Supporting Information For

Iridium-Catalyzed Asymmetric Hydrogenation of Racemic α-Substituted Lactones to Chiral Diols

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General: All reactions and manipulations which are sensitive to moisture or air were performed under inert atmosphere of nitrogen. All chemicals were purchased from J & K, Acros and Aldrich, and were used as received. Hydrogen gas (99.999%) was purchased from Boc Gas Inc., Tianjin. Anhydrous THF was distilled from sodium benzophenone ketyl. Anhydrous CH₂Cl₂, nPrOH and Et₃N were freshly distilled from calcium hydride. Anhydrous EtOH was freshly distilled from magnesium. Melting points were measured on a RY-I apparatus and uncorrected. ¹H NMR spectra were recorded at 400 MHz on Bruker AV 400 spectrometer. ¹³C NMR spectra were recorded at 100 MHz on Bruker AV 400 spectrometer. NMR spectra were recorded in deuterated chloroform (CDCl₃) as a solvent, with residual chloroform (δ 7.26 ppm. for ¹H NMR and δ 77.00 ppm. for ¹³C NMR) or tetramethylsilane (TMS, δ 0.00 ppm. for ¹H NMR) taken as the inert standard, and were reported in ppm. Abbreviations for signal coupling are as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Coupling constants were taken from the spectra directly and are uncorrected. Optical rotations were determined using a Perkin Elmer 341 polarimeter. HRMS were recorded on APEXII and ZAB-HS spectrometer. HPLC analyses were performed using Hewlett Packard Model HP1100 instruments with Chiralcel OJ-H, OD-H, AD-H, AS-H column.
(A) Preparation of racemic α-substituted δ-valerolactones

The racemic α-aryl substituted δ-valerolactones were prepared according to the literature method illustrated below.¹

\[
\begin{align*}
\text{Ar} - \text{CO}_2\text{H} & \xrightarrow{\text{THF, } -60 \, ^\circ\text{C to rt}} \text{BrCH}_2\text{CH}_2\text{CH}_2\text{Cl} \xrightarrow{\text{DBU}} \text{Ar} - \text{CO}_2\text{H} \xrightarrow{\text{THF, } 60 \, ^\circ\text{C}} \text{2a-l}
\end{align*}
\]

To a solution of arylacetic acids (25.0 mmol) in dry THF (100 mL) was added nBuLi (20.8 mL, 50.0 mmol, 2.4 M in hexane) dropwise at −60 °C under N₂ atmosphere and the temperature was maintained below −40 °C. After complete addition, the resultant mixture was slowly warmed to 0 °C and stirred at that temperature for 2 h. 1-Bromo-3-chloropropane (4.71 g, 30.0 mmol) was then added and the reaction allowed to warm to room temperature and stirred for 18 h. The reaction was quenched with 1N NaOH (50 mL) and transferred to a separatory funnel. The aqueous layer was collected and the organic extracted again with 1N NaOH (50 mL). The combined aqueous were re-acidified with 2N HCl (70 mL) and extracted with EtOAc (75 mL). The organic layer was washed with water (50 mL) and then concentrated in vacuo to yield an oil. The oil was redissolved in THF (50 mL), treated with DBU (3.74 mL, 25.0 mmol) and heated to 60 °C for 18 h. The resultant slurry was cooled to room temperature and filtered through a suction funnel. The solvent was concentrated in vacuo and the residue was purified by flash chromatography to offer the corresponding racemic α-aryl δ-valerolactones.

3-(Phenyl)tetrahydro-2H-pyran-2-one (2a)¹

\[\text{3H} \, \text{NMR (400 MHz, CDCl}_3\text{)} \, \delta \, 7.38 – 7.32 \, (m, \, 2\text{H}), \, 7.30 \, – \, 7.21 \, (m, \, 3\text{H}), \, 4.52 \, – \, 4.38 \, (m, \, 2\text{H}), \, 3.78 \, (dd, \, J = 10.0, \, 7.2 \, Hz, \, 1\text{H}), \, 2.34 \, – \, 2.23 \, (m, \, 1\text{H}), \, 2.14 \, – \, 1.92 \, (m, \, 3\text{H}). \]

13C NMR (100 MHz, CDCl₃) δ 172.5, 135.8, 134.2, 129.6, 129.0, 69.1, 46.5, 28.1, 21.9.

3-(4-Chlorophenyl)tetrahydro-2H-pyran-2-one (2b)

White solid, mp 50–52 °C, 78% yield. ¹H NMR (400 MHz, CDCl₃) δ 7.34–7.30 (m, 2H), 7.20–7.15 (m, 2H), 4.52–4.39 (m, 2H), 3.74 (dd, J = 10.4, 6.8 Hz, 1H), 2.34–2.21 (m, 1H), 2.11–1.95 (m, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 172.1, 137.2, 133.2, 129.6, 128.8, 69.2, 46.4, 28.1, 21.9. HRMS (ESI) Calcd for C₁₁H₉ClO₂Na ([M + Na]⁺): 233.0340, Found: 233.0339.

3-(4-Tolyltetrahydro-2H-pyran-2-one (2c)

White solid, mp 42–44 °C, 77% yield. ¹H NMR (400 MHz, CDCl₃) δ 7.19–7.10 (m, 4H), 4.52–4.37 (m, 2H), 3.74 (dd, J = 10.0, 7.2 Hz, 1H), 2.34 (s, 3H), 2.31–2.22 (m, 1H), 2.13–1.94 (m, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 172.7, 136.80, 135.8, 129.3, 128.0, 69.1, 46.5, 28.0, 21.8, 20.9. IR (KBr): 2955, 2931, 2856, 1513, 1415, 1354, 1219, 1161, 1039, 817, 734 cm⁻¹. HRMS (ESI) Calcd for C₁₂H₁₂O₂Na ([M + Na]⁺): 213.0886, Found: 213.0892.

3-(4-Methoxyphenyl)tetrahydro-2H-pyran-2-one (2d)²
3-(3-Chlorophenyl)tetrahydro-2H-pyran-2-one (2e)

Colorless oil, 81% yield. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.32–7.22 (m, 3H), 7.13 (dt, $J = 6.4$, 2.0 Hz, 1H), 4.52–4.41 (m, 2H), 3.75 (dd, $J = 10.4$, 6.8 Hz, 1H), 2.34–2.23 (m, 1H), 2.11–1.97 (m, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 171.8, 140.7, 134.4, 129.9, 128.5, 127.5, 126.5, 69.2, 46.7, 28.1, 21.9. HRMS (ESI) Calcd for C$_{11}$H$_{11}$ClO$_2$Na ([M + Na$^+$]): 233.0340, Found: 233.0345.

3-(3-Methoxyphenyl)tetrahydro-2H-pyran-2-one (2g)$^2$

Colorless oil, 77% yield. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.26 (t, $J = 7.2$ Hz, 1H), 7.10–6.99 (m, 3H), 4.47–4.36 (m, 2H), 3.72 (dd, $J = 9.6$, 6.8 Hz, 1H), 2.33 (s, 3H), 2.29–2.20 (m, 1H), 2.11–1.91 (m, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 172.5, 138.8, 138.1, 128.8, 128.4, 127.9, 125.1, 69.1, 46.9, 28.1, 21.8.

HRMS (ESI) Calcd for C$_{12}$H$_{12}$O$_2$Na ([M + Na$^+$]): 229.0836, Found: 229.0839.

3-(3,4-Dichlorophenyl)tetrahydro-2H-pyran-2-one (2h)

White solid, mp 96–98 °C, 43% yield. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.42 (d, $J = 8.4$ Hz, 1H), 7.34 (d, $J = 2.0$ Hz, 1H), 7.09 (dd, $J = 8.4$, 2.0 Hz, 1H), 4.52–4.40 (m, 2H), 3.72 (dd, $J = 10.4$, 7.2 Hz, 1H), 2.36–2.22 (m, 1H), 2.11–1.96 (m, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 171.5, 138.8, 132.6, 131.5, 130.6, 130.4, 127.8, 69.2, 46.2, 27.9, 22.0. IR (KBr): 2956, 1732, 1473, 1400, 1258, 1225, 1158, 1133, 1078, 1031, 961, 823 cm$^{-1}$. HRMS (ESI) Calcd for C$_{11}$H$_{10}$ClO$_2$Na ([M + Na$^+$]): 266.9951, Found:266.9954.

3-(3,4-Dimethoxyphenyl)tetrahydro-2H-pyran-2-one (2i)

White solid, mp 98–100 °C, 47% yield. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 6.86–6.80 (m, 1H), 6.79–6.72 (m, 2H), 4.49–4.38 (m, 2H), 3.89–3.82 (m, 6H), 3.75–3.67 (m, 1H), 2.35–2.21 (m, 1H), 2.12–1.92 (m, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 172.7, 148.9, 148.2, 131.2, 120.2, 111.4, 111.2, 69.1, 55.8, 46.6, 28.0, 21.9. IR (KBr): 2940, 1731, 1592, 1518, 1464, 1420, 1259, 1143, 1078, 1026, 961, 810, 759 cm$^{-1}$. HRMS (ESI) Calcd for C$_{13}$H$_{16}$O$_2$Na ([M + Na$^+$]): 259.0941, Found: 259.0945.

3-(2-Chlorophenyl)tetrahydro-2H-pyran-2-one (2j)

Colorless oil, 34% yield. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.19–7.13 (m, 2H), 6.92–6.85 (m, 2H), 4.50–4.38 (m, 2H), 3.80 (s, 3H), 3.73 (dd, $J = 10.0$, 6.8 Hz, 1H), 2.32–2.21 (m, 1H), 2.12–1.95 (m, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 172.9, 158.7, 130.8, 129.2, 114.1, 69.1, 55.2, 46.2, 28.1, 22.0.
Colorless oil, 76% yield. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.56–7.34 (m, 1H), 7.27–7.18 (m, 3H), 4.56–4.43 (m, 2H), 4.07 (dd, $J$ = 10.4, 7.2 Hz, 1H), 2.28–2.18 (m, 1H), 2.14–1.96 (m, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 171.2, 137.2, 133.2, 130.4, 129.94, 128.7, 127.2, 69.7, 45.6, 27.3, 22.6. IR (KBr): 2957, 1732, 1475, 1443, 1215, 1168, 1036, 751 cm$^{-1}$. HRMS (ESI) Calcd for C$_{11}$H$_{14}$ClO$_2$Na ([M + Na]$^+$): 233.0340, Found: 233.0344.

3-(2-Tolyl)tetrahydro-2H-pyran-2-one (2k)

Colorless oil, 82% yield. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.22–7.17 (m, 3H), 7.17–7.13 (m, 1H), 4.57–4.44 (m, 2H), 3.94 (dd, $J$ = 9.6, 7.2 Hz, 1H), 2.33 (s, 3H), 2.29–2.17 (m, 1H), 2.10–1.96 (m, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 172.2, 137.8, 135.6, 130.78, 128.1, 127.3, 126.3, 69.7, 44.5, 27.6, 22.3, 19.6. IR (KBr): 2957, 1731, 1491, 1462, 1208, 1160, 759, 733 cm$^{-1}$. HRMS (ESI) Calcd for C$_{12}$H$_{14}$O$_2$Na ([M + Na]$^+$): 213.0886, Found: 213.0890.

3-(2-Methoxyphenyl)tetrahydro-2H-pyran-2-one (2l)

White solid, mp 86–88 °C, 55% yield. $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.29–7.23 (m, 1H), 7.16 (dd, $J$ = 7.2, 1.6 Hz, 1H), 6.96–6.88 (m, 2H), 4.54–4.40 (m, 2H), 3.83 (s, 3H), 3.77 (dd, $J$ = 10.4, 7.6 Hz, 1H), 2.18–2.09 (m, 1H), 2.08–1.91 (m, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 172.2, 156.2, 129.9, 128.9, 128.6, 120.8, 111.2, 69.8, 55.4, 43.9, 27.8, 23.0. IR (KBr): 2945, 1729, 1495, 1463, 1246, 1147, 1087, 1025, 960, 755 cm$^{-1}$. HRMS (ESI) Calcd for C$_{13}$H$_{15}$O$_2$Na ([M + Na]$^+$): 229.0836, Found: 229.0840.

The racemic $\alpha$-alkyl substituted $\delta$-valerolactones were prepared via $\alpha$-alkylation of $\delta$-valerolactones according to the literature method illustrated below.$^5$

![Chemical Reaction Diagram]

To a solution of diisopropylamine (5.05 g, 50 mmol) in dry THF (80 mL) was added n-BuLi (20 mL, 48 mmol, 2.4 M in hexane) dropwise at 0 °C under N$_2$ atmosphere and the result mixture was stirred at that temperature for 10 min. Then HMPA (8.96 g, 50 mmol) was added to the solution with stirring over a period of 10 min. The reaction mixture was cooled to −78 °C and $\delta$-valerolactone (4.00 g, 40 mmol) in dry THF (160 mL) was added dropwise to the solution. After stirring 20 min, alkyl iodides (RI, 44 mmol) was added dropwise to the result solution and the result mixture was stirred at that temperature for 1 h. Then, the reaction solution was allowed to warm to −78 °C and stirred for further 1 h. The reaction mixture was quenched with saturated NH$_4$Cl (50 mL). The residue was extracted with EtOAc (50 mL × 3). The combined organic layers were washed with brine, dried over anhydrous MgSO$_4$, and concentrated in vacuo. The residue was chromatographed on silica gel column with EtOAc/petroleum ether as an eluent to offer the corresponding racemic $\alpha$-alkyl $\delta$-valerolactones.

3-Methyltetrahydro-2H-pyran-2-one (2m)$^5$

Colorless oil, 86% yield, $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 4.28–4.16 (m, 2H), 2.55–2.42 (m, 1H), 2.07–1.95 (m, 1H), 1.87–1.76 (m, 2H), 1.51–1.35 (m, 1H), 1.14 (d, $J$ = 6.8 Hz, 3H).
3-Ethyltetrahydro-2H-pyran-2-one (2n)\(^6\)

Colorless oil, 40% yield, \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta 4.35-4.17\) (m, 2H), 2.43-2.28 (m, 1H), 2.12-1.99 (m, 1H), 1.94-1.77 (m, 3H), 1.58-1.44 (m, 2H), 0.94 (t, \(J = 7.6\) Hz, 3H).

3-Isopropyltetrahydro-2H-pyran-2-one (2o)\(^7\)

Colorless oil, 11% yield, \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta 4.40-4.17\) (m, 2H), 2.49-2.32 (m, 2H), 2.01-1.81 (m, 3H), 1.71-1.52 (m, 1H), 0.99 (d, \(J = 5.6\) Hz, 3H), 0.94 (d, \(J = 5.6\) Hz, 3H).

3-(But-3-en-1-yl)tetrahydro-2H-pyran-2-one (2p)\(^8\)

Colorless oil, 51% yield, \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta 5.81-5.68\) (m, 1H), 5.04-4.90 (m, 2H), 4.31-4.19 (m, 2H), 2.49-2.37 (m, 1H), 2.19-1.93 (m, 4H), 1.92-1.79 (m, 2H), 1.57-1.43 (m, 2H).

(B) Asymmetric hydrogenation of racemic \(\alpha\)-substituted lactones

**General procedure:** To a 20 mL hydrogenation vessel in an autoclave was added racemic \(\alpha\)-substituted 6-valerolactone 2 (1.0 mmol), a solution of iridium catalyst (\(R\))-1d in \(^{t}\)PrOH (dried with MS 4Å for 12 h, 0.002 mmol/mL, 1.0 mL, 0.002 mmol), a solution of \(^{t}\)BuOK in \(^{t}\)PrOH (0.5 mmol/mL, 2.0 mL, 1.0 mmol) and \(^{t}\)PrOH (1.0 mL). The autoclave was purged with hydrogen by pressurizing to 5 atm and releasing the pressure. This procedure was repeated three times and then pressurized to 10 atm of H\(_2\). The reaction mixture was stirred at room temperature (25–30 °C) until no obvious hydrogen pressure drop was observed. The reaction mixture was then quenched with saturated NH\(_4\)Cl (5 mL) and extracted with EtOAc (5 mL \(\times\) 3). The combined extracts were washed with brine, dried over anhydrous MgSO\(_4\) and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel with petroleum ether/ethyl acetate as an eluent to afford the chiral diols 3.

The ee values of the chiral diols 3m, 3n, 3o, 3p and 3r were determined by transformation of them into the corresponding benzoyl esters. The general procedure was shown as follows: The chiral diols 3 (0.2 mmol) was reacted with benzoyl chloride (70 mg, 0.5 mmol) in the presence of pyridine (47 mg, 0.6 mmol) in DCM (5 mL) for 2 h. The reaction mixture was then quenched with saturated NH\(_4\)Cl (5 mL) and extracted with DCM (5 mL \(\times\) 3). The combined extracts were washed with brine, dried over anhydrous MgSO\(_4\) and concentrated in vacuo. After a flash chromatography on silica gel (petroleum ether/ethyl acetate = 10:1), the desired benzoyl esters were obtained in nearly quantitative yields.

\((R)-2\)-Phenylpentane-1,5-diol (3a)\(^9\)

Colorless oil, 10 h, 92% yield, 93% ee, \([\alpha]_D^{20} = 20.0\) (c 1.0, EtOH) [lit.\(^9\) \([\alpha]_D^{20} = +55.0\) (c 0.1, EtOH) for S-isomer]. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta 7.36-7.29\) (m, 2H), 7.27-7.17 (m, 3H), 3.73 (dd, \(J = 6.4, 2.4\) Hz, 2H), 3.58 (t, \(J = 6.4\) Hz, 2H), 2.84-2.72 (m, 1H), 1.89-1.73 (m, 3H), 1.69-1.56 (m, 1H), 1.54–
1.39 (m, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 142.1, 128.7, 128.0, 126.8, 67.4, 62.6, 48.3, 30.3, 28.1. HPLC conditions: Chiralcel AS-H column (25 cm × 0.46 cm ID); n-hexane/2-propanol = 80:20; temp, rt; flow rate = 1.0 mL/min; 220 nm UV detector; $t_R$ (S) = 5.63 min; $t_R$ (R) = 6.03 min

**(R)-2-(4-Chlorophenyl)pentane-1,5-diol (3b)**

White solid, mp 66–68 °C, 7 h, 93% yield, 93% ee, $[\alpha]^0_{D} = -15.2$ (c 1.0, EtOH). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.32–7.27 (m, 2H), 7.17–7.11 (m, 2H), 3.75–3.66 (m, 2H), 3.58 (t, $J$ = 6.4 Hz, 2H), 2.83–2.69 (m, 1H), 1.88–1.66 (m, 3H), 1.64–1.52 (m, 1H), 1.50–1.37 (m, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 140.7, 132.4, 129.3, 128.8, 67.2, 62.6, 47.7, 30.2, 28.1. IR (KBr): 3284, 2929, 2879, 1491, 1091, 1055, 1040, 1013, 824 cm$^{-1}$. HPLC conditions: Chiralcel AS-H column (25 cm × 0.46 cm ID); n-hexane/2-propanol = 94:6; temp, rt; flow rate = 1.0 mL/min; 220 nm UV detector; $t_R$ (S) = 21.16 min and $t_R$ (R) = 22.82 min. HRMS (ESI) Caled for C$_{11}$H$_{15}$ClO$_2$Na ([M + Na]$^+$): 237.0653, Found: 237.0658.

**(R)-2-(4-Tolyl)pentane-1,5-diol (3c)**

Colorless oil, 9 h, 92% yield, 93% ee, $[\alpha]^0_{D} = -20.6$ (c 1.0, EtOH). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.17–7.07 (m, 4H), 3.78–3.65 (m, 2H), 3.57 (t, $J$ = 6.4 Hz, 2H), 2.81–2.69 (m, 1H), 2.32 (s, 3H), 1.87–1.76 (m, 3H), 1.65–1.54 (m, 1H), 1.52–1.39 (m, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 138.9, 136.3, 129.4, 127.9, 67.5, 62.7, 47.9, 30.4, 28.1, 21.0. IR (KBr): 3331, 2936, 2868, 1514, 1453, 1056, 1036, 815 cm$^{-1}$. HPLC conditions: Chiralcel OJ-H column (25 cm × 0.46 cm ID); n-hexane/2-propanol = 92:8; temp, rt; flow rate = 1.0 mL/min; 220 nm UV detector; $t_R$ (S) = 13.81 min and $t_R$ (R) = 15.47 min. HRMS (ESI) Caled for C$_{13}$H$_{16}$O$_2$Na ([M + Na]$^+$): 217.1199, Found: 217.1202.

**(R)-2-(4-Methoxyphenyl)pentane-1,5-diol (3d)**

White solid, m.p. 48–50 °C, 10 h, 93% yield, 93% ee, $[\alpha]^0_{D} = -19.6$ (c 1.0, EtOH). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.18–7.08 (m, 2H), 6.91–6.81 (m, 2H), 3.80 (s, 3H), 3.75–3.63 (m, 2H), 3.59 (t, $J$ = 6.4 Hz, 2H), 2.81–2.67 (m, 1H), 1.88–1.71 (m, 3H), 1.69–1.55 (m, 1H), 1.53–1.41 (m, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 158.4, 143.4, 128.9, 114.1, 67.6, 62.8, 55.2, 47.5, 30.5, 28.2. HPLC conditions: Chiralcel AS-H column (25 cm × 0.46 cm ID); n-hexane/2-propanol = 80:20; temp, rt; flow rate = 1.0 mL/min; 220 nm UV detector; $t_R$ (S) = 7.78 min; $t_R$ (R) = 8.64 min.

**(R)-2-(3-Chlorophenyl)pentane-1,5-diol (3e)**

Colorless oil, 7 h, 95% yield, 92% ee, $[\alpha]^0_{D} = -14.2$ (c 1.0, EtOH). $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.33–7.22 (m, 3H), 7.16–7.11 (m, 1H), 3.81–3.72 (m, 2H), 3.63 (t, $J$ = 6.4 Hz, 2H), 2.86–2.75 (m, 1H), 2.00–1.82 (m, 3H), 1.69–1.57 (m, 1H), 1.56–1.42 (m, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 144.5, 134.4, 129.9, 128.1, 126.9, 126.3, 67.1, 62.5, 48.1, 30.21, 28.0. IR (KBr): 3319, 2839, 2871, 1596, 1571, 1474, 1430, 1055, 1037, 785, 746, 698 cm$^{-1}$. HPLC conditions: Chiralcel OJ-H column (25 cm × 0.46 cm ID); n-hexane/2-propanol = 92:8; temp, rt; flow rate = 1.0 mL/min; 220 nm
UV detector; \( t_R (S) = 11.84 \) min and \( t_R (R) = 12.42 \) min. HRMS (ESI) Calcd for \( C_{11}H_{15}ClO_2Na ([M + Na]^+) \): 237.0653, Found: 237.0658.

**(R)-2-(3-Toly)pentane-1,5-diol (3f)**

Colorless oil, 10 h, 91% yield, 93% ee, \([\alpha]_D^{20} = -21.0 \) (c 1.0, EtOH). \(^1^H\) NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.25–7.18 (m, 1H), 7.08–6.97 (m, 3H), 3.77–3.68 (m, 2H), 3.59 (t, \( J = 6.4 \) Hz, 2H), 2.80–2.70 (m, 1H), 2.34 (s, 3H), 1.87–1.76 (m, 1H), 1.71 (s, 2H), 1.67–1.57 (m, 1H), 1.53–1.41 (m, 2H). \(^{13}^C\) NMR (100 MHz, CDCl\(_3\)) \( \delta \) 142.0, 138.3, 128.8, 128.6, 127.6, 125.0, 67.5, 62.7, 48.3, 30.4, 28.1, 21.5. IR (KBr): 3331, 2937, 2868, 1607, 1454, 1056, 1038, 785, 704 cm\(^{-1}\). HPLC conditions: Chiralcel AS-H column (25 cm × 0.46 cm ID); \( n \)-hexane/2-propanol = 90:10; temp; rt; flow rate = 1.0 mL/min; 220 nm UV detector; \( t_R (S) = 10.03 \) min; \( t_R (R) = 11.44 \) min. HRMS (ESI) Calcd for \( C_{12}H_{16}O_2Na ([M + Na]^+) \): 217.1199, Found: 217.1201.

**(R)-2-(3-Methoxyphenyl)pentane-1,5-diol (3g)**\(^\text{10}^\)

Colorless oil, 10 h, 93% yield, 92% ee, \([\alpha]_D^{20} = -10.2 \) (c 1.0, CHCl\(_3\)). [lit.\(^\text{10}^\) \([\alpha]_D^{20} = +10.7 \) (c 1.0, CHCl\(_3\)) for \( S \)-isomer]. \(^1^H\) NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.27–7.22 (m, 1H), 6.83–6.74 (m, 3H), 3.80 (s, 3H), 3.73 (dd, \( J = 6.8, 2.7 \) Hz, 2H), 3.59 (t, \( J = 6.4 \) Hz, 2H), 2.83–2.71 (m, 1H), 1.88–1.72 (m, 3H), 1.68–1.56 (m, 1H), 1.53–1.41 (m, 2H). \(^{13}^C\) NMR (100 MHz, CDCl\(_3\)) \( \delta \) 159.8, 143.8, 129.7, 120.3, 114.0, 111.7, 67.4, 62.7, 55.1, 48.4, 30.4, 28.1. HPLC conditions: Chiralcel OD-H column (25 cm × 0.46 cm ID); \( n \)-hexane/2-propanol = 90:10; temp, rt; flow rate = 1.0 mL/min; 220 nm UV detector; \( t_R (S) = 17.07 \) min and \( t_R (R) = 19.76 \) min.

**(R)-2-(3,4-Dichlorophenyl)pentane-1,5-diol (3h)**

Colorless oil, 7 h, 94% yield, 92% ee, \([\alpha]_D^{20} = -8.8 \) (c 1.0, EtOH). \(^1^H\) NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.40 (d, \( J = 8.0 \) Hz, 1H), 7.32 (d, \( J = 2.0 \) Hz, 1H), 7.07 (dd, \( J = 8.0, 2.0 \) Hz, 1H), 3.81–3.68 (m, 2H), 3.62 (t, \( J = 6.4 \) Hz, 2H), 2.82–2.71 (m, 1H), 1.89–1.78 (m, 1H), 1.68–1.55 (m, 1H), 1.53–1.38 (m, 3H), 1.32 (s, 1H). \(^{13}^C\) NMR (100 MHz, CDCl\(_3\)) \( \delta \) 142.9, 132.5, 130.5, 130. 5, 129. 9, 127.4, 66.7, 62.3, 47.4, 30.0, 27.9. IR (KBr): 3319, 2937, 2872, 1470, 1403, 1132, 1057, 1029, 821, 618 cm\(^{-1}\). HPLC conditions: Chiralcel OD-H column (25 cm × 0.46 cm ID); \( n \)-hexane/2-propanol = 97:3; temp, rt; flow rate = 1.0 mL/min; 220 nm UV detector; \( t_R (S) = 54.51 \) min and \( t_R (R) = 57.04 \) min. HRMS (ESI) Calcd for \( C_{11}H_{13}Cl_3O_2Na ([M + Na]^+) \): 271.0264, Found: 271.0265.

**(R)-2-(3,4-Dimethoxyphenyl)pentane-1,5-diol (3i)**

Colorless oil, 10 h, 91% yield, 91% ee, \([\alpha]_D^{20} = -17.6 \) (c 1.0, EtOH). \(^1^H\) NMR (400 MHz, CDCl\(_3\)) \( \delta \) 6.82 (d, \( J = 8.4 \) Hz, 1H), 6.78–6.70 (m, 2H), 3.87 (s, 3H), 3.85 (s, 3H), 3.76–3.65 (m, 2H), 3.59 (t, \( J = 6.4 \) Hz, 2H), 2.79–2.66 (m, 1H), 1.85–1.75 (m, 1H), 1.72–1.54 (m, 3H), 1.52–1.42 (m, 2H). \(^{13}^C\) NMR (100 MHz, CDCl\(_3\)) \( \delta \) 149.1, 147.8, 134.5, 119.9, 111.4, 111.0, 67.5, 62.7, 55.9, 48.0, 30.4, 28.2. IR (KBr): 3347, 2936, 2871, 1517, 1461, 1261, 1234, 1141, 1027, 810, 763 cm\(^{-1}\). HPLC conditions: Chiralcel OJ-H column (25 cm × 0.46 cm ID);
\( n\)-hexane/2-propanol = 90:10; temp, rt; flow rate = 1.0 mL/min; 220 nm UV detector; \( t_R (R) = 45.61 \) min and \( t_R (S) = 52.24 \) min. HRMS (ESI) Calcd for C\(_{12}\)H\(_{30}\)O\(_2\)Na ([M + Na]\(^+\)): 263.1254, Found: 263.1258.

\((R)-2-(2\text{-Chlorophenyl})\)pentane-1,5-diol (3j)

Colorless oil, 13 h, 89% yield, 78% ee, \([\alpha]_D^{20} -20.0 (c 1.0, \text{EtOH})\). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.41–7.36 (m, 1H), 7.30–7.23 (m, 2H), 7.21–7.13 (m, 1H), 3.83–3.73 (m, 2H), 3.62 (t, \(J = 6.4, 2H\), 3.53–3.43 (m, 1H), 1.98–1.87 (m, 1H), 1.84–1.61 (m, 3H), 1.60–1.41 (m, 2H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 139.6, 134.9, 129.8, 128.0, 127.7, 127.1, 66.2, 62.7, 43.2, 30.1, 27.5. IR (KBr): 3318, 2940, 2869, 1475, 1439, 1043, 754, 687 cm\(^{-1}\). HPLC conditions: Chiralcel OJ-H column (25 cm \(\times\) 0.46 cm ID); \(n\)-hexane/2-propanol = 90:10; temp, rt; flow rate = 1.0 mL/min; 220 nm UV detector; \(t_R (S) = 10.00 \) min and \( t_R (R) = 13.11 \) min. HRMS (ESI) Calcd for C\(_{11}\)H\(_{15}\)ClO\(_2\)Na ([M + Na]\(^+\)): 237.0653, Found: 237.0660.

\((R)-2-(2\text{-Tolyl})\)pentane-1,5-diol (3k)

Colorless oil, 36 h, 84% yield, 77% ee, \([\alpha]_D^{20} -20.9 (c 1.0, \text{EtOH})\). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.23–7.08 (m, 4H), 3.69 (d, \(J = 6.8 \) Hz, 2H), 3.55 (td, \(J = 6.4, 1.6 \) Hz, 2H), 3.19–3.09 (m, 1H), 2.34 (s, 3H), 2.24 (s, 2H), 1.94–1.81 (m, 1H), 1.69–1.56 (m, 1H), 1.52–1.35 (m, 2H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 140.3, 137.0, 130.5, 126.3, 126.2, 125.8, 67.0, 62.6, 42.5, 30.2, 28.1, 19.9. IR (KBr): 3315, 2941, 2868, 1490, 1461, 1265, 1061, 1035, 756, 733 cm\(^{-1}\). HPLC conditions: Chiralcel AD-H column (25 cm \(\times\) 0.46 cm ID); \(n\)-hexane/2-propanol = 90:10; temp, rt; flow rate = 1.0 mL/min; 220 nm UV detector; \(t_R (S) = 15.89 \) min and \( t_R (R) = 16.77 \) min. HRMS (ESI) Calcd for C\(_{12}\)H\(_{19}\)O\(_2\)Na ([M + Na]\(^+\)): 217.1199, Found: 217.1203.

\((R)-2-(2\text{-Methoxyphenyl})\)pentane-1,5-diol (3l)

White solid, m.p. 88–90°C, 20 h, 88% yield, 86% ee, \([\alpha]_D^{20} -21.8 (c 1.0, \text{EtOH})\). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.23–7.14 (m, 2H), 6.93 (td, \(J = 7.6, 0.8 \) Hz, 1H), 6.87 (dd, \(J = 8.4, 0.8 \) Hz, 1H), 3.80 (s, 3H), 3.73 (dd, \(J = 6.4, 3.2 \) Hz, 2H), 3.58 (td, \(J = 6.4, 1.6 \) Hz, 2H), 3.56–3.27 (m, 2H), 1.90–1.79 (m, 1H), 1.71–1.60 (m, 1H), 1.53–1.43 (m, 2H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 157.6, 130.2, 127.9, 127.4, 120.7, 110.7, 66.4, 62.7, 55.4, 40.5, 30.3, 27.1. IR (KBr): 3325, 2938, 2868, 1492, 1462, 1240, 751 cm\(^{-1}\). HPLC conditions: Chiralcel OJ-H column (25 cm \(\times\) 0.46 cm ID); \(n\)-hexane/2-propanol = 90:10; temp, rt; flow rate = 1.0 mL/min; 220 nm UV detector; \(t_R (S) = 10.20 \) min and \( t_R (R) = 12.40 \) min. HRMS (ESI) Calcd for C\(_{12}\)H\(_{18}\)O\(_3\)Na ([M + Na]\(^+\)): 233.1149, Found: 233.1152.

\((S)-2\text{-Methylpentane-1,5-diol} (3m)\)

Colorless oil, 8 h, 92% yield, 91% ee, \([\alpha]_D^{20} -16.7 (c 1.0, \text{CHCl}_3)\). [lit. \([\alpha]_D^{20} -18 (c 0.8, \text{CHCl}_3)\)]. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 3.58 (t, \(J = 6.0 \) Hz, 2H), 3.46–3.36 (m, 4H), 1.66–1.55 (m, 2H), 1.54–1.44 (m, 2H), 1.18–1.06 (m, 1H), 0.87 (d, \(J = 6.8 \) Hz, 3H). HPLC conditions: Chiralcel OD-H column (25 cm \(\times\) 0.46 cm ID); \(n\)-hexane/2-propanol = 90:10; temp, rt; flow rate = 1.0 mL/min; 220 nm UV detector; \(t_R (R) = 11.54 \) min; \(t_R (S) = 12.66 \) min

\((S)-2\text{-Ethylpentane-1,5-diol} (3n)\)
Colorless oil, 12 h, 90% yield, 87% ee, [α]_D^20 = -3.0 (c 1.0, CHCl₃). ¹H NMR (400 MHz, CDCl₃) δ 3.62–3.53 (m, 3H), 3.49–3.39 (m, 3H), 1.58–1.49 (m, 2H), 1.44–1.35 (m, 2H), 1.35–1.25 (m, 3H), 0.86 (t, J = 7.2 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃) δ 64.5, 62.7, 41.5, 23.4, 23.4, 11.2. IR (KBr): 3305, 2930, 2873, 1456, 1379, 1052 cm⁻¹. HPLC conditions: Chiralcel OD-H column (25 cm × 0.46 cm ID); n-hexane/2-propanol = 99:1; temp, rt; flow rate = 1.0 mL/min; 220 nm UV detector; tₚ (R) = 18.58 min; tₚ (S) = 19.85 min.

(R)-2-Isopropylpentane-1,5-diol (3o)¹¹

Colorless oil, 12 h, 90% yield, 95% ee, [α]_D^20 = -7.3 (c 1.0, CHCl₃). [lit.¹¹ [α]_D^20 = -7.11 (c 0.6, CHCl₃)]. ¹H NMR (400 MHz, CDCl₃) δ 3.72–3.60 (m, 3H), 3.58–3.51 (m, 1H), 2.07 (s, 2H), 1.83–1.68 (m, 1H), 1.66–1.54 (m, 2H), 1.50–1.29 (m, 3H), 0.91 (s, 3H), 0.90 (s, 3H). HPLC conditions: Chiralcel OD-H column (25 cm × 0.46 cm ID); n-hexane/2-propanol = 98:2; temp, rt; flow rate = 1.0 mL/min; 220 nm UV detector; tₚ (R) = 12.02 min.

(S)-2-(But-3-en-1-yl)pentane-1,5-diol (3p)²

Colorless oil, 12 h, 91% yield, 88% ee, [α]_D^20 = -4.3 (c 1.0, CHCl₃). [lit.² [α]_D^20 = 11.24 min; 1,4-HPLC conditions: Chiralcel OD-H column (25 cm × 0.46 cm ID); n-hexane/2-propanol = 99:1; temp, rt; flow rate = 1.0 mL/min; 220 nm UV detector; tₚ (R) = 23.17 min; tₚ (S) = 24.95 min. HRMS (ESI) Calcd for C₁₉H₂₀O₄Na ([M + Na]⁺): 318.1199, Found: 318.1195.

(R)-2-Phenylbutane-1,4-diol (3q)²¹

Colorless oil, 10 h, 80% yield, 80% ee, [α]_D^20 = -19.0 (c 1.0, CHCl₃). [lit.²¹ [α]_D^20 = -39 (c 0.3, CHCl₃)]. ¹H NMR (400 MHz, CDCl₃) δ 7.34–7.28 (m, 2H), 7.25–7.19 (m, 3H), 3.73 (dd, J = 6.8, 2.8 Hz, 2H), 3.69–3.61 (m, 1H), 3.57–3.49 (m, 1H), 3.27 (brs, 2H), 2.99–2.87 (m, 1H), 2.09–1.95 (m, 1H), 1.93–1.79 (m, 1H). HPLC conditions: Chiralcel AD-3 column (25 cm × 0.46 cm ID); n-hexane/2-propanol = 97:3; temp, rt; flow rate = 1.0 mL/min; 220 nm UV detector; tₚ (S) = 50.70 min; tₚ (R) = 50.78 min.

(S)-2-Methylbutane-1,4-diol (3r)²²

Colorless oil, 10 h, 82% yield, 69.1% ee, [α]_D^20 = -9.4 (c 1.0, CHCl₃). [lit.²² [α]_D^20 = +22.6 (c 0.6, CHCl₃) for R-isomer]. ¹H NMR (400 MHz, CDCl₃) δ 3.81–3.70 (m, 1H), 3.67–3.58 (m, 2H), 3.56–3.50 (m, 2H), 3.39 (dd, J = 10.8, 7.6 Hz, 1H), 1.85–1.74 (m, 1H), 1.66–1.45 (m, 2H), 0.91 (d, J = 6.8 Hz, 3H). HPLC conditions: Chiralcel OD-H column (25 cm × 0.46 cm ID); n-hexane/2-propanol = 95:5; temp, rt; flow rate = 1.0 mL/min; 220 nm UV detector; tₚ (R) = 7.89 min; tₚ (S) = 8.65 min.

(C) Investigation the pathway of hydrogenation of racemic α-substituted lactones

Monitoring of the hydrogenation of rac-2a by NMR

According to the general procedure for the asymmetric hydrogenation of rac-2, the hydrogenations
of rac-2a (1.0 mmol-scale) were performed in parallel with (R)-1d as a catalyst and stopped after reaction for 0.5, 1, 2, 4, 6, 8, 10 h, respectively. The conversions or yields and ee values were determined by 1H NMR and HPLC. The data and the plot are outlined in Table S1. For the reason of the lactone rac-2a was readily alcoholized with alcohol under the reaction conditions, we observed the formation of propyl 5-hydroxy-2-phenylpentanoate (4) during the hydrogenations.

Propyl 5-hydroxy-2-phenylpentanoate (4):

\[
\text{Ph} \quad \text{O}_{\text{Pr}} \quad \text{O} \quad \text{OH}
\]

Colorless oil. 1H NMR (400 MHz, CDCl_3) δ 7.38–7.20 (m, 5H), 4.20–3.87 (m, 2H), 3.66 (t, 2H), 3.59 (t, J = 7.7 Hz, 1H), 2.29–2.07 (m, 1H), 2.00–1.79 (m, 1H), 1.67–1.49 (m, 4H), 0.88 (t, J = 7.4 Hz, 3H). 13C NMR (400 MHz, CDCl_3) δ 174.2, 139.1, 128.6, 127.9, 127.29, 66.4, 62.4, 51.5, 30.7, 29.7, 22.0, 10.3. IR (KBr): 3310, 2919, 1731, 1455, 1261, 1160, 750 cm\(^{-1}\). HRMS (ESI) Calcd for C_{14}H_{20}O_{3}H ([M + H]+): 237.1485, Found: 237.1483.

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Table S1 The data of asymmetric hydrogenation of rac-2a.

Asymmetric hydrogenation of hydroxyl ester rac-4 and MOM-protected hydroxyl ester rac-5

\[
\text{Ph} \quad \text{O}_{\text{Pr}} \quad \text{O} \quad \text{H}_2 \quad \text{Ph} \quad \text{OH} \quad \text{OR}
\]

\[4 \text{ (R = H)} \quad 0.2 \text{ mol\% (R)-1d} \quad \text{NTP, NTPH, 25–30 °C, 10 h} \quad 6 \text{ (R = CH}_2\text{OMe), no reaction}\]

The hydrogenations of hydroxyl ester rac-4 and MOM-protected hydroxyl ester rac-5 were performed according to the general procedure for the asymmetric hydrogenation of rac-2 (1.0 mmol-scale) with (R)-1d as a catalyst in nPrOH.

**Hydroxyl ester rac-4**: 10 h, 93% yield, 93% ee.

**MOM-protected hydroxyl ester rac-5**: 10 h, no reaction.

The MOM-protected hydroxyl ester rac-5 was synthesized as below according to literature method.\(^{14}\)
To a stirred solution of DMAP (61 mg, 0.5 mmol) and compound 4 (118 mg, 0.5 mol) in DMF (2 mL) was added \( \text{Pr}_2\text{NEt} \) (1.1 mL) and MOMCl (190 \( \mu \)L, 2.5 mmol) at room temperature under N\(_2\) atmosphere. The resulting mixture was allowed to warm up to 90 °C. After the reaction mixture stirred for 3 h, DMF was removed in vacuo and the residue was diluted with EtOAc (10 mL) and washed with saturated NaHCO\(_3\), brine and dried over MgSO\(_4\) and concentrated in vacuo to afford a crude product, which was purified by flash column chromatography on silical gel (petroleum ether/ethyl acetate = 8:1) to afford the compound 5 (123 mg, 88% yield). \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.36–7.15 (m, 5H), 4.59 (s, 2H), 4.13–3.86 (m, 2H), 3.54 (dt, \( J \) = 12.8, 7.1 Hz, 3H), 3.34 (s, 3H), 2.27–2.00 (m, 1H), 1.98–1.75 (m, 1H), 1.64–1.38 (m, 4H), 0.85 (t, \( J \) = 7.4 Hz, 3H), \(^{13}\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 173.0, 138.1, 127.6, 126.9, 126.2, 95.3, 66.2, 65.3, 54.1, 50.5, 29.1, 26.7, 20.9. IR (KBr): 2931, 2879, 1731, 1454, 1147, 1110, 1039, 917, 698 cm\(^{-1}\). HRMS (ESI) Calcd for C\(_{16}\)H\(_{24}\)O\(_4\)H ([M + H]\(^+\)): 281.1747, Found: 281.1743.

(D) Asymmetric synthesis of \((-\)-preclamol and compound 8

Asymmetric synthesis of \((-\)-preclamol

The asymmetric synthesis of \((-\)-preclamol was outlined below.

The asymmetric hydrogenation of \( \text{rac-2g} \) at 1.65 g (80 mmol) scale was according to the general procedure for the asymmetric hydrogenation of racemic \( \alpha \)-substituted \( \delta \)-valerolactones and under the same reaction conditions (10 atm, 10 h), and yielded (S)-3g in 89% yield (1.50 g) with 93% ee.

To a solution of (S)-3g (1.49 g, 7.1 mmol) in DCM (40 mL) was added NEt\(_3\) (3.0 mL, 21.3 mmol) and MsCl (1.4 mL, 17.8 mmol) at –20 °C under N\(_2\) atmosphere. After the reaction mixture was stirred for 2 h, saturated NaHCO\(_3\) (20 mL) was added. The layers were separated and the aqueous layer was extracted with DCM (20 mL \( \times \) 3). The combined organic layers were washed with brine, dried over MgSO\(_4\) and concentrated in vacuo. To the crude residue was added 48% HBr (20 mL) and the mixture was stirred at 120 °C for 2 h. After cooling to room temperature, saturated NaHCO\(_3\) was added to the reaction mixture to pH 7 at 0 °C. The solution was extracted with DCM (20 mL \( \times \) 3), and the combined extracts were washed with brine, dried over anhydrous MgSO\(_4\) and concentrated in vacuo to afford a crude product, which was purified by flash column chromatography on silical gel (petroleum ether/ethyl acetate = 1:1) to afford the \((-\)-preclamol (1.31 g, 84% yield over three
steps) as a yellow oil,\textsuperscript{4} [\(\alpha\)]\textsubscript{D}\textsuperscript{20} = -19.1 (c 2.0, CHCl\textsubscript{3}) [lit.\textsuperscript{4} [\(\alpha\)]\textsubscript{D}\textsuperscript{20} = -20.9 (c 1.8, CHCl\textsubscript{3})]. \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 9.35 (s, 1H), 7.18 (t, \(J = 8.0\) Hz, 1H), 6.79 (s, 1H), 6.76–6.68 (m, 2H), 3.24 (d, \(J = 11.2\) Hz, 1H), 3.09 (d, \(J = 10.8\) Hz, 1H), 2.97–2.90 (m, 1H), 2.47–2.27 (m, 2H), 2.07–1.91 (m, 3H), 1.89–1.70 (m, 2H), 1.61–1.48 (m, 3H), 0.87 (t, \(J = 7.2\) Hz, 3H). \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) \(\delta\) 157.0, 145.3, 129.8, 117.2, 114.7, 114.3, 61.4, 61.2, 54.0, 41.8, 29.8, 25.2, 19.2, 12.0.

### Asymmetric synthesis of compound 9

The asymmetric synthesis of compound 9 was outlined below.

\[
\text{(S)-3p (88% ee)} \overset{\text{I₂, NaHCO₃}}{\text{CH₃CN, 0 °C to rt, 2 h}} \overset{7 (\text{trans/cis} = 2:1)}{\text{NaCN}} \overset{\text{DMSO, 80 °C, 3 h}}{\text{9 (\text{trans/cis} = 5:1)}} \overset{9\text{MeO}_2\text{C}^\text{O}}{\text{MeO}_2\text{C}^\text{O}} \overset{\text{8 (\text{trans/cis} = 2:1)}}{\text{reflux, 20 h}} \overset{79\% (2\text{ steps})}{\text{MeO}_2\text{C}^\text{O}}
\]

To a solution of (S)-3p (790 mg, 5.0 mmol) in CH₃CN (60 mL) was added NaHCO₃ (1.26 g, 15 mmol) at room temperature under N\textsubscript{2} atmosphere. The reaction mixture was vigorously stirred for 15 min and cooling to 0 °C followed by addition of I\textsubscript{2}. After at room temperature stirring for 2 h, saturated Na\textsubscript{2}SO\textsubscript{4} was added to the solution. The layers were separated and the aqueous layer was extracted with DCM (30 mL \(\times\) 3). The combined organic layers were washed with brine, dried over MgSO\textsubscript{4} and concentrated in vacuo to afford the desired compound 7 (1.33 g, 94% yield) as a mixture of trans and cis-isomer in a ratio of 2:1. Colorless oil. [\(\alpha\)]\textsubscript{D}\textsuperscript{20} +5.4 (c 1.0, CHCl\textsubscript{3}). \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 4.07–3.99 (m, 0.7H), 3.87–3.80 (m, 0.3H), 3.73–3.60 (m, 2.3H), 3.43–3.33 (m, 0.3H), 3.31–3.18 (m, 2.7H), 3.12 (t, \(J = 11.2\) Hz, 0.7H), 2.00–1.91 (m, 0.7H), 1.90–1.83 (m, 0.7H), 1.79–1.72 (m, 0.6H), 1.68–1.47 (m, 5H), 1.43–1.12 (m, 3H). \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) \(\delta\) 76.8, 76.7, 73.6, 70.8, 62.7, 62.7, 35.1, 33.0, 31.45, 30.6, 29.8, 29.6, 28.1, 26.8, 26.8, 26.8, 26.1, 9.73, 9.67. HRMS (ESI) Calcd for C\textsubscript{2}H\textsubscript{13}O\textsubscript{2} ([M + H\textsuperscript{+}]): 285.0346, Found: 285.0346.

To the solution of 7 (1.33 g, 4.7 mmol) in DMSO (50 mL) was added NaCN (490 mg, 10 mmol). The reaction mixture was heated at 80 °C for 3 h and then cooled to room temperature. The solvent was removed in vacuo and the resulting was added H\textsubscript{2}O (20 mL). The solution was extracted with EtOAc (20 mL \(\times\) 3) and the combined extracts were washed with brine, dried over anhydrous MgSO\textsubscript{4} and concentrated in vacuo to afford the desired compound 8 as a colorless oil (0.78 g, 91% yield). [\(\alpha\)]\textsubscript{D}\textsuperscript{20} +1.0 (c 1.0, CHCl\textsubscript{3}). \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 4.03–3.95 (m, 0.65 H), 3.80 (d, \(J = 11.2\) Hz, 0.35H), 3.71–3.57 (m, 2.70H), 3.53–3.48 (m, 0.65H), 3.08 (t, \(J = 11.2\) Hz, 0.65H), 2.52 (m, 2H), 2.02–1.92 (m, 0.65H), 1.83–1.71 (m, 1.35H), 1.67–1.52 (m, 4H), 1.51–1.40 (m, 1H), 1.28–1.11 (m, 2H). \textsuperscript{13}C NMR (101 MHz, CDCl\textsubscript{3}) \(\delta\) 117.4, 73.6, 72.8, 71.0, 62.8, 62.7, 35.0, 32.8, 30.9, 30.7, 29.7, 29.6, 28.3, 26.7, 26.3, 26.0, 24.7, 24.5. HRMS (ESI) Calcd for C\textsubscript{2}H\textsubscript{10}N\textsubscript{2}O\textsubscript{2} ([M + NH\textsuperscript{+}]): 201.1603, Found: 201.1598.

The compound 8 (0.78 g, 4.3 mmol) was then added to a solution of NaOH (2.0 g, 50.0 mmol) in 50 mL of a 3:1 mixture of EtOH/H\textsubscript{2}O. The reaction mixture was heated to reflux for 20 h. After cooling to 0 °C, the reaction mixture was acidified with 2 N HCl to pH > 1. The solution was concentrated in vacuo again and the remaining solution was extracted with EtOAc (20 mL \(\times\) 3). The combined extracts
were washed with brine, dried over anhydrous MgSO$_4$ and concentrated in vacuo to afford the desired carboxylic acid as a crude product. The crude carboxylic acid was then redissolved in MeOH (20 mL) and several drops of conc. H$_2$SO$_4$ (0.5–1.0 mL) was added. The reaction mixture was refluxed for 20 h and concentrated in vacuo to yield a residue. The residue was diluted with EtOAc (20 mL), and neutralized with 1 N NaOH solution to pH 7 at 0 °C. The organic solution was separated and the aqueous solution was extracted with EtOAc (20 mL × 3). The combined organic solution was then dried over anhydrous MgSO$_4$, concentrated in vacuo and the residue was purified by flash chromatography (petroleum ether/ethyl acetate = 10:1) to offer the corresponding compound 9 (0.73 g, 79% yield) as a colorless oil (trans/cis = 5:1). $[\alpha]_{D}^{20}$ −10.9 (c 1.0, CHCl$_3$). $^1$H NMR (400 MHz, CDCl$_3$) δ 3.91–3.83 (m, 1H), 3.71–3.59 (m, 4H), 3.54 (t, $J = 8.4$ Hz, 2H), 3.01 (t, $J = 11.2$ Hz, 1H), 2.47 (dd, $J = 15.2, 8.0$ Hz, 1H), 2.35 (dd, $J = 15.2, 4.8$ Hz, 1H), 2.14 (s, 1H), 2.14–1.80 (m, 1H), 1.70–1.58 (m, 1H), 1.57–1.38 (m, 3H), 1.35–1.22 (m, 1H), 1.21–1.01 (m, 3H). $^1$C NMR (100 MHz, CDCl$_3$) δ 171.8, 74.1, 73.4, 62.6, 51.6, 41.1, 35.2, 31.3, 30.0, 29.6, 28.3. HRMS (ESI) Calcd for C$_{11}$H$_{20}$O$_4$Na ([M + Na]$^+$): 239.1254, Found: 239.1252.

References:
(E) NMR spectra of new compounds

3-(4-Chlorophenyl)tetrahydro-2H-pyran-2-one (2b)
3-(4-Tolyl)tetrahydro-2H-pyran-2-one (2c)
3-(3-Chlorophenyl)tetrahydro-2H-pyran-2-one (2e)
3-(3,4-Dichlorophenyl)tetrahydro-2H-pyran-2-one (2h)
3-(2-Chlorophenyl)tetrahydro-2H-pyran-2-one (2j)
3-(2-Toly1)tetrahydro-2H-pyran-2-one (2k)
3-(2-Methoxyphenyl)tetrahydro-2H-pyran-2-one (2l)
3-(But-3-en-1-yl)tetrahydro-2H-pyran-2-one (2p)

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5 Owner | mnr
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7 Spectrometer | spect
8 Author | test
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(R)-2-(4-Chlorophenyl)pentane-1,5-diol (3b)
(R)-2-(4-Tolyl)pentane-1,5-diol (3c)
(R)-2-(3-Chlorophenyl)pentane-1,5-diol (3e)
(R)-2-(3-Toly)pentane-1,5-diol (3f)
(R)-2-(3-Methoxyphenyl)pentane-1,5-diol (3g)
(R)-2-(3,4-Dichlorophenyl)pentane-1,5-diol (3h)
(R)-2-(3,4-Dimethoxyphenyl)pentane-1,5-diol (3i)
(R)-2-(2-Chlorophenyl)pentane-1,5-diol (3j)
(R)-2-(2-Toly)pentane-1,5-diol (3k)
(R)-2-(2-Methoxyphenyl)pentane-1,5-diol (3l)
Compound 4
(F) HPLC charts for hydrogenation products

(R)-2-Phenylpentane-1,5-diol (3a)
(R)-2-(4-Chlorophenyl)pentane-1,5-diol (3b)

Peak RetTime Type Width Area Height Area %
# [min] [min] [mAU*s] [mAU] %
1 21.159 BV 0.5393 1223.11536 35.37984 3.2675
2 22.824 VB 0.6200 3.62100e4 910.54260 96.7325
(R)-2-(4-Tolyl)pentane-1,5-diol (3c)

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(R)-2-(4-Methoxyphenyl)pentane-1,5-diol (3d)

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1  7.780 BV  0.2493 388.67471 23.95855 3.3540
2  8.643 VB  0.2573 1.11996e4 675.92743 96.6460
(R)-2-(3-Chlorophenyl)pentane-1,5-diol (3e)
(R)-2-(3-Tolyl)pentane-1,5-diol (3f)
(R)-2-(3-Methoxyphenyl)pentane-1,5-diol (3g)

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(R)-2-(3,4-Dichlorophenyl)pentane-1,5-diol (3h)
(R)-2-(3,4-Dimethoxyphenyl)pentane-1,5-diol (3i)

**Graph 1:**
- Peak RetTime Type Width Area Height Area
- # [min] [min] [mAU*s] [mAU] %
- 1 45.606 BV 1.3241 3.48732e4 371.19522 95.3972
- 2 52.239 VB 1.3059 1682.60229 19.05971 4.6028
(R)-2-(2-Chlorophenyl)pentane-1,5-diol (3j)

![Chemical Structure]

**Table:**

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(R)-2-(2-Tolyl)pentane-1,5-diol (3k)

Peak RetTime Type Width Area Height Area %
# [min] [min] [mAU*s] [mAU] %
1 15.892 BV 0.3228 3226.01245 155.02222 11.5618
2 16.768 VV 0.3849 2.46763e4 1010.63812 88.4382
(R)-2-(2-Methoxyphenyl)pentane-1,5-diol (3l)
(S)-2-Methylpentane-1,5-diol (3m)

Peak RetTime Type Width Area Height Area
# [min] [min] [mAU*s] [mAU] %

1 11.314 BV 0.3051 487.04681 24.38050 4.6194
2 12.231 VB 0.3399 1.00565e4 454.88486 95.3806
(S)-2-Ethylpentane-1,5-diol (3n)

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(R)-2-Isopropylpentane-1,5-diol (3o)
(S)-2-(But-3-en-1-yl)pentane-1,5-diol (3p)
**[(R)-2-Phenylbutane-1,4-diol (3q)]**(3q)

![Graph A](image1)

![Graph B](image2)

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(S)-2-Methylbutane-1,4-diol (3r)

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1 7.888 BV 0.1700 3533.73608 322.14230 84.5679
2 8.649 VB 0.1865 644.84155 52.79661 15.4321
The HPLC of asymmetric hydrogenation of hydroxyl ester 4 to (R)-2-phenylpentane-1,5-diol (3a)

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