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## **Catalyst-Free and Solvent-Free Facile Hydroboration of Imines**

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#### Dedication ((optional))

**Abstract:** A facile process for the catalyst-free and solvent-free hydroboration of aromatic as well as heteroaromatic imines is reported. This atom-economic methodology is scalable, compatible with sterically and electronically diverse imines displaying excellent tolerance towards various functional groups, and works efficiently at ambient temperature for majority cases affording secondary amines in good to excellent yield after hydrolysis.

Hydrogenation of imines is an important reaction in synthetic organic chemistry as the produced amine compounds find versatile utility in several fields such as natural products, pharmaceuticals, agrochemicals, polymers, and dyes.<sup>[1]</sup> Although traditional hydrogenation process using either stoichiometric reducing agents or pressurized hydrogen gas as hydrogen source are well-exploited, the efficacy of these methodologies is restricted due to poor selectivity over other potentially reducible unsaturated functionalities, requirement of high-pressure setup, and formation of inorganic byproducts.<sup>[1c-e]</sup> In contrary, catalytic hydroboration of imines offers a moderate and efficient way to get access of diverse secondary amines.[2a-b] However, only few examples of imine hydroboration have been described<sup>[2]</sup> when compared to a variety of protocols having been developed for catalytic hydroboration of other unsaturated functionalities like carbonyl, alkyne, and alkene.<sup>[3]</sup>

catecholborane (H-Bcat) was utilized as Initially. hydroboration agent for coinage metal catalyzed hydroboration of imines<sup>[4a]</sup> and later on, pinacolborane (H-Bpin) having lower Lewis acidity got much attention for the same purpose.<sup>[2a,4b]</sup> Among metal catalyzed processes, transition metal<sup>[5]</sup> and even rare earth metal complexes<sup>[6]</sup> have been studied (Scheme 1). There is also a recent surge in utilization of s- and p-block elements<sup>[7]</sup> and till date, several research groups have studied the hydroboration of carbonyl<sup>[3a]</sup> and to some extent imine compounds using maingroup element (Ca,<sup>[7b]</sup> Mg,<sup>[8a]</sup> Al,<sup>[7c-d]</sup> Si<sup>[8b]</sup>) based systems (Scheme 1). Alkali metal based compounds e.g. "BuLi and NaOH have also been utilized for the same process.<sup>[9]</sup> Although substantial efforts have been directed towards exploitation of main-group based systems as an alternative to precious transition metal catalysts, area of metal-free catalysis is also emerging expeditiously in recent years due to environmental and economic demands.<sup>[4b,10]</sup> In this area, frustrated Lewis pairs (FLPs) have demonstrated themselves as prominent catalytic systems for the reduction of imines.<sup>[10d]</sup> In 2012, Crudden and co-workers reported an efficient FLP system generated from DABCO, pinacolborane and B(C<sub>6</sub>F<sub>5</sub>)<sub>3</sub>.<sup>[11]</sup> After this report, various protocols

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[b] Supporting information (experimental details, characterization data, NMR spectra of the synthesized compounds) for this article is given via a link at the end of the document utilizing Lewis acid (mainly boron based), Brønsted acid, and recently, diazaphospholene-based phosphorus hydride as catalyst have been reported (Scheme 1).<sup>[7a,10c,12]</sup> However, hydroboration of imines with most of these catalysts demands either elevated reaction temperature or longer reaction duration along with high catalyst loading.<sup>[5-8]</sup> Thus, development of alternative atom-economic and catalyst-free green process for the hydroboation of imines with broad functional group tolerance under mild conditions is desirable for future sustainable catalytic methods.



Scheme 1. Overview of prior reports on hydroboration reaction of imines and this work.

A solvent as well as catalyst-free approach not only leads to an environment-friendly greener process by diminishing waste generation but also produces reactions, which are practically more convenient.<sup>[13a-b]</sup> However, catalyst-free processes to attain target molecules did not get much momentum over the years after pioneering works on hydroboration of alkenes and alkynes by the group of Knochel and Piers.<sup>[13c-d]</sup> Only in recent years, development of and solvent-free) areen (catalyst-free organic transformations such as dehydrocoupling of protic substrates with boranes,<sup>[14a-c]</sup> hydroboration of aldehydes/ketone,<sup>[14d-e]</sup> and reduction of carboxylic acid via hydroboration<sup>[14f-h]</sup> has gained attention from the researchers. In line with these efforts, we delved in developing a green protocol for the hydroboration of imine and herein, we present the catalystfree and solvent-free ambient temperature hydroboration of imines with excellent functional group tolerance.

To explore the feasibility of aldimine hydroboration under catalyst-free condition, initially, we performed the hydroboration of *N*-benzylideneaniline using H-Bpin as hydroborating agent at ambient temperature. Hydroboration using 1.1 equiv. of H-Bpin in organic solvents resulted in moderate conversion and after hydrolysis *N*-benzylaniline was attained in about 60% yield (Table 1; entry 1-2). However, to our delight, reaction under neat condition goes smoothly and the desired amine was isolated in

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excellent yield of 89% which increases marginally when 1.3 equiv. H-Bpin was used (entry 3-4). Reactions at higher temperature (60 °C) require less time to complete (entry 5-6). Although reaction under neat condition using 1.1 eqiv. H-Bpin with respect to *N*-benzylideneaniline delivered competent yield of the *N*-benzylaniline, use of 1.3 eqiv. of H-Bpin was chosen as optimized condition for the hydroboration process at ambient temperature due to solubility problem of some other aldimines.

Table 1. Optimization of the hydroboration reaction.[a]

Entry	Solvent	Temperature	Time (h)	Yield (%) <sup>[b]</sup>
1 2 3 4 <sup>[c]</sup> 5	Acetonitrile THF - -	RT RT RT 60 ℃	6 6 6 3 2	62 56 89 92 93
6	-	60 °C	2	80

[a] Reaction condition: *N*-Benzylideneaniline (0.5 mmol), H-Bpin (0.55 mmol), room temperature (RT). [b] all are isolated yields. [c] 1.3 equiv. H-Bpin was used.

With this optimized reaction condition in hand, we then probed the potential of this protocol and investigated a wide range of imines, synthesized via condensation of readily available aldehydes and amines following reported procedure, <sup>[15a]</sup> under catalyst-free and solvent-free condition. We were delighted to find that the hydroboration of electronically and sterically diverse amines, which include aromatic and heteroaromatic amines with varying substituents was realized efficiently. After hydrolysis followed by purification via column chromatography provided the corresponding secondary amines in good to excellent yields (Table 2).

Both the C- and N-phenyl ring of the imine moiety bearing diverse substituents resulted the desired products. Various substituents on C-phenyl ring afforded the secondary amines (3ae) in excellent yields of 85-92% and these results are significantly better than those observed for Co(II)-CP,[5a] Ru(II),[5b] and (MeCp)<sub>3</sub>La<sup>[6c]</sup> systems which require higher temperature (60-70 °C) and longer reaction duration. Presence of substituents at the *N*-phenyl ring demands longer reaction span than their analogues C-phenyl substituted imines (3h-j vs 3a-e). However, substrates having both N- and C-phenyl rings substituents gave excellent yield of the products at the same reaction duration as required for only C-phenyl substituents (31-m vs 3c-d). Notably, variation of substituents on the C- and N-phenyl ring of the imine moiety (3ae and 3h-j) does not have much effect on the reaction outcome. Importantly, position of the C-phenyl substituents does not have any influence on the reaction (3d vs 3g) and compounds with moderate steric congestion around the imine moiety can be reduced efficiently at ambient temperature (3k and 3n) although sterically more congested imine (10) requires higher temperature (30, 92%). It is important to note that Mg-based catalyst performs sluggishly for this type of bulky substrates although found to be suitable for other aldimines.<sup>[8a]</sup> Possibly because of low solubility of 1p, reaction temperature of 60 °C is necessary for the completion of reaction and the amine 3p was isolated in 90% vield. Hydroboration of N-benzyl substituted imine 1g proceeds at 60 °C and the dibenzylamine (3q) could be isolated in 65% yield.

Table 2. Substrate scope for catalyst-free and solvent-free hydroboration of various aldimines.  $\ensuremath{^{[a]}}$ 



[a] Reaction condition: imine (0.5 mmol), H-Bpin (0.65 mmol), 6-24 h. The hydroborated products were hydrolysed with SiO<sub>2</sub> in methanol; all are isolated yields. [b] 1.5 equiv. H-Bpin was used. [c] Reactions were performed at 60 °C. [d] 2.3 equiv. H-Bpin was used.

Our catalyst-free and solvent-free approach can also be utilized for the reduction of heteroaromatic-substituted imines although higher temperature (60 °C) is required to realize decent yields in 24 h (**3r-3t**) possibly due to change in electrophilicity of the imine moiety. Poly-aromatic compound 1-naphthyl substituted imine **1u** is also reactive and yielded the corresponding amine **3u** after hydrolysis in 93% yield at ambient temperature. Satisfyingly, this approach can also be extended to diimine compound and the corresponding diamine compound **3v** could be attained in excellent yield of 96%.

Table 3. Substrate scope for catalyst-free hydroboration of ketimines.  $\ensuremath{^{[a]}}$ 



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[a] Reaction condition: imine (0.5 mmol), H-Bpin (0.75 mmol), 60  $^{\rm o}$ C, 24-48 h. The hydroborated products were hydrolysed with SiO\_2 in methanol; all are isolated yields.

Catalyst-free hydroboration of ketimines is expected to be difficult as compared to analogues aldimines<sup>[15b]</sup> due to less electrophilicity coupled with more steric congestion around the imine moiety. After having success with aldimines, we focused on the hydroboration of ketimines using our catalyst-free and solvent-free approach. As expected, hydroboration at ambient temperature using 1.5 equiv. of H-Bpin with respect to ketimine was not successful. However, hydroboration was realized when reaction was performed at higher temperature of 60 °C (Table 3) although effectiveness is much lower than previously reported catalyzed reactions<sup>[8a,10c,12c]</sup> and the corresponding amines were obtained in moderate to good yields after hydrolysis. Reduction of N-(α-methylbenzylidene)aniline 4a followed by hydrolysis yielded the *N*-( $\alpha$ -methylbenzyl)aniline **6a** in good yield of 70%. Hydroboration of imines with both electron withdrawing and donating substituents on the C-phenyl ring (4b-4d) was attained. However, presence of methoxy group substantially reduces the activity<sup>[4b]</sup> and corresponding amine (6d) could only be isolated in 37% yield even after prolonged reaction time (48 h) which may be due to reduced electrophilicity of the imine moiety. Similarly, presence of ethyl (4e) instead of methyl group at the  $\alpha$ -position as well as N-benzyl (4f) instead of phenyl group required longer time to realize the corresponding amines (6e and 6f) in moderate yield.



Scheme 2. Intermolecular chemoselective hydroboration of imine. [a] Isolated yield.

To explore the suitability of the developed process in hydroboration, chemoselective 1:1 mixture Nof benzylideneaniline and 4-bromostyrene/diphenyl acetylene/4methylacetophenone were reacted with H-Bpin under our standard condition. To our delight, essentially quantitative hydroboration of only N-benzylideneaniline was observed (based on <sup>1</sup>H NMR analysis) and we could isolate the N-benzylaniline 3a after hydrolysis in about 90% yield (Scheme 2). No hydroboration of other potential functional moieties was observed which was confirmed by 95% recovery of diphenyl acetylene along with <sup>1</sup>H NMR analysis of the reaction mixture (see Supporting Information).



Scheme 2. Intramolecular chemoselective hydroboration of imine (isolated yield). Yield at 60  $^{\circ}\text{C}$  are given in parenthesis.

After having success in intermolecular chemoselective hydroboration, we then targeted substrates installed with both aldimine and nitro/nitrile moiety<sup>[15a]</sup> at the *p*-positions of a phenyl ring. Gratifyingly, we found excellent functional group tolerance of our present method for nitro and nitrile moiety. The corresponding secondary amines **8a** and **8b** having the nitro/nitrile group unaltered were exclusively obtained in moderate yields at ambient temperature which can be improved by conducting the reaction at higher temperature of 60 °C (Scheme 3). It is worth to mention that the efficiency our protocol is much higher when compared to previously reported Er, Ca, and Si-based catalyst systems.<sup>[6a,7b,8b]</sup>

Importantly, the present system also works for large-scale synthesis as demonstrated by gram scale reaction of *N*-benzylideneaniline (**1a**) under optimized conditions providing *N*-benzylaniline (**3a**) upon hydrolysis in 85% isolated yield (Scheme 4).



Scheme 4. Gram scale hydroboration of *N*-benzylideneaniline.

Based on previously reported related literatures,<sup>[2b,4b,9b,14d]</sup> a plausible mechanistic pathway for this catalyst-free process is depicted in Scheme 5. It is proposed that a Lewis adduct between the imine and H-Bpin of type **A** is first formed, which possibly enhances the hydridic character of the B-H moiety of H-Bpin via weakening of the bond<sup>[9b,14d-e]</sup> and thereby, promotes the hydride transfer to reduce the imine functionality likely via four membered cyclic transition state (**B**) in the next step.



Scheme 5. A plausible mechanistic pathway.

#### Conclusion

In conclusion, we have developed a general, ambient temperature catalyst-free and solvent-free efficient protocol for the hydroboration of imines, which upon hydrolysis produces the corresponding secondary amines. This simple

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protocol is pertinent to synthetically diverse imines which include aromatic and heteroaromatic aldimines as well as ketimines and offers excellent chemoselectivities (conversion of imine over alkene, alkyne, ketone, nitro, and nitrile).

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#### **Conflict of Interest**

The author declares no conflict of interest.

**Keywords:** Catalyst-free • Hydroboration • Imines • Green chemistry • Chemoselective

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A general method for catalyst-free and solvent-free ambient temperature hydroboration of imines has been developed which after hydrolysis gives access to sterically and electronically diverse secondary amines



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