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Transition-metal-free PhI(OAc)$_2$-promoted highly selective hydroboration of terminal alkynes under air†

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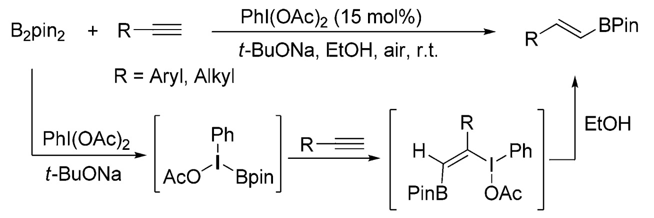
A new transition-metal-free PhI(OAc)$_2$-promoted hydroboration reaction of terminal alkynes with bis(pinacolato)diboron has been developed at room temperature under air. A series of vinyl boronates could be conveniently and efficiently obtained in moderate to good yields with good regioselectivity and stereoselectivity as well as favorable functional group tolerance. The key I–B intermediates were first demonstrated in the present reaction system that explains the proposed mechanism.

Alkenylboronates are important building blocks in the Suzuki–Miyaura cross-coupling reaction for complex molecule synthesis in organic semiconductors and pharmaceuticals.[1] The catalytic hydroboration of alkynes represents one of the most straightforward and powerful tools for the construction of alkenylboronates.[2] Over the past several years, considerable efforts have been made in this area and some transition-metal-catalyzed synthetic methods have been successfully developed, such as Cu,[3] Pd,[4] Ag,[5] Ir,[4a] Pt[3a,6] and Au[7] catalyzed addition of boron reagents to alkynes. Nevertheless, the cost, toxicity and environmental impact of these metal-catalysts might thereby limit their wide applications on a large scale in the field of synthetic and pharmaceutical chemistry.

Recently, transition-metal-free methods have attracted increasingly attention of chemists for the synthesis of alkenylboronates through direct hydroboration reactions of alkynes.[8] For instance, Sun and co-workers reported the hydroboration of terminal alkynes with bis(pinacolato)diboron using *N*-heterocyclic carbene (NHC) as the catalyst.[8a] Jin's group presented a carboxylic acid-catalyzed hydroboration of alkynes with pinacolborane at 100 °C under an argon atmosphere.[8b] In 2016, Deng described a *t*-BuOLi mediated hydroboration of terminal alkynes in toluene under argon.[8c] Nevertheless, most of those transition-metal-free methods required relatively harsh reaction conditions, inert atmosphere protection or toxic solvents. Therefore, the development of a new, simple, convenient, and environmentally-benign transition-metal-free method to access alkenylboronates is still high desirable.

On the other hand, hypervalent iodine reagents have been increasingly employed for various organic transformations due to their ready available, cost-effective and environmentally friendly properties.[9] They are generally used as stoichiometric oxidizing reagents and recognized as alternatives to highly toxic heavy-metal oxidants.[10] However, to our knowledge, only a few strategies for the reactions using a catalytic amount of hypervalent iodine reagents have been exploited, in which *m*-CPBA (*m*-chloroperoxybenzoic acid) was mostly used as a stoichiometric chemical oxidant to accomplish the catalytic cycle.[11] As our continued interests in metal-free functionalization of unsaturated hydrocarbons,[12] here, we wish to report a new PhI(OAc)$_2$-promoted highly selective hydroboration of terminal alkynes with bis(pinacolato)diboron in EtOH under transition-metal and external-oxidant free conditions. The present protocol provides an attractive and efficient approach to various *E*-vinyl boronates in moderate to good yields with favorable functional group tolerance, which does not require inert atmosphere (Scheme 1).

Initially, phenylacetylene **1a** and B$_2$Pin$_2$ **2** were used as the model substrates for the screening of reaction conditions (Table 1). In the absence of the catalyst, only 8% yield of **3a** was obtained when the reaction was performed in EtOH using



Scheme 1 PhI(OAc)$_2$-promoted hydroboration of terminal alkynes.

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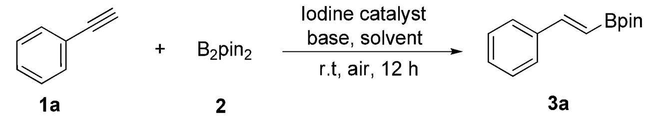
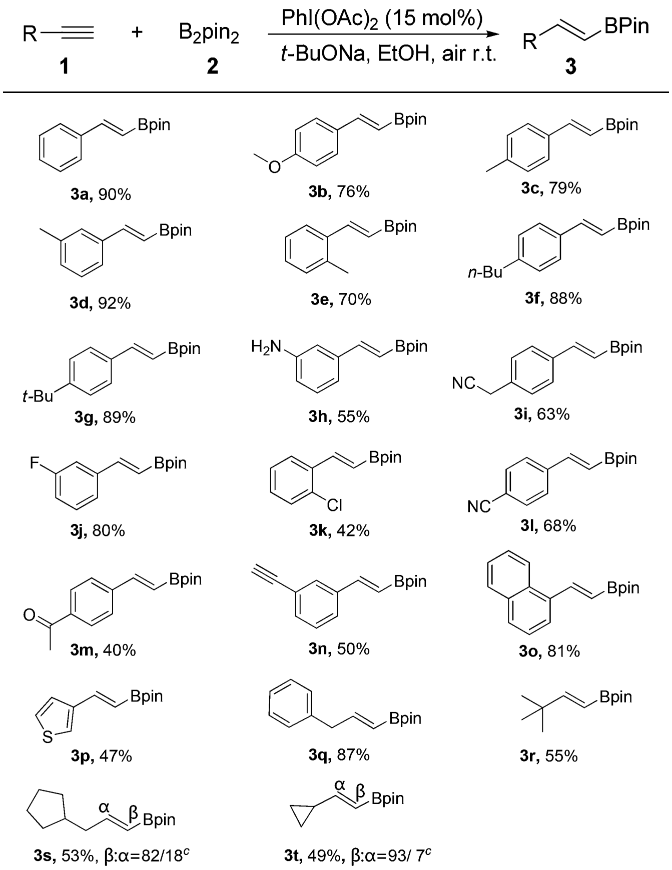
Table 1 Optimization of reaction conditions[a]



Entry	Catalyst	Base	Solvent	Yield[b] (%)
1	—	*t*-BuONa	EtOH	8
2	PhI	*t*-BuONa	EtOH	17
3	TBAI	*t*-BuONa	EtOH	13
4	KIO_3	*t*-BuONa	EtOH	35
5	$PhI(OTFA)_2$	*t*-BuONa	EtOH	36
6	DMP	*t*-BuONa	EtOH	12
7	$PhI(OAc)_2$	*t*-BuONa	EtOH	90
8	$PhI(OAc)_2$	KOH	EtOH	31
9	$PhI(OAc)_2$	DBU	EtOH	7
10	$PhI(OAc)_2$	MeONa	EtOH	50
11	$PhI(OAc)_2$	*t*-BuOLi	EtOH	5
12	$PhI(OAc)_2$	—	EtOH	0
13	$PhI(OAc)_2$	*t*-BuONa	EtOH	42[c]
14	$PhI(OAc)_2$	*t*-BuONa	EtOH	73[d]
15	$PhI(OAc)_2$	*t*-BuONa	EtOH	90[e]
16	$PhI(OAc)_2$	*t*-BuONa	MeOH	40
17	$PhI(OAc)_2$	*t*-BuONa	*n*-PrOH	71
18	$PhI(OAc)_2$	*t*-BuONa	i-PrOH	12
19	$PhI(OAc)_2$	*t*-BuONa	EtOH	82[f]
20	**$PhI(OAc)_2$**	***t*-BuONa**	**EtOH**	**90[g]**

[a] Reaction conditions: **1a** (0.5 mmol), **2** (0.75 mmol), iodine reagents (15 mol%), base (2 equiv.), solvent (4 mL), r.t., air, 12 h; TBAI: tetrabutyl ammoniuiodide; DMP: Dess–Martin periodinane; DBU: 1,5-diaza(5,4,0)undec-5-ene. [b] Isolated yields based on **1a**, isomers were not detected in crude ^1H NMR. [c] $PhI(OAc)_2$ (5 mol%). [d] $PhI(OAc)_2$ (10 mol%). [e] $PhI(OAc)_2$ (20 mol%). [f] *t*-BuONa (1.5 equiv.). [g] *t*-BuONa (1.8 equiv.).

Table 2 $PhI(OAc)_2$-promoted hydroboration of various terminal alkynes[a,b]



[a] Reaction conditions: **1** (0.5 mmol), **2** (0.75 mmol), $PhI(OAc)_2$ (15 mol%), *t*-BuONa (1.8 equiv.), EtOH (4 mL), r.t., air, 12 h. [b] Isolated yields based on **1**. [c] Determined by ^1H NMR.

t-BuONa as base at room temperature under air (entry 1). Then, various iodine reagents (15 mol%) such as PhI, TBAI, KIO_3, $PhI(OTFA)_2$, DMP, and $PhI(OAc)_2$ were tested (entries 2–7). To our delight, among those iodine reagents examined, $PhI(OAc)_2$ could provide excellent catalytic activity for the formation of product **3a** with an exclusive regioselectivity and stereoselectivity (entry 7). Subsequently, the screening of a range of bases showed that the reaction performed in the presence of *t*-BuONa was significantly better than those promoted by KOH, DBU, MeONa, or *t*-BuOLi (entries 7–11). None of **3a** was obtained when the reaction was performed in the absence of base (entry 12). Notably, the reaction efficiency was obviously low with the decreasing of $PhI(OAc)_2$ loading to 5 mol% or 10 mol% (entries 13 and 14). The further increase of $PhI(OAc)_2$ loading to 20 mol% did not improve the reaction efficiency (entry 15). The optimization of solvents demonstrated that other solvents such as MeOH, *n*-PrOH, and i-PrOH were all inferior to EtOH (entries 16–18). In addition, the reaction activity was slightly lower when the amount of *t*-BuONa was decreased to 1.5 equiv. and 1.8 equiv. of *t*-BuONa was the best choice (entries 19 and 20).

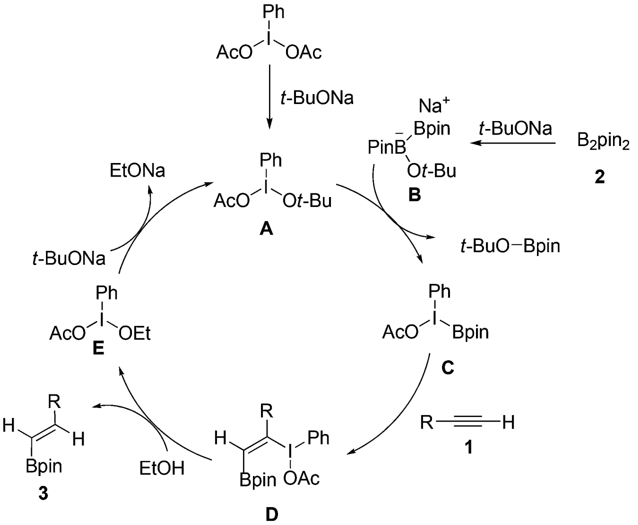
With the optimized reaction conditions in hand (Table 1, entry 20), the substrate scope of hydroboration of alkynes was investigated. As shown in Table 2, a variety of *E*-vinyl boronates could be conveniently and efficiently obtained by this novel $PhI(OAc)_2$-promoted regioselective hydroboration of terminal alkynes. Generally, both electron-rich and electron-deficient aromatic alkynes were suitable for this process, and the corresponding hydroboration products were obtained in moderate to good yields (**3b–3n**). It should be noted that various functional groups including unprotected amino, cyano, fluoro, chloro and keto groups were all compatible with this protocol to give the corresponding products (**3h–3m**), which could be employed for further transformations. In addition, when 1,3-diethynylbenzene was used in this reaction, the monoalkynyl substituted *E*-vinyl boronate **3n** was isolated in 50% yield. Furthermore, 1-ethynylnaphthalene and heterocyclic alkyne such as 3-ethynylthiophene were also tolerated in this reaction to provide the desired products (**3o** and **3p**) in 81% and 47% yields, respectively. Notably, the aliphatic terminal alkynes were all suitable substrates, and generated the corresponding products in good yields (**3q–3t**).

A radical trapping experiment was conducted to investigate the possible reaction mechanism. When TEMPO (2,2,6,6-tetramethyl-1-piperidinyloxy) was added into the model reaction of **1a** and B_2Pin_2 **2** under air or N_2 conditions, the corresponding product **3a** was still obtained in 88% or 89% yield, respectively. This result indicated that a radical process might not be involved in the present hydroboration reaction.

On the basis of our experimental results and previous reports,[13] a possible reaction pathway was proposed as shown in Scheme 2. Initially, $PhI(OAc)_2$ reacted with *t*-BuONa leading to intermediate **A**. Subsequently, the interaction of intermediate **A** with ate complex **B**, which was generated from the reaction of B_2Pin_2 with *t*-BuONa, gave the key intermediate **C**. Then, the selective addition of **C** to alkyne **1** would lead to the formation of addition intermediate **D**. Next, ethanol acted as hydrogen donor reagent to provide target product **3** and iodine(III) compound **E**. Finally, compound **E** was activated by another *t*-BuONa to accomplish the catalytic circle.

LC-MS analysis technology was employed to investigate the existence of possible intermediates described in Fig. 1. The reaction mixture was detected by LC-MS when the reaction of 4-methoxyphenylacetylene **1b** and **2** was conducted under standard conditions for **4h**. Fortunately, the $[M + H]^+$ ion peaks (m/z = 337.2, 309.1) for intermediates **A** and **E**, and the $[M + Na]^+$ ion peaks (m/z = 413.3, 545.1) for intermediate **C** and **D** were detected by LC-MS analysis, respectively (Fig. 1).

In conclusion, we have developed a new transition-metal-free $PhI(OAc)_2$-promoted hydroboration reaction of terminal alkynes with bis(pinacolato)diboron under air. A series of vinyl boronates could be conveniently and efficiently obtained in moderate to good yields with good regioselectivity and stereoselectivity at room temperature. Taking into account the following desirable features including operation simplicity, cheap catalyst, broad functional group tolerance and mild reaction conditions, this novel reaction system provides a highly attractive approach to access *E*-vinyl boronates. The present protocol also expands the scope of potential applications of hypervalent iodine reagents in the synthetic chemistry. Further investigations on increasing the reaction scope, synthetic applications and mechanistic details are undergoing in our laboratory.



Scheme 2 Proposed reaction mechanism.

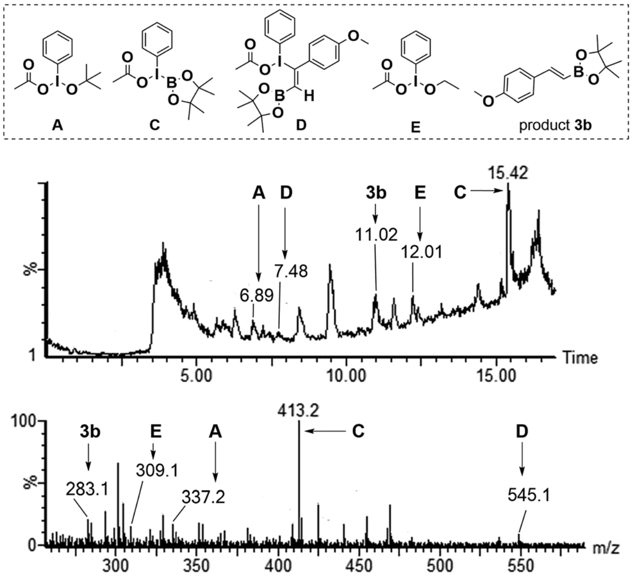


Fig. 1 LC-MS spectrum.

Acknowledgements

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