Organic & Biomolecular Chemistry

Accepted Manuscript

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Cite this: DOI: 10.1039/c0xx00000x

www.rsc.org/xxxxxx

View Article Online
DOI: 10.1039/C4OB02419B

ARTICLE TYPE

A Chiral Borane Catalyzed Asymmetric Hydrosilylation of Imines†

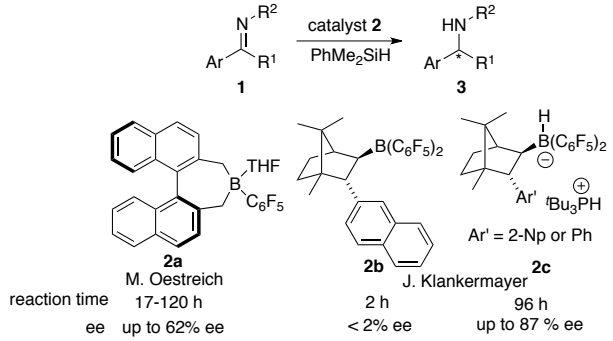
Xiaxia Zhu and Haifeng Du*[a]

Received (in XXX, XXX) Xth XXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX
DOI: 10.1039/b000000x

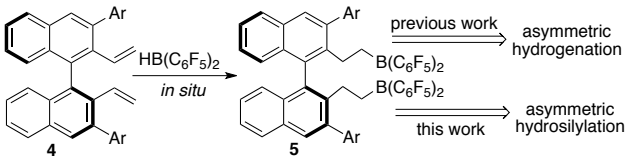
An enantioselective hydrosilylation of imines was successfully achieved using a chiral borane catalyst generated by the in situ hydroboration of a binaphthyl-based chiral diene with Piers' borane $HB(C_6F_5)_2$ to furnish a variety of optically active amines in 70->99% yields and 44-82% ee's.

Catalytic hydrosilylation of unsaturated molecules represents a very important and useful transformation in organic chemistry, and numerous excellent metal or metal-free catalytic systems have been well established.[1-3] Among these methodologies, the Piers type hydrosilylation has both synthetic and mechanistic interest for chemists. In 1996, Piers and Parks reported a $B(C_6F_5)_3$-catalyzed hydrosilylation of carbonyl compounds, in which the Lewis acid activated the silane instead of carbonyl function.[4] This Si-H bond activation by $B(C_6F_5)_3$ was further extended to the reduction of imines, the dehydrocoupling reaction, the hydrosilylation of olefins, the deoxygenative hydrosilylation of carbon dioxide, and the deoxygenation of carbohydrates.[5] Interestingly, the Si-H bond activation in the hydrosilylation is similar to the H-H bond activation in the latterly emerging chemistry of frustrated Lewis pairs (FLPs).[6,7] In 2010, Alcarazo and co-workers described such a silane activation using the FLPs of hexaphenylcarbodiphosphorane and $B(C_6F_5)_3$.[8] Recently, Erker and co-workers also described a reversible heterolytic Si-H bond activation by an intramolecular FLP.[9] Despite these advances, the first asymmetric version of this type of hydrosilylation was not disclosed until 2008.[10] Oestreich and co-workers reported a $B(C_6F_5)_3$-catalyzed hydrosilylation of acetophenone using a chiral silane to afford the chiral alcohol with 38% ee.[11] In a later study, the combination of $B(C_6F_5)_3$ and chiral silanes for the reduction of imines gave racemic products.[12] In 2012, the authors also developed a novel borane **2a** for the asymmetric reduction of imines **1** using $PhMe_2SiH$ or chiral silanes to give chiral amines with up to 62% ee (Scheme 1).[13] Recently, Klankermayer and co-workers employed the camphor derived borane catalyst **2b** for this asymmetric hydrosilylation of imines. The borane **2b** exhibited an extremely high catalytic activity, but led a racemic product (Scheme 1).[14] However, the FLP catalysts **2c** gave up to 87% ee (Scheme 1).[14] The Lewis base tri-*tert*-butylphosphine largely improved the enantioselectivity but diminished the reactivity. However, the development of highly reactive and enantioselective hydrosilylation is still a challenge.

As our interest in developing novel borane catalysts for the FLP-catalyzed hydrogenation,[15] very recently, we reported the asymmetric hydrogenation of imines, silyl enol ethers, and 2,3-disubstituted quinoxalines.[16] The borane catalysts **5** were generated in situ by the hydroboration of binaphthyl-based chiral dienes **4** with Piers' borane (Scheme 2).[17,18] Since the Si-H bond activation is similar to H-H bond, we envisioned that boranes **5** would be also likely one class of effective catalysts for the asymmetric hydrosilylation of imines. Herein, we reported our efforts on this subject.



Scheme 1 Representative asymmetric hydrosilylation of imines

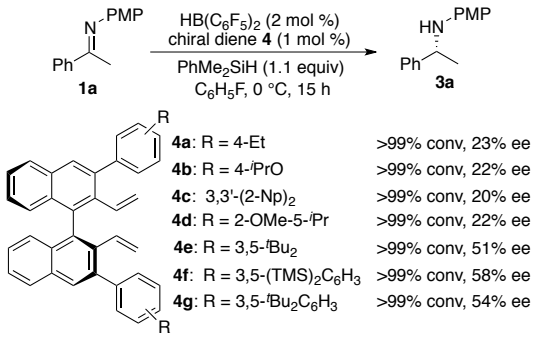


Scheme 2 Chiral borane catalyst for asymmetric reactions

The asymmetric hydrosilylation of imine **1a** with $PhMe_2SiH$ was initially examined using 1 mol % of chiral dienes **4a-g** and 2 mol % of Piers' borane (Scheme 3). It was found that all these reactions can proceed efficiently at 0 °C to give the desired amine **2a** in quantitative conversions. Chiral dienes **4a-d** bearing less bulky substituents gave very low ee's. The more bulky chiral dienes **4e-g** gave 51-58% ee's. In sharp contrast to borane **2b** reported by Klankermayer and co-workers (Scheme 1),[12] boranes **5** generated in situ from chiral dienes **4** gave a promising enantioselectivity instead of racemic products, and additional Lewis bases were unnecessary in the current catalytic system.

The reaction conditions including concentration, solvents, temperature, and catalyst loading were carefully optimized to further improve the enantioselectivities. It was found that the

reaction concentration had an obvious impact on the enantioselectivities when chiral diene **4g** was used, and 67% ee was obtained at the concentration of 0.5 M (Table 1, entries 1-3). However, for chiral diene **4f**, such an improvement was not observed. Solvents were found to affect the enantioseletivities obviously but have little influence on the reactivities, and C_6H_5F proved to be a better solvent (Table 1, entries 4-9). Decreasing the reaction temperature to -20 °C did not improve the enantioselectivity (Table 1, entry 10). The catalyst loading can be reduced to 0.5 mol % without loss of enantioselectivity, but a longer reaction time was required (Table 1, entry 11). In fact, the asymmetric hydrosilylation of imine **1a** using 1 mol % of borane **4g** and Piers' borane can be completed in 6.5 h (Table 1, entry 12). Moreover, silanes Ph_3SiH and Ph_2MeSiH were examined, but no reaction was observed under the current conditions. The substituents on the nitrogen atom of imines were also evaluated. Electron-deficient groups such as 4-chlorophenyl and 4-bromophenyl gave a very low reactivity (<10% conversion). Several electron-rich groups (4-isopropoxylphenyl, 4-piperidin-1-ylphenyl, and cyclohexanyl) gave a similar reactivity with the PMP group but an obviously lower enantioselectivity (31-57% ee's).



Scheme 3 Evaluation of chiral dienes for asymmetric hydrosilylations

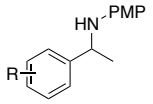
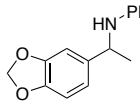
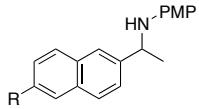
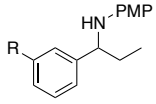
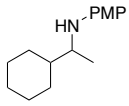
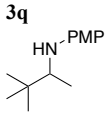
Table 1 Optimization of reaction conditions[a]

Entry	Solvent	Conc. (M)	Time (h)	Conv (%)[b]	Ee (%)[c]
1	C_6H_5F	0.25	15	>99	54
2	C_6H_5F	0.5	15	>99	67
3	C_6H_5F	1.0	15	>99	62
4	C_6H_5Cl	0.5	15	>99	63
5	C_6H_5Br	0.5	15	>99	58
6	Toluene	0.5	15	>99	56
7	CH_2Cl_2	0.5	15	>99	58
8	Et_2O	0.5	15	91	30
9	Pentane	0.5	15	>99	14
10[d]	C_6H_5F	0.5	24	87	68
11[e]	C_6H_5F	0.5	21	>99	67
12	C_6H_5F	0.5	6.5	>99	67

[a] All the reactions were carried out with imine **1a** (0.50 mmol), $PhMe_2SiH$ (0.55 mmol), chiral diene **4g** (0.005 mmol), and Piers' borane (0.010 mmol) at 0 °C unless otherwise noted. [b] The conversion was determined by crude ^1H NMR. [c] The ee was determined by chiral HPLC (Chiralcel OD-H column). [d] At -20 °C. [e] 0.5 mol % of chiral diene **4g** and 1.0 mol % of Piers' borane were used.

The asymmetric hydrosilylation of imines **1** was next investigated using chiral diene **4g** under the optimal reaction conditions. As shown in Table 2, a wide range of imines **1** can be efficiently reduced to furnish the desired amines **3a-r** in 70->99% yields with 44-82% ee's. Both electron-donating and withdrawing substituents on the *para* and/or *meta* positions of phenyl group were well tolerant for this reaction (Table 2, entries 2-12). Imines derived from 1-(nathphthalen-2-yl)ethanones were suitable substrates (Table 2, entries 13 and 14). The reaction of imines derived from phenylpropanones gave relatively lower ee's (Table 2, entries 15 and 16). In particular, the asymmetric hydrosilylation can be extended to the challenging dialkylketoimine substrates to give reasonable yields and ee's (Table 2, entries 17 and 18).

Table 2 Chiral borane catalyzed asymmetric hydrosilylation of imines[a]

Entry	Product (**3**)	Yield (%)[b]	Ee (%)[c,d]
			
1	**3a**: R = H	>99	67
2	**3b**: R = 4-Me	99	61
3	**3c**: R = 4-OMe	99	65
4	**3d**: R = 4-Ph	>99	61
5	**3e**: R = 4-Br	97	59
6	**3f**: R = 3-Me	97	68
7	**3g**: R = 3-OMe	>99	72
8	**3h**: R = 3-Br	96	68
9	**3i**: R = 3,4-Me_2	>99	71
10	**3j**: R = 3,4-$(OMe)_2$	90	78
11	**3k**: R = 3,4,5-$(OMe)_3$	96	82
			
12	**3l**	>99	59
			
13	**3m**: R = H	>99	71
14	**3n**: R = OMe	>99	74
			
15	**3o**: R = H	>99	50
16	**3p**: R = Me	90	55
			
17	**3q**	86	44
			
18[e]	**3r**	70	60

[a] All the reactions were carried out with imine **1** (0.50 mmol), $PhMe_2SiH$ (0.55 mmol), chiral diene **4g** (0.005 mmol) and Piers' borane (0.010 mmol) in C_6H_5F (1.0 mL) at 0 °C for 8 h unless otherwise noted. [b] Isolated yield based on imine **1**. [c] The ee was determined by chiral HPLC. [d] The absolute configuration was determined as *R* except for entries 12,14, 16 and 18 by comparing the optical rotation or the retention time in HPLC with the reported one. [e] 2.5 mol % of chiral diene **4g** and 5.0 mol % of Piers' borane were used, and the reaction time was 24 h.

Conclusions

In summary, a simple chiral borane catalyst generated in situ by the hydroboration of a chiral diene **4g** with Piers' borane was highly effective for the asymmetric hydrosilylation of imines to furnish the desired optically active amines in 70->99% yields and 44-82% ee's. It is noteworthy that the usage of highly reactive chiral borane as a catalyst without addition of any other Lewis bases can give promising enantioselectivies. Further efforts to improve the enantioselectivity and expand the substrate type are underway in our laboratory.

Acknowledgements

This work was supported by the National Science Foundation of China (20802079, 21222207), the National Basic Research Program of China (2011CB808600).

Notes and references

[a] *Beijing National Laboratory of Molecular Sciences, CAS Key Laboratory of Molecular Recognition and Function, Institute of Chemistry, Chinese Academy of Sciences, Beijing 100190, China. Fax: 0086-10-62554449; Tel: 0086-10-62652117; E-mail: haifengdu@iccas.ac.cn*

† Electronic Supplementary Information (ESI) available: The procedure for the asymmetric hydrosilylation and the characterization and data for the determination of enantiomeric excess of amine products along with the NMR spectra. See DOI: 10.1039/b000000x/

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