Highly Enantioselective Synthesis of Heteroaromatic Alcohols Catalyzed by Chiral Diaminodiphosphine–Ruthenium(II) Complexes

Wei-Yi Shen, Yan-Yun Li, Zhen-Rong Dong, Jing-Xing Gao*

State Key Laboratory of Physical Chemistry of Solid Surfaces and Department of Chemistry,
College of Chemistry and Chemical Engineering, Xiamen University, Xiamen 361005, Fujian, P. R. of China
Fax +86(592)2183047; E-mail: cuihua@xmu.edu.cn

Received 12 February 2009; revised 24 March 2009

Abstract: Chiral diaminodiphosphine–ruthenium(II) complexes were found to be excellent catalysts for the asymmetric transfer hydrogenation of heteroaromatic ketones in propan-2-ol. In the presence of potassium hydroxide, the enantioselective reduction of heteroaromatic ketones proceeded smoothly to give chiral alcohols with excellent enantiomeric excess (up to 97% ee) under mild conditions without reduction of the heterocycle.

Key words: asymmetric, transfer hydrogenation, catalysis, heteroaromatic ketones, heteroaromatic alcohols

Chiral heteroaromatic alcohols are valuable intermediates and building blocks for a variety of biologically active compounds and chiral auxiliaries.[1] Hitherto the preparation of these compounds involved resolution of racemic alcohols,[2] enantioselective addition of dialkylzinc to aldehydes,[3] catalytic asymmetric reduction of prochiral ketones, etc. [4] The inherent disadvantage of resolution of racemic alcohols is that the maximum yield will be only 50% and the separation of the product is often problematic. The enantioselective alkylation is limited to only a few dialkylzinc derivatives. However, enantioselective reduction of prochiral ketones represents one of the simplest routes. In recent years, several highly efficient catalytic systems consisting of a chiral diphosphine–ruthenium–diamine complex and an inorganic base, which were developed by Noyori and others, have been used for the asymmetric hydrogenation of heteroaromatic ketones.[4j–r] Using these catalytic systems, a wide range of heteroaromatic alcohols were obtained in high yields with excellent enantioselectivities. Compared with asymmetric hydrogenation, asymmetric transfer hydrogenation (ATH) using nonhazardous organic molecules such as propan-2-ol, provides a useful complement to catalytic reduction using molecular hydrogen, particularly for small-to-medium-scale reactions. It also produces alcohols with high enantiomeric excess and the operation is simpler.[5–8] Some research groups have achieved success in obtaining enantiopure heteroaromatic alcohols by ATH of the corresponding ketones.[4b,d,f–h,j]

In the past decade, we have successfully prepared a class of chiral $C_6P_2(NH)_2$–Ru(II), –Rh(I), –Ir(I), or –Ir(III) complexes, which were used as catalysts in the ATH of aromatic ketones and in the kinetic resolution of racemic secondary alcohols.[9] These catalytic systems have been found to be excellent for the enantioselective reduction of a series of aromatic ketones, leading to the corresponding chiral alcohols with up to 99% ee and the molar ratio of ketone to catalyst up to 10000:1. These systems were also used for oxidative kinetic resolution of the alcohols with excellent enantioselectivity of up to 98% ee. These good results prompt us to explore their applications in the ATH of heteroaromatic ketones.

In an initial experiment, the ATH of 4-acetylpyridine (**3e**) was chosen as a model reaction. Various chiral diaminodiphosphine–Ru, –Rh, or –Ir catalysts were tested for the ATH of 4-acetylpyridine (**3e**). Typical results are listed in Table 1.

As shown in Table 1 (see also Figure 1 for the structures of **1** and **2**), for the rhodium catalysts, the $RhH(CO)(PPh_3)_3$/(*R*,*R*)-**1** system showed low activity and moderate enantioselectivity (Table 1, entry 1), while $[RhCl(COD)]_2$ exhibited higher activity but even lower enantiomeric excess (Table 1, entry 2). As for iridium catalysts, both $[IrCl(COD)]_2$/(*R*,*R*)-**1** and $[IrHCl_2(COD)]_2$/(*R*,*R*)-**1** systems gave good activity but poor enantioselectivity (Table 1, entries 3 and 4). Fortunately, the (*R*,*R*)-**2** system displayed excellent enantioselectivity giving (*S*)-1-(pyridin-4-yl)ethanol (**4e**) in high yield (97% ee, 99% conversion, Table 1, entry 5). Without the addition of base, no reaction occurred (Table 1, entry 6), but when the ratio of potassium hydroxide to catalyst varied from 5:1 to 10:1, the enantiomeric excess values of the desired product were essentially identical, while the lower ratio of potassium hydroxide to catalyst resulted in a somewhat slower rate (Table 1, entry 5 vs 7). Increasing the reaction temperature from 40–55 °C caused deterioration in the performance of the catalyst. This indicates that an appropriate reaction temperature is crucial for obtaining high enantioselectivity of the catalytic system (Table 1, entry 5 vs 8).

The preliminary results encouraged us to apply the chiral $C_6P_2(NH)_2$–Ru(II) catalyst **2** (Figure 1) to the ATH of a wide range of heteroaromatic ketones. The results are summarized in Table 2. We found that the reactivity and enantioselectivity were affected by the kind of heteroatom in the heterocycle of the ketones. The furan-2-yl ketone **3a** and thiophen-2-yl ketone **3b** were reduced smoothly with 87% ee and 95% ee, respectively, but hydrogenation of

SYNTHESIS 2009, No. 14, pp 2413–2417
Advanced online publication: 27.05.2009
DOI: 10.1055/s-0029-1216833; Art ID: F04109SS

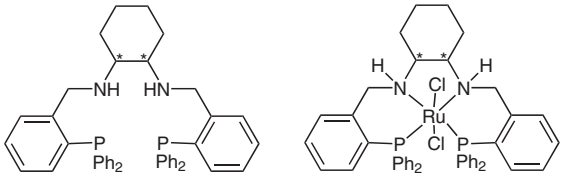


Figure 1

pyridin-2-yl ketone **3c** only gave moderate enantioselectivity. The reason is probably that the nitrogen atom of the heteroaromatic ring coordinates to the ruthenium in the catalytic transition state more strongly than a sulfur atom or an oxygen atom, which would result in a deterioration of the induced enantioselectivity (Table 2, entries 1–3). The enantiomer excess of the products **4c**–**e** improves as the distance of the acyl group from the nitrogen atom in the pyridinyl ring increases; the pyridin-3-yl and pyridin-4-yl ketones **3d** and **3e** were smoothly reduced to the corresponding alcohols **4d** and **4e** with 90% and 97% ee in almost quantitative conversion respectively (Table 2, entries 4 and 5). The introduction of either an electron-donating substituent, such as methyl, to the furan ring or an electron-withdrawing chloro substituent to the thiophene ring decreases the enantioselectivity (from 87% ee to 82% ee and from 95% ee to 90% ee, respectively, Table 2, entry 1 vs 7 and entry 2 vs 8). The steric properties of the alkyl moiety in the substrates also affected the enantioselectivity of the reduction reaction. As the bulkiness of the alkyl group increased from Me, Et, to Pr, the enantioselectivity gradually increased (from 95% ee to 97% ee), but the activity varied little (Table 2, entries 2, 9, and 10). In addition, when using chiral complexes (*R*,*R*)-**2** or (*S*,*S*)-**2** as catalysts respectively, similar activity and enantioselectivity were obtained (Table 2, entry 5 vs 6).

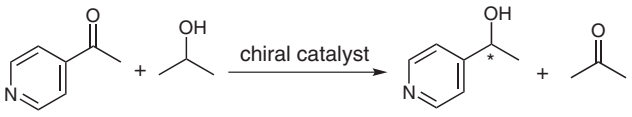
In summary, this work presents that chiral $C_6P_2(NH)_2$–Ru(II) complexes are excellent catalysts for the ATH of heteroaromatic ketones in propan-2-ol. Several heteroaromatic ketones can be effectively reduced to the corresponding chiral alcohols with up to 97% ee under mild conditions without reduction of the heterocycle. These experimental results provide another attractive method for obtaining very useful chiral heteroaromatic alcohols and a practical tool for stereocontrolled organic synthesis.

All experiments were carried out in an N_2 atmosphere with Schlenk techniques, all solvents were dried and purified according to standard methods before use. The heteroaromatic ketones were purchased from Alfa Aesar, and used directly without further purification. Racemic heteroaromatic alcohols were synthesized by $NaBH_4$ reduction in EtOH from their respective ketones. Enantiomeric excesses were determined by GC analysis using a chiral CP-Chirasil-Dex CB column, or by HPLC analysis with a Daicel Chiralcel OD column. NMR spectra were recorded on a Bruker AV 400 instrument using TMS as an internal standard in $CDCl_3$.

Asymmetric Transfer Hydrogenation; General Procedure

(*R*,*R*)-$C_6P_2(NH)_2$–Ru(II) (8.4 mg, 0.01 mmol) and *i*-PrOH (10 mL) were added to a Schlenk tube (50 mL) under N_2. The soln was stirred at 40 °C for 5 min and then 0.1 M KOH in *i*-PrOH (0.5 mL, 0.05 mmol) was added followed by ketone **3** (1 mmol). The soln was stirred at the desired temperature for the required reaction time. The conversion and ee of the product was determined by chiral GC analysis on a CP-Chirasil-Dex CB column. Then the reaction was quenched with sufficient AcOH. The solvent was removed under reduced pressure. The residue was purified by column chromatography (silica gel) to give alcohols **4**.

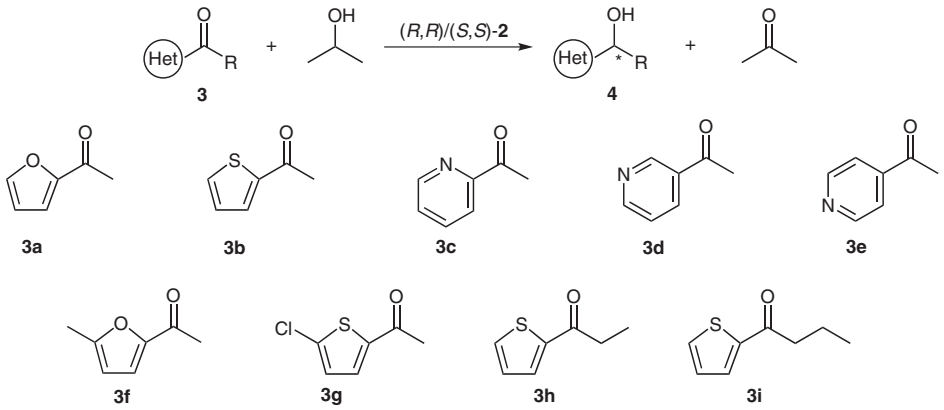
Table 1 ATH of 4-Acetylpyridine (**3e**) Catalyzed by Chiral Diaminodiphosphine–Ru, –Rh, or –Ir Containing Complexes[a]



Entry	Catalyst	Ratio **3e**/catalyst/KOH	Temp. (°C)	Time (h)	Conv.[b] (%)	ee[b] (%)
1	$RhH(CO)(PPh_3)_3$/(*R*,*R*)-**1**	100:1:5	45	3	40	53 (*R*)
2	$[RhCl(COD)]_2$/(*R*,*R*)-**1**	100:1:5	45	3	99	15 (*R*)
3	$[IrCl(COD)]_2$/(*R*,*R*)-**1**	100:1:5	30	2	99	40 (*S*)
4	$[IrHCl_2(COD)]_2$/(*R*,*R*)-**1**	100:1:5	30	2	99	49 (*S*)
5	(*R*,*R*)-**2**	100:1:5	40	4	99	97 (*S*)
6	(*R*,*R*)-**2**	100:1:0	40	4	–	–
7	(*R*,*R*)-**2**	100:1:10	40	2.5	99	96 (*S*)
8	(*R*,*R*)-**2**	100:1:5	55	1.5	99	92 (*S*)

[a] Reaction conditions: 4-acetylpyridine (**3e**, 1.0 mmol), *i*-PrOH (10 mL).
[b] Conversions and enantiomeric excesses were determined by GC analysis using a chiral CP-Chirasil-Dex CB column. The absolute configuration was determined by comparison of the retention time with literature data.

Table 2 ATH of Various Heteroaromatic Ketones Catalyzed by (*R*,*R*)/(*S*,*S*)-**2**[a]



Entry	Substrate	Catalyst	Temp. (°C)	Time (h)	Product	Conv.[b] (%) [Yield[c] (%)]	ee[b] (%)
1	**3a**	(*R*,*R*)-**2**	40	12	**4a**	90 [82]	87 (*S*)
2	**3b**	(*R*,*R*)-**2**	40	12	**4b**	86 [79]	95 (*S*)
3	**3c**	(*R*,*R*)-**2**	40	6	**4c**	96 [92]	78 (*S*)[d]
4	**3d**	(*R*,*R*)-**2**	40	6	**4d**	99 [94]	90 (*S*)
5	**3e**	(*R*,*R*)-**2**	40	4	**4e**	99 [93]	97 (*S*)
6	**3e**	(*S*,*S*)-**2**	45	4	**4f**	99 [94]	96 (*R*)
7	**3f**	(*R*,*R*)-**2**	40	20	**4g**	80 [71]	82 (*S*)
8	**3g**	(*S*,*S*)-**2**	40	7	**4h**	92 [83]	90 (*R*)
9	**3h**	(*R*,*R*)-**2**	40	20	**4i**	90 [81]	96 (*S*)
10	**3i**	(*S*,*S*)-**2**	40	12	**4j**	81 [68]	97 (*R*)

[a] Reaction conditions: substrate **3** (1.0 mmol), *i*-PrOH (10 mL, ratio substrate/catalyst/KOH, 100:1:5.
[b] Conversions and enantiomeric excesses were determined by GC analysis using a chiral CP-Chirasil-Dex CB column. The absolute configuration was determined by the sign of the specific rotation and comparison of the retention time with literature data.
[c] Isolated yield.
[d] The ee value was determined by HPLC analysis with a Daicel Chiralcel OD column.

(*S*)-1-(Furan-2-yl)ethanol [(*S*)-4a][4e,j]
GC [chiral CP-Chirasil-Dex CB column, 0.25 mm × 25 m; column temperature = 80 °C (isothermal); inject temperature = 250 °C; detector temperature = 250 °C; inlet pressure = 0.12 MPa]: t_R = 4.47 (substrate), 10.24 (*R*-isomer), 10.69 min (*S*-isomer); 90% conversion, 87% ee (*S*). The residue was purified by column chromatography (silica gel, EtOAc–hexane, 1:5) to give (*S*)-**4a** (92 mg, 82%) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.54 (d, *J* = 6.8 Hz, 3 H, CH_3), 2.01 (s, 1 H, OH), 4.88 (q, *J* = 6.8 Hz, 1 H, CH), 6.22–6.24 (m, 1 H), 6.32 (dd, *J* = 3.2, 2.0 Hz, 1 H), 7.37 (dd, *J* = 2.0, 0.8 Hz, 1 H).

(*S*)-1-(Thiophen-2-yl)ethanol [(*S*)-4b][4e]
GC [chiral CP-Chirasil-Dex CB column, 0.25 mm × 25 m, column temperature = 110 °C (isothermal), inject temperature = 250 °C, detector temperature = 250 °C, inlet pressure = 0.12 MPa]: t_R = 4.57 (substrate), 8.95 (*R*-isomer), 9.49 min (*S*-isomer); 86% conversion, 95% ee (*S*). The residue was purified by column chromatography (silica gel, EtOAc–hexane, 1:15) to give (*S*)-**4b** (101 mg, 79%) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.59 (d, *J* = 6.4 Hz, 3 H, CH_3), 2.14 (s, 1 H, OH), 5.12 (q, *J* = 6.4 Hz, 1 H, CH), 6.94–6.98 (m, 2 H), 7.22–7.24 (m, 1 H).

(*S*)-1-(Pyridin-2-yl)ethanol [(*S*)-4c][4e]
HPLC [Daicel Chiralcel OD column, 4.6 mm i.d. × 250 mm; eluent = *i*-PrOH–hexane, 5:95; *T* = 25 °C; flow rate = 0.9 mL/min; λ = 254 nm]: t_R = 10.73 (*R*-isomer), 11.81 min (*S*-isomer); 78% ee (*S*).

Conversion was determined by GC [chiral CP-Chirasil-Dex CB column, 0.25 mm × 25 m; column temperature = 110 °C (isothermal); inject temperature = 250 °C; detector temperature = 250 °C; inlet pressure = 0.12 MPa]: t_R = 2.87 (substrate), 6.95 min (alcohol); 96% conversion. The residue was purified by column chromatography (silica gel, EtOAc–hexane, 4:1) to give (*S*)-**4c** (113 mg, 92%) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.51 (d, *J* = 6.4 Hz, 3 H, CH_3), 4.40 (s, 1 H, OH), 4.90 (q, *J* = 6.4 Hz, 1 H, CH), 7.18–7.22 (m, 1 H), 7.29 (d, *J* = 8.4 Hz, 1 H), 7.66–7.71 (m, 1 H), 8.53 (d, *J* = 4.0 Hz, 1 H).

(*S*)-1-(Pyridin-3-yl)ethanol [(*S*)-4d][4e,j]
GC [chiral CP-Chirasil-Dex CB column, 0.25 mm × 25 m; column temperature = 110 °C (isothermal); inject temperature = 250 °C; detector temperature = 250 °C; inlet pressure = 0.12 MPa]: t_R = 2.87 (substrate), 7.67 (*R*-isomer), 8.00 min (*S*-isomer); 99% conversion, 90% ee (*S*). The residue was purified by column chro-

matography (silica gel, EtOAc–hexane, 4:1) to give (*S*)-**4d** (116 mg, 94%) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.50 (d, *J* = 5.6 Hz, 3 H, CH_3), 4.21 (br, s, 1 H, OH), 4.91 (q, *J* = 5.6 Hz, 1 H, CH), 7.26 (dd, *J* = 11.2, 6.8 Hz, 1 H), 7.74 (d, *J* = 6.8 Hz, 1 H), 8.36–8.45 (m, 2 H).

(*S*)-1-(Pyridin-4-yl)ethanol [(*S*)-4e] and (*R*)-1-(Pyridin-4-yl)ethanol [(*R*)-4e][4e]

GC [chiral CP-Chirasil-Dex CB column, 0.25 mm × 25 m; column temperature = 120 °C (isothermal); inject temperature = 250 °C; detector temperature = 250 °C; inlet pressure = 0.12 MPa]: t_R = 14.71 (*R*-isomer), 15.31 min (*S*-isomer); >99% conversion, 97% ee (*S*); t_R = 3.95 (substrate), 14.85 (*R*-isomer), 16.97 (*S*)-isomer), 99% conversion, 96% ee (*R*). The residue was purified by column chromatography (silica gel, EtOAc–hexane, 4:1) to give **4e** as a white solid [(*S*)-**4e**: 115 mg, 93%; (*R*)-**4e**: 116 mg, 94%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.50 (d, *J* = 6.4 Hz, 3 H, CH_3), 3.07 (br, s, 1 H, OH), 4.90 (q, *J* = 6.4 Hz, 1 H, CH), 7.30 (d, *J* = 4.0 Hz, 2 H), 8.50 (d, *J* = 4.0 Hz, 2 H).

(*S*)-1-(5-Methylfuran-2-yl)ethanol [(*S*)-4f][2d]

GC [chiral CP-Chirasil-Dex CB column, 0.25 mm × 25 m; column temperature = 80 °C (isothermal); inject temperature = 250 °C; detector temperature = 250 °C; inlet pressure = 0.12 MPa]: t_R = 7.92 (substrate), 15.00 (*R*-isomer), 15.29 min (*S*-isomer); 80% conversion, 82% ee (*S*). The residue was purified by column chromatography (silica gel, EtOAc–hexane, 1:15) to give (*S*)-**4f** (90 mg, 71%) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.52 (d, *J* = 6.8 Hz, 3 H, CHCH_3), 2.00 (s, 1 H OH), 2.28 (s, 3 H, CH_3), 4.82 (q, *J* = 6.8 Hz, 1 H, CH), 5.89 (d, *J* = 2.4 Hz, 1 H), 6.09 (d, *J* = 2.4 Hz, 1 H).

(*R*)-1-(5-Chlorothiophen-2-yl)ethanol [(*R*)-4g]

GC [chiral CP-Chirasil-Dex CB column, 0.25 mm × 25 m; column temperature = 120 °C (isothermal); inject temperature = 250 °C; detector temperature = 250 °C; inlet pressure = 0.12 MPa]: t_R = 5.48 (substrate), 13.56 (*R*-isomer),16.07 (*S*-isomer); 92% conversion, 90% ee (*R*). The residue was purified by column chromatography (silica gel, EtOAc–hexane, 1:15) to give (*R*)-**4g** (135 mg, 83%) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.55 (d, *J* = 6.4 Hz, 3 H, CH_3), 2.13 (s, 1 H, OH), 5.01 (q, *J* = 6.4 Hz, 1 H, CH), 6.72 (d, *J* = 4.0 Hz, 1 H), 6.76 (d, *J* = 4.0 Hz, 1 H).

(*S*)-1-(Thiophen-2-yl)propan-1-ol [(*S*)-4h][4a]

GC [chiral CP-Chirasil-Dex CB column, 0.25 mm × 25 m; column temperature = 110 °C (isothermal); inject temperature = 250 °C; detector temperature = 250 °C; inlet pressure = 0.12 MPa]: t_R = 6.81 (substrate), 15.12 (*R*-isomer), 15.81 min (*S*-isomer); 90% conversion, 96% ee (*S*). The residue was purified by column chromatography (silica gel, EtOAc–hexane, 1:15) to give (*S*)-**4h** (115 mg, 81%) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.97 (t, *J* = 7.2 Hz, 3 H, CH_3), 1.79–1.96 (m, 2 H, CH_2), 2.05 (s, 1 H, OH), 4.84 (t, *J* = 6.4 Hz, 1 H, CH), 6.95–6.99 (m, 2 H), 7.24–7.26 (m, 1 H).

(*R*)-1-(Thiophen-2-yl)butan-1-ol [(*R*)-4i]

GC [chiral CP-Chirasil-Dex CB column, 0.25 mm × 25 m; column temperature = 110 °C (isothermal); inject temperature = 250 °C; detector temperature = 250 °C; inlet pressure = 0.12 MPa]: t_R = 10.56 (substrate), 24.07 (*S*-isomer), 24.31 min (*R*-isomer); 81% conversion, 97% ee (*R*). The residue was purified by column chromatography (silica gel, EtOAc–hexane, 1:15) to give (*R*)-**4i** (106 mg, 68%) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.95 (t, *J* = 7.2 Hz, 3 H, CH_3), 1.29–1.54 (m, 2 H, CH_2CH$_3$), 1.74–1.92 (m, 2 H, CHCH_2), 2.05 (br, s, 1 H, OH), 4.92 (t, *J* = 6.8 Hz, 1 H, CH), 6.94–6.97 (m, 2 H), 7.24 (dd, *J* = 4.4, 2.0 Hz, 1 H).

Acknowledgment

We would like to thank the National Natural Science Foundation of China (No. 20423002; 20703034), Natural Science Foundation of Fujian Province of China (No. 2008J0235) and State Key Laboratory of Physical Chemistry of Solid Surfaces for financial support.

References

(1) (a) Uskoković, M. R.; Lewis, R. L.; Partridge, J. J.; Despreaux, C. W.; Pruess, D. L. *J. Am. Chem. Soc.* **1979**, *101*, 6742. (b) Kusakabe, M.; Kitano, Y.; Kobayashi, Y.; Sato, F. *J. Org. Chem.* **1989**, *54*, 2085. (c) Waldmann, H. *Tetrahedron Lett.* **1989**, *30*, 3057. (d) Deeter, J.; Frazier, J.; Staten, G.; Staszak, M.; Weigel, L. *Tetrahedron Lett.* **1990**, *31*, 7101. (e) Shioiri, T.; Hayashi, K.; Hamada, Y. *Tetrahedron* **1993**, *49*, 1913. (f) Sablong, R.; Newton, C.; Dierkes, P.; Osborn, J. A. *Tetrahedron Lett.* **1996**, *37*, 4933. (g) Sablong, R.; Osborn, J. A. *Tetrahedron Lett.* **1996**, *37*, 4937. (h) Astleford, B. A.; Weigel, L. O. In *Chirality in Industry II*; Collins, A. N.; Sheldrake, G. N.; Crosby, J., Eds.; Wiley: Chichester, **1997**, Chap. 6. (i) Corey, E. J.; Roberts, B. E. *J. Am. Chem. Soc.* **1997**, *119*, 12425. (j) Wishka, D. G.; Graber, D. R.; Seest, E. P.; Dolak, F. H.; Morris Watt, W. J. *J. Org. Chem.* **1998**, *63*, 7851. (k) Uenishi, J.; Takagi, T.; Ueno, T.; Hiraoka, T.; Yonemitsu, O.; Tsukube, H. *Synlett* **1999**, 41. (l) Chen, G.-M.; Brown, H. C.; Ramachandran, P. V. *J. Org. Chem.* **1999**, *64*, 721.

(2) (a) Kitano, Y.; Kusakabe, M.; Kobayashi, Y.; Sato, F. *J. Org. Chem.* **1989**, *54*, 994. (b) Kobayashi, Y.; Kusakabe, M.; Kitano, Y.; Sato, F. *J. Org. Chem.* **1988**, *53*, 1586. (c) Fantin, G.; Fogagnolo, M.; Medici, A.; Pedrini, P.; Poli, S. *Tetrahedron Lett.* **1993**, *34*, 883. (d) Fantin, G.; Fogagnolo, M.; Medici, A.; Pedrini, P.; Poli, S.; Gardini, F. *Tetrahedron: Asymmetry* **1993**, *4*, 1607. (e) Fantin, G.; Fogagnolo, M.; Guerzoni, M. E.; Medici, A.; Pedrini, P.; Poli, S. *J. Org. Chem.* **1994**, *59*, 924. (f) Kaminska, J.; Gornicka, I.; Sikora, M.; Gora, J. *Tetrahedron: Asymmetry* **1996**, *7*, 907. (g) Kang, S.-K.; Jeon, J.-H.; Yamaguchi, T.; Kim, J.-S.; Ko, B.-S. *Tetrahedron: Asymmetry* **1995**, *6*, 2139. (h) Nakamura, K.; Inoue, Y.; Matsuda, T.; Misawa, I. *J. Chem. Soc., Perkin Trans. 1* **1999**, 2397. (i) Allan, G. R.; Carnell, A. J. *J. Org. Chem.* **2001**, *66*, 6495. (j) Mandal, S. K.; Jensen, D. R.; Pugsley, J. S.; Sigman, M. S. *J. Org. Chem.* **2003**, *68*, 4600. (k) Mandal, S. K.; Sigman, M. S. *J. Org. Chem.* **2003**, *68*, 7535. (l) Ghanem, A.; Schurig, V. *Tetrahedron: Asymmetry* **2003**, *14*, 2547. (m) Shioji, K.; Kurauchi, Y.; Terada, K.; Kodera, Y.; Okuma, K. *Synth. Commun.* **2007**, *37*, 2163.

(3) (a) Wallbaum, S.; Martens, J. *Tetrahedron: Asymmetry* **1993**, *4*, 637. (b) Behnen, W.; Mehler, T.; Martens, J. *Tetrahedron: Asymmetry* **1993**, *4*, 1413. (c) Rijnberg, E.; Jastrzebski, J. T. B. H.; Janssen, M. D.; Boersma, J.; van Koten, G. *Tetrahedron Lett.* **1994**, *35*, 6521. (d) Nakano, H.; Kumagai, N.; Matsuzaki, H.; Kabuto, C.; Hongo, H. *Tetrahedron: Asymmetry* **1997**, *8*, 1391. (e) Huang, W.-S.; Hu, Q.-S.; Pu, L. *J. Org. Chem.* **1998**, *63*, 1364. (f) Reddy, K. S.; Sola, L.; Moyano, A.; Pericas, M. A.; Riera, A. *J. Org. Chem.* **1999**, *64*, 3969. (g) Dangel, B. D.; Polt, R. *Org. Lett.* **2000**, *2*, 3003. (h) Dai, W.-M.; Zhu, H.-J.; Hao, X.-J.

Tetrahedron: Asymmetry **2000**, *11*, 2315. (i) Palmieri, G. *Tetrahedron: Asymmetry* **2000**, *11*, 3361. (j) Hatano, M.; Miyamoto, T.; Ishihara, K. *Adv. Synth. Catal.* **2005**, *347*, 1561. (k) Hatano, M.; Miyamoto, T.; Ishihara, K. *J. Org. Chem.* **2006**, *71*, 6474. (l) Tanaka, T.; Yasuda, Y.; Hayashi, M. *J. Org. Chem.* **2006**, *71*, 7091.

(4) (a) Prasad, K. R. K.; Joshi, N. N. *Tetrahedron: Asymmetry* **1997**, *8*, 173. (b) Okano, K.; Murata, K.; Ikariya, T. *Tetrahedron Lett.* **2000**, *41*, 9277. (c) Lipshutz, B. H.; Lower, A.; Noson, K. *Org. Lett.* **2002**, *4*, 4045. (d) Stampfer, W.; Edegger, K.; Kosjek, B.; Faber, K.; Kroutil, W. *Adv. Synth. Catal.* **2004**, *346*, 57. (e) Soni, P.; Kaur, G.; Chakraborti, A. K.; Banerjee, U. C. *Tetrahedron: Asymmetry* **2005**, *16*, 2425. (f) Morris, D. J.; Hayes, A. M.; Wills, M. *J. Org. Chem.* **2006**, *71*, 7035. (g) Wu, X.; Li, X.; Zanotti-Gerosa, A.; Pettman, A.; Liu, J.; Mills, A. J.; Xiao, J. *Chem.–Eur. J.* **2008**, *14*, 2209. (h) Wu, X.; Li, X.; King, F.; Xiao, J. *Angew. Chem. Int. Ed.* **2005**, *44*, 3407. (i) Matharu, D. S.; Morris, D. J.; Clarkson, G. J.; Wills, M. *Chem. Commun.* **2006**, 3232. (j) Ohkuma, T.; Koizumi, M.; Yoshida, M.; Noyori, R. *Org. Lett.* **2000**, *2*, 1749. (k) Burk, M. J.; Hems, W.; Herzberg, D.; Malan, C.; Zanotti-Gerosa, A. *Org. Lett.* **2000**, *2*, 4173. (l) Wu, J.; Ji, J. X.; Guo, R. W.; Yeung, C. H.; Chan, A. S. C. *Chem.–Eur. J.* **2003**, *9*, 2963. (m) Chen, C.-y.; Reamer, R. A.; Chilenski, J. R.; McWilliams, C. J. *Org. Lett.* **2003**, *5*, 5039. (n) Xie, J.-H.; Wang, L.-X.; Fu, Y.; Zhu, S.-F.; Fan, B.-M.; Duan, H.-F.; Zhou, Q.-L. *J. Am. Chem. Soc.* **2003**, *125*, 4404. (o) Jing, Q.; Zhang, X.; Sun, J.; Ding, K. *Adv. Synth. Catal.* **2005**, *347*, 1193. (p) Xu, Y. J.; Clarkson, G. C.; Docherty, G.; North, C. L.; Woodward, G.; Wills, M. *J. Org. Chem.* **2005**, *70*, 8079. (q) Cheemala, M. N.; Gayral, M.; Brown, J. M.; Rossen, K.; Knochel, P. *Synthesis* **2007**, 3877. (r) Doherty, S.; Knight, J. G.; Bell, A. G.; Harrington, R. W.; Clegg, W. *Organometallics* **2007**, *26*, 2465.

(5) Noyori, R.; Hashiguchi, S. *Acc. Chem. Res.* **1997**, *30*, 97.

(6) Rautenstrauch, V.; Hoang-Cong, X.; Churland, R.; Abdur-Rashid, K.; Morris, R. H. *Chem.–Eur. J.* **2003**, *9*, 4954.

(7) Wu, X.; Xiao, J. *Chem. Commun.* **2007**, 2449.

(8) Ikariya, T.; Blacker, A. J. *Acc. Chem. Res.* **2007**, *40*, 1300.

(9) (a) Gao, J.-X.; Ikariya, T.; Noyori, R. *Organometallics* **1996**, *15*, 1087. (b) Gao, J.-X.; Yi, X.-D.; Xu, P.-P.; Tang, C.-L.; Zhang, H.; Wan, H.-L.; Ikariya, T. *J. Mol. Catal. A: Chem.* **2000**, *159*, 3. (c) Gao, J.-X.; Zhang, H.; Yi, X.-D.; Xu, P.-P.; Tang, C.-L.; Wan, H.-L.; Tsai, K.-R.; Ikariya, T. *Chirality* **2000**, 383. (d) Chen, J.-S.; Li, Y.-Y.; Dong, Z.-R.; Li, B.-Z.; Gao, J.-X. *Tetrahedron Lett.* **2004**, *45*, 8415. (e) Dong, Z.-R.; Li, Y.-Y.; Chen, J.-S.; Li, B.-Z.; Xing, Y.; Gao, J.-X. *Org. Lett.* **2005**, *7*, 1043. (f) Xing, Y.; Chen, J.-S.; Dong, Z.-R.; Li, Y.-Y.; Gao, J.-X. *Tetrahedron Lett.* **2006**, *47*, 4501. (g) Li, Y.-Y.; Zhang, X.-Q.; Dong, Z.-R.; Shen, W.-Y.; Chen, G.; Gao, J.-X. *Org. Lett.* **2006**, *8*, 5565.