Catalytic, Asymmetric *trans*-Selective Hetero Diels-Alder Reactions Using a Novel Chiral Zirconium Catalyst

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Supporting Information

Experimental Details

General

Melting points were uncorrected. ^1H and ^{13}C NMR spectra were recorded on a JEOL JNM-LA300, JNM-LA400, or JNM-LA500 spectrometer in CDCl_3 unless otherwise noted. Tetramethylsilane (TMS) served as internal standard ($\delta = 0$) for ^1H NMR, and CDCl_3 was used as internal standard ($\delta = 77.0$) for ^{13}C NMR. IR spectra were measured with JASCO FT/IR-610 spectrometers. Optical rotations were measured with a JASCO P-1010 polarimeter. High-performance liquid chromatography was carried out using following apparatuses; SHIMADZU LC-10AT (liquid chromatograph), SHIMADZU SPD-10A (UV detector), and SHIMADZU C-R6A Chromatopac. Mass spectrometry analysis was carried out using SHIMADZU GCMS-QP5050A. Column chromatography was conducted on Silica gel 60 (Merck) and preparative thin-layer chromatography was carried out using Wakogel B-5F. Toluene was distilled and dried over MS 4A. $\text{Zr}(\text{O}^i\text{Bu})_4$ was purchased from Trichemical Laboratory Co., Ltd.. Employed aldehydes were purchased from Tokyo Kasei Kogyo Co., Ltd. Danishefsky's dienes were prepared according to the

literature.¹ Propanol was distilled in the presence of magnesium propoxide. All reactions were carried out under argon atmosphere in dried glassware.

Typical experimental procedure for asymmetric hetero Diels–Alder reactions using a chiral zirconium catalyst prepared from $\text{Zr}(\text{O}^i\text{Bu})_4$ and (*R*)-3,3'- I_2 BINOL: A typical experimental procedure is described for the reaction of benzaldehyde with Danishefsky's diene **1b**. To a suspension of (*R*)-3,3'-diiodo-1,1'-binaphthalene-2,2'-diol ((*R*)-3,3'- I_2 BINOL, 0.048 mmol) in toluene (0.5 mL), was added $\text{Zr}(\text{O}^i\text{Bu})_4$ (0.040 mmol) in toluene (0.5 mL) at room temperature, and the solution was stirred for 30 min. Then propanol (0.32 mmol) and H_2O (0.080 mmol) in toluene (0.3 mL) were added and the whole was stirred for 3 h at room temperature. After cooling at $-78\text{ }^\circ\text{C}$, benzaldehyde (0.40 mmol) in toluene (0.35 mL) and diene **1b** (0.48 mmol) in toluene (0.35 mL) were successively added. The mixture was warmed to $-20\text{ }^\circ\text{C}$ and stirred for 18 h, then saturated aqueous NaHCO_3 (10 mL) was added to quench the reaction. After added dichloromethane (10 mL), the organic layer was separated and the aqueous layer was extracted twice with dichloromethane (10 mL x 2). The organic layers were combined and dried over anhydrous Na_2SO_4 . After filtration and concentration under reduced pressure, the residue was treated with TFA (0.5 mL) in dichloromethane (8 mL) for 1 h at $0\text{ }^\circ\text{C}$. After the solution was basicified with saturated aqueous NaHCO_3 (20 mL), the organic layer was separated and extracted with dichloromethane (10 mL x 2). The organic layers were combined and dried over anhydrous Na_2SO_4 . After filtration and concentration under reduced pressure, the crude product was purified by preparative thin layer chromatography (benzene-ethyl acetate=20:1) to afford the desired product. The optical purity was determined by HPLC analysis using a chiral column (see following analytical data).

Typical experimental procedure for asymmetric hetero Diels–Alder reactions using a chiral zirconium catalyst prepared from $\text{Zr}(\text{O}^i\text{Bu})_4$ and (*R*)-3,3'- I_2 -6,6'- X_2 BINOL ($\text{X}=\text{I}$, C_2F_5): A typical experimental procedure is described for the reaction of benzaldehyde with Danishefsky's diene **1d**. To a suspension of

(*R*)-3,3'-diiodo-6,6'-disubstituted-1,1'-binaphthalene-2,2'-diol ((*R*)-3,3'-I₂-6,6'-X₂BINOL (X: C₂F₅, I), 0.060 mmol) in toluene (0.5 mL), was added Zr(O^{*i*}Bu)₄ (0.040 mmol) in toluene (0.5 mL) at room temperature, and the solution was stirred for 3 h. Then propanol (0.32 mmol) and H₂O (0.080 mmol) in toluene (0.3 mL) were added and the whole was stirred for 30 min at room temperature. After cooling at –78 °C, benzaldehyde (0.40 mmol) in toluene (0.35 mL) and diene **1d** (0.48 mmol) in toluene (0.35 mL) were successively added. The mixture was warmed to –20 °C and stirred for 18 h, then saturated aqueous NaHCO₃ (10 mL) was added to quench the reaction. After added dichloromethane (10 mL), the organic layer was separated and the aqueous layer was extracted twice with dichloromethane (10 mL x 2). The organic layers were combined and dried over anhydrous Na₂SO₄. After filtration and concentration under reduced pressure, the residue was treated with TFA (0.5 mL) in dichloromethane (8 mL) for 1 h at 0 °C. In case of the reaction of α,β-unsaturated aldehyde, Sc(OTf)₃ (0.040 mmol, 10 mol% to employed aldehyde) was used instead of TFA in dichloromethane at room temperature for 12 h. After the solution was basified with saturated aqueous NaHCO₃ (20 mL) the organic layer was separated and extracted with dichloromethane (10 mL x 2). The organic layers were combined and dried over anhydrous Na₂SO₄. After filtration and concentration under reduced pressure, the desired *trans* and *cis* diastereomers were separated and purified by preparative thin layer chromatography (benzene-ethyl acetate=20:1). The optical purity was determined by HPLC analysis using a chiral column (see below).

(*R*)-2-Phenyl-2,3-dihydro-4*H*-pyran-4-one:² [α]_D²⁶ = –97.1 (c 0.69, CHCl₃) (97% ee). lit.)² [α]_D²³ = +88.4 (c 0.529, CHCl₃) (87% ee, *S*-form); IR [cm^{–1}] 3063, 2902, 1680, 1595, 1496, 1455, 1403, 1270, 1227, 1209; ¹H NMR (CDCl₃) δ 2.66 (dd, 1H, *J* = 17, 3.5 Hz), 2.90 (dd, 1H, *J* = 17, 14 Hz), 5.42 (dd, 1H, *J* = 15, 3.7 Hz), 5.52 (d, 1H, *J* = 6.0 Hz), 7.3 - 7.4 (m, 5H), 7.48 (d, 1H, *J* = 6.0 Hz); ¹³C NMR (CDCl₃) δ 43.3, 81.0, 107.3, 126.0, 128.8, 128.9, 137.8, 163.1, 192.1; HPLC, Daicel Chiralcel OD, hexane/*i*PrOH = 40/1, flow rate = 1.0 mL/min : *t*_R = 25.1 min (*S*), *t*_R = 30.1 min (*R*).

2-(*p*-Chlorophenyl)-2,3-dihydro-4*H*-pyran-4-one:² $[\alpha]_{\text{D}}^{19} = -62.4$ (c 0.56, CHCl₃) (84% ee); IR [cm⁻¹] 3063, 2906, 1907, 1675, 1599, 1494, 1402, 1267, 1227, 1208; ¹H NMR (CDCl₃) δ 2.64 (dd, 1H, *J* = 17, 3.7 Hz), 2.85 (dd, 1H, *J* = 17, 14 Hz), 5.41 (dd, 1H, *J* = 14, 3.5 Hz), 5.53 (d, 1H, *J* = 6.1 Hz), 7.34 (d, 2H, *J* = 8.7 Hz), 7.39 (d, 2H, 8.7 Hz), 7.47 (d, 1H, *J* = 6.1 Hz); ¹³C NMR (CDCl₃) δ 43.3, 80.2, 107.5, 127.4, 129.0, 134.7, 136.3, 162.9, 191.6; HPLC, Daicel Chiralcel OD, hexane/*i*PrOH = 40/1, flow rate = 1.0 mL/min : *t*_R = 27.2 min (minor), *t*_R = 35.9 min (major).

(*S*)-2-Phenethyl-2,3-dihydro-4*H*-pyran-4-one:² $[\alpha]_{\text{D}}^{19} = -93.4$ (c 1.34, CHCl₃) (85% ee); IR [cm⁻¹] 3023, 2931, 2632, 1674, 1599, 1495, 1455, 1402, 1274. ¹H NMR (CDCl₃) δ 1.95 (m, 1H), 2.15 (m, 1H), 2.42 (dd, 1H, *J* = 17, 3.8 Hz), 2.55 (dd, 1H, *J* = 17, 13 Hz), 2.80 (m, 2H), 4.39 (m, 1H), 5.40 (d, 1H, *J* = 6.0 Hz), 7.1 - 7.3 (m, 5H), 7.38 (d, 1H, *J* = 6.1 Hz); ¹³C NMR (CDCl₃) δ 30.9, 36.0, 41.8, 78.4, 107.1, 126.2, 128.4, 128.6, 140.6, 163.1, 192.4; HPLC, Daicel Chiralcel OD, hexane/*i*PrOH = 9/1, flow rate = 1.0 mL/min : *t*_R = 21.7 min (*R*), *t*_R = 43.8 min (*S*).

2-(*p*-Tolyl)-2,3-dihydro-4*H*-pyran-4-one: $[\alpha]_{\text{D}}^{19} = -27.5$ (c 0.26, CHCl₃) (92% ee); IR [cm⁻¹] 2921, 1672, 1596, 1515, 1405, 1271, 1220; ¹H NMR (CDCl₃) δ 2.28 (s, 3H), 2.53 (dd, 1H, *J* = 17, 3.5 Hz), 2.81 (dd, 1H, *J* = 17, 15 Hz), 5.29 (dd, 1H, *J* = 14, 3.3 Hz), 5.43 (dd, 1H, *J* = 6.1, 1.3 Hz), 7.1 - 7.3 (m, 4H), 7.37 (d, 1H, *J* = 6.1 Hz); ¹³C NMR (CDCl₃) δ 21.2, 43.3, 81.0, 107.3, 126.1, 129.5, 134.8, 138.9, 163.2, 192.3; HPLC, Daicel Chiralcel OD, hexane/*i*PrOH = 40/1, flow rate = 1.0 mL/min : *t*_R = 22.2 min (minor), *t*_R = 27.1 min (major); HRMS (*m/z*) calcd. for C₁₂H₁₂O₂ (M⁺): 188.0837; found: 188.0832.

2-Pentyl-2,3-dihydro-4*H*-pyran-4-one: $[\alpha]_{\text{D}}^{19} = -131.4$ (c 0.54, CHCl₃) (83% ee); IR [cm⁻¹] 2935, 2865, 1678, 1599, 1466, 1403, 1274; ¹H NMR (CDCl₃) δ 0.90 (t, 3H, *J* = 6.8 Hz), 1.3 - 1.5 (m, 6H), 1.66 (m, 1H), 1.81 (m, 1H), 2.4 - 2.5 (m, 1H), 4.4 (m, 1H), 5.4 (dd, 4H, *J* = 5.9, 0.7 Hz), 7.35 (d, 1H, *J* = 6.1 Hz); ¹³C NMR (CDCl₃) δ 13.9, 22.4, 24.4, 31.4, 34.3, 41.8, 79.5, 106.9, 163.3, 192.7; HPLC, Daicel Chiralcel OD, hexane/*i*PrOH = 40/1, flow rate = 0.5 mL/min : *t*_R = 19.0 min (minor),

t_R = 21.1 min (major); HRMS (m/z) calcd. for $C_{10}H_{16}O_2$ (M^+): 168.1150; found: 168.1132.0

3,5-Dimethyl-2-phenyl-2,3-dihydro-4H-pyran-4-one: *trans* isomer: $[\alpha]_D^{26} = -35.1$ (c 0.77, $CHCl_3$) (96% ee); IR [cm^{-1}] 3037, 2926, 1964, 1725, 1670, 1625, 1496, 1455, 1377, 1307, 1272, 1232; 1H NMR ($CDCl_3$) *trans* isomer: δ 0.92 (d, 3H, J = 6.8 Hz), 1.73 (s, 3H), 2.80 (dq, 1H, J = 13, 6.6 Hz), 4.91 (d, 1H, J = 13 Hz), 7.31 (s, 1H), 7.3 - 7.5 (m, 5H); *cis* isomer: δ 0.90 (d, 3H, J = 7.6 Hz), 1.74 (s, 3H), 2.60 (dq, 1H, J = 7.3, 3.2 Hz), 5.47 (d, 1H, J = 3.2 Hz), 7.26 (s, 1H), 7.3 - 7.5 (m, 5H); ^{13}C NMR ($CDCl_3$); *trans* isomer: δ 10.3, 10.7, 44.7, 86.9, 113.1, 127.3, 128.7, 129.0, 137.5, 158.7, 194.9. *cis* isomer: δ 9.9, 10.7, 45.7, 82.9, 112.5, 125.4, 127.9, 128.5, 136.8, 158.8, 197.7; *cis* isomer HPLC, Daicel Chiralcel OD, hexane/*i*PrOH = 40/1, flow rate = 0.6 mL/min : t_R = 22.3 min (minor), t_R = 27.1 min (major); *trans* isomer HPLC, Daicel Chiralcel OD, hexane/*i*PrOH = 19/1, flow rate = 0.3 mL/min : t_R = 29.3 min (minor), t_R = 31.2 min (major); *trans* isomer: HRMS (m/z) calcd. for $C_{13}H_{14}O_2$ (M^+): 202.0994; found: 202.0993.

3,5-Dimethyl-2-(*p*-chlorophenyl)-2,3-dihydro-4H-pyran-4-one: *trans* isomer: $[\alpha]_D^{26} = -59.5$ (c 1.03, $CDCl_3$) (97% ee); IR [cm^{-1}] 2930, 1668, 1630, 1455, 1384, 1306, 1232; 1H NMR ($CDCl_3$) *trans* isomer: δ 0.92 (d, 3H, J = 6.8 Hz), 1.72 (s, 3H), 2.74 (dq, 1H, J = 14, 6.8 Hz), 4.89 (d, 1H, J = 13 Hz), 7.30 (s, 1H), 7.3 - 7.4 (m, 4H); *cis* isomer: δ 0.88 (d, 3H, J = 7.3 Hz), 1.74 (s, 3H), 2.56 (dq, 1H, J = 7.3, 3.2 Hz), 5.44 (d, 1H, J = 2.9 Hz), 7.2 - 7.4 (m, 5H); ^{13}C NMR ($CDCl_3$); *trans* isomer: δ 10.3, 10.7, 44.7, 86.0, 113.3, 128.7, 128.9, 134.8, 136.1, 158.5, 194.5; *cis* isomer: δ 9.9, 10.6, 45.5, 82.2, 112.7, 126.8, 128.7, 133.8, 135.3, 158.5, 197.3; *cis* isomer HPLC, Daicel Chiralcel OD, hexane/*i*PrOH = 40/1, flow rate = 0.6 mL/min : t_R = 14.5 min (minor), t_R = 27.8 min (major); *trans* isomer HPLC, Daicel Chiralcel OD, hexane/*i*PrOH = 19/1, flow rate = 0.3 mL/min : t_R = 23.9 min (minor), t_R = 24.9 min (major); *trans* isomer: HRMS (m/z) calcd. for $C_{13}H_{13}ClO_2$ (M^+): 236.0604; found: 236.0590; *trans* isomer: Elemental analysis for $C_{13}H_{13}ClO_2$, calcd.: C 65.97, H 5.54; found: C 65.75, H 5.75.

3,5-Dimethyl-2-(*p*-tolyl)-2,3-dihydro-4*H*-pyran-4-one: *trans* isomer: $[\alpha]_D^{23} = -48.6$ (c 1.48, CHCl₃) (90% ee); IR [cm⁻¹] 3445, 2974, 2324, 1671, 1626, 1517, 1456, 1376, 1305, 1270, 1233; ¹H NMR (CDCl₃) *trans* isomer: δ 0.92 (d, 3H, *J* = 6.9 Hz), 1.72 (s, 3H), 2.73 (s, 3H), 2.80 (dq, 1H, *J* = 13, 6.8 Hz), 4.87 (d, 1H, *J* = 13 Hz), 7.2 - 7.3 (m, 5H); *cis* isomer: δ 0.90 (d, 3H, *J* = 7.3 Hz), 1.73 (s, 3H), 2.37 (s, 3H), 2.57 (dq, 1H, *J* = 7.3, 3.3 Hz), 5.43 (d, 1H, *J* = 3.1 Hz), 7.2 - 7.3 (m, 4H), 7.37 (s, 1H); ¹³C NMR (CDCl₃); *trans* isomer: δ 10.4, 10.7, 21.2, 44.6, 86.8, 113.0, 127.3, 129.3, 134.6, 138.9, 158.8, 195.1. *cis* isomer: δ 9.9, 10.7, 21.1, 45.7, 83.0, 112.4, 125.4, 129.1, 133.8, 137.7, 158.9, 197.9; *cis* isomer HPLC, Daicel Chiralcel OD, hexane/*i*PrOH = 40/1, flow rate = 0.6 mL/min : *t*_R = 15.7 min (major), *t*_R = 18.1 min (minor); *trans* isomer HPLC, Daicel Chiralcel OD, hexane/*i*PrOH = 19/1, flow rate = 0.3 mL/min : *t*_R = 22.9 min (major), *t*_R = 26.1 min (minor); *trans* isomer: HRMS (m/z) calcd. for C₁₄H₁₆O₂ (M⁺): 216.1150; found: 216.1128.

3,5-Dimethyl-2-styryl-2,3-dihydro-4*H*-pyran-4-one: *trans* isomer: $[\alpha]_D^{19} = -28.9$ (c 0.3, CHCl₃) (78% ee); IR [cm⁻¹] 3034, 2816, 2741, 2355, 1675, 1627, 1497, 1450, 1382, 1302; ¹H NMR (CDCl₃) *trans* isomer: δ 1.13 (d, 3H, *J* = 7.0 Hz), 1.69 (s, 3H), 2.57 (dd, 1H, *J* = 12, 7.0 Hz), 4.57 (dd, 1H, *J* = 13, 7.7 Hz), 6.27 (dd, 1H, *J* = 16, 7.7 Hz), 6.71 (d, 1H, *J* = 16 Hz), 7.2 - 7.4 (m, 6H); *cis* isomer: δ 1.1 (d, 3H, *J* = 7.3 Hz), 1.70 (s, 3H), 2.58 (dd, 1H, *J* = 7.3, 3.7 Hz), 5.01 (dd, 1H, *J* = 6.2, 3.7 Hz), 6.25 (dd, 1H, *J* = 16, 6.4 Hz), 6.74 (d, 1H, *J* = 16 Hz), 7.2 - 7.4 (m, 6H); ¹³C NMR (CDCl₃); *trans* isomer: δ 10.70, 10.74, 43.9, 85.1, 113.0, 125.3, 126.7, 128.4, 128.7, 135.0, 135.7, 158.4, 194.8. *cis* isomer: δ 10.1, 10.6, 44.1, 82.3, 112.4, 123.2, 126.6, 128.2, 128.6, 133.7, 135.9, 158.3, 196.9; HPLC, Daicel Chiralcel OD, hexane/*i*PrOH = 40/1, flow rate = 1.0 mL/min : *cis* isomer *t*_R = 12.8 min (minor), *t*_R = 31.7 min (major); *trans* isomer *t*_R = 18.7 min (major), *t*_R = 22.0 min (minor); *trans* isomer: HRMS (m/z) calcd. for C₁₅H₁₆O₂ (M⁺): 228.1150; found: 228.1131.

3,5-Dimethyl-2-phenethyl-2,3-dihydro-4*H*-pyran-4-one: *trans* isomer: $[\alpha]_D^{22} = -121.0$ (c 1.01, CHCl₃) (87% ee); IR [cm⁻¹] 3441, 3026, 2927, 1670, 1626, 1496, 1455, 1382, 1311, 1273, 1232; ¹H NMR (CDCl₃) *trans* isomer: δ 1.16 (d, 3H, *J*

= 7.1 Hz), 1.67 (s, 3H), 2.02 (dt, 2H, J = 14, 7.3 Hz), 2.43 (dt, 1H, J = 12, 7 Hz), 2.67-2.93 (m, 2H), 4.01 (m, 1H), 7.2 - 7.4 (m, 6H); ^{13}C NMR (CDCl_3); *trans* isomer: δ 10.7, 30.8, 34.3, 43.5, 82.8, 112.7, 126.0, 128.4, 128.5, 141.2, 158.4, 195.3; HPLC, Daicel Chiralcel OD, hexane/*i*PrOH = 40/1, flow rate = 1.0 mL/min : *cis* isomer t_R = 12.8 min (minor), t_R = 31.7 min (major); *trans* isomer t_R = 18.7 min (major), t_R = 22.0 min (minor); *trans* isomer: HRMS (m/z) calcd. for $\text{C}_{15}\text{H}_{18}\text{O}_2$ (M^+): 230.1307; found: 230.1315.

3,5-Dimethyl-2-pentyl-2,3-dihydro-4H-pyran-4-one: *trans* isomer: $[\alpha]_D^{22} = -109.0$ (c 1.00, CHCl_3) (88% ee); IR [cm^{-1}] 3324, 2929, 2860, 1671, 1628, 1458, 1380, 1312, 1271, 1228; ^1H NMR (CDCl_3) *trans* isomer: δ 0.90 (t, 3H, J = 7.1 Hz), 1.11 (d, 3H, J = 6.8 Hz), 1.3 – 1.6 (m, 8H), 1.60 (d, 3H, J = 1.0 Hz), 2.35-2.44 (m, 1H), 4.01 (dt, 1H, J = 12, 5.6 Hz), 7.21 (s, 1H); ^{13}C NMR (CDCl_3); *trans* isomer: δ 10.69, 10.77, 13.9, 22.5, 24.1, 31.6, 32.3, 43.4, 83.8, , 112.4, 158.6, 195.7; *cis* isomer HPLC, Daicel Chiralcel OD, hexane/*i*PrOH = 1000/1, flow rate = 1.0 mL/min : t_R = 13.7 min (minor), t_R = 17.6 min (major); *trans* isomer HPLC, Daicel Chiralcel OB-H, hexane/*i*PrOH = 200/1, flow rate = 0.5 mL/min : t_R = 13.0 min (major), t_R = 14.5 min (minor); *trans* isomer: HRMS (m/z) calcd. for $\text{C}_{12}\text{H}_{20}\text{O}_2$ (M^+): 196.1463; found: 196.1464.

(2R, 3R)-3-methyl-2-((E)-1-propenyl)-2,3-dihydro-4H-pyran-4-one (*trans*-3): *trans*-3: IR [cm^{-1}] 1677, 1599, 1457, 1409, 1377, 1308, 1285, 1250, 1217. ^1H NMR (CDCl_3) δ 1.04 (d, 3H, J = 7.1 Hz), 1.76 (dd, 3H, J = 6.6, 1.7 Hz), 2.46 (dq, 1H, J = 12, 7.1 Hz), 4.39 (dd, 1H, J = 12, 8.3), 5.36 (d, 1H, J = 5.8 Hz), 5.57 (ddq, 1H, J = 15, 8.3, 1.7 Hz), 5.86 (ddq, 1H, J = 15, 6.6, 0.7 Hz), 7.30 (d, 1H, J = 6.1 Hz). ^{13}C NMR (CDCl_3) δ 10.6, 17.7, 43.9, 85.5, 106.2, 127.4, 132.9, 162.2, 194.7. MS [m/z] 152 (M^+), $[\alpha]_D^{22} = +83.1$ (c 1.35, CHCl_3 , 87% ee). . HRMS (m/z) calcd. for $\text{C}_9\text{H}_{12}\text{O}_2$ (M^+): 152.0837; found: 152.0831. The ratio of *trans*- and *cis*- isomers was determined by ^1H NMR analysis, and the optical purity was determined by HPLC analysis (Daicel Chiralcel AS, hexane/*i*PrOH = 100/1, flow rate = 1.0 mL/min: *trans* isomer t_R = 23.1 min (major), t_R = 19.5 min (minor); *cis* isomer t_R = 30.0 min

(major), t_R = 48.0 min (minor)). Then, *trans*-**3** was separated by column chromatography (silica gel, P.E.-diethyl ether=9:1) and used in the next reaction.

(2R, 3S, 4S)-4-Hydroxy-3-methyl-2-((E)-1-propenyl)-2,3-dihydro-4H-pyran (4): m.p. 88 °C. IR [cm^{-1}] (KBr) 3246, 1651, 1457, 1378, 1357, 1335, 1312, 1282, 1268, 1233. ^1H NMR (CDCl_3) δ 0.98 (d, 3H, J = 6.8 Hz), 1.38 (d, 1H, J = 8.0 Hz), 1.65 (m, 1H), 1.75 (dd, 3H, J = 6.6, 1.7 Hz), 3.88 (m, 1H), 4.01 (m, 1H), 4.77 (dd, 1H, J =6.1, 2.2 Hz), 5.49 (ddq, 1H, J = 15, 8.0, 1.7 Hz), 5.79 (dq, 1H, J = 15, 6.4 Hz), 6.39 (dd, 1H, J = 6.3, 1.2 Hz). ^{13}C NMR (CDCl_3) δ 14.9, 17.8, 40.7, 69.1, 81.0, 104.8, 128.9, 130.9, 144.7. MS [m/z] 154 (M^+), $[\alpha]_D^{22}$ = -88.9 (c 0.65, THF, >99% ee after recrystallization). HRMS (m/z) calcd. for $\text{C}_9\text{H}_{14}\text{O}_2$ (M^+): 154.0994; found: 154.0997. The enantiomeric excess of the product was determined by HPLC analysis (Daicel Chiralpak AD, hexane/*i*PrOH = 1000/1, flow rate = 1.0 mL/min: t_R = 20.5 min (major), t_R = 15.5 min (minor)) after benzylation using benzoyl chloride and pyridine, DMAP.

(4R,5S,6R)-4-Hydroxy-5-methyl-6-((E)-1-propenyl)-tetrahydro-2H-pyran-2-one ((+)-Prelactone C, 6): IR [cm^{-1}] (neat) 3434, 1730, 1454, 1376, 1244. ^1H NMR (CDCl_3) δ 1.03 (d, 3H, J = 6.7 Hz), 1.65 (m, 1H), 1.75 (dd, 3H, J = 6.8, 1.6 Hz), 2.49 (dd, 1H, J = 17, 8.6 Hz), 2.57 (br, 1H), 2.91 (dd, 1H, J = 17, 5.8 Hz), 3.77 (m, 1H), 4.19 (dd, 1H, J = 10.8, 6 Hz), 5.43 (ddq, 1H, J = 15, 8.2, 1.9 Hz), 5.80 (dq, 1H, J = 15, 6.7 Hz). ^{13}C NMR (CDCl_3) δ 13.7, 17.6, 39.1, 41.5, 69.5, 84.1, 127.6, 132.4, 170.4. MS [m/z] 170 (M^+), 152 ($(\text{M}-\text{H}_2\text{O})^+$). $[\alpha]_D^{24}$ = +65.4 (c 0.71, MeOH). lit.)³ $[\alpha]_D^{20}$ = +57.6 (c 0.5, MeOH). HRMS (m/z) calcd. for $\text{C}_9\text{H}_{14}\text{O}_3$ (M^+): 170.0943; found: 170.0972.

References

- (1) Danishefsky's dienes employed were prepared according to the procedures reported in the literatures. (a) Danishefsky, S.; Kitahara, T. *J. Am. Chem. Soc.* **1974**, *96*, 7807. (b) Bednarski, M.; Maring, C.; Danishefsky, S. *Tetrahedron Lett.* **1983**, *24*, 3451. (c) Myles, D. C.; Bigham, M. H. *Organic Synthesis* Vol.

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