


Cite this: *RSC Adv.*, 2022, 12, 9815

Palladium-catalyzed hydroboration reaction of unactivated alkynes with bis (pinacolato) diboron in water†

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Received 17th December 2021
Accepted 14th March 2022

DOI: 10.1039/d1ra09136k

rsc.li/rsc-advances

A highly efficient and mild palladium-catalyzed hydroboration of unactivated internal alkynes in water is described. Both aryl- and alkyl-substituted alkynes proceeded smoothly within the reaction time to afford the desired vinylboronates in moderate to high yields. Bis (pinacolato) diboron was used to afford α - and β -hydroborated products in the presence of HOAc. These reactions showed high reactivities and tolerance, thus providing a promising method for the synthesis of alkenyl boron compounds.

Introduction

In the past few decades, organoboron compounds have received extensive attention due to their diverse biological activities and important synthetic intermediates in the fields of organic synthesis, materials science and drug development, especially as important synthetic intermediates in organic synthesis, the versatility shown by the structure is very eye-catching.^{1,2} Organoboron compounds could be used as essential carbon nucleophiles for the introduction of functional groups and the C–C bond formation process such as Suzuki–Miyaura coupling and Petasis reaction. The current research provides numerous feasible and effective new methods for preparing organoboron compounds, such as asymmetric catalytic reaction to prepare a chiral borane. In this circumstance, vinyl boronates, which are versatile organic synthetic intermediates, are now gaining increasing attention and have been widely used in various carbon–carbon bond forming reactions.³ Compared with the previous methods that used organic halides (I, Br, Cl) as reagents, our method of using organic boron reagents is more effective for the formation of C–C bonds and direct hydroboration reactions. High-yield products can be obtained by the method. The method we developed is very compatible with various functional groups.⁴ The organoboron reagent can be used as a necessary carbon nucleophile in the reaction of introducing functional groups and the formation of C–C bonds (such as Suzuki–Miyaura coupling and Petasis reaction); it is an

excellent borohydride reagent.⁵ It is very important to develop synthetic methods for organoboron compounds because these compounds can be directly used in various transformations, such as the construction of C–C bonds and C–B bonds.⁶

Considerable attention was focused on alkenylboron compounds, whose versatility has been demonstrated by the stereodefined construction of valuable multi-substituted alkenes including biologically active molecules, natural products, and functional materials.⁷ Cobalt,⁸ ruthenium,⁹ aluminum,¹⁰ copper,¹¹ iron,¹² manganese,¹³ and ytterbium¹⁴ were used in the hydroboration reaction of alkenes recently. For example, oxazolinyl phenyl picolinic acid amide as a ligand, styrene was subjected to a highly Markovnikov selective hydroboration reaction under iron catalysis to provide the branched borohydride product (Scheme 1, eqn (1)),^{15a} and Jiang *et al.* have successfully developed the regioselective palladium(II)-catalyzed hydroboration of aryl alkenes with B₂pin₂.^{15b} Alkenyl boron reagents are ubiquitous in synthesis and very important in stereospecific cross-coupling reactions to generate olefins. The hydroboration of alkynes is a useful and concise method for the preparation of alkenyl boranes, which are versatile organic building blocks in subsequent couplings.¹⁶ For example, Arase and Hoshi reported that at room temperature, in THF, Cy₂BH and 9-BBN catalyzed the regioselective *cis* hydroboration reaction of alkynes, thereby preparing the *E*-alkenyl pinacol borate in high yields without being polluted by metal catalysts.^{17a} In the past two decades, the Arase–Hoshi R₂BH-catalyzed alkyne hydroboration reaction has been widely used (Scheme 1, eqn (2)–(4)).^{17b–d} Recently, the groups of Yun Sawamura and Hoveyda have made great contributions to the borohydride reaction with Cu as a catalyst. In the case of adding MeOH, the organoboron reagent combined with α,β -unsaturated carbonyl compounds,¹⁸ olefins¹⁹ and alkyne²⁰ underwent an addition reaction, respectively.

In general, the type of alkyne insertion in the transition metal-catalyzed borohydride reaction determines the *cis* configuration

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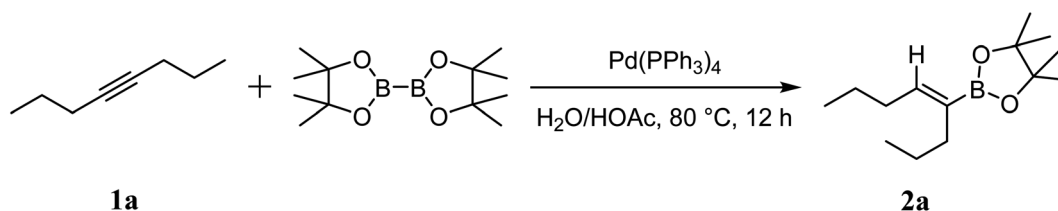
† Electronic supplementary information (ESI) available: Experimental procedures, analytical data, and copies of ¹H, ¹³C spectra (PDF). See DOI: 10.1039/d1ra09136k

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Table 1 Optimization of the reaction conditions using 4-octyne **1** and bis(pinacolato)-diboron **2**^a

Entry	Catalysts	Solvents	Temperature	Reaction time	Yield ^b (%)
1	Pd(PPh ₃) ₄	THF/HOAc	80 °C	12 h	45
2	Pd(PPh₃)₄	H₂O/HOAc	80 °C	12 h	58
3	Pd(PPh ₃) ₄	MeOH/HOAc	80 °C	12 h	52
4	Pd(PPh ₃) ₄	EA/HOAc	80 °C	12 h	50
5	Pd(PPh ₃) ₄	H ₂ O/CF ₃ CO ₂ H	80 °C	12 h	12
6	Pd(PPh ₃) ₄	H ₂ O/PTSA·H ₂ O	80 °C	12 h	5
7	Pd(PPh ₃) ₄	H ₂ O/EtCO ₂ H	80 °C	12 h	39
8	Pd(PPh ₃) ₄	DMF/HOAc	80 °C	12 h	48
9	Pd(PPh ₃) ₄	HOAc	80 °C	12 h	23
10	Pd(PPh ₃) ₄	H ₂ O	80 °C	12 h	12
11	Pd(OAc) ₂	H ₂ O/HOAc	80 °C	12 h	Trace
12	Pd ₂ (dba) ₃	H ₂ O/HOAc	80 °C	12 h	Trace
13	—	H ₂ O/HOAc	80 °C	12 h	0
14	Pd(PPh ₃) ₄	H ₂ O/HOAc	60 °C	12 h	37
15	Pd(PPh ₃) ₄	H ₂ O/HOAc	70 °C	12 h	51
16	Pd(PPh ₃) ₄	H ₂ O/HOAc	90 °C	12 h	57
17	Pd(PPh ₃) ₄	H ₂ O/HOAc	80 °C	3 h	32
18	Pd(PPh ₃) ₄	H ₂ O/HOAc	80 °C	6 h	41
19	Pd(PPh ₃) ₄	H ₂ O/HOAc	80 °C	18 h	57
20	Pd(PPh ₃) ₄	H ₂ O/HOAc	80 °C	24 h	59

^a Reaction conditions: Pd catalyst (5%), solvent (1.5 mL), **1a** (1 eq.), B₂(pin)₂ (2 eq.), HOAc (4 eq.). ^b Isolated yield.

obtained with longer reaction time periods of 18 h and 24 h (Table 1, entry 19 and 20). With an optimal reaction protocol in hand, numerous unactivated alkynes were examined.

As shown in Table 2, Pd(PPh₃)₄ efficiently catalyzed the hydroboration reactions of various alkynes and B₂(pin)₂ in H₂O at 80 °C to afford the corresponding products in moderate to good yields. Both aryl- and alkyl-substituted alkynes proceeded smoothly within the reaction time to provide the desired products in good to high yields (Table 2, entries 1 and 2). With 1-phenyl-1-butyne and 1-phenyl-1-pentyne substrates, under the optimal catalytic conditions, α -vinyl boronate could be exclusively furnished in excellent yields of 85% and 70%, respectively (Table 2, entries 5 and 6). For the activated substrates (Table 2, entries 7 and 8), the reaction proceeded smoothly with 68% and 60% yields to afford the desired products. When 1-phenyl-1-heptyne and 1-phenyl-1-propyne were used as substrates, under the optimal catalytic conditions, the desired products were provided with yields of 62% and 60%, respectively (Table 2, entries 11 and 13). For **1j**, the corresponding product **2j** was produced under the structure of the 1,4-bisarylation group. The reaction proceeded smoothly with a yield of 74%. It further demonstrated that this reaction had a wide range of substrates. It was gratifying to find that for the substrate **1l**, the reaction delivered only one regioisomer **2l** (Table 2, entries 12), which



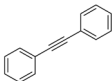

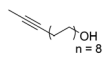

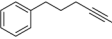

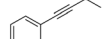



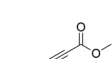
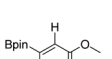

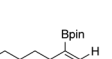
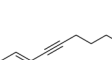
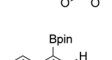

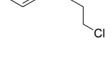

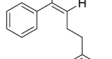
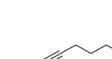
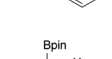

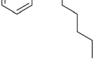
may be due to the complexation effect of the *ortho* olefin substituent with the palladium catalyst.

It is exciting to find that with the substrate **1l**, the reaction delivered only one regioisomer **2l** (Table 2, entry 12) and **2l** was in the *Z* configuration. Therefore, this result can inspire us to use this type of substrate to produce the product we need, without producing other by-products, and to conduct a strongly targeted synthesis. Such a high yield product can be applied in industrial synthesis. Furthermore, functional groups such as hydroxyl, ester and halide were all tolerated in this reaction, which further proved the high compatibility of this transformation (Table 2, entries 3 and 7–9).

On the basis of our experiments as well as literature precedents,^{15b} we proposed the mechanism, which is shown in Scheme 2. The palladium(0) complex initially delivers the palladium hydride complex (intermediate **1**) after the reaction with acetic acid, and the hydrogen atom transfers from AcOH to palladium, providing the [PdH] species **1**. Next, intermediate **1** subsequently produces intermediate **2** after complexation and migratory insertions with alkyne **1**. Then, intermediate **2** undergoes a transmetalation with B₂pin₂ and furnishes intermediate **3**. Lastly, intermediate **3**, after a reductive elimination would generate the desired product **II** and regenerate the palladium(0) complex to close the catalytic cycle.

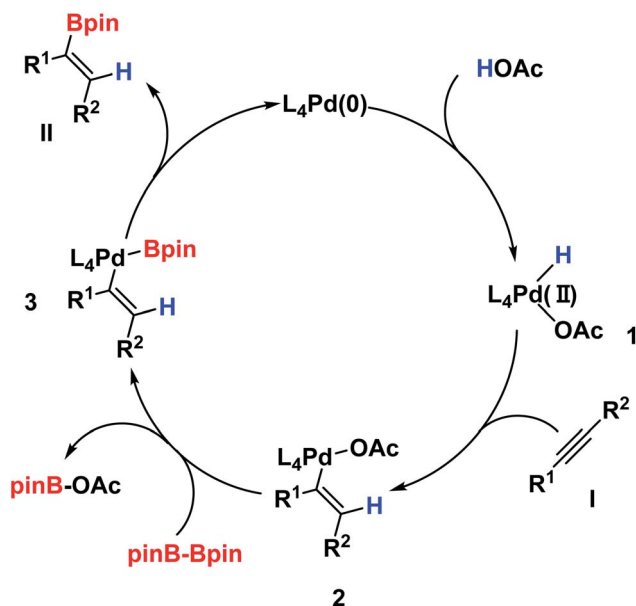


Table 2 Screening the reactivity of various alkynes in the boron addition catalyzed by Pd(PPh₃)₄^a

$R^1 \equiv R^2 + \text{Bpin-Bpin} \xrightarrow[\text{H}_2\text{O/HOAc, 80 } ^\circ\text{C, 12 h}]{\text{Pd(PPh}_3)_4} \begin{matrix} \text{Bpin} \\ \\ R^1 - C = C - H \\ \\ R^2 \\ \text{A} \end{matrix} + \begin{matrix} H \\ \\ R^1 - C = C - \text{Bpin} \\ \\ R^2 \\ \text{B} \end{matrix}$				
1a-1m		2a-2m		
Entry	Alkyne	Product ^b	Yield ^c (%)	A ^d : B
1	 1a	 2a	58	—
2	 1b	 2b	70	—
3	 1c	 2c	68	52 : 48
4	 1d	 2d	75	60 : 40
5	 1e	 2e	85	75 : 25
6	 1f	 2f	70	84 : 16
7	 1g	 2g	68	90 : 10
8	 1h	 2h	60	84 : 16
9	 1i	 2i	62	86 : 14
10	 1j	 2j	74	75 : 25
11	 1k	 2k	60	75 : 25
12	 1l	 2l	61	100 : 0
13	 1m	 2m	62	53 : 47

^a Reaction conditions: 5 mol% Pd(PPh₃)₄, 1 equiv. Alkyne, 2 equiv. B₂pin₂, 4 equiv. HOAc in 1.5 mL H₂O at 80 °C for 12 h. ^b The drawing structure is the major regioisomer. ^c Isolated yield. ^d Determined by ¹H-NMR of the crude product.





Scheme 2 Proposed reaction mechanism.

Conclusion

In summary, we have developed an efficient procedure for the hydroboration reactions with unactivated alkynes based on a palladium catalyst, which provides a route for the synthesis of α -borylated- α,β -alkenes in water. These studies suggested that H_2O is a suitable solvent for the palladium-catalyzed hydroboration reaction. Studies are underway to extend the application of the boron derivatives in organic syntheses.

Author contributions

MY, YY, WM and GZ executed the synthesis of the compounds and analysis of spectral data. MY, YY, YY and DL conceptualized the research work, wrote the main text. MY, YF, YW and FZ were involved in troubleshooting the synthesis and writing the ESI.† YY and DL provided the funding acquisition. All authors reviewed the manuscript and the ESI.†

Conflicts of interest

The authors declare no conflicts of interest.

Acknowledgements

This work was supported by the Wuhan Textile University (017/202127, 017/202161J), the Nanyang Technological University, Ministry of Education (No. M45110000), and A*STAR S. E. R. C. (No. 0721010024) and the Hubei Superior and Distinctive Discipline Group of "Mechatronics and Automobiles" (No. XKQ2019009).

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