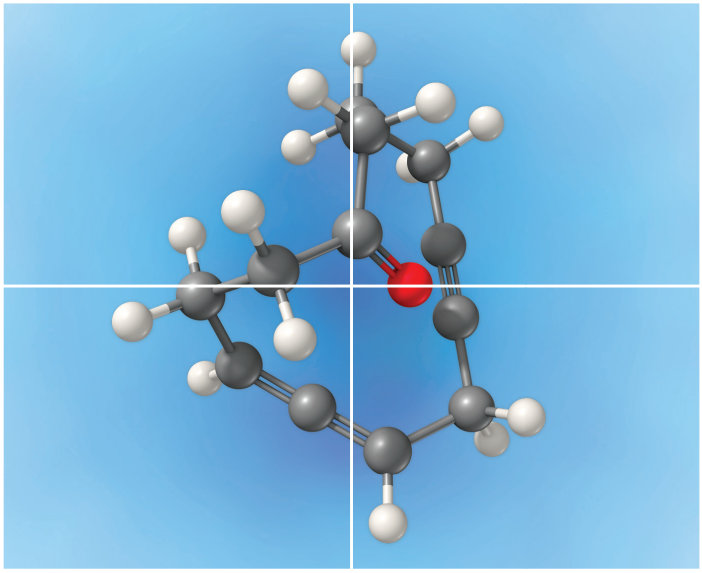
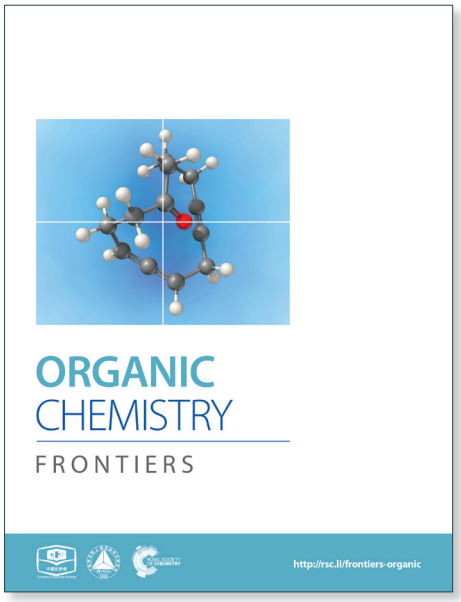
ORGANIC CHEMISTRY

FRONTIERS



Accepted Manuscript



This is an *Accepted Manuscript*, which has been through the Royal Society of Chemistry peer review process and has been accepted for publication.

Accepted Manuscripts are published online shortly after acceptance, before technical editing, formatting and proof reading. Using this free service, authors can make their results available to the community, in citable form, before we publish the edited article. We will replace this *Accepted Manuscript* with the edited and formatted *Advance Article* as soon as it is available.

You can find more information about *Accepted Manuscripts* in the **Information for Authors**.

Please note that technical editing may introduce minor changes to the text and/or graphics, which may alter content. The journal's standard **Terms & Conditions** and the **Ethical guidelines** still apply. In no event shall the Royal Society of Chemistry be held responsible for any errors or omissions in this *Accepted Manuscript* or any consequences arising from the use of any information it contains.

Organic Chemistry Frontiers

RSCPublishing

COMMUNICATION

Asymmetric hydrogenation of 3-substituted 2*H*-1,4-benzoxazines with chiral cationic Ru-MsDPEN catalysts: remarkable counteranion effect

Cite this: DOI: 10.1039/x0xx00000x

Received 00th January 2012,
Accepted 00th January 2012

DOI: 10.1039/x0xx00000x

www.rsc.org/

Jie Qin,[a,b] Fei Chen,[a] Yan-Mei He,[a] Qing-Hua Fan*[a,c]

The enantioselective hydrogenation of 3-aryl and 3-styryl-substituted-2*H*-1,4-benzoxazines was developed by using the chiral cationic Ru(η^6-cymene)(MsDPEN)(Ar_2PO_2) system in high yields with up to 99% ee. The counteranion was found to be critically important for the high enantioselectivity. Furthermore, the regioselectivity could be regulated by the counteranion of catalyst in the asymmetric hydrogenation of 3-styryl-2*H*-1,4-benzoxazines.

Optically active 3,4-dihydro-2*H*-1,4-benzoxazines are ubiquitous structural moieties in biologically interesting natural alkaloids and chiral pharmaceuticals.[1-2] Some important representative examples include Obscurinervine, Levofloxacin, WIN-55212-2 and compound **A** (Fig. 1). Consequently, many research efforts have been devoted to the asymmetric synthesis of these chiral compounds over the past decades.[3-9] Among them, asymmetric hydrogenation represents one of the most convenient and atom-economic approaches,[8,9] and the transition-metal-catalyzed reduction of corresponding readily available benzoxazines has attracted much attention over the past few years.[9] In 1998, Satoh and co-workers first reported the Ir-BPPM (*N*-(*t*-butoxy-carbonyl)-4-(diphenylphosphino)-2-[(siphwnylphoaphino)methyl]pyrrolidine) and bismuth(III) iodide system catalyzed hydrogenation of 7,8-difluoro-3-methyl-2*H*-1,4-benzoxazine affording the product as a key intermediate for the synthesis of Levofloxacin with 90% ee.[9a] Most recently, a variety of chiral metal catalysts, including Ir, Ru and Fe complexes,[9b-f] have been developed to successfully catalyze the enantioselective hydrogenation of 3-aryl benzoxazine derivatives with good to excellent enantioselectivities. Despite great progress achieved in this field, all these metallic catalysts contained phosphorus ligand around the metal center which are often air sensitive. Furthermore, in most cases, only the 3-aryl benzoxazines were studied with these reported catalysts.[9c-g] From the viewpoint of both scientific interest and practical applications, it is desirable to develop more efficient and stable catalysts for the asymmetric hydrogenation of a broad range of 3-substituted benzoxazine derivatives.

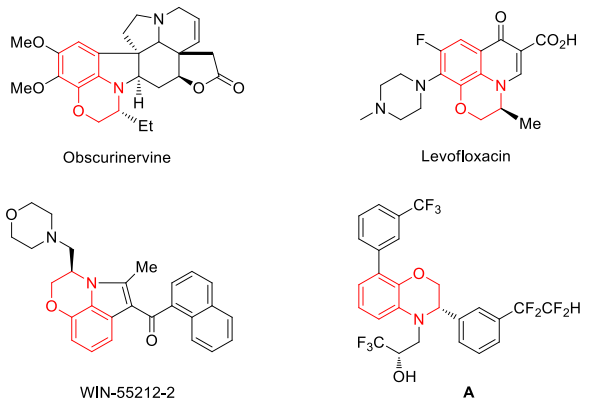


Fig. 1 Selected examples of alkaloids and bioactive compounds containing 3,4-dihydro-2*H*-1,4-benzoxazines frameworks.

In the past few years, we have found that cationic ruthenium complexes of chiral mono-tosylated diamines[10] are very efficient catalysts for the asymmetric hydrogenation of various *N*-containing heterocycles.[11-12] This catalytic system was also demonstrated to be highly enantioselective for the asymmetric hydrogenation of a broad range of acyclic ketimines and cyclic imines.[13] The achiral counteranions were found to influence the enantioselectivity significantly in the hydrogenation of imines and quinoxalines.[12c,13] Interestingly, in the hydrogenation of 2,4-diaryl substituted-3*H*-1,5-benzodiazepines, the choice of achiral counteranions determined the sense of asymmetric induction.[13e] Encouraged by these results and as a continuation of ongoing endeavour to prepare chiral *N*-containing heterocycles and amines, herein, we report the details of enantioselective hydrogenation of a variety of 2*H*-1,4-benzoxazines

by using the chiral cationic Ru-MsDPEN complexes with excellent enantioselectivities (up to 99% ee). Unexpectedly, it was found that the achiral counteranion regulated both the regioselectivity and enantioselectivity in the hydrogenation of 3-styryl-substituted-2*H*-1,4-benzoxazines.

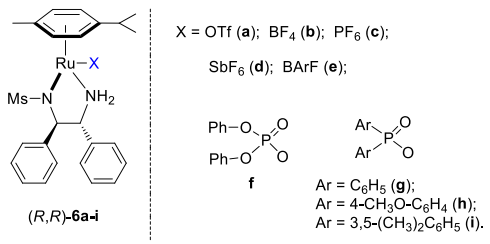
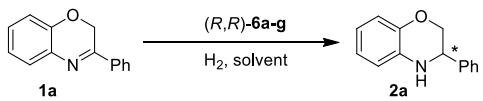


Fig. 2 Chiral cationic Ru-MsDPEN catalysts used in this study.

Based on our previous work,[13b] (*R*,*R*)-**6e** was firstly chosen to catalyze the asymmetric hydrogenation of 3-phenyl-2*H*-1,4-benzoxazine (**1a**) in different solvent under 50 atm H_2 pressure at 20 ^oC for 12 h. This reaction was found to be sensitive to solvent and higher enantioselectivity (65% ee) was observed in THF (entry 1 in Table 1 and Table S1 in Supporting Information (SI)). Further investigation of a variety of catalysts, (*R*,*R*)-**6a-g**, showed that the counteranion of the catalyst had a significant effect on the stereochemical outcome of the reaction (entries 1-7 in Table 1 and Table S2 in SI). The catalyst (*R*,*R*)-**6g**, bearing an achiral Ph_2PO_2 anion, turned out to be optimal in enantioselectivity but with low reactivity (entry 7 in Table 1).

Table 1 Optimization of the reaction conditions[a]

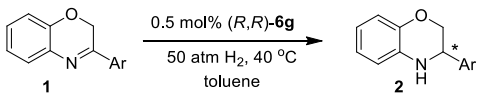


entry	catalyst	solvent	H_2 (atm)/ temp (^oC)	conv. (%)[b]	ee (%)[c]
1	(*R*,*R*)-**6e**	THF	50; 20	>95	65
2	(*R*,*R*)-**6a**	THF	50; 20	>95	8
3	(*R*,*R*)-**6b**	THF	50; 20	>95	13
4	(*R*,*R*)-**6c**	THF	50; 20	>95	47
5	(*R*,*R*)-**6d**	THF	50; 20	>95	55
6	(*R*,*R*)-**6f**	THF	50; 20	92	83
7	(*R*,*R*)-**6g**	THF	50; 20	19	92
8	(*R*,*R*)-**6g**	CH_2Cl_2	50; 20	32	82
9	(*R*,*R*)-**6g**	CH_2ClCH_2Cl	50; 20	57	88
10	(*R*,*R*)-**6g**	toluene	50; 20	>95	94
11	**(*R*,*R*)-6g**	**toluene**	**50; 40**	**>95**	**94**
12	(*R*,*R*)-**6g**	toluene	80; 20	>95	94
13	(*R*,*R*)-**6g**	toluene	10; 20	74	94
14[d]	(*R*,*R*)-**6g**	toluene	50; 40	>95	94
15[e]	(*R*,*R*)-**6g**	toluene	50; 40	40	93

[a] Reaction conditions: **1a** (0.1 mmol) in solvent (1 mL), catalyst (1.0 mol%), stirred for 12 h. [b] The conversions were determined by ^1H NMR spectroscopy of the crude reaction mixture. [c] The enantiomeric excesses were determined by chiral HPLC with a chiral OD-H column. [d] With catalyst (0.2 mol%) for 24 h. [e] With catalyst (0.1 mol%) for 24 h.

To further improve the catalytic performance of (*R*,*R*)-**6g**, the influences of solvent was studied once again (entries 7-10 in Table 1 and Table S3 in SI). To our great delight, full conversion and the highest enantioselectivity (94% ee) were obtained in toluene (entry 10 in Table 1). In addition, the influences of temperature and hydrogen pressure were studied and it was found that the enantioselectivity is insensitive to hydrogen pressure and temperature (entries 10-13 in Table 1 and Table S4 in SI). Remarkably, good reactivities and identical enantioselectivities were observed when the hydrogenation was carried out at a substrate/catalyst ratio of 500 upon prolonged reaction time (entry 14 in Table 1). Similar enantioselectivity was observed when the reaction proceeded at a lower catalyst loading of 0.1 mol% (entry 15 in Table 1).

Table 2 Asymmetric hydrogenation of 3-aryl-substituted-2*H*-1,4-benzoxazines catalyzed by (*R*,*R*)-**6g**[a]



entry	Ar	yield (%)[b]	ee (%)[c]
1	C_6H_5 (**1a**)	95	94
2	4-F-C_6H_4 (**1b**)	98	95
3	4-Cl-C_6H_4 (**1c**)	97	96
4	4-Br-C_6H_4 (**1d**)	95	96
5	4-MeO-C_6H_4 (**1e**)	96	98
6	4-CF_3-C_6H_4 (**1f**)	97	92
7	4-C_6H_5-C_6H_4 (**1g**)	95	97
8	3-MeO-C_6H_4 (**1h**)	95	90
9	3-Cl-C_6H_4 (**1i**)	94	82
10	3,4-Cl_2-C_6H_4 (**1j**)	98	86
11	2-MeO-C_6H_4 (**1k**)	<5	nd
12	2-Cl-C_6H_4 (**1l**)	<5	nd

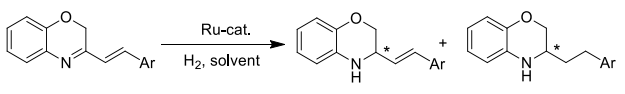
[a] Reaction conditions: substrate **1a-l** (0.2 mmol) in toluene (2 mL), (*R*,*R*)-**6g** (0.5 mol%), H_2 (50 atm), stirred at 40 ^oC for 12 h. [b] Isolated yield. [c] Determined by chiral HPLC.

Under the optimized reaction conditions (entry 11 in Table 1), a variety of 3-aryl-substituted-2*H*-1,4-benzoxazines were efficiently hydrogenated in the presence of 0.5 mol% (*R*,*R*)-**6g** to afford the corresponding chiral heterocycles with good to excellent enantioselectivities in most cases (82-98% ee, entries 1-10 in Table 2). It was evident that the electronic properties of the substituents at the *para* position of the phenyl ring had no apparent effect on activity and enantioselectivity (entries 1-7), and 3-(4-MeO-C_6H_4)-2*H*-1,4-benzoxazine (**1e**) gave the highest ee value (98% ee, entry 5). When the substituent is located at the *meta* position, the enantiomeric excess slightly dropped (entries 8-10). However, for the *ortho* substituted substrates (**1k-l**), reaction even could not occur (entries 11-12). This was probably due to the undesirable steric effect of the *ortho* substituent.

After establishing the successful catalyst system for the asymmetric hydrogenation of 3-aryl-substituted-2*H*-1,4-benzoxazines, we further expanded the substrate scope to 3-styryl-substituted-2*H*-1,4-benzoxazine derivatives (Table 3). Recently, Zhou et al. reported that the $[Ir(COD)Cl]_2$/(*S*)-SegPhos/I_2 system could catalyze this reaction and full conversions were obtained, but with mixtures of partially (**4a**) and completely hydrogenated products (**5a**).[9b] In our initial study, the hydrogenation of **3a** in toluene with 1.0 mol% (*R*,*R*)-**6e** also afforded the partially (**4a**) and completely hydrogenated products (**5a**) with a ratio of approximately 1:2 in 75% and 92% ee, respectively (entry 1 in Table 3). Interestingly, the catalyst screening demonstrated that the counteranion played an important role in both the regioselectivity and enantioselectivity control of this reduction (entries 1-7 in Table 3). Significantly, catalyst (*R*,*R*)-**6h** exhibited extremely high 1,2-selectivity (**4a**/**5a**, 97:3) and afforded **4a** in enantiopure form (entry 6). Next, we optimized the reaction conditions by varying the solvents, hydrogen pressure and reaction time. In contrast to MeOH, weakly polar solvents, such as CH_2Cl_2, $ClCH_2CH_2Cl$ and apolar toluene, are suitable to obtain high enantioselectivities and regioselectivities (entry 8 *vs* entries 6 and 9-10). Higher

regioselectivity was achieved when the reaction was carried out under ascending hydrogen pressure and decreasing reaction temperature (entry 12 in Table 3 and Table S6 in SI). Notably, the enantioselectivity and regioselectivity maintained when catalyst loading was reduced to 0.2 mol % (entry 11).

Table 3 Asymmetric hydrogenation of 3-styryl-substituted-2*H*-1,4-benzoxazines[a]



Ar = C_6H_5 (**3a**); 4-Br-C_6H_4 (**3d**); 4-F-C_6H_4 (**3b**); 4-MeO-C_6H_4 (**3e**); 4-Cl-C_6H_4 (**3c**); 3,4-$(MeO)_2$-C_6H_4 (**3f**)

entry	catalyst	substrate	solvent	conv. (%)[b]	**4**/**5**[c]	ee (%)[d]
1	(*R*,*R*)-**6e**	(**3a**)	toluene	>99	33:67	75/92
2	(*R*,*R*)-**6c**	(**3a**)	toluene	>99	70:30	8/14
3	(*R*,*R*)-**6a**	(**3a**)	toluene	>99	89:11	47/10
4	(*R*,*R*)-**6f**	(**3a**)	toluene	>99	91:9	75/nd
5	(*R*,*R*)-**6g**	(**3a**)	toluene	>99	95:5	98/nd
6	(*R*,*R*)-**6h**	(**3a**)	toluene	>99	97:3	99/nd
7	(*R*,*R*)-**6i**	(**3a**)	toluene	>99	96:4	98/nd
8	(*R*,*R*)-**6h**	(**3a**)	MeOH	>99	53:47	28/50
9	(*R*,*R*)-**6h**	(**3a**)	DCM	>99	97:3	95/nd
10	(*R*,*R*)-**6h**	(**3a**)	DCE	>99	97:3	94/nd
11[e]	(*R*,*R*)-**6h**	(**3a**)	toluene	>99	97:3	98/nd
12[f]	**(*R*,*R*)-6h**	**(3a)**	**toluene**	**>99 95**[g]	**98:2**	**99/nd**
13[f]	(*R*,*R*)-**6h**	(**3b**)	toluene	96[g]	95:5	91/nd
14[f]	(*R*,*R*)-**6h**	(**3c**)	toluene	94[g]	95:5	98/nd
15[f]	(*R*,*R*)-**6h**	(**3d**)	toluene	93[g]	97:3	98/nd
16[f]	(*R*,*R*)-**6h**	(**3e**)	toluene	95[g]	97:3	97/nd
17[f]	(*R*,*R*)-**6h**	(**3f**)	toluene	97[g]	97:3	98/nd

[a] Reaction conditions: **3a** (0.1 mmol) in solvent (1 mL), catalyst (1.0 mol%), H_2 (50 atm), stirred at 20 °C for 12 h. [b] Determined by ^{1}H NMR of the crude reaction mixture. [c] Determined by ^{1}H NMR spectroscopy of the crude reaction mixture. [d] Determined by chiral HPLC. [e] 0.2 mol% catalyst was used. [f] Reaction conditions: substrate **3a-f** (0.2 mmol) in toluene (2 mL), (*R*,*R*)-**6h** (0.5 mol%), H_2 (80 atm), stirred at 20 °C for 12 h. [g] Isolated yield.

Under the optimized reaction conditions (entry 12 in Table 3), several 3-styryl-substituted-2*H*-1,4-benzoxazine derivatives were reduced at 20 °C for 12 h in toluene under 80 atm of hydrogen using 0.5 mol% (*R*,*R*)-**6h**. Generally, excellent enantioselectivities (91-99% ee) and regioselectivities (95/5-98/2) were achieved, no matter the substrates with either an electron-donating or electron-withdrawing substituent on the phenyl group (entries 12-17 in Table 3).

Conclusions

In summary, the half-sandwich Ru(II) complexes of monosulfonylated chiral diamines bearing a Ar_2PO_2 anion have been disclosed to be highly efficient for the asymmetric hydrogenation of a variety of 3-aryl and 3-styryl-substituted-2*H*-1,4-benzoxazines, providing a convenient access to the corresponding optically active 3,4-dihydro-2*H*-1,4-benzoxazines with biological importance. Remarkable counteranion effect was found to be critically important for tuning of the enantioselectivity and regioselectivity. Extending application of these catalyst systems in the asymmetric hydrogenation of other heteroaromatic compounds and investigation for detailed insight into the nature of this remarkable counteranion effect are in progress.

Notes and references

[a] Beijing National Laboratory for Molecular Sciences, CAS Key Laboratory of Molecular Recognition and Function, Institute of Chemistry, Chinese Academy of Sciences (CAS), Beijing 100190, P. R. China; E-mail: fanqh@iccas.ac.cn; Fax: (+86)-10-62554449.
[b] Technical Center, China State Construction Engineering Co., Ltd., No. 15 Linhe Street, Shunyi District, Beijing 101300, P. R. China.
[c] Collaborative Innovation Center of Chemical Science and Engineering, Tianjin 300071, P. R. China.

† Financial support from the National Natural Science Foundation of China (Grant Nos. 21232008 and 21302190), the National Basic Research Program of China (973 Program, No. 2010CB833300), and the Chinese Academy of Sciences (CMS-PY-201303) is greatly acknowledged.
‡ Electronic Supplementary Information (ESI) available: See DOI: 10.1039/c000000x/

1 For selected examples of the alkaloids, see: (a) R. H. F. Manske, *Chemistry and Physiology*, Vol. **8**, Academic Press, New York, 1965; (b) K. S. Brown and C. Djerassi, *J. Am. Chem. Soc.*, 1964, **86**, 2451.
2 For selected reviews of the chiral pharmaceuticals, see: (a) K. Krohn, H. A. Kirst and H. Maag, *Antibiotics and Antiviral Compounds*, VCH, Weinheim, 1993; (b) A. Kleemann, J. Engel, B. Kutscher and D. Reichert, *Pharmaceutical Substances*, 4th ed., Thieme, Stuttgart, New York, 2001. For selected examples of the chiral pharmaceuticals, see: (c) S. Atarashi, S. Yokohama, K. Yamazaki, K. Sakano, M. Imamura and I. Hayakawa, *Chem. Pharm. Bull.*, 1987, **35**, 1896; (d) J.-Y. Shim, E. R. Collantes, W. J. Welsh, B. Subramaniam, A. C. Howlett, M. A. Eissenstat and S. J. Ward, *J. Med. Chem.*, 1998, **41**, 4521; (e) S. D. McAllister, G. Rizvi, S. Anavi-Goffer, D. P. Hurst, J. Barnett-Norris, D. L. Lynch, P. H. Reggio and M. E. Abood, *J. Med. Chem.*, 2003, **46**, 5139; (f) P.-F. Jiao, B.-X. Zhao, W.-W. Wang, D.-S. Shin, Q.-X. He, M.-S. Wan, D.-S. Shin and J.-Y. Miao, *Bioorg. Med. Chem. Lett.*, 2006, **16**, 2862; (g) A. Wang, C. P. Prouty, P. D. Pelton, M. Yong, K. T. Demarest, W. V. Murray and G.-H. Kuo, *Bioorg. Med. Chem. Lett.*, 2010, **20**, 1432.
3 For recent reviews, see: (a) B. Achari, S. B. Mandal, P. K. Dutta and C. Chowdhury, *Synlett*, 2004, 2449; (b) J. Ilaš, P. Š. Anderluh, M. S. Dolenc and D. Kikelj, *Tetrahedron*, 2005, **61**, 7325.
4 For selected examples of kinetic resolution: (a) A. Miyadera and A. Imura, *Tetrahedron: Asymmetry*, 1999, **10**, 119; (b) V. N. Charushin, V. P. Krasnov, G. L. Levit, M. A. Korolyova, M. I. Kodess, O. N. Chupakhin, M. H. Kim, H. S. Lee, Y. J. Park and K.-C. Kim, *Tetrahedron: Asymmetry*, 1999, **10**, 2691; (c) V. P. Krasnov, G. L. Levit, I. M. Bukrina, I. N. Andreeva, L. S. Sadretdinova, M. A. Korolyova, M. I. Kodess, V. N. Charushin and O. N. Chupakhin, *Tetrahedron: Asymmetry*, 2003, **14**, 1985; (d) V. P. Krasnov, G. L. Levit, M. I. Kodess, V. N. Charushin and O. N. Chupakhin, *Tetrahedron: Asymmetry*, 2004, **15**, 859; (e) V. A. Potemkin, V. P. Krasnov, G. L. Levit, E. V. Bartashevich, I. N. Andreeva, M. B. Kuzminsky, N. A. Anikin, V. N. Charushin and O. N. Chupakhin, *Mendeleev Commun.*, 2004, **14**, 69.
5 For selected examples of stoichiometric synthesis: (a) S. Atarashi, H. Tsurumi, T. Fujiwara and I. Hayakawa, *J. Heterocycl. Chem.*, 1991, **28**, 329; (b) L. J. Xie, *Chin. Chem. Lett.*, 1995, **6**, 857; (c) S. B. Kang, E. J. Ahn, Y. Kim and Y. H. Kim, *Tetrahedron Lett.*, 1996, **37**, 9317; (d) J. Adrio, J. C. Carretero, J. L. G. Ruano, A. Pallarés and M. Vicioso, *Heterocycles*, 1999, **51**, 1563; (e) J. F. Bower, P. Szeto and

T. Gallagher, *Org. Lett*., 2007, **9**, 3283; (f) M. K. Parai and G. Panda, *Tetrahedron Lett*., 2009, **50**, 4703; (g) J. C. Kim, H. G. Choi, M. S. Kim, H.-J. Ha and W. K. Lee, *Tetrahedron*, 2010, **66**, 8108; and ref. 2c.

6 For examples of the hydrosilylation of benzoxazines, see: (a) A. V. Malkov, K. Vranková, S. Stončius and P. Kočovský, *J. Org. Chem.*, 2009, **74**, 5839; (b) Y. Jiang, L.-X. Liu, W.-C. Yuan and X.-M. Zhang, *Synlett*, 2012, **23**, 1797; (c) X.-W. Liu, C. Wang, Y. Yan, Y.-Q. Wang and J. Sun, *J. Org. Chem.*, 2013, **78**, 6276.

7 For examples of the organocatalytic asymmetric transfer hydrogenation of benzoxazines, see: (a) M. Rueping, A. P. Antonchick and T. Theissmann, *Angew. Chem., Int. Ed.*, 2006, **45**, 6751; (b) M. Rueping, F. Tato and F. R. Schoepke, *Chem.-Eur. J.*, 2010, **16**, 2688; (c) M. Rueping, E. Sugiono, A. Steck and T. Theissmann, *Adv. Synth. Catal.*, 2010, **352**, 281; (d) M. Rueping, M. Stoeckel, E. Sugiono and T. Theissmann, *Tetrahedron*, 2010, **66**, 6565; (e) M. Rueping and T. Theissmann, *Chem. Sci.*, 2010, **1**, 473; (f) C. Bleschke, J. Schmidt, D. S. Kundu, S. Blechert and A. Thomas, *Adv. Synth. Catal.*, 2011, **353**, 3101; (g) D. S. Kundu, J. Schmidt, C. Bleschke, A. Thomas and S. Blechert, *Angew. Chem., Int. Ed.*, 2012, **51**, 5456.

8 (a) R. Noyori, *Acta Chem. Scand.*, 1996, **50**, 380; (b) Y.-G. Zhou, P.-Y. Yang and X.-W. Han, *J. Org. Chem.*, 2005, **70**, 1679; (c) J. Xie and Q. Zhou, *Acta Chim. Sinica*, 2012, **70**, 1427.

9 (a) K. Satoh, M. Inenaga and K. Kanai, *Tetrahedron: Asymmetry*, 1998, **9**, 2657; (b) K. Gao, C.-B. Yu, D.-S. Wang and Y.-G. Zhou, *Adv. Synth. Catal.*, 2012, **354**, 483; (c) J. Hu, D. Wang, Z. Zheng and X. Hu, *Chinese J. Chem.*, 2012, **30**, 2664; (d) J. L. Núñez-Rico and A. Vidal-Ferran, *Org. Lett.*, 2013, **15**, 2066; (e) S. Fleischer, S. Zhou, S. Werkmeister, K. Junge and M. Beller, *Chem.-Eur. J*., 2013, **19**, 4997; (f) N. Arai, Y. Saruwatari, K. Isobe and T. Ohkuma, *Adv. Synth. Catal*., 2013, **355**, 2769; (g) Q.-A. Chen, K. Gao, Y. Duan, Z.-S. Ye, L. Shi, Y. Yang and Y.-G. Zhou, *J. Am. Chem. Soc.*, 2012, **134**, 2442.

10 (a) R. Noyori and S. Hashiguchi, *Acc. Chem. Res.*, 1997, **30**, 97; (b) T. Ikariya and A. J. Blacker, *Acc. Chem. Res*., 2007, **40**, 1300; (c) S. Hashiguchi, A. Fujii, J. Takehara, T. Ikariya and R. Noyori, *J. Am. Chem. Soc*., 1995, **117**, 7562; (d) T. Ohkuma, N. Utsumi, K. Tsutsumi, K. Murata, C. Sandoval and R. Noyori, *J. Am. Chem. Soc*., 2006, **128**, 8724.

11 For recent reviews on asymmetric hydrogenation of heteroaromatic compounds, see: (a) D.-S. Wang, Q.-A. Chen, S.-M. Lu and Y.-G. Zhou, *Chem. Rev.*, 2012, **112**, 2557; (b) Y.-M. He, F.-T. Song and Q.-H. Fan, *Top. Curr. Chem*., 2014, **343**, 145.

12 (a) H. Zhou, Z. Li, Z. Wang, T. Wang, L. Xu, Y. He, Q.-H. Fan, J. Pan, L. Gu and A. S. C. Chan, *Angew. Chem., Int. Ed.*, 2008, **47**, 8464; (b) T. Wang, L. Zhuo, Z. Li, F. Chen, Z. Ding, Y. He, Q.-H. Fan, J. Xiang, Z.-X. Yu and A. S. C. Chan, *J. Am. Chem. Soc*., 2011, **133**, 9878; (c) J. Qin, F. Chen, Z. Ding, Y. He, L. Xu and Q.-H. Fan, *Org. Lett.*, 2011, **13**, 6568; (d) T. Wang, F. Chen, J. Qin, Y.-M. He and Q.-H. Fan, *Angew. Chem., Int. Ed*., 2013, **52**, 7172.

13 (a) F. Chen, T. Wang, Y. He, Z. Ding, Z. Li, L. Xu and Q.-H. Fan, *Chem.-Eur. J*., 2011, **17**, 1109; (b) F. Chen, Z. Ding, J. Qin, T. Wang, Y. He and Q.-H. Fan, *Org. Lett*., 2011, **13**, 4348; (c) F. Chen, Z. Li, Y. He and Q.-H. Fan, *Chin. J. Chem*., 2010, **28**, 1529; (d) Z.-Y. Ding, T. Wang, Y.-M. He, F. Chen, H.-F. Zhou, Q.-H. Fan, Q. Guo and A. S. C. Chan, *Adv. Synth. Catal.*, 2013, **355**, 3727; (e) Z.-Y. Ding, F. Chen, J. Qin, Y.-M. He and Q.-H. Fan, *Angew. Chem., Int. Ed*., 2012, **51**, 5706.

