Hydrogenation

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Spiro-Bicyclic Bisborane Catalysts for Metal-Free Chemoselective and Enantioselective Hydrogenation of Quinolines

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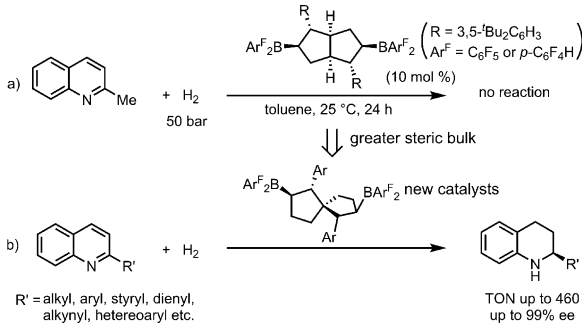
Dedicated to the 100th anniversary of Nankai University

Abstract: *A new series of spiro-bicyclic bisborane catalysts has been prepared by means of hydroboration reactions of C_2-symmetric spiro-bicyclic dienes with $HB(C_6F_5)_2$ and $HB(p\text{-}C_6F_4H)_2$. When used for hydrogenation of quinolines, these catalysts give excellent yields and enantiomeric excesses, and show turnover numbers of up to 460. The most attractive feature of these metal-free hydrogenation reactions was the broad functional-group tolerance, making this method complementary to existing methods for quinoline hydrogenation.*

Because of the prevalence of chiral tetrahydroquinoline scaffolds in natural products and drugs,[1] the development of methods for enantioselective hydrogenation of quinolines is an important area of research. Methods that use transition-metal catalysts with chiral ligands have been extensively investigated,[2] and the good performing catalysts are generally iridium- and ruthenium-centered.[3–5] However, the need to use precious metals, especially when the turnover numbers are not high, limits the attractiveness of these methods, for both economic and environmental reasons. More important, because other unsaturated functional groups, such as olefins, alkynes, and electron-rich heteroarenes, are reactive under metal-catalyzed hydrogenation conditions, it is very difficult to preserve these groups during hydrogenation of the quinoline core. Indeed, most of the existing methods have been used only on substrates that have relatively inert substituents and thus lack handles for further elaboration.[2–5]

With the emergence of frustrated Lewis pair chemistry,[6] studies on metal-free borane-catalyzed hydrogenations of N-heteroarenes have grown rapidly.[7] Particularly, chiral borane Lewis acids have been tested for enantioselective hydrogenation of quinolines. The first report appeared in 2011: the group of Repo used a chiral ansa-ammonium borate as a catalyst for hydrogenation of 2-phenylquinoline, and obtained an *ee* value of 37%.[8] Subsequently, the group of Du made a breakthrough by using binaphthyl-diene-derived bisborane catalysts. They reported excellent enantioselectivities in the hydrogenations of 2,3- and 2,4-disubstituted quinolines, 2,3,4-trisubstituted quinolines, and 2,3-disubstituted quinoxalines.[9] However, the methods described in these pioneering studies have limitations. First, monosubstituted quinolines remain mostly unexplored. Besides the results for 2-phenylquinoline reported by Repo (37% *ee*),[8] there is only one report from Du, who tested their catalysts with methyl quinoline-2-carboxylate but obtained an *ee* of merely 14%.[10] By comparison, the success with di- and trisubstituted quinolines using Du's catalysts[9a,b] implies that the steric influence from additional substituents might be essential for enantiocontrol. Second, the compatible di- and trisubstituted quinolines in Du's studies all have an aryl substituent at the 2-position. We suspect that the 2-aryl substituent increases the steric bulk around the nitrogen atom, thereby preventing undesired coordination of the nitrogen center to the Lewis acid catalyst. Third, the functional-group tolerance is limited. Therefore, the development of more effective catalytic systems is highly desirable.

Recently, we developed a series of chiral C_2-symmetric bisborane catalysts that are prepared by hydroboration reactions of bicyclic [3.3.0] dienes with $HB(C_6F_5)_2$ and $HB(p\text{-}C_6F_4H)_2$.[11] These catalysts are highly effective and selective in asymmetric imine hydrogenations. We attempted to use them for the hydrogenation of 2-methylquinoline, a less bulky substrate that was not studied by either Repo[8] or Du.[9,10] Disappointingly, we observed no reaction (Scheme 1 a). We hypothesized that our catalysts were not sterically hindered enough to prevent the coordination of this quinoline to the boron center. To increase the steric bulk, we intended to change the fused bicyclic structure to a spiro-bicyclic structure because the latter consists of two perpendicular rings, which produce a steric environment similar to that in



Scheme 1. Hydrogenation of quinolines with chiral bicyclic bisborane catalysts.

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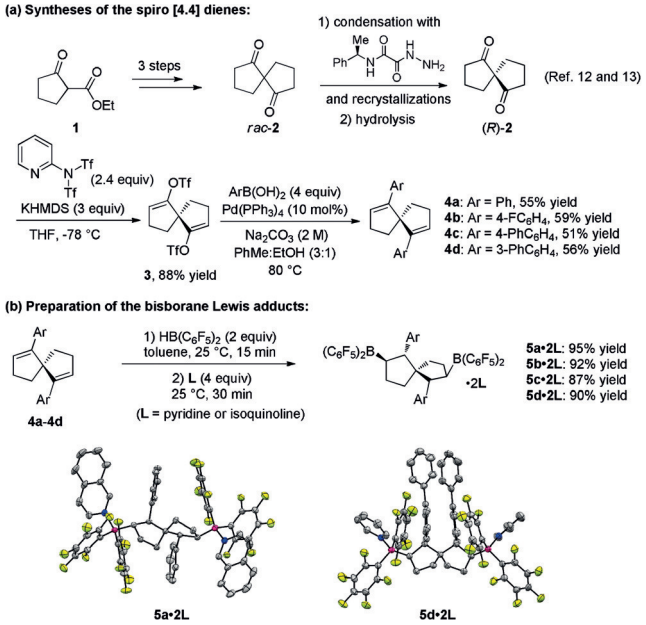
compounds with geminal dialkyl substituents. Furthermore, the presence of Ar and BAr^F_2 groups attached to the rings would further increase the steric bulkiness. We hoped that such catalysts would show better activities than the existing borane catalysts. Herein, we report that these new spiro-bicyclic bisboranes have now been synthesized and that, to our delight, they exhibit excellent catalytic activities and selectivities for the hydrogenation reactions of quinolines (Scheme 1b).

We began our study by synthesizing the necessary spiro [4.4] diene precursors (Scheme 2a) as follows. First, the racemic spiro [4.4]nonane-1,6-dione **2** was prepared from



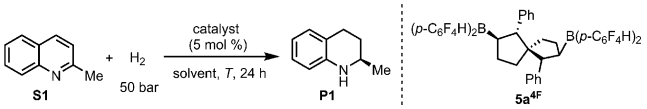
Scheme 2. Preparation and characterization of bisborane catalysts. Tf = trifluoromethanesulfonyl, THF = tetrahydrofuarn.

ethyl 2-oxocyclopentanecarboxylate (**1**) by a previously reported three-step synthesis.[12] Then **2** was resolved by condensation with (*R*)-2-hydrazinyl-2-oxo-N-(1-phenylethyl)acetamide and multiple recrystallizations of the obtained diastereomeric mixture.[13] After hydrolysis of the pure hydrazone diastereomer, (*R*)-**2** was obtained in enantiopure form. (*R*)-**2** was then transformed into the enol triflate **3** by reaction with *N*-(2-pyridyl)triflimide in the presence of potassium bis(trimethylsilyl)amide (KHMDS). It is worth mentioning that for this step, we tested several triflyl sources under various reaction conditions, and only *N*-(2-pyridyl)triflimide gave the desired product in a high yield without the loss of enantiomeric purity.[14] From the common intermediate **3**, we were able to prepare four aryl-substituted spiro [4.4] dienes, **4a**–**d**, by Suzuki coupling reactions. These dienes served as precursors for the corresponding bisborane catalysts.

To study the process for catalyst formation, we subjected **4a**–**d** in their racemic form to hydroboration with Piers borane, $HB(C_6F_5)_2$ (Scheme 2b).[15] In toluene at 25 °C, the dienes were completely consumed within 15 minutes, at which point a strongly coordinative base (isoquinoline or pyridine) was added to the reaction mixture to capture the resulting bisborane species as stable Lewis acid/base adducts **5a·2L**–**5d·2L**. Remarkably, despite the possibility for formation of multiple regioisomers and diastereomers, single isomers of the bisborane adducts were obtained in high yields as determined by NMR analyses using CH_2Br_2 as an internal standard. Single crystals of **5a·2L** and **5d·2L** were obtained by recrystallization from 20:1 (v/v) *n*-hexane/dichloromethane at room temperature. X-ray crystallographic analyses revealed that the aryl groups were *trans* to the $B(C_6F_5)_2$ groups in both cyclopentane rings and that the overall structures were C_2-symmetric.[16] Notably, unlike hydroboration reactions of bicyclic [3.3.0] dienes,[11] these hydroborations gave the same isomers when they were performed at higher temperatures (e.g., 80 °C).

Knowing that hydroboration reactions of the spiro [4.4] dienes could efficiently generate single bisborane isomers, we investigated the use of in situ generated bisborane compounds for enantioselective hydrogenation with 2-methylquinoline (**S1**; Table 1). For each reaction, an enantiopure diene and

Table 1: Study of reaction conditions for hydrogenation of 2-methylquinoline.[a]



Entry	Catalyst	Solvent	*T* [°C]	Conv. [%][b]	*ee* [%][c]
1	**5a**	toluene	25	100	63
2	**5b**	toluene	25	30	45
3	**5c**	toluene	25	100	62
4	**5d**	toluene	25	100	53
5	**5a**^{4F}	toluene	25	100	78
6	**5a**^{4F}	toluene	0	100	81
7	**5a**^{4F}	toluene	−20	100	84
8	**5a**^{4F}	*n*-hexane	−20	95	79
9	**5a**^{4F}	$PhCF_3$	−20	100	92
10[d]	**5a**^{4F}	$PhCF_3$	−20	100	92

[a] Unless otherwise specified, all hydrogenations were performed with 0.1 mmol of **S1** in 2 mL of solvent in a 30 mL autoclave. [b] Determined by NMR spectroscopy. [c] Determined by HPLC with a Chiralcel OD-H column. [d] H_2 pressure, 20 bar.

$HB(C_6F_5)_2$ were first reacted in toluene at 25 °C for 15 minutes to generate the active catalyst, and then 2-methylquinoline was added. The resulting mixture was hydrogenated in an autoclave. We were pleased to find that these spiro-bicyclic bisborane catalysts were active and selective: the use of 5 mol% of the catalyst **5a** resulted in complete conversion into the corresponding tetrahydroquinoline product (**P1**) with 63% *ee* (entry 1). Although **5b** exhibited markedly diminished activity (entry 2), both **5c** and **5d** were very active, providing **P1** in complete conversion (entries 3 and 4). However, the enantioselectivities of these catalysts were no better than that of **5a**. Gratifyingly, after an extensive optimization study, we discovered that changing the $B(C_6F_5)_2$ group in **5a** to $B(p\text{-}C_6F_4H)_2$ to afford **5a**^{4F} improved the enantioselectivity to 78% *ee* (entry 5).[17] With this

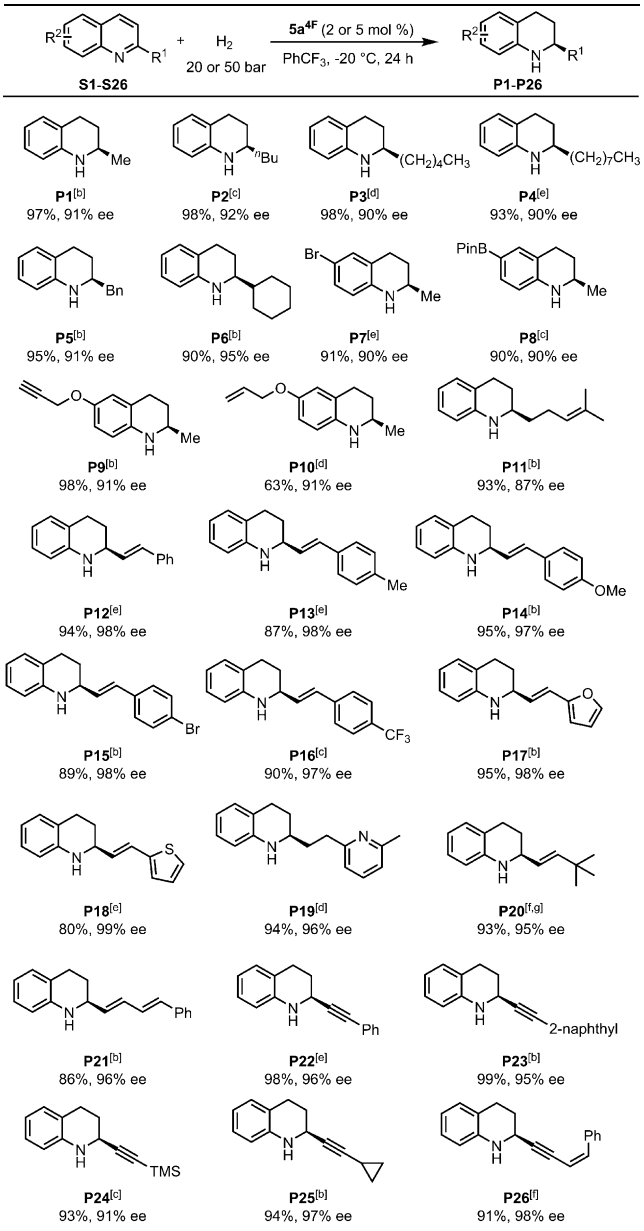
catalyst, the *ee* gradually increased with decreasing reaction temperature (entries 6 and 7). At −20 °C, the substrate was completely consumed, and **P1** was obtained with 84 % *ee*. Moreover, switching the solvent to $PhCF_3$ markedly improved the enantioselectivity (entry 9). Under these reaction conditions, the same result was obtained even when the hydrogen pressure was decreased from 50 to 20 bar (entry 10).

With the optimal reaction conditions in hand, we investigated the generality of this borane-catalyzed enantioselective hydrogenation reaction by testing various quinoline substrates (Table 2). A number of 2-alkyl substituents, including *n*-butyl, *n*-pentyl, *n*-octyl, benzyl, and cyclohexyl, were compatible with the reaction conditions. The corresponding products (**P2**–**P6**, respectively) were obtained in 90–98 % yields with 90–95 % *ee* values. Substrates with various coexisting substituents at the 6-position of the 2-methylquinolines were then studied (**S7**–**S10**). Gratifyingly, bromo, Bpin, and terminal alkyne and alkene substituents were preserved, giving the desired products (**P7**–**P10**, respectively) with high *ee* values. Similarly, when a substrate possessing an unconjugated internal olefin at the 2-position was used, the double bond remained untouched when the heterocycle was hydrogenated (**P11**).

Various quinolines with conjugated olefins at the 2-position (**S12**–**S20**) were subsequently tested (Table 2). These olefin units are highly susceptible to hydride reduction because of the activation by the adjacent heteroarene.[3e,4b,7b] In fact, only a transfer-hydrogenation protocol that uses chiral phosphoric acids and Hantzsch ester can enantioselectively reduce 3-nitro-2-styrylquinolines while preserving the olefin group.[18] However, we were gratified to find that when 2-styrylquinolines were tested with our bisborane catalyst, hydrogenation preferentially occurred at the heteroaromatic ring regardless of the electronic nature of the substituents on the phenyl ring, and styryl-substituted tetrahydroquinolines (**P12**–**P16**) were obtained in high yields with excellent *ee* values. Furthermore, the presence of a furyl (**P17**) or thiophenyl (**P18**) moiety did not inhibit the reaction. Although the hydrogenation reaction of a pyridyl-substituted substrate reduced the conjugated olefin to afford **P19**, the reaction of a substrate with a terminal alkyl substituent left the olefin unit untouched (**P20**). Moreover, the reaction was feasible with 2-dienyl- (**P21**) and alkynyl-substituted (**P22**–**P25**) quinolines, and even with a quinoline bearing consecutive double and triple bonds (**P26**). Note that, the asymmetric hydrogenation reactions of **S12**–**S26** with retention of the unsaturated functional groups are unprecedented with any kind of catalysis.

2-Aryl-substituted quinolines were next studied (Table 3). We discovered that **5d** provided the highest enantioselectivities, and addition of tris[3,5-bis(trifluoromethyl)phenyl]phosphine improved the yields. Phenyl rings bearing various electron-donating and electron-withdrawing groups were tolerated, giving the products **P27**–**P35** in high yields and *ee* values. The presence of a Bpin moiety (**P36**) or internal and terminal double and triple bonds (**P37**–**P40**) did not influence the reactivity or selectivity. Furthermore, coordinative MeS (**P41**) and heterocyclic substituents (**P42**–**P45**) were compatible.

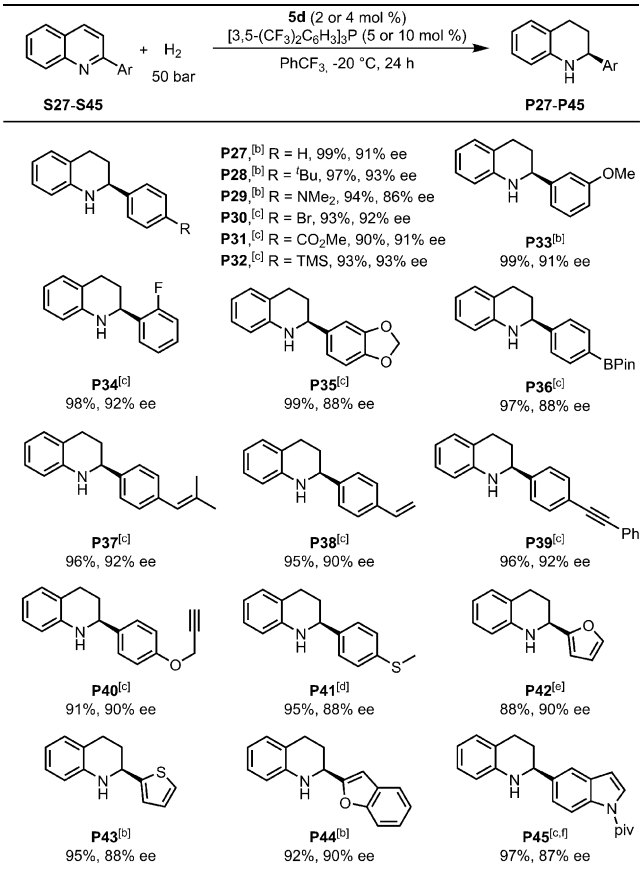
Table 2: Investigation of quinolines with various substituents.[a]



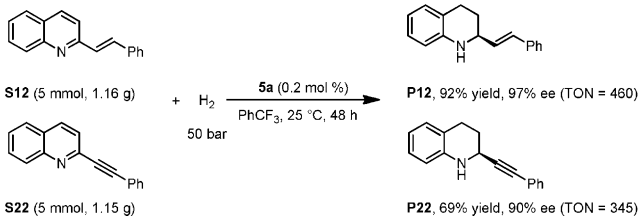
[a] Unless otherwise specified, hydrogenations were performed with 0.25 mmol of the quinoline substrate in 5 mL of $PhCF_3$ in a 30 mL autoclave. The percentages shown are yields of isolated products and enantiomeric excesses, in that order. [b] Used 5 mol % of **5a**^{4F} and 20 bar of H_2. [c] Used 2 mol % of **5a**^{4F}, 50 bar of H_2, and 2 mL of $PhCF_3$. [d] Used 5 mol % of **5a**^{4F} and 50 bar of H_2. [e] Used 2 mol % of **5a**^{4F}, 20 bar of H_2, and 2 mL of $PhCF_3$. [f] Used 5 mol % of **5a** and 50 bar of H_2. [g] Reaction temperature, 25 °C. TMS = trimethylsilyl.

To further demonstrate the power of our catalytic system, we performed gram-scale reactions with styryl- (**S12**) and alkynyl-substituted (**S22**) quinolines (Scheme 3). We discovered that running these hydrogenations at 25 °C did not compromise the enantioselectivities substantially. In addition, by using only 0.2 mol % of **5a**[19] and extending the reaction time to 48 hours, we obtained **P12** and **P22** in high yields with excellent *ee* values. Notably, the turnover number of 460, obtained in the hydrogenation reaction of **S12** represents the

Table 3: Investigation of 2-aryl-substituted quinolines.[a]



[a] Unless otherwise specified, hydrogenations were performed with 0.25 mmol of substrate in 2 mL of $PhCF_3$ in a 30 mL autoclave. The percentages shown are the yields of the isolated products and enantiomeric excesses, in that order. [b] Used 2 mol% of **5 d** and 5 mol% of the phosphine. [c] Used 4 mol% of **5 d** and 10 mol% of the phosphine. [d] Used 6 mol% of **5 d**, 12 mol% of the phosphine, 60 bar of H_2, and 4 mL of $PhCF_3$. [e] Used 4 mol% of **5 d**^{4F} and 10 mol% of the phosphine. [f] Used 60 bar of H_2 and 4 mL of $PhCF_3$.



Scheme 3. Gram-scale reactions with 0.2 mol% catalyst.

highest turnover number so far for asymmetric hydrogenation reactions promoted by a chiral borane catalyst. We reason that the rigidity of the bicyclic scaffold and the steric bulk, which shields boron centers from attack or coordination by nucleophiles (e.g., tetrahydroquinolines), might have contributed to the enhanced stability and activity of these catalysts.

In conclusion, we have synthesized a new class of spirobicyclic bisborane catalysts that exhibit excellent activities and selectivities in asymmetric hydrogenation reactions of 2-substituted quinolines. The unprecedented broad functional-group tolerance observed in these hydrogenation reactions demonstrates the unique advantages of these catalysts over transition metals and other borane catalysts. Our group is currently investigating the origin of this excellent chemoselectivity, as well as the potential applications of these catalysts in other enantioselective transformations.

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Conflict of interest

The authors declare no conflict of interest.

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[1] a) E. Vitaku, D. T. Smith, J. T. Njardarson, *J. Med. Chem.* **2014**, *57*, 10257; b) V. Sridharan, P. A. Suryavanshi, J. C. Menéndez, *Chem. Rev.* **2011**, *111*, 7157.

[2] For selected reviews, see: a) D.-S. Wang, Q.-A. Chen, S.-M. Lu, Y.-G. Zhou, *Chem. Rev.* **2012**, *112*, 2557; b) Y.-M. He, F.-T. Song, Q.-H. Fan, *Top. Curr. Chem.* **2013**, *343*, 145.

[3] For selected studies using iridium catalysts, see: a) W.-B. Wang, S.-M. Lu, P.-Y. Yang, X.-W. Han, Y.-G. Zhou, *J. Am. Chem. Soc.* **2003**, *125*, 10536; b) S.-M. Lu, Y.-Q. Wang, X.-W. Han, Y.-G. Zhou, *Angew. Chem. Int. Ed.* **2006**, *45*, 2260; *Angew. Chem.* **2006**, *118*, 2318; c) L.-J. Xu, K. H. Lam, J. X. Ji, J. Wu, Q.-H. Fan, W.-H. Lo, A. S. C. Chan, *Chem. Commun.* **2005**, 1390; d) L. Q. Qiu, F. Y. Kwong, J. Wu, W. H. Lam, S. Chan, W.-Y. Yu, Y.-M. Li, R. W. Guo, Z. Zhou, A. S. C. Chan, *J. Am. Chem. Soc.* **2006**, *128*, 5955; e) D.-W. Wang, X.-B. Wang, D.-S. Wang, S.-M. Lu, Y.-G. Zhou, Y.-X. Li, *J. Org. Chem.* **2009**, *74*, 2780.

[4] For selected studies using ruthenium catalysts, see: a) H.-F. Zhou, Z.-W. Li, Z.-J. Wang, T.-L. Wang, L.-J. Xu, Y.-M. He, Q.-H. Fan, J. Pan, L.-Q. Gu, A. S. C. Chan, *Angew. Chem. Int. Ed.* **2008**, *47*, 8464; *Angew. Chem.* **2008**, *120*, 8592; b) T.-L. Wang, L. G. Zhuo, Z.-W. Li, F. Chen, Z.-Y. Ding, Y.-M. He, Q.-H. Fan, J.-F. Xiang, Z.-X. Yu, A. S. C. Chan, *J. Am. Chem. Soc.* **2011**, *133*, 9878; c) Q.-A. Chen, K. Gao, Y. Duan, Z.-S. Ye, L. Shi, Y. Yang, Y.-G. Zhou, *J. Am. Chem. Soc.* **2012**, *134*, 2442; d) W. Ma, J. Zhang, C. Xu, F. Chen, Y.-M. He, Q.-H. Fan, *Angew. Chem. Int. Ed.* **2016**, *55*, 12891; *Angew. Chem.* **2016**, *128*, 13083.

[5] For selected reports using other metals as well as enantioselective transfer hydrogenations, see: a) M. Rueping, A. P. Antonchick, T. Theissmann, *Angew. Chem. Int. Ed.* **2006**, *45*, 3683; *Angew. Chem.* **2006**, *118*, 3765; b) C. Wang, C. Li, X. Wu, A. Pettman, J. Xiao, *Angew. Chem. Int. Ed.* **2009**, *48*, 6524; *Angew. Chem.* **2009**, *121*, 6646; c) X.-F. Tu, L.-Z. Gong, *Angew. Chem. Int. Ed.* **2012**, *51*, 11346; *Angew. Chem.* **2012**, *124*, 11508; d) X.-F. Cai, W.-X. Huang, Z.-P. Chen, Y.-G. Zhou, *Chem. Commun.*

2014, *50*, 9588; e) J. Wen, R. Tan, S. Liu, Q. Zhao, X. Zhang, *Chem. Sci.* **2016**, *7*, 3047.

[6] For recent reviews, see: a) D. W. Stephan, G. Erker, *Angew. Chem. Int. Ed.* **2015**, *54*, 6400; *Angew. Chem.* **2015**, *127*, 6498; b) D. W. Stephan, *Science* **2016**, *354*, aaf7229; c) J. Lam, K. M. Szkop, E. Mosaferi, D. W. Stephan, *Chem. Soc. Rev.* **2019**, https://doi.org/10.1039/C8CS00277K; d) M. Oestreich, J. Hermeke, J. Mohr, *Chem. Soc. Rev.* **2015**, *44*, 2202; e) W. Meng, X. Feng, H. Du, *Acc. Chem. Res.* **2018**, *51*, 191; f) J. Paradies, *Coord. Chem. Rev.* **2019**, *380*, 170; g) J. R. Lawson, R. L. Melen, *Inorg. Chem.* **2017**, *56*, 8627.

[7] For selected reports, see: a) S. J. Geier, P. A. Chase, D. W. Stephan, *Chem. Commun.* **2010**, *46*, 4884; b) G. Erős, K. Nagy, H. Mehdi, I. Pápai, P. Nagy, P. Király, G. Tárkányi, T. Soós, *Chem. Eur. J.* **2012**, *18*, 574; c) T. Mahdi, J. N. del Castillo, D. W. Stephan, *Organometallics* **2013**, *32*, 1971; d) Y. Liu, H. Du, *J. Am. Chem. Soc.* **2013**, *135*, 12968; e) P. Eisenberger, B. P. Bestvater, E. C. Keske, C. M. Crudden, *Angew. Chem. Int. Ed.* **2015**, *54*, 2467; *Angew. Chem.* **2015**, *127*, 2497; f) W. Wang, X. Feng, H. Du, *Org. Biomol. Chem.* **2016**, *14*, 6683; g) W. Wang, W. Meng, H. Du, *Dalton Trans.* **2016**, *45*, 5945; h) X. Liu, T. Liu, W. Meng, H. Du, *Org. Lett.* **2018**, *20*, 5653.

[8] V. Sumerin, K. Chernichenko, M. Nieger, M. Leskelä, B. Rieger, T. Repo, *Adv. Synth. Catal.* **2011**, *353*, 2093.

[9] a) Z. Zhang, H. Du, *Org. Lett.* **2015**, *17*, 2816; b) Z. Zhang, H. Du, *Org. Lett.* **2015**, *17*, 6266; c) Z. Zhang, H. Du, *Angew. Chem. Int. Ed.* **2015**, *54*, 623; *Angew. Chem.* **2015**, *127*, 633.

[10] C. Han, E. Zhang, X. Feng, S. Wang, H. Du, *Tetrahedron Lett.* **2018**, *59*, 1400.

[11] X.-S. Tu, N.-N. Zeng, R.-Y. Li, Y.-Q. Zhao, D.-Z. Xie, Q. Peng, X.-C. Wang, *Angew. Chem. Int. Ed.* **2018**, *57*, 15096; *Angew. Chem.* **2018**, *130*, 15316.

[12] J. A. Nieman, B. A. Keay, *Synth. Commun.* **1999**, *29*, 3829.

[13] N. Harada, N. Ochiai, K. Takada, H. Uda, *J. Chem. Soc. Chem. Commun.* **1977**, 495.

[14] Because the spiro-bicyclic structure forms by a reversible ring-closure reaction, the erosion of enantiomeric excesses may have occurred by a sequential ring-opening and reclosing process.

[15] For Piers borane, see: a) D. J. Parks, R. E. von H. Spence, W. E. Piers, *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 809; *Angew. Chem.* **1995**, *107*, 895; b) D. J. Parks, W. E. Piers, G. P. A. Yap, *Organometallics* **1998**, *17*, 5492; For pioneering studies of using this hydroboration for preparation of chiral catalysts, see: c) D. Chen, J. Klankermayer, *Chem. Commun.* **2008**, 2130; d) D. Chen, Y. Wang, J. Klankermayer, *Angew. Chem. Int. Ed.* **2010**, *49*, 9475; *Angew. Chem.* **2010**, *122*, 9665.

[16] CCDC 1872176 and 1872179 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.

[17] For in situ generation of the catalyst **5a**^{4F}, diene **4a** was allowed to react with H(p-C_6F_4H)$_2$ in toluene at 80 °C for 10 min. The structure of **5a**^{4F} was confirmed by a crystal structure of its adduct with isoquinoline (CCDC 1872178). For preparation of H(p-C_6F_4H)$_2$, see: D. Winkelhaus, B. Neumann, H.-G. Stammler, N. W. Mitzel, *Dalton Trans.* **2012**, *41*, 8609.

[18] X.-F. Cai, M.-W. Chen, Z.-S. Ye, R.-N. Guo, L. Shi, Y.-Q. Li, Y.-G. Zhou, *Chem. Asian J.* **2013**, *8*, 1381.

[19] For these reactions, **5a** and **5a**^{4F} gave similar enantioselectivities, but **5a** gave higher turnover numbers than **5a**^{4F}.

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