Supporting Information General Remarks

Pyruvic aldehyde (ca. 40 % in water), which was purchased from ACROS catalog number: 175791000 was used directly. All liquid aldehydes and solvents were distilled before use except pyruvic aldehyde. All reactions were monitored by thin-layer chromatography using Merck 60 F₂₅₄ precoated silica gel plates (0.25 mm thickness). Preparative thin layer chromatography was performed using Wakogel B-5F purchased from Wako Pure Chemical Industries, Tokyo, Japan. Flash chromatography was performed using silica gel 60N of Kanto Chemical Co. Int., Tokyo Japan. FT-IR spectra were recorded on a JASCO FT/IR-410 spectrometer. ¹H and ¹³C NMR spectra were recorded on a Bruker AM400 (400 MHz for ¹H NMR, 100 MHz for ¹³C NMR) instrument. Data for ¹H NMR are reported as chemical shift (δ ppm), integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant (Hz). Data for ¹³C NMR are reported as chemical shift. High-resolution mass spectral analyses (HRMS) were carried out using Bruker ESI-TOF MS. HPLC analysis was performed on a HITACHI Elite LaChrom Series HPLC, UV detection monitored at appropriate wavelength respectively, using CHIRALPAK AD-H (0.46 cm x 25 cm), CHIRALPAK IA (0.46 cm x 25 cm) and CHIRALPAK IC (0.46 cm x 25 cm).

Typical procedure of aldol / Wittig reaction (Table 2)

To pyruvic aldehyde (0.5 mmol, 75 µL, 40 wt% aqueous solution) in THF (0.50 mL, 1.0 M) were added (*S*)-2-[bis(3,5-bis-trifluoromethyl-phenyl)hydroxymethyl]pyrrolidine (26.3 mg, 0.05 mmol), and aldehyde (1.0 mmol). After stirring the reaction mixture for 12 hours at 23 °C. Wittig reagent (435 mg, 1.25 mmol) was added and reaction mixture was stirred for 2 hours at 23 °C. Upon completion, the Wittig reaction was quenched by passing through silica gel pad, and concentrated in vacuo. Purification by preparative thin layer chromatography (ethyl acetate : hexane = 1 : 6) gave corresponding α , β -unsaturated ester. The diastereomeric ratio was determined from crude NMR and is same after purification. After careful preparative thin layer chromatography, the *anti* and *syn* isomers were partially separated. The physical data were collected after the partial separation of major diastereomer (*anti* isomer) and these diastereomeric ratios are written in the following data. Enantiomeric excess of major diastereomer (*anti* isomer) was determined by HPLC equipped with chiral column. Racemic compound was obtained using (*S*)-2-[bis(3,5-bis-trifluoromethyl-phenyl)hydroxymethyl]pyrrolidine (13.2 mg, 0.025 mmol) and (*R*)-2-[bis(3,5-bis-trifluoromethyl-phenyl)hydroxymethyl]pyrrolidine (13.2 mg, 0.025 mmol) by following the identical procedure as described above.

(R,E)-ethyl 5-hydroxy-6-oxohept-2-enoate (table 2-entry 1)

60% yield; ¹H NMR (CDCl₃, 400 MHz): δ 1.28 (3H, t, J = 7.2 Hz), 2.23 (3H, s), 2.46-2.54 (1H, m), 2.77 (1H, ddq, J = 1.4, 7.6, 14.8 Hz), 4.18 (2H, q, J = 7.2 Hz), 4.32 (1H, dt, J = 4.8, 7.2 Hz), 5.94 (1H, dt, J = 1.4, 15.6 Hz), 6.90 (1H, dt, J = 7.6, 15.6 Hz); ¹³C NMR(CDCl₃, 100 MHz): 14.1, 25.4, 36.4, 60.6, 75.6, 124.9, 142.5, 166.3, 208.3; IR (neat): v_{max} 3446, 2924, 1717, 1655, 1369, 1269, 1165, 1096, 1041, 981, 668, 701 cm⁻¹; HRMS (ESI): [M+Na]⁺ calcd for [C₉H₁₄NaO₄]⁺: 209.0784, found: 209.0792; [α]_D¹⁷-19.5° (c = 0.81, CHCl₃); Enantiomeric excess of major diastereomer (*anti* isomer) was determined after 3,5-dinitrobenzoylation of Wittig product by HPLC with a CHIRALCEL OD-H column (^{*i*}PrOH : hexane = 1 : 40), 1 mL/min, major enantiomer $t_R = 37.5$ min, minor enantiomer $t_R = 56.4$ min.

(4R,5R,E)-ethyl 5-hydroxy-4-methyl-6-oxohept-2-enoate (table 2-entry 2)

As diastereomer mixture (*anti* : *syn* =11 : 1); 84% yield; ¹H NMR (CDCl₃, 400 MHz): δ 1.27 (3H, d, J = 6.8 Hz), 1.28 (3H, t, J = 7.2 Hz), 2.19 (3H, s), 2.84-2.91 (1H, m), 4.17 (2H, q, J = 7.2 Hz), 4.20 (1H, d, J = 6.8 Hz), 5.84 (1H, d, J = 15.6 Hz), 6.79 (1H, dd, J = 8.0, 15.6 Hz); ¹³C NMR (CDCl₃, 100 MHz): 14.6, 16.8, 25.8, 40.1, 60.7, 80.2, 122.9, 146.9, 166.1, 208.2; IR (neat): v_{max} 3467, 2979, 1716, 1654, 1459, 1369, 1276, 1181, 1035, 981 cm⁻¹; HRMS (ESI): [M+Na]⁺ calcd for [C₁₀H₁₆NaO₄]⁺: 223.0941, found: 223.0933; [α] $_{D}$ ¹⁷-26.2° (c = 0.57, CHCl₃); Enantiomeric excess of major diastereomer (*anti* isomer) was determined by HPLC with a CHIRALPAK IC column (^{*i*}PrOH : hexane = 1 : 30), 1 mL/min, minor enantiomer $t_{R} = 33.9$ min, major enantiomer $t_{R} = 46.0$ min.

(4R,5R,E)-ethyl 4-ethyl-5-hydroxy-6-oxohept-2-enoate (table 2-entry 4)

As diastereomer mixture (*anti* : *syn* = >20 : 1); 82% yield; ¹H NMR (CDCl₃, 400 MHz): δ 0.98 (3H, t, J = 7.2 Hz), 1.28 (3H, t, J = 7.2 Hz), 1.61-1.82 (2H, m), 2.18 (3H, s), 2.49-2.56 (1H, m), 4.16 (2H, q, J = 7.2 Hz), 4.28 (1H, d, J = 1.6 Hz), 5.80 (1H, d, J = 15.6 Hz), 6.69 (1H, dd, J = 9.6, 15.6 Hz); ¹³C NMR (CDCl₃, 100 MHz): δ 11.9, 14.2, 24.6, 25.4, 47.2, 60.5 78.7, 123.8, 145.5, 165.7, 208.1; IR (neat): v_{max} 3461, 2965, 1716, 1653, 1459, 1370, 1237, 1176, 1137, 1038, 990 cm⁻¹; HRMS (ESI): [M+Na]⁺ calcd for [C₁₁H₁₈NaO₄]⁺: 237.1097, found: 237.1089; [α] $_{0}$ ¹⁷-38.6° (c = 1.15, CHCl₃); Enantiomeric excess of major diastereomer (*anti* isomer) was determined by HPLC with a CHIRALPAK AD-H column (^{*i*}PrOH : hexane =1 :30), 1mL/min, major enantiomer *t*_R =26.1 min., minor enantiomer *t*_R =32.7 min.

(4R,5R,E)-ethyl 5-hydroxy-6-oxo-4-propylhept-2-enoate (table 2-entry 5)

As diastereomer mixture (*anti* : *syn* = 14 : 1); 80% yield; ¹H NMR (CDCl₃, 400 MHz): δ 0.94 (3H, t, *J* = 7.2 Hz), 1.27 (3H, t, *J* = 7.2 Hz), 1.33-1.39 (2H, m), 1.61-1.68 (2H, m), 2.18 (3H, s), 2.61-2.67 (1H, m), 4.17 (2H, q, *J* = 7.2 Hz), 4.25 (1H, dd, *J* = 2.4, 4.4 Hz), 5.79 (1H, d, *J* = 16.0 Hz), 6.70 (1H, dd, *J* = 9.6, 16.0 Hz); ¹³C NMR (CDCl₃, 100 MHz): 13.7, 14.0, 20.3, 25.3, 33.4, 45.1. 60.3, 78.9, 123.4, 145.5, 165.6, 207.9; IR(neat): v_{max} 3457, 2959, 1717, 1654, 1370, 1279, 1176, 1138, 1039, 990 cm⁻¹; HRMS (ESI): [M+Na]⁺ calcd for [C₁₂H₂₀O₄Na]⁺: 251.1254, found: 251.1257 ; [*α*]_D¹⁷ -81.1° (c = 1.02, CHCl₃); Enantiomeric excess was of major diastereomer (*anti* isomer) determined after 3,5-dinitrobenzoylation of Wittig product by HPLC with a CHIRALPAK IA column (^{*i*}PrOH : hexane = 1 : 50), 1 mL/min, major enantiomer *t*_R = 41.4 min, minor enantiomer *t*_R = 74.8 min.

(4R,5R,E)-ethyl 5-hydroxy-4-isopropyl-6-oxohept-2-enoate (table 2-entry 6)

As diastereomer mixture (*anti* : *syn* = >20 : 1); 96% yield; ¹H NMR (CDCl₃, 400 MHz): δ 0.91 (3H, d, *J* = 6.8 Hz), 1.11 (3H, d, *J* = 6.8 Hz), 1.27 (3H, t, *J* = 7.2 Hz), 1.97-2.07 (1H, m), 2.07-2.21 (1H, m), 2.15 (3H, s), 4.15 (2H, q, *J* = 7.2 Hz), 4.42 (1H, dd, *J* = 2.0, 4.4 Hz), 5.75 (1H, d, *J* = 16.0 Hz), 6.71 (1H, dd, *J* = 10.4, 16.0 Hz); ¹³C NMR (CDCl₃, 100 MHz): δ 14.1, 20.5, 21.2, 25.1, 28.6, 52.6, 60.4, 77.4, 123.9, 145.4, 165.5, 208.4; IR (neat): v_{max} 3457, 2961, 1716, 1369, 1278, 1177, 1140, 1086, 1037, 994, 750 cm⁻¹; HRMS (ESI): [M+Na]⁺ calcd for [C₁₂H₂₀O₄Na]⁺: 251.1254, found: 251.1259; [α] $_{D}^{17}$ -89.9° (c = 0.79, CHCl₃); Enantiomeric excess of major diastereomer (*anti* isomer) was determined by HPLC with a CHIRALPAK IC column (ⁱPrOH : hexane = 1 : 30), 1 mL/min, minor enantiomer *t*_R = 23.0 min, major enantiomer *t*_R = 45.0 min.

(4R,5R,E)-ethyl 4-benzyl-5-hydroxy-6-oxohept-2-enoate (table 2-entry 7)

O Bn CO2Et

As diastereomer mixture (*anti* : *syn* = >20 : 1); 79% yield; ¹H NMR (CDCl₃, 400 MHz): δ 1.27 (3H, t, *J* = 7.2 Hz), 2.09 (3H, s), 2.84-2.92 (2H, m), 3.04 (1H, dt, *J* = 4.0, 11.0 Hz), 4.09 (1H, s), 4.16 (2H, q, *J* = 7.2 Hz), 5.78 (1H, d, *J* = 15.8 Hz), 6.79 (1H, dd, *J* = 9.0, 15.8 Hz), 7.22-7.34 (5H, m); ¹³C NMR (CDCl₃, 100 MHz): δ 14.1, 25.4, 37.8, 47.4, 60.3, 77.0, 123.7, 126.7, 128.7, 129.4, 138.0, 145.2, 165.3, 208.0, ; IR (neat): v_{max} 3448, 1717, 1653, 1496, 1455, 1369, 1313, 1281, 1239, 1177, 1108, 1033, 989, 872, 740, 702, 683, 418 cm⁻¹; HRMS (ESI): [M+Na]⁺ calcd for [C₁₆H₂₀O₄Na]⁺: 299.1254, found: 299.1279; [α]p²²-97.1° (c = 0.52, CHCl₃); Enantiomeric excess of major diastereomer (*anti* isomer) was determined by HPLC with a CHIRALPAK AD-H column (^{*i*}PrOH : hexane = 1 : 30), 1 mL/min, major enantiomer *t*_R = 16.1 min, minor enantiomer *t*_R = 23.2 min.

(4R,5R,E)-ethyl 4-benzyloxy-5-hydroxy-6-oxohept-2-enoate (table 2-entry 8)

CO₂Et

Tri-n-butyl(carbethoxymethylidene)phosphorane was employed as a Wittig reagent instead of Tri-phenyl (carbethoxymethylidene)phosphorane.

As diastereomer mixture (*anti* : *syn* = 2.8 : 1) ; 78% yield; ¹H NMR (CDCl₃, 400 MHz): δ 1.31 (3H, t, *J* = 7.2 Hz), 2.23 (3H, s), 4.19-4.25 (3H, m), 4.31 (1H, d, *J* = 4.8 Hz), 4.46 (1H, d, *J* = 12.0 Hz), 4.65 (1H, d, *J* = 12.0 Hz), 6.13 (1H, d, *J* = 16.0 Hz), 6.94 (1H, dd, *J* = 6.0, 16.0 Hz), 7.28-7.36 (5H, m); ¹³C NMR (CDCl₃, 100 MHz): δ 14.2, 27.8, 60.7, 72.1, 78.9, 79.8, 124.5, 127.8, 128.0 128.5, 136.9, 143.3, 165.5, 207.3 ; IR (neat): v_{max} 3448, 2985, 2924, 1712, 1365, 1273, 1180, 1095, 1034, 987, 741, 702 cm⁻¹; HRMS (ESI): [M+Na]⁺ calcd for [C₁₆H₂₀NaO₅]⁺: 315.1203, found: 315.1199; Enantiomeric excess of major diastereomer (*anti* isomer) was determined by HPLC with a CHIRALCEL OD-H column (^{*i*}PrOH : hexane = 1 : 50), 1 mL/min, minor enantiomer *t*_R = 35.4 min, major enantiomer *t*_R = 43.0 min.

(4S,5R,E)-ethyl 5-hydroxy-4-((4-methoxybenzyloxy)methyl)-6-oxohept-2-enoate (table 2-entry 9)



As diastereomer mixture (*anti* : *syn* = 7.5 : 1); 76% yield; ¹H NMR (CDCl₃, 400 MHz): δ 1.27 (3H, t, *J* = 7.2 Hz), 2.17 (3H, s), 2.95-3.01 (1H, m), 3.56 (1H, dd, *J* = 5.6, 8.8 Hz), 3.72 (1H, dd, *J* = 8.4 Hz), 3.81 (3H, s), 4.16 (2H, q, *J* = 7.2 Hz), 4.48 (2H, dd, *J* = 11.6, 22.4 Hz), 5.88 (1H, d, *J* = 15.6 Hz), 6.72 (1H, dd, *J* = 9.0, 15.6 Hz), 7.29-7.41 (5H, m); ¹³C NMR (CDCl₃, 100 MHz): δ 14.2, 25.6, 45.6, 55.3, 60.5, 69.2, 73.2, 76.5, 113.8, 124.9, 129.4, 129.8, 142.1, 159.4, 165.6, 208.5; IR (neat): v_{max} 3456, 2931, 1712, 1511, 1365, 1250, 1180, 1095, 1034, 818 cm⁻¹; [α]p²²-41.7° (c = 0.83, CHCl₃); HRMS (ESI): [M+Na]⁺ calcd for [C₁₈H₂₄NaO₆]⁺: 359.1465, found: 359.1465; Enantiomeric excess of major diastereomer (*anti* isomer) was determined by HPLC with a CHIRALPAK AS-H column (^{*i*}PrOH : hexane = 1 : 10), 1 mL/min, minor enantiomer *t*_R = 12.6 min, major enantiomer *t*_R = 18.1 min.

(R,E)-ethyl 4-((R)-1-hydroxy-2-oxopropyl)-7-phenylhept-2-en-6-ynoate (table 2-entry 10)



As diastereomer mixture (*anti* : *syn* = 14 : 1); 65% yield; ¹H NMR (CDCl₃, 400 MHz): δ 1.28 (3H, t, J = 7.2 Hz), 2.23 (3H, s), 2.68 (1H, dd, J = 6.0, 16.4 Hz), 2.88 (1H, dd, J = 8.8, 16.4 Hz), 2.95-3.02 (1H, m), 4.18 (2H, q, J = 7.2 Hz), 4.58 (1H, dd, J = 2.4, 4.4 Hz), 5.92 (1H, d, J = 15.6 Hz), 6.73 (1H, dd, J = 9.0, 15.6 Hz), 7.29-7.41 (5H, m); ¹³C NMR (CDCl₃, 100 MHz): δ 14.4, 22.4, 25.5, 45.0, 60.7, 77.7, 83.3, 86.4, 124.6, 128.1, 128.3, 131.7, 143.4, 165.5, 207.8; IR (neat): v_{max} 3460, 2924, 1717, 1654, 1491, 1370, 1280, 1173, 1032, 981, 758, 692 cm⁻¹; $[\alpha]_D^{18}$ -63.8° (c = 0.85, CHCl₃); HRMS (ESI): [M+Na]⁺ calcd for [C₁₈H₂₀NaO₄]⁺: 323.1254, found: 323.1262; Enantiomeric excess of major diastereomer (*anti* isomer) was determined by HPLC with a CHIRALPAK IC column (^{*i*}PrOH : hexane = 1 : 30), 1 mL/min, minor enantiomer $t_R = 33.7$ min, major enantiomer $t_R = 41.8$ min.

(R,2E,7Z)-ethyl 4-((R)-1-hydroxy-2-oxopropyl)deca-2,7-dienoate (table 2-entry 11)

CO₂Et

As diastereomer mixture (*anti* : *syn* = 11 : 1); 92% yield; ¹H NMR (CDCl₃, 400 MHz): δ 0.96 (3H, t, *J* = 7.2 Hz), 1.27 (3H, t, *J* = 7.2 Hz), 1.67-1.82 (2H, m), 1.98-2.12 (4H, m), 2.17 (3H, s), 2.64-2.69 (1H, m), 4.16 (2H, q, *J* = 7.2 Hz), 4.24 (1H, dd, *J* = 2.0, 4.4 Hz), 5.27-5.46 (2H, m), 5.79 (1H, d, *J* = 16.0 Hz), 6.70 (1H, dd, *J* = 9.6, 16.0 Hz); ¹³C NMR (CDCl₃, 100 MHz): δ 14.1, 14.3, 20.6, 24.5, 25.3, 31.3, 44.6, 60.4, 78.8, 123.7, 127.5, 132.9, 145.3, 165.6, 207.9; IR (neat): v_{max} 3446, 2933, 1718, 1450, 1370, 1280, 1162, 1095, 1038, 668 cm⁻¹; HRMS (ESI): [M+Na]⁺ calcd for [C₁₅H₂₄O₄Na]⁺: 291.1567, found: 291.1566; [α]p¹⁶-31.7° (c = 0.47, CHCl₃); Enantiomeric excess of major diastereomer (*anti* isomer) was determined after 3,5-dinitrobenzoylation of Wittig product by HPLC with a CHIRALPAK AD-H column (^{*i*}PrOH : hexane = 1 : 30), 1 mL/min, major enantiomer *t*_R = 20.5 min, minor enantiomer *t*_R = 24.9 min.

(4R,5R,E)-ethyl 5-hydroxy- 4-methyl -6-oxooct-2-enoate (table 2-entry 13)

2-oxo-butanal was prepared according to procedure A. This aldehyde was used for reaction as 17wt% aqueous solution.

As diastereomer mixture (*anti* : *syn* = >20 : 1); 80% yield; ¹H NMR (CDCl₃, 400 MHz): δ 1.10 (3H, t, *J* = 7.2 Hz), 1.25 (3H, d, *J* = 7.2 Hz), 1.27 (3H, t, *J* = 7.2 Hz), 2.45 (2H, q, *J* = 7.2 Hz), 2.82-2.89 (1H, m), 4.16 (2H, q, *J* = 7.2 Hz), 4.19 (1H, d, *J* = 4.0 Hz), 5.81 (1H, d, *J* = 16.0 Hz), 6.78 (1H, dd, *J* = 8.0, 16.0 Hz); ¹³C NMR (CDCl₃, 100 MHz): δ 7.3, 14.1, 16.6, 31.7, 40.0, 60.4, 79.4, 122.6, 146.7, 165.9, 210.8; IR (neat): v_{max} 3464, 2978, 2939, 2360, 1712, 1651, 1458, 1373, 1273, 1180, 1142, 1103, 1034 cm⁻¹; [α] σ ²³ -69.3° (c = 0.75, CHCl₃); HRMS (ESI): [M+Na]⁺ calcd for [C₁₁H₁₈NaO₄]⁺: 237.1089, found: 237.1097; Enantiomeric excess of major diastereomer (*anti* isomer) was determined by HPLC with a CHIRALPAK IC column (^{*i*}PrOH : hexane = 1 : 10), 1 mL/min, minor enantiomer *t*_R = 10.4 min, major enantiomer *t*_R = 13.7 min.

(4R,5R,E)-ethyl 6-cyclohexyl-5-hydroxy-4-methyl-6-oxohex-2-enoate(table 2-entry 15)

OH O Me CO₂Et

2-cyclohexyl-2-oxoacetaldehyde was prepared according to procedure B. This aldehyde was used for reaction with 12.2 eq. H_2O (table 2-entry14) or 6.1 eq. H_2O (table 2-entry15).

As diastereomer mixture (*anti* : *syn* = 20 : 1); 86% yield; ¹H NMR (CDCl₃, 400 MHz): δ 1.26-1.30 (8H, m), 1.45-1.84 (8H, m), 2.49-2.55 (1H, m), 2.85-2.92 (1H, m), 4.17 (2H, q, *J* = 7.2 Hz), 4.32 (1H, d, *J* = 2.4 Hz), 5.80 (1H, d, *J* = 16.0 Hz), 6.78 (1H, dd, *J* = 8.0, 16.0 Hz); ¹³C NMR (CDCl₃, 100 MHz): δ 14.2, 16.9, 25.0, 25.6, 25.9, 26.9, 30.1, 39.8, 46.5, 60.4, 70.8, 122.7, 146.9, 165.9, 213.4; IR (neat): v_{max} 3456, 2931, 2854, 1712, 1651, 1450, 1373, 1304, 1273, 1180, 1034, 1003 cm⁻¹; [α]_D²³-50.8° (c = 0.50, CHCl₃);

HRMS (ESI): $[M+Na]^+$ calcd for $[C_{15}H_{24}NaO_4]^+$: 291.1567, found: 291.1565; Enantiomeric excess of major diastereomer (*anti* isomer) was determined by HPLC with a CHIRALPAK IA column (^{*i*}PrOH : hexane = 1 : 30), 1 mL/min, minor enantiomer $t_R = 11.3$ min, major enantiomer $t_R = 13.5$ min.

(4R,5R,E)-ethyl 5-hydroxy-4-methyl-6-oxododec-2-enoate(table 2-entry 17)

2-oxo-octanal was prepared as per the literature procedure ^{a)}. This aldehyde was used for reaction with 12.2 eq. H_2O (table 2-entry16) or 6.1 eq. H_2O (table 2-entry17).

As diastereomer mixture (*anti* : *syn* = 20 : 1); 74% yield; ¹H NMR (CDCl₃, 400 MHz): δ 0.87 (3H, t, *J* = 7.2 Hz), 1.24-1.28 (12H, m), 1.56-1.61 (2H, m), 2.41 (2H, t, *J* = 7.2 Hz), 2.81-2.88 (1H, m), 4.13-4.18 (3H, m), 5.80 (1H, d, *J* = 16.0 Hz), 6.77 (1H, dd, *J* = 8.0, 16.0 Hz); ¹³C NMR (CDCl₃, 100 MHz): δ 13.9, 14.1, 16.7, 22.3, 23.3, 28.8, 31.4, 38.4, 39.9, 60.3, 79.5, 122.7, 146.7, 165.8, 210.4; IR (neat): v_{max} 3448, 2931, 1712, 1651, 1458, 1373, 1273, 1180, 1034, 872, 725 cm⁻¹; [α] $_{D}^{22}$ -31.3° (c = 0.69, CHCl₃); HRMS (ESI): [M+Na]⁺ calcd for [C₁₅H₂₆NaO₄]⁺: 293.1723, found: 293.1726; Enantiomeric excess of major diastereomer (*anti* isomer) was determined by HPLC with a CHIRALPAK IC column (^{*i*}PrOH : hexane = 1 : 30), 1 mL/min, minor enantiomer *t*_R = 19.4 min, major enantiomer *t*_R = 27.6 min.

Procedure A; Preparation of 2-oxo-butanal

This is a modified procedure by Rosowsky, A. et. al.^{a)} and Russell, G. A. et. al.^{b)}.

To ethyl propionate (6.74 ml, 0.0587 mol) in DMSO (58.7 mL, 1 M) was added NaH (5.23 g, 0.117 mol) at 23 °C. After the reaction mixture was heated for 2 hours at 75 °C, the reaction was quenched by addition of ice water. After diethyl ether extraction to remove unreacted ester, the aqueous phase was cooled and acidified to pH 2 with 12 N HCl. The organic materials were extracted five times with chloroform, washed with water and brine, dried over anhydrous Na₂SO₄, and concentrated in vacuo.

The residue was dissolved in DMSO (22.5 mL, 2.6 M) and treated with 1.4 N HCl (196 mL, 0.3 M) at 23 °C. After stirring the reaction mixture for 24 hours at 23 °C, the organic materials were extracted three times with diethyl ether, washed with 5% aqueous NaHCO₃ solution and water, dried over anhydrous Na₂SO₄, and concentrated in vacuo.

The residue was dissolved in CH_2Cl_2 (29.4 mL, 2.0 M) and added $Cu(OAc)_2$ (5.88 g, 0.0294 mol) at 23 °C. After stirring the reaction mixture for 1 hour at 23 °C, it was filtered and then quenched by small portion of saturated aqueous NaHCO₃ solution. After evaporation of organic layer, extraction with water (5 mL) from organic materials gave 2-ethyl-2-oxoacetaldehyde as a 17wt% aqueous solution.

Procedure B; Preparation of 2-cyclohexyl-2-oxo-acetaldehyde

This is a modified procedure by Rosowsky, A. et. al.^{a)} and Russell, G. A. et. al.^{b)}.

To methyl cyclohexanecarboxylate (10.2 mL, 0.07 mol) in DMSO (70.4 mL, 1 M) was added NaH (6.27

g, 0.14 mol) at 23 °C. After the reaction mixture was heated for 2 hours at 75 °C, the reaction was quenched by addition of ice water. After diethyl ether extraction to remove unreacted ester, the aqueous phase was cooled and acidified to pH 2 with 12 N HCl. The organic materials were extracted five times with chloroform, washed with water and brine, dried over anhydrous Na_2SO_4 , and concentrated in vacuo.

The residue was dissolved in DMSO (26.9 mL, 2.6 M) and treated with 1.4 N HCl (233 mL, 0.3 M) at 23 °C. After stirring the reaction mixture for 24 hours at 23 °C, the organic materials were extracted three times with diethyl ether, washed with 5% aqueous NaHCO₃ solution and water, dried over anhydrous Na₂SO₄, and concentrated in vacuo.

The residue was dissolved in CH_2Cl_2 (35.0 mL, 2.0M) and added $Cu(OAc)_2$ (6.99 g, 0.035 mol) at 23 °C. After stirring the reaction mixture for 1 hour at 23 °C, it was filtered and then quenched by small portion of saturated aqueous NaHCO₃ solution. After evaporation of organic layer, The residue is distilled under reduced pressure to give 2-cyclohexyl-2-oxoacetaldehyde as a yellow oil.

(4R,5R,6S,E)-ethyl 5,6-dihydroxy-4-methylhept-2-enoate (Eq. 3)

OH OH Me

To (4R,5R,E)-ethyl 5-hydroxy-4-methyl-6-oxohept-2-enoate (34.6 mg, 0.17 mmol) as diastereomer mixture (*anti* : *syn* = 10 : 1) in THF (0.7 mL, 0.25 M) was added Zn(BH₄)₂ (1.5 ml, 0.5 M in THF) at 0 °C. After stirring the reaction mixture for 30 min at 0 °C, it was quenched by addition of water and then 10% HCl. The organic materials were extracted four times with chloroform, washed with saturated aqueous NaHCO₃ solution and brine, dried over anhydrous MgSO₄, and concentrated in vacuo after filtration. Purification by column chromatography (ethyl acetate : hexane = 1 : 2) gave (4*R*,5*R*,6*S*,*E*)-ethyl 5,6-dihydroxy-4-methylhept-2-enoate in 80% yield with dr = 10 : 1.

As diastereomer mixture (dr = 10 : 1); ¹H NMR (CDCl₃, 400 MHz): δ 1.08 (3H, d, J = 6.8 Hz), 1.21 (3H, d, J = 6.4 Hz), 1.29 (3H, t, J = 7.2 Hz), 2.43-2.54 (1H, m), 3.48 (1H, dd, J = 4.8, 6.8 Hz), 3.85 (1H, dd, J = 4.8, 6.0 Hz), 4.19 (2H, q, J = 7.2 Hz), 5.85 (1H, d, J = 16.0 Hz), 6.97 (1H, dd, J = 8.0, 16.0 Hz); ¹³C NMR (CDCl₃, 100MHz): δ 14.2, 16.0, 17.1, 38.9, 60.4, 68.4, 77.7, 122.0, 150.5, 166.7 ; IR(neat): v_{max} 3417, 2970, 1705, 1651, 1458, 1373, 1281, 1188, 1041, 995, 771 cm⁻¹; HRMS (ESI): [M+Na]⁺ calcd for [C₁₀H₁₈NaO₄]⁺: 225.1097, found: 225.1088; [α]p²⁴ +10.5° (c = 0.44, CHCl₃).

(R,E)-ethyl 4-((4R,5S)-2,2,5-trimethyl-1,3-dioxolan-4-yl)pent-2-enoate

Determination of relative configuration of anti-reduction product.

-0 ← CO₂Et



(4R,5R,6S,E)-ethyl 5,6-dihydroxy-4-methylhept-2-enoate (22.4 mg, 0.11 mmol) as diastereomer mixture (*anti* : *syn* = 10 : 1) was dissolved in CH₂Cl₂ (440 µL, 0.25 M) and treated with 2,2-dimethoxy-propane (16 µL, 0.13 mmol) and *p*-toluenesulfonic acid (2.1 mg, 0.011 mmol) at 23 °C. After stirring the reaction mixture for 30 min at 23 °C, it was quenched by addition of 5% aqueous NaHCO₃ solution. The organic materials were extracted three times with ethyl acetate, washed with brine, dried over unhydrous Na₂SO₄, and concentrated in vacuo. Purification by column chromatography (ethyl acetate : hexane = 1 : 4) gave (*R*,*E*)-ethyl 4-((4*R*,5*S*)-2,2,5-trimethyl-1,3-dioxolan-4-yl)pent-2-enoate in 89% yield with *anti* : *syn* = 10 : 1.

As single diastereomer; ¹H NMR (CDCl₃, 400 MHz): δ 1.03 (3H, d, J = 6.8 Hz), 1.17 (3H, d, J = 6.4 Hz), 1.28 (3H, t, J = 7.2 Hz), 1.30 (3H, s), 1.42 (3H, s), 2.49 (1H, ddq, J = 6.8, 7.2, 8.4 Hz), 3.86 (1H, dd, J = 5.6, 8.4 Hz), 4.17 (2H, q, J = 7.2 Hz), 4.25 (1H, dq, J = 5.6, 6.4 Hz), 5.85 (1H, d, J = 16.0 Hz), 7.02 (1H, dd, J = 7.2, 16.0 Hz); ¹³C NMR (CDCl₃, 100MHz): δ 13.9, 15.5, 16.1, 25.6, 28.0, 35.9, 59.9, 73.3, 80.6, 107.6, 120.7, 150.6, 166.4 ;IR(neat): v_{max} 2985, 1720, 1651, 1458, 1373, 1250, 1180, 1065, 987, 856, 517 cm⁻¹; HRMS (ESI): [M+Na]⁺ calcd for [C₁₃H₂₂NaO₄]⁺: 265.1410, found: 265.1417; [α] $_{D}^{24}$ +15.8° (c = 1.03, CHCl₃).

(4R,5R,E)-ethyl 4-methyl-6-oxo-5-(triisopropylsilyloxy)hept-2-enoate

O Me

To (4R,5R,E)-ethyl 5-hydroxy-4-methyl-6-oxohept-2-enoate (261 mg, 1.31 mmol) as a diastereo mixture (*anti* : *syn* = 10 : 1) in CH₂Cl₂ (2.6 ml, 0.5 M) were added TIPSOTf (0.52 ml, 1.96 mmol) and 2,6-lutidine (0.38 ml, 3.26 mmol) at 0 °C. After stirring the reaction mixture for 12 h at 23 °C, it was quenched by addition of saturated aqueous NH₄Cl solution. The organic materials were extracted three times with CHCl₃, washed with brine, dried over anhydrous Na₂SO₄, and concentrated in vacuo after filteration. Purification by column chromatography (ethyl acetate : chloroform= 1 : 40) gave (4*R*,5*R*,*E*)-ethyl 4-methyl-6-oxo-5-(triisopropylsilyloxy)hept-2-enoate in 38% yield with *anti* : *syn* = 10 : 1.

As single diastereomer; ¹H NMR (CDCl₃, 400 MHz): δ 1.04-1.10 (24H, d, J = 6.8 Hz), 1.27 (3H, d, J = 7.2 Hz), 2.16 (3H, s), 2.58-2.67 (1H, m), 4.08 (1H, d, J = 4.8 Hz), 4.17 (2H, q, J = 7.2 Hz), 5.86 (1H, d, J = 16.0 Hz), 6.95 (1H, dd, J = 8.0, 16.0 Hz); ¹³C NMR (CDCl₃, 100MHz): δ 12.3, 14.2, 14.7, 18.0, 26.1, 41.8, 60.3, 82.5, 122.0, 148.8, 166.2, 210.6; IR(neat): v_{max} 2947, 2870, 1720, 1466, 1365, 1273, 1180, 1111, 1041, 987, 879, 818, 679 cm⁻¹; HRMS (ESI): [M+Na]⁺ calcd

for $[C_{19}H_{36}NaO_4Si]^+$: 379.2275, found: 379.2288; $[\alpha]_D^{22}$ +15.1° (c = 0.77, CHCl₃).

(4R,5R,6R,E)-ethyl 6-hydroxy-4-methyl-5-(triisopropylsilyloxy)hept-2-enoate (Eq. 4)

OH Me

A single diastereomer of (4R,5R,E)-ethyl 4-methyl-6-oxo-5-(triisopropylsilyloxy)hept-2-enoate (31.5 mg, 0.088mmol) in toluene (0.9 ml, 0.1 M) was treated with sodium bis(2-methoxyethoxy) aluminum hydride (0.04 ml, 65 wt% in toluene) at -78 °C. After stirring the reaction mixture for 30 minute at -78 °C, it was quenched by addition of saturated aqueous solution of potassium sodium tartrate. The organic materials were extracted three times with CHCl₃, washed with brine, dried over anhydrous Na₂SO₄, and concentrated in vacuo after filtration. Purification by column chromatography (ethyl acetate : hexane = 1 : 4) gave (4R,5R,E)-ethyl 4-methyl-6-oxo-5-(triisopropylsilyloxy)hept-2-enoate in 94% yield.

¹H NMR (CDCl₃, 400 MHz): δ 1.10-1.18 (27H, m), 1.17 (3H, t, *J* = 7.2 Hz), 2.64-2.67 (1H, m), 3.67-3.71 (2H, m), 4.19 (2H, q, *J* = 7.2 Hz), 5.83 (1H, d, *J* = 16.0 Hz), 6.99 (1H, dd, *J* = 7.2, 16.0 Hz); ¹³C NMR (CDCl₃, 100MHz): δ 13.4, 14.3, 14.4, 18.2, 18.3, 21.0,

60.3, 67.7, 79.3, 121.4, 150.3, 166.6 ;IR(neat): v_{max} 3487, 2939, 2870, 1720, 1651, 1466, 1373, 1265, 109 5, 1041, 879, 679 cm⁻¹; HRMS (ESI): [M+Na]⁺ calcd for [C₁₉H₃₈NaO₄Si]⁺: 381.2432, found: 381.2435; [α] p^{26} +7.0° (c = 1.31, CHCl₃).

(4R,5R,8R,E)-ethyl-8-hydroxy-4,9-dimethyl-6-oxo-5-(triisopropylsilyloxy)dec-2-enoate(Eq.5)

To (4R,5R,E)-ethyl 4-methyl-6-oxo-5-(triisopropylsilyloxy)hept-2-enoate (44.5 mg, 0.116 mmol) as a diastereo mixture (anti : syn = 8.5 : 1) in CH₂Cl₂ (0.77 mL, 0.15 M), was added ⁱPr₂NEt (37 μ L, 0.216 mmol) and "Bu2BOTf (0.185 ml, 0.185 mol) at -78 °C. After stirring the reaction mixture for 3 hours at 0 °C, the reaction was cooled to -78 °C. Isobutyraldehyde (28 μ L, 0.308 mmol) was added dropwise. After stirring the reaction mixture for 30 min at -78 to -20 °C, quenched by the addition of aqueous buffer (pH = 7). After separation, the aqueous layer was extracted with CH_2Cl_2 . The combined organic layers were concentrated in vacuo, and the residue was dissolved in a mixture of MeOH (6 M of ketone), aqueous buffer (pH = 7) (6 M of ketone), and aqueous 30% H₂O₂ (30%, 3 M of ketone). The solution was stirred for 2 h, and after separation of the layers, the aqueous phase was extracted with CH_2Cl_2 and the combined organic layers. Organic layers were washed with satured aqueous NaHCO₃ and brine, dried over anhydrous MgSO₄, and concentrated in vacuo after filtration. Purification by preparative thin layer chromatography (ethyl 1 acetate hexane ٠ 6) gave (4R,5R,8R,E)-ethyl-8-hydroxy-4,9-dimethyl-6-oxo-5-(triisopropyl-

silyloxy)dec-2-enoate in 70% yield with anti : syn = 14.3 : 1. Starting material was recovered 19% with

anti / syn = 5.6 / 1. Diastereomeric ratio decreased at purification stage due to isomerization.

As diastereomer mixture (*anti* : *syn* = 4.0 : 1); ¹H NMR (CDCl₃, 400 MHz): δ 0.83 (3H, d, *J* = 6.8 Hz), 0.84 (3H, d, *J* = 6.8 Hz), 0.98-1.05 (24H, m), 1.22 (3H, t, *J* = 7.2 Hz), 1.60-1.66 (1H, m), 2.50 (1H, dd, *J* = 6.0, 18.4 Hz), 2.57-2.62 (1H, m), 2.66 (1H, dd, *J* = 2.0, 18.4 Hz), 3.65-3.69 (1H, m), 4.11 (2H, q, *J* = 7.2 Hz), 4.14 (1H, d, *J* = 4.8 Hz), 5.73 (1H, d, *J* = 15.6 Hz), 6.89 (1H, dd, *J* = 8.0, 15.6 Hz); ¹³C NMR (CDCl₃,100MHz): δ 12.5, 14.2, 14.9, 17.9, 18.0, 32.9, 42.1, 42.3, 60.4, 71.6, 82.3, 122.0, 148.4, 166.1, 21 5.0 ;IR(neat): v_{max} 4327, 3525, 2947, 2870, 1720, 1651, 1466, 1373, 1265, 1180, 1111, 1041, 995, 879, 8 18, 679, 579, 509 cm⁻¹; HRMS (ESI): [M+Na]⁺ calcd for [C₂₃H₄₄NaO₅Si]⁺: 451.2850, found: 451.2856.

Determination of relative and absolute configuration of aldol product

The absolute configuration was determined by comparison of the optical rotation after conversion of the aldol product into the known compound^{c)}, which was prepared according to Scheme 1.



(S,E)-ethyl 5-(*tert*-butyldimethylsilyloxy)-6-oxohept-2-enoate

OTBS CO₂Et

To (*S*,*E*)-ethyl 5-hydroxy-6-oxohept-2-enoate (405 mg, 2.17 mmol) in DMF (4.34 mL, 0.5 M) was added TBSCl (1.31 g, 8.68 mmol) and imidazole (739 mg, 10.85 mmol) at 0 °C. After stirring the reaction mixture for 1 h at 0 °C, it was quenched by addition of buffer (pH = 7.0). The organic materials were extracted three times with ethyl acetate, washed with water and brine, dried over anhydrous Na₂SO₄, and concentrated in vacuo. Purification by column chromatography (ethyl acetate : hexane = 1 : 10) gave (*S*,*E*)-ethyl 5-(*tert*-butyldimethylsilyloxy)-6-oxohept-2-enoate as a pale yellow oil in 86% yield.

¹H NMR (CDCl₃, 400 MHz): δ 0.06 (6H, s), 0.92 (9H, s), 1.27 (3H, t, J = 7.2 Hz), 2.17 (3H, s), 2.50 (2H, dd, J = 6.4, 7.2 Hz), 4.10 (1H, t, J = 6.4 Hz), 4.17 (2H, q, J = 7.2 Hz), 5.85 (1H, d, J = 15.6 Hz), 6.86 (1H, dt, J = 7.2, 15.6 Hz); ¹³C NMR (CDCl₃, 100MHz): δ –5.1, –5.0, 14.2, 18.0, 25.6, 37.4, 60.2, 77.6, 124.5, 143.2, 165.9, 210.9 δ ;IR(neat): v_{max} 2931, 2862, 1720, 1658, 1466, 1358, 1257, 1165, 1103, 1041, 987, 8 41,779 cm⁻¹; HRMS (ESI): [M+Na]⁺ calcd for [C₁₅H₂₈NaO₄Si]⁺: 323.1649, found: 323.1645; [α]_D²²-31.6^o (c = 1.00, CHCl₃).

(E)-ethyl 4-((4S,5S)-2,2,5-trimethyl-1,3-dioxolan-4-yl)but-2-enoate

To (*S*,*E*)-ethyl 5-(*tert*-butyldimethylsilyloxy)-6-oxohept-2-enoate (97 mg, 0.323 mmol) in toluene (3.23 mL, 0.1 M) was added sodium bis(2-methoxyethoxy)aluminium hydride (147.7 μ L, 65wt% in toluene) at -78 °C. After stirring the reaction mixture for 1 hat -78 °C, the reaction mixture was allowed to come to 23 °C. Reaction mixture was quenched by addition of saturated aqueous solution of potassium sodium tartrate at -78 °C. Organic materials were extracted three times with ethyl acetate, washed with brine, dried over unhydrous Na₂SO₄, and concentrated in vacuo.

The residue was dissolved in ethanol (323 μ L, 1.0 M) and treated with trimethyl silyl chloride (6.1 μ L, 0.05 mmol) at 23 °C. After stirring the reaction mixture for 8 h at 40 °C, it was concentrated in vacuo and the crude residue was forwarded for next step.

The crude residue was dissolved in acetone (323 μ L, 1.0 M) and treated with 2,2-dimethoxy-propane (59.4 μ L, 0.484 mmol) and *p*-toluenesulfonic acid (6.1 mg, 0.032 mmol) at 23 °C. After stirring the reaction mixture for 30 min at 23 °C, it was quenched by addition of 5% NaHCO₃ aqueous solution. The organic materials were extracted three times with ethyl acetate, washed with brine, dried over unhydrous Na₂SO₄, and concentrated in vacuo. Purification by column chromatography (ethyl acetate : hexane = 1 : 4) gave (*E*)-ethyl 4-((4*S*,5*S*)-2,2,5-trimethyl-1,3-dioxolan-4-yl)but-2-enoate as a pale yellow oil in 89% yield over three steps.

¹H NMR (CDCl₃, 400 MHz): δ 1.24 (3H, d, J = 5.6 Hz), 1.27 (3H, t, J = 7.2 Hz), 1.36 (3H, s), 1.38 (3H, s), 2.41-2.46 (2H, m), 3.61-3.65 (1H, m), 3.71-3.77 (1H, m), 4.17 (2H, q, J = 7.2 Hz), 5.90 (1H, d, J = 15.6 Hz), 6.96 (1H, dt, J = 7.2, 15.6 Hz); ¹³C NMR (CDCl₃,100MHz): δ 14.2, 17.3, 27.0, 27.2, 34.7, 60.2, 76.3, 80.5, 108.2, 123.7, 143.9, 166.1 ;IR(neat): v_{max} 2985, 1720, 1658, 1450, 1373, 1265, 1219, 1180, 1 095, 1041, 987, 856, 671 cm⁻¹; HRMS (ESI): [M+Na]⁺ calcd for [C₁₂H₂₀NaO₄]⁺: 251.1254, found: 251.1259; [α]p²⁴-14.8° (c = 0.99, CHCl₃).

2-((45,55)-2,2,5-trimethyl-1,3-dioxolan-4-yl)ethyl benzoate



(*E*)-ethyl 4-((4*S*,5*S*)-2,2,5-trimethyl-1,3-dioxolan-4-yl)but-2-enoate (44 mg, 0.19 mmol) in MeOH (1.9 mL, 0.1 M) was cooled to -78 °C, and ozone was bubbled into the stirred solution. When the solution turned blue, ozone bubbling was stopped. Excess ozone was removed by purging with argon and then NaBH₄ (14 mg, 0.38 mmol) was added at 0 °C. After stirring the reaction mixture for 30 min at 0 °C, it was quenched by addition of buffer (pH = 7.0). Organic materials were extracted three times with chloroform, washed with brine, dried over unhydrous Na₂SO₄, and concentrated in vacuo.

The residue was dissolved in pyridine (190 μ L, 1.0 M) and benzoyl chloride (37.4 μ L, 0.29 mmol) was added at 0 °C. After stirring the reaction mixtuire for 2 hours at 23 °C, it was quenched by addition of buffer (pH = 7.0). The organic materials were extracted three times with ethyl acetate, washed with brine,

dried over unhydrous Na_2SO_4 , and concentrated in vacuo. Purification by Preparative thin layer chromatography (acetone : hexane = 1 : 5) gave 2-((4*S*,5*S*)-2,2,5-trimethyl-1,3-dioxolan-4-yl)ethyl benzoate as a pale yellow oil in 59% yield over two steps.

¹H NMR (CDCl₃, 400 MHz): δ 1.28 (3H, d, J = 6.0 Hz), 1.39 (3H, s), 1.40 (3H, s), 1.93-2.07 (2H, m), 3.67-3.83 (2H, m), 4.39-4.54 (2H, m), 7.42-8.04 (5H, m); ¹³C NMR (CDCl₃,100MHz): δ 17.3, 27.2, 27.3, 31.5, 62.0, 79.3, 108.2, 128.4, 128.4, 129.6, 130.2, 133.0, 166.5 ; IR(neat): v_{max} 2985, 2931, 1720, 1604, 1 450, 1373, 1273, 1173, 1095, 1026, 1003, 856, 710, 517 cm⁻¹; HRMS (ESI): [M+Na]⁺ calcd for [C₁₅H₂₀NaO₄]⁺: 287.1254, found: 287.1247; [α] $_{D}^{24}$ -24.5° (c = 1.00, CHCl₃), lit ^c) : -25.6° (c = 4.95, CHCl₃)

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table 2-entry 2,3











table 2-entry 5











table 2-entry 7





















table 2-entry 12,13





table 2-entry 14,15



































