Supporting Information

Catalytic Enantioselective Alkylative Aldol Reaction: Efficient Multicomponent-Assembling of Dialkylzincs, Allenic Esters, and Ketones toward Highly Functionalized δ-Lactones with Tetrasubstituted Chiral Centers

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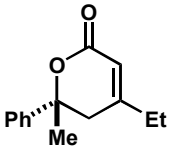
General: ^{1}H NMR spectra were recorded on a JEOL JNM-LA500 spectrometer, operating at 500 MHz for ^{1}H NMR and 125.65 MHz for ^{13}C NMR. Chemical shifts were reported downfield from TMS (δ = 0 ppm) for ^{1}H NMR. For ^{13}C NMR, chemical shifts were reported in the scale relative to the solvent used as an internal reference. Optical rotations were measured on a JASCO P-1010 polarimeter. Column chromatographies were performed with silica gel Merck 60 (230-400 mesh ASTM). The enantiomeric excess (ee) was determined by HPLC analysis. HPLC analysis was performed on JASCO HPLC systems consisting of the following: pump, 880-PU or PU-980; detector, 875-UV or UV-970, measured at 254 nm or 220 nm; mobile phase, hexane–2-propanol. In general, reactions were carried out in THF (freshly distilled from sodium benzophenone ketyl) under an argon atmosphere, unless noted otherwise. Ethyl 2,3-butadienoate (Aldrich) was distilled before use. MS4A powder (Nakalai tesque) was used after activation by heating gun under reduced press (5 mmHg). $Cu(OAc)_2$ (Wako Pure Chemical Industries, Ltd.), (*R*)-DIFLUORPHOS (Strem Chemicals, Inc.), dimethylzinc and diethylzinc (1.0 M in hexane; Kanto Chemical Co. Inc.), di(*n*-butyl)zinc (1.0 M in heptane ; Fluka), di(*i*-propyl)zinc (1.0 M in toluene; Aldrich) and Ph_2S=O (ACROS) were used as purchased. DMSO and HMPA were distilled over CaH_2 before use. Copper thiophen-2-carboxylate (CuTC) was prepared by following the literature procedure.[1]

Typical Procedure for Catalytic Enantiolselective Alkylative Aldol Reaction: A catalyst solution was generated from $Cu(OAc)_2$ (0.01 mmol, 5.0 mol%), (*R*)-DIFLUORPHOS (0.012 mmol, 6.0 mol%), a Lewis base additive (0.04 mmol, 20 mol%), and activated MS4A (40 mg, 200mg/mmol of **1**) in THF (0.25 mL) under stirring at room temperature for 10 min. Ethyl 2,3-butadienoate **2** (0.3 mmol, 1.5 equiv) and ketone **1** (0.2 mmol) were then added successively to the catalyst solution. Another 10 min later, dialkylzinc solution (**3**: 0.24 mmol, 1.2 equiv) was added slowly to the reaction mixture via syringe pump for 1.5 h at –20 °C. The mixture was allowed to stir for the indicated time. MeOH was added to quench the reaction then the generated precipitate was filtered off over celite pad. After evaporation of solvent, the NMR yield was determined by ^{1}H NMR analysis of the crude product with 1,1,2,2-tetrachloroethane as an internal standard. Purification by silica gel column chromatography (eluent: AcOEt/hexane) gave the analytically pure lactone **4**. Enantiomeric excess was determined by chiral HPLC analysis with 220 nm UV.

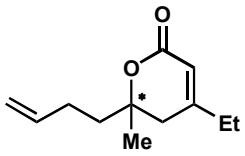
Characterization of Products:

(*R*)-4-Ethyl-6-methyl-6-phenyl-5,6-dihydropyran-2-one (4aa)



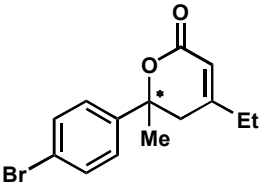
Colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.05 (t, J = 7.6 Hz, 3H), 1.70 (s, 3H), 2.15-2.25 (m, 2H), 2.73 (d, J = 17.7 Hz, 1H), 2.84 (d, J = 17.7 Hz, 1H), 5.76, (s, 1H), 7.23-7.30 (m, 1H), 7.31-7.40 (m ,4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ:10.49, 29.74, 30.04, 39.39, 82.31, 114.93, 124.27, 127.47, 128.49, 144.07, 160.24, 164.99; IR (neat, cm^{-1}): ν 865, 1140, 1262, 1712, 2975; MS (ESI) m/z 239 $(M+Na)^+$; HRMS (FAB) calcd for $C_{14}H_{17}O_2$ $(M+H)^+$ 217.1223. Found 217.1222; $[\alpha]_D^{25}$ = +2.5 (c = 0.53, $CHCl_3$) for 92% ee; HPLC condition: Chiralpak OJ-H column, flow rate: 0.5 mL / min, *n*-hexane / *i*-PrOH = 20 / 1, t = 34.3 min (*R*, major), 40.6 min (*S*, minor). λ = 220nm.

6-(3-Butenyl)-4-ethyl-6-methyl-5,6-dihydropyran-2-one (4ba)



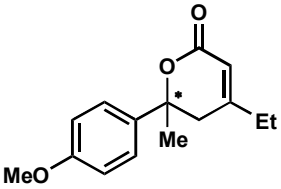
Colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.11 (t, J = 7.6 Hz, 3H), 1.38 (s. 3H), 1.68-1.77 (m, 1H), 1.79-1.88 (m, 1H), 2.10-2.26 (m, 5H), 2.44 (d, J = 18.0 Hz, 1H), 4.96 (dd, J = 1.2, 10.0 Hz, 1H), 5.02 (dd, J = 1.5, 17.0 Hz, 1H), 5.74-5.87 (m, 1H), 5.79 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ:10.66, 25.00, 27.90, 29.74, 37.91, 39.74, 81.06, 114.07, 114.97, 137.71, 160.07, 164.72; IR (neat, cm^{-1}): ν 1712, 2937, 2974, 3076; MS (ESI) m/z 217 $(M+Na)^+$, 411 $(2M+Na)^+$; HRMS (FAB) calcd for $C_{12}H_{19}O_2$ $(M+H)^+$ 195.1380. Found 195.1385; $[\alpha]_D^{25}$ = +16.8 (c = 0.49, $CHCl_3$) for 87% ee; HPLC condition: Chiralpak OJ-H column, flow rate: 1.0 mL / min, *n*-hexane / *i*-PrOH = 50 / 1, t = 15.9 min (minor), 19.2 min (minor). λ = 220nm.

6-(4-Bromophenyl)-4-ethyl-6-methyl-5,6-dihydropyran-2-one (4ca)



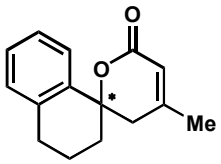
Pale yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.04 (t, J = 7.6 Hz, 3H), 1.66 (s, 3H), 2.11-2.26 (m, 2H), 2.71 (d, J = 17.4 Hz, 1H), 2.77 (d, J = 17.4 Hz, 1H), 5.75 (s, 1H), 7.24 (d, J = 8.3 Hz, 2H), 7.45 (d, J = 8.3 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 10.45, 29.71, 29.81, 39.24, 81.93, 114.84, 121.49, 126.10, 131.60, 143.24, 160.20, 164.55; IR (neat, cm^{-1}): ν 1714, 2934, 2974; MS (ESI) m/z 317 $(M+Na)^+$, 611 $(2M+Na)^+$; HRMS (FAB) calcd for $C_{14}H_{16}BrO_2$ $(M+H)^+$ 295.0328. Found 295.0322; $[\alpha]_D^{25}$ = +6.8 (c = 0.24, $CHCl_3$) for 90% ee; HPLC condition: Chiralpak OJ-H column, flow rate: 1 mL / min, *n*-hexane / *i*-PrOH = 20 / 1, t = 20.7 min (major), 25.2 min (minor). λ = 220nm.

4-Ethyl-6-(4-methoxyphenyl)-6-methyl-5,6-dihydropyran-2-one (4da)



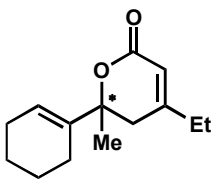
Colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.04 (dt, J = 0.6, 7.3 Hz, 3H), 1.68 (s, 3H), 2.19 (m, 2H), 2.70 (d, J = 17.7 Hz, 1H), 2.80 (d, J = 17.7 Hz, 1H), 3.77 (s, 1H), 5.74 (s, 1H), 6.84 (d, J = 8.3 Hz, 2H), 7.26 (d, J = 8.3 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 10.42, 29.67, 30.11, 39.31, 55.10, 82.18, 113.63, 114.69, 125.45, 136.09, 158.71, 160.37, 165.03; IR (neat, cm^{-1}): ν 1714, 2837, 2935, 2937; MS (ESI) m/z 269 $(M+Na)^+$, 515 $(2M+Na)^+$; HRMS (FAB) calcd for $C_{15}H_{19}O_3$ $(M+H)^+$ 247.1256. Found 247.1330; $[\alpha]_D^{25}$ = –13.6 (c = 0.71, $CHCl_3$) for 92% ee; HPLC condition: Chiralpak OJ-H column, flow rate: 0.5 mL / min, *n*-hexane / *i*-PrOH = 4 / 1, t = 20.9 min (major), 23.6 min (minor). λ = 220nm.

spirodihydropyranone (4ea)



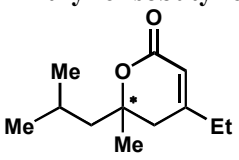
Pale yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.14 (t, J = 7.4 Hz, 3H), 1.65-1.80 (m, 1H), 1.93-2.05 (m, 1H), 2.06-2.15 (m, 1H), 2.18-2.32 (m, 3H), 2.52 (d, J = 17.7 Hz, 1H), 2.73-2.81 (m, 1H), 2.82-2.91 (m, 1H), 2.86 (d, J = 17.7 Hz, 1H), 5.90 (s, 1H), 7.05-7.12 (m, 1H), 7.17-7.25 (m, 2H), 7.48-7.56 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 10.63, 19.97, 29.15, 29.67, 33.11, 39.74, 81.41, 114.26, 126.32, 127.28, 127.95, 128.75, 136.80, 138.31, 159.87, 164.50; IR (neat, cm^{-1}): ν 1714, 2938, 3022, 3061; MS (ESI) m/z 243 $(M+H)^+$, 265 $(M+Na)^+$, 507 $(2M+Na)^+$; HRMS (FAB) calcd for $C_{16}H_{19}O_2$ $(M+H)^+$ 243.1380. Found 243.1379; $[\alpha]_D^{25}$ = +116.6 (c = 0.45, $CHCl_3$) for 90% ee; HPLC condition: Chiralpak AD-H column, flow rate: 1.0 mL / min, *n*-hexane / *i*-PrOH = 20 / 1, t = 20.2 min (major), 31.0 min (minor). λ = 220nm.

6-(1-Cyclohexenyl)-4-ethyl-6-methyl-5,6-dihydropyran-2-one (4fa)



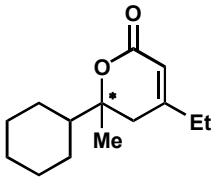
Colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.10 (t, J = 7.4 Hz, 3H), 1.47 (s, 3H), 1.42-1.68 (m, 4H),1.90-2.10 (m, 4H), 2.21 (q, J = 7.4 Hz, 2H), 2.36 (d, J = 18.0 Hz, 1H), 2.56 (d, J = 18.0 Hz, 1H), 5.69-5.74 (m, 1H), 5.76 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 10.71, 21.94, 22.79, 24.72, 24.97, 26.61, 29.67, 37.00, 83.19, 114.54, 122.28, 138.68, 160.10, 165.38; IR (neat, cm^{-1}): ν 1712, 2931; MS (ESI) m/z 221 $(M+H)^+$, 243 $(M+Na)^+$, 463 $(2M+Na)^+$; HRMS (FAB) calcd for $C_{14}H_{21}O_2$ $(M+H)^+$ 221.1536. Found 221.1533; $[\alpha]_D^{25}$ = –7.5(c = 0.20, $CHCl_3$) for 98% ee; HPLC condition: Chiralpak OJ-H column, flow rate: 0.5 mL / min, *n*-hexane / *i*-PrOH = 99 / 1, t = 48.7 min (major), 58.0 min (minor). λ = 220nm.

4-Ethyl-6-isobutyl-6-methyl-5,6-dihydro-pyran-2-one (4ga)



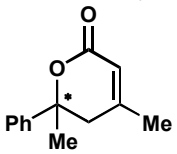
Colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ: 0.95 (dd, J = 0.9, 6.7 Hz, 3H), 0.98 (dd, J = 0.9, 6.7 Hz, 3H), 1.40 (s, 3H), 1.54 (dd, J = 6.0, 14.6 Hz, 1H), 1.67 (dd, J = 6.0, 14.6 Hz, 1H), 1.80-1.90 (m, 1H), 2.16-2.27 (m, 3H), 2.42 (d, J = 18.0 Hz, 1H), 5.78-5.81 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 10.65, 24.07, 24.38, 24.58, 25.50, 29.77, 38.69, 48.89, 81.80, 114.12, 160.07, 164.87; IR (neat, cm^{-1}): ν 1714, 2956; MS (ESI) m/z 219 $(M+Na)^+$, 415 $(2M+Na)^+$; HRMS (FAB) calcd for $C_{12}H_{21}O_2$ $(M+H)^+$ 197.1536. Found 197.1535; $[\alpha]_D^{25}$ = +14.0 (c = 0.19, $CHCl_3$) for 97% ee; HPLC condition: Chiralpak OJ-H column, flow rate: 0.5 mL / min, n-hexane / i-PrOH = 99 / 1, t = 16.6 min (major), 19.3 min (minor). λ = 220nm.

6-Cyclohexyl-4-ethyl-6-methyl-5,6-dihydropyran-2-one (4ha)



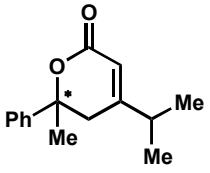
Colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ: 0.96-1.32 (m, 7H), 1.13 (t, J = 7.3 Hz, 3H), 1.30 (s, 3H), 1.59-1.72 (m, 2H), 1.75-1.85 (m, 3H), 1.87-1.95 (m, 1H), 2.08 (d, J = 17.7 Hz, 1H), 2.15-2.27 (m, 2H), 2.50 (d, J = 17.7 Hz, 1H), 5.80 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 10.73, 21.92, 26.36, 26.38, 26.40, 26.82, 27.48, 29.88, 35.75, 47.35, 83.86, 114.11, 160.15, 164.94; IR (neat, cm^{-1}): ν 1713, 2854, 2929; MS (ESI) m/z 245 $(M+Na)^+$, 467 $(2M+Na)^+$; HRMS (FAB) calcd for $C_{14}H_{23}O_2$ $(M+H)^+$ 223.1693. Found 223.1688; $[\alpha]_D^{25}$ = +30.1 (c = 0.25, $CHCl_3$) for 97% ee; HPLC condition: Chiralpak OJ-H column, flow rate: 1.0 mL / min, n-hexane / i-PrOH = 99 / 1, t = 17.2 min (major), 22.1 min (minor). λ = 220 nm.

4,6-Dimethyl-6-phenyl-5,6-dihydropyran-2-one (4ab)



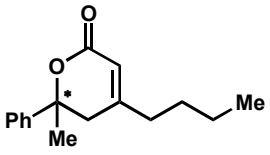
Colorless solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.70 (s, 3H), 1.92 (s, 3H), 2.74 (d, J = 17.7 Hz, 1H), 2.83 (d, J = 17.7 Hz, 1H), 5.78 (s, 1H), 7.23-7.30 (m, 1H), 7.31-7.40 (m, 4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 23.17, 30.13, 40.49. 82.41, 116.83, 124.22, 127.51, 128.53, 144.08, 155.27, 164.71; IR (neat, cm^{-1}): ν 848, 1141, 1261, 1445, 1708, 2979; MS (ESI) m/z 225 $(M+Na)^+$; HRMS (FAB) calcd for $C_{13}H_{15}O_2$ $(M+H)^+$ 203.1067. Found 203.1060; $[\alpha]_D^{25}$ = –6.0 (c = 0.64, $CHCl_3$) for 94% ee; HPLC condition: Chiralpak OJ-H column, flow rate: 1.0 mL / min, n-hexane / i-PrOH = 20 / 1, t = 22.9 min (major), 25.3 min (minor). λ = 220nm.

4-Isopropyl-6-methyl-6-phenyl-5,6-dihydropyran-2-one (4ac)



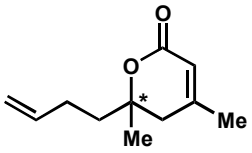
Colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.01 (d, J = 7.0 Hz, 3H), 1.02 (d, J = 7.0 Hz, 3H), 1.70 (s, 3H), 2.36 (qq, J = 7.0, 7.0 Hz, 1H), 2.71 (d, J = 17.7 Hz, 1H), 2.83 (d, J = 17.7 Hz, 1H), 5.76 (s, s1H), 7.23-7.28 (m, 1H), 7.30-7.39 (m, 4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 19.66, 19.82, 29.83, 34.56, 37.64, 82.34, 114.00, 124.30, 127.42, 128.42, 144.01, 163.89, 165.24; IR (neat, cm^{-1}): ν 1713, 2966; MS (ESI) m/z 253 $(M+Na)^+$, 483 $(2M+Na)^+$; HRMS (FAB) calcd for $C_{15}H_{19}O_2$ $(M+H)^+$ 231.1380. Found 231.1383; $[\alpha]_D^{25}$ = +21.9 (c = 0.25, $CHCl_3$) for 84% ee; HPLC condition: Chiralpak OJ-H column, flow rate: 1.0 mL / min, n-hexane / i-PrOH = 99 / 1, t = 31.1 min (major), 48.1 min (minor). λ = 220nm.

4-Butyl-6-methyl-6-phenyl-5,6-dihydropyran-2-one (4ad)



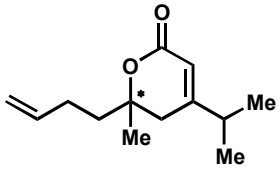
Pale yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ: 0.86 (t, J = 7.4 Hz, 3H), 1.12-1.30 (m, 2H), 1.34-1.48 (m, 2H), 1.70 (s, 3H), 2.16 (t, J = 7.5 Hz, 2H), 2.72 (d, J = 17.7 Hz, 1H), 2.82 (d, J = 17.7 Hz, 1H), 5.75 (s, 1H), 7.22-7.29 (m, 1H), 7.31-7.38 (m, 4H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 13.70, 22.05, 28.13, 30.06, 36.46, 39.40, 82.40, 115.90, 124.27, 127.45, 128.47, 144.10, 159.04, 164.92; IR (neat, cm^{-1}): ν 1714, 2871, 2931, 2957; MS (ESI) m/z 267 $(M+Na)^+$, 511 $(2M+Na)^+$; HRMS (FAB) calcd for $C_{16}H_{21}O_2$ $(M+H)^+$ 245.1536. Found 245.1539; $[\alpha]_D^{25}$ = +32.4 (c = 0.05, $CHCl_3$) for 92% ee; HPLC condition: Chiralpak OJ-H column, flow rate: 0.5 mL / min, n-hexane / i-PrOH = 99 / 1, t = 114.5 min (minor), 125.8 min (major). λ = 220nm.

6-(3-Butenyl)-4,6-dimethyl-5,6-dihydropyran-2-one (4bb)



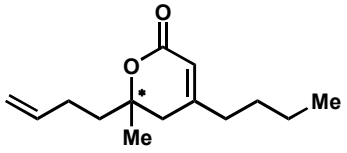
Colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.38 (s, 3H), 1.66-1.86 (m, 2H), 1.84 (s, 3H), 2.08-2.25 (m, 2H), 2.20 (d, J = 17.0 Hz, 1H), 2.43 (d, J = 17.0 Hz, 1H), 4.95 (dlike, J = 11.0 Hz, 1H), 5.02 (dlike, J = 18.0 Hz, 1H), 5.72-5.83 (m, 1H), 5.78 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 23.16, 25.09, 27.87, 39.15, 39.77, 81.06, 114.95, 115.91, 137.66, 155.03, 164.44; IR (neat, cm^{-1}): ν 1714, 2936, 2977, 3076; MS (ESI) m/z 203 $(M+Na)^+$, 383 $(2M+Na)^+$; HRMS (FAB) calcd for $C_{11}H_{17}O_2$ $(M+H)^+$ 181.1223. Found 181.1228; $[\alpha]_D^{25}$ = +15.6 (c = 0.56, $CHCl_3$) for 84% ee; HPLC condition: Chiralpak OJ-H column, flow rate: 0.75 mL / min, *n*-hexane / *i*-PrOH = 50 / 1, t = 31.7 min (major), 38.0 min (minor). λ = 220nm.

6-(3-Butenyl)-4-isopropyl-6-methyl-5,6-dihydropyran-2-one (4bc)



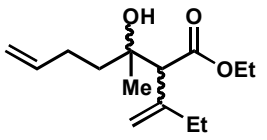
Colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.11 (d, J = 7.0 Hz, 6H), 1.58 (s, 3H), 1.70-1.79 (m, 1H), 1.80-1.88 (m, 1H), 2.11-2.26 (m, 2H), 2.23 (d, J = 17.6 Hz, 1H), 2.37-2.47 (m, 1H), 2.43 (d, J = 17.6 Hz, 1H), 4.97 (dd, J = 1.3, 10.0 Hz, 1H), 5.03 (dd, J = 1.3, 17.0 Hz, 1H), 5.75-5.85 (m, 1H), 5.80 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 19.86, 19.93, 24.83, 27.94, 34.61, 35.93, 39.67, 81.05, 113.21, 114.99, 137.73, 163.83, 164.99; IR (neat, cm^{-1}): ν 1713, 2966, 3076; MS (ESI) m/z 231 $(M+Na)^+$, 439 $(2M+Na)^+$; HRMS (FAB) calcd for $C_{13}H_{21}O_2$ $(M+H)^+$ 209.1536. Found 209.1540; $[\alpha]_D^{25}$ = +1.0 (c = 0.30, $CHCl_3$) for 76% ee; HPLC condition: Chiralpak OJ-H column, flow rate: 0.5 mL / min, *n*-hexane / *i*-PrOH = 99 / 1, t = 33.1 min (major), 40.7 min (minor). λ = 220nm.

6-(3-Butenyl)-4-butyl-6-methyl-5,6-dihydropyran-2-one (4bd)



Colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ: 0.92 (dt, J = 0.9, 7.6 Hz, 3H), 1.31-1.42 (m, 2H), 1.38 (s, 3H), 1.44-1.52 (m, 2H), 1.69-1.78 (m, 1H), 1.79-1.87 (m, 1H), 2.10-2.25 (m, 5H), 2.43 (d, J = 17.7 Hz, 1H), 4.97 (dt, J = 1.5, 10.5 Hz, 1H), 5.03 (dt, J = 1.5, 17.4 Hz, 1H), 5.74-5.84 (m, 1H), 5.76 (s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 13.75, 22.25, 25.04, 27.93, 28.41, 36.50, 37.88, 39.76, 81.08, 114.99, 137.72, 158.92, 164.67; IR (neat, cm^{-1}): ν 1714, 2872, 2932, 3076; MS (ESI) m/z 223 $(M+H)^+$, 245 $(M+Na)^+$, 467 $(2M+Na)^+$; HRMS (FAB) calcd for $C_{14}H_{23}O_2$ $(M+H)^+$ 223.1693. Found 223.1692; $[\alpha]_D^{25}$ = +24.8 (c = 0.18, $CHCl_3$) for 88% ee; HPLC condition: Chiralpak OJ-H column, flow rate: 0.5 mL / min, *n*-hexane / *i*-PrOH = 50 / 1, t = 27.3 min (major), 31.4 min (minor). λ = 220nm.

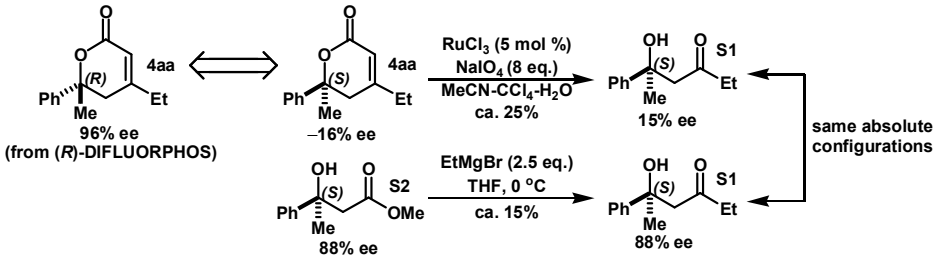
3-Hydroxy-3-methyl-2-(1-methylenepropyl)-hept-6-enoic acid ethyl ester (6) (underlined chemical shift for major isomer of diastereomixture)



Colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.03-1.08 (m, <u>3H</u>+3H), <u>1.10</u> (s, <u>3H</u>), 1.21-1.28 (m, <u>3H</u>+3H), 1.26 (s, 3H), 1.36-1.67 (m, <u>2H</u>+2H), 2.02-2.30 (m, <u>4H</u>+4H), <u>3.02</u> (s, <u>1H</u>), 3.05 (s, 1H), 3.83 (s, 1H), <u>3.89</u> (s, <u>1H</u>), 4.05-4.22 (m, <u>2H</u>+2H), 4.93 (dlike, J = 10.0 Hz, <u>1H</u>+1H), 5.02 (dlike, J = 17.3 Hz, <u>1H</u>+1H), 5.04 (s, <u>1H</u>+1H), 5.14 (s, <u>1H</u>+1H), 5.74-5.86 (m, <u>1H</u>+1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 12.18, 14.01, 23.30, 26.52, 27.89, 28.49, 29.27, 29.60, 38.13, 41.78, 58.80, 59.46, 60.80, 73.13, 73.30, 113.49, 114.11, 114.29, 114.37, 138.79, 138.80, 145.12, 174.60; IR (neat, cm^{-1}): ν 906, 1179, 1640, 1710, 2975, 3076, 3508; MS (ESI) m/z 263 $(M+Na)^+$; HPLC condition: Chiralpak AS-H–OJ-H sequential column, flow rate: 0.3 mL / min, *n*-hexane / *i*-PrOH = 1000 / 1, t = 45.5, 53.1 min (minor diastereomer), 50.6, 56.3 min (major diastereomer). λ = 220nm.

Determination of Absolute Configuration of 4aa:

Scheme S1.



Conversion from δ-lactone 4aa to β-hydroxyketone S1:

To a solution of lactone **4aa** (21 mg, 0.1 mmol, –16% ee) in $MeCN/CCl_4/H_2O$=2/2/3 (net. 0.5 mL) was added $NaIO_4$ (168mg, 0.8 mmol) and $RuCl_3$ hydrate (1mg, ca. 0.005 mmol), and then stirred at room temperature. After consumption of **4aa**, reaction mixture was filtered through short pad silica gel and the residues were washed with AcOEt thoroughly. The organic layers were combined and the solvents were evaporated under reduced pressure to afford crude mixture. Purification with preparative TLC (eluent: hexane/AcOEt) gave **S1** as a colorless oil (~5 mg, ~25% yield). Enantiomers were separable with chiral HPLC (see HPLC Chart S3).

Conversion from β-hydroxyester S2 to β-hydroxyketone S1:

A solution of β-hydroxyester (*S*)-**S2**[2] (13 mg, 0.068 mmol, 0% ee or 88% ee) in THF (0.3 mL) was cooled to 0 °C and EtMgBr (0.17 mL, 0.170 mmol, 1.0 M in THF, 2.5 equiv) was added dropwise. The resulting mixture was stirred for 1 h, and then silica gel was added to quench the reaction. Silica gel was filtered off and washed with AcOEt thoroughly. The organic layers were combined and the solvents were evaporated under reduced pressure to afforded crude mixture. Purification with preparative TLC (eluent: hexane/AcOEt) gave **S1** as an inseparable mixture with starting ester **S2** (estimated yield of **S1** was ca. 15%). These compounds were separable with chiral HPLC (see HPLC Chart S1 and S2)

Characterization of β-hydroxyketone S1:

Colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ: 0.92 (t, J = 7.3 Hz, 3H), 1.50 (s, 3H), 2.19-2.29 (m, 1H), 2.33-2.43 (m, 1H), 2.75 (d, J = 16.0 Hz, 1H), 3.13 (d, J = 16.0 Hz, 1H), 4.65 (s, 1H), 7.20 (dd, J = 7.3, 7.3 Hz, 1H), 7.30 (dd, J = 7.3, 7.6 Hz, 2H), 7.40 (d, J = 7.6 Hz, 2H); MS (ESI) m/z 215 $(M+Na)^+$; HPLC condition: Chiralpak AS-H column, flow rate: 0.5 mL / min, *n*-hexane / *i*-PrOH = 50 / 1, t = 33.0 min (*R*, minor), 34.9 mi n (*S*, major). λ = 254nm.

HPLC condition of **S2**: Chiralpak AS-H column, flow rate: 0.5 mL / min, *n*-hexane / *i*-PrOH = 50 / 1, t = 26.7 min (*R*, minor), 42.9 min (*S*, major). λ = 254nm.

HPLC analyses demonstrated that **4aa** used for conversion (–16% ee) was (*S*)-enantiomer. The absolute configuration of **4aa** produced from optimized conditions (96% ee) was determined to be (*R*) as shown in Scheme S1.

References

[1] Gallagher, W. P.; Maleczka, R. E., Jr. *J. Org. Chem.* **2003**, *68*, 6775-6779.

[2] Oisaki, K.; Zhao, D.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2006**, *128*, 7164-7165.