. Colorless oil; R_f 0.36 (33% EtOAc in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.98-4.97 (m, 1H), 4.79 (d, *J* = 0.9 Hz, 1H), 4.59 (dd, *J* = 20.0, 4.8 Hz, 1H), 4.46 (dd, *J* = 20.0, 4.8 Hz, 1H), 2.96 (t, *J* = 4.8 Hz, 1H), 2.74 (s, 1H), 2.62 (d, *J* = 14.0 Hz, 1H), 2.35 (d, *J* = 14.0 Hz, 1H), 1.70 (s, 3H), 1.38 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 214.8, 140.8, 116.6, 78.1, 65.5, 47.9, 26.6, 24.2; IR (Neat Film NaCl) 3429, 3078, 2976, 2917, 1720, 1644, 1452, 1373, 1229, 1135, 1101, 1024, 898 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_8H_{14}O_3$ $[M]^+$: 1580943, found 158.0943; $[\alpha]_D^{23.3}$ –24.2° (*c* 0.420 CH_2Cl_2, 89% ee).



(*S*)-5-chloro-1,3-dihydroxy-3-methylhex-5-en-2-one (Table 3, entry 5). 97% yield. Colorless oil; R_f 0.30 (33% EtOAc in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.38 (d, *J* = 0.9 Hz, 1H), 5.28 (d, *J* = 0.9 Hz, 1H), 4.65 (dd, *J* = 19.8, 5.1 Hz, 1H), 4.54 (dd, *J* = 19.8, 4.8 Hz, 1H), 2.96-2.91 (m, 3H), 2.74 (d, *J* = 14.7 Hz, 1H), 1.42 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 213.5, 136.0, 118.4, 78.0, 65.6, 49.2, 26.3; IR (Neat Film NaCl) 3422, 2981, 2922, 1722, 1633, 1452, 1416, 1371, 1267, 1167, 1087, 1021, 981, 895 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_7H_9ClO_2$ $[M-H_2O]^+$: 160.0291, found 160.0298; $[\alpha]_D^{21.2}$ –16.7° (*c* 1.000, CH_2Cl_2, 91% ee).



(*S*)-1,3-dihydroxy-3-methyl-phenylhex-5-en-2-one (Table 3, entry 6). 92% yield. Colorless oil; R_f 0.27 (33% EtOAc in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35-7.26 (m, 5H), 5.41 (d, *J* = 1.2 Hz, 1H), 5.17 (d, *J* = 0.9 Hz, 1H), 4.41 (dd, *J* = 20.3, 5.0 Hz, 1H), 4.18 (dd, *J* = 20.3, 5.0 Hz, 1H), 3.12 (d, *J* = 14.0 Hz, 1H), 2.86 (d, *J* = 14.0 Hz, 1H), 2.66 (t, *J* = 5.0 Hz, 1H), 2.46 (s, 1H), 1.33 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 214.5, 143.7, 140.8, 128.9, 128.4, 126.8, 118.8, 78.7, 65.7, 45.6, 26.4; IR (Neat Film NaCl) 3431, 2977, 2931, 1719, 1625, 1494, 1445, 1406, 1369, 1142, 1021, 908, 780, 700 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_{13}H_{16}O_3$ $[M]^+$: 220.1100, found 220.1116; $[\alpha]_D^{20.6}$ –9.82° (*c* 0.355, CH_2Cl_2, 94% ee).

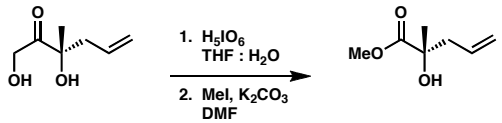


(*S,E*)-methyl 5,7-dihydroxy-5-methyl-6-oxohept-2-enoate (Table 3, entry 7). 80% yield. Colorless oil; R_f 0.58 (50% EtOAc in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.85 (m, 1H), 5.94-5.88 (m, 1H), 4.52 (d, *J* = 5.1 Hz, 2H), 3.73 (s, 3H), 2.99-2.90 (m, 2H), 2.69-2.50 (m, 2H), 1.42 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 213.5, 166.6, 142.1, 125.5, 78.2, 65.1, 51.9, 42.4, 25.7; IR (Neat Film NaCl) 3436, 2954, 1721, 1658, 1439, 1339, 1280, 1204, 1021 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_9H_{15}O_5$ $[M+H]^+$: 203.0919, found

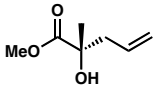
203.0918; $[\alpha]_D^{18.5}$ –8.35° (*c* 0.695, CH_2Cl_2, 92% ee).

Synthesis of Hydroxyesters by Oxidation and Methylation.

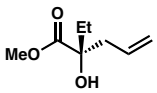
Representative Procedure for the Synthesis of α-Hydroxy Esters 8.



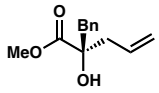
(2*S*)-Hydroxy-2-methyl-4-pentanoate (Table 3, entry 1).
To a solution of diol **7a** (53.4 mg, 0.37 mmol, 1 equiv) in THF and water (THF/H_2O, 2:1, 11.1 mL, 0.033 M) was added H_5IO_6 (127 mg, 0.50 mmol, 1.5 equiv) at room temperature. After the mixture was stirred at room temperature (ca. 25 °C) for 24 h, the mixture was extracted with Et_2O (3 x 30 mL). The organic layer was washed with water (3 mL) and brine (3 mL), dried over Na_2SO_4 and concentrated under reduced pressure. To a suspension of the residue and K_2CO_3 (27.6 mg, 0.44 mmol, 1.2 equiv) in DMF (3.7 mL, 0.1 M) was added MeI (27.6 μL, 0.44 mmol, 1.2 equiv) at room temperature (ca. 25 °C). After stirring for 1 h, water (5 mL) was added, and the reaction was extracted with Et_2O (3 x 30 mL). The organic layer was washed with water (3 mL) and brine (3 mL), dried over Na_2SO_4 and concentrated under reduced pressure (~80 mmHg). The residue was purified by flash chromatography (10% Et_2O in petroleum ether on silica gel) to give methyl ester **8a** (28.9 mg, 54% yield, 90% ee).



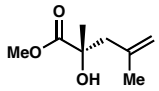
(2*S*)-Hydroxy-2-methyl-4-pentanoate (Table 3, entry 1).[8] 54% yield. Colorless oil; R_f 0.48 (20% EtOAc in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.84-5.70 (m, 1H), 5.15 (s, 1H), 5.12-5.07 (m, 1H), 3.77 (s, 3H), 3.10 (s, 1H), 2.35-2.54 (m, 2H), 1.43 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.1, 132.6, 119.3, 74.7, 52.9, 44.9, 25.7; IR (Neat Film NaCl) 3504, 2982, 2955, 1736, 1642, 1455, 1437, 1372, 1271, 1227, 1170, 1143, 1069, 1000, 980, 920 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_7H_{13}O_3$ $[M+H]^+$: 145.0865, found 145.0867; $[\alpha]_D^{22.7}$ +25.6° (*c* 0.365, CH_2Cl_2, 90% ee).



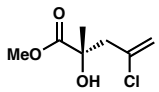
(2*S*)-Hydroxy-2-ethyl-4-pentanoate (Table 3, entry 2). 60% yield. Colorless oil; R_f 0.59 (33% EtOAc in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.84-5.70 (m, 1H), 5.13-5.06 (m, 2H), 3.77 (s, 3H), 3.16 (s, 1H), 2.51-2.37 (m, 2H), 1.85-1.63 (m, 2H), 0.86 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.8, 132.7, 119.0, 78.2, 52.8, 43.8, 32.0, 8.1; IR (Neat Film NaCl) 3524, 2956, 1735, 1641, 1446, 1246, 1225, 1163, 1028, 999, 974, 919 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_8H_{15}O_3$ $[M+H]^+$: 159.1021, found 159.1026; $[\alpha]_D^{20.4}$ +24.3° (*c* 0.350, CH_2Cl_2, 93% ee).



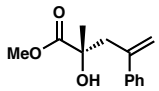
(2*S*)-Hydroxy-2-benzyl-4-pentanoate (Table 3, entry 3). 85% yield. Colorless oil; R_f 0.52 (20% EtOAc in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31-7.11 (m, 5H), 5.88-5.74 (m, 1H), 5.16-5.11 (m 2H), 3.72 (s, 3H), 3.07 (d, *J* = 13.5 Hz, 1H), 3.07 (s, 1H), 2.95 (d, *J* = 13.5 Hz, 1H), 2.65-2.46 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.7, 135.9, 132.5, 130.3, 128.4, 127.2, 119.2, 78.4, 52.7, 45.3, 43.8; IR (Neat Film NaCl) 3522, 3030, 2954, 1736, 1640, 1495, 1455, 1442, 1272, 1229, 1142, 1093, 920, 701 cm^{-1}; HRMS (EI+) *m*/*z* calc'd for $C_{13}H_{16}O_3$ $[M]^+$: 220.1100, found 220.1105; $[\alpha]_D^{23.4}$ +41.8° (*c* 0.890, CH_2Cl_2, 86% ee).



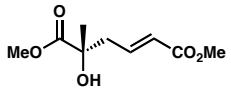
Methyl (*S*)-2-hydroxy-2,4-dimethyl-pent-4-enoic acid methyl ester (Table 3, entry 4).[9] 84% yield. Colorless oil; R_f 0.38 (20% EtOAc in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.89-4.88 (m, 1H), 4.75 (s, 1H), 3.77 (s, 3H), 3.12 (s, 1H), 2.53 (d, *J* = 13.8 Hz, 1H), 2.37 (d, *J* = 13.8 Hz, 1H), 1.74 (s, 3H), 1.44 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.4, 141.4, 115.2, 74.9, 52.8, 48.2, 26.6, 24.0; IR (Neat Film NaCl) 3514, 2954, 1736, 1644, 1452, 1375, 1266, 1212, 1156, 1114, 896 cm^{-1}; HRMS (EI+) *m*/*z* calc'd for $C_8H_{14}O_3$ $[M]^+$: 158.0943, found 158.0946; $[\alpha]_D^{22.0}$ +11.4° (*c* 0.220, CH_2Cl_2, 89% ee).



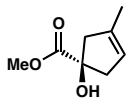
2-(2-Chloroallyl)-2-hydroxymalonic acid dimethyl ester (Table 3, entry 5).[10] 76% yield. Colorless oil; R_f 0.48 (33% EtOAc in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.33 (d, *J* = 0.9 Hz, 1H), 5.26 (d, *J* = 0.9 Hz, 1H), 3.80 (s, 3H), 3.32 (s, 1H), 2.86 (d, *J* = 14.3 Hz, 1H), 2.72 (d, *J* = 14.3 Hz, 1H), 1.47 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.4, 136.6, 117.2, 73.6, 53.1, 49.6, 26.4; IR (Neat Film NaCl) 3507, 2987, 2955, 1738, 1633, 1454, 1436, 1278, 1230, 1167, 887 cm^{-1}; HRMS (EI+) *m*/*z* calc'd for $C_7H_{11}ClO_3$ $[M]^+$: 178.0397, found 178.0399; $[\alpha]_D^{19.0}$ +0.79° (*c* 1.190, CH_2Cl_2, 91% ee).



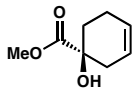
Methyl (*S*)-2-hydroxy-2-methyl-4-phenyl-4-pentanoate (Table 3, entry 6).[9,11] 77% yield. Colorless oil; R_f 0.52 (33% EtOAc in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36-7.24 (m, 5H), 5.34 (d, *J* = 1.5 Hz, 1H), 5.17 (s, 1H), 3.18 (s, 3H), 3.07 (d, *J* = 13.5 Hz, 2H), 2.80 (d, *J* = 13.5 Hz, 1H), 1.45 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.4, 144.1, 141.4, 128.3, 127.7, 126.9, 118.1, 74.3, 52.3, 46.4, 26.1; IR (Neat Film NaCl) 3514, 2981, 2952, 1736, 1626, 1494, 1447, 1269, 1214, 1129, 980, 906, 778, 709 cm^{-1}; HRMS (EI+) *m*/*z* calc'd for $C_{13}H_{16}O_3$ $[M]^+$: 220.1100, found 220.1108; $[\alpha]_D^{19.9}$ –4.09° (*c* 0.610, CH_2Cl_2, 94% ee).



(5*S*)-Hydroxy-5-methyl-hex-2-endioic acid dimethyl ester (Table 3, entry 7).[12] 51% yield. Colorless oil; R_f 0.44 (50% EtOAc in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.89 (dt, *J* = 15.6, 7.7 Hz, 1H), 5.89 (dt, *J* = 15.6, 1.5 Hz, 1H), 3.80 (s, 3H), 3.73 (s, 3H), 3.19 (s, 1H), 2.67-2.52 (m, 2H), 1.44 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.7, 166.6, 142.9, 124.9, 74.3, 53.3, 51.7, 42.8, 26.2; IR (Neat Film NaCl) 3485, 2955, 1725, 1659, 1438, 1336, 1271, 1198, 1179, 1123, 1059, 1038, 983 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_9H_{15}O_5$ $[M+H]^+$: 203.0919, found 203.0911; $[\alpha]_D^{20.2}$ –1.06° (*c* 0.220, CH_2Cl_2, 92% ee).

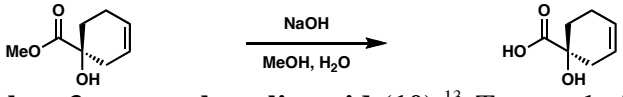


(*R*)-methyl 1-hydroxy-3-methylcyclopent-3-enecarboxylate (Table 3, entry 8). 48% yield. Colorless oil; R_f 0.52 (33% EtOAc in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.30-5.25 (m, 1H), 3.81 (s, 3H), 3.24 (s, 1H), 2.94-2.89 (m, 2H), 2.54-2.46 (m, 1H), 2.42 (d, *J* = 16.8 Hz, 1H), 1.76 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.6, 137.4, 121.1, 80.8, 53.1, 50.9, 47.5, 16.5; IR (Neat Film NaCl) 3469, 2916, 1735, 1437, 1285, 1211, 1090, 1018, 960, 901 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_8H_{12}O_3$ $[M]^+$: 156.0786, found 156.0786; $[\alpha]_D^{21.1}$ +2.51° (*c* 0.360, CH_2Cl_2, 86% ee).



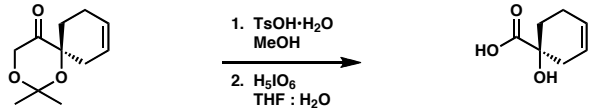
(1*S*)-Hydroxy-cyclohex-3-ene carboxylic acid methyl ester (Table 3, entry 9).[13] 61% yield. Colorless oil; R_f 0.56 (33% EtOAc in hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.86-5.74 (m, 1H), 5.70-5.58 (m, 1H), 3.80 (s, 1H), 2.98 (s, 1H), 2.65-2.54 (m, 1H), 2.40-2.24 (m, 1H), 2.17-2.05 (m, 2H), 2.00-1.89 (m, 1H), 1.84-1.71 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.5, 126.6, 123.0, 72.5, 53.0, 35.2, 30.9, 21.6; IR (Neat Film NaCl) 3471, 3029, 2954, 2915, 1732, 1437, 1278, 1258, 1223, 1096, 1058, 887 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_8H_{12}O_3$ $[M]^+$: 156.0786, found 156.0794; $[\alpha]_D^{20.9}$ +32.7° (*c* 0.660, CH_2Cl_2, 92% ee).

Synthesis of Hydroxyacid.



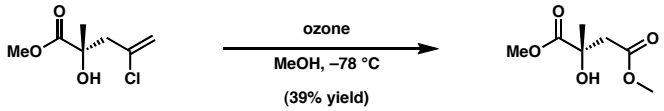
(1*S*)-Hydroxy-cyclohex-3-ene carboxylic acid (**10**).[13] To a solution of methyl ester (48.0 mg, 0.307 mmol, 1 equiv) in MeOH (3.0 mL, 0.1 M) was added 1N NaOH (0.37 mL, 0.37 mmol, 1.2 equiv) at room temperature (ca. 25 °C). After stirring for 18 h, the mixture was concentrated under reduced pressure. To the residue was added 1N HCl (1.0 mL) and the mixture was extracted with Et_2O (3 x 20 mL). The organic layer was washed with brine (5.0 mL), dried over Na_2SO_4, and concentrated under reduced pressure to give carboxylic acid **10** (41.5 mg, 95% yield, 92% ee) as a white solid: mp 79-81 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.88-5.79 (m, 1H), 5.72-5.61 (m, 1H), 2.79-2.62 (m, 1H), 2.37-2.11 (m, 4H), 1.95-1.80 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 181.5, 126.6, 122.6, 72.6, 34.9, 30.6, 21.4; IR (Neat Film NaCl) 3432, 3032, 2929, 2624, 1736, 1443, 1370, 1356,

1318, 1253, 1216, 1092, 1064, 982, 939, 886, 773, 746, 650, 736 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_8H_{12}O_3$ $[M]^+$: 143.0708, found 143.0708; $[\alpha]_D^{20.7}$ +31.7° (*c* 0.310, CH_2Cl_2, 92% ee).



(1*S*)-Hydroxy-cyclohex-3-ene carboxylic acid (10).[13] To a solution of acetonide **6d** (40 mg, 0.20 mmol, 1.0 equiv) in MeOH (4 mL, 0.05 M) was added *p*-toluenesulfonic acid monohydrate (3.9 mg, 0.02 mmol, 0.1 equiv) at room temperature (24 °C). After the mixture was stirred for 3 h, Et_3N (0.1 mL) was added. The mixture was concentrated under reduced pressure to give a yellow oil. The oil was diluted with EtOAc (10 mL), filtered through SiO_2 (1 mL), and concentrated under reduced pressure to furnish a white solid (35 mg). The solid was dissolved in THF (0.4 mL) and water (0.2 mL), and the colorless solution was cooled to 0 °C (ice water bath). H_5IO_6 (46 mg, 0.20 mmol, 1 equiv) was added to the solution. The mixture was allowed to warm to room temperature (26 °C) over 10 minutes, and then stirred for 2 h. The reaction was diluted with water (0.5 mL), and extracted with EtOAc (4 x 15 mL). Extracts were dried over Na_2SO_4 and concentrated under reduced pressure. The white solid was purified by column chromatography over silica gel (ca. 9 mL) with 2:1 Hexanes:EtOAc to give carboxylic acid **10** (16.3 mg, 56% yield, 92% ee) as a white solid.

Determination of Absolute Stereochemistry.

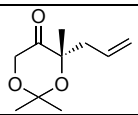
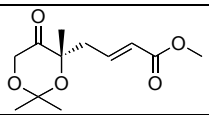
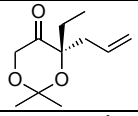
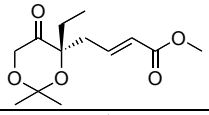
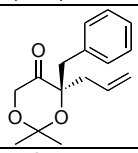
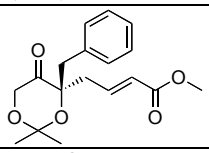
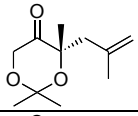
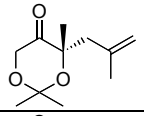
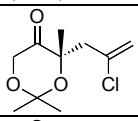
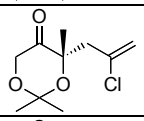
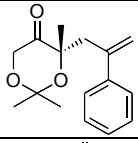
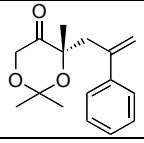
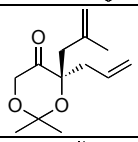
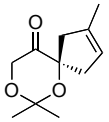
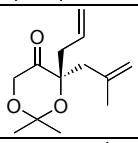
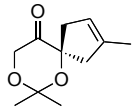
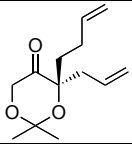
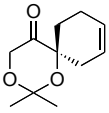
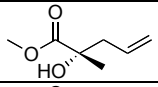
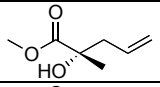
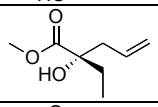
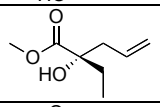
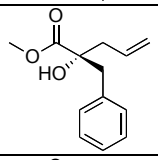
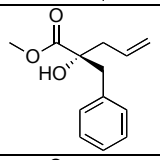
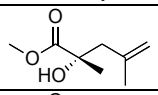
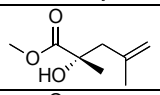
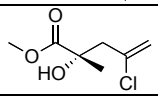
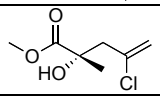


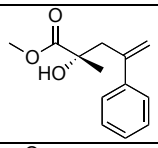
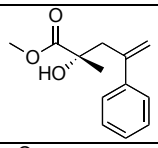
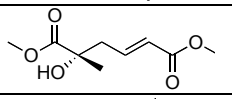
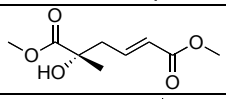
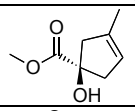
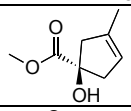
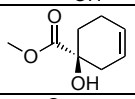
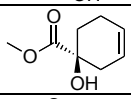
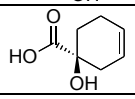
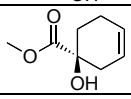
(*S*)-dimethyl citramalate (SI 6).[14] Ozone was bubbled through a colorless solution of alkene (25 mg, 0.14 mmol, 1 equiv) in MeOH (0.52 mL, 0.27 M) at –78 °C until the solution turned blue (50 minutes). The blue solution was flushed with nitrogen gas until it turned colorless, at which point it was treated with sodium sulfite (79 mg, 4.5 equiv). The mixture was allowed to warm to room temperature overnight (ca. 25 °C), at which point it was diluted with Et_2O (to 30 mL), filtered, and concentrated under vacuum to a colorless oil (9.7 mg, 39% yield). ^1H NMR (500 MHz, $CDCl_3$) δ 3.81 (s, 3H), 3.80 (s, 3H), 2.97 (d, *J*=16.5 Hz, 1H), 2.67 (d, *J*=16.5 Hz, 1H), 1.44 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.2, 171.7, 72.8, 53.2, 52.2, 44.2, 26.5; IR (Neat Film NaCl) 3500, 2988, 2957, 2851, 1740, 1439, 1356, 1292, 1207, 1120, 1012, 983 cm^{-1}; HRMS (EI+) *m/z* calc'd for $C_8H_{12}O_3$ $[M]^+$: 170.0763, found 170.0750; $[\alpha]_D^{23.6}$ +13.4° (*c* 0.485, $CHCl_3$).

Methods for the Determination of Enantiomeric Excess.

Table SI 3. Methods for determination of enantiomeric excess

Entry	Product	Compound assayed	Assay conditions	Retention Time of major isomer [min]	Retention Time of minor isomer [min]	*ee* [%]

1			HPLC Chiralcel OD-H 5% EtOH in hexanes isocratic, 1.0 mL/min	7.283	9.200	90
2			HPLC Chiralcel OD-H 5% EtOH in hexanes isocratic, 1.0 mL/min	6.332	7.197	93
3			HPLC Chiralcel OD-H 5% EtOH in hexanes isocratic, 1.0 mL/min	9.846	12.111	85
4			GC, G-TA 65 °C isotherm	71.824	67.568	89
5			GC, G-TA 100 °C isotherm	23.425	21.998	92
6			HPLC Chiralcel OD-H 1% IPA in hexanes isocratic, 1.0 mL/min	7.256	6.818	94
7			GC, G-TA 80 °C isotherm	69.974	62.451	85
8			GC, G-TA 80 °C isotherm	62.170	71.087	88
9			HPLC CHIRALPAK AD Hexanes (220nm) isocratic, 1.0 mL/min	11.462	10.307	92
9			GC, G-TA 100 °C isotherm	5.184	4.959	90
10			GC, G-TA 100 °C isotherm	6.314	6.128	93
11			GC, G-TA 110 °C isotherm	57.801	63.226	86
12			GC, G-TA 100 °C isotherm	6.321	6.064	89
13			GC, G-TA 100 °C isotherm	14.338	13.530	91

14			HPLC CHIRALPAK AD 3% EtOH in hexanes isocratic, 1.0 mL/min	10.652	9.773	94
15			GC, G-TA 100 °C isotherm	84.186	92.457	92
16			GC, G-TA 110 °C isotherm	8.300	10.900	86
17			GC, G-TA 85°C isotherm	59.568	58.072	92
18			GC, G-TA 85°C isotherm	59.995	58.135	92

References:

[1] a) M. Peer, J. C. de Jong, M.Kiefer, T. Langer, H. Rieck, H. Schell, P. Sennhenn, J. Sprinz, H. Steinhagen, B. Weise, G. Helmchen, *Tetrahedron* **1996**, *52*, 7547–7583; b) K. Tani, D. C. Behenna, R. M. McFadden, B. M. Stoltz, *Org. Lett.* **2007**, *9*, 2529–2531.

[2] D. C. Forbes, D. G. Ene, M. P. Doyle, *Synthesis* **1998**, *6*, 879–882.

[3] Previous preparations include: a) D. Enders, B. Bernhard, *Synthesis* **1989**, *7*, 493–496; b) D. Enders, C. Herriger, *Eur. J. Org. Chem.* **2007**, *7*, 1085–1090.

[4] Previous preparations include: a) D. Enders, M. Voith, *Synthesis* **2002**, *11*, 1571–1577; b) D. Enders, A. Muller-Huwen, *Eur. J. Org. Chem.* **2004**, *8*, 1732–1739.

[5] Previous preparations include: a) I. Ibrahem, A. Córdova, *Angew. Chem. Int. Ed.* **2006**, *45*, 1952–1956; b) D. Enders, M. Voith, S. J. Ince, *Synthesis* **2002**, *12*, 1775–1779.

[6] Previous preparations include: D. Enders, T. Hundertmark, R. Lazny, *Synth. Commun.* **1999**, *29*, 27–34.

[7] J. Eames, H. J. Mitchell, A. Nelson, P. O'Brien, S. Warren, P. Wyatt, *J. Chem. Soc. Perkin Trans. 1* **1999**, *8*, 1095–1104.

[8] Previous preparations of the racemate include: a) K. Uneyama, H. Matsuda, S. Torii, *Tetrahedron Lett.* **1984**, *25*, 6017–6020; b) I. Ojima, Y. Miyazawa, M. Kumagai, *J. Chem. Soc. Chem. Commun.* **1976**, 927–928.

[9] Previous enantioenriched preparations include: D. A. Evans, S. W. Tregay, C. S. Burgey, N. A. Paras, T. Vojkovsky, *J. Am. Chem. Soc.* **2000**, *122*, 7936–7943.

[10] Previous preparations of the racemate have been reported: O. Achmatowitz, P. Cieplak, J. Rozwadowski, *Pol. J. Chem.* **1989**, *63*, 531–539.

[11] Previous enantioenriched preparations include: M. Langner, P. Remy, C. Bolm, *Synlett* **2005**, *5*, 781–784.

[12] Previous preparations of the racemate have been reported: Y. Naruta, H. Uno, K. Maruyama, *Chem. Lett.* **1982**, 961–964.

[13] a) L. P. Rapado, V. Bulugahapitiya, P. Renauld, *Helv. Chim. Acta* **2000**, *83*, 1625-1623; b) J. Wolinsky, R. Novak, R. Vasilev, *J. Org. Chem.* **1964**, *29*, 3596-3598.

[14] J. E. Baldwin, R. M. Adlington, D. G. Marquess, A. R. Pitt, M. J. Porter, A. T. Russell, *Tetrahedron* **1996**, *52*, 2515–2536.