Asymmetric Catalysis

DOI: 10.1002/ange.200803872

Iridium-Catalyzed Highly Enantioselective Hydrogenation of the C=C Bond of α, β-Unsaturated Ketones**

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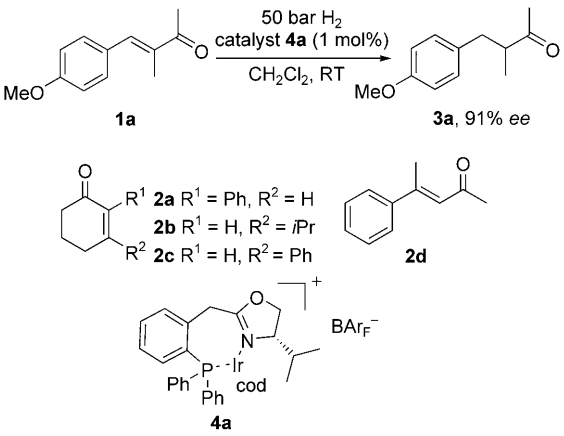
Ketones with α-chiral carbon centers are an important group of compounds in organic synthesis,[1] and many efforts have been focused on their preparation. However, high enantioselectivity has seldom been reported for the synthesis of α-substituted ketones,[2–5] because the products undergo racemization of the chiral carbon center through enolization. Installing chiral centers at the α-position of ketones in high enantioselectivity remains a great challenge. Conversely, asymmetric hydrogenation is a very practical method and has attracted much attention. Many transition metals have been used in catalysts for such conversions, and a variety of unsaturated compounds have been hydrogenated in the presence of chiral transition-metal complexes.[6] Among them, chiral iridium complexes have unique properties, both in asymmetric induction and catalytic activity.[7] Not only alkenes but also imines and ketones are suitable substrates for the hydrogenation reaction. Seemingly, ketones with α-chiral carbon centers are accessible from asymmetric hydrogenation of corresponding α-substituted α,β-unsaturated ketones. However, few examples were found to establish chiral centers at the α position of ketones using the hydrogenation strategy.[8,9] Although asymmetric hydrogenation of α,β-unsaturated ketones has been well documented, in most cases, the carbonyl group is reduced preferentially to afford the allyl alcohol.[10] In studying the effectiveness of chiral ligands in asymmetric catalysis, we investigated whether or not the carbon–carbon double bond of α,β-unsaturated ketones is hydrogenated selectively to provide ketones with chiral center at the α position of carbonyl group. Herein, we address this important issue and disclose preliminary results on the asymmetric hydrogenation of α,β-unsaturated ketones, using chiral iridium complexes to provide ketones with α-carbon chiral center in high enantioselectivity.[7]

Initially, asymmetric hydrogenation of α,β-unsaturated ketones **1a** and **2** were investigated by using 1 mol% of the Ir catalyst **4a** in dichloromethane under 50 bar of H_2 pressure at room temperature [Eq. (1)].[7d] Hydrogenation of **1a** provided the ketone **3a** in 91% *ee*, whereas that of **2d** afforded a mixture of the alkyl ketone, the alkyl alcohol, and residual substrate. No reaction took place for **2a–c**. These results demonstrated that the reaction, under the aforementioned conditions, preferentially reduces carbon–carbon double bonds of acyclic α-substituted α,β-unsaturated ketones, such as **1a**.



(1)

Based upon these results, screening of solvents and catalyst counterions was carried out (Table 1). Only the reactions in weakly polar solvents toluene (Table 1, entry 2) and CH_2Cl_2 (Table 1, entry 7) afforded high conversion and high enantioselectivity, with the reaction in CH_2Cl_2 furnishing

Table 1: The effect of various solvents and counterions on the asymmetric hydrogenation of α,β-unsaturated ketone **1a**.[a]

Entry	Solvent	Counterion	Conv. [%][b]	*ee* [%][c]
1	MeOH	BAr_F^-	0	–
2	toluene	BAr_F^-	100	86
3	*n*-hexane	BAr_F^-	6	–
4	THF	BAr_F^-	20	n.d.[d]
5	ethyl acetate	BAr_F^-	58	n.d.[d]
6	acetone	BAr_F^-	0	–
7	CH_2Cl_2	BAr_F^-	100	91
8	CH_2Cl_2	Cl^-	9	n.d.[d]
9	CH_2Cl_2	BF_4^-	16	n.d.[d]
10	CH_2Cl_2	PF_6^-	13	n.d.[d]

[a] **1a** (0.2 mmol), **4a** (1 mol%, counterions vary), H_2 (50 bar) in 2 mL of solvent at room temperature for 24 h. [b] Determined by ^{1}H NMR spectroscopy. [c] Determined by chiral HPLC. [d] n.d. = not determined.

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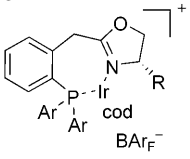
[**] This work was financially supported by the Major Basic Research Development Program (2006CB806106), National Natural Science Foundation of China (20532050, 20672130), Chinese Academy of Sciences, Croucher Foundation of Hong Kong, and Science and Technology Commission of Shanghai Municipality. Y.-W. C. is a participant of the undergraduate program of Shanghai Normal University.

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.200803872.

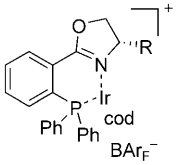
better results. Reactions in other nonpolar and polar solvents, such as hexane, THF, ethyl acetate, MeOH, and acetone, gave either product in low conversion or no product (Table 1, entries 1,3–6). Among the counterions tested, only tetrakis-[3,5-bis(trifluoromethyl)phenyl]borate (BAr_F) resulted in a high-yielding, enantioselective reaction (Table 1, entries 7–10). These results reflect the same tendency as reported.[7d,11,12]

The impact of changes in the phosphane ligands developed by our group,[13] having different substituents on the oxazoline ring and different aryl groups on P , as well as phosphinooxazoline (PHOX) ligands, was investigated.[7d,11] (Table 2). Catalysts **4a**–**f**, from benzylic-substituted ligands, and catalyst **4h**, from the *t*Bu-substituted PHOX ligand, achieved complete conversion of α,β-unsaturated ketones **1a** (Table 2, entries 1–6 and 8), whereas the conversion was only 93% using catalyst **4g**, from *i*Pr-substituted PHOX (Table 2, entry 7). Using catalyst **4h** led to formation of product **3a** with 98% *ee*, the highest enantioselectivity among the catalysts screened, (Table 2, entry 8), whereas catalyst **4g** gave **3a** in only 79% *ee* (Table 2, entry 7). For benzylic ligands, catalyst **4a**, with *i*Pr-substituted oxazoline, and catalyst **4e**, with *i*Pr-substituted oxazoline and two *p*-anisyl groups on P, provided **3a** in 91% and 92% *ee* respectively (Table 2, entries 1 and 5), whereas catalyst **4b**, with Me-substituted oxazoline, provided **3a** in 34% *ee* (Table 2, entry 2). The other catalysts **4c** and **4d**, incorporating *i*Bu and *t*Bu oxazoline substituents, afforded **3a** with 89% and 86% *ee* (Table 2, entries 3 and 4). Notably, the two types of ligands showed different tendencies towards enantioselectivity. Catalyst **4a**, derived from benzylic substituted ligands with *i*Pr-substituted oxazoline, gave better enantioselectivity than catalyst **4g**, derived from *i*Pr-substituted PHOX (Table 2, entry 1 vs. entry 7), whereas catalyst **4h**, derived from *t*Bu PHOX gave better enantioselectivity than the analogous benzylic substituted catalyst **4d** (Table 2, entry 8 vs. entry 4).

Table 2: The effect of the catalyst structures on the asymmetric hydrogenation of α,β-unsaturated ketone **1a**.[a]



4a. Ar = Ph, R = *i*Pr
4b. Ar = Ph, R = Me
4c. Ar = Ph, R = *i*Bu
4d. Ar = Ph, R = *t*Bu
4e. Ar = *p*-$MeOC_6H_4$, R = *i*Pr
4f. Ar = *o*-Tol, R = *i*Pr



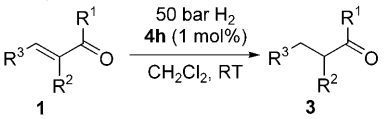
4g. R = *i*Pr
4h. R = *t*Bu

Entry	Catalyst	Conv. [%][b]	*ee* [%][c]
1	**4a**	100	91
2	**4b**	100	34
3	**4c**	100	89
4	**4d**	100	86
5	**4e**	100	92
6	**4f**	100	75
7	**4g**	93	79
8	**4h**	100	98

[a] **1a** (0.2 mmol), catalyst (1 mol%), H_2 (50 bar) in 2 mL of CH_2Cl_2 at room temperature for 24 h. BAr_F^- = tetrakis[3,5-bis(trifluoromethyl)phenyl]borate; cod = cyclooctadiene. [b] Determined by ^{1}H NMR spectroscopy. [c] Determined by chiral HPLC.

Under the above reaction conditions, different substrates were subjected to hydrogenation using **4h** as a catalyst, (Table 3). All reactions of ketones incorporating aryl β-substituents, including cyclic ketones **1e**, **1f**, and **1h–j** (Table 3, entries 5, 6, and 8–10) and acyclic ketones **1a–d** and **1g** (Table 3, entries 1–4 and 7), afforded chiral ketones in 95–99% *ee*. Heteroaryl substituted **1j** was also a suitable substrate (Table 3,entry 10), affording **3j** in 98% *ee*. However, hydrogenation of ketone **1k**, with *i*Pr at the β position, gave **3k** in 40% *ee* with 78% conversion using catalyst **4h** (Table 3, entry 11), and with 100% conversion but no enantioselectivity using catalyst **4a** (not shown in Table), No reaction took place for ketone substrate **1l**, with *n*Pr at the β position (Table 3, entry 12). Interestingly, α,α′-bis(benzylidene) ketones **1h** and **1i** were smoothly hydrogenated to provide corresponding ketones in high diastereo- and enan-

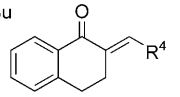
Table 3: Asymmetric hydrogenation of α,β-unsaturated ketone **1** using catalyst **4h**.[a]



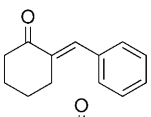
(2)

1 **3**

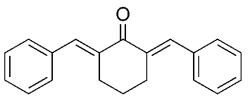
a R^1 = Me, R^2 = Me, R^3 = *p*-$MeOC_6H_4$
b R^1 = Me, R^2 = Me, R^3 = Ph
c R^1 = Et, R^2 = Me, R^3 = *p*-$MeOC_6H_4$
d R^1 = *n*Pr, R^2 = Et, R^3 = *p*-$MeOC_6H_4$
g R^1 = Ph, R^2 = Me, R^3 = Ph
l R^1 = Et, R^2 = Me, R^3 = *n*Pr



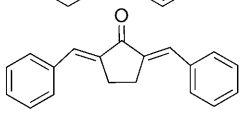
1e R^4 = Ph
1j R^4 = furan
1k R^4 = *i*Pr



1f



1h



1i

Entry	Substrate	Under 50 bar of H_2 Conv. [%][b]	*ee* [%][c]	Under ambient pressure of H_2 Conv. [%][b]	*ee* [%][c]
1	**1a**	100	98	100	98[f]
2	**1b**	100	98	100	98
3	**1c**	100	97	100	97[f]
4	**1d**	100	98	100	98
5	**1e**	100	98	100	99
6	**1f**	100	98	100	97[f]
7	**1g**	100	97	95	97
8	**1h**	100	>99[d]	100	>99[f,g]
9	**1i**	100	95[e,f]	100	>99[h,i]
10	**1j**	100	98	100	98[f]
11	**1k**	78	40	–	–
12[j]	**1l**	0	–	–	–

[a] Conditions unless otherwise stated: substrate (0.2 mmol), catalyst **4h** (1 mol%), CH_2Cl_2 (2 mL), room temperature for 24 h. [b] Determined by ^{1}H NMR spectroscopy. [c] Determined by chiral HPLC. [d] *cis*/*trans* = 1:49, determined by ^{1}H NMR spectroscopy. [e] *cis*/*trans* = 1:10. [f] 3 mol% of catalyst was used. [g] *cis*/*trans* = 1:>50. [h] 5 mol% of catalyst was used. [i] *cis*/*trans* = 1:38. [j] Catalyst **4a** was used.

tioselectivities; > 99 % *ee* with a ratio of 1:49 in favor of the *trans* product for **3h** (Table 3, entry 8), and 95 % *ee* with 1:10 diastereoselectivity in favor of the *trans* product for **3i** (Table 3, entry 9). Even under 50 bar pressure of H_2, no reduction of the carbonyl group was detected by ^1H NMR spectroscopy for any substrate. These reaction conditions are chemospecific for reduction of the carbon–carbon double bond.

Hydrogenation under mild conditions, especially under ambient pressure of hydrogen, is extremely desirable in industry. Thus, the reaction was investigated at this pressure (Table 3). Most substrates delivered the products in comparable *ee* values or, in the cases of **1e** and **1i** (Table 3, entries 5 and 9), even higher *ee* values than under 50 bar H_2, although higher catalyst loading was required in the reactions of **1c**, **1f**, and **1h–j** (Table 3, entries 3, 6 and 8–10).

The high activity of the catalytic system is also evident in the reaction of **1a** under 20 bar of H_2 using 0.3 mol % of **4h**, giving the product in 97 % *ee* with 84 % conversion.

In summary, a method has been developed for the installation of chiral centers at the α-position of ketones, by Ir-catalyzed asymmetric hydrogenation of α, β-unsaturated ketones. High enantioselectivity was achieved, even under ambient pressure of hydrogen. The PHOX ligand with a *t*Bu-substituted oxazoline moiety afforded the system excellent asymmetric induction ability. Further investigations on the understanding and applications of these ligands in asymmetric hydrogenation are currently in progress.

Received: August 6, 2008
Revised: October 13, 2008
Published online: November 19, 2008

Keywords: enantioselectivity · enones · hydrogenation · iridium · N,P-ligands

[1] a) K. C. Nicolaou, D. J. Edmonds, A. Li, G. S. Tria, *Angew. Chem.* **2007**, *119*, 4016; *Angew. Chem. Int. Ed.* **2007**, *46*, 3942; b) S. H. Lim, M. D. Curtis, P. Beak, *Org. Lett.* **2001**, *3*, 711; c) U. Schneider, X. Pannecoucke, J. C. Quirion, *Synlett* **2005**, 1853.

[2] a) W. Oppolzer, C. Darcel, P. Rochet, S. Rosset, J. de Brabander, *Helv. Chim. Acta* **1997**, *80*, 1319; b) M. Kossenjans, J. Martens, *Tetrahedron: Asymmetry* **1999**, *10*, 3409; c) A. G. Myers, B. H. Yang, H. Chen, J. L. Gleason, *J. Am. Chem. Soc.* **1994**, *116*, 9361; d) D. A. Evans, M. D. Ennis, D. J. Mathre, *J. Am. Chem. Soc.* **1982**, *104*, 1737; e) P. E. Sonnet, R. R. Heath, *J. Org. Chem.* **1980**, *45*, 3137; f) H. Kaku, S. Takaoka, T. Tsunoda, *Tetrahedron* **2002**, *58*, 3401; g) P. C. Hutchison, T. D. Heightman, D. J. Procter, *Org. Lett.* **2002**, *4*, 4583; h) A. M. McGhee, J. C. Kizirian, D. J. Procter, *Org. Biomol. Chem.* **2007**, *5*, 1021.

[3] Some examples of alkylation of ketones by transition-metal-catalyzed asymmetric allylic alkylation: a) B. M. Trost, G. M. Schroeder, *J. Am. Chem. Soc.* **1999**, *121*, 6759; b) M. Braun, F. Laicher, T. Meier, *Angew. Chem.* **2000**, *112*, 3637; *Angew. Chem. Int. Ed.* **2000**, *39*, 3494; c) U. Kazmaier, *Curr. Org. Chem.* **2003**, *7*, 317; d) E. C. Burger, J. A. Tunge, *Org. Lett.* **2004**, *6*, 4113; e) D. C. Behenna, B. M. Stoltz, *J. Am. Chem. Soc.* **2004**, *126*, 15044; f) B. M. Trost, J. Xu, *J. Am. Chem. Soc.* **2005**, *127*, 2846; g) B. M. Trost, J. Xu, *J. Am. Chem. Soc.* **2005**, *127*, 17180; h) M. Braun, T. Meier, *Synlett* **2005**, 2968; i) T. Graening, J. F. Hartwig, *J. Am. Chem. Soc.* **2005**, *127*, 17192; j) D. Liu, F. Xie, W. Zhang, *Tetrahedron Lett.* **2007**, *48*, 7591; k) D. J. Weix, J. F. Hartwig, *J. Am. Chem. Soc.* **2007**, *129*, 7720; l) H. He, X.-J. Zheng, Y. Li, L.-X. Dai, S.-L. You, *Org. Lett.* **2007**, *9*, 4339; m) M. Braun, T. Meier, F. Laicher, P. Meletis, M. Fidan, *Adv. Synth. Catal.* **2008**, *350*, 303.

[4] a) S.-L. You, X.-L. Hou, L.-X. Dai, X.-Z. Zhu, *Org. Lett.* **2001**, *3*, 149; b) X. X. Yan, C. G. Liang, Y. Zhang, W. Hong, B. X. Cao, L. X. Dai, X. L. Hou, *Angew. Chem.* **2005**, *117*, 6702; *Angew. Chem. Int. Ed.* **2005**, *44*, 6544; *Angew. Chem.* **2005**, *117*, 6702; c) W.-H. Zheng, B.-H. Zheng, Y. Zhang, X. L. Hou, *J. Am. Chem. Soc.* **2007**, *129*, 7718.

[5] Asymmetric alkylation of ketones by using imines was also reported: a) for a review: A. Job, C. F. Janeck, W. Bettray, R. Peters, D. Enders, *Tetrahedron* **2002**, *58*, 2253; b) A. I. Meyers, D. R. Williams, M. Druelinger, *J. Am. Chem. Soc.* **1976**, *98*, 3032; c) A. I. Meyers, D. R. Williams, G. W. Erickson, S. White, M. Druelinger, *J. Am. Chem. Soc.* **1981**, *103*, 3081; d) S.-I. Hashimoto, K. Koga, *Tetrahedron Lett.* **1978**, *19*, 573; e) D. Lim, D. M. Coltart, *Angew. Chem.* **2008**, *120*, 5285; *Angew. Chem. Int. Ed.* **2008**, *47*, 5207.

[6] For reviews, see: a) *The Handbook of Homogeneous Hydrogenation* (Eds.: J. G. de Vries, C. J. Elsevier), Wiley-VCH, Weinheim, **2007**; b) S. Kobayashi, H. Ishitani, *Chem. Rev.* **1999**, *99*, 1069 – 1094; c) R. Noyori, T. Ohkuma, *Angew. Chem.* **2001**, *113*, 40; *Angew. Chem. Int. Ed.* **2001**, *40*, 40; d) H. U. Blaser, C. Malan, B. Pugin, F. Spindler, H. Steiner, M. Studer, *Adv. Synth. Catal.* **2003**, *345*, 103; e) W. Tang, X. Zhang, *Chem. Rev.* **2003**, *103*, 3029; f) T. Jerphagnon, J. L. Renaud, C. Bruneau, *Tetrahedron: Asymmetry* **2004**, *15*, 2101; g) W. Zhang, Y. Chi, X. Zhang, *Acc. Chem. Res.* **2007**, *40*, 1278; h) A. J. Minnaard, B. L. Feringa, L. Lefort, J. G. de Vries, *Acc. Chem. Res.* **2007**, *40*, 1267; i) W. P. Hems, M. Groarke, A. Zanotti-Gerosa, G. A. Grasa, *Acc. Chem. Res.* **2007**, *40*, 1340; j) F. D. Klingler, *Acc. Chem. Res.* **2007**, *40*, 1367; k) Y. G. Zhou, *Acc. Chem. Res.* **2007**, *40*, 1357.

[7] For reviews on Ir-catalyzed asymmetric hydrogenation, see: a) A. Pfaltz, J. Blankenstein, R. Hilgraf, E. Hörmann, S. McIntyre, F. Menges, M. Schönleber, S. P. Smidt, B. Wüstenberg, N. Zimmermann, *Adv. Synth. Catal.* **2003**, *345*, 33; b) X. Cui, K. Burgess, *Chem. Rev.* **2005**, *105*, 3272; c) K. Källström, I. Munslow, P. G. Andersson, *Chem. Eur. J.* **2006**, *12*, 3194; For examples of Ir-catalyzed asymmetric hydrogenation, see: d) A. Lightfoot, P. Schnider, A. Pfaltz, *Angew. Chem.* **1998**, *110*, 3047; *Angew. Chem. Int. Ed.* **1998**, *37*, 2897; e) S. Kainz, A. Brinkmann, W. Leitner, A. Pfaltz, *J. Am. Chem. Soc.* **1999**, *121*, 6421; f) D. Xiao, X. Zhang, *Angew. Chem.* **2001**, *113*, 3533; *Angew. Chem. Int. Ed.* **2001**, *40*, 3425; g) W. B. Wang, S. M. Lu, P. Y. Yang, X. W. Han, Y. G. Zhou, *J. Am. Chem. Soc.* **2003**, *125*, 10536; h) Y. Fan, X. Cui, K. Burgess, M. B. Hall, *J. Am. Chem. Soc.* **2004**, *126*, 16688; i) S. M. Lu, X. W. Han, Y. G. Zhou, *Adv. Synth. Catal.* **2004**, *346*, 909; j) K. H. Lam, L. Xu, L. Feng, Q. H. Fan, F. L. Lam, W. Lo, A. S. C. Chan, *Adv. Synth. Catal.* **2005**, *347*, 1755; k) C. Moessner, C. Bolm, *Angew. Chem.* **2005**, *117*, 7736; *Angew. Chem. Int. Ed.* **2005**, *44*, 7564; l) L. Xu, K. H. Lam, J. Ji, J. Wu, Q. H. Fan, W. H. Lo, A. S. C. Chan, *Chem. Commun.* **2005**, 1390; m) M. T. Reetz, X. Li, *Chem. Commun.* **2006**, 2159; n) S. Bell, B. Wüstenberg, S. Kaiser, F. Menges, T. Netscher, A. Pfaltz, *Science* **2006**, *311*, 642; o) S. F. Zhu, J. B. Xie, Y. Z. Zhang, S. Li, Q. L. Zhou, *J. Am. Chem. Soc.* **2006**, *128*, 12886; p) C. Hedberg, K. Källström , P. Brandt, L. K. Hansen, P. G. Andersson, *J. Am. Chem. Soc.* **2006**, *128*, 2995; q) S. M. Lu, Y. Q. Wang, X. W. Han, Y. G. Zhou, *Angew. Chem.* **2006**, *118*, 2318; *Angew. Chem. Int. Ed.* **2006**, *45*, 2260; r) G. H. Hou, J. H. Xie, L. X. Wang, Q. L. Zhou, *J. Am. Chem. Soc.* **2006**, *128*, 11774; s) M. N. Cheemala, P. Knochel, *Org. Lett.* **2007**, *9*, 3089; t) M. Engman, J. S. Diesen, A. Paptchikhine, P. G. Andersson, *J. Am. Chem. Soc.* **2007**, *129*, 4536; u) Z. J. Wang, G. J. Deng, Y. Li, Y. M. He, W. J. Tang, Q. H. Fan, *Org. Lett.* **2007**, *9*, 1243; v) F. Giacomina,

A. Meetsma, L. Panella, L. Lefort, A. H. M. de Vries, J. G. de Vries, *Angew. Chem.* **2007**, *119*, 1519; *Angew. Chem. Int. Ed.* **2007**, *46*, 1497; w) M. G. Schrems, E. Neumann, A. Pfaltz, *Angew. Chem.* **2007**, *119*, 8422; *Angew. Chem. Int. Ed.* **2007**, *46*, 8274; x) S. Li, S. F. Zhu, C. M. Zhang, S. Song, Q. L. Zhou, *J. Am. Chem. Soc.* **2008**, *130*, 8584; y) Y. Wang, T. Sturm, M. Steurer, V. B. Arion, K. Mereiter, F. Spindler, W. Weissensteiner, *Organometallics* **2008**, *27*, 1119; z) X. B. Wang, W. Zeng, Y. G. Zhou, *Tetrahedron Lett.* **2008**, *49*, 4922.

[8] For examples of organocatalyzed asymmetric hydrogenation, see: a) J. B. Tuttle, S. G. Ouellet, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2006**, *128*, 12662; b) N. J. A. Martin, B. List, *J. Am. Chem. Soc.* **2006**, *128*, 13368.

[9] a) A. Tungler, T. Máthé, J. Petró, T. Tarnai, *J. Mol. Catal.* **1990**, *61*, 259; b) T. Ohta, T. Miyake, N. Seido, H. Kumobayashi, H. Takaya, *J. Org. Chem.* **1995**, *60*, 357; c) G. Fogassy, A. Tungler, A. Lévai, G. Tóth, *J. Mol. Catal. A* **2002**, *179*, 101; d) C. Thorey, S. Bouquillon, A. Helimi, F. Hénin, J. Muzart, *Eur. J. Org. Chem.* **2002**, 2151; e) R. Hilgraf, A. Pfaltz, *Adv. Synth. Catal.* **2005**, *347*, 61; f) A. I. McIntosh, D. J. Watson, J. W. Burton, R. M. Lambert, *J. Am. Chem. Soc.* **2006**, *128*, 7329; g) L. Qiu, F. Y. Kwong, J. Wu, W. H. Lam, S. Chan, W. Y. Yu, Y. M. Li, R. Guo, Z. Zhou, A. S. C. Chan, *J. Am. Chem. Soc.* **2006**, *128*, 5955; h) B. H. Lipshutz, B. A. Frieman, A. E. Tomaso Jr. , *Angew. Chem.* **2006**, *118*, 1281; *Angew. Chem. Int. Ed.* **2006**, *45*, 1259; i) Y. Tsuchiya, Y. Hamashima, M. Sodeoka, *Org. Lett.* **2006**, *8*, 4851; j) T. Ikariya, A. J. Blacker, *Acc. Chem. Res.* **2007**, *40*, 1300; k) T. Ohshima, H. Tadaoka, K. Hori, N. Sayo, K. Mashima, *Chem. Eur. J.* **2008**, *14*, 2060; l) S. M. Lu, C. Bolm, *Chem. Eur. J.* **2008**, *14*, 7513.

[10] a) K. Mashima, T. Akutagawa, X. Zhang, H. Takaya, T. Taketomi, H. Kumobayashi, S. Akutagawa, *J. Organomet. Chem.* **1992**, *428*, 213; b) T. Ohkuma, H. Ooka, T. Ikariya, R. Noyori, *J. Am. Chem. Soc.* **1995**, *117*, 10417; c) T. Ohkuma, M. Koizumi, H. Doucet, T. Pham, M. Kozawa, K. Murata, E. Katayama, T. Yokozawa, T. Ikariya, R. Noyori, *J. Am. Chem. Soc.* **1998**, *120*, 13529; d) M. J. Burk, W. Hems, D. Herzberg, C. Malan, A. Zanotti-Gerosa, *Org. Lett.* **2000**, *2*, 4173; e) J. Xie, L. Wang, Y. Fu, S. Zhu, B. Fan, H. Duan, Q. Zhou, *J. Am. Chem. Soc.* **2003**, *125*, 4404.

[11] a) G. Helmchen, A. Pfaltz, *Acc. Chem. Res.* **2000**, *33*, 336; b) S. J. Roseblade, A. Pfaltz, *Acc. Chem. Res.* **2007**, *40*, 1402.

[12] S. P. Smidt, N. Zimmermann, M. Studer, A. Pfaltz, *Chem. Eur. J.* **2004**, *10*, 4685.

[13] a) X. L. Hou, D. X. Dong, K. Yuan, *Tetrahedron: Asymmetry* **2004**, *15*, 2189; b) W. Q. Wu, Q. Peng, D. X. Dong, X. L. Hou, Y. D. Wu, *J. Am. Chem. Soc.* **2008**, *130*, 9717.

