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## Palladium-catalyzed addition of organoboronic acids to allenes

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The palladium-catalyzed addition reaction of alkenyl- or aryl-boronic acids into various allenes is described, which allows C–C bond formation in a highly regioselective manner under very mild conditions.

Miyaura discovered the addition of organoboronic acids to  $\alpha$ , $\beta$ unsaturated ketones by a rhodium-phosphine complex in 1997.<sup>1</sup> Since then, transition metal-catalyzed addition to unsaturated bonds with organoboronic acids has been a subject of intensive work in the area of organic and organometallic chemistry. Very recently, we reported Pd-catalyzed hydroarylation which is widely applicable to terminal as well as to internal alkynes.<sup>2</sup>

Allenes are a class of compounds with unique reactivities due to the existence of two orthogonal  $\pi$ -bonds and they are very useful intermediates in organic synthesis.<sup>3</sup> Transition-metal catalyzed reactions of allenes have attracted increasing interest during the last two decades.<sup>4</sup> However, to the best of our knowledge reports on transition metal-catalyzed additions of boronic acids to allenes is not known. On the other hand conjugated addition to enones,<sup>5</sup> addition to aldehydes,<sup>6</sup> allylic substitution,<sup>7</sup> carbonylation<sup>8</sup> and cross coupling reactions with alkenes or acid chlorides<sup>9</sup> are well known. In continuing palladium-catalyzed allene chemistry,<sup>10</sup> we wish to report here an efficient regioselective palladium-catalyzed addition of boronic acids to allenes under very mild conditions.

For our initial survey, we conducted the Pd-catalyzed hydroalkenylation of allene  $1a^{\dagger}$  with hexenylboronic acid (2a) under a variety of conditions, where we expected to obtain a mixture of stereoisomers of products **3aa** and **4aa** (eqn. 1).



From a series of studies, we found that the yield of product **3aa** depends greatly on the palladium catalyst as well as the reaction solvent as summarized in Table 1. After we screened this reaction in several solvents, the reaction in DMF or in THF in

 Table 1 Pd-Catalyzed hydroalkenylation of allene 1a with organoboronic acid 2a in the presence of 10 mol% AcOH

Entry	Catalyst (3 mol%)	Solvent	<i>T</i> /°C	<i>t/</i> h	Yield (%) <sup>a</sup>
1	$Pd(PPh_3)_4$	Chloroform	35	20	20
2	Pd(PPh <sub>3</sub> ) <sub>4</sub>	DMF	80	3	53
3	Pd(PPh <sub>3</sub> ) <sub>4</sub>	1,4-Dioxane	50	3	89
4	$Pd(PPh_3)_4$	Toulene	45	20	25
5	$Pd(PPh_3)_4$	THF	50	3	82
6	Pd(OAc) <sub>2</sub> /PPh <sub>3</sub> <sup>b</sup>	1,4-Dioxane	50	3	78
7	Pd(OAc) <sub>2</sub> /dppb <sup>c</sup>	1,4-Dioxane	60	3	81
a Isolata	d vialds of the isome	b The catalyst was prepared			

by mixing 3 mol% Pd(OAc)<sub>2</sub> and 6 mol% of PPh<sub>3</sub>. c The catalyst was prepared by mixing 3 mol% Pd(OAc)<sub>2</sub> and 3 mol% of dppe.

the presence of catalytic amounts of acetic acid afforded **3aa** with an excellent selectivity, albeit in low yields (entries 2 and 5). However, it was interesting to observe that the reaction in 1,4-dioxane worked nicely for most cases. The effect of Pd complex and ligand on the catalytic activity was also investigated. Both Pd(II) complexes such as  $Pd(OAc)_2/2PPh_3$  and  $Pd(OAc)_2/dppb$  and the Pd(0) complex,  $Pd(PPh_3)_4$ , catalyze the reaction smoothly. Gratifyingly, the use of  $Pd(PPh_3)_4$  in 1,4 dioxane showed more promise resulting in the formation of product **3aa** in excellent overall yield (entry 3).

Subsequently we tested the generality of the reaction with some commercially available boronic acids 2 to various allenes 1 (eqn. 2) and the results are summarized in Table 2. First of all, we tested the addition reaction of various organoboronic acids to the allene 1a. All reactions afforded the corresponding addition products in good yields (entries 1–5). This addition reaction occurs in a highly regioselective manner, with the organic group on boronic acid adding to the middle carbon of the allene moiety. However, fine tuning of the reaction conditions is required for each boronic acid employed in order to achieve high yield. It was of interest to investigate the reactions of other substituted allenes (1b-j) with boronic acids (2a-b) under these catalytic conditions of 3 mol% Pd(PPh<sub>3</sub>)<sub>4</sub> and 10 mol% of AcOH in 1,4-dioxane.

Table 2 Pd-Catalyzed hydroalkenylation of allenes 1 with organoboronic acids 2 in the presence of 10 mol% AcOH  $\,$ 

Entry	Allenes	R <sup>2</sup> B(OH) <sub>2</sub>	T/°C	t/h	Products	Yield (%)
1	1a	2b	60	3	3ab	65
2	1a	2c	60	12	3ab	55
3	1a	2d	60	11	3ab	64
4	1a	2e	60	3	3ab	66
5	1a	2f	60	5	3ab	55
6	1b	2a	50	3	3ba	78
7	1b	2b	50	3	3bb	65
8	1c	2a	60	7	3ca	83
9	1c	2b	60	9	3cb	74
10	1d	2a	60	3	3da	75
11	1d	2b	60	3	3db	63
12	1e	2a	50	3	3ea	65
13	1e	2b	50	3	3eb	59
14	1f	2a	60	5	3fa	78
15	1f	2b	60	5	3fb	69
16	1g	2a	60	8	3ga	68
17	1g	2b	60	10	3gb	59
18	1h	2a	60	3	3ha	62
19	1h	2b	60	3	3hb	58
20	1i	2a	80	10	3ia,4ia	$78^{a}$
21	1i	2b	80	12	3ib,4ib	63 <sup>a</sup>
22	1j	2a	70	12	3ja,4ja	61 <sup>a</sup>
23	1j	2b	70	12	3jb,4jb	57 <i>a</i>
a Thore	tio of 2 and	4 was almost	1 · 1 in a	ach and	10	

<sup>*a*</sup> The ratio of **3** and **4** was almost 1 : 1 in each case

Initially, we invesigated the reaction of monosubstituted allenes (1b–f). The reaction of 1b with hexenyl boronic acid 2a and phenyl boronic acid 2b afforded the addition products 3ba and 3bb in 78 and 65% yields, respectively (entries 6 and 7). Under similar reaction conditions, allenic nitrile (1c), allenic ethylester (1d), allenol (1e), and allenal (1f) smoothly reacted with boronic acids 2a and 2b gave the corresponding addition products in good to excellent yields (entries 8–15). In all these cases only one stereoisomer with (E)-configuration was observed.



Under these conditions, two 1,1-disubstituted allenes (1g and 1h) afforded 1,3-butadiene derivatives 3ga and 3ha with hexenylboronic acid 2a and styrene derivatives 3gb and 3hb with phenyl boronic acid 2b in good yields (entries 16–19).

We were interested in extending this process to 1,3-disubstituted allenes (1i and 1j) and found that, unlike the other allenes, these required higher temperature and longer reaction time to proceed to completion. Notably, we have observed that the corresponding reactions with boronic acids 2a and 2b afforded a stereoisomeric mixture of products 3ia and 4ia, 3ja and 4ja, 3ib and 4ib, and 3jb and 4jb, respectively (entries 20–23). The formation rate of these 1,3-disubstituted allenes was greatly slowed probably due to the steric hindrance of the allenes.

Here the catalytic reaction was highly regioselective with the organic group on boronic acid adding to the middle carbon of the allene moiety. We observed the formation of *E*-isomer solely from the mono and 1,1-disubstituted allenes which was in contrast to the fact that most carbopalladation reactions of mono- and di-substituted allenes are reported to give *E* and *Z* isomeric products with low selectivity.<sup>11</sup> A plausible explanation for the formation of the exclusive *E*-isomer is based on face-selective addition of organoboronic acids to the allenes (Fig. 1).

The relative stereochemistry was confirmed by temperature dependent (-60 to 30 °C) NOESY experiments with 150, 200, 250 ms mixing times. Direct NOE enhancements for **3aa** were found between H<sub>a</sub> and H<sub>c</sub> and between H<sub>b</sub> and H<sub>d</sub>, while no such NOE was found between H<sub>c</sub> and H<sub>d</sub> (Fig. 2) which clearly shows a *trans* relationship.





In conclusion, we have demonstrated a new palladiumcatalyzed addition of alkenyl- and aryl-organoboronic acids to various allenes. This reaction proceeds under mild conditions, to provide *E*-tri-substituted dienes and styrenes in good to excellent yields and with good regio- and stereo-control (in the case of monosubstituted allenes).

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## Notes and references

† General procedure: A 10 mL round-bottomed flask was charged with tetrakis(triphenylphosphine)palladium(0) (7.6 mg, 0.0066 mmol), allenic benzylether (1a, 38.3 mg, 0.22 mmol), hexenyl boronic acid (2a, 34 mg, 0.26 mmol) and 1,4-dioxane (1.0 mL) and then purged the system with a dry argon atmosphere. The resulting mixture was treated with acteic acid (1.3  $\mu$ L, 0.022 mmol) *via* a 10  $\mu$ L GC syringe. This was then stirred at 50 °C for 3 h. On completion of the reaction, the mixture was allowed to cool to 0 °C, quenched with water, and then extracted with ether. The organic portion was washed with water and brine successively, dried over magnesium sulfate, and concentrated *in vacuo*. The crude product was then purified by flash chromatography (ethyl acetate/hexane = 1/10) to give the addition product **3aa** (50.0 mg, 89%) as a colorless oil. All products **3aa-4jb** have been satisfactorily characterised by means of <sup>1</sup>H NMR, <sup>13</sup>C NMR, IR and HRMS.

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