

## Kinetic Resolution of Axially Chiral 5- or 8-Substituted Quinolines via Asymmetric Transfer Hydrogenation

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# Kinetic Resolution of Axially Chiral 5- or 8-Substituted Quinolines *via* Asymmetric Transfer Hydrogenation

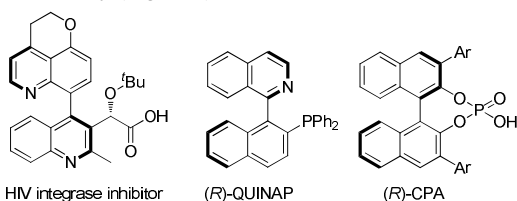
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**ABSTRACT:** An efficient kinetic resolution of axially chiral 5- or 8-substituted quinoline derivatives was developed through asymmetric transfer hydrogenation of heteroaromatic moiety, simultaneously obtaining two kinds of axially chiral skeletons with up to 209 of selectivity factor. This represents the first successful application of asymmetric transfer hydrogenation of heteroaromatics in kinetic resolution of axially chiral biaryls.

Axially chiral biaryl scaffolds are prevalent in materials, natural products, pharmaceuticals, and also play an important part in organic synthesis as chiral catalysts and ligands.<sup>1</sup> The quinoline-based HIV integrase inhibitor with a rotation inhibited axis has special biological activity and is being investigated to target the LEDGF/p75 binding site.<sup>1c</sup> The privileged ligands and catalysts such as QUINAP and chiral phosphoric acid (CPA) are widely applied to an array of reactions with high activity and enantioselectivity (Figure 1).<sup>1f-1g</sup>



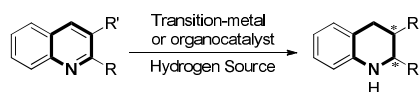
**Figure 1.** Selected privileged axially chiral biaryls.

Accordingly, these axially chiral compounds have attracted widespread attention and a variety of methods have been successfully developed to synthesize axially chiral frameworks,<sup>2</sup> including classical resolution,<sup>3</sup> stereoselective construction of biaryl linkages,<sup>4</sup> asymmetric functionalization of prochiral compounds,<sup>5</sup> central-to-axial chirality transfer strategy,<sup>6</sup> dynamic kinetic resolution of atropisomers,<sup>7</sup> kinetic resolution of racemic biaryls<sup>5a, 8</sup> and so on.<sup>9</sup> Among them, kinetic resolution of biaryls as a powerful and reliable method has gradually become a hot field in recent years. Compared to the others, kinetic resolution would improve the enantioselectivity of the substrate or the product through adjusting the conversion so that various methods have been involved in kinetic resolution. You, Virgil and Tsuji groups successfully incorporated C-H activation,<sup>8f</sup> C-P coupling,<sup>7e</sup> alcoholysis<sup>8g</sup> into the kinetic resolution using transition-metal catalysts, respectively. In addition, substantial efforts were also made toward the development of organocatalysts for kinetic

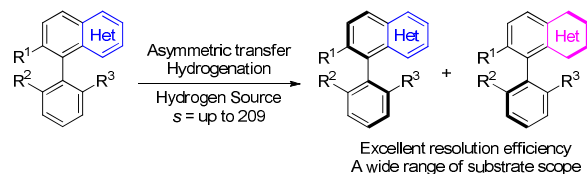
resolution. Phase-transfer catalyst catalyzed *N*-allylation,<sup>8c</sup> *N*-heterocyclic carbene catalyzed *N*-acylation,<sup>8e</sup> Brønsted acid catalyzed reductive amination,<sup>8h</sup> bromination<sup>5b</sup> have realized the kinetic resolution of the amino and hydroxyl biaryls. Although these strategies have gained substantial progress, some of them are limited in substrate scope and resolution efficiency. Therefore, it's still necessary to develop new approaches to realize the kinetic resolution of axially chiral biaryls, which remains a great challenge.

## Scheme 1. Kinetic Resolution of Axially Chiral Biaryls *via* Asymmetric Transfer Hydrogenation of Heteroaromatics

**Previous work:** Construction of central chirality



**This work:** Construction of axial chirality *via* kinetic resolution

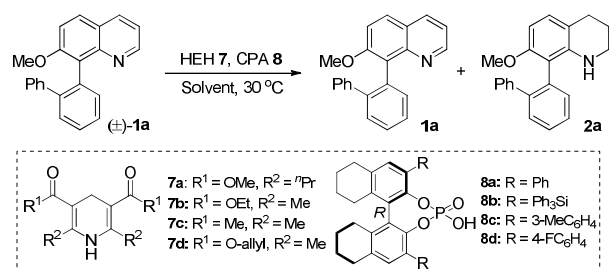


Recently, asymmetric hydrogenation of heteroaromatics has been regarded as a promising method to chiral heterocycles using transition-metal catalysts and organocatalysts.<sup>10</sup> Considering that axially chiral biaryl compounds containing heteroaromatics are prevalent in organocatalyst and biologically active molecules,<sup>1a</sup> we envisaged that asymmetric (transfer) hydrogenation of heteroaromatics would be intergrated into the kinetic resolution of axially chiral biaryls, which has not been achieved so far (Scheme 1). As for the heterocyclic compounds afforded, they would conveniently return to the heteroaromatics by simple oxidation. The key point in the development of an efficient kinetic resolution method is to find a suitable catalyst to activate heteroaromatics which have high resonance stability. In addition, the catalyst should be able to distinguish the chiral axis of the biaryls to provide high kinetic resolution efficiency. Herein, we first apply the asymmetric transfer hydrogenation of heteroaromatics to kinetic resolution of axially chiral biaryls with up to 209 of kinetic resolution selectivity factor.

To validate the feasibility of the hypothesis, we initiated our research on kinetic resolution of (±)-8-([1,1'-biphenyl]-2-yl)-7-methoxyquinoline **1a** using the iridium-based catalytic system developed by our group.<sup>11</sup> Disappointedly, poor resolution

efficiency was obtained. Inspired by Rueping group's work on organocatalytic asymmetric transfer hydrogenation, we turned our attention to organocatalysts.<sup>12</sup> The reaction system CPA/Hantzsch ester (HEH) would activate the substrate by hydrogen bond and the opposite configuration of the biaryls maybe exhibit the different energy barrier when matching with the chiral phosphoric acid. In this context, the experiment was conducted in 1,4-dioxane using (*R*)-CPA **8a** as the catalyst and HEH **7a** as the hydrogen source. Fortunately, the desirable product **2a** was afforded with 97% ee at 29% conversion (Table 1, entry 1, *s* = 112). Then, we examined the effect of solvents such as THF, benzene, CH<sub>2</sub>Cl<sub>2</sub>, and so on (entries 2-5). To our delight, the reaction showed a high selectivity in CH<sub>2</sub>Cl<sub>2</sub> (entry 5, *s* = 125, *conv.* = 51%, *ee*<sub>1a</sub> = 96%, *ee*<sub>2a</sub> = 94%). Since Hantzsch esters usually played a vital role in asymmetric transfer hydrogenation, various HEH **7** were also investigated to study the steric and electronic effect of R<sup>1</sup> and R<sup>2</sup> on reactivity and enantioselectivity (entries 5-8). Obviously, introducing <sup>*i*</sup>Pr onto the 2,6-position of HEH **7** would improve the kinetic resolution selectivity. Further examination was focused on some commercially available chiral phosphoric acids, showing that the (*R*)-CPA **8a** was the best catalyst (entries 5, 9-11). Finally, the optimal conditions were established: CH<sub>2</sub>Cl<sub>2</sub>/HEH **7a**/*R*-CPA **8a**/30 °C.

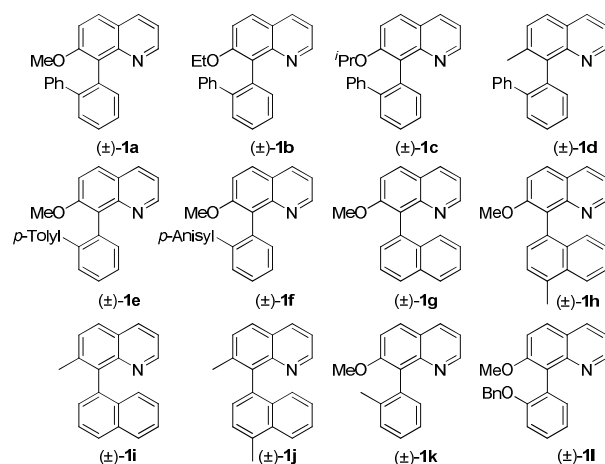
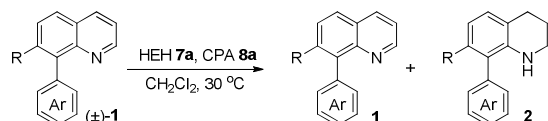
**Table 1. Condition Optimization<sup>a</sup>**



entry	solvent	HEH <b>7</b> / CPA <b>8</b>	<b>1a</b> ee % <sup>b</sup>	<b>2a</b> ee % <sup>b</sup>	<i>conv.</i> % <sup>c</sup>	<i>s</i> <sup>c</sup>
1	dioxane	<b>7a/8a</b>	40	97	29	112
2	THF	<b>7a/8a</b>	38	97	28	111
3	benzene	<b>7a/8a</b>	99	83	55	73
4	CH <sub>3</sub> OH	<b>7a/8a</b>	-	-	-	-
5	CH <sub>2</sub> Cl <sub>2</sub>	<b>7a/8a</b>	96	94	51	125
6	CH <sub>2</sub> Cl <sub>2</sub>	<b>7b/8a</b>	78	81	49	23
7	CH <sub>2</sub> Cl <sub>2</sub>	<b>7c/8a</b>	31	92	25	34
8	CH <sub>2</sub> Cl <sub>2</sub>	<b>7d/8a</b>	65	73	47	12
9	CH <sub>2</sub> Cl <sub>2</sub>	<b>7a/8b</b>	-	-	-	-
10	CH <sub>2</sub> Cl <sub>2</sub>	<b>7a/8c</b>	60	96	38	90
11	CH <sub>2</sub> Cl <sub>2</sub>	<b>7a/8d</b>	85	95	47	99

<sup>a</sup>Reaction conditions: (**±**)-**1a** (0.1 mmol), HEH **7** (0.12 mmol), CPA **8** (5 mol%), solvent (2 mL), 24 h, 30 °C. <sup>b</sup>The ee value was determined by HPLC. <sup>c</sup>Calculated conversion and selectivity factors<sup>13</sup>: *conv.* = *ee*<sub>1a</sub>/(*ee*<sub>1a</sub>+*ee*<sub>2a</sub>), *s* = ln[(1-*C*)(1-*ee*<sub>1a</sub>)]/ln[(1-*C*)(1+*ee*<sub>1a</sub>)].

**Table 2. Substrate Scope for the Kinetic Resolution of 8-Substituted Quinoline-derived Biaryls<sup>a</sup>**

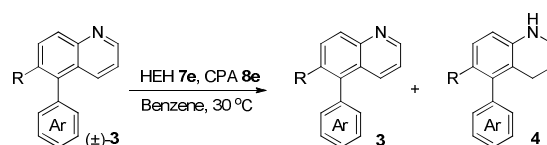


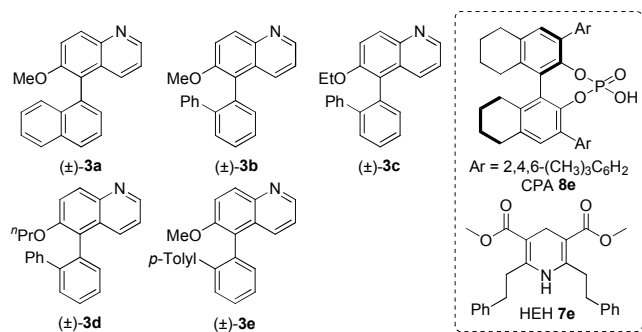
entry	( <b>±</b> )- <b>1</b>	<b>2</b>	<b>1</b> ee % <sup>b</sup>	<b>1</b> yield % <sup>c</sup>	<b>2</b> ee % <sup>b</sup>	<b>2</b> yield % <sup>c</sup>	<i>s</i>
1	<b>1a</b>	<b>2a</b>	96	47	94	49	125
2	<b>1b</b>	<b>2b</b>	97	49	95	49	169
3	<b>1c</b>	<b>2c</b>	86	51	97	45	187
4	<b>1d</b>	<b>2d</b>	96	45	94	48	131
5	<b>1e</b>	<b>2e</b>	86	49	97	45	209
6	<b>1f</b>	<b>2f</b>	99	43	81	51	50
7	<b>1g</b>	<b>2g</b>	62	53	90	33	36
8	<b>1h</b>	<b>2h</b>	91	44	81	47	29
9	<b>1i</b>	<b>2i</b>	93	45	88	50	51
10	<b>1j</b>	<b>2j</b>	89	44	79	47	25
11	<b>1k</b>	<b>2k</b>	89	46	78	51	23
12	<b>1l</b>	<b>2l</b>	97	37	72	51	25

<sup>a</sup>Reaction conditions: (**±**)-**1** (0.15 mmol), HEH **7a** (0.18 mmol), CPA **8a** (5 mol%), CH<sub>2</sub>Cl<sub>2</sub> (3 mL), 24 h, 30 °C. <sup>b</sup>The ee value was determined by HPLC. <sup>c</sup>Isolated yield.

With the optimal conditions in hand, we set out to explore the substrate generality of the kinetic resolution of quinoline-derived biaryls by asymmetric transfer hydrogenation. Gratifyingly, the strategy was suitable for the kinetic resolution of different kinds of substrates and high selectivities (*s* >20) were obtained. As shown in Table 2, the substrates bearing 2-biphenyl were well tolerated. With the increasing the steric hindrance from MeO to O<sup>*i*</sup>Pr, there was a substantial rise of kinetic resolution selectivity (entries 1-3, *s* = 125, 169, 187). Switching the strong electron-donating alkoxy group to the simple methyl led to an excellent selectivity (entry 4, *s* = 131). Besides, introducing various substituents to phenyl could also give a high selectivity (entries 5-6, *s* = 209, 50). Moreover, biaryl substrates bearing naphthalene moiety also afforded the corresponding hydrogenation products with *s* arranging from to 25-51 (entries 7-10). In addition, for the 2-methylphenyl, 2-benzyloxy-phenyl substituted quinolines, high selectivity factors were also obtained (entries 11, 12, *s* = 23, 25).

**Table 3. Substrate Scope for the Kinetic Resolution of 5-Substituted Quinoline-derived Biaryls<sup>a</sup>**

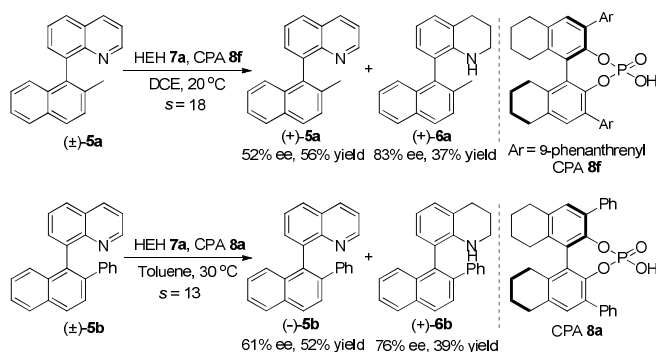




entry	(±)-3	4	3	3	4	4	<i>s</i>
			ee% <sup>b</sup>	yield% <sup>c</sup>	ee% <sup>b</sup>	yield% <sup>c</sup>	
1	<b>3a</b>	<b>4a</b>	46	62	79	37	14
2	<b>3b</b>	<b>4b</b>	51	62	84	36	20
3	<b>3c</b>	<b>4c</b>	53	59	86	35	22
4	<b>3d</b>	<b>4d</b>	53	57	87	37	24
5	<b>3e</b>	<b>4e</b>	48	61	87	35	23

<sup>a</sup>Reaction conditions: (±)-3 (0.15 mmol), HEH 7e (0.17 mmol), CPA 8e (5 mol%), benzene (3 mL), 24-72 h, 30 °C. <sup>b</sup>The ee value was determined by HPLC. <sup>c</sup>Isolated yield.

### Scheme 2. 2',6'-Substituted Quinoline-based Biaryls



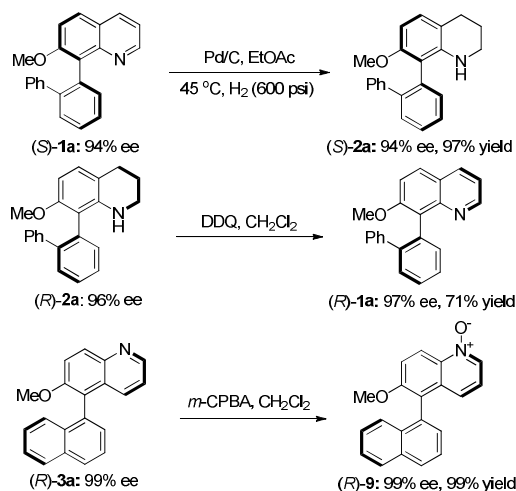
To extend the substrate scope, 5-substituted quinoline derived biaryls (±)-**3** were also synthesized to test the kinetic resolution (Table 3). It would be challengeable for the nitrogen atom far away from the *non-C*<sub>2</sub> symmetry axis. To our delight, the kinetic resolution could perform smoothly at 30 °C for 24-72 h. The results were insensitive to the chain length of the alkoxy group (entries 2-4, R = MeO, EtO and <sup>n</sup>PrO). Substrates bearing 1-naphthyl or 2-biphenyl were also tolerated with moderate to high selectivities (entries 1-5, *s* = 14-24).

To further estimate the application possibility, 2',6'-substituted quinoline-based biaryls (±)-**5a** and **5b** were synthesized. As for the simple quinoline and 2',6'-substituted phenyl combined axially chiral compounds, the reduced-recognition between the substituents at 2',6' position would extremely increase the kinetic resolution difficulty. Fortunately, the reaction also worked well with moderate selectivity (*s* = 13, 18) (Scheme 2).

An indication of configuration stability of the recovered substrates and products (-)-**1i**, (-)-**3a**, (+)-**2d** and (+)-**2i** was obtained by heating them in DCE at 80 °C for 4 hours and the HPLC analysis showed all the ee values were retained.<sup>14</sup> Thus, the quinoline-based axially chiral scaffold would provide a potential application in organic synthesis. To demonstrate the potential of this new strategy, a scale-up resolution experiment of (±)-**1a** on 2 mmol was carried out to afford corresponding hydrogenation product **2a** (95% ee) in 49% yield and enantiopure recovered

substrate **1a** (>99% ee) in 48% yield. For the axially chiral compounds obtained above, these could be easy for reciprocal transformations (Scheme 3). The recovered substrate (*S*)-**1a** (94% ee) could be hydrogenated to the product (*S*)-**2a** (94% ee) with Pd/C at 45 °C under 600 psi of hydrogen,<sup>15</sup> and the corresponding hydrogenation product (*R*)-**2a** (96% ee) could be reoxidized to the substrate (*R*)-**1a** (97% ee) using DDQ in dichloromethane.<sup>16</sup> In this way, the substrates and corresponding products with different axial skeletons could each get two enantiomers with excellent ee. As for the axially chiral 5-substituted quinolines, a derivatization reaction was carried out. Treatment of **3a** with *m*-CPBA led to a quantitative formation of the corresponding axially chiral quinoline *N*-oxide **9**, which would be convenient for the other series of transformations.<sup>17</sup>

### Scheme 3. Transformation Experiments



In summary, we have developed a highly efficient chiral phosphoric acid-catalyzed kinetic resolution of axially chiral 5-, or 8-substituted quinoline-based biaryl compounds with excellent selectivity factor (*s* up to 209). Two different kinds of axially chiral skeletons could be simultaneously obtained in the kinetic resolution process. To the best of our knowledge, this strategy provides the first example to achieve axially chiral skeleton *via* asymmetric transfer hydrogenation of heteroaromatics. Further investigations of this strategy toward kinetic resolution of other similar axially chiral biaryl compounds are currently ongoing in our laboratory.

## ASSOCIATED CONTENT

### Supporting Information

Procedures and spectral (NMR, HRMS, HPLC) data. This material is available free of charge *via* the Internet at <http://pubs.acs.org>.

## AUTHOR INFORMATION

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## REFERENCES

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51  
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- (1) For recent reviews and selected papers on axially chiral biaryls, see: (a) Bringmann, G.; Gulder, T.; Gulder, T. A. M.; Breuning, M. *Chem. Rev.* **2011**, *111*, 563. (b) Tang, W.; Zhang, X. *Chem. Rev.* **2003**, *103*, 3029. (c) Terada, M. *Synthesis* **2010**, *12*, 1929. (d) Rueping, M.; Kuenkel, A.; Atodiressei, L. *Chem. Soc. Rev.* **2011**, *40*, 4539. (e) Christ, F.; Voet, A.; Marchand, A.; Nicolet, S.; Desimmié, B. A.; Marchand, D.; Bardirot, D.; Van der Veken, N. J.; Van Remoortel, B.; Strelkov, S. V.; De Maeyer, M.; Chaltin, P.; Debyser, Z. *Nat. Chem. Biol.* **2010**, *6*, 442. (f) Chen, Y.; Yekta, S.; Yudin, A. K. *Chem. Rev.* **2003**, *103*, 3155. (g) Brunel, J. M. *Chem. Rev.* **2005**, *105*, 857; Update 1: Brunel, J. M. *Chem. Rev.* **2007**, *107*, PR1.
- (2) For recent reviews on the enantioselective synthesis of axially chiral compounds, see: (a) Wencel-Delord, J.; Panossian, A.; Leroux, F. R.; Colobert, F. *Chem. Soc. Rev.* **2015**, *44*, 3418. (b) Bencivenni, G. *Synlett* **2015**, *26*, 1915. (c) Kumarasamy, E.; Raghunathan, R.; Sibi, M. P.; Sivaguru, J. *Chem. Rev.* **2015**, *115*, 11239. (d) Ma, G.; Sibi, M. P. *Chem. Eur. J.* **2015**, *21*, 11644.
- (3) For selected papers on classical resolution, see: (a) Miyashita, A.; Yasuda, A.; Takaya, H.; Toriumi, K.; Ito, T.; Souchi, T.; Noyori, R. *J. Am. Chem. Soc.* **1980**, *102*, 7932. (b) Takaya, H.; Mashima, K.; Koyano, K.; Yagi, M.; Kumobayashi, H.; Taketomi, T.; Akutagawa, S.; Noyori, R. *J. Org. Chem.* **1986**, *51*, 629.
- (4) (a) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457. (b) Cammidge, A. N.; Crépy, K. V. L. *Chem. Commun.* **2000**, 1723. (c) Mulrooney, C. A.; Li, X.; DiVirgilio, E. S.; Kozlowski, M. C. *J. Am. Chem. Soc.* **2003**, *125*, 6856. (d) Shen, X.; Jones, G. O.; Watson, D. A.; Bhayana, B.; Buchwald, S. L. *J. Am. Chem. Soc.* **2010**, *132*, 11278. (e) Xu, G.; Fu, W.; Liu, G.; Senanayake, C. H.; Tang, W. *J. Am. Chem. Soc.* **2014**, *136*, 570. (f) Fang, Z.-J.; Zheng, S.-C.; Guo, Z.; Guo, J.-Y.; Tan, B.; Liu, X.-Y. *Angew. Chem. Int. Ed.* **2015**, *54*, 9528. (g) Feng, J.; Li, B.; He, Y.; Gu, Z. *Angew. Chem. Int. Ed.* **2016**, *55*, 2186.
- (5) (a) Hayashi, T.; Niizuma, S.; Kamikawa, T.; Suzuki, N.; Uozumi, Y. *J. Am. Chem. Soc.* **1995**, *117*, 9101. (b) Mori, K.; Ichikawa, Y.; Kobayashi, M.; Shibata, Y.; Yamanaka, M.; Akiyama, T. *J. Am. Chem. Soc.* **2013**, *135*, 3964. (c) Osako, T.; Uozumi, Y. *Org. Lett.* **2014**, *16*, 5866. (d) Armstrong, R. J.; Smith, M. D. *Angew. Chem. Int. Ed.* **2014**, *53*, 12822. (e) Zheng, J.; Cui, W.-J.; Zheng, C.; You, S.-L. *J. Am. Chem. Soc.* **2016**, *138*, 5242.
- (6) (a) Guo, F.; Konkol, L. C.; Thomson, R. J. *J. Am. Chem. Soc.* **2011**, *133*, 18. (b) Chen, Y.-H.; Cheng, D.-J.; Zhang, J.; Wang, Y.; Liu, X.-Y.; Tan, B. *J. Am. Chem. Soc.* **2015**, *137*, 15062. (c) Quinonero, O.; Jean, M.; Vanthuyne, N.; Roussel, C.; Bonne, D.; Constantieux, T.; Bressy, C.; Bugaut, X.; Rodriguez, J. *Angew. Chem. Int. Ed.* **2016**, *55*, 1401. (d) Wang, J.-Z.; Zhou, J.; Xu, C.; Sun, H.; Kürti, L.; Xu, Q.-L. *J. Am. Chem. Soc.* **2016**, *138*, 5202.
- (7) (a) Zheng, J.; You, S.-L. *Angew. Chem. Int. Ed.* **2014**, *53*, 13244. (b) Cozzi, P. G.; Emer, E.; Gualandi, A. *Angew. Chem. Int. Ed.* **2011**, *50*, 3847. (c) Clayden, J.; Fletcher, S. P.; McDouall, J. J. W.; Rowbottom, S. J. M. *J. Am. Chem. Soc.* **2009**, *131*, 5331. (d) Gustafson, J. L.; Lim, D.; Miller, S. J. *Science* **2010**, *328*, 1251. (e) Bhat, V.; Wang, S.; Stoltz, B. M.; Virgil, S. C. *J. Am. Chem. Soc.* **2013**, *135*, 16829. (f) Ros, A.; Estepa, B.; Ramírez-López, P.; Álvarez, E.; Fernández, R.; Lassaletta, J. M. *J. Am. Chem. Soc.* **2013**, *135*, 15730. (g) Hazra, C. K.; Dherbassy, Q.; Wencel-Delord, J.; Colobert, F. *Angew. Chem. Int. Ed.* **2014**, *53*, 13871.
- (8) (a) Schlosser, M.; Bailly, F. *J. Am. Chem. Soc.* **2006**, *128*, 16042. (b) Arseniyadis, S.; Mahesh, M.; McDaid, P.; Hampel, T.; Davey, S. G.; Spivey, A. C. *Collect. Czech. Chem. Commun.* **2011**, *76*, 1239. (c) Shirakawa, S.; Wu, X.; Maruoka, K. *Angew. Chem. Int. Ed.* **2013**, *52*, 14200. (d) Ma, G.; Deng, J.; Sibi, M. P.; *Angew. Chem. Int. Ed.* **2014**, *53*, 11818. (e) Lu, S.; Poh, S. B.; Zhao, Y. *Angew. Chem. Int. Ed.* **2014**, *53*, 11041. (f) Gao, D.-W.; Gu, Q.; You, S.-L. *ACS Catal.* **2014**, *4*, 2741. (g) Aoyama, H.; Tokunaga, M.; Kiyosu, J.; Iwasawa, T.; Obora, Y.; Tsuji, Y. *J. Am. Chem. Soc.* **2005**, *127*, 10474. (h) Cheng, D.-J.; Yan, L.; Tian, S.-K.; Wu, M.-Y.; Wang, L.-X.; Fan, Z.-L.; Zheng, S.-C.; Liu, X.-Y.; Tan, B. *Angew. Chem. Int. Ed.* **2014**, *53*, 3684. (i) Lu, S.; Poh, S. B.; Siau, W.-Y.; Zhao, Y. *Angew. Chem. Int. Ed.* **2013**, *52*, 1731.
- (9) (a) Nishida, G.; Noguchi, K.; Hirano, M.; Tanaka, K. *Angew. Chem. Int. Ed.* **2007**, *46*, 3951. (b) Ashizawa, T.; Tanaka, S.; Yamada, T. *Org. Lett.* **2008**, *10*, 2521. (c) Ashizawa, T.; Yamada, T. *Chem. Lett.* **2009**, *38*, 246.
- (10) For selected reviews on hydrogenation of aromatic compounds, see: (a) Wang, D.-S.; Chen, Q.-A.; Lu, S.-M.; Zhou, Y.-G. *Chem. Rev.* **2012**, *112*, 2557. (b) He, Y.-M.; Song, F.-T.; Fan, Q.-H. *Top. Curr. Chem.* **2014**, *343*, 145. (c) Xie, J.; Zhou, Q. *Acta Chim. Sinica* **2012**, *70*, 1427. (d) Kuwano, R. *Heterocycles* **2008**, *76*, 909. (e) Glorius, F. *Org. Biomol. Chem.* **2005**, *3*, 4171. (f) Chen, Q.-A.; Ye, Z.-S.; Duan, Y.; Zhou, Y.-G. *Chem. Soc. Rev.* **2013**, *42*, 497.
- (11) (a) Wang, W.-B.; Lu, S.-M.; Yang, P.-Y.; Han, X.-W.; Zhou, Y.-G. *J. Am. Chem. Soc.* **2003**, *125*, 10536. (b) Zhou, Y.-G. *Acc. Chem. Res.* **2007**, *40*, 1357.
- (12) (a) Rueping, M.; Antonchick, A. P.; Theissmann, T. *Angew. Chem. Int. Ed.* **2006**, *45*, 3683. (b) Rueping, M.; Theissmann, T.; Raja, S.; Bats, J. W. *Adv. Synth. Catal.* **2008**, *350*, 1001. (c) Guo, Q.-S.; Du, D.-M.; Xu, J. *Angew. Chem. Int. Ed.* **2008**, *47*, 759. (d) Metallinos, C.; Barrett, F. B.; Xu, S. *Synlett* **2008**, 720. (e) Rueping, M.; Theissmann, T. *Chem. Sci.* **2010**, *1*, 473. (f) Tu, X.-F.; Gong, L.-Z. *Angew. Chem. Int. Ed.* **2012**, *51*, 11346. (g) Stemper, J.; Isaac, K.; Pastor, J.; Frison, G.; Retailleau, P.; Voituriez, A.; Betzer, J.-F.; Marinetti, A. *Adv. Synth. Catal.* **2013**, *355*, 3613. (h) Ferry, A.; Stemper, J.; Marinetti, A.; Voituriez, A.; Guinchard, X. *Eur. J. Org. Chem.* **2014**, 188. (i) Shugrue, C. R.; Miller, S. J. *Angew. Chem. Int. Ed.* **2015**, *54*, 11173. (j) Cai, X.-F.; Chen, M.-W.; Ye, Z.-S.; Guo, R.-N.; Shi, L.; Li, Y.-Q.; Zhou, Y.-G. *Chem. Asian J.* **2013**, *8*, 1381. (k) Chen, M.-W.; Cai, X.-F.; Chen, Z.-P.; Shi, L.; Zhou, Y.-G. *Chem. Commun.* **2014**, *50*, 12526.
- (13) Kagan, H. B.; Fiaud, J. C. *Top. Stereochem.* **1988**, *18*, 249.
- (14) (a) For the detailed stability experiments, please see Supporting Information; (b) CCDC 1427846 and CCDC 1455885 contain supplementary crystallographic data of (-)-**3b** and (-)-**1i**. These data can be obtained free of charge from Cambridge Crystallographic Data Centre via [www.ccdc.cam.ac.uk/data\\_request/cif](http://www.ccdc.cam.ac.uk/data_request/cif).
- (15) Xiao, J.; Loh, T.-P. *Org. Lett.* **2009**, *11*, 2876.
- (16) Kise, N.; Isemoto, S.; Sakurai, T. *Org. Lett.* **2009**, *11*, 4902.
- (17) Zhang, X.; Qi, Z.; Li, X. *Angew. Chem. Int. Ed.* **2014**, *53*, 10794.

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**Table of Contents (TOC) Graphic:**

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