Supplementary Information For:

Asymmetric Hydrogenation of Ketones with Polymer-Supported Chiral 1,2-diphenylethylene-diamine

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General:

[RuCl₂(benzene)]₂ and ketones, diphosphines, except (*R*)-MeO-BIPHEP which was prepared according to the literature,¹ were obtained from Aldrich or Lancaster. The hydrogenation products were analyzed by a Varian CP-3380 GC equipped with a Chrompack Chirasil-Dex CB (25 m × 0.25 mm) column.

(A) Preparation of Ligand

Synthesis of (*R,R*)-*N,N*-Bis-Boc-1,2-di(3-benzyloxyphenyl)ethane-1,2-diamine (**4**)

To a solution of (*R,R*)-1,2-di(3-benzyloxyphenyl)ethane-1,2-diamine (**3**) (1.32 g, 3.1 mmol) and *N,N*-diisopropylethylamine (1.21 ml, 7.0 mmol) in CH_2Cl_2 (10 ml) was added di-*tert*-butyl dicarbonate (1.42 g, 6.5 mmol). The reaction mixture was stirred overnight at room temperature. And the mixture was then washed with 1N HCl (5 ml), brine (5 ml). The combined organic layer was dried over MgSO_4 and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (hexane/EtOAc = 4:1) to give the product (1.88 g, 97%) as white solid. $[\alpha]_{\text{D}}^{22} = +12.5$ (c 1.2, CHCl_3). ^1H NMR (CDCl_3 , 400 MHz): δ 7.29~7.36 (m, 10H), 7.10 (t, $J = 8.0$, 2H), 6.78 (dm, $J = 8.0$, 2H), 6.66 (d, $J = 8.0$, 2H), 6.65 (s, 2H), 5.50 (br. s, 2H), 4.93 (d, $J = 11.6$, 2H), 4.88 (d, $J = 11.6$, 2H), 4.81 (s, 2H), 1.44 (s, 18 H). ^{13}C NMR (CDCl_3 , 400 MHz): δ 158.79, 140.86, 136.89, 129.49, 128.57, 127.95, 127.47, 120.03, 114.35, 114.05, 79.81, 70.01, 60.48, 28.42. Acc. Mass: Calcd. for $\text{C}_{38}\text{H}_{44}\text{N}_2\text{O}_6\text{Na}$ ($\text{M}+\text{Na}$) 647.3097; Found: 647.3098.

Synthesis of (*R,R*)-*N,N*-Bis-Boc-1,2-di(3-hydroxyphenyl)ethane-1,2-diamine (**5**):

A suspension of (*R,R*)-*N,N*-Bis-Boc-1,2-di(3-benzyloxyphenyl)ethane-1,2-diamine (**4**) (1.50 g, 2.4 mmol) and 10% Pd-C (50 mg) in EtOAc (10 ml) was stirred for 2 h at room temperature under 10 bar of hydrogen. The reaction mixture was then filtered through a pad of Celite, and the solvent was removed under reduced pressure. The residue was purified by flash silica gel column chromatography (hexane-EtOAc = 1:1) to give the product (1.00 g, 94%) as a white foam. $[\alpha]_{\text{D}}^{22} = -22.9$ (c 1.3, CHCl_3). ^1H NMR (CDCl_3 , 400 MHz): δ 6.97 (s, 4H), 6.55~6.61 (m, 6H), 5.71 (s, 2H), 5.78 (s, 2H), 4.78 (s, 2H), 1.43 (s, 18H). ^{13}C NMR (CDCl_3 , 400 MHz): δ 156.44, 140.94, 130.01, 119.75, 115.37, 114.97,

80.66, 60.81, 28.77. Acc. Mass: Calcd. for $C_{24}H_{32}N_2O_6Na$ (M+Na): 467.2158; found: 467.2170.

Synthesis of Polyethylene glycol 2000 monomethyl ether mesylate:

To a solution of polyethylene glycol 2000 monomethyl ether (20.00 g, 10 mmol) and tri-*n*-octylamine (13.1 ml, 30 mmol) in CH_2Cl_2 (50 ml) was added MsCl (1.55 ml, 20 mmol) at 0 °C. The reaction mixture was stirred for 24 h at room temperature and poured into Et_2O (1000 ml) with stirring. After stirring for 30 min at 0 °C, the precipitate was collected by filtration, washed with Et_2O (5×200 ml), and dried in vacuum to give the product (20.50 g) as white solid.

Synthesis of Polymer 6:

A suspension of (*R,R*)-N,N-Bis-Boc-1,2-di(3-hydroxyphenyl)ethane-1,2-diamine (**5**) (222 mg, 0.5 mmol), polyethylene glycol 2000 monomethyl ether mesylate (2.00 g, 1.0 mmol) and Cs_2CO_3 (978 mg, 3.0 mmol) in DMF (10 ml) was stirred overnight at 50 °C. Most of DMF were removed under reduced pressure and CH_2Cl_2 (10 ml) was added. The insoluble salts were filtered off, and the filtrate was poured into Et_2O (150 ml) with stirring. After stirring for 30 min at 0 °C, the precipitate was collected by filtration, washed with Et_2O (5×20 ml), and dried in vacuum to give the product (2.10 g) as off-white solid.

Synthesis of (*R,R*)-Polymer-supported PEG-2:

A solution of polymer **6** (2.00 g) in CH_2Cl_2 (5 ml) and $\text{CF}_3\text{CO}_2\text{H}$ (5 ml) was stirred for 4 h at room temperature. Most of solvents were removed under reduced pressure. The

residue was dissolved in CH₂Cl₂ (10 ml) and tri-*n*-octylamine (5 ml) was added. The mixture was stirred for 30 min at room temperature and poured into Et₂O (150 ml) with stirring. After stirring for 30 min at 0 °C, the precipitate was collected by filtration, washed with Et₂O (5 × 20 ml) and dried in vacuum to give the product (1.95 g) as white solid (nitrogen content from elemental analysis: 0.61%).

(B) General Procedure for Preparation of Diphosphine-Ru-Diamine Precatalysts²

Method A: Diphosphine (0.055 mmol) and [(C₆H₆)RuCl₂]₂ (0.025 mmol) were dissolved in anhydrous and degassed DMF (2 ml) under argon. The mixture was heated to 100 °C for 3-4 hours, then the polymer-supported diamine **2** (0.055 mmol) was added and the reaction was allowed to reach room temperature and stirred for 12-15 hours. The solvent was removed under high vacuum and the residue was used for hydrogenations without further purification.

Method B: Diphosphine (0.055 mmol) and [(C₆H₆)RuCl₂]₂ (0.025 mmol) were dissolved in anhydrous and degassed DMF (2 ml) under argon. The reaction was heated to 100 °C for 10-20 minutes and then the solvent removed under high vacuum. The complex obtained was used directly to react with the polymer-supported diamine **2** *in situ* to generate the diphosphine-Ru-Diamine precatalyst.

(C) Asymmetric Hydrogenation of Acetonaphthone

Standard procedure at S/C = 2000: An autoclave containing a glass liner was charged with [(Diphosphine)RuCl₂((*R,R*)-**2**)] (0.0025 mmol), *i*-PrOH (3 ml), acetonaphthone (5 mmol) and *t*-BuOK in *i*-PrOH (0.1 M, 0.3 ml, 0.03 mmol) under argon. The reaction mixture was degassed with 10 bar H₂ five times and finally the autoclave was pressurized to 10 bar with H₂. After stirring at room temperature for a certain time, the H₂ was carefully released. The reaction mixture was diluted with Et₂O and passed through a short silica gel column before being subjected to chiral GC analysis (Chirasil Dex CB; carrier gas: helium, 30 psi; injection temperature: 250 °C; column temperature: 150 °C; *t*_R of (*S*)-1-(1'-naphthyl)ethanol, 7.71 min; *t*_R of (*R*)-1-(1'-naphthyl)ethanol, 8.88 min).^{2,3}

Hydrogenation with [(*S*)-PhanePhos)RuCl₂((*R,R*)-**2**)] at S/C = 2000: (19.0 mg, 0.0025 mmol), acetonaphthone (0.85 g, 5 mmol), *i*-PrOH (3.0 ml), *t*-BuOK in *i*-PrOH (0.1 mmol/ml, 0.3 ml, 0.03 mmol), 10 bar H₂, r.t., 2 h. (*S*)-1-(1'-naphthyl)ethanol, 98%

conversion, 97% ee.

Hydrogenation with $[(S)\text{-PhanePhos}]\text{RuCl}_2((R,R)\text{-2})$ at S/C = 10000: (19.0 mg, 0.0025 mmol), acetonaphthone (4.25 g, 25 mmol), *i*-PrOH (6.0 ml), *t*-BuOK in *i*-PrOH (0.1 mmol/ml, 1.0 ml, 0.10 mmol), 50 bar H₂, r.t., 10 h. (*S*)-1-(1'-naphtyl)ethanol, 100% conversion, 97% ee.

Hydrogenation with $[(R)\text{-BINAP}]\text{RuCl}_2((R,R)\text{-2})$ at S/C = 2000: (19.0 mg, 0.0025 mmol), acetonaphthone (0.85 g, 5 mmol), *i*-PrOH (3.0 ml), *t*-BuOK in *i*-PrOH (0.1 mmol/ml, 0.3 ml, 0.03 mmol), 10 bar H₂, r.t., 4 h. (*S*)-1-(1'-naphtyl)ethanol, 99% conversion, 98% ee.

Hydrogenation with $[(R)\text{-Tol-BINAP}]\text{RuCl}_2((R,R)\text{-2})$ at S/C = 2000: (19.0 mg, 0.0025 mmol), acetonaphthone (0.85 g, 5 mmol), *i*-PrOH (3.0 ml), *t*-BuOK in *i*-PrOH (0.1 mmol/ml, 0.3 ml, 0.03 mmol), 10 bar H₂, r.t., 12 h. (*S*)-1-(1'-naphtyl)ethanol, 100% conversion, 91% ee.

Hydrogenation with $[(R)\text{-14}]\text{RuCl}_2((R,R)\text{-2})$ at S/C = 2000: $[(R)\text{-14}]\text{RuCl}_2(\text{DMF})_n$ (2.3 mg, 0.0025 mmol), $((R,R)\text{-2})$ (16 mg, 0.003 mmol), acetonaphthone (0.85 g, 5 mmol), *i*-PrOH (3.0 ml), *t*-BuOK in *i*-PrOH (0.1 mmol/ml, 0.3 ml, 0.03 mmol), 10 bar H₂, r.t., 12 h. (*S*)-1-(1'-naphtyl)ethanol, 99% conversion, 92% ee.

Hydrogenation with $[(15)]\text{RuCl}_2((R,R)\text{-2})$ at S/C = 2000: $[(15)]\text{RuCl}_2(\text{DMF})_n$ (2.2 mg, 0.0025 mmol), $((R,R)\text{-2})$ (16 mg, 0.003 mmol), acetonaphthone (0.85 g, 5 mmol), *i*-PrOH (3.0 ml), *t*-BuOK in *i*-PrOH (0.1 mmol/ml, 0.3 ml, 0.03 mmol), 10 bar H₂, r.t., 4 h. (*S*)-1-(1'-naphtyl)ethanol, 99% conversion, 61% ee.

(D) Asymmetric Hydrogenation of other ketones

Hydrogenations of other ketones with $[(S)\text{-PhanePhos}]\text{RuCl}_2((R,R)\text{-2})$ were carried out using the same standard procedure as for acetophenone. When the reaction completed, the reaction mixture was filtered through a short silica gel column, the filtrate was concentrated and the residue was analyzed by NMR and chiral GC. The stereochemistry of products was assigned by comparing the GC retention time with literature data.

(*S*)-1-(2'-naphthyl)ethanol:⁴ $[(S)\text{-PhanePhos}]\text{RuCl}_2((R,R)\text{-2})$ (19.0 mg, 0.0025 mmol), 2-acetophenone (0.85 g, 5 mmol), *i*-PrOH (3.0 ml), *t*-BuOK in *i*-PrOH (0.1 mmol/ml, 0.3 ml, 0.03 mmol), 10 bar H₂, r.t., 2 h. (*S*)-1-(2'-naphthyl)ethanol, 100% conversion, 96% ee. GC (Chirasil Dex CB); carrier gas: helium, 30 psi; injection temperature: 250 °C; column temperature: 150 °C; 7.11 min (*R*); 7.46 min (*S*).

(*S*)-1-(4'-Bromophenyl)ethanol:⁵ $[(S)\text{-PhanePhos}]\text{RuCl}_2((R,R)\text{-2})$ (19.0 mg, 0.0025 mmol), 4-Bromoacetophenone (1.0 g, 5 mmol), *i*-PrOH (3.0 ml), *t*-BuOK in *i*-PrOH (0.1 mmol/ml, 0.3 ml, 0.03 mmol), 10 bar H₂, r.t., 2 h. (*S*)-1-(4'-Bromophenyl)ethanol, 99% conversion, 94% ee. GC (Chirasil Dex CB; carrier gas: helium, 30 psi; injection temperature: 250 °C; column temperature: 135 °C; 5.19 min (*R*); 5.56 min (*S*).

(*S*)-1-(2'-Methylphenyl)ethanol:⁶ $[(S)\text{-PhanePhos}]\text{RuCl}_2((R,R)\text{-2})$ (19.0 mg, 0.0025 mmol), 2-Methylacetophenone (0.67 g, 5 mmol), *i*-PrOH (3.0 ml), *t*-BuOK in *i*-PrOH (0.1 mmol/ml, 0.3 ml, 0.03 mmol), 10 bar H₂, r.t., 4 h. (*S*)-1-(2'-Methylphenyl)ethanol, 100% conversion, 93% ee. GC (Chirasil Dex CB; carrier gas: helium, 30 psi; injection temperature: 250 °C; column temperature: 120 °C; 4.43 min (*R*); 5.42 min (*S*).

(*S*)-1-(4'-Methylphenyl)ethanol:⁷ $[(S)\text{-PhanePhos}]\text{RuCl}_2((R,R)\text{-2})$ (19.0 mg, 0.0025 mmol), 4-Methylacetophenone (0.67 g, 5 mmol), *i*-PrOH (3.0 ml), *t*-BuOK in *i*-PrOH (0.1 mmol/ml, 0.3 ml, 0.03 mmol), 10 bar H₂, r.t., 4 h. (*S*)-1-(4'-Methylphenyl)ethanol, 100% conversion, 97% ee. GC (Chirasil Dex CB; carrier gas: helium, 30 psi; injection temperature: 250 °C; column temperature: 120 °C; 2.87 min (*R*); 3.14 min (*S*).

(*S*)-1-(4'-Methoxyphenyl)ethanol:⁷ $[(S)\text{-PhanePhos}]\text{RuCl}_2((R,R)\text{-2})$ (19.0 mg, 0.0025 mmol), 4-Methoxyacetophenone (0.75 g, 5 mmol), *i*-PrOH (3.0 ml), *t*-BuOK in *i*-PrOH (0.1 mmol/ml, 0.3 ml, 0.03 mmol), 10 bar H₂, r.t., 4 h. (*S*)-1-(4'-Methoxyphenyl)ethanol, 100% conversion, 90% ee. GC (Chirasil Dex CB; carrier gas: helium, 30 psi; injection temperature: 250 °C; column temperature: 125 °C; 5.24 min (*R*); 5.45 min (*S*).

(*S*)-1-(4'-Trifluoromethylphenyl)ethanol:⁶ $[(S)\text{-PhanePhos}]\text{RuCl}_2((R,R)\text{-2})$ (19.0 mg, 0.0025 mmol), 4-Trifluoromethylacetophenone (0.94 g, 5 mmol), *i*-PrOH (3.0 ml), *t*-BuOK in *i*-PrOH (0.1 mmol/ml, 0.3 ml, 0.03 mmol), 10 bar H₂, r.t., 4 h. (*S*)-1-(4'-Trifluoromethylphenyl)ethanol, 99% conversion, 90% ee. GC (Chirasil Dex CB; carrier gas: helium, 30 psi; injection temperature: 250 °C; column temperature: 110 °C; 5.66 min (*R*); 6.86 min (*S*).

(*S*)-1-phenylethanol:⁴ [((*S*)-PhanePhos)RuCl₂((*R,R*)-**2**)] (19.0 mg, 0.0025 mmol), acetophenone (0.60 g, 5 mmol), *i*-PrOH (3.0 ml), *t*-BuOK in *i*-PrOH (0.1 mmol/ml, 0.3 ml, 0.03 mmol), 10 bar H₂, r.t., 4 h. (*S*)-1-phenylethanol, 100% conversion, 94% ee. GC (Chirasil Dex CB; carrier gas: helium, 30 psi; injection temperature: 250 °C; column temperature: 105 °C; 4.92 min (*R*); 5.41 min (*S*).

(*S*)-Phenylpropanol:⁴ [((*S*)-PhanePhos)RuCl₂((*R,R*)-**2**)] (19.0 mg, 0.0025 mmol), phenylpropanone (0.67 g, 5 mmol), *i*-PrOH (3.0 ml), *t*-BuOK in *i*-PrOH (0.1 mmol/ml, 0.3 ml, 0.03 mmol), 10 bar H₂, r.t., 4 h. (*S*)-Phenylpropanol, 100% conversion, 92% ee. GC (Chirasil Dex CB; carrier gas: helium, 30 psi; injection temperature: 250 °C; column temperature: 95 °C; 12.76 min (*R*); 13.14 min (*S*).

The results are also tabulated on page 8.

(E) Catalyst recycle

A mini-autoclave containing a glass liner was charged with [(Diphosphine)RuCl₂((*R,R*)-**2**)] (0.005 mmol), *i*-PrOH (5 ml), acetophenone (0.85 g, 5 mmol) and *t*-BuOK in *i*-PrOH (0.1 M, 0.6 ml, 0.06 mmol) under argon. The reaction mixture was degassed with 9 bar H₂ five times and finally the autoclave was pressurized to 9 bar with H₂. After stirring at room temperature for 3 h, the H₂ was carefully released. After removal of the solvent under vacuum, Et₂O (3 x 10 ml) was added to extract the organic materials. The product was analyzed as in C. To start a new run, a previous degassed *i*-PrOH (5 ml), degassed acetophenone (0.85 g, 5 mmol) and *t*-BuOK in *i*-PrOH (0.1 M, 0.6 ml, 0.06 mmol, degassed) were added to the catalyst-containing glass liner under argon. The reaction was repeated under 9 bar H₂ as above. The third run was performed in the same manner as the second one.

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Ketones	diphosphine	S/C	H ₂ (bar)	Time(h)	conv.(%)	e.e.(%)	config
(<i>S</i>)-PhanePhos	2000	10	2	98	97	<i>S</i>
(<i>S</i>)-PhanePhos	10000	10	10	100	97	<i>S</i>
(<i>S</i>)-PhanePhos	2000	10	2	100	96	<i>S</i>
(<i>S</i>)-PhanePhos	2000	10	2	99	94	<i>S</i>
(<i>S</i>)-PhanePhos	2000	10	4	100	93	<i>S</i>
(<i>S</i>)-PhanePhos	2000	10	4	100	97	<i>S</i>
(<i>S</i>)-PhanePhos	2000	10	4	100	90	<i>S</i>
(<i>S</i>)-PhanePhos	2000	10	4	99	90	<i>S</i>
(<i>S</i>)-PhanePhos	2000	10	2	100	94	<i>S</i>
(<i>S</i>)-PhanePhos	2000	10	2	100	92	<i>S</i>
(<i>R</i>)-BINAP	2000	10	4	99	98	<i>S</i>
(<i>R</i>)-Tol-BINAP	2000	10	12	100	91	<i>S</i>
(<i>R</i>)-MeO-BIPHEP	2000	10	12	99	92	<i>S</i>
DPPF	2000	10	4	99	61	<i>S</i>