

Heterocycles

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Highly Enantioselective Synthesis of Indolines: Asymmetric Hydrogenation at Ambient Temperature and Pressure with Cationic Ruthenium Diamine Catalysts

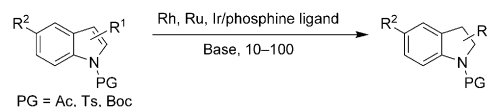
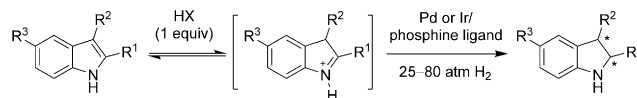
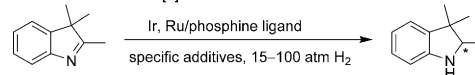
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Abstract: A highly enantioselective synthesis of indolines by asymmetric hydrogenation of 1*H*-indoles and 3*H*-indoles at ambient temperature and pressure, catalyzed by chiral phosphine-free cationic ruthenium complexes, has been developed. Excellent enantio- and diastereoselectivities (up to > 99% ee, > 20:1 d.r.) were obtained for a wide range of indole derivatives, including unprotected 2-substituted and 2,3-disubstituted 1*H*-indoles, as well as 2-alkyl- and 2-aryl-substituted 3*H*-indoles.

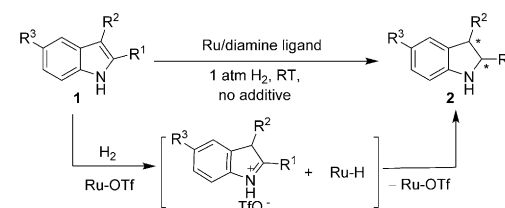
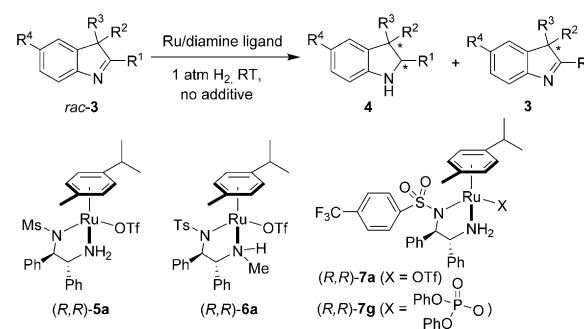
Optically active indoline derivatives are ubiquitous structural moieties in chiral pharmaceuticals and biologically interesting natural alkaloids.^[1] In addition, optically active indolines serving as either organocatalysts or chiral auxiliaries have been successfully used in a number of asymmetric transformations.^[2] Consequently, a variety of protocols have been devoted to the asymmetric synthesis of enantioenriched indolines by both the synthetic and medicinal chemistry communities.^[1e,3]

Among the various reported methods,^[4–7] the direct asymmetric hydrogenation (AH) of the corresponding readily available indoles represents one of the most straightforward, efficient, and atom-economic approaches for attaining optically active indolines.^[6,7] However, because of the inherent aromatic stability and the poisoning effects of indoles and/or indolines on metal catalysts, this transformation still represents a challenge.^[8] In 2000, Kuwano and co-workers developed the first highly effective hydrogenation of *N*-protected indoles catalyzed by a Rh/PhTRAP complex in the presence of a base.^[6a] Since this pioneering work, a few transition metal/chiral phosphine catalysts have been successfully employed in the AH of *N*-protected indoles (Scheme 1a).^[6] Most recently, Zhou and co-workers demonstrated that the simple unprotected indoles (1*H*-indoles) could be reduced via

Previous work:

a) AH of *N*-protected indoles: Ref. [6]b) AH of unprotected indoles (1*H*-indoles): Ref. [7]c) AH of 3*H*-indoles: Ref. [9]

This work:

d) AH of unprotected indoles (1*H*-indoles):e) AH of 3*H*-indoles ($R^2 \neq R^3$, kinetic resolution):

Scheme 1. Enantioselective synthesis of indolines by AH. Boc = *tert*-butoxycarbonyl, Tf = trifluoromethanesulfonyl, Ts = 4-toluenesulfonyl.

iminium salt intermediates generated in situ by addition of a stoichiometric amount of a Brønsted acid (Scheme 1b).^[7] Despite the significant progress achieved, these catalytic systems still suffer from some drawbacks, such as high hydrogen pressure, need of a protecting group, or use of basic or acidic additives. Moreover, only monosubstituted or 2,3-disubstituted indolines could be synthesized by these protocols (Scheme 1a,b), and asymmetric synthesis of 2,3,3-trisubstituted indolines by AH has been less developed.

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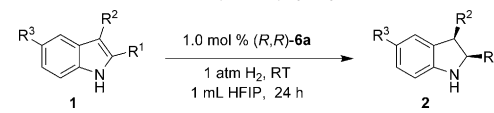
Although a number of iridium and ruthenium complexes with different chiral phosphine ligands have been employed in the AH of trisubstituted 3*H*-indoles over the past two decades,^[9] only one substrate, 2,3,3-trimethyl 3*H*-indole, was reported in all cases (Scheme 1 c). So far, there is limited success in the AH of unprotected indoles, and to the best of our knowledge, the AH of racemic 3,3-disubstituted 3*H*-indoles has not been documented yet.

Most recently, we have found that the cationic ruthenium complexes of chiral monosulfonylated diamines^[10] are very efficient catalysts for the AH of several types of N-containing heteroaromatic compounds and ketimines with excellent enantioselectivity.^[11] Further mechanism study indicated that dihydrogen could be activated by the cationic ruthenium complex with the aid of substrate to generate the Ru–H active species and the iminium salt, and the in situ activated substrate was then reduced by a stepwise H⁺/H[−] transfer process.^[11b] We thus envisioned that such cationic ruthenium complex could be used to hydrogenate 1*H*-indoles and 3*H*-indoles, via iminium salts, without the addition of acid (Scheme 1 d,e). Herein, we communicate the highly effective AH of a wide range of 1*H*-indoles and 3*H*-indoles under very mild reaction conditions. A kinetic resolution was also observed when racemic 3,3-disubstituted 3*H*-indoles were hydrogenated.

In our initial study, the AH of 2-methyl-indole (**1a**) with the catalyst (*R,R*)-**5a** (see Scheme 1) was chosen as the model reaction for the optimization of the reaction conditions (see Table S1 in the Supporting Information). The solvent influenced the catalytic performance significantly, and full conversion and high enantioselectivity were observed in hexafluoroisopropanol (HFIP).^[12] Upon the screening of a variety of catalysts, (*R,R*)-**6a** was found to be optimal in terms of both reactivity and enantioselectivity. In addition, the enantioselectivity was insensitive to hydrogen pressure and temperature. Remarkably, even if the reaction was conducted at ambient temperature and pressure,^[13] full conversion and the same *ee* value were obtained within 3 hours. To the best of our knowledge, this is the first example for AH of heteroaromatic compounds at ambient temperature and pressure. Furthermore, when the substrate to catalyst ratio was increased to 1000, only very slight erosion of the *ee* value was observed (see entry 27 in Table S1).

Under the optimized reaction conditions, the AH of a variety of 1*H*-indoles was examined, and good to excellent enantioselectivities were obtained (Table 1). 2-Alkyl-substituted indoles were hydrogenated in very good yields with excellent enantioselectivities (entries 1–11), regardless of either the length of side chain or the position of substituents at the phenyl ring. Notably, excellent results were also achieved with 2,3-disubstituted fused ring indolines (entries 12–16). It was found that the enantiomeric excess increased from 89 to 99% when increasing the ring size from five- to six- and seven-membered rings. In addition, the hydrogenation of 2,3-dimethylindole could be carried out under harsh reaction conditions (entry 17). More difficult substrates such as 3-methyl and 2-phenyl indoles were also tested, and moderate *ee* values were obtained (entries 18 and 19).

Table 1: AH of 1*H*-indoles catalyzed by (*R,R*)-**6a**.^[a]



Entry	R ¹ /R ²	R ³	Yield [%] ^[b]	<i>ee</i> [%] ^[c]
1	Me/H	H	94 (2a)	96 (<i>R</i>)
2	<i>n</i> Pr/H	H	88 (2b)	96 (<i>R</i>)
3	<i>n</i> Bu/H	H	92 (2c)	97 (<i>R</i>)
4	<i>n</i> -Pentyl/H	H	89 (2d)	96 (<i>R</i>)
5	C ₆ H ₅ CH ₂ /H	H	93 (2e)	97 (<i>R</i>)
6	4-FC ₆ H ₄ CH ₂ /H	H	92 (2f)	97 (<i>R</i>)
7	4-MeC ₆ H ₄ CH ₂ /H	H	90 (2g)	96 (<i>R</i>)
8	3-MeC ₆ H ₄ CH ₂ /H	H	93 (2h)	97 (<i>R</i>)
9	Me/H	Me	93 (2i)	95 (<i>R</i>)
10	Me/H	OMe	93 (2j)	95 (<i>R</i>)
11	Me/H	F	94 (2k)	94 (<i>R</i>)
12 ^[d]	-(CH ₂) ₃ -	H	92 (2l)	89 (<i>R,R</i>)
13 ^[d]	-(CH ₂) ₄ -	H	91 (2m)	95 (<i>R,R</i>)
14 ^[d]	-(CH ₂) ₄ -	CH ₃	94 (2n)	90 (<i>R,R</i>)
15 ^[d]	-(CH ₂) ₄ -	F	92 (2o)	94 (<i>R,R</i>)
16 ^[d]	-(CH ₂) ₅ -	H	73 (2p)	99 (<i>R,R</i>)
17 ^[e,f]	Me/Me	H	95 (2q)	97 (<i>R,R</i>)
18 ^[g]	H/Me	Me	85 (2r)	40 (<i>R</i>)
19 ^[g]	Ph/H	H	53 (2s)	42 (<i>S</i>)

[a] Reaction conditions: substrates **1a–s** (0.2 mmol) and (*R,R*)-**6a** in HFIP, and H₂ (1 atm). Stirred at RT for 24 h. [b] Yield of isolated product.

[c] The *ee* values were determined by HPLC with a chiral-phase column.

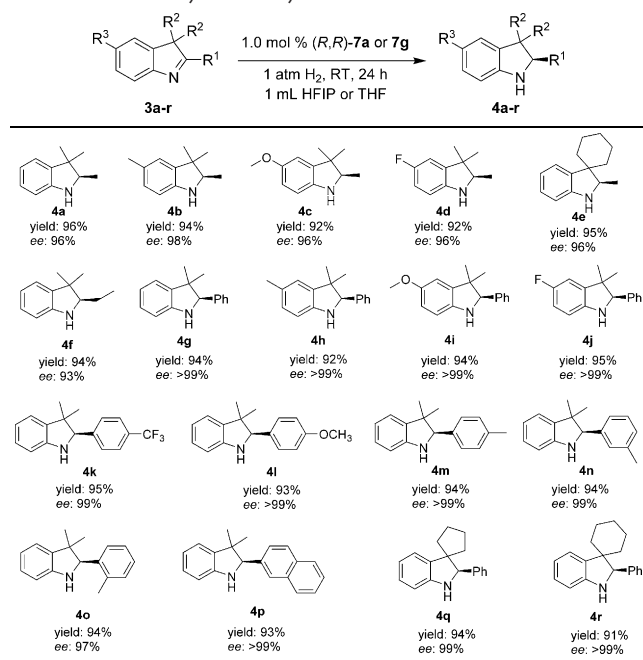
[d] *cis/trans* isomer > 20:1. [e] (*R,R*)-**6a** (2.0 mol %) and H₂ (50 atm).

Stirred at 50 °C for 24 h. [f] *cis/trans* isomer = 8:1. [g] (*R,R*)-**6a** (5.0 mol %), H₂ (50 atm), stirred at 50 °C for 24 h.

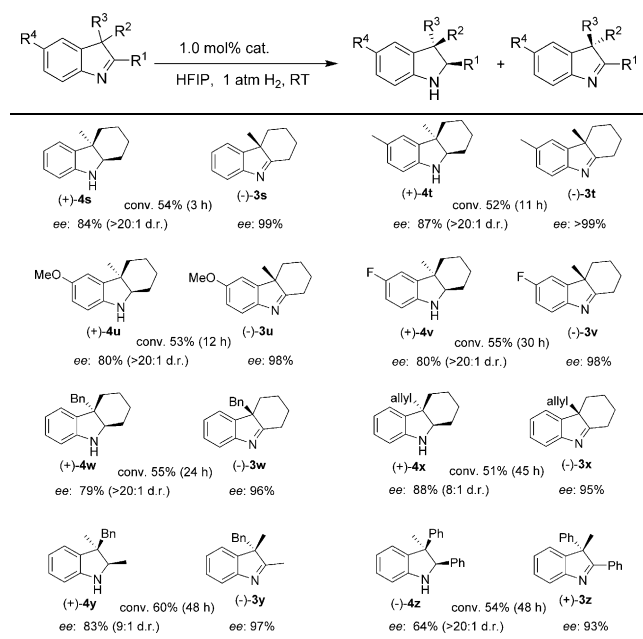
Encouraged by the above excellent results, we then extended this catalytic system to the synthesis of chiral 2,3,3-trisubstituted indolines, which are more commonly found in alkaloids and other natural products. So far, the AH of 3*H*-indoles is still limited to only one substrate.^[9] A quick survey with **3a** as the model substrate revealed that (*R,R*)-**7a** was the optimal catalyst (see Table S2). As shown in Table 2, a series of 2-alkyl-substituted 3*H*-indole derivatives (**3a–f**) were hydrogenated at ambient temperature and pressure in HFIP with excellent reactivity and enantioselectivity (93–98% *ee*).

This catalytic system was further applied to the AH of 2-aryl-substituted 3*H*-indoles (Table 2), which are much more difficult substrates for hydrogenation, and transition-metal-catalyzed AH of this class of substrates has not been reported yet.^[5a] In contrast to 2-alkyl-substituted 3*H*-indoles, the AH of **3g** proceeded smoothly in THF instead of HFIP (see Table S3). Interestingly, (*R,R*)-**7g** with a (PhO)₂PO₂[−] anion was found to be optimal catalyst, thus indicating that the counteranion played an important role on catalytic performance.^[11e–f,14] Under the optimized reaction conditions, high yields and excellent enantioselectivities (97–>99% *ee*) were obtained for a range of 2-aryl-substituted 3*H*-indoles (**3g–r**).

Finally, the AH of a range of racemic 3*H*-indoles bearing different substituents at C3 was carried out. Interestingly, a kinetic resolution of 3*H*-indoles by AH was observed for the first time.^[15,16] After optimizing the reaction conditions, several substrates were resolved with high selectivity (Table 3), thus providing the reduced products with very

Table 2: AH of 2-alkyl- and 2-aryl-substituted 3*H*-indoles.

Reaction conditions. For substrates **3a–e** (0.2 mmol): (*R,R*)-**7a** in HFIP, and H₂ (1 atm). Stirred at RT for specified time. For **3f**: H₂ (50 atm), stirred at 50°C. For substrates **3g–n** and **3p–r** (0.2 mmol): (*R,R*)-**7g** in THF, and H₂ (1 atm). Stirred at RT for 24 h. For **4o**: H₂ (50 atm), stirred at 50°C for 24 h. Yields of isolated products are given in all cases.

Table 3: Kinetic resolution of racemic 3,3-disubstituted 3*H*-indoles by AH.

Reaction conditions: Substrates **3s–y** (0.2 mmol) and (*R,R*)-**7a** in HFIP (1 mL), and H₂ (1 atm). Stirred at RT. Substrate **3z** and (*R,R*)-**7g** in toluene, and H₂ (50 atm). Stirred at 50°C. Conversions were determined by ¹H NMR spectroscopy.

good enantioselectivities (64–88% *ee*) and the recovered substrates with excellent enantioselectivities (93–>99% *ee*). When the reaction was stopped at lower conversion, indolines

were obtained with higher enantioselectivity (see Table S4). Notably, both the products and recovered starting materials are valuable chiral compounds bearing C3 quaternary chiral centers of indoline and indole cores, respectively.

An isotope-labeling experiment was carried out (see Scheme S3). When **1a** was subjected to hydrogenation with D₂, the incorporation of deuterium was observed only at the 2-position. All results indicate that the reaction proceeds through the generation of an iminium salt, by C3 protonation with the in situ generated TfOH acid, which was subsequently reduced by the ruthenium complex to afford the desired indolines.

In summary, we have developed a highly enantioselective synthesis of indolines, by AH of unprotected 1*H*-indoles and 3*H*-indoles catalyzed by chiral ruthenium diamine complexes at ambient temperature and pressure. Excellent enantio- and diastereoselectivities were obtained for a wide range of indole derivatives. Moreover, a kinetic resolution of racemic 3,3-disubstituted 3*H*-indoles was achieved with high selectivity for the first time. The unique features of this protocol, including broad substrate scope, excellent enantioselectivity and diastereoselectivity, mild reaction conditions, and operational simplicity, make it very useful and practical for both academic and industrial applications.

Acknowledgments

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Keywords: heterocycles · hydrogenation · indoles · N ligands · ruthenium

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- [1] For reviews, see: a) I. W. Southon, J. Buckingham, *Dictionary of Alkaloids*, Chapman and Hall, New York, **1989**; b) N. Neuss, M. N. Neuss, *The Alkaloids* (Eds.: H. A. Brossi, M. Suffness), Academic Press, San Diego, **1990**, p. 229; c) F. Gueritte, J. Fahy, *Anticancer Agents from Natural Products* (Eds.: G. M. Cragg, D. G. I. Kingston, D. J. Newman), CRC Press, Boca Raton, FL, **2005**, p. 123; d) *Modern Alkaloids* (Eds.: E. Fattorusso, O. Tagliatella-Scafati), Wiley-VCH, Weinheim, **2008**; e) D. Zhang, H. Song, Y. Qin, *Acc. Chem. Res.* **2011**, 44, 447. For some examples, see: f) J. Dunlop, K. L. Marquis, H. K. Lim, L. Leung, J. Kao, C. Cheesman, S. Rosenzweig-Lipson, *CNS Drug Rev.* **2006**, 12, 167; g) H. Zhao, A. Thurkauf, X. He, K. Hodgetts, X. Zhang, S. Rachwal, R. X. Kover, A. Hutchison, J. Peterson, A. Kieltyka, R. Brodbeck, R. Primus, J. W. F. Wasley, *Bioorg. Med. Chem. Lett.* **2002**, 12, 3105; h) D. Ramanitrahasimbola, P. Rasoanaivo, S. Ratsimamanga, H. Vial, *Mol. Biochem. Parasitol.* **2006**, 146, 58; i) J. P. Marino, M. B. Rubio, G. Cao, A. de Dios, *J. Am. Chem. Soc.* **2002**, 124, 13398; j) D. Kato, Y. Sasaki, D. L. Boger, *J. Am. Chem. Soc.* **2010**, 132, 3685.
- [2] For selected examples, see: a) R. K. Kunz, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2005**, 127, 3240; b) F. Andersson, E. Hedenström, *Tetrahedron: Asymmetry* **2006**, 17, 1952; c) A. Hartikka, P. I. Arvidsson, *J. Org. Chem.* **2007**, 72, 5874; d) J. Pietruszka, R. C. Simon, *ChemCatChem* **2010**, 2, 505.

- [3] a) D. Liu, G. Zhao, L. Xiang, *Eur. J. Org. Chem.* **2010**, 3975; b) S. Anas, H. B. Kagan, *Tetrahedron: Asymmetry* **2009**, *20*, 2193, and references therein.
- [4] For selected examples, see: a) F. O. Arp, G. C. Fu, *J. Am. Chem. Soc.* **2006**, *128*, 14264; b) X. L. Hou, B. H. Zheng, *Org. Lett.* **2009**, *11*, 1789; c) K. Saito, Y. Shibata, M. Yamanaka, T. Akiyama, *J. Am. Chem. Soc.* **2013**, *135*, 11740; d) M. López-Iglesias, E. Busto, V. Gotor, V. Gotor-Fernández, *J. Org. Chem.* **2012**, *77*, 8049; e) G. S. Gil, U. M. Groth, *J. Am. Chem. Soc.* **2000**, *122*, 6789; f) K.-T. Yip, M. Yang, K.-L. Law, N.-Y. Zhu, D. Yang, *J. Am. Chem. Soc.* **2006**, *128*, 3130; g) M. Nakanishi, D. Katayev, C. Besnard, E. P. Kündig, *Angew. Chem. Int. Ed.* **2011**, *50*, 7438; *Angew. Chem.* **2011**, *123*, 7576; h) T. Saget, S. J. Lemouzy, N. Cramer, *Angew. Chem. Int. Ed.* **2012**, *51*, 2238; *Angew. Chem.* **2012**, *124*, 2281; i) E. E. Maciver, S. Thompson, M. D. Smith, *Angew. Chem. Int. Ed.* **2009**, *48*, 9979; *Angew. Chem.* **2009**, *121*, 10164; j) E. Ascic, S. L. Buchwald, *J. Am. Chem. Soc.* **2015**, *137*, 4666; k) A. Martínez, M. J. Webber, S. Müller, B. List, *Angew. Chem. Int. Ed.* **2013**, *52*, 9486; *Angew. Chem.* **2013**, *125*, 9664; l) Y.-C. Xiao, C. Wang, Y. Yao, J. Sun, Y.-C. Chen, *Angew. Chem. Int. Ed.* **2011**, *50*, 10661; *Angew. Chem.* **2011**, *123*, 10849.
- [5] a) M. Rueping, C. Brinkmann, A. P. Antonchick, I. Atodiresei, *Org. Lett.* **2010**, *12*, 4604; b) A. D. Lackner, A. V. Samant, F. D. Toste, *J. Am. Chem. Soc.* **2013**, *135*, 14090.
- [6] a) R. Kuwano, K. Sato, T. Kurokawa, D. Karube, Y. Ito, *J. Am. Chem. Soc.* **2000**, *122*, 7614; b) R. Kuwano, K. Kaneda, T. Ito, K. Sato, T. Kurokawa, Y. Ito, *Org. Lett.* **2004**, *6*, 2213; c) R. Kuwano, M. Kashiwabara, *Org. Lett.* **2006**, *8*, 2653; d) N. Mršić, T. Jerphagnon, A. J. Minnaard, B. L. Feringa, J. G. de Vries, *Tetrahedron: Asymmetry* **2010**, *21*, 7; e) A. Baeza, A. Pfaltz, *Chem. Eur. J.* **2010**, *16*, 2036.
- [7] a) D.-S. Wang, Q.-A. Chen, W. Li, C.-B. Yu, Y.-G. Zhou, X. Zhang, *J. Am. Chem. Soc.* **2010**, *132*, 8909; b) D.-S. Wang, J. Tang, Y.-G. Zhou, M.-W. Chen, C.-B. Yu, Y. Duan, G.-F. Jiang, *Chem. Sci.* **2011**, *2*, 803; c) Y. Duan, L. Li, M.-W. Chen, C.-B. Yu, H.-J. Fan, Y.-G. Zhou, *J. Am. Chem. Soc.* **2014**, *136*, 7688.
- [8] For recent reviews on AH of heteroaromatic compounds, see: a) F. Glorius, *Org. Biomol. Chem.* **2005**, *3*, 4171; b) Y.-G. Zhou, *Acc. Chem. Res.* **2007**, *40*, 1357; c) R. Kuwano, *Heterocycles* **2008**, *76*, 909; d) D.-S. Wang, Q.-A. Chen, S.-M. Lu, Y.-G. Zhou, *Chem. Rev.* **2012**, *112*, 2557; e) Y.-M. He, F.-T. Song, Q.-H. Fan, *Top. Curr. Chem.* **2014**, *343*, 145.
- [9] Selected examples, see: a) F. Spindler, B. Pugin, H.-U. Blaser, *Angew. Chem. Int. Ed. Engl.* **1990**, *29*, 558; *Angew. Chem.* **1990**, *102*, 561; b) T. Morimoto, N. Nakajima, K. Achiwa, *Synlett* **1995**, 748; c) G. Zhu, X. Zhang, *Tetrahedron: Asymmetry* **1998**, *9*, 2415; d) A. M. Kluwer, R. J. Detz, Z. Abiri, A. M. van der Burg, J. N. H. Reek, *Adv. Synth. Catal.* **2012**, *354*, 89.
- [10] For seminal works on asymmetric transfer hydrogenation (ATH) of ketones and imines with Ru(diamine) complexes, see: a) S. Hashiguchi, A. Fujii, J. Takehara, T. Ikariya, R. Noyori, *J. Am. Chem. Soc.* **1995**, *117*, 7562; b) N. Uematsu, A. Fujii, S. Hashiguchi, T. Ikariya, R. Noyori, *J. Am. Chem. Soc.* **1996**, *118*, 4916; c) R. Noyori, S. Hashiguchi, *Acc. Chem. Res.* **1997**, *30*, 97; d) T. Ikariya, A. J. Blacker, *Acc. Chem. Res.* **2007**, *40*, 1300; For a pioneering work on AH of ketones, see: e) M. Ito, M. Hirakawa, K. Murata, T. Ikariya, *Organometallics* **2001**, *20*, 379; f) T. Ohkuma, N. Utsumi, K. Tsutsumi, K. Murata, C. Sandoval, R. Noyori, *J. Am. Chem. Soc.* **2006**, *128*, 8724.
- [11] a) H. Zhou, Z. Li, Z. Wang, T. Wang, L. Xu, Y.-M. He, Q.-H. Fan, J. Pan, L. Gu, A. S. C. Chan, *Angew. Chem. Int. Ed.* **2008**, *47*, 8464; *Angew. Chem.* **2008**, *120*, 8592; b) T. Wang, L.-G. Zhuo, Z. Li, F. Chen, Z. Ding, Y.-M. He, Q.-H. Fan, J. Xiang, Z.-X. Yu, A. S. C. Chan, *J. Am. Chem. Soc.* **2011**, *133*, 9878; c) T. Wang, F. Chen, J. Qin, Y.-M. He, Q.-H. Fan, *Angew. Chem. Int. Ed.* **2013**, *52*, 7172; *Angew. Chem.* **2013**, *125*, 7313; d) J. Zhang, F. Chen, Y.-M. He, Q.-H. Fan, *Angew. Chem. Int. Ed.* **2015**, *54*, 4622; *Angew. Chem.* **2015**, *127*, 4705; e) F. Chen, T. Wang, Y.-M. He, Z. Ding, Z. Li, L. Xu, Q.-H. Fan, *Chem. Eur. J.* **2011**, *17*, 1109; f) Z.-Y. Ding, F. Chen, J. Qin, Y.-M. He, Q.-H. Fan, *Angew. Chem. Int. Ed.* **2012**, *51*, 5706; *Angew. Chem.* **2012**, *124*, 5804.
- [12] For recent reviews, see: a) T. Sugiishi, M. Matsugi, H. Hamamoto, H. Amii, *RSC Adv.* **2015**, *5*, 17269. For dramatic improvements in both product yield and enantioselectivity in the AH of imines in fluorinated solvents, b) H. Abe, H. Amii, K. Uneyama, *Org. Lett.* **2001**, *3*, 313; c) M.-W. Chen, Y. Duan, Q.-A. Chen, D.-S. Wang, C.-B. Yu, Y.-G. Zhou, *Org. Lett.* **2010**, *12*, 5075; d) L. Pauli, R. Tannert, R. Scheil, A. Pfaltz, *Chem. Eur. J.* **2015**, *21*, 1482.
- [13] Few examples of AH of imines at ambient pressure, see: a) S.-F. Zhu, J.-B. Xie, Y.-Z. Zhang, S. Li, Q.-L. Zhou, *J. Am. Chem. Soc.* **2006**, *128*, 12886; b) A. Dervisi, C. Carcedo, L. Ooi, *Adv. Synth. Catal.* **2006**, *348*, 175; c) T. Imamoto, N. Iwade, K. Yoshida, *Org. Lett.* **2006**, *8*, 2289.
- [14] a) F. Chen, Z. Ding, J. Qin, T. Wang, Y.-M. He, Q.-H. Fan, *Org. Lett.* **2011**, *13*, 4348; b) F. Chen, Z. Ding, Y.-M. He, J. Qin, T. Wang, Q.-H. Fan, *Tetrahedron* **2012**, *68*, 5248; c) J. Qin, F. Chen, Z. Ding, Y.-M. He, L. Xu, Q.-H. Fan, *Org. Lett.* **2011**, *13*, 6568; d) J. Qin, F. Chen, Y.-M. He, Q.-H. Fan, *Org. Chem. Front.* **2014**, *1*, 952.
- [15] J. M. Keith, J. F. Larrow, E. N. Jacobsen, *Adv. Synth. Catal.* **2001**, *343*, 5.
- [16] Few examples of kinetic resolution of imines via asymmetric hydrosilylation, ATH or asymmetric imine amidation, see: a) J. Yun, S. L. Buchwald, *J. Org. Chem.* **2000**, *65*, 767; b) J. Yun, S. L. Buchwald, *Chirality* **2000**, *12*, 476; c) A. Bongers, P. J. Moon, A. M. Beauchemin, *Angew. Chem. Int. Ed.* **2015**, *54*, 15516; *Angew. Chem.* **2015**, *127*, 15736; d) H. Hu, Y. Liu, L. Lin, Y. Zhang, X. Liu, X. Feng, *Angew. Chem. Int. Ed.* **2016**, *55*, 10098; *Angew. Chem.* **2016**, *128*, 10252.

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