



**Ligand-Free Hydroboration of Alkynes Catalyzed by Heterogeneous Copper Powder with High Efficiency**

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ARTICLE TYPE

# Ligand-free hydroboration of alkynes catalyzed by heterogeneous copper powder with high efficiency

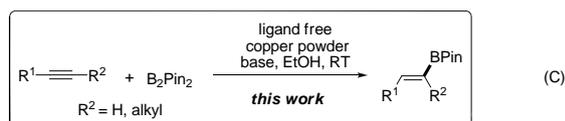
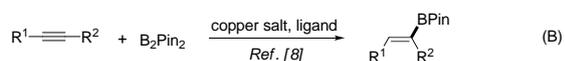
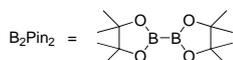
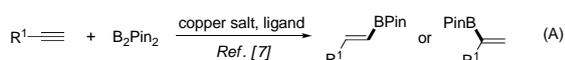
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Regioselective hydroboration of terminal and internal alkynes is realized by using 10 mol% copper powder (0.3–1 μm) at room temperature. 24 examples were efficiently converted into vinylboronates in yield up to 96% without addition of any ligand or additive.

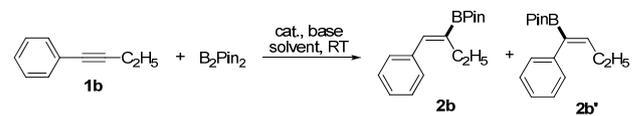
Organoboron compounds play a significant role in organic synthesis because they are generally nontoxic, stable under atmospheric condition and highly reactive.<sup>1</sup> Among them, vinylboronates have drawn much attention for they are versatile intermediates in the construction of numerous complex molecules, such as organic semiconductors and pharmaceuticals.<sup>2</sup> Transition metal-catalyzed addition of boron-containing reagents to carbon-carbon multiple bonds represents an important strategy for synthesis of organoboron compounds.<sup>3,4</sup> Notably, copper is preferred in organic synthesis for its low cost and low toxicity.<sup>5</sup> Over the past few years, big progress has been made in copper-catalyzed hydroboration of either terminal alkynes (Scheme 1A)<sup>6</sup> or internal asymmetrical alkynes (Scheme 1B)<sup>7</sup> with bis(pinacolato)diboron (B<sub>2</sub>Pin<sub>2</sub>). For example, Yun's group used CuCl as catalyst for addition of B<sub>2</sub>Pin<sub>2</sub> to disubstituted alkynes and α,β-ethylenic carbonyl compounds.<sup>7a–c</sup> Hoveyda's group reported an efficient method for the synthesis of internal (α-) vinylboronates catalyzed by NHC-Cu complex.<sup>6b</sup> Corma and Garcia's group explored CuO nanoparticles together with PPh<sub>3</sub> in the hydroboration of alkynes.<sup>6a</sup> It should be noted that most of these protocols are exclusively performed in the presence of organic ligands and proceed via homogeneous pathways.



**Scheme 1** Copper-catalyzed hydroboration of (A) terminal alkynes and (B) internal alkynes. (C) Our protocol for hydroboration of terminal and internal alkynes by heterogeneous micro copper powder

From the perspective of practical applications, heterogeneous hydroboration of alkynes which may reduce metal contamination of products and avoid the use of toxic ligands, is highly desired but has not been reported thus far. Herein, we report a ligand-free hydroboration of terminal and internal alkynes catalyzed by micro copper powder at room temperature (Scheme 1C).

**Table 1** Hydroboration of but-1-ynylbenzene: optimization of conditions<sup>a</sup>



Entry	Cat.	Base	Solvent	Yield of <b>2b</b> (%)	Yield of <b>2b'</b> (%) <sup>b</sup>
1	Cu	NaOBu <sup>t</sup>	EtOH	24	n.d.
2	Cu	LiOBu <sup>t</sup>	EtOH	61	2
3	<b>Cu</b>	<b>MeONa</b>	<b>EtOH</b>	<b>90</b>	<b>n.d.</b>
4	Cu	Cs <sub>2</sub> CO <sub>3</sub>	EtOH	56	n.d.
5	Cu	K <sub>2</sub> CO <sub>3</sub>	EtOH	66	n.d.
6	Cu	-	EtOH	trace	n.d.
7	Cu(α) <sup>c</sup>	MeONa	EtOH	61	n.d.
8	Cu(β) <sup>d</sup>	MeONa	EtOH	79	n.d.
9	Cu(γ) <sup>e</sup>	MeONa	EtOH	79	n.d.
10	-	MeONa	EtOH	8	n.d.
11	Cu	MeONa	CH <sub>2</sub> Cl <sub>2</sub>	trace	n.d.
12	Cu	MeONa	THF	trace	n.d.
13	Cu	MeONa	MeOH	67	n.d.
14	Cu <sup>f</sup>	MeONa	EtOH	29	n.d.

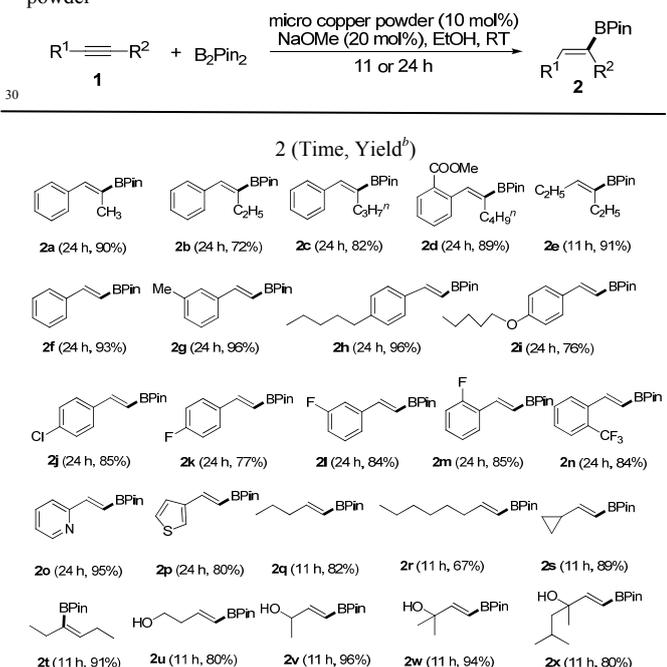
<sup>a</sup> Reaction conditions: but-1-ynylbenzene (0.5 mmol), B<sub>2</sub>Pin<sub>2</sub> (0.75 mmol), micro copper powder (0.05 mmol) (0.3–1 μm, Ningbo Guangbo New Nanomaterials Stock Co., Ltd.), base (0.1 mmol), solvent (2 mL), room temperature (~25 °C), under Ar atmosphere. <sup>b</sup> Yield was determined by GC analysis using n-tridecane as the internal standard. <sup>c</sup> Copper powder (-100 mesh, Sinopharm Chemical Reagent Beijing Co., Ltd). <sup>d</sup> Copper powder (-170+270 mesh, Alfa Aesar). <sup>e</sup> Copper powder (-625 mesh, 0.5–1.5 μm, Alfa Aesar). <sup>f</sup> Under air.

At the outset, but-1-ynylbenzene and B<sub>2</sub>Pin<sub>2</sub> were used as the model substrates for the screening of reaction conditions including catalysts, bases, solvents and atmospheres. As shown in Table 1, five bases were tested using 10 mol% micro copper powder (0.3–1 μm, Ningbo Guangbo New Nanomaterials Stock Co., Ltd.) as the catalyst, EtOH as the solvent under Ar atmosphere at room temperature (entries 1–5). Sodium methoxide (MeONa) provided the highest yield of **2b** without detection of regioisomeric product **2b'** (entry 3). No product was observed in the absence of the base (entry 6). As shown in entries 7–9, three other kinds of copper catalyst were tested: copper (α) (size: -100 mesh, Sinopharm Chemical Reagent Beijing Co. Ltd) exhibited

weaker catalytic activity than micro copper powder (cf. entries 3 and 7), copper ( $\beta$ ) and copper ( $\gamma$ ) (Alfa Aesar) of which shape and size was not as well-distributed as micro copper powder also showed less activity (cf. entries 3, 8 and 9, Figure S1). Only 8% yield was observed in the absence of catalyst (entry 10). Other solvents screened (entries 11–13) were inferior to ethanol. The yield decreased significantly when the reaction was carried out under air as compared to that under argon protection (entry 14).

After obtaining the optimum reaction conditions (using 10 mol% micro copper powder as the catalyst, 20 mol% MeONa as the base, and 2 mL EtOH as the solvent at room temperature under Ar atmosphere), the substrate scope for hydroboration of alkynes was investigated. As shown in Table 2, the examined substrates provided good to excellent yields with high regioselectivity. For internal alkynes, hydroboration occurred at the  $\beta$ -carbon to the aryl and yielded only the (*Z*)-isomers (**2a-d**, **2t**). Hydroboration of terminal alkynes led to *E*-vinylboronates via *anti*-Markovnikov and *syn*-addition of the boron reagents. For the aryl terminal alkynes, electronic effect of the substrates on the aromatic rings including neutral, electron-donating and electron-withdrawing groups did not show obvious difference in reactivity. The aliphatic terminal alkynes displayed higher reactivity than the aromatic ones, and they finished the reactions within 11 h. The hydroboration of alkynes under catalysis of micro copper powder could tolerate various functional groups including ester (**2d**), ether (**2i**), C-Cl bond (**2j**), C-F bond (**2k-m**), trifluoromethyl (**2n**), *N,S*-heterocycles (**2o**, **2p**), hydroxyl (**2u-x**) in the substrates.

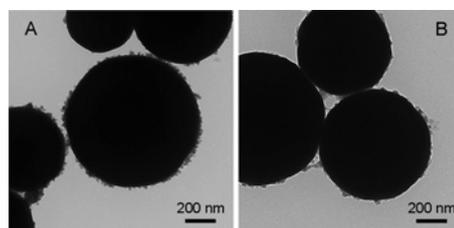
**Table 2** Hydroboration of various alkynes catalyzed by micro copper powder<sup>a</sup>



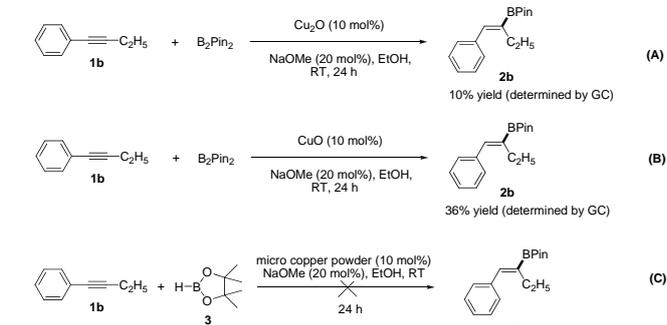
<sup>a</sup> Reaction conditions: alkyne (0.5 mmol),  $\text{B}_2\text{Pin}_2$  (0.75 mmol), micro copper powder (0.05 mmol, Ningbo Guangbo New Nanomaterials Stock Co. Ltd.), NaOMe (0.1 mmol), ethanol (2 mL), room temperature (~25 °C), reaction time (11 or 24 h), under Ar atmosphere. <sup>b</sup> Isolated yield.

To investigate if the reaction was catalyzed by heterogeneous copper, at first we studied the structural variation of the catalyst before and after the reaction by transmission electron microscopy

(TEM). As shown in Figure 1, the shape and size of the copper powder mainly remained. Moreover, the colour of the final reaction solution didn't turn to green or blue, which indicated that the catalyst had not been oxidized (Figure S2). The filtration test was then performed. The reaction solution was filtrated when the reaction proceeded at about 13% conversion and the liquid phase was allowed to react under the same condition to the final time. It turned out that the liquid phase did not continue to generate the product. Encouraged by these results, we subsequently tested the metal residue in the reaction solution by using ICP-AES. The copper concentration in the solution of the micro copper powder system was below 0.05 ppm, which was much lower than that of common  $\text{CuCl}/\text{PPh}_3$  catalyst system (33.35 ppm). Noting that copper easily undergoes surface oxidation at ambient atmosphere,<sup>8</sup> we used  $\text{Cu}_2\text{O}$  and  $\text{CuO}$  as the catalysts (Scheme 2A and 2B), and the poor yields suggested that the oxide species on the surface of micro copper powder was not essential for the catalytic activity. These evidences collectively implied the hydroboration catalyzed by micro copper powder was not under traditional homogeneous conditions.



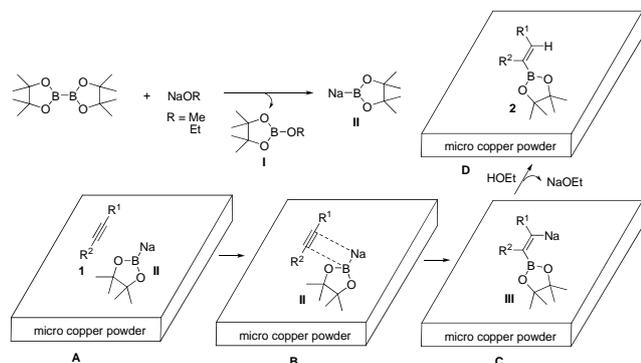
**Figure 1** TEM images of micro copper powder: (A) before reaction and (B) after reaction



**Scheme 2** (A) 10 mol%  $\text{Cu}_2\text{O}$  was used as catalyst. (B) 10 mol%  $\text{CuO}$  was used as catalyst. (C) Reaction of but-1-ynylbenzene (**1b**) and pinacolborane under our standard condition

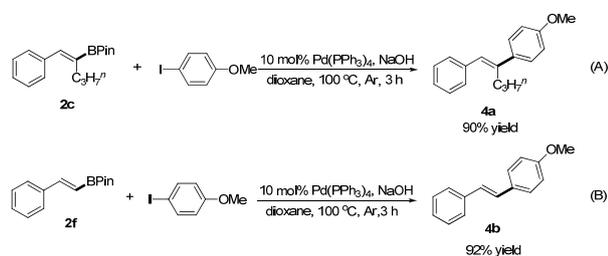
We further treated but-1-ynylbenzene with pinacolborane under our standard conditions, and the reaction did not work (Scheme 2C), indicating the reaction did not undergo a pinacolborane intermediate process. A possible mechanism for hydroboration of alkynes is therefore proposed in Scheme 3. First, reaction of NaOR (R = Me or Et) with  $\text{B}_2\text{Pin}_2$  provides **I** and **II**. Adsorption of alkyne (**1**) and **II** on the surface of micro copper powder gives **A**, and synergetic effect of **I** and **II** occurs, leading to **B** till the formation of **III**. Finally, treatment of **III** with ethanol affords the target product (**2**). The present regioselective boron addition to alkynes is in agreement with the Yun's reports under homogeneous catalysis.<sup>7a-c</sup>

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**Scheme 3** Possible mechanism for hydroboration of alkynes on the surface of copper powder

It is well known that vinylboronates are important intermediates in organic synthesis and usually used in Suzuki coupling reactions. Application of the synthesized products (Table 2) was demonstrated in Scheme 4. Coupling reactions of two synthesized compounds (**2c** and **2f**) were attempted under the catalysis of Pd(PPh<sub>3</sub>)<sub>4</sub>, and the corresponding products (**4a** and **4b**) were obtained in high yields.



**Scheme 4** Application of the synthesized products: (A) Coupling reaction of **2c** and 1-iodo-4-methoxybenzene. (B) Coupling reaction of **2f** and 1-iodo-4-methoxybenzene

In summary, we discovered that micro copper powder was a robust and efficient catalyst for the preparation of vinylboronates under heterogeneous conditions. This protocol avoids the use of any ligand or additive, and is applied to a wide spectrum of alkynes, including terminal and internal ones as well as alkynols. Moreover, compared with copper salts or copper complexes that are mainly used in hydroboration reactions, the metal contamination of the products was greatly reduced. We believe this work will greatly benefit the synthesis of organic semiconductors and drugs, further application of this heterogeneous hydroboration and mechanism study are in progress in our laboratory.

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## Notes and references

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- † Electronic Supplementary Information (ESI) available: details of synthesis procedures and characterizations of compounds by H-NMR, C-NMR, GC-MS (or ESI-MS). See DOI: 10.1039/b000000x/
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