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Facile Development of Chiral Alkenylboranes from Chiral Diynes for Asymmetric Hydrogenation of Silyl Enol Ethers

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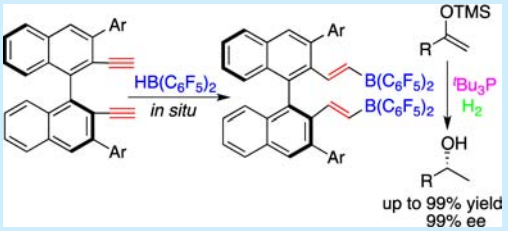
Supporting Information

ABSTRACT: A facile development of chiral alkenylboranes by the hydroboration of chiral diynes with Piers' borane was successfully achieved for the first time. With the combination of the in situ generated chiral alkenylboranes and tri-*tert*-butylphosphine as frustrated Lewis pair catalysts, the metal-free asymmetric hydrogenation of silyl enol ethers was realized to furnish a wide range of optically active secondary alcohols in high yields and up to 99% ee.



The chemistry of frustrated Lewis pairs (FLPs) provides a unique metal-free approach for the hydrogenation with molecule H_2, which has been dominated by the transition-metal catalysis to date.[1,2] Numerous unsaturated materials proved to be suitable substrates for the metal-free hydrogenation.[3] However, in contrast to these great advances, the chiral FLP-catalyzed asymmetric hydrogenation is just in the start-up stage.[4] Only a few catalytic systems have been reported for the asymmetric hydrogenation of imines, 2-phenylquinoline, silyl enol ethers, and 2,3-disubstitued quinoxalines, and even few of them can give more than 90% ee.[3−9] The development of versatile chiral FLP catalysts is undoubtedly the most important goal to ensure the rapid growth of this field. The key issue is how to develop them. At present, the synthesis of chiral boranes can be categorized into two types of transformations (Figure 1). One is the hydroboration of chiral alkenes with Piers' borane HB-$(C_6F_5)_2$.[5,6,10] Chiral boranes **1a−c** can be generated from chiral internal alkenes, but isomers of **1a** and **1b** were also formed at the same time, which required an additional isolation.[5,10] Very recently, our group accessed chiral boranes **2** by the in situ hydroboration of chiral terminal alkenes which avoids the production of isomers and ensures the rapid discovery of optimal catalysts. Chiral boranes **2** were highly effective for the asymmetric hydrogenation of imines, silyl enol ethers, and 2,3-disubstituted quinoxalines.[6] The other is the substitution reaction of $(C_6F_5)_nBCl_{3-n}$ with chiral organometallic reagents. Chiral boranes **3** and **4** were prepared by this protocol.[7,11] The lack of readily accessible methods for the chiral borane synthesis seems to be the major difficulty to be overcome. Exploring novel approaches for quick access to chiral boranes is therefore of prime importance.

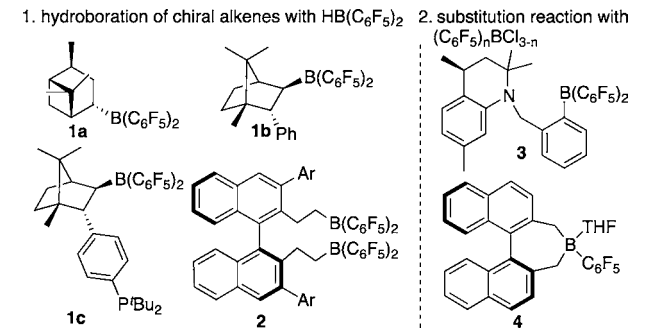
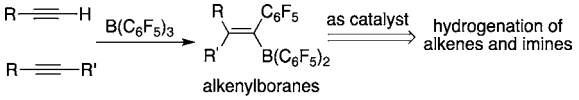


Figure 1. Chiral FLP catalysts for asymmetric hydrogenation and hydrosilylation.

Recently, Erker, Stephan, and co-workers reported an interesting 1,1-carboboration of alkynes with $B(C_6F_5)_3$ to furnish alkenylboranes (Scheme 1).[12,13] Significantly, they found these alkenylboranes to be effective for the hydrogenation of imines and electron-deficient alkenes.[14] In 1998, Piers and co-workers described the synthesis of alkenylboranes by the hydroboration of alkynes with $HB(C_6F_5)_2$.[10b] Erker and co-workers also reported the hydroboration of alkynes using $HB(C_6F_5)_2$.[15] Inspired by these discoveries, and based on our previous work as well, we envisioned that chiral alkenylboranes **6** generated by the in situ hydroboration of chiral diynes **5** with $HB(C_6F_5)_2$ were likely one efficient class of catalysts for the asymmetric metal-free hydrogenation (Scheme 2). In comparison with the C−C single bond in chiral boranes **2**, the C−C double bond in boranes **6** makes

Scheme 1. Alkenylboranes for Metal-Free Hydrogenations



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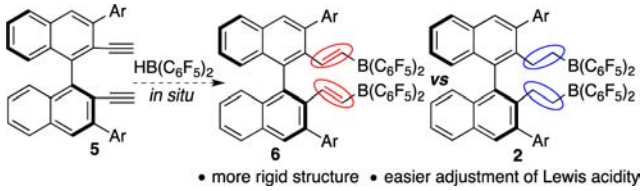
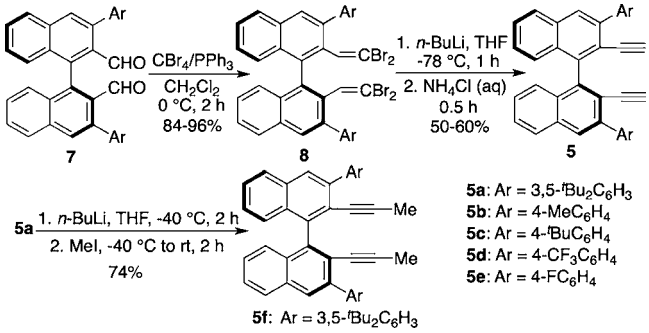
Scheme 2. Strategy for Developing Chiral Boranes by Hydroboration of Chiral Diynes



the structures more rigid. In particular, the conjugation of the C−C double bond and the binaphthyl moieties makes it easier to adjust the Lewis acidity of borane **6** by introducing electron-rich or deficient substituents on chiral diynes. Herein, we report our efforts on the development of chiral alkenylboranes from chiral diynes for the asymmetric hydrogenation of silyl enol ethers.

Chiral diynes **5** were synthesized as shown in Scheme 3. Compounds **8** can be obtained in high yields through the

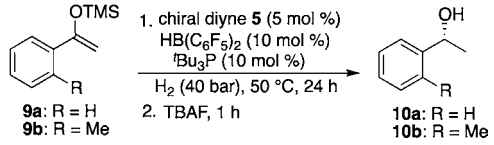
Scheme 3. Synthesis of Chiral Diynes



Corey−Fuchs reactions of chiral dialdehydes **7**, which were also the intermediates for the chiral diene synthesis.[16] Further treatment of compounds **8** with *n*-butyllithium and quenching with aqueous ammonium chloride gave chiral diynes **5a−e** in moderate yields. An internal chiral diyne **5f** was prepared in 74% yield by the reaction of chiral diyne **5a** with *n*-butyllithium and iodomethane. With these chiral diynes in hand, the reaction of chiral diyne **5a** with Piers' borane $HB(C_6F_5)_2$ was subsequently checked. It was pleasing to find that the desired chiral alkenylborane **6a** can be formed quickly at room temperature (see the Supporting Information).

To examine the catalytic activity and selectivity of the in situ generated chiral alkenylboranes, the asymmetric hydrogenation of silyl enol ethers was selected as a model reaction.[6b,17,18] Using chiral diyne **5a** (5 mol %) and $HB(C_6F_5)_2$ (10 mol %) with the combination of $^tBu_3P$ (10 mol %), the asymmetric hydrogenation of silyl enol ether **9a** under H_2 (40 bar) in toluene for 24 h gave the desired product **10a** in 70% conversion and 94% ee (Table 1, entry 1). Chiral diynes **5b−e** were also effective for this reaction to give alcohol **10a** with 88−94% ee's (Table 1, entries 2−5). It seems that both steric hindrance and Lewis acidity have an impact on the reactivity and enantioselectivity. Interestingly, chiral diyne **5f** with an internal triple C−C bond gave a very low ee (Table 1, entry 6). Increasing the concentration would largely improve the reactivity without loss of enantioselectivity, and a quantitative conversion was obtained at the concentration of 2.0 M (Table 1, entries 7 and 8). Using silyl enol ether **9b** as a substrate, the solvent effect was checked, and mesitylene proved to be the optimal solvent (Table 1, entries 9−13). Under these conditions, the hydrogenation of silyl enol ether **9a** also gave the best result (Table 1, entry 14).

Table 1. Asymmetric Hydrogenation of Enol Ethers 9a and 9b[a]



entry	enol ether	chiral diyne	solvent	concn (M)	conv[b] (%)	ee[c] (%)
1	**9a**	**5a**	toluene	0.2	70	94
2	**9a**	**5b**	toluene	0.2	67	94
3	**9a**	**5c**	toluene	0.2	41	88
4	**9a**	**5d**	toluene	0.2	88	89
5	**9a**	**5e**	toluene	0.2	87	89
6	**9a**	**5f**	toluene	0.2	75	13
7	**9a**	**5a**	toluene	0.8	89	95
8	**9a**	**5a**	toluene	2.0	>99	95
9	**9b**	**5a**	toluene	2.0	65	92
10	**9b**	**5a**	CH_2Cl_2	2.0	39	91
11	**9b**	**5a**	Et_2O	2.0	94	92
12	**9b**	**5a**	*n*-hexane	2.0	72	75
13	**9b**	**5a**	mesitylene	2.0	98	98
14	**9a**	**5a**	mesitylene	2.0	>99	95

[a]All reactions were carried out with silyl enol ethers (0.20 mmol), $HB(C_6F_5)_2$ (0.02 mmol), chiral diyne (0.01 mmol), and $^tBu_3P$ (0.02 mmol) under H_2 (40 bar) at 50 °C for 24 h. [b]Determined by crude ^1H NMR. [c]The ee was determined by chiral HPLC.

A broad range of silyl enol ethers **9** were subjected to asymmetric hydrogenation under the optimal conditions. As shown in Table 2, all of the reactions proceeded smoothly to give the desired alcohols **10a−v** in 80−99% yields and 87−99% ee's. Electron-rich and -deficient substituents were both well tolerated for this reaction (Table 2, entries 1−15). Acetonaphthone-derived silyl enol ethers were suitable substrates (Table 2, entries 16 and 17). Aromatic heterocycle moieties were also tolerated to give 93−96% ee's (Table 2, entries 18−20). Moreover, the reaction of silyl enol ethers derived from 1-indanone and 1-cyclohexenylethanone furnished alcohols **10u** and **10v** in high yields with 97% ee (Table 2, entries 21 and 22).

In summary, a novel approach for the synthesis of chiral boranes has been successfully developed by the in situ hydroboration of chiral diynes and Piers' borane. The resulting chiral alkenylboranes were highly effective for the asymmetric hydrogenation of silyl enol ethers with the combination of $^tBu_3P$ to furnish a variety of optically active secondary alcohols in high yields with 87−99% ee's. Some interesting features such as the relatively rigid structures and the ease adjustment of Lewis acidity make the chiral alkenylboranes a class of potentially useful catalysts for the metal-free asymmetric hydrogenation. Further efforts on the application of these boranes in other asymmetric reactions are underway in our laboratory.

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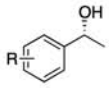
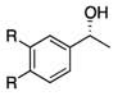
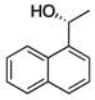
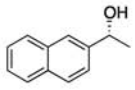
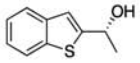
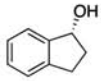
Table 2. Asymmetric Hydrogenation of Silyl Enol Ethers[a]

entry	product (**10**)	yield (%)[b]	ee (%)[c]
			
1	**10a**: R = H	90	95
2	**10b**: R = 2-Me	93	98
3	**10c**: R = 2-OMe	92	99
4	**10d**: R = 2-F	85	99
5	**10e**: R = 2-Cl	90	99
6	**10f**: R = 2-Br	88	99
7	**10g**: R = 3-Me	93	89
8	**10h**: R = 3-Cl	91	97
9	**10i**: R = 3-Br	92	98
10	**10j**: R = 4-Et	84	92
11	**10k**: R = 4-F	80	98
12	**10l**: R = 4-Cl	89	93
13	**10m**: R = 4-Br	92	94
			
14	**10n**: R = Me	89	91
15	**10o**: R,R = $(CH_2)_4$	97	92
			
16	**10p**	98	98
			
17	**10q**	97	87
			
18	**10r**: X = O	85	94
19	**10s**: X = S	95	96
			
20	**10t**	99	93
			
21	**10u**	92	98
			
22	**10v**	82	97

[a]All reactions were carried out with silyl enol ethers **9** (0.40 mmol), $HB(C_6F_5)_2$ (0.04 mmol), chiral diyne **5a** (0.02 mmol), and $^tBu_3P$ (0.04 mmol) under H_2 (40 bar) in mesitylene (0.2 mL) at 50 °C for 24 h. [b]Isolated yield. [c]Determined by chiral HPLC.

■ ASSOCIATED CONTENT

Supporting Information

Procedure for the synthesis of chiral diyne, the metal-free catalytic asymmetric hydrogenation of silyl enol ethers, characterization of chiral diynes, alkenylboranes and products, and data for the determination of enantiomeric excesses along with the NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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