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An efficient metal-free reduction using diphenylsilane with (tris–perfluorophenyl)borane as catalyst

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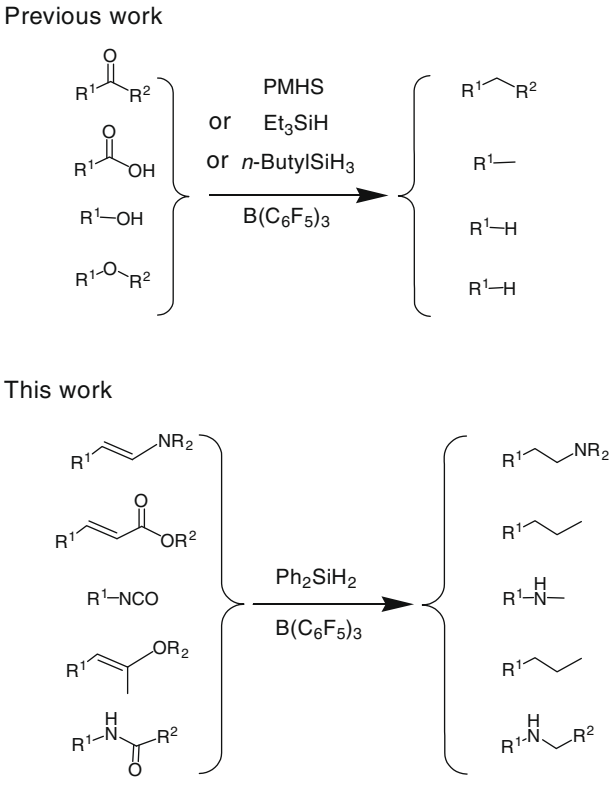
ABSTRACT

An efficient metal-free reduction of various C=X (X = O, N, C) bonds into their corresponding amines or hydrocarbons using the $Ph_2SiH_2/B(C_6F_5)_3$ catalytic system is demonstrated. This protocol reduces enamines, enol esters, carbonyls, amides, and isocyanates.

Reductions of unsaturated organic compounds by hydrogenation, hydroboration, and hydrosilylation are well-known protocols in organic synthesis.[1] Among various methods, the widely used transition metal-catalyzed reductions play a key role in these transformations. However, the use of transition metal catalysts has several shortcomings, such as metal leaching, expensive catalysts, and difficulty in catalyst recycling.[2] Other protocols also suffer from various challenges. Main group hydride reagents such as $NaBH_4$ and $LiAlH_4$ provide stoichiometric reductions that are plagued by high costs, tedious procedures, and toxic chemical wastes.[3] Recently, metal-free catalytic systems for unsaturated bond reduction have attracted considerable attention. Organocatalysts have been developed for the hydrogenation of enones and imines with dihydropyridine as the hydrogen source.[4–6] The groups of Stephan and Rieger reported 'frustrated Lewis pairs' consisting of a bulky Lewis acid $B(C_6F_5)_3$ and a base (amine, phosphine, or *N*-heterocyclic carbene), which demonstrated significant potential in dihydrogen activation and metal-free catalytic hydrogenation of imines.[7–11] In this context, $B(C_6F_5)_3$ has also been shown to catalyze the hydrosilylation of imines,[12] reduction of alcohols with silane,[13] and hydrogenation of imines.[14] In these protocols, Lewis acidic $B(C_6F_5)_3$ was critical for the formation of a hydridoborate counterion with different hydride sources, and further served as a reductant in various reduction reactions. This concept opened a new method for metal-free catalytic hydrogenation reactions. However, it has been limited to imine and nitrile substrates.

It is known that $B(C_6F_5)_3$ can extract a hydride from hydrosilane to form a $[R_3Si–H–B(C_6F_5)]$ ion pair.[12–14] We are interested in extending the borane-based Lewis acid catalyst concept to examine different hydrosilane reagents for the reduction of a broader range of functional groups. Previous studies were focused on using alkyl silanes $R_{4-n}SiH_n$ [polymethylhydrosiloxane (PMHS),[15] Et_3SiH,[12,16] and *n*-butylSiH_3[17]]. However, more active phenylsilanes[18] have rarely been used in this protocol. Herein, we report a powerful $B(C_6F_5)_3$-catalyzed hydrogenation protocol utilizing phenylhydrosilanes for the reduction of various groups, such as enamines (indoles), enol esters, carbonyls, amides, and isocyanates (Scheme 1). Hydrogenation products were obtained instead of hydrosilyla-



Scheme 1.

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tion products using our system. The $B(C_6F_5)_3$-catalyzed reduction protocol would be a particularly attractive process due to its mild reaction conditions, broad applicability to different substrates, and easy-to-handle silane reducing agent, as compared to the use of stoichiometric hydride reagents for reduction and other conventional catalytic systems.

Indole was chosen as the substrate to test this catalytic system. It was reduced quantitatively to indoline at 75 °C with 2 equiv of diphenylsilane in the presence of 2 mol % of $B(C_6F_5)_3$ in toluene for 16 h. The hydrogenation product, indoline was confirmed by gas chromatography–mass spectrometry (GC–MS) and NMR spectroscopy. An NMR tube-scale reaction (Fig. 1) also clearly showed that indole was fully consumed, and indoline was formed as the only product. Different hydrosilanes were screened under the same reaction conditions (see Table 1). The very bulky triphenylsilane and less active triethylsilane did not promote any conversion. Phenylsilane and diphenylsilane gave quantitative yields of the reduction product, while phenyldimethylsilane and diphenylmethylsilane gave only 72–80% yields, probably due to steric hindrance effects. Diphenylsilane was selected as the reducing agent in subsequent studies. It was found that the solvent effect played a very significant role in the reaction. The less active *N*-methylindole was used for solvent screening (see Supplementary data). Generally, this reaction proceeded well in polar solvents. Dichloromethane and 1,1,2,2-tetrachloroethane gave better conversions (72–75%) than solvents such as acetonitrile (60%) and toluene (35%). However, the use of oxygen-containing solvents, such as *N*,*N*-dimethylformamide and THF resulted in none of the desired products. In

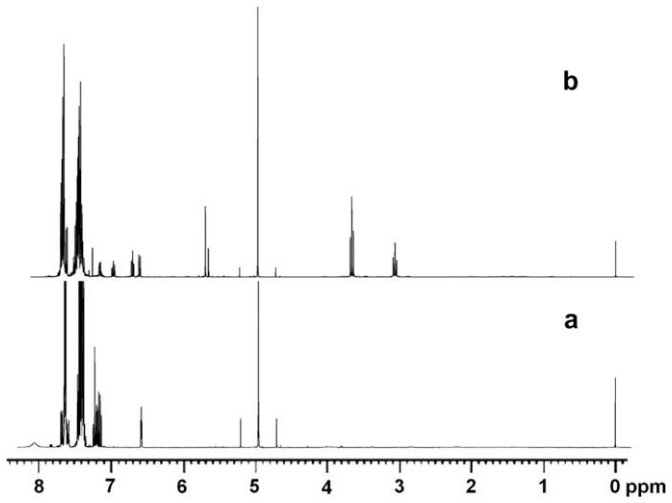
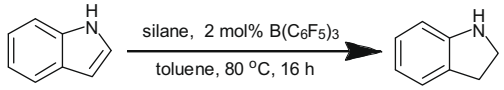


Figure 1. ^{1}H NMR spectra of the NMR tube-scale reaction of indole, diphenylsilane, and $B(C_6F_5)_3$ catalyst (5 mol %) in $CDCl_3$: (a) before reaction, and (b) after heating at 75 °C overnight.

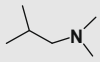
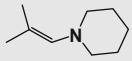
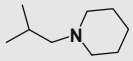
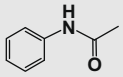
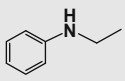
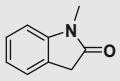
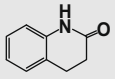
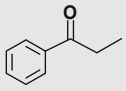
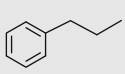
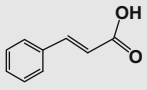
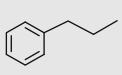
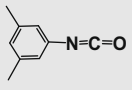
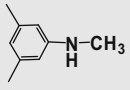
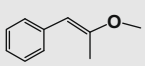
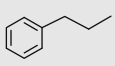
Table 1
$B(C_6F_5)_3$-catalyzed indole reduction with various hydrosilanes[a]



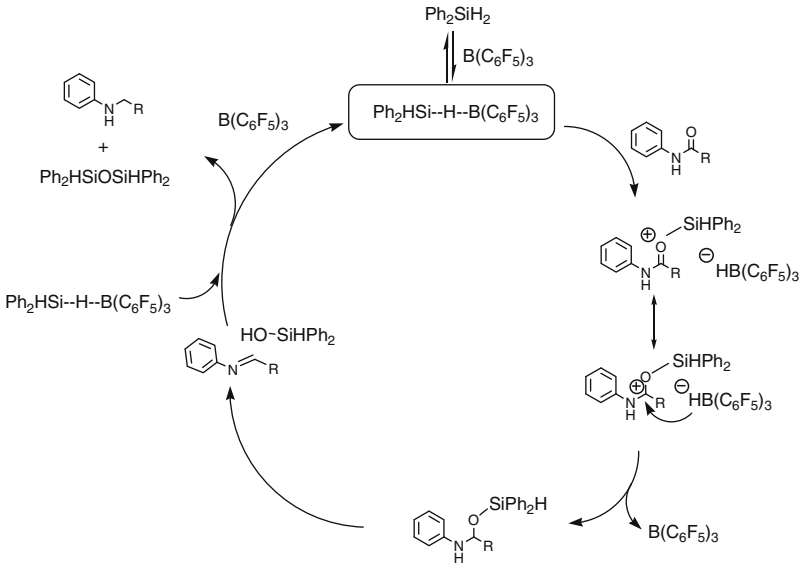
Entry	Silane	Yield[b] (%)
1	$Ph(Me)_2SiH$	80
2	$PhSiH_3$	99
3	Ph_2SiH_2	99
4	Ph_3SiH	0
5	Et_3SiH	0
6	$Ph_2(Me)SiH$	72

[a] Reaction conditions: 0.2 mmol of indole, 0.004 mmol of borane, 0.4 mmol of silane, 2 ml of toluene, 75 °C, 16 h.
[b] Yield was determined by GC and GC–MS.

Table 2
$B(C_6F_5)_3$-catalyzed reduction of various functional groups with diphenylsilane[a]

Entry	Substrate	Product	Yield[b] (%)
1			99
2			75
3			85
4			99
5			(80)
6			(80)
7			(80)
8			99
9			99
10			99
11			99 (92)
12			99[c]

[a] Reaction conditions: 1 mmol of substrate, 0.02 mmol of $B(C_6F_5)_3$, 2–6 mmol of diphenylsilane, 2 ml of CH_2Cl_2, 75 °C, 16 h.
[b] Yield was determined by GC or NMR integrations; isolated yield given in the parentheses.
[c] Reaction was performed at room temperature.



Scheme 2. Suggested mechanism for amide reduction using the $Ph_2SiH_2/B(C_6F_5)_3$ system.

addition, 2 mol % of borane catalyst was sufficient for this reaction, achieving a similar yield as 5 mol % of catalyst. Other compounds such as enamines were reduced to tertiary amines in 85–99% yields, as observed by ^1H NMR (Table 2, entries 3 and 4).

The $B(C_6F_5)_3/R_3SiH$ system has been applied for the reduction of alcohols,[13] esters,[13] carbonyls,[15] and carboxylic acids[16] under different conditions. Herein, the $B(C_6F_5)_3/(Ph)_2SiH_2$ protocol was extended to reduce a broader range of oxygen-containing compounds (see Table 2). 1-Phenylethanol and propiophenone were reduced quantitatively to ethylbenzene and propylbenzene under standard reaction conditions (Table 2, entries 8 and 9). Interestingly, an α,β-unsaturated aldehyde and a carboxy acid group (within the same substrate) were reduced to a saturated hydrocarbon (Table 2, entry 10). For the α,β-unsaturated methoxy-containing substrate, β-methoxy-β-methylstyrene (Table 2, entry 12), two reduction products, propylbenzene and (1-phenylpropan-2-yloxy)-diphenylhydrosilane were observed at reaction temperatures of 40 °C and 80 °C. However, when the reaction was performed at room temperature in CH_2Cl_2, propylbenzene was obtained as the only product.

Remarkably, the reduction system was also applicable to the reduction of amides. Various *N*-phenylamides (Table 2, entries 5–7) were successfully reduced under standard conditions, yielding the corresponding amines in good yields of ~80%. On the other hand, benzamide did not undergo any reduction under the reaction conditions, even when heated at a higher temperature of 120 °C. This was likely due to the carbonyl group being conjugated to the phenyl ring, thus requiring greater activation, which cannot be achieved with the hydrosilane/$B(C_6F_5)_3$ catalytic system. However, an arylisocyanate was reduced to the corresponding amine in quantitative yield under the standard conditions (entry 11).

A silylium–hydridoborate ion pair [$Ph_2HSi–H–B(C_6F_5)_3$], formed by borane abstracting hydride from the hydrosilane, should play a key role in the reaction mechanism. Piers and co-workers have reported previously that their substrates were activated via the silylium cation,[19,20] instead of via a Lewis acid-borane complex.[21] A possible mechanism for amide reduction is suggested (Scheme 2). The silylium cation initially activates the C=O bond, followed by hydride transfer to form an aminal-hydrosilylation intermediate. The resulting imine formed from the aminal underwent hydride addition to form the amine product. $[Ph_2HSi]_2O$ was detected as a by-product by GC–MS. While the reduction of oxygen-containing compounds such as amides, alcohols, and ethers could be rationalized with the formation of siloxane by-products, the reduction of activated C=C double bonds (enamine or enol) would require a more in-depth study of the quenching of silylium ions after the reaction. A suggested mechanism for enamine reduction is provided in the Supplementary data, however, it requires confirmation.

In conclusion, we have demonstrated an efficient metal-free system for reducing various C=X (X = O, N, C) bonds to their corresponding amines or hydrocarbons using the $Ph_2SiH_2/B(C_6F_5)_3$ catalytic system. This $B(C_6F_5)_3$-catalyzed reduction system has a potential in organic synthesis due to the mild reaction conditions, broad applicability to different substrates, and easy-to-handle silane reducing agent, as compared to reduction by stoichiometric hydride reagents or other conventional catalytic systems. Further work is underway to investigate the reaction mechanism in detail.

Acknowledgments

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2009.06.066.

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