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Palladium-Catalyzed Oxidative Allylation of Bis[(pinacolato)boryl]methane: Synthesis of Homoallylicboronic Esters

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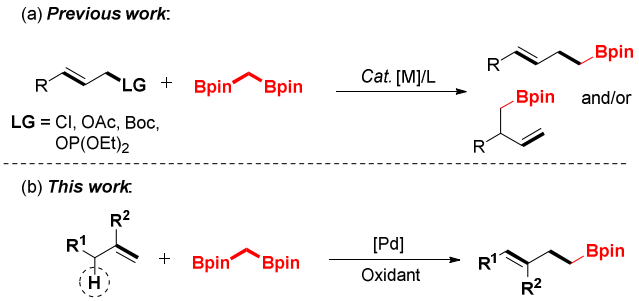
A palladium-catalyzed oxidative allylation of bis[(pinacolato)boryl]methane to afford the corresponding homoallylic organoboronic esters with moderate to excellent yields is reported. This novel transformation provides an efficient strategy for the construction of homoallylic organoboronic esters in one-step with a broad substrate scope. It is proposed that palladium-catalyzed oxidative allylic C-H bond activation process may be involved in the catalytic cycle.

1,1-Bisborylalkanes have emerged as a valuable synthon in contemporary organic synthesis due to its easy access to highly functionalized, complicated organoboron molecules.[1-3] Shibata and co-workers reported the pioneering work on the allylation of bis[(pinacolato)boryl]methane with allyl halides under mild conditions, giving highly valuable homoallyicboronic esters.[4] Hoveyda *et al.* reported the Cu-catalyzed enantioselective allylic substitution (EAS) of allylic electrophiles with 1,1-bisborylalkanes.[5] Niu's group developed the iridium-catalyzed asymmetric allylation strategy to prepare *β*-substituted chiral homoallyl boronic esters.[6] Despite the significant progress that has been achieved along this line, all of these elegant developments employed the unique and high reactivity of 1,1-bisborylalkanes toward electrophiles. However, the application of 1,1-bisborylalkanes as soft nucleophiles in the allylic C-H activation process has not been investigated, and is still highly desirable.

Transition metal-catalyzed oxidative functionalization of allylic C-H bonds has been recognized as a powerful method toward the construction of carbon-carbon or carbon-heteroatom bonds in a concise manner.[7, 8] Most notably, palladium-catalyzed oxidative allylic C-H bond activation has been defined as an expedient and atom-economic strategy for the synthesis of complex molecules.[9] As a class of high activity electrophiles, the key allylpalladium intermediate could undergo cross-coupling reactions with various nucleophiles.[10-13] Recently, our group has realized the palladium-catalyzed direct coupling of terminal alkenes with water[11c], amines[12h] and alcohols[10a, 11g]. On the basis of the previous endeavours, we envision that the allyl-Pd intermediate could be captured by the 1,1-bisborylalkanes to afford the organoboron compounds by introducing an *α*-boroalkyl group. Herein, we disclose a strategically distinct approach to synthesize homoallylicboronic esters through palladium-catalyzed oxidative allylic C-H functionalization of terminal olefins.



Scheme 1. Strategies for the synthesis of homoallyicboronic esters

Inspired by these advances and our previous work[6, 11g, 12h], we investigated the oxidative *α*-boroalkylation reaction of allylbenzene (**1a**) and bisborylmethane (**2a**). At first, the reaction was initially carried out with the combination of $Pd(OAc)_2$, AgOTf and ^tBuOK in 1,4-dioxane at 50 °C for 24 h under 1 atm of oxygen. Unfortunately, no desired product **3a** was detected (Table 1, entry 1). Subsequently, a series of silver salts were screened, such as AgTFA, AgOAc and $AgBF_4$ (Table 1, entries 2-4), among which $AgBF_4$ was the optimal one and afforded the desired product **3a** in trace yield (entry 4). Next, various bases were surveyed, and KH_2PO_4 was found to be the most effective base for this reaction (Table 1, entry 8). Further examination of oxidants revealed that NQ (1,4-naphthoquinone) increased the yield of **3a** distinctly (Table 1, entry 15). After screening of different ligands (Table 1, entries 16-20), 1,2-bis(phenylsulfinyl)ethane was identified as the optimal ligand for the present transformation (Table 1, entry 20). Screening of various solvents indicated that 1,4-dioxane giving the best result for this reaction (see the Supporting Information for details). Thus, the standard condition was obtained as $Pd(OAc)_2$ (10 mol %), $AgBF_4$ (20 mol %), KH_2PO_4 (2.0 equiv), NQ (2 equiv) and 1,2-bis(phenylsulfinyl)ethane (15 mol %) in 1,4-dioxane (2.0 mL) at 50 °C with stirring for 24 h.

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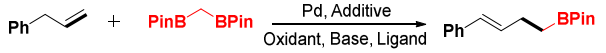
Table 1. Screening for optimal reaction conditions[a]



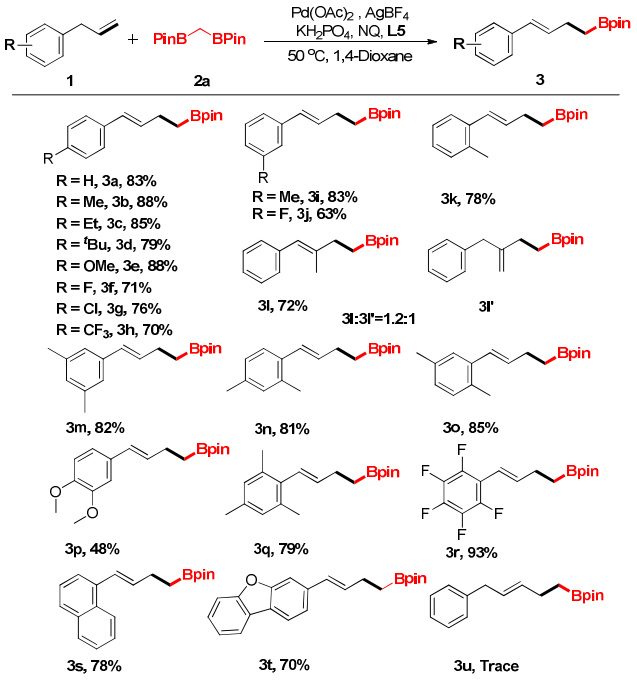
1a 2a 3a

Entry	Additive	Ligand	Base	Oxidant	Yield (%) [b]
1	AgOTf	-	^{t}BuOK	O_2	N.D.
2	AgTFA	-	^{t}BuOK	O_2	N.D.
3	AgOAc	-	^{t}BuOK	O_2	N.D.
4	$AgBF_4$	-	^{t}BuOK	O_2	Trace
5	$AgBF_4$	-	Cs_2CO_3	O_2	Trace
6	$AgBF_4$	-	CF_3COONa	O_2	12
7	$AgBF_4$	-	KPF_6	O_2	23
8	$AgBF_4$	-	KH_2PO_4	O_2	30
9	$AgBF_4$	-	KH_2PO_4	$PhI(OAc)_2$	N.D.
10	$AgBF_4$	-	KH_2PO_4	BQ	Trace
11	$AgBF_4$	-	KH_2PO_4	DDQ	Trace
12	$AgBF_4$	-	KH_2PO_4	DMBQ	Trace
13	$AgBF_4$	-	KH_2PO_4	BQ/DDQ	35
14	$AgBF_4$	-	KH_2PO_4	BQ/DDQ	55
15	$AgBF_4$	-	KH_2PO_4	NQ	60
16	$AgBF_4$	**L1**	KH_2PO_4	NQ	N.D.
17	$AgBF_4$	**L2**	KH_2PO_4	NQ	N.D.
18	$AgBF_4$	**L3**	KH_2PO_4	NQ	N.D.
19	$AgBF_4$	**L4**	KH_2PO_4	NQ	43
20	$AgBF_4$	**L5**	**KH_2PO_4**	**NQ**	**83**

[a] A mixture of **1a** (0.25 mmol, 2.5 equiv), **2a** (0.1 mmol), base (0.2 mmol, 2 equiv), $Pd(OAc)_2$ (10 mol %), additive (20 mol %), ligand (15 mol %), oxidant (2 equiv) and anhydrous 1,4-dioxane (2 mL) was sealed in a 25 mL Schlenk tube at 50 °C for 24 h. N.D. = not detected. L1: PPh_3. **L2**: dppf. **L3**: 4,4'-bipyridine. **L4**: 1,2-bis(phenylsulphonyl)ethane. **L5**: 1,2-bis(phenylsulfinyl)ethane. [b] Isolated yield based on **2a**. [c] BQ: DDQ = 2: 1; [d] BQ: DDQ = 4: 1.

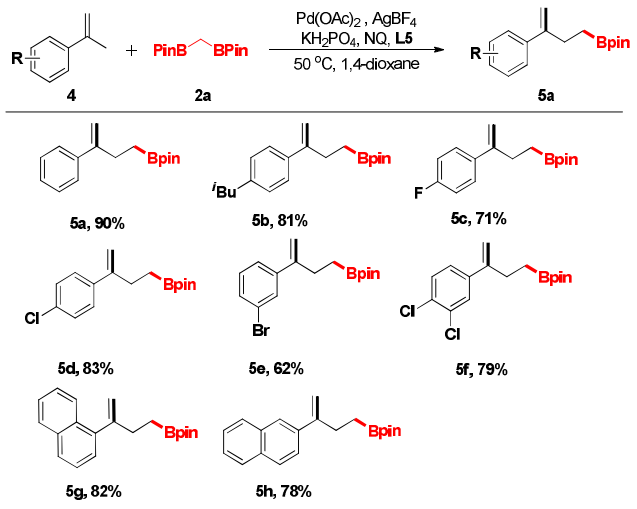
The generality of the new protocol was next tested as the optimized conditions established. Several structurally diverse allylbenzenes were initially explored, and the representative results are summarized in Table 2. Generally, both electron-donating (Me, Et, OMe) and electron-withdrawing groups (F, Cl, CF_3) were compatible with this method (**3a-3k**). In addition, when (2-methylallyl)benzene (**1l**) was treated with **2a** under the optimized condition, two regioisomeric products **3l** and **3l'** were obtained (dr = 1.2: 1, determined by NMR spectrum). Disubstituted allylbenzenes could also undergo this transformation, furnishing the corresponding boronic ester derivatives in good yields (**3m-3q**). Notably, functionalized allylbenzene derivatives, such as 1-allyl-2,3,4,5,6-pentafluorobenzene (**3r**) transferred to the desired products with excellent yields. Only a trace amount of the desired product was detected by GC-MS when but-3-en-1-ylbenzene (**1u**) was surveyed.

Table 2. Substrate scope of various allylbenzenes.[a, b]



[a] Reaction conditions: **1** (0.25 mmol, 2.5 equiv), **2a** (0.1 mmol), $Pd(OAc)_2$ (10 mol %), $AgBF_4$ (20 mol %), **L5** (15 mol %), KH_2PO_4 (0.2 mmol, 2 equiv), NQ (0.2 mmol, 2 equiv) and anhydrous 1,4-dioxane (2 mL) was sealed in a 25 mL Schlenk tube at 50 °C for 24 h. [b] Isolated yields based on **2a**.

Table 3. Substrate Scope of α-Methylstyrenes.[a b]



[a] Reaction conditions: **4** (0.25 mmol, 2.5 equiv), **2a** (0.1 mmol), $Pd(OAc)_2$ (10 mol %), $AgBF_4$ (20 mol %), **L5** (15 mol %), KH_2PO_4 (0.2 mmol, 2 equiv), NQ (0.2 mmol, 2 equiv) and anhydrous 1,4-dioxane (2 mL) was sealed in a 25 mL Schlenk tube at 50 °C for 24 h. [b] Isolated yields based on **2a**.

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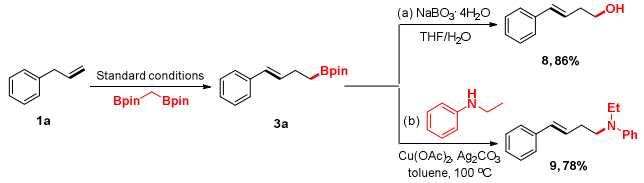
In view of the further applications of this transformation, the substrate scope was expanded to different substituted α-methylstyrenes (Table 3). *α*-Methylstyrene was first surveyed, which delivered a good yield of product **5a** under our optimized conditions. Moreover, *α*-methylstyrenes bearing different functional groups such as F, Cl and Br at the *para* or *ortho* positions of the phenyl ring could also react smoothly to give the corresponding products **5c**-**5e** in good yields ranging from 62% to 83%. Pleasingly, the reactions of 1-(prop-1-en-2-yl)naphthalene and 2-(prop-1-en-2-yl)naphthalene proceeded efficiently to give the corresponding products **5g** and **5h** in 82% and 78% yields, respectively.

trans-β-Methylstyrene derivatives could be recognized as a precursor of allylic electrophile. Thus, **6a** and **6b** were applied in this process and converted into the organoboronic esters in moderate yields (Scheme 2).

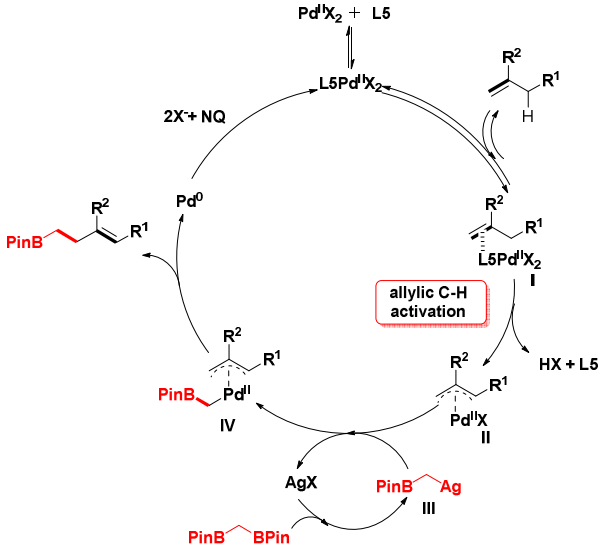
Scheme 2. Substrate Scope of *trans-β*-Methylstyrenes. Reaction conditions: **6** (0.25 mmol, 2.5 equiv), **2a** (0.1 mmol), $Pd(OAc)_2$ (10 mol %), $AgBF_4$ (20 mol %), **L5** (15 mol %), KH_2PO_4 (0.2 mmol, 2 equiv), NQ (0.2 mmol, 2 equiv) and 1,4-dioxane (2 mL) was sealed in a 25 mL Schlenk tube at 50 °C for 24 h. [b] Isolated yields based on **2a**.

To demonstrate the synthetic utility of this protocol further, the homoallylic boronic esters were transferred into other desired synthons using the established chemistry (Scheme 3). For example, compound **3a** could be oxidized by $NaBO_3{\cdot}4H_2O$ to homoallylic alcohol **8**, which has been engaged in a wide range of chemical reactions to synthesize structurally complex products. Moreover, **3a** could undergo amination to form homoallylic amine **9** in 78% yield.



Scheme 3. Elaboration of Homoallyl Boronates. Conditions: (a) **3a** (0.2 mmol), $NaBO_3{\cdot}4H_2O$ (6.0 equiv) in THF/H_2O (2 mL/2 mL) at room temperature for 12 h. (b) **3a** (0.2 mmol), *N*-ethylaniline (0.1 mL), $Cu(OAc)_2$ (10 mol %), Ag_2CO_3 (2.0 equiv) in toluene at 100 °C stirred for 20 h.

In light of the previous literature, a plausible mechanism is outlined in Scheme 4. Initially, the catalytic cycle would begin with the coordination of palladium with olefins to generate the intermediate **I**. Next, the corresponding π-allylpalladium species II is formed by the electrophilic allylic C-H cleavage in the presence of ligand **L5**.[10b, 11a, 14] With the addition of silver salt, 1,1-bis[(pinacolato)boryl]methane undergoes a deborylative transmetallation process to form an alkyl silver species **III**.[6, 15] Then, π-allylpalladium intermediate **II** reacts with intermediate **III** by transmetallation to give a Pd-(*α*-boroalkyl) complex **IV**. The product homoallylic organoboronic ester would be obtained through the reductive elimination process. Finally, the reactive Pd(II) species is regenerated by the oxidation of NQ.[16] (see the Supporting Information for details)



Scheme 4. Possible Reaction Mechanism.

In summary, a practical Pd-catalyzed oxidative *α*-boroalkylation reaction of simple olefins with 1,1-bis[(pinacolato)boryl]methane is presented. This novel procedure provides an efficient and attractive protocol for the construction of functionalized homoallylicboronic esters in good to excellent yields from readily available olefins with broad substrate scope and excellent functional group compatibility. Remarkably, an efficient construction of Csp^3-Csp^3 bond has been realized *via* the Pd-catalyzed oxidative functionalization of allylic C-H bond.

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Notes and references

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† Electronic Supplementary Information (ESI) available: Experimental section, characterization of all compounds, copies of ^1H and ^{13}C NMR spectra for selected compounds. See DOI: 10.1039/b000000x/

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