Hydroboration of nitriles and imines by highly active zinc dihydride catalysts†

Xiaoming Wang and Xin Xu † *

Eco-friendly zinc dihydrides stabilized by N-heterocyclic carbenes were demonstrated to be highly efficient catalysts for the double hydroboration of nitriles with pinacolborane, exhibiting turnover frequencies up to 3000 h⁻¹ at room temperature under solvent-free conditions. The reactions afforded corresponding diborated amines with excellent yields and good functional group tolerance. A single Zn–H insertion product was isolated from a stoichiometric reaction of zinc dihydride with nitrile, and was proved to be an active species in this transformation. Kinetic studies were performed to give some insights into the catalytic reactions. In addition, zinc dihydride species also showed high activity for the hydroboration of imines to boronated amines.

Introduction

The development of efficient synthetic approaches for amines is of great significance because this class of compounds has a widespread application in the fine chemical, agrochemical, and pharmaceutical industries. ¹ ² In this context, catalytic reduction of unsaturated compounds containing e.g. C≡N or C≡N bonds with borane has recently emerged and attracted extensive attention, because it usually affords high reaction selectivity and employs mild reaction conditions.³ Moreover, corresponding hydroboration products, i.e. borylamines, can be used for the synthesis of a variety of organic compounds.⁴ The first example of nitrile dihydroboration was reported by Nikonov et al. using a molybdenum complex 2,6-iPr₂-C₆H₃N)Mo(H)(Cl)(PMe₃)_3 (1a, Fig. 1), achieving a turnover frequency (TOF) up to 1.7 h⁻¹.⁵ Since then, many efforts have been made for the development of catalysts used for this transformation.⁶ Over the last few years, it has been expanded to include a variety of metal complexes, including s-, p-, d- and f-block elements, and the representatives of effective complexes for the dihydroboration of nitriles are shown in Fig. 1. However, most of above complexes show low to moderate catalytic activity and some of them are unattractive due to their precious or combustible nature.

Considering the biocompatibility, environmental friendliness and abundance of zinc ion, it is attractive to use zinc-based catalysts for various organic transformations. Zinc-based complexes have been successfully used in the hydroboration of a series of unsaturated molecules, including ketones,⁷ imines,⁸ alkenes,⁹ and N-heterocycles,¹⁰ but are rarely seen to be used in the hydroboration of organic nitriles. To the best of our knowledge, only one precedent was reported by Panda et al.¹¹ recently by disclosing that the imidazoline-2-iminato ligand-based zinc alkyl complexes were active toward hydroboration of nitriles under heating conditions (60 °C), achieving a maximum TOF of 50 h⁻¹. In our previous work, we synthesized two molecular zinc(II) dihydrides supported by phosphine-functionalized N-heterocyclic carbene ligands (Fig. 2), that were found to be efficient for hydroboration of thermodynamic stable and kinetic inert CO₂ under mild conditions.¹² Being inspired by this result, we herein investigated further of these complexes for the catalytic hydroboration of nitriles and imines. Gratifyingly, zinc dihydrides 2 exhibit remarkably high activity for hydroboration of a variety of nitriles and imines, producing boronated amines with a TOF of up to 3000 h⁻¹ at room temperature in the absence of solvent. A plausible mechanism is also proposed based on the isolation of a catalytic intermediate and kinetic studies.

Fig. 1 Selected metal complexes effective for the hydroboration of nitriles (reaction temperature and maximum TOF obtained were also listed).
Results and discussion

We initiated our study by using complex 2a (1 mol% based on Zn) for the reaction of benzonitrile with pinacolborane (HBpin) at room temperature in various solvents and the results are summarized in Table 1. The reactions gave low conversions of benzonitrile in the employed solvents (entries 1–3; 54% in C₆D₆, 29% in PhF, 26% in THF) in 2 h. It’s noteworthy that in all of these cases, no intermediate species, i.e. PhCH=N=NBpin, was detected. Excitingly, a significant increase in activity was achieved when reaction was conducted in the absence of any solvent, which consumed all of the benzonitrile in a short time (8 min; entry 4), exclusively affording diboronated amine PhCH=NN(Bpin)₂ ([5a] with a TOF of 750 h⁻¹. To our knowledge, this represents the highest activity reported to date for the hydroboration of benzonitrile. Complex 2b was also applied in this reaction under similar conditions, which resulted in a lower conversion of benzonitrile (85%; entry 5) probably due to the sterically bulky NHC ligand employed for complex 2b. To make a comparison, a tridentate monoanionic ligand-based zinc monohydride, i.e. L^{NPP}ZnH [L^{NPP} = CH₃C(2,6-iPr₂C₆H₃)CHC(CH₃)(-NCH₂CH₂PPh₂)], previously reported by our group, was also prepared and examined under neat conditions. However, it is almost ineffective toward the current reaction with 1 mol% loading in 2 h (entry 6). NHC ligand employed in 2a alone was found inert for the reaction under the same conditions (entry 7).

Subsequently, reactions of a variety of nitriles with HBpin promoted by complex 2a were examined under our typical conditions (0.5 mol% catalyst loading, room temperature, in the absence of any solvent; Table 2). Reactions of para- or ortho-methyl-substituted benzonitriles with HBpin offered the corresponding diboronated amines 5b and 5c in 93% and 86% isolated yields, respectively. Additionally, benzonitriles containing polar functional groups are tolerated in the reaction. For example, methoxy, dimethylamino, halogen (F, Cl, and Br) substituted benzonitriles gave corresponding hydroboration products 5d–5h in 5–40 min with high isolated yields. Notably, the reaction was significantly accelerated when using para-trifluoromethyl substituted benzonitrile, leading to a full conversion of substrate only in 2 min. As a result, it afforded compound 5i with a TOF of 3000 h⁻¹, which is the maximum value reported to date in nitrile hydroboration. For polycyclic 1-naphthonitrile, the quantitative conversion was observed in 40 min, producing 5j in 90% isolated yield. Heterocyclic aromatic substrates comprised of a furan, thiophene or pyridine framework are applicable in current study to give anticipated dihydroboration products 5k–5m. The selectivity in the reduction of the nitriles when containing other unsaturated functional groups was also investigated. In the case of 4-acetylbazonitrile, hydroboration of both C=O and C≡N groups occurred at a comparable rate, and only 5n was isolated. In contrast, methyl 4-cyanobenzooate underwent selective hydroboration reaction only at C≡N moiety even with excess amount of HBpin, affording compound 5o and keeping ester.

Table 2 Hydroboration of various organic nitriles with HBpin catalyzed by 2a

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Loading (mol%)</th>
<th>Solvent</th>
<th>Time (min)</th>
<th>Conv. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2a</td>
<td>0.5</td>
<td>C₆D₆</td>
<td>120</td>
<td>54</td>
</tr>
<tr>
<td>2</td>
<td>2a</td>
<td>0.5</td>
<td>C₆H₆</td>
<td>120</td>
<td>29</td>
</tr>
<tr>
<td>3</td>
<td>2a</td>
<td>0.5</td>
<td>THF</td>
<td>120</td>
<td>26</td>
</tr>
<tr>
<td>4</td>
<td>2a</td>
<td>0.5</td>
<td></td>
<td>8</td>
<td>99</td>
</tr>
<tr>
<td>5</td>
<td>2b</td>
<td>0.5</td>
<td></td>
<td>8</td>
<td>85</td>
</tr>
<tr>
<td>6</td>
<td>L^{NPP}ZnH</td>
<td>1</td>
<td></td>
<td>120</td>
<td>Trace</td>
</tr>
<tr>
<td>7</td>
<td>NHC</td>
<td>1</td>
<td></td>
<td>120</td>
<td>Trace</td>
</tr>
</tbody>
</table>

a Reaction conditions: nitrile (0.30 mmol), pinacolborane (0.63 mmol), room temperature. b Conversions were determined by ¹H NMR spectroscopy (integration of residual benzonitrile vs diborylammine product).

d Reaction conditions: [2a] = 0.0015 mmol, [HBpin] = 0.63 mmol, [RN=CN] = 0.30 mmol, room temperature. Conversions were determined by ¹H NMR spectroscopy (integration of residual 3 vs. 5). Isolated yields were shown in the parentheses. c 3.1 eq. HBpin was used. d Reaction was conducted at 80 °C.
motif intact. Moreover, an intermolecular competition reaction between benzonitrile, styrene, and HBpin (1:1:2 molar ratio) was examined under above conditions. The hydroboration product 5a was exclusively formed while the styrene remained intact, thus indicating a preference of nitrile reduction over the alkene in the reaction. Furthermore, the scope of the substrates was expanded to the more challenging aliphatic nitriles. As shown in Table 2, all three selected nitriles were also successfully converted to the target borylamines 5p-5r, although the reactions required an elevated temperature (80 °C) and a prolonged reaction time (240 min) to achieve a complete conversion of nitriles.

Inspired by the excellent performance of complex 2a in the hydroboration of C=N bond, we next examined its application in the imine hydroboration, which provides an efficient method for the synthesis of secondary amines.18 It was found that 2a also showed high activity toward reduction of a variety of imines with HBpin under neat condition, affording hydroborated product 7 at room temperature (Table 3). Reaction of N-benzylideneaniline with 1.1 equiv. of HBpin gave 7a in the presence of 0.5 mol% of zinc dihydride (2a), with complete consumption of imine in 15 min (TOF = 400 h⁻¹).19 Subsequently, a wide range of C- and N-substituted imines were subjected to the reactions. For the imines bearing diverse substituents at C-phenyl ring, the expected hydroborated amines 7b-7h could be obtained in excellent isolated yields (82–94%) from 10 to 40 min. Among them, substrates with electron-withdrawing groups (−Cl, −Br, −CF₃, or −NO₂) proceeded rapidly in comparison to those with electron-donating groups (−OMe or −NMe₂). Introduction of the substituent at N-phenyl of imine, either p-Cl or p-Me, slightly suppressed the rate of hydroboration reactions as in the cases of generation of 7i and 7j. Aliphatic N-substituted imines are also tolerated with current catalytic system and produced corresponding products 7k-7m, albeit requiring an elevated temperature (80 °C) and a prolonged reaction time (6–16 h). Heterocyclic C-substituted imine was applied under the given conditions, providing boronated aniline 7n in 40 min. When introducing an ester group to C-phenyl of imine, hydroboration reaction still occurred at C=N moiety even with excess amount of HBpin, affording compound 7o with 82% isolated yield.

To gain more insights into the reaction mechanism, we conducted a stoichiometric reaction between the zinc dihydrides 2a and two equimolar amounts of p-MePhCN in toluene. The reaction rapidly occurred and gave complex 8 in 93% isolated yield (Scheme 1) through the insertion of one Zn-H into the −C=N moiety. It was fully characterized by multinuclear NMR spectroscopy and elemental analysis. Addition of an excessive amount of the nitrile did not lead to a further insertion reaction probably due to the steric hindrance. The ¹H NMR spectrum showed a sharp signal at δ 9.39 ppm which was identified as a characteristic imine N=CH-R, while the signal of remaining Zn-H was located at δ 4.81 ppm. This was further confirmed by a control experiment using deuterium labeling complex 2a-D as a starting materiel (see the ESI for details†).

Subsequently, complex 8 was directly employed as a catalyst for the reaction of p-MePhCN with pinacolborane under standard conditions. As expected, it efficiently provided the diborated amine p-MePhCH₂N(Bpin)₂ (5b) in 88% isolated yield (Scheme

![Scheme 1 Synthesis of complex 8 and its use in the hydroboration.](image)

### Table 3 Hydroboration of various imines with HBpin catalyzed by 2a

<table>
<thead>
<tr>
<th>Imine</th>
<th>Reaction Conditions</th>
<th>Isolated Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>7a</td>
<td>[2a] = 0.0015 mmol, [HBpin] = 0.33 mmol, [imine] = 0.30 mmol, room temperature. Conversions were determined by ¹H NMR spectroscopy (integration of residual 6 vs. 7). Isolated yields were shown in the parentheses.</td>
<td>90 (92)</td>
</tr>
<tr>
<td>7b</td>
<td>[2a] = 0.0015 mmol, [HBpin] = 0.33 mmol, [imine] = 0.30 mmol, room temperature. Conversions were determined by ¹H NMR spectroscopy (integration of residual 6 vs. 7). Isolated yields were shown in the parentheses.</td>
<td>90 (92)</td>
</tr>
<tr>
<td>7c</td>
<td>[2a] = 0.0015 mmol, [HBpin] = 0.33 mmol, [imine] = 0.30 mmol, room temperature. Conversions were determined by ¹H NMR spectroscopy (integration of residual 6 vs. 7). Isolated yields were shown in the parentheses.</td>
<td>90 (92)</td>
</tr>
<tr>
<td>7d</td>
<td>[2a] = 0.0015 mmol, [HBpin] = 0.33 mmol, [imine] = 0.30 mmol, room temperature. Conversions were determined by ¹H NMR spectroscopy (integration of residual 6 vs. 7). Isolated yields were shown in the parentheses.</td>
<td>90 (92)</td>
</tr>
</tbody>
</table>

† Reaction was conducted at 80 °C.

![Fig. 3 Plots of ln([p-MePhCN]/[p-MePhCN]₀) versus time for the hydroboration of p-MePhCN by catalyst 2a.](image)

© 2021 The Author(s). Published by the Royal Society of Chemistry
conducted and showed a KIE value of 3.1 (ESI, Fig. S119†). The experimental evidence herein implied that the B–H bond breaking processes might be the rate-determining step.\textsuperscript{7a,10b}

Based on our observations and previous literature report-s,\textsuperscript{7a–w,15} a plausible mechanistic framework for zinc dihydrides-catalyzed nitrile hydroboration is depicted in Scheme 2. The reaction of zinc dihydride 2 with nitrile gave single insertion product 8, which then reacted with one molecule of HBpin to possibly give a zinc mixed hydride/amine 9. Finally, complex 9 underwent a σ-bond metathesis reaction with another molecule of HBpin to afford final product 5 with the regeneration of catalyst 2.

### Conclusions

In summary, the double hydroboration of nitriles to the corresponding diborated amines have been achieved with broad substrate scope by using a molecular zinc dihydride based on NHC ligand at room temperature under solvent-free conditions. Complex 2a showed extremely high activity for this transformation, affording TOFs of up to 3000 h\textsuperscript{−1}. In addition, complex 2a was also effective for the hydroboration of imines to boronated amines. The stoichiometric reaction of 2a with a nitrile led to the isolation of a single Zn–H insertion product 8, which was proved to be an active intermediate in the catalysis. Kinetic studies revealed a pseudo second-order dependence on the catalyst concentration. Further mechanistic studies and application to other catalytic reactions of this molecular zinc dihydride are underway in our laboratory.

### Conflicts of interest

There are no conflicts to declare.

### Acknowledgements

This work was supported by the National Natural Science Foundation of China (21871204).

### Notes and references


---

**Fig. 4** Plots of \(\ln k_{\text{obs}}\) vs. \(\ln[2a]\) for the hydroboration of \(p\)-MePhCN by catalyst 2a.

**Scheme 2** The proposed mechanism of hydroboration of nitriles catalyzed by 2.


6 (a) M. Itazaki and H. Nakazawa, Selective double addition reaction of an E–H bond (E = Si, B) to a C≡N triple bond of organonitriles, Molecules, 2018, 23, 2769; (d) D. Hayrapetyan and A. Y. Khalimon, Catalytic nitrile hydroboration: a route to N,N-diborylamine and uses thereof, Chem. – Asian J., 2020, 15, 2575–2587.


19 Hydroboration of N-benzylideneaniline with HBpin occurred under catalyst-free and solvent-free conditions, however, prolonged reaction time (6 h) was required to achieve a high yield. For comparisons, see ref. 18j.