

# Green Chemistry

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## COMMUNICATION

## Lithium Triethylborohydride as Catalyst for Solvent-Free Hydroboration of Aldehydes and Ketones

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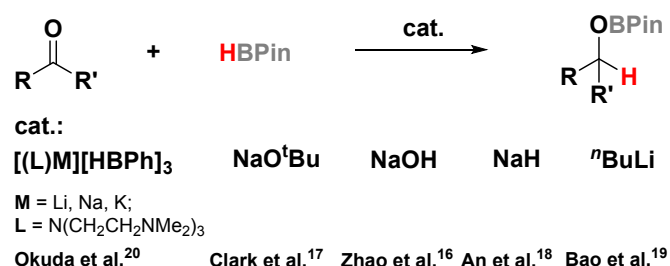
Commercially available and inexpensive lithium triethylborohydride (LiHBEt<sub>3</sub>) acts as efficient catalyst for the solvent-free hydroboration of a wide range of aldehydes and ketones, which were subsequently transformed to corresponding 1° and 2° alcohols in one-pot procedure at room temperature (rt).

## Introduction

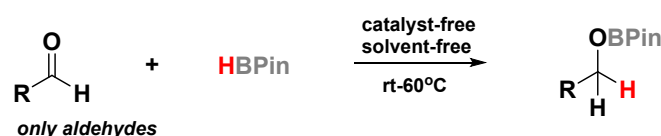
The hydroboration of unsaturated compounds has become increasingly trendy in the past 5 years and is currently intensively explored by many scientists.<sup>1–4</sup> A wide variety of transition metal complexes,<sup>5–19</sup> as well as s-,<sup>20–33</sup> p-<sup>34–41</sup> and f-block<sup>42–45</sup> element species have already been documented as efficient catalysts for the hydroboration of carbonyls, nitriles and imines. The Okuda group has described pioneering work about well-defined series of light alkali metal hydridotriphenylborates with coordinated tetradentate ligand L (L = tris{2-(dimethylamino)ethyl}amine), that act as highly efficient catalysts for the hydroboration of a wide range of aldehydes and ketones.<sup>27</sup> Unfortunately, this unique efficiency directly translates into a significantly reduced applicative potential (due to the preparation of such complexes and the need for specific ligand). On the other hand, Wu et al., have reported that commercially available NaOH powder can be utilized in hydroboration. However, all reactions were performed in highly toxic deuterated benzene.<sup>20</sup> Lastly, the An group has described efficient addition of hydroboranes to carbonyls,<sup>22,25</sup> although required highly sensitive catalysts (sodium hydride and n-butyllithium). Currently, there is a very clear focus on the development of hydroelementation processes in accordance with green chemistry principles.<sup>46–52</sup> More recently, our studies concerning the use of hydroboranes<sup>53,54</sup> have shown, that addition of B-H bond into C=O bonds in

aldehydes can be efficiently performed under catalyst-free and solvent-free conditions (Fig. 1).<sup>55</sup>

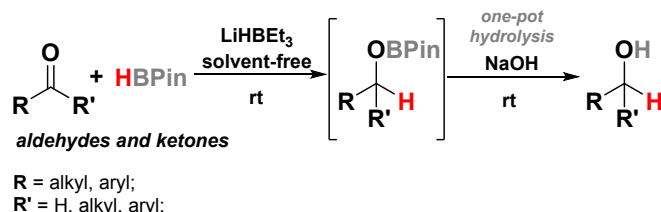
## Selected examples of alkali metal based catalysts



## Our previous work



## This work



**Figure 1.** Selected examples of alkali metal catalysts utilized in hydroboration of carbonyls.

However, this green methodology required a higher temperature to ensure complete conversion of most aldehydes in a short time. What is more, this was completely ineffective for ketones and gave only trace amounts of the desired boronic esters, even at elevated temperature.

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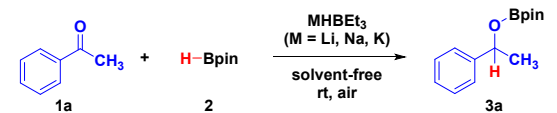
## Green Chemistry

Therefore, in view of mentioned reports, the aim of this work was to check the possibility of utilizing inexpensive and easily accessible main group species in addition of hydroboranes to carbonyls. In this paper, we present an efficient method for the hydroboration of ketones and aldehydes (Fig. 1) at ambient temperature and air atmosphere, mediated by catalytic amounts of commercially available and inexpensive lithium triethylborohydride ( $\text{LiHBEt}_3$ ).

## Results and Discussion

We began our studies by exploring reaction conditions for the envisioned hydroboration of acetophenone **1a** with pinacolborane **2** under solvent-free conditions using commercially accessible alkali metal triethylborohydrides ( $\text{M} = \text{Li, Na, K}$ ) as the catalysts (Table 1).

Table 1 Optimization of the reaction conditions.<sup>a</sup>

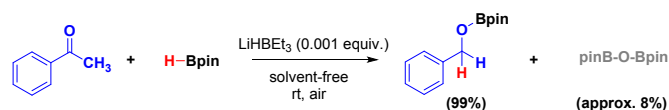
|  |                            |             |                             |
|-----------------------------------------------------------------------------------|----------------------------|-------------|-----------------------------|
| Entry                                                                             | Equiv. of $\text{MHBET}_3$ | Time (min.) | Conversion (%) <sup>b</sup> |
| <b><math>\text{LiHBEt}_3</math></b>                                               |                            |             |                             |
| 1                                                                                 | 0.1                        | 5           | 99                          |
| 2                                                                                 | 0.01                       | 5           | 99                          |
| 3                                                                                 | 0.001                      | 5           | 99                          |
| 4 <sup>c</sup>                                                                    | 0.001                      | 60          | 90                          |
| 5 <sup>d</sup>                                                                    | 0.001                      | 5           | 99                          |
| 6                                                                                 | 0.0001                     | 60          | 65                          |
| <b><math>\text{NaHBEt}_3</math></b>                                               |                            |             |                             |
| 7                                                                                 | 0.1                        | 5           | 99                          |
| 8                                                                                 | 0.01                       | 30          | 96                          |
| 9                                                                                 | 0.001                      | 5           | 10                          |
| <b><math>\text{KHBEt}_3</math></b>                                                |                            |             |                             |
| 10                                                                                | 0.1                        | 5           | 99                          |
| 11                                                                                | 0.01                       | 30          | 98                          |
| 12                                                                                | 0.001                      | 5           | 10                          |

<sup>a</sup>Reaction conditions: rt, **1a** (1.0 equiv.), **2** (1.15 equiv.), solvent-free. <sup>b</sup>Determined by GC. <sup>c</sup>1.0 equiv. of **2**. <sup>d</sup>THF as the solvent.

It turned out that lithium triethylborohydride (Table 1, entry 3) is the most active catalyst. Other triethylborohydrides were less active in this process (see and compare the conversion of acetophenone, when the amount of the catalyst was decreased to 0.1 mol% - Table 1, entries 3, 9 and 12). Next, a control experiment confirmed that reaction can also be carried out in THF (Table 1, entry 5), as an alternative to solvent-free conditions, what can be particularly useful in case of solid substrates. On the other hand, the amount of pinacolborane was also examined. After few testing attempts, we decided to use 1.15 equiv. of HBPin in our further tests, due to the fact of slightly lower conversion of acetophenone to its boronic ester, when 1.0 equiv. of HBPin was utilized (Table 1, entry 4). Such result was surprising, in particular since GC analysis suggested the formation of desired boronic ester as a single product. However, the NMR spectroscopic analysis clearly confirmed the formation of symmetrical diboraxane (pinB-O-Bpin) as the by-product (approx. 8% of diboraxane,  $^1\text{H}$  NMR signal at 1.30;

see Scheme 1 and  $^1\text{H}$  NMR spectra illustrated on Figure 1 in ESI).

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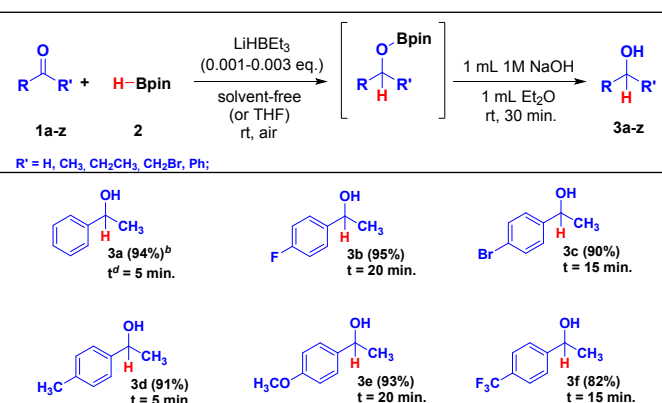


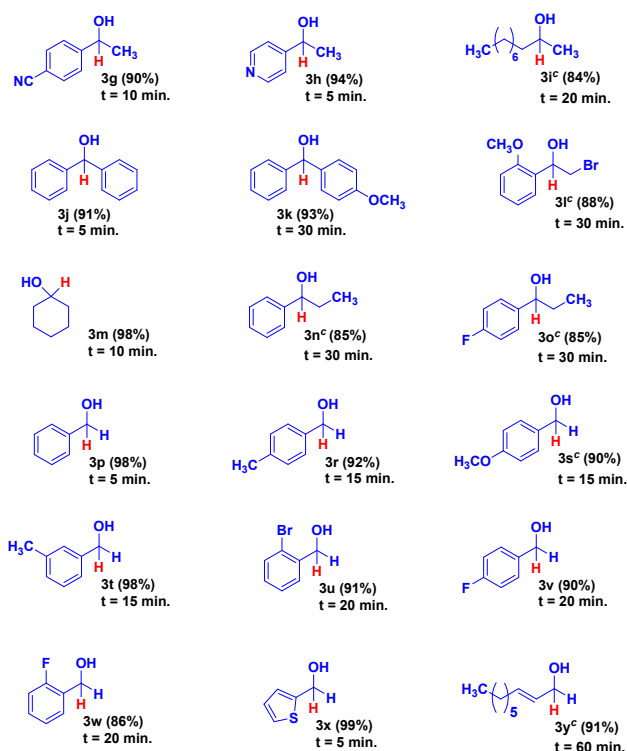
Scheme 1. The hydroboration of acetophenone catalyzed by  $\text{LiHBEt}_3$ .

In overall, the formation of diboraxane was observed in all tests (approx. 5–8%), but it was hardly detected by GC analysis (due to similar retention time of both compounds). As the result, the separation process *via* distillation could be very difficult, and only use of ketones with higher boiling points allowed to observe a single, clean GC peak derived from pinB-O-Bpin. Inherently, alcohols (not boronic esters) were indeed envisioned to be the final products of each reaction. Therefore, as it was scheduled, we transformed all of afforded boronic esters (despite their isolation) directly to corresponding alcohols *via* one-pot hydrolysis. Of course, the complete removal of oxygen and water would cause an overall decrease in the formation of unwanted by-products. However, this would require an additional inert atmosphere, and preferably glove-box system, in order to obtain satisfactory results from the test. And that in turn could significantly reduce an applicative potential of our approach.

With the optimized reaction conditions in hand, we evaluated the versatility of  $\text{LiHBEt}_3$ -catalyzed hydroboration of carbonyls, followed by one-pot hydrolysis (Table 2). In each case, after the hydroboration step, 1M solution of NaOH was added to get corresponding alcohols. Thus, the reaction smoothly proceeded with various ketones and aldehydes **1a–z** bearing electron-donating or electron-withdrawing groups. In case of solid substrates, we used THF as the solvent. We were particularly delighted that derivatives possessing other potentially reactive functional groups (**1g**, **1h**, **1y**) could be chemoselectively converted only to desired alcohols (**3g**, **3h**, **3y**).

Table 2 Hydroboration of various carbonyl derivatives with HBPin.<sup>a</sup>

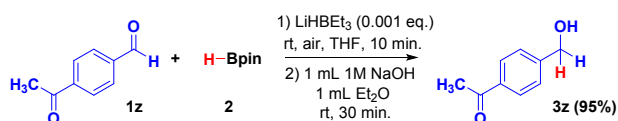




<sup>a</sup>Reaction conditions: **1** (1.0 equiv.), **2a** (1.15 equiv.), 5–60 minutes. <sup>b</sup>Isolated yields of all products. <sup>c</sup>0.003 equiv. of LiHBEt<sub>3</sub>. <sup>d</sup>Time of hydroboration step for all products.

Finally, the reaction of acetophenone **1a** with pinacolborane **2** also proceeded well on a gram scale, providing 1-phenylethanol (**3a**, 1.46 g) in 97% yield (see the ESI).

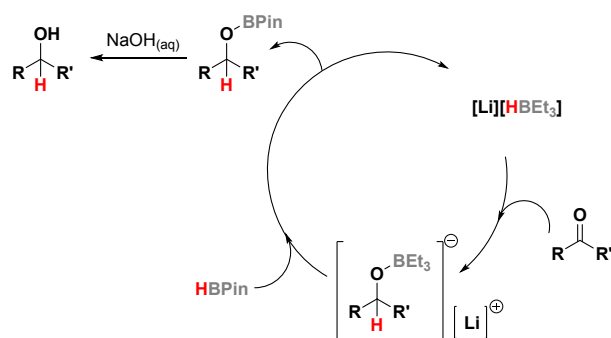
Next, intramolecular competition experiment was conducted (Scheme 2). 4-acetylbenzaldehyde (**1z**) underwent hydroboration selectively at the aldehyde, while preserving the ketone functionality. This finding indicates that our catalytic system allows the chemoselective conversion of aldehyde to boronic ester (and subsequently to alcohol (**3z**)), even in the presence of ketone group.



**Scheme 2.** Intramolecular competition experiment.

Based on our findings and the previously published literature,<sup>27,33,55,56</sup> we assume the plausible mechanism (Figure 2). LiHBEt<sub>3</sub> acts as the catalyst and addition of carbonyl derivative is proposed in the first step. This was confirmed by <sup>11</sup>B NMR analysis (see ESI). Subsequently, obtained intermediate reacts with pinacolborane to form the corresponding boryl ether.

**Figure 2.** Proposed catalytic cycle for the carbonyl hydroboration.



## Conclusions

In summary, we have disclosed the accessibility of lithium triethylborohydride (LiHBEt<sub>3</sub>) as an efficient and simple catalyst for hydroboration of numerous ketones and aldehydes, bearing a wide array of electron-withdrawing and electron-donating groups. The key advantages of this process are its exclusive aldehyde selectivity over ketone, wide reducible functional group tolerance, mild reaction conditions (air atmosphere, rt), one-pot hydrolysis to desired alcohols, and very low loading of the catalyst, as well as its wide availability. Most of these transformations were additionally performed under solvent-free conditions. This simple LiHBEt<sub>3</sub>-catalyzed hydroboration system will therefore be attractive to chemists and non-chemists alike, highlighting great potential for future applications to chemical synthesis. Further studies on the hydroboration of functional groups are currently underway.

## Conflicts of interest

There are no conflicts to declare.

## Acknowledgements

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Lithium triethylborohydride as an efficient and easily accessible catalyst for hydroboration of numerous carbonyls under solvent-free conditions at room temperature.

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