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A Highly Stereoselective Metal-Free Hydrogenation of Diimines for the Synthesis of *Cis*-Vicinal Diamines

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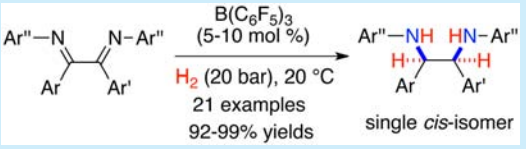
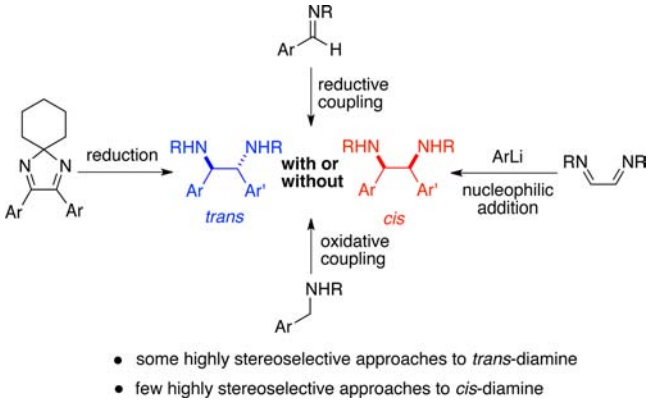
Supporting Information

ABSTRACT: A highly stereoselective metal-free hydrogenation of vicinal diimines has been successfully realized for the first time using 5−10 mol % of Piers' borane as a catalyst under mild conditions, and a variety of *cis*-1,2-diamines were obtained in 92−99% yields. The current work provides a novel and efficient approach for the synthesis of vicinal diamines.



Vicinal diamines are extremely important moieties present in many natural products with notable biological activities and a large number of drugs.[1] Meanwhile, they can also be used as effective ligands or catalysts in asymmetric catalysis, and as building blocks in synthetic chemistry.[1] Various methodologies have been well established for their synthesis, for example, reduction of imidazoles or diimines,[2] the nitro-Mannich reaction,[3] reductive coupling of imines,[4] oxidative coupling of amines,[5] nucleophilic addition of diimines,[6] substitution of diols,[7] C−H amination,[8] and direct diamination of olefins.[1g−j] For the important 1,2-diarylethane-1,2-diamines, many approaches can provide *trans*-isomers as predominate products, but few can give *cis*-isomers in high selectivities (Scheme 1). In

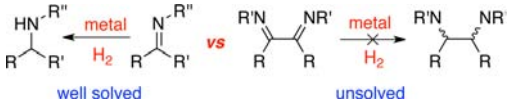
Scheme 1. Representative Approaches to 1,2-Diarylethane-1,2-diamines



fact, some unique properties for *cis*-1,2-diarylethane-1,2-diamines in catalysis have been reported, and some other usages still await further exploration.[9] The development of stereospecific access to *cis*-diamines is therefore of great interest.

The transition-metal catalyzed hydrogenation of imines as well as its asymmetric version has become one of the most useful tools for the synthesis of amines.[10] Accordingly, the direct hydrogenation of vicinal diimines seems to be an efficient and straightforward approach for the synthesis of vicinal diamines (Scheme 2). Strangely, to the best of our knowledge,

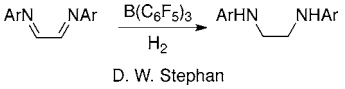
Scheme 2. Metal-Catalyzed Hydrogenation of Imines



the catalytic hydrogenation of vicinal diimines has been rarely reported, which might be partially attributed to the bulky steric hindrance and/or the poison of the catalyst by a chelating coordination with vicinal diimines. Exploration for an effective catalytic system for the hydrogenation of vicinal diimines is a challenging but highly desirable subject.

The frustrated Lewis pair (FLP) chemistry provides a novel and powerful approach for the metal-free hydrogenation.[11] Numerous classes of unsaturated compounds can be successfully hydrogenated under FLP catalysis, and imines have been among the most widely investigated substrates.[12,13] Some important advances in asymmetric transformation have also been achieved.[14,15] Significantly, in 2011, Stephan and coworkers reported a $B(C_6F_5)_3$-catalyzed metal-free hydrogenation of ethane-1,2-diimines (Scheme 3).[12e] Recently, our group reported the stereo- or enantioselective hydrogenation of imines, 2,6-disubstituted pyridines, silyl enol ethers, 2,3-disubstituted quinoxalines, and 2,3,4-trisubstituted quinolines using borane catalysts derived *in situ* from alkenes or

Scheme 3. Metal-Free Hydrogenation of Ethane-1,2-diimines



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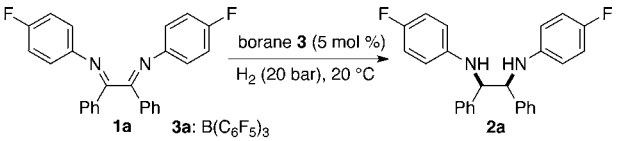
alkynes.[16−18] In comparison with transition metal catalysts, FLP catalysts are not necessary to coordinate with substrates and more compatible with the bulky steric hindrance, which therefore provides good potential in solving the challenging hydrogenation of vicinal diimines. Herein, we report our preliminary efforts on this subject.

Initially, the reduction of vicinal diimine **1a** with 6 equiv of $NaBH_4$ or $NaBH_3CN$ in ethanol at room temperature or 60 °C was first conducted, but this reaction did not occur. The metal-free hydrogenation of vicinal diimine **1a** using 5 mol % of $B(C_6F_5)_3$ (**3a**)[19] under H_2 (20 bar) in toluene at 20 °C was then examined. To our pleasure, this reaction proceeded very quickly to furnish the *cis*-1,2-diamine product **2a** in a quantitative conversion (Table 1, entry 1). It was noteworthy

Table 1. Metal-Free Hydrogenation of Diimine 1a[a]



entry	borane **3**	solvent	time (h)	conv (%)[b]	*cis*/*trans*[b]
1	**3a**	toluene	0.5	>99	>99:1
2	**3b**	toluene	2	29	>99:1
3	**3c**	toluene	2	65	>99:1
4	**3a**	CH_2Cl_2	2	nr[c]	–
5	**3a**	Et_2O	2	nr[c]	–
6	**3a**	pentane	2	60	>99:1
7	**3a**	mesitylene	2	90	>99:1
8	**3a**	C_6H_5F	2	>99	>99:1
9[d]	**3a**	toluene	2	54	>99:1

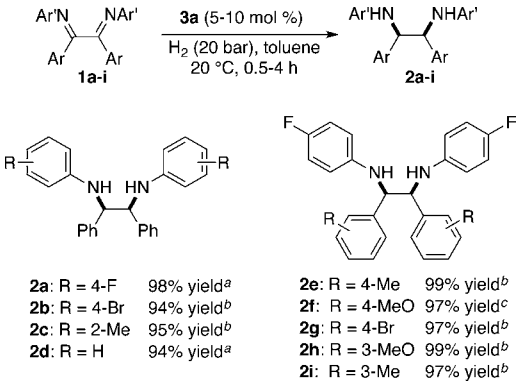
[a]Diimine **1a** (0.25 mmol), borane (5 mol %), and H_2 (20 bar) in solvent (1.0 mL) at 20 °C. [b]By crude ^1H NMR. [c]No reaction. [d]1 mol % of borane **3a**.

that this hydrogenation gave only a single *cis*-isomer. The bulky steric hindrance of the diimine substrates might be a possible explanation for the observed high *cis*-stereoselectivities. Using *in situ* generated borane catalysts **3b** and **3c** derived from styrene or 1,2,3,4,5-pentafluorostyrene with $HB(C_6H_5)_2$ gave a relatively lower conversion (Table 1, entries 2 and 3). Solvents had a large impact on the reactivity: dichloromethane and diethyl ether were not suitable solvents, while toluene proved to be the optimal solvent for this hydrogenation (Table 1, entries 4−8). Further reducing the catalyst loading to 1 mol % can also give a reasonable conversion (Table 1, entry 9).

A variety of symmetrical vicinal diimines **1a−i** were next subjected to the metal-free hydrogenation under the optimal reaction conditions. As shown in Scheme 4, all these reactions went smoothly to produce the desired *cis*-1,2-diaryl-1,2-diamines **2a−i** as single isomers in 94−99% yields. To afford chiral 1,2-diamines, various unsymmetrical vicinal diimines were employed as substrates for this hydrogenation. Both electron-donating and -withdrawing substituents on the phenyl group were well tolerated to give 1,2-diamine products **2j−u** in 92−99% yields (Scheme 5). The stereochemistry for the obtained vicinal diamines was determined to be *cis* by an X-ray structure of compound **2b** (Figure 1).

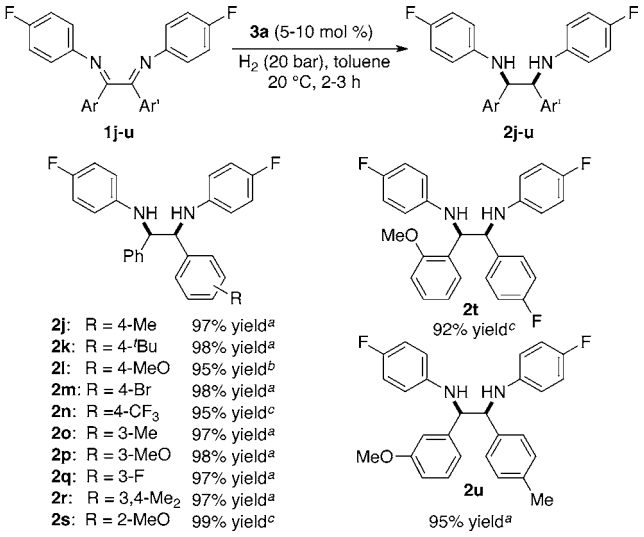
With these excellent results in hand, the asymmetric hydrogenation of diimine **1v** using 10 mol % of the chiral

Scheme 4. Hydrogenation of Symmetrical Diimines



[a]**3a** (5 mol %), 0.5 h. [b]**3a** (5 mol %), 2 h. [c]**3a** (10 mol %), 4 h.

Scheme 5. Hydrogenation of Unsymmetrical Diimines



[a]**3a** (5 mol %), 2 h. [b]**3a** (10 mol %), 3 h. [c]**3a** (10 mol %), 2 h.

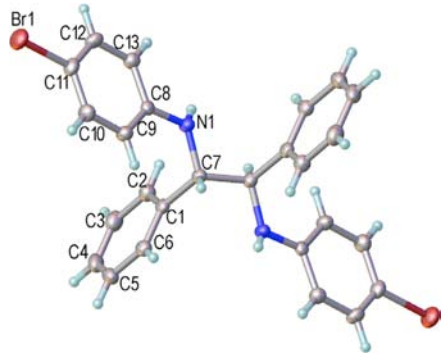


Figure 1. X-ray structure of compound **2b**.

borane catalyst formed *in situ* by the hydroboration of chiral diene **4** with $HB(C_6F_5)_2$ was further studied. It was found that vicinal diamine **2v** can be obtained in a quantitative conversion with 10% ee (Scheme 6). Further efforts are still needed to explore more efficient chiral catalysts.

In summary, a metal-free hydrogenation of 1,2-diaryl-1,2-diimines was realized for the first time by using 5−10 mol % of $B(C_6F_5)_3$ as the catalyst under mild conditions. Significantly, this hydrogenation is a highly stereoselective reaction to furnish

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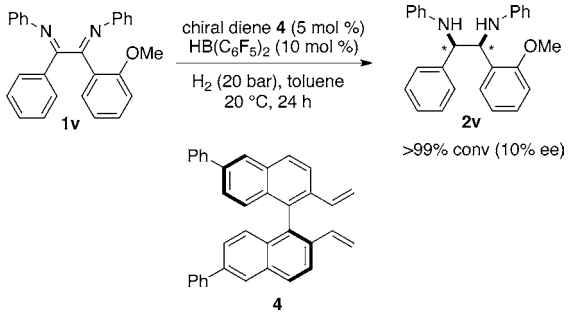
Scheme 6. Asymmetric Hydrogenation of Diimine 1v



a broad range of *cis*-1,2-diaryl-1,2-diamines as single isomers in 92−99% yields. The current work provides a novel and straightforward approach to *cis* vicinal diamines. Studies to further understand the mechanism and explore highly enantioselective hydrogenation reactions are underway in our laboratory.

■ ASSOCIATED CONTENT

Supporting Information

Procedure for the synthesis of diimines and the metal-free hydrogenation of diimines, characterization of diimines and products, a CIF file for the single crystal, and data for the determination of enantiomeric excesses along with the NMR spectra. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.5b01380.

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Notes

The authors declare no competing financial interest.

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