

Metal-free catalytic reduction of aldehydes, ketones, aldimines, and ketimines

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Abstract

The metal-free combination of catalytic amounts of PPh_3 , $\text{B}(\text{C}_6\text{F}_5)_3$, and PhSiH_3 can efficiently hydrosilylate aldehydes, ketones, aldimines and ketimines to afford the corresponding reduction products in good yields.

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Reduction of $\text{C}=\text{O}$ and $\text{C}=\text{N}$ bonds to alcohols and amines, respectively, is an important reaction in organic synthesis [1]. Among the available reduction methods, hydrosilylation is very useful because of its less excessive reaction, as compared with other reduction methods such as the one that uses LiAlH_4 . Thus far, considerable research has focused on the development of hydrosilylation using metals [1]. Herein, we report the metal-free catalytic reduction (hydrosilylation) [2–4] of aldehydes, ketones, aldimines and ketimines.

1. Results and discussion

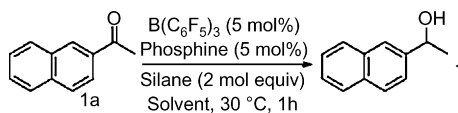
We investigated the combinations of non-metal Lewis acids and bases in the activation of a substrate and a silane, respectively [5]. After intensive screening, the combination of $\text{B}(\text{C}_6\text{F}_5)_3$ as a Lewis acid, PPh_3 as a Lewis base [6], PhSiH_3 as a hydride source and toluene as a solvent was found to afford the best yield: the reaction conversion within 2 mol equiv of PhSiH_3 was low. Representative screening results are shown in entries 1–8 of Table 1. Absence of PPh_3 or $\text{B}(\text{C}_6\text{F}_5)_3$ resulted in no reaction (entries 7 and 8). Although bis-phosphines were also found to be effective as shown in entries 9 and 10, PPh_3 was chosen from the cost perspective.

As shown in Table 2, the reaction under the optimized conditions proved to be general and may be applied to a broad range of ketones, aldehydes, aldimines and ketimines. Specifically, the reaction proceeds smoothly under mild conditions with a synthetically acceptable catalyst loading (5 mol.%). Various acetophenone derivatives **1b–1e**, aliphatic acyclic and cyclic ketones **1f–1h**, aromatic aldehydes, aliphatic and α,β -unsaturated aldehydes **1i–1o**,

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Table 1
Effects of differing silane, phosphine and solvent on reaction yield.

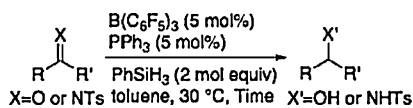


Entry	Silane	Phosphine	Solvent	Yield (%)
1	$(\text{EtO})_3\text{SiH}$	PPh_3	Toluene	Trace
2	Ph_2SiH_2	PPh_3	Toluene	74
3	PhSiH_3	PPh_3	Toluene	90
4	PhSiH_3	PPh_3	DMF	Trace
5	PhSiH_3	PPh_3	Dioxane	25 ^a
6	PhSiH_3	PCy_3	Toluene	Trace
7	PhSiH_3	None	Toluene	Trace
8 ^b	PhSiH_3	PPh_3	Toluene	Trace
9	PhSiH_3	dppf	Toluene	83
10	PhSiH_3	(±)-BINAP	Toluene	87

^a TLC revealed the major component to be the starting ketone.

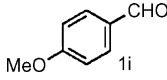
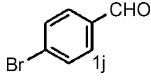
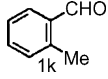
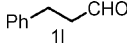
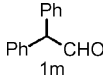
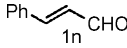
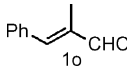
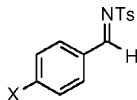
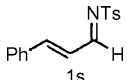
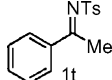
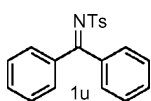
^b No $\text{B}(\text{C}_6\text{F}_5)_3$ was used.

Table 2
Substrate generality.



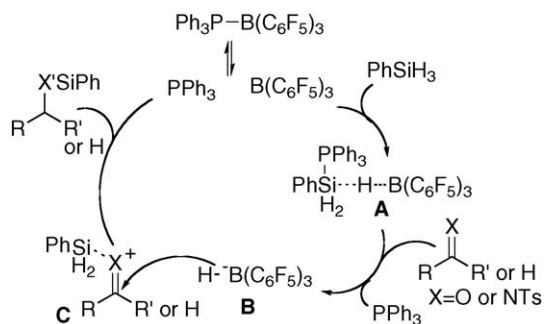
Entry	Substrate	Time (h)	Yield (%)
1		1	90
2		1	79
	1b: X=OMe 1c: X=CF ₃		
3		1	92
4		1	86
5		1	93
6		1	93
7		1	87

Table 2 (Continued)

Entry	Substrate	Time (h)	Yield (%)
8		1	91
9		1	93
10		1	90
11		1	90
12		3	90
13		1	93
14		1	90
15		1	91
16		1	95
17		2	90
	1p: X=H 1q: X=MeO 1r: X=Cl		
18		6	87
19		1	94
20		4	90

aldimines **1p–1s**, and ketimines **1t** and **1u** were employable, affording the corresponding reduction products in good yields. The α,β -unsaturated aldehydes **1n** and **1o** and the aldimine **1s** were reduced in only the 1,2-mode.

Although Piers' group has previously reported the hydrosilylation of carbonyl compounds with the combination of Ph_3SiH and a catalytic amount of $\text{B}(\text{C}_6\text{F}_5)_3$ [3], our protocol has the following advantages as follows: (1) Unlike Piers' protocol, slow addition over 1 h of silane is not required. (2) From the viewpoint of atom economy, the use of PhSiH_3 is more desirable than the use of Ph_3SiH . (3) The process may be applied to aldimines, ketimines and easily enolizable β -teralone (**1h**). Considering Piers' and Oestreich's results [3,4] and those reported herein [7], we assume that the mechanism for the reduction is as follows (Scheme 1). Initially, both $\text{B}(\text{C}_6\text{F}_5)_3$ and PPh_3 activate the Si–H bond to form **A**. The carbonyl- and imino-substrates are then activated by the Si group and the activated substrate **C** is attacked by $\text{H}^-\text{B}(\text{C}_6\text{F}_5)_3$ **B**, affording the corresponding product.



In summary, the combination of $B(C_6F_5)_3$ and PPh_3 was found to function as an effective catalyst in the reduction (hydrosilylation) of aldehydes, ketones, aldimines and ketimines with $PhSiH_3$ [8]. Development of an asymmetric version is now in progress [9–11].

References

- [1] P.G. Andersson, I.J. Munslow, *Modern Reduction Methods*, Wiley-VCH, New York, 2008.
- [2] M. Tan, Y. Zhang, J.Y. Ying, *Adv. Synth. Catal.* 351 (2009) 1390.
- [3] D.J. Parks, J.M. Blackwell, W.E. Piers, *J. Org. Chem.* 65 (2000) 3090.
- [4] S. Rendler, M. Oestreich, *Angew. Chem. Int. Ed.* 47 (2008) 5997.
- [5] M. Shibasaki, *Enantiomer* 4 (2000) 513.
- [6] V. Sumerin, F. Schultz, M. Nieger, et al. *Angew. Chem. Int. Ed.* 6001 (2008) 47.
- [7] When $B(C_6F_5)_3$ (1 mol. equiv. to **1a**) was added to the solution of PPh_3 (1 mol. equiv. to **1a**) in toluene- d_8 , the signal in the ^{11}B NMR changed from 42.91 ppm to -0.52 ppm. Further, when ketone **1a** was added to this solution, no change of the signal change was observed. This result implies that the complex of $B(C_6F_5)_3$ and PPh_3 , even in the presence of ketone **1a**, is formed preferentially.
- [8] Representative procedure for the hydrosilylation (entry 3, Table 1). To a stirred solution of PPh_3 (2.60 mg, 0.0100 mmol) in toluene (0.50 mL), $B(C_6F_5)_3$ (5.40 mg, 0.0100 mmol), **1a** (34.0 mg, 0.200 mmol) and $PhSiH_3$ (49 μ L, 0.400 mmol) were added at rt. The reaction mixture was stirred for 1 h at 30 $^\circ$ C and diluted with 1 mol/L NaOH. After usual work-up, purification by SiO_2 column (hexane:EtOAc = 4:1) afforded 1-(naphthalen-2-yl)ethanol (31.0 mg, 90%) as a white solid.
- [9] C.T. Lee, B.H. Lipshutz, *Org. Lett.* 10 (2008) 4187.
- [10] N.S. Shaikh, S. Enthaler, K. Junge, et al. *Angew. Chem. Int. Ed.* 47 (2008) 2497.
- [11] T. Inagaki, Y. Yamada, L.T. Phong, et al. *Synlett* (2009) 253.