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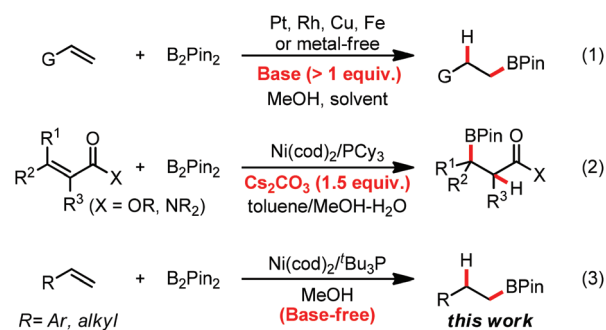
Base-free nickel-catalyzed hydroboration of simple alkenes with bis(pinacolato)diboron in an alcoholic solvent†

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A base-free nickel-catalyzed hydroboration of unreactive simple alkenes with bis(pinacolato)diboron using methanol as the hydride source under mild conditions has been developed. Methanol as the solvent proved to be critical for the base-free conditions and high reactivity. A series of linear alkylboronates were synthesized in moderate to excellent yields with high regioselectivity.

Different from air- and moisture-sensitive pinacoborane (HBPin) used in the hydroboration of π -unsaturated compounds,^{1–4} diboron reagents display better stability to air and moisture, higher functional group tolerance, and more versatile transformations, such as diboration⁵ and borylative couplings.⁶ In this context, the transition-metal-catalyzed borylation of the π -unsaturated compounds with diboron reagents, especially bis(pinacolato)diboron (B_2Pin_2), represents one of the most attractive approaches to construct organoborane, a versatile building block in organic synthesis.⁷ Recently, the development of the formal hydroboration of π -unsaturated compounds with B_2Pin_2 using alcohol as a hydride source has received increasing attention. A wide range of transition metals have been explored in this reaction, such as precious metals Pt⁸ and Rh,⁹ base metals Cu¹⁰ and Fe¹¹ and even recently non-metal catalysis¹² (Scheme 1, eqn (1)). However, all of these protocols require stoichiometric amounts of bases, like Cs_2CO_3 and KO^tBu , to facilitate the hydroboration reaction, which leads to not only high reaction cost but also to stoichiometric amounts of waste in the reaction. Accordingly, the development of a greener and more environment-friendly hydroboration of π -unsaturated compounds with B_2Pin_2 that uses a catalytic amount of base or base-free conditions would be in high demand.

On the other hand, nickel is one of the most commonly used base metals and it has been widely applied in various



Scheme 1 Hydroboration of alkenes with B_2Pin_2 .

coupling reactions,¹³ while nickel-catalyzed hydroboration reactions of alkenes with diboron reagents are quite scarce.^{14,15} The earliest example was reported by Oshima and co-workers on the hydroboration of activated alkene, α,β -unsaturated ester or amide (Scheme 1, eqn (2)).^{14a} A little later, Fernández and co-workers performed an asymmetric version with up to 98% ee.^{14b} However, a nickel-catalyzed hydroboration of simple alkene with B_2Pin_2 still remains elusive. Herein we report a nickel-catalyzed base-free hydroboration of simple alkene with B_2Pin_2 using MeOH as the hydrogen source under simple and mild conditions (Scheme 1, eqn (3)). This hydroboration method eliminates the need for excess of base and an air-moisture-sensitive metallic hydride reagent.

Initially, the reaction of styrene (**1a**) with B_2Pin_2 in toluene catalyzed using 5 mol% of $Ni(cod)_2$ and 10 mol% of PCy_3 was selected as the model reaction for the investigation. With no external proton source, there is no reaction observed, not even diboration (Table 1, entry 1). When one equivalent of methanol was added, only trace amounts of the product with sole anti-Markovnikov selectivity were obtained (entry 2). We reasoned that low yield could have resulted from the slow transmetalation of the alkylnickel species; so we proposed to increase the amount of methanol to accelerate this step. Pleasingly, more than one equivalent of methanol did improve

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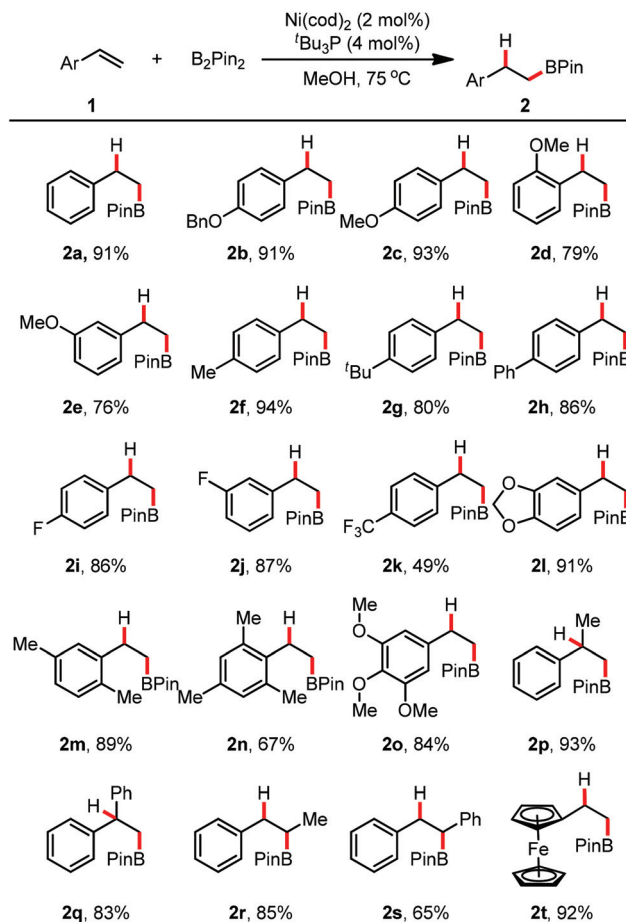
Table 1 Conditions optimization

Entry	Ligand	Solvent	Yield ^a (%)
1	Cy ₃ P	Toluene	0
2	Cy ₃ P	Toluene/MeOH (1 eq.)	Trace
3	Cy ₃ P	Toluene/MeOH (2 eq.)	4
4	Cy ₃ P	Toluene/MeOH (5 eq.)	7
5	Cy ₃ P	Toluene/MeOH (10 eq.)	32
6	Cy ₃ P	Toluene/MeOH (20 eq.)	34
7	Cy ₃ P	MeOH	58
8 ^b	Cy ₃ P	MeOH	49
9 ^c	Cy ₃ P	MeOH	58
10	Cy ₃ P	EtOH	38
11	Cy ₃ P	ⁿ PrOH	Trace
12	Cy ₃ P	ⁱ PrOH	Trace
13	Cy ₃ P	CF ₃ CH ₂ OH	0
14	^t Bu ₃ P	MeOH	32
15	^t Bu ₃ P	MeOH	97
16 ^d	^t Bu ₃ P	MeOH	95
17 ^e	^t Bu ₃ P	MeOH	88
18	^t Bu ₃ P	H ₂ O	59
19	PPh ₃	MeOH	26
20	dppe	MeOH	12
21	IPr	MeOH	14

^a Conditions: Styrene (0.5 mmol), B₂Pin₂ (0.55 mmol), solvent (1 mL), at 75 °C under N₂ for 10 h, and ¹H NMR yield using CH₂Br₂ as the internal standard. ^b Cs₂CO₃ (1 equiv.). ^c KO^tBu (1 equiv.). ^d Ni(cod)₂ (2 mol%) and ^tBu₃P (4 mol%). ^e Ni(cod)₂ (1 mol%) and ^tBu₃P (2 mol%).

the reaction significantly (entries 3–6). Ten equivalents of methanol afforded the borylated product in 32% yield (entries 5 and 6). And when methanol was used as the solvent, a better yield was provided (58%, entry 7). In this case, additional bases, whether Cs₂CO₃ or KO^tBu, showed no accelerating effect on the reaction at all (entries 8 and 9). This result demonstrated for the first time that the use of alcoholic solvent could significantly accelerate this reaction and completely avoid the use of stoichiometric amounts of base. Notably, the structure of the alcohol proved critical to the reaction. Neither the longer-chain alcohol (ethanol, normal propanol and isopropanol) nor the more acidic alcohol (trifluoroethanol) gave good yields (entries 10–13). Considering that the ligand often plays a vital role in nickel-catalyzed coupling reactions, we next screened a series of phosphine and carbene ligands to optimize the reaction conditions (entries 14–21). Tri(*tert*-butyl) phosphine (entry 15) was shown to be the optimal one, providing the corresponding product in 97% yield. And in this case, even decreasing the loadings of the catalyst to 2 mol% and 1 mol% did not have a significant effect on the reaction yield (entries 16 and 17). Furthermore, under the optimal conditions, water was also found to be a suitable solvent for this reaction, providing the desired product in 59% yield (entry 18). Other common ligands, such as triarylphosphines, bisphosphines and carbenes, were not suitable for this reaction.

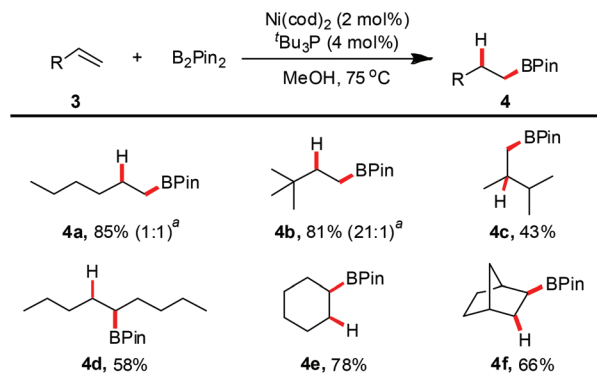
With the optimal conditions in hand, a variety of substituted styrene derivatives were investigated (Scheme 2). Various



Scheme 2 Base-free hydroboration of arylalkene. Conditions: Arylalkene (1.0 mmol), B₂Pin₂ (1.1 mmol), MeOH (2 mL), at 75 °C under N₂ for 10 h, and isolated yield for all the products.

electron-donating groups on different positions of the aryl ring of styrene, such as BnO (**2b**), MeO (**2c–2e**), Me (**2f**), ^tBu (**2g**) and Ph (**2h**), were well tolerated to deliver the corresponding product in good to excellent yields. Although the electron-withdrawing group, F (**2i** and **2j**), also gave a very good yield, a more electron-deficient group, CF₃ (**2k**), greatly deactivated this reaction, providing the desired product in 49% yield. Multisubstituted aryl olefins also proved to be good substrates (**2l–2o**); especially the steric-hindered mesityl olefin (**2n**) still worked well to produce 67% yield. Surprisingly, more challenging olefins, steric-hindered 1,1-disubstituted olefins (**2p** and **2q**) and 1,2-disubstituted olefins (**2r** and **2s**), were compatible with the current method, providing the corresponding products in 65–93% yields. Notably, ferrocenyl alkene also proved to be a good substrate and afforded the desired product in 92% yield (**2t**).

Next, we examined alkyl olefins under the optimized reaction conditions (Scheme 3). Owing to the relatively low reactivity of alkyl olefins, an external base is often required to promote their hydroboration with B₂Pin₂; otherwise low yields would be obtained or no reaction would occur. However, our alcohol-promoted, nickel-catalyzed protocol was still well com-

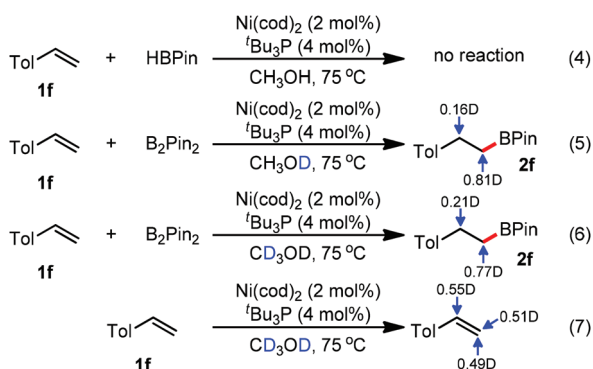


Scheme 3 Base-free hydroboration of alkylalkene. Conditions: Alkene (1 mmol), B_2Pin_2 (1.1 mmol), MeOH (2 mL), at 75 °C under N_2 for 10 h, and isolated yield for all the products. ^a Determined using GC analysis.

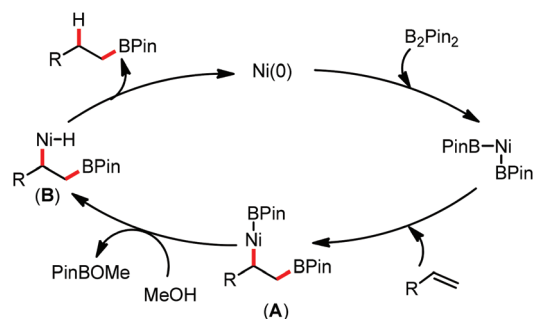
patible with alkyl olefins, like 1-hexene (**4a**) and 3,3-dimethylbut-1-ene (**4b**), providing the corresponding products in very good yields, while the product selectivity was highly dependent on the steric hindrance of the substituted group. For example, 1-hexene with a sterically less-hindered alkyl group led to regioselective isomers in almost 1:1 ratio, but more sterically hindered 3,3-dimethylbut-1-ene elevated the ratio to 21:1. Gratifyingly, disubstituted olefins, either 1,1-disubstituted alkyl olefin (**4c**), or symmetrical 1,2-disubstituted alkyl olefin (**4d–4f**) also worked well under the current conditions, providing a completely and solely regioselective borylated product. All these characteristics, including low catalyst loading, base-free conditions and a broad substrate scope, demonstrate that the current nickel-catalyzed base-free hydroboration is a practical and useful synthetic method.

To further understand the mechanism of this reaction, we conducted some additional mechanistic reactions (Scheme 4). Firstly, *p*-methylstyrene **1f** was treated with HBPiPin under the optimized conditions, but there was no reaction and only the starting alkene was fully recovered (eqn (4)).

This suggested that the current reaction would not take place through HBPiPin that could be formed *in situ* during the course of the reaction. In addition, no reaction occurred in the absence of the nickel catalyst, suggesting that the phosphine



Scheme 4 Mechanistic experiments.



Scheme 5 Proposed mechanism.

ligand itself would not catalyse this reaction.^{12b} Secondly, two isotope-labelling experiments were conducted to track the hydride transfer pathway. Using CH_3OD as the solvent (eqn (5)), 0.81 D was observed at the position adjacent to the boron atom and 0.16 D was observed at the benzylic position. Using CD_3OD as the solvent (eqn (6)), a similar distribution of deuterium was presented, which implied that all hydrides that transferred into the product came from the proton of methanol, not the α -hydride of methanol. Thirdly, to clarify whether that deuterium exchange could happen before boron insertion, a deuterium-labelling experiment was performed. *p*-Methylstyrene **1f** was mixed with CD_3OD under the optimal conditions without B_2Pin_2 (eqn (7)). Deuterium scrambling in all the three positions of alkene was finally observed, suggesting that the equilibrium of Ni-H insertion and β -H elimination in styrene could occur before the boron insertion into styrene, and thus the final deuterium scrambling of the product would appear.

Based on these experiments, we proposed a plausible mechanism for the current reaction. As shown in Scheme 5, the oxidative addition of nickel with B_2Pin_2 and the subsequent insertion into styrene results in intermediate **A**.¹⁶ The transmetalation of **A** with methanol produces the intermediate **B**, which delivers the desired product through a reductive elimination.

Conclusions

In summary, we have developed a base-free Ni-catalyzed hydroboration of simple alkene with B_2Pin_2 . The use of methanol solvent proved to be critical for the reaction's success and the elimination of stoichiometric amounts of base. Low catalyst loading, non-toxic nickel metal, base-free conditions, and high regioselectivity for styrene derivatives demonstrated that the current reaction is a useful and environment-friendly synthetic method. Efforts to further enhance the regioselectivity of the sterically less-hindered alkyl alkene are underway in the lab.

Conflicts of interest

There are no conflicts to declare.

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