SUPPORTING INFORMATION

for

The Hydrogenation/Transfer Hydrogenation Network:
Asymmetric Hydrogenation of Ketones with Chiral
$\eta^6$-Arene/N-Tosylethlenediamine–Ruthenium(II) Catalysts

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(1) Procedure for silanization of glassware

The use of a silanized glass reaction vessel was necessary to secure the reproducibility. Although HMDS (hexamethyldisilazide) and TMSCl gave similar results, the HMDS treatment was more convenient. A 100-mL glass vessel was charged with 0.5 mL of HMDS, capped with a silicon rubber, and heated at 30 °C for 24 h. Then the vessel was washed with water and acetone, heated at 100 °C for 30 min, and dried under reduced pressure for 2 h. The vessel was stored under Ar gas.

(2) Procedure for the preparation of (S,S)-8b

A solution of TfOH (70 µL, 0.79 mmol) in CH$_2$Cl$_2$ (10 mL) was added dropwise to a solution of (S,S)-9 (570 mg, 0.95 mmol) in CH$_2$Cl$_2$ (55 mL) under an Ar atmosphere at room temperature over a period of 30 min. Then the solution was stirred for 30 min and evaporated to a volume of 15 mL. Cooling the solution to 0 °C gave an orange precipitate. The precipitate was filtered and dried under reduced pressure to give (S,S)-8b (380 mg, 65% yield).

$^1$H NMR (400 MHz, 21 mM in CD$_2$Cl$_2$) δ 1.30, 1.33 (each d, $J = 7$ Hz, 3H x 2, CH(CH$_3$)$_2$), 2.12 (s, 3H, CH$_3$), 2.27 (s, 3H, CH$_3$ of Ts), 2.76 (m, 1H, CH(CH$_3$)$_2$), 3.75 (m, 1H, CHNH$_2$), 4.21 (d, $J = 8$ Hz, 1H, CHNTs), 4.71 (m, 1H, NH), 5.68 (m, 1H, NH$H$). 5.84 (d, $J = 6$ Hz, 1H, aromatic proton), 5.94 (m, 2H, aromatic proton), 6.11 (d, $J = 6$ Hz, 1H, aromatic proton), 6.63–7.25 (m, 14H, aromatic protons).

$^1$H NMR (400 MHz, 10 mM in THF-$d_8$) δ 1.37, 1.43 (each d, $J = 7$ Hz, 3H x 2, CH(CH$_3$)$_2$), 2.18 (s, 3H, CH$_3$), 2.29 (s, 3H, CH$_3$ of Ts), 2.98 (m, 1H, CH(CH$_3$)$_2$), 3.55 (m, 1H, CHNH$_2$), 3.85 (m, 1H, NH$H$), 3.94 (d, $J = 11$ Hz, 1H, CHNTs), 5.78 (d, $J = 6$ Hz, 1H, aromatic proton), 5.92–5.93 (m, 2H, aromatic protons), 6.15 (d, $J = 6$ Hz, 1H, aromatic proton), 6.5–7.1 (m, 14H, aromatic protons), 7.16 (m, 1H, NH$H$).

$^1$H NMR (400 MHz, 21 mM in CD$_3$OH) δ 1.40, 1.43 (each d, $J = 7$ Hz, 3H x 2, CH(CH$_3$)$_2$), 2.24 (s, 3H, CH$_3$), 2.37 (s, 3H, CH$_3$ of Ts), 3.02 (m, 1H, CH(CH$_3$)$_2$), 3.45 (m, 1H, NH$H$), 3.68 (m, 1H, CHNH$_2$), 4.02 (d, $J = 11$ Hz, 1H, CHNTs), 5.63 (d, $J = 6$ Hz, 1H, aromatic proton), 6.11 (d, $J = 6$ Hz, 1H, aromatic proton), 6.63–7.25 (m, 14H, aromatic protons), 7.16 (m, 1H, NH$H$).
Hz, 1H, aromatic proton), 6.00–6.05 (m, 3H, aromatic protons), 6.60–7.19 (m, 14H, aromatic protons), 7.60 (m, 1H, NH).

$^{13}$C NMR (100.4 MHz, THF-$d_8$) δ 18.6, 21.1, 22.6, 22.8, 31.4, 70.3, 73.2, 82.4, 82.9, 84.2, 84.3, 97.0, 101.2, 127.0, 127.8, 128.1, 128.6, 128.7, 128.8, 129.2, 130.0, 139.7, 139.9, 140.3, 143.6.

Anal. calcd. for: C 51.26, H 4.70, N 3.74, found: C 51.09, H 4.47, N 3.74.

(3) Procedure for the asymmetric hydrogenation of 4-chromanone (6a) with (S,S)-8a

4-Chromanone (6a) (0.89 g, 6.0 mmol) and (S,S)-8a (1.3 mg, 2 µmol) were placed in a 100-mL glass autoclave. The atmosphere was replaced with Ar gas, and methanol (19.3 mL) was added to this mixture. Hydrogen was initially introduced into the autoclave at a pressure of 10 atm, before being reduced to 1 atm. This procedure was repeated three times. Then the autoclave was pressurized with H$_2$ gas (10 atm), and the solution was stirred vigorously at 60 °C for 15 h. The $^1$H-NMR and HPLC analysis indicated that (S)-4-chromanol [(S)-7a] with 95% ee was obtained in 64% yield.

Pure (S)-7a (0.52 g, 58% yield) was obtained by silica gel chromatography.

$^1$H NMR (400 MHz, CDCl$_3$) δ 1.99 (m, 1H, CHHCH(OH)), 2.08 (m, 1H, CHHCH(OH)), 2.31 (br, 1H, OH), 4.23 (m, 2H, CH$_2$O), 4.74 (m, 1H, CHOH), 6.8–6.9 (m, 2H, aromatic protons), 7.2–7.3 (m, 2H, aromatic protons).

The HPLC analytical conditions were used as follows: column, CHIRALCEL OJ-H (4.6 mm i.d. x 250 mm); eluent, hexane/2-propanol = 99/1; flow rate, 1.5 mL/min; temp, 35 °C; detection, UV (220 nm). The retention times were as follows: 6a, 11.8 min, (S)-7a, 26.7 min, (R)-7a, 30.8 min.

[$\alpha$]$_{D}^{25}$ -77 (c 0.5, C$_2$H$_5$OH), (lit. [$\alpha$]$_{D}^{25}$ +80.4, c 0.5, C$_2$H$_5$OH, 100% ee (R), Zhang, X.; Takemoto, T.; Yoshizumi, T.; Kumobayashi, H.; Akutagawa, S.; Mashima, K.; Takaya, H. J. Am. Chem. Soc. 1993, 115, 3318–3319).
(4) Procedure for the asymmetric hydrogenation of 4-chromanone (6a) with (S,S)-8b

4-Chromanone (6a) (0.89 g, 6.0 mmol) and (S,S)-8b (1.5 mg, 2 µmol) were placed in a 100-mL glass autoclave. The atmosphere was replaced with Ar gas, and methanol (5.3 ml) was added to this solution. Hydrogen was initially introduced into the autoclave at a pressure of 10 atm, before being reduced to 1 atm. This procedure was repeated three times. Then the autoclave was pressurized with H₂ gas (10 atm), and the solution was stirred vigorously at 60 °C for 15 h to give (S)-4-chromanol [(S)-7a] with 97% ee in 100% yield. The solvent was removed under reduced pressure and the Ru catalyst was removed by silica gel chromatography, giving (S)-7a (0.84 g, 93% yield).

(5) Analytical data of hydrogenation products

(S)-6-Methyl-4-chromanol [(S)-7b]

¹H NMR (400 MHz, CDCl₃) δ 1.97–2.13 (m, 2H, CH₂HCH(OH)), 2.27 (s, 3H, CH₃), 4.21 (m, 2H, CH₂O), 4.72 (m, 1H, CHOH), 6.73 (d, J = 8.3 Hz, 1H, aromatic proton), 7.00 (d, J = 8.3 Hz, 1H, aromatic proton), 7.10 (s, 1H, aromatic proton).

The HPLC analytical conditions were as follows: column, CHIRALCEL OJ-H (4.6 mm i.d. x 250 mm); eluent, hexane/2-propanol = 99/1; flow rate, 1.5 mL/min; temp, 35 °C; detection, UV (220 nm). The retention times were: 6b, 8.6 min, (S)-7b, 23.4 min, (R)-7b, 29.2 min.


(S)-6-Chloro-4-chromanol [(S)-7c]

¹H NMR (400 MHz, CDCl₃) δ 1.82 (br, 1H, OH), 2.00–2.16 (m, 2H, CH₂HCH(OH)), 4.26 (m, 2H, CH₂O), 4.77 (m, 1H, CHOH), 6.77 (d, J = 8.8 Hz, 1H, aromatic ring proton), 7.15 (d, J = 8.3 Hz, 1H, aromatic proton), 7.30 (s, 1H, aromatic proton).

The HPLC analytical conditions were as follows: column, CHIRALCEL OJ-H (4.6 mm i.d. x 250 mm); eluent, hexane/2-propanol = 99/1; flow rate, 1.5 mL/min; temp, 35 °C;
detection, UV (220 nm). The retention times were: 6c, 9.9 min, (R)-7c, 33.7 min, (S)-7c, 36.9 min, 
\([\alpha]D^{25} -24 \ (c \ 1.0, \ CHCl_3), \) (lit. \([\alpha]D^{25} -24, \ c \ 1.0, \ CHCl_3, \ 80\% \ ee \ (S), \) Ramadas, S.; 

(6) Procedure for the large–scale asymmetric hydrogenation of 4-chromanone (6a)

4-Chromanone (6a) (2.37 kg, 16 mol), (S,S)-9 (9.6 g, 16 mmol), and TfOH (1.42 
ml, 16 mmol) were added to methanol (8 L) placed in a 20-L SUS autoclave. 
Hydrogen was initially introduced into the autoclave at a pressure of 10 atm, before 
being reduced to 1 atm. This procedure was repeated three times. Then the 
aucoclave was pressurized with H\(_2\) gas (17 atm), and the solution was stirred vigorously 
at 60 °C for 15 h. The \(^1\)H-NMR and HPLC analysis indicated that (S)-4-chromanol 
[(S)-7a] with 97% ee was produced in 99% yield.