Supporting information for

Efficient Asymmetric Transfer Hydrogenation of Ketones in Ethanol with Chiral Iridium Complexes of SpiroPAP Ligands as Catalysts

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A. General procedure for asymmetric transfer hydrogenation of ketones………………………S1
B. Monitored the asymmetric transfer hydrogenation with ReactIR and GC…………………S4
C. GC and HPLC charts for hydrogenation products…………………………………………S6

General: All reactions and manipulations which are sensitive to moisture or air were performed in an argon-filled glovebox (VAC DRI-LAB HE 493) or using standard Schlenk techniques. Anhydrous THF was distilled from sodium benzophenone ketyl. Anhydrous CH₂Cl₂ and Et₃N were freshly distilled from calcium hydride. Anhydrous EtOH was freshly distilled from magnesium. [Ir(COD)Cl]₂ was purchased from J&K Chemical Company. tBuOK, and other chemical reagents were purchased from Acros and Aldrich Chemical Company. Melting points were measured on a RY-I apparatus and uncorrected. ¹H and ¹³C NMR spectra were recorded on Bruker AMX-400 spectrometers. Chemical shifts were reported in ppm downfield from internal Si(CH₃)₄ and external 85% H₃PO₄, respectively. Optical rotations were determined using a Perkin Elmer 341 polarimeter. GC analyses were performed using a Hewlett Packard Model HP 6890 Series. HPLC analyses were performed using Hewlett Packard Model HP 1100 instruments. For the ReactIR stepwise stoichiometric reaction experiments, the reaction spectra were recorded using an IC 15 from Mettler-Toledo AutoChem. Data manipulation was carried out using the iC IR software, version 4.2 and 4.3.

A. Asymmetric transfer hydrogenation of simple ketones.

![Diagram](https://via.placeholder.com/150)

**General procedure for S/C = 1000:** To a dry 25 mL Schlenk tube flushed with nitrogen was added (S)-1a (2.0 mg, 2.0 µmol) and 1 mL EtOH. Then, ketones 1 (2.0 mmol) in 1 mL EtOH and tBuOK (22.4 mg, 0.2 mmol) in 3 mL EtOH were added via a syringe successively. The reaction solution was stirred at 40 °C for 4–10 h (monitored by GC). The solvent was removed in vacuo and the residue was purified by flash column chromatography on silical gel with petroleum ether/ethyl acetate (5:1) as the eluent to afford the chiral alcohols 3. The enantioselectivity was determined by HPLC or GC with chiral column.

**(R)-1-Phenylethanol ((R)-3a)**

4 h, 99% yield, 98% ee (R). [α]₂⁰⁺ + 44.5 (c 1.0, CH₂Cl₂). GC conditions: Supelco β-DEX™225, df = 0.25 μm, 0.25 mm i.d. × 25 m, carrier gas, N₂ (flow 2 mL/min); injection temp, 230 °C; initial column temperature, 100 °C; progress rate, 1 °C/min; final column temperature, 120 °C; progress rate, 10 °C/min; final column temperature, 200 °C; detector temperature, 250 °C); tₚ(R) = 9.32 min; tₚ(S) = 10.01 min.
(R)-1-Phenylpropanol ((R)-3b)\(^1\)

\[
\begin{align*}
\text{10 h, 95\% yield, 97\% ee (R). } & [\alpha]^{20}_D + 44.5 (c 1.0, \text{CHCl}_3). \text{ SFC conditions: Chiralcel OJ-H column; eluent, } i\text{-propanol/CO}_2 = 1.99, \text{ temp, r.t.; flow rate, 2.0 mL/min; detection, 220 nm light); t_r (S) = 7.45 \text{ min; } t_r (R) = 8.14 \text{ min.} \\
\end{align*}
\]

(R)-1-(4-Chlorophenyl)ethanol ((R)-3c)\(^1\)

\[
\begin{align*}
\text{10 h, 95\% yield, 96\% ee (R). } & [\alpha]^{20}_D + 43.5 (c 1.0, \text{CHCl}_3). \text{ HPLC conditions: Chiralcel OD-H column; eluent, } i\text{-propanol/hexane = 2.98; temp, r.t.; flow rate, 1.0 mL/min; detection, 220 nm light); t_r (S) = 15.08 \text{ min; } t_r (R) = 16.91 \text{ min.} \\
\end{align*}
\]

(R)-1-(4-Bromophenyl)ethanol ((R)-3d)\(^1\)

\[
\begin{align*}
\text{10 h, 95\% yield, 91\% ee (R). } & [\alpha]^{20}_D + 36.5 (c 1.0, \text{CHCl}_3). \text{ GC conditions: Supelco } \beta\text{-DEX}^{\text{TM} 225, df = 0.25 \mu m, 0.25 mm i.d. x 25 m, carrier gas, N}_2 \text{ (flow 2 mL/min; injection temp, 230 °C; initial column temperature, 100 °C; progress rate, 1 °C/min; final column temperature, 160 °C; progress rate, 10 °C/min; final column temperature, 200 °C; detector temperature, 250 °C); } t_r (R) = 35.43 \text{ min; } t_r (S) = 36.98 \text{ min.} \\
\end{align*}
\]

(R)-1-(4-Methylphenyl)ethanol ((R)-3e)\(^1\)

\[
\begin{align*}
\text{10 h, 98\% yield, 90\% ee (R). } & [\alpha]^{20}_D + 53.8 (c 1.0, \text{CHCl}_3). \text{ HPLC conditions: Chiralcel OJ-H column; eluent, } i\text{-propanol/hexane = 5.95; temp, r.t.; flow rate, 1.0 mL/min; detection, 220 nm light); t_r (S) = 10.51 \text{ min; } t_r (R) = 11.95 \text{ min.} \\
\end{align*}
\]

(R)-1-(4-Methoxyphenyl)ethanol ((R)-3f)\(^1\)

\[
\begin{align*}
\text{10 h, 93\% yield, 95\% ee (R). } & [\alpha]^{20}_D + 56.8 (c 1.0, \text{CHCl}_3). \text{ HPLC conditions: Chiralcel OJ-H column; eluent, } i\text{-propanol/hexane = 10.90; temp, r.t.; flow rate, 1.0 mL/min; detection, 220 nm light); t_r (S) = 15.11 \text{ min; } t_r (R) = 16.54 \text{ min.} \\
\end{align*}
\]

(R)-1-(3-Chlorophenyl)ethanol ((R)-3g)\(^2\)

\[
\begin{align*}
\text{10 h, 93\% yield, 96\% ee (R). } & [\alpha]^{20}_D + 56.8 (c 1.0, \text{CHCl}_3). \text{ HPLC conditions: Chiralcel OJ-H column; eluent, } i\text{-propanol/hexane = 5.95; temp, r.t.; flow rate, 1.0 mL/min; detection, 220 nm light); t_r (S) = 15.92 \text{ min; } t_r (R) = 16.74 \text{ min.} \\
\end{align*}
\]

(R)-1-(3-Bromophenyl)ethanol ((R)-3h)\(^1\)

\[
\begin{align*}
\text{10 h, 96\% yield, 93\% ee (R). } & [\alpha]^{20}_D + 33.3 (c 1.0, \text{CHCl}_3). \text{ HPLC conditions: Chiralcel OJ-H column; eluent, } i\text{-propanol/hexane = 2.98; temp, r.t.; flow rate, 1.0 mL/min; detection, 220 nm light); t_r (S) = 7.45 \text{ min; } t_r (R) = 8.47 \text{ min.} \\
\end{align*}
\]

(R)-1-(3-Methylphenyl)ethanol ((R)-3i)\(^1\)

\[
\begin{align*}
\end{align*}
\]

\(52\)
(R)-1-(3-Methoxyphenyl)ethanol ((R)-3j)

10 h, 95% yield, 97% ee (R). [α]$_D^{20}$ + 42.7 (c 1.0, CHCl$_3$). SFC conditions: Chiralcel OJ-H column; eluent, i-propanol / CO$_2$ = 1:99; temp, r.t.; flow rate, 2.0 mL/min; detection, 220 nm light; $t_k$ (S) = 15.25 min; $t_k$ (R) = 12.76 min.

(R)-1-(2-Chlorophenyl)ethanol ((R)-3k)

10 h, 99% yield, 98% ee (R). [α]$_D^{20}$ + 66.8 (c 1.0, CHCl$_3$). HPLC conditions: Chiralcel OD-H column; eluent, i-propanol/hexane = 2:98; temp, r.t.; flow rate, 1.0 mL/min; detection, 220 nm light; $t_k$ (S) = 16.3 min.

(R)-1-(2-Bromophenyl)ethanol ((R)-3l)

10 h, 94% yield, 96% ee (R). [α]$_D^{20}$ + 54.3 (c 1.0, CHCl$_3$). HPLC conditions: Chiralcel OD-H column; eluent, i-propanol/hexane = 2:98; temp, r.t.; flow rate, 1.0 mL/min; detection, 220 nm light; $t_k$ (S) = 14.92 min.

(R)-1-(2-Methylphenyl)ethanol ((R)-3m)

10 h, 96% yield, 98% ee (R). [α]$_D^{20}$ + 79.8 (c 1.0, CHCl$_3$). GC conditions: Coating CP Chirasil-DEX CB, CP7502, df = 0.25 μm, 0.25 mm i.d. x 25 m; carrier gas, N$_2$ (flow 2.0 mL/min); injection temp, 250 °C; initial column temperature, 100 °C; progress rate, 1.0 °C/min; final column temperature, 160 °C; $t_k$ (R) = 19.00 min; $t_k$ (S) = 22.91 min.

(R)-1-(2-Methoxylphenyl)ethanol ((R)-3n)

10 h, 99% yield, 96% ee (R). [α]$_D^{20}$ +23.7 (c 1.0, CHCl$_3$). HPLC conditions: Chiralcel OD-H column; eluent, i-propanol/hexane = 2:98; temp, r.t.; flow rate, 1.0 mL/min; detection, 220 nm light; $t_k$ (S) = 20.89 min; $t_k$ (R) = 21.9 min.

(R)-1-(3,5-bis(trifluoromethyl)phenyl)ethanol ((R)-3o)

10 h, 98% yield, 93% ee (R). [α]$_D^{20}$ +22.7 (c 1.0, CHCl$_3$). HPLC conditions: Chiralcel OD-H column; eluent, i-propanol/hexane = 2:98; temp, r.t.; flow rate, 1.0 mL/min; detection, 220 nm light; $t_k$ (S) = 14.74 min; $t_k$ (R) = 12.43 min.
10 h, 99% yield, 95% ee (R). [α]_D^20 +48.9 (c 1.0, CHCl₃). HPLC conditions: Chiralcel OD-H column; eluent, i-propanol/hexane = 2:98; temp, r.t.; flow rate, 1.0 mL/min; detection, 220 nm light); tᵣ(S) = 50.52 min; tᵣ(R) = 52.98 min.

(R)-1-(Pyridin-3-yl)ethan-1-ol ((R)-3q)

10 h, 87% yield, 93% ee (R). [α]_D^20 +19.6 (c 1.0, CHCl₃). HPLC conditions: Chiralcel OD-H column; eluent, i-propanol/hexane = 25:75; temp, r.t.; flow rate, 1.0 mL/min; detection, 220 nm light); tᵣ(R) = 3.97 min; tᵣ(S) = 4.56 min.

(R)-1-Cyclohexylethan-1-ol ((R)-3r)

10 h, 97% yield, 83% ee (R). [α]_D^20 −25.2 (c 1.2, CHCl₃). HPLC conditions (To the corresponding benzylacelated derivatives): Chiralcel OD-H column; eluent, i-propanol/hexane = 2:98; temp, r.t.; flow rate, 1.0 mL/min; detection, 220 nm light); tᵣ(S) = 6.17 min; tᵣ(R) = 6.79 min.

(R)-3,3-Dimethylbutan-2-ol ((R)-3s)

10 h, 90% yield, 80% ee (R). [α]_D^20 −3.7 (c 1.0, CHCl₃). GC condition (Supelco beta-DEX™ 225, df = 0.25 μm, 0.25 mm i.d. x 25 m, fused silica capillary column); carrier gas, N₂ (flow 1 mL/min); injection temp, 250 °C; initial column temperature, 70 °C; progress rate, hold for 40 min then 0.5 °C/min; final column temperature, 180 °C); tᵣ(R) = 24.27 min; tᵣ(S) = 27.97 min.

Asymmetric transfer hydrogenation of 2a on a gram scale (S/C = 2000): To a dry 500 mL three-necked round flask flushed with nitrogen was added (S)-1a (50 mg, 0.1 mmol) in 10 mL EtOH. Then, 2a (12.0 g, 0.1 mol) in 200 mL EtOH and tBuOK (22.4 mg, 0.2 mmol) in 40 mL EtOH were added via a syringe successively. The reaction solution was stirred at 40 °C stirred for 16 h (monitored by GC, 99% conversion). The solvent was removed in vacuo and the residue was purified by flash column chromatography on silical gel with petroleum ether/ethyl acetate (5:1) as the eluent to afford (R)-3a (11.7 g, 96% yield, 98% ee) as a colorless oil.

B. Monitored the asymmetric transfer hydrogenation using online IR techniques

The IR probe was inserted through an adapter into the middle neck of a 25 mL three-necked reaction flask which contained a befitting magnetic stirring bar, another neck were capped by rubber plug for injections and the last neck was connected to a nitrogen line. Following evacuation under vacuum and flushing with nitrogen for three times. Then, (S)-1a (2.0 mg, 2.0 μmol) in 1 mL EtOH and tBuOK (22.4 mg, 0.2 mmol) in 3 mL EtOH was injected to the reaction flask, followed by additions of acetophenone (240 mg, 2.0 mmol) in 1 mL EtOH. The resulting mixture was allowed to stir at 40 °C and the whole process was monitored by operando IR though the probe.
Monitored the asymmetric transfer hydrogenation using GC

The tBuOK (22.4 mg, 0.2 mmol), (S)-1a (2.0 mg, 2.0 μmol) were introduced into 15 mL anoven-dried Schlenk tube in an argon-filled glove box. EtOH (5 mL) was injected and the solution was stirred at 50 °C under the argon atmosphere for 5 min, followed by additions of acetophenone (240 mg, 2.0 mmol). The resulting mixture was stirred for 10 h at 50 °C. The conversion and enantiomeric excess was determined by GC with chiral column every 10 min. GC [(Supelco β-DEX™ 225, df = 0.25 μm, 0.25 mm i.d. × 25 m, N2 (2 mL/min); injection temp, 230 °C; initial column temperature, 100 °C; progress rate, 1.0 °C /min; final column temperature, 120 °C; progress rate, 10.0 °C /min; final column temperature, 200 °C; detector temperature, 250 °C); \( t_1 (R) = 9.21 \) min; \( t_2 (S) = 9.94 \) min].

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References
C) GC and HPLC charts for hydrogenation products

(R)-1-Phenylethanol ((R)-3a)
(R)-Phenylpropanol ((R)-3b)

Peaks:

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(R)-1-(4-Chlorophenyl)ethanol ((R)-3c)
(R)-1-(4-Bromophenyl)ethanol ((R)-3d)
(R)-1-(4-Methylphenyl)ethanol ((R)-3e)
(R)-1-(4-Methoxyphenyl)ethanol ((R)-3f)
(\textit{R})-1-(3-Chlorophenyl)ethanol ((\textit{R})-3g)
(R)-1-(3-Bromophenyl)ethanol ((R)-3h)
(R)-1-(3-Methylphenyl)ethanol ([(R)-3i])
(R)-1-(3-Methoxyphenyl)ethanol ((R)-3j)

\[
\text{MeO} \quad \text{OH}
\]

### Chromatogram Details

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(R)-1-(2-Chlorophenyl)ethanol ((R)-3k)
(R)-1-(2-Bromophenyl)ethanol ((R)-31)
(R)-1-(2-Methylphenyl)ethanol ((R)-3m)
(R)-1-(2-Methoxyphenyl)ethanol ((R)-3n)
(R)-1-(3,5-bis(trifluoromethyl)phenyl)ethanol ((R)-3o)

\[
\begin{align*}
\text{OH} & \quad \text{CF}_3 \\
\text{F}_3\text{C} & \quad \text{C} \quad \text{H} \\
\text{CF}_3 & \quad \text{H} \\
\end{align*}
\]

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(R)-1-(2-Naphtyl)ethanol ((R)-3p)
(R)-1-(Pyridin-3-yl)ethan-1-ol ((R)-3q)

**Panel 1:**
![Graph 1](image1)

**Panel 2:**
![Graph 2](image2)

**Table:**

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(R)-1-Cyclohexylethan-1-ol ((R)-3r)
(R)-3,3-Dimethylbutan-2-ol ((R)-3s)