



# Cationic Pd(II)-catalyzed arylyative cyclization of 1,6-enynes with arylboronic acids



Kun Shen, Xiuling Han<sup>\*</sup>, Xiyan Lu<sup>\*</sup>, Zhiyong Hu

State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, University of Chinese Academy of Sciences, Chinese Academy of Sciences, 345 Lingling Road, Shanghai 200032, China

## ARTICLE INFO

### Article history:

Received 15 June 2017

Revised 9 August 2017

Accepted 14 August 2017

Available online 19 August 2017

### Keywords:

Cationic palladium

1,6-Enyne

Arylboronic acid

Carbopalladation

$\beta$ -Heteroatom elimination

## ABSTRACT

A cationic Pd(II)-catalyzed redox neutral arylyative cyclization of enynes by using  $\beta$ -acetoxy elimination as the quenching step has been developed. The reaction offers an efficient method to access a variety of carbocycles and *N*-heterocycles bearing an exocyclic double bond.

© 2017 Elsevier Ltd. All rights reserved.

## Introduction

Transition-metal-catalyzed tandem reactions are powerful methods for the construction of structurally complex frameworks from relatively simple materials and have attracted great scientific interest from chemists.<sup>1</sup> Among which, enyne coupling has been achieved with a wide range of transition-metal complexes, which represents a versatile approach to a variety of products by a simple manipulation.<sup>2,3</sup> With our interests in developing transition metal-catalyzed tandem reactions, here we report our recent progress on cationic palladium-catalyzed redox neutral 1,6-enyne couplings.

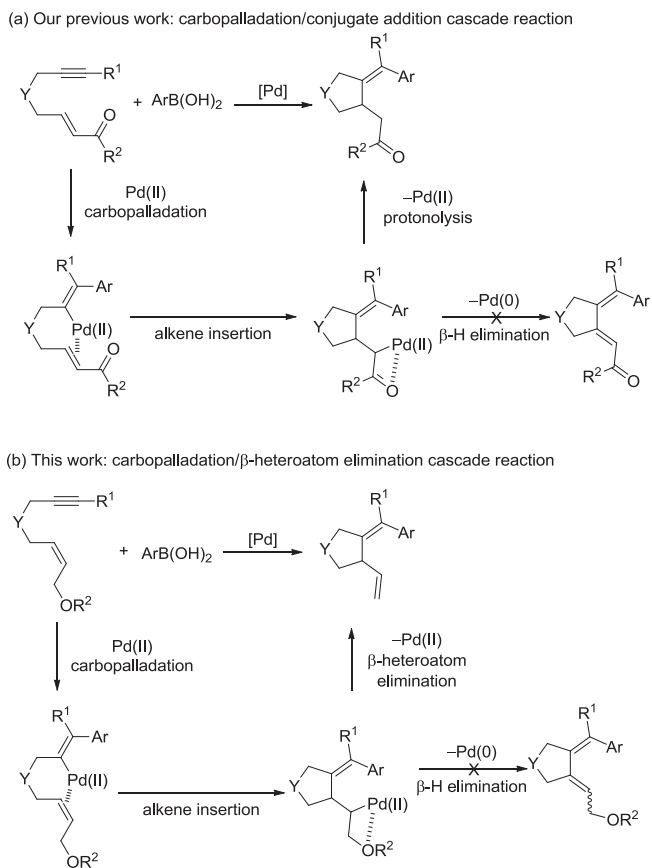
In our previous work, we reported a cationic Pd(II)-catalyzed intramolecular arylyative alkyne- $\alpha$ ,  $\beta$ -unsaturated carbonyl coupling (Scheme 1, a).<sup>4</sup> In the course of the reaction, carbopalladation of the alkyne gives vinylpalladium intermediate, which undergoes intramolecular alkene insertion to form a cyclic alkylpalladium intermediate. Protonolysis of the newly formed carbon-palladium bond would yield the product and regenerate the Pd(II) catalytic species. It is worth noting that protonolysis of the carbon-palladium bond, rather than  $\beta$ -H elimination, occurred preferentially in the quenching step for the process, which may be due to the strong Lewis acidity of the cationic palladium complex.<sup>5</sup> Inspired by above study, we are wondering if the redox neutral enyne cyclization is possible when the newly formed C–Pd bond is

quenched by  $\beta$ -heteroatom elimination (Scheme 1, b). Such type of arylyative cyclization of 1,6-enynes was previously reported by the Murakami group,<sup>6</sup> where Rh(I) was used as the catalyst to achieve different carbocycles. Zhang group also described a Pd(0)-catalyzed 1,6-enyne arylyative cyclization through a Pd(0)/Pd(II) redox process, where the reaction was proposed to go through a 1,6-enyne cyclization-arylation cascade process via a  $\pi$ -allylpalladium intermediate.<sup>7</sup>

Our studies began with the arylyative cyclization of 1,6-enyne **1a** with phenylboronic acid **2a** (Table 1). Preliminary studies showed that the desired arylyative cyclization product **3aa** was isolated in 25% yield in toluene at 80 °C when cationic palladium complex [Pd(dppp)(H<sub>2</sub>O)<sub>2</sub>](OTf)<sub>2</sub> was used as the catalyst (Table 1, entry 1). Then several additives were examined. In the presence of K<sub>2</sub>CO<sub>3</sub>, the yield was raised to 82% (Table 1, entry 2). When K<sub>3</sub>PO<sub>4</sub> was used, the yield decreased significantly (Table 1, entry 3). KF gave a similar result as K<sub>2</sub>CO<sub>3</sub> (Table 1, entry 4). Next, cationic palladium catalysts were screened. A dramatically decreased yield was obtained when the reaction was catalyzed by [Pd(dppe)(H<sub>2</sub>O)<sub>2</sub>](OTf)<sub>2</sub> (43% yield, Table 1, entry 5). However, the reaction afforded **3aa** in a higher yield with [Pd(dppp)(H<sub>2</sub>O)<sub>2</sub>](BF<sub>4</sub>)<sub>2</sub> as the catalyst (91% yield, Table 1, entry 6). In addition to the OAc group, other leaving groups were tested. Ester **1b** or carbonate **1c** can also react with phenylboronic acid **2a** successfully to produce **3aa** in good yields (Table 1, entries 7 and 8). When the leaving group was a methoxy (**1d**) or hydroxy (**1e**),<sup>8</sup> the reaction was very slow and gave low yields of the product

<sup>\*</sup> Corresponding authors.

E-mail addresses: [xlhan@sioc.ac.cn](mailto:xlhan@sioc.ac.cn) (X. Han), [xylu@sioc.ac.cn](mailto:xylu@sioc.ac.cn) (X. Lu).



**Scheme 1.** Cationic Pd(II)-catalyzed redox neutral enyne coupling reaction.

(Table 1, entries 9 and 10). These results suggest that OAc is the best leaving group among the screened groups for this reaction and the elimination of which would be assisted by the intramolec-

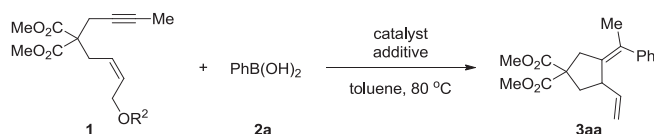
ular coordination with palladium.<sup>9</sup> Thus, enyne **1** (0.2 mmol), arylboronic acid **2** (0.4 mmol, 2.0 equiv), [Pd(dppp)(H<sub>2</sub>O)<sub>2</sub>](BF<sub>4</sub>)<sub>2</sub> (0.01 mmol, 5 mol%), KF (0.4 mmol, 2 equiv) and toluene (1 mL) at 80 °C were chosen as the optimized conditions.

With optimal reaction conditions in hand, we studied the scope of the arylyative cyclization of a variety of arylboronic acids and enynes bearing acetoxy as the leaving group and the results were summarized in Table 2. The catalytic process worked well with a sterically and electronically diverse array of arylboronic acids to give the corresponding products **3aa–3ag** in moderate to good yields (Table 2, entries 1–7). Arylboronic acids with electron-donating groups (e.g. **2b**, **2c** and **2d**) gave lower yields than phenylboronic acid **2a** (Table 2, entries 2–4). Arylboronic acids with halogen substituents were compatible in this reaction, offering opportunities for further transformations (Table 2, entries 5 and 6). Then, enynes bearing other substituents on the alkyne were used to react with phenylboronic acid **2a**. Slightly lower yields were obtained with **1f** (R<sup>1</sup> = *n*-Pr) and **1g** (R<sup>1</sup> = Ph) (Table 2, entries 8 and 9). The stereochemistry of the exocyclic double bond in the products was assigned as *E* as confirmed by NOESY spectra of **3aa** (See the Supporting Information). In contrast to the Rh(I)-catalyzed enyne cyclization, the reaction of aza-1,6-enyne **1h**, bearing a sulfonamide group in the skeleton, gave the product **3ha** in a very good yield (93%, Table 2, entry 10).<sup>10</sup> While the arylyative cyclization of enyne **Z-1a** was very efficient (91% yield, Table 2, entry 1), the reaction of enyne **E-1a** was less effective under the same reaction conditions (47% yield, Table 2, entry 11). The decent yield might be due to the weaker coordinating ability of (*E*)-olefins compared to (*Z*)-olefins.<sup>11</sup>

Next, the asymmetric version of this arylyative cyclization reaction was studied by using enyne **1a** and phenylboronic acid **2a** as substrates (Scheme 2). Our preliminary results showed that product **3aa** can be obtained in a high *ee* value (97%) under the catalysis of Pd(CH<sub>3</sub>CN)<sub>4</sub>(BF<sub>4</sub>)<sub>2</sub>/(*R*)-BINAP, whereas the yield was low.

A possible mechanism for the cationic Pd(II)-catalyzed arylyative enyne cyclization is proposed in Scheme 3. The catalytic cycle is initiated by transmetalation between the cationic palladium(II) complex **A** and arylboronic acids **2** to form the arylpalladium(II)

**Table 1**  
Reaction condition optimization.<sup>a</sup>



Entry	<b>1</b>	Catalyst	Additive	Time (h)	Yield <sup>b</sup> (%)
1	<b>1a</b> , R <sup>2</sup> = Ac	[Pd(dppp)(H <sub>2</sub> O) <sub>2</sub> ](OTf) <sub>2</sub>	–	24	25
2	<b>1a</b>	[Pd(dppp)(H <sub>2</sub> O) <sub>2</sub> ](OTf) <sub>2</sub>	K <sub>2</sub> CO <sub>3</sub>	3	82
3	<b>1a</b>	[Pd(dppp)(H <sub>2</sub> O) <sub>2</sub> ](OTf) <sub>2</sub>	K <sub>3</sub> PO <sub>4</sub>	24	52
4	<b>1a</b>	[Pd(dppp)(H <sub>2</sub> O) <sub>2</sub> ](OTf) <sub>2</sub>	KF	3	84
5	<b>1a</b>	[Pd(dppe)(H <sub>2</sub> O) <sub>2</sub> ](OTf) <sub>2</sub>	KF	24	43
<b>6</b>	<b>1a</b>	<b>[Pd(dppp)(H<sub>2</sub>O)<sub>2</sub>](BF<sub>4</sub>)<sub>2</sub></b>	<b>KF</b>	<b>3</b>	<b>91</b>
7	<b>1b</b> , R <sup>2</sup> = Bz	[Pd(dppp)(H <sub>2</sub> O) <sub>2</sub> ](BF <sub>4</sub> ) <sub>2</sub>	KF	5	80
8	<b>1c</b> , R <sup>2</sup> = CO <sub>2</sub> Me	[Pd(dppp)(H <sub>2</sub> O) <sub>2</sub> ](BF <sub>4</sub> ) <sub>2</sub>	KF	5	84
9	<b>1d</b> , R <sup>2</sup> = Me	[Pd(dppp)(H <sub>2</sub> O) <sub>2</sub> ](BF <sub>4</sub> ) <sub>2</sub>	KF	24	8
10	<b>1e</b> , R <sup>2</sup> = H	[Pd(dppp)(H <sub>2</sub> O) <sub>2</sub> ](BF <sub>4</sub> ) <sub>2</sub>	KF	24	26

<sup>a</sup> Reaction conditions: **1** (0.2 mmol, 1.0 equiv), **2a** (0.4 mmol, 2.0 equiv), catalyst (0.01 mmol, 5 mol%), additive (0.4 mmol, 2 equiv), toluene (1 mL), 80 °C.

<sup>b</sup> Isolated yield.

Download English Version:

<https://daneshyari.com/en/article/5258915>

Download Persian Version:

<https://daneshyari.com/article/5258915>

[Daneshyari.com](https://daneshyari.com)