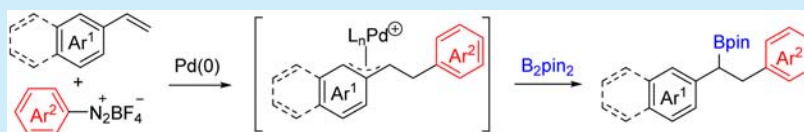


Pd-Catalyzed Regioselective Arylboration of Vinylarenes

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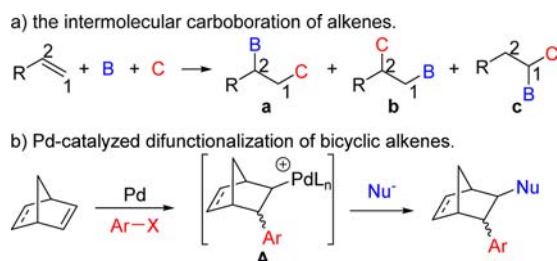
Supporting Information



ABSTRACT: A palladium-catalyzed 1,2-arylboration of vinylarenes with aryldiazonium tetrafluoroborates and bis(pinacolato)-diboron has been disclosed. It is reported for the first time that styrene derivatives can be successfully employed as good substrates for 1,2-arylboration of alkenes. Mechanistic studies suggest that no Pd–H reinsertion occurred under our standard conditions, which is the key for the success of this transformation.

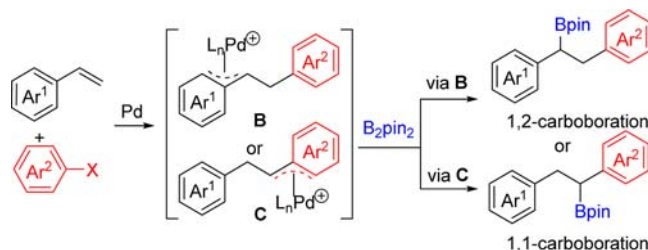
Transition-metal-catalyzed difunctionalization of alkenes has become an efficient and expedient strategy to construct molecular complexities in one step in organic synthesis.¹ Among them, carboboration of alkenes has attracted great attention since diversified alkyl boronates, which are important intermediates and building blocks in organic chemistry, were found to be readily accessible.² Significant progress on transition-metal-catalyzed carboboration has been achieved recently by Fu,^{3a} Toste,^{3b} Cheng,^{3c} Yoshida,^{3d} Hoveyda,^{3e} Brown,^{3f} Liao,^{3g} Semba and Nakao,^{3h} et al., rendering 1,2-carboboration (a),^{3a} 2,1-carboboration (b),^{3d–h} and 1,1-carboboration (c)^{3b} products (Scheme 1a). Recently,

Scheme 1. Transition-Metal-Catalyzed Carboboration of Alkenes



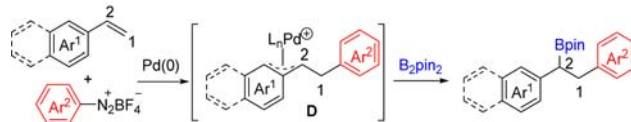
our group reported a Pd-catalyzed arylboration of unactivated bicyclic alkenes through the Catellani intermediate A⁴ (Scheme 1b).⁵ However, in all of these pioneering examples, 1,2-arylboration of vinylarenes has not been investigated due to the unselectivity and complexity of the reactions: two isomers via different π -allyl-Pd intermediates, which come from a tandem process of high-oxidative-state Pd-aryl Heck insertion of vinylarenes, β -hydride elimination, and reinsertion of Pd–H, always exist owing to their similarity (Scheme 2).^{6,3b} How to find a good way to differentiate the two intermediates and make one of them stable enough for further coupling becomes the

Scheme 2. Challenges in Pd-Catalyzed Arylboration of Vinylarenes



key to solving this challenge. We envisioned that the electron effects of Ar¹ and Ar² will highly influence the stability of two intermediates due to their cationic properties.⁷ Therefore, vinylnaphthalenes come to mind: compared to benzene counterparts, naphthalene has more room to accommodate the cationic charge.^{7a} Herein, we report the first Pd-catalyzed 1,2-arylboration of vinylarenes under very mild conditions with high regioselectivity and excellent functional group tolerance.

This work: Pd(0)-catalyzed highly regioselective intermolecular 1,2-arylboration of vinylarenes



To evaluate our hypothesis, we commenced our study with 2-vinylnaphthalene (1a), 4-fluorophenyldiazonium tetrafluoroborate (2a), and B₂pin₂ as substrates (Table 1). Starting with Pd₂(dba)₃ as the catalyst and Na₂CO₃ as the base in *t*-amyl-OH, to our delight, the desired product 3aa was formed in 56% GC yield, which indicated 1,2-arylboration product 3aa

Received: August 24, 2016

Published: October 27, 2016

Table 1. Development of Optimized Conditions for 1,2-Arylboration^a

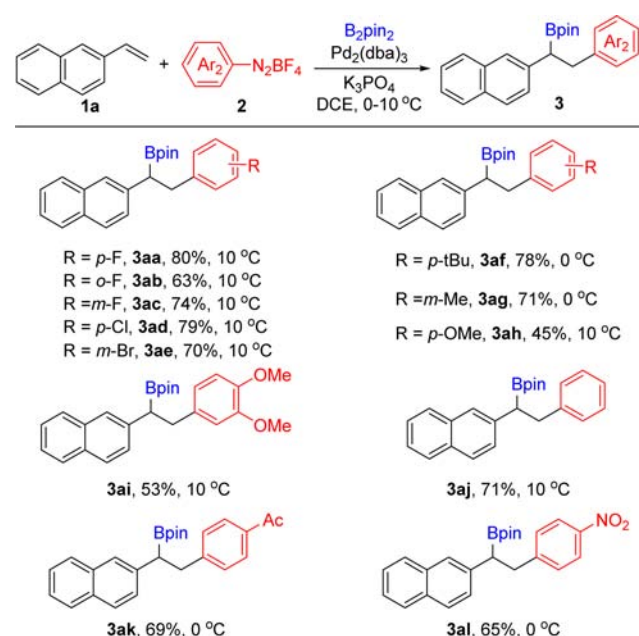
entry	base	solvent	temp (°C)	3a ^c (%)	4aa ^c (%)	5a ^c (%)
1	Na ₂ CO ₃	<i>tert</i> -amyl-OH	60	56	22	21
2	K ₂ CO ₃	<i>tert</i> -amyl-OH	60	59	20	20
3	Cs ₂ CO ₃	<i>tert</i> -amyl-OH	60	41	20	22
4	NaOAc	<i>tert</i> -amyl-OH	60	51	13	14
5	K ₃ PO ₄	<i>tert</i> -amyl-OH	60	61	18	20
6	K ₂ HPO ₄	<i>tert</i> -amyl-OH	60	52	21	23
7	KOH	<i>tert</i> -amyl-OH	60	57	21	21
8	K ₃ PO ₄	THF	60	59	18	17
9	K ₃ PO ₄	EtOH	60			
10	K ₃ PO ₄	DMF	60			
11	K ₃ PO ₄	dioxane	60	35	11	9
12	K ₃ PO ₄	toluene	60	69	14	13
13	K ₃ PO ₄	<i>p</i> -xylene	60	22	0	0
14	K ₃ PO ₄	DCE	60	76	6	7
15	K ₃ PO ₄	DCE	25	87	7	6
16	K ₃ PO ₄	DCE	10	90	5	3
17 ^b	K ₃ PO ₄	DCE	10	89 (80) ^d	5	5

^aReaction conditions: 2-vinylnaphthalene **1a** (0.2 mmol), aryldiazonium salt **2a** (1 equiv), B₂pin₂ (1.5 equiv), base (1 equiv), solvent (1 mL), N₂, 12 h. ^bB₂pin₂ (1.1 equiv). ^cGC yield. ^dIsolated yield.

predominated over hydroboration product **5a**, Heck product **4aa**, and trace Suzuki–Miyaura borylative product (Table 1, entry 1).

Further base screening suggested that K₃PO₄ was optimal compared to K₂CO₃, Cs₂CO₃, NaOAc, K₂HPO₄, and KOH (Table 1, entries 2–7). Subsequently, solvent optimization demonstrated that DCE was the best one among THF, EtOH, DMF, dioxane, toluene, and *p*-xylene (Table 1, entries 8–14). Interestingly, a significant improvement in yield of **3aa** was observed when the temperature was decreased from 60 to 10 °C (GC yield from 76 to 90%), and superior selectivity of the desired product over other byproducts was also detected simultaneously (Table 1, entry 14–16). When the loading of B₂pin₂ was dropped to 1.1 equiv, the yield of desired product **3aa** was not affected and obtained in 89% in GC with 80% isolated yield (Table 1, entry 17). It is of note that when aryl iodide and triflate such as PhI and PhOTf took place of aryldiazonium salt **2a** no reaction occurred under the current conditions.

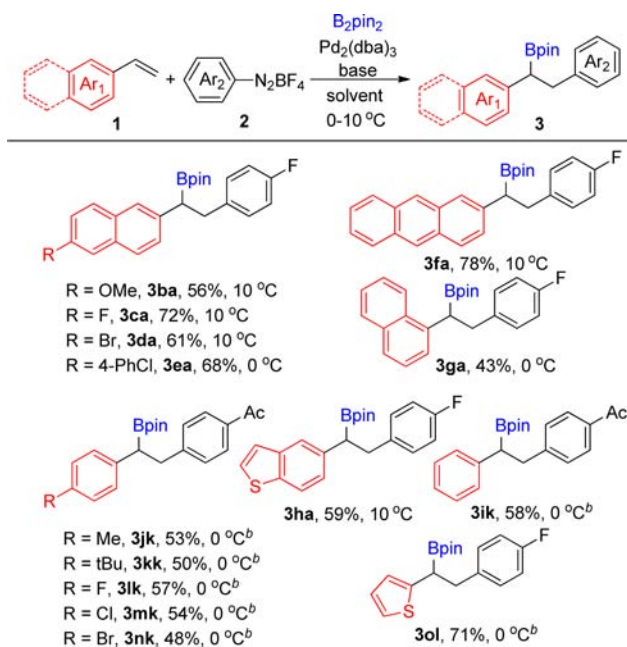
With the optimized conditions in hand, we next turned our attention to the substrate scope of this palladium-catalyzed regioselective 1,2-arylboration. A very broad range of substituted aryldiazonium tetrafluoroborates (**2a–n**, Scheme 3) with **1a** and B₂pin₂ could be smoothly converted into the corresponding 1,2-arylboration products with high regioselectivity. To our delight, halo-substituted aryldiazonium tetra-

Scheme 3. Substrate Scope of Aryldiazonium Tetrafluoroborates **2**^a

^aReaction conditions: 2-vinylnaphthalene (**1a**) (0.2 mmol), aryldiazonium salt **2a** (1 equiv), Pd₂(dba)₃ (5 mol %), B₂pin₂ (1.1 equiv), K₃PO₄ (1 equiv), DCE (1 mL), N₂, 12 h, isolated yield.

fluoroborates were demonstrated to be well-tolerated under our standard conditions, and *para*, *meta*, and *ortho* substitutions all provided the corresponding products in good yields (**3aa–ae**, Scheme 3) that provide feasibility for further structural manipulation. Moreover, aryldiazonium tetrafluoroborates with electron-rich substituents (like *t*Bu, Me, and MeO) on the aromatic rings could proceed smoothly to afford the corresponding 1,2-arylboration products in moderate to good yields (**3af–aj**, Scheme 3), and aryldiazonium tetrafluoroborates bearing strong electron-withdrawing groups (such as ketone and nitro) were found to be good candidates as well for this transformation, rendering **3ak** and **3al** in 69% and 65% yields, respectively.

Subsequently, the scope of vinylarenes was evaluated with (4-fluorophenyl)diazonium tetrafluoroborate (**2a**) or (4-acetylphenyl)diazonium tetrafluoroborate (**2k**) under the standard conditions (Scheme 4). To our delight, 2-vinylnaphthalenes bearing both electron-rich and electron-poor substituents worked well with (4-fluorophenyl)diazonium tetrafluoroborate (**2a**) and B₂pin₂, affording the corresponding desired products in decent yields (**3ba–ea**). Both 2-vinylnaphthalene (**1f**) and 1-vinylnaphthalene (**1g**) were good candidates for this transformation as well. Furthermore, heteroaromatics, such as 5-vinylbenzo[*b*]thiophene (**1h**), were compatible under the standard conditions, leading to the desired product **3ha** in 59% yield. To our delight, this catalytic system could be employed for styrenes, whose preparation has met with hurdles and challenges for 1,2-carboboration products in previous reports,⁸ after simple condition optimization (see Table S1 for details). Byproducts arising from Heck reaction or hydroboration reactions also existed in these reactions; however, interestingly, 1,1-arylboration product was not detected, which is in sharp contrast to the precedents. Both electron-donating and electron-withdrawing groups were

Scheme 4. Substrate Scope of Vinylarenes **1**^a

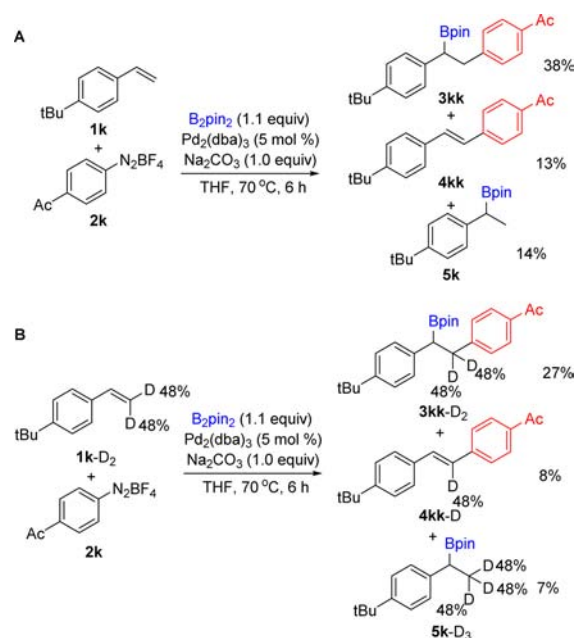
^aReaction conditions: 2-vinylarene **1** (0.2 mmol), aryldiazonium salt **2** (1 equiv), Pd₂(dba)₃ (5 mol %), B₂pin₂ (1.1 equiv), K₃PO₄ (1 equiv), DCE (1 mL), N₂, 12 h, isolated yield. ^bReaction conditions: 2-vinylarene **1** (0.2 mmol), aryldiazonium salt **2** (1 equiv), Pd₂(dba)₃ (15 mol %), B₂pin₂ (1.1 equiv), Na₂CO₃ (1 equiv), THF (1 mL), N₂, 24 h, isolated yield. Using 4-acetylphenyldiazonium tetrafluoroborate was convenient for isolation, and 1,1-arylboration product was not observed when other aryldiazonium salts were used.

introduced into the corresponding products smoothly in moderate to good yields (**1j–n**). Moreover, a heteroaromatic alkene, such as 2-vinylthiophene, was also a good substrate for this transformation without generating any byproducts (**3ol**).

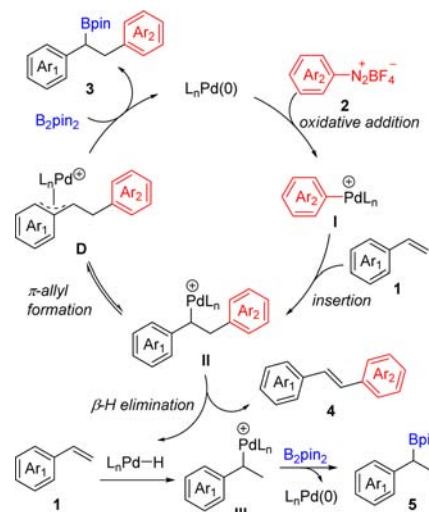
To understand the inference for the high regioselectivity of this 1,2-arylboration, isotope-labeled experiments were carried out with 4-*t*-Bu β,β-bisdeuterated styrene (**1k-D**₂) (Scheme 5B). To improve the yields of the Heck product and hydroboration product, we decreased the loading of Pd₂(dba)₃ to 5 mol % and raised the temperature to 70 °C. Under these conditions, we purified the reaction mixture and obtained 38% yield of **3kk**, 13% yield of **4kk**, and 14% yield of **5k** (Scheme 5A). At the same time, with deuterated styrene **1k-D**₂, similar results were obtained. It was surprising that the hydroboration product **5k-D** is the branched boronate (α-boronate) with three deuterium atoms observed on the same carbon (methyl group); meanwhile, 1,1-bisdeuterated 1,2-arylboration product **3kk-D**₂ was obtained in 27% yield along with 8% of 1-deuterated Heck product **4kk-D**. On the basis of previous experiments, the additional deuterium atom on **5k-D**₃ might come from the Pd-D intermediate which was generated from β-D elimination of the Heck reaction between **1k-D** and **2k**, leading to product **4kk-D**. This reaction also explained why Heck product **4kk** and hydroboration product **5k** always appear in identical amounts.

According to the previous literature reports⁹ as well as our control experimental results, we gave a proposed mechanism (Scheme 6): oxidative addition of aryldiazonium tetrafluoroborate **2** over Pd(0) affords aryl-Pd intermediate **I**. Heck reaction between vinylarene **1** and intermediate **I** would yield intermediate **II**, which further can convert into π-allyl-Pd

Scheme 5. Related Mechanistic Experiments



Scheme 6. Plausible Catalytic Cycle for 1,2-Arylboration of Vinylarenes



intermediate **D**. The intermediate **D** directly reacts with a nucleophile, diboron, under basic conditions to generate the desired 1,2-arylboration product **3**. Meanwhile, β-H elimination of the intermediate **II** will lead to Heck product **4** as a byproduct along with 1 equiv of L_nPd-H, which attacks vinylarene **1** to render intermediate **III**, and eventually branched alkyl boronate **5** was obtained in the presence of B₂pin₂. Interestingly, reinsertion of L_nPd-H over Heck product **4** was not observed at all under our standard conditions, which is in sharp contrast to the previous report, probably owing to the steric hindrance of Heck product **4** over vinylarene **1**. Therefore, this reaction can highly regioselectively afford 1,2-arylboration product without the formation of 1,1-arylboration product.

In conclusion, a highly regioselective palladium-catalyzed 1,2-arylboration of vinylarenes with aryldiazonium tetrafluoroborates and bis(pinacolato)diboron has been disclosed for the first time. Isotope-labeled experiments clearly demonstrated that no

Pd–H reinsertion occurred under the standard conditions perhaps due to the steric hindrance of Heck product **4** over vinylarenes **1**, which also explained why this protocol can highly regioselectively afford 1,2-arylboration product. Enantioselective 1,2-arylboration of vinylarenes with aryldiazonium tetrafluoroborates and bis(pinacolato)diboron is underway in our laboratory and will be reported in due course.

■ ASSOCIATED CONTENT

■ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: [10.1021/acs.orglett.6b02527](https://doi.org/10.1021/acs.orglett.6b02527).

General procedures, mechanistic experiments, and NMR spectroscopic data (PDF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

Financial support from the National Natural Science Foundation of China (21202049), the Recruitment Program of Global Experts (1000 Talents Plan), the Natural Science Foundation of Fujian Province (2016J01064), Fujian Hundred Talents Plan and Program of Innovative Research Team of Huaqiao University (Z14X0047), and Graduate Innovation Fund (for K.Y.) of Huaqiao University are gratefully acknowledged. We also thank the Instrumental Analysis Center of Huaqiao University for analysis support.

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