

The Pd(OAc)₂-catalyzed homocoupling of arylboronic acids in water and ionic liquid

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Abstract

The homocoupling reaction of the arylboronic acids proceeded smoothly in a mixture of water and ionic liquids in the presence of ethyl bromoacetate ester using Pd(OAc)₂ as catalyst in high yield at 60 °C for 3 h. The separation of desired products was easily performed by extraction with diethyl ether and Pd(OAc)₂-[bmim][PF₆] (1-butyl-3-methylimidazolium hexafluorophosphate) can be reused eight times accompanied with only a slight decrease in activity.

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Keywords: Dimerization of arylboronic acid; Ionic liquid; Pd(OAc)₂ catalyst

1. Introduction

Biaryls are important building blocks of natural products and functional materials [1–5], and the development of new methods for the preparation of biaryls continues to be the subject of intense investigations. Good results have been achieved by transition metal-catalyzed transformations, which include the Suzuki reaction, modified Ullmann reaction, Stille reaction and so on. Recently, the homocoupling of arylboronic acids has aroused interest because the arylboronic acids are nontoxic, stable and readily available from commercial sources. Song and Wong first turned the self-coupling of arylboronic acid into a useful method by applying it to the preparation of furan-3,4-diyl dimers [6]. From then on, several reports utilizing the homocoupling of boronic acids for the preparation of symmetrical biaryls have appeared in the literature. For example, Jackson and co-workers reported Pd(II) catalyzed homocoupling of arylboronic acids under oxygen atmosphere [7]. Later, Wong and Zhang found that the phosphine ligands enhanced the catalytic activity of Pd(OAc)₂ for the homocoupling reaction in a *N,N*-dimethyl formamide (DMF) solvent [8]. However, Koza and Carita revealed that Pd(PPh₃)₄ had a poor catalytic activity in the homocoupling reaction of arylboronic acids, and

that Cu(NO₃)₂ was a useful co-catalyst for the reaction using Pd(OAc)₂ in DMF [9]. A similar dimerization initiated by transmetallation of palladium enolates was reported by Lei and Zhang [10]. Recently, the oxidative dimerization of arylboronic acids in aqueous media was presented by using oxygen and phase transformation catalysts [11], and the use of *p*-toluenesulfonyl chloride as the additive was shown to be beneficial to the reaction in aqueous media [12]. The homocoupling under base-free condition has been shown to provide high yields of biaryls by using palladium-1,3-bis(diphenylphosphino) propane (DPPP) complex in dimethyl sulfoxide (DMSO) under an oxygen atmosphere [13]. Very recently, the homocoupling reaction of arylboronic acids mediated by Mn(III) [14], Au(III) [15–17], and Ag₂O/CrCl₂ was reported [18].

Ionic liquids have attracted considerable attention as a new type of reaction media in green chemistry [19–23]. We recently reported the Suzuki reaction and cross-coupling reaction of arylboronic acid with carboxylic anhydride in high efficiency in the presence of ionic liquids [24–26]. These catalytic systems are air stable, insensitive to moisture, and reusable with excellent activity for a wide range of substrates. Water was proved to play a crucial role in the reaction, and the formation of biphasic with other traditional solvents such as diethyl ether significantly simplified the purification of the desired products. In this paper, we present an efficient method for the synthesis of symmetrical biaryls by the homocoupling reaction of arylboronic acids in water and ionic liquid in high yields under mild reaction

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conditions in short reaction times. The use of ionic liquids significantly simplified the separation process and good recyclable efficiency was obtained.

2. Experimental

Starting materials and solvents were purchased from common commercial sources and were used without additional purification. ^1H NMR spectra were recorded at 400 MHz, using TMS as internal standard. Mass spectroscopy data of the product of homocoupling reaction was collected on an EI-MS instrument.

Representative procedure for the homocoupling reaction **A**: a mixture of arylboronic acid (2 mmol), $\text{Pd}(\text{OAc})_2$ (4 mg, 3.6 mol%), K_2CO_3 (0.55 g, 4 mmol), and $[\text{bmim}][\text{PF}_6]/\text{H}_2\text{O}$ (3/3 g) were stirred at 60°C for 3 h. After the reaction the solution was cooled to room temperature and the resulting solid was extracted with anhydrous diethyl ether (4×15 mL). The residue was subjected to a second run with the same substrates without further addition of $\text{Pd}(\text{OAc})_2$ and $[\text{bmim}][\text{PF}_6]$ in the cycle. The combined diethyl ether phase was concentrated. Further purification of the product was achieved by flash chromatography on a silica gel column.

B: a mixture of arylboronic acid (2 mmol), $\text{Pd}(\text{OAc})_2$ (4 mg, 3.6 mol%), K_2CO_3 (0.55 g, 4 mmol), ethyl 2-bromoacetate (0.167 g, 1 mmol), and $[\text{bmim}][\text{PF}_6]/\text{H}_2\text{O}$ (3/3 g) were stirred at 60°C for 3 h. Subsequently the same procedure as **A** was followed.

3. Results and discussions

In the initial studies, phenylboronic acid was treated with 3.6 mol% of $\text{Pd}(\text{OAc})_2$ and 2 equiv. of K_2CO_3 in $[\text{bmim}][\text{PF}_6]$ at 80°C for 3 h under normal air atmosphere. Like the Suzuki reaction in ionic liquids, water played the crucial role in the reaction (Fig. 1). It was seen that the addition of water clearly enhanced

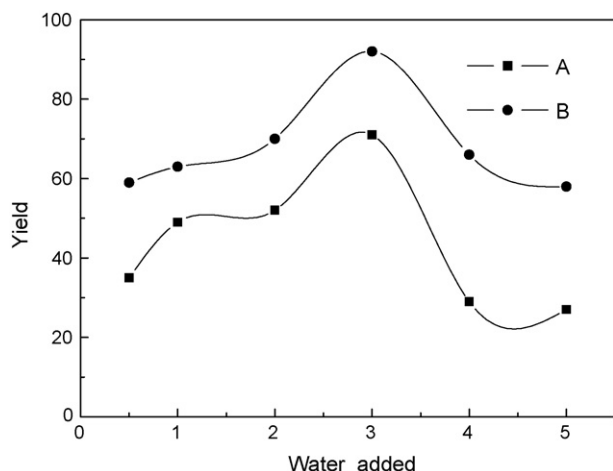


Fig. 1. Effect of water on the homocoupling reaction of phenylboronic acid in H_2O - $[\text{bmim}][\text{PF}_6]$. Reaction conditions: $\text{PhB}(\text{OH})_2$ (2 mmol), K_2CO_3 (4 mmol), $\text{Pd}(\text{OAc})_2$ (3.6 mol%), $[\text{bmim}][\text{PF}_6]$ (3 g), 3 h. (A) Without the use of ethyl 2-bromoacetate, 80°C (external). (B) 1 mmol ethyl 2-bromoacetate was added, 60°C (external).

Table 1

Effect of ionic liquids and bases on the homocoupling reaction

Entry	Ionic liquid	Base	Temperature ($^\circ\text{C}$)	Yield $_{\text{Ph-Ph}}$ (%) ^a
1	$[\text{bmim}][\text{PF}_6]$	K_2CO_3	60	92
2	$[\text{bmim}][\text{BF}_4]$	K_2CO_3	60	49
3	$[\text{bmim}][\text{Cl}]$	K_2CO_3	60	21
4	$[\text{bmim}][\text{PF}_6]$	K_2CO_3	60	92
5	$[\text{bmim}][\text{PF}_6]$	Na_2CO_3	60	82
6	$[\text{bmim}][\text{PF}_6]$	NaOAc	60	69
7	$[\text{bmim}][\text{PF}_6]$	KOH	60	67
8	$[\text{bmim}][\text{PF}_6]$	NEt_3	60	19
9	$[\text{bmim}][\text{PF}_6]$	K_3PO_4	60	47
10	$[\text{bmim}][\text{PF}_6]$	None	60	42
11	$[\text{bmim}][\text{PF}_6]$	K_2CO_3	r.t.	78
12	$[\text{bmim}][\text{PF}_6]$	K_2CO_3	90	88

Reaction conditions: $\text{PhB}(\text{OH})_2$ (2 mmol), base (4 mmol), 3.6 mol% $\text{Pd}(\text{OAc})_2$, ethyl 2-bromoacetate (1 mmol), ionic liquid/ H_2O = 3/3 g, 3 h.

^a Isolated yield.

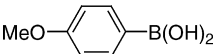
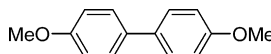
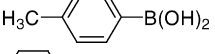
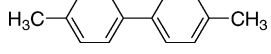
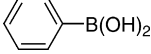
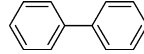
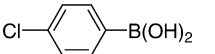
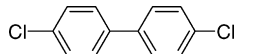
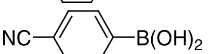
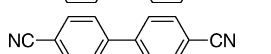
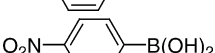
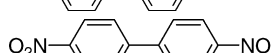
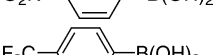
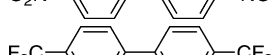
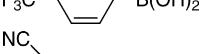
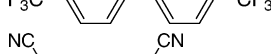
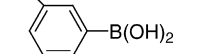
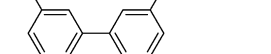
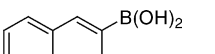
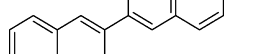
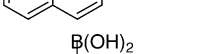
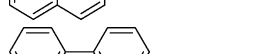
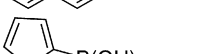
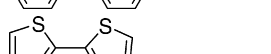
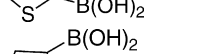
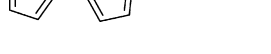
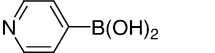
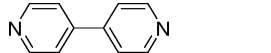
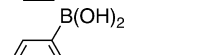
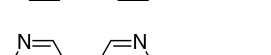

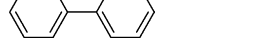
the activity of the homocoupling reaction and an optimum yield was obtained when the ratio of water and $[\text{bmim}][\text{PF}_6]$ was 3:3 (Fig. 1, ●). Further increase in the amount of water was deleterious to the reaction.

Although the homocoupling reaction in $[\text{bmim}][\text{PF}_6]$ was accelerated by the addition of water, only a moderate yield was obtained under the reaction conditions. The previous researches by other groups showed that the palladium-catalyzed dimerization of arylboronic acid could be promoted by the utilization of suitable oxidizing agents [10–13,28]. We therefore examined the effect of different oxidizing agents on the homocoupling reaction, including O_2 , I_2 , H_2O_2 , 2-chloroacetate and 2-bromoacetate. Detailed optimization studies showed that 1 mmol ethyl 2-bromoacetate presented a significant accelerating effect on the homocoupling reaction of phenylboronic acid while the effect of the amount of water on the reaction was similar to that without ethyl 2-bromoacetate. An isolated yield of 92% was obtained in a mixture of water and $[\text{bmim}][\text{PF}_6]$ (3:3 g) (Fig. 1, ■). The mechanism of the reaction might involve the initial step of the oxidative addition of ethyl 2-bromoacetate to a palladium (0) species [27], which caused the double transmetalation with arylboronic acid and generate homocoupling product via the reductive elimination [10,29].

On the other hand, the anion of ionic liquids influenced the activity strongly (Table 1). The $[\text{bmim}][\text{BF}_4]$ (1-butyl-3-methylimidazolium tetrafluoroborate) and $[\text{bmim}][\text{Cl}]$ (1-butyl-3-methylimidazolium chloride) was proved to be less active in the reaction (Table 1, entries 2–3), and $[\text{bmim}][\text{PF}_6]$ was superior to $[\text{bmim}][\text{BF}_4]$ or $[\text{bmim}][\text{Cl}]$. Among the bases tested, K_2CO_3 was the best even though Na_2CO_3 , NaOAc and KOH also gave the good yields (Table 1, entries 1, 5–7). Et_3N and K_3PO_4 delivered low yields (Table 1, entries 8, 9). The reaction was sluggish in the absence of base (Table 1, entry 10). A moderate yield was obtained at room temperature (Table 1, entry 11), but by-products of phenol and biphenyl ether increased when the temperature increased to 90°C , which led to the decrease in the yield of biphenyl (Table 1, entry 12).

Table 2
The homocoupling reaction of arylboronic acids

$$2\text{ArB(OH)}_2 \xrightarrow[\text{K}_2\text{CO}_3, \text{BrCH}_2\text{COOEt}]{\text{Pd(OAc)}_2, 60^\circ\text{C}} \text{Ar-Ar}$$

Entry	Substrate	Product	Yield (%) ^a
1			95 (74)
2			97 (79)
3			92 (76)
4			90 (68)
5			90 (72)
6			91 (69)
7			87 (66)
8			87 (70)
9			90 (62)
10			88 (70)
11			86 (72)
12			68 (47)
13			90 (75)
14			71 (46)
15			73 (49)
16			75 (45)

Reaction conditions: arylboronic acid (2 mmol), Pd(OAc)₂ (3.6 mol%), K₂CO₃ (4 mmol), ethyl 2-bromoacetate (1 mmol), [bmim][PF₆]/H₂O (3:3 g), 60 °C (external), 3 h, in air. The isolated yield without ethyl 2-bromoacetate was given in the parentheses.

^a Isolated yield.

With the optimum reaction conditions in hand, we next studied the homocoupling reaction of various arylboronic acids in H₂O–[bmim][PF₆] in the presence or absence of ethyl 2-bromoacetate. The results are summarized in Table 2. The isolated yields for all substrates were obviously decreased in the absence of ethyl 2-bromoacetate (Table 2, in parentheses). In the presence of 1 mmol ethyl 2-bromoacetate, the formation of the desired homocoupling product was accelerated (Table 2). It was seen that the homocoupling reaction of arylboronic

acids having either electron-donating or electron-withdrawing groups afforded the desired symmetrical biaryls in good to excellent yields (Table 2, entries 1–9). The dimerization of naphthalen-2-ylboronic acid and naphthalen-1-ylboronic acid had also successfully performed in 3 h and provided good yields (Table 2, entries 10, 11). The thiophen-2-ylboronic acid gave the lower yield and thiophen-3-ylboronic acid delivered the higher yield (Table 2, entries 12, 13). The pyridinylboronic acids showed the good reactivity and allowed for the homocoupling

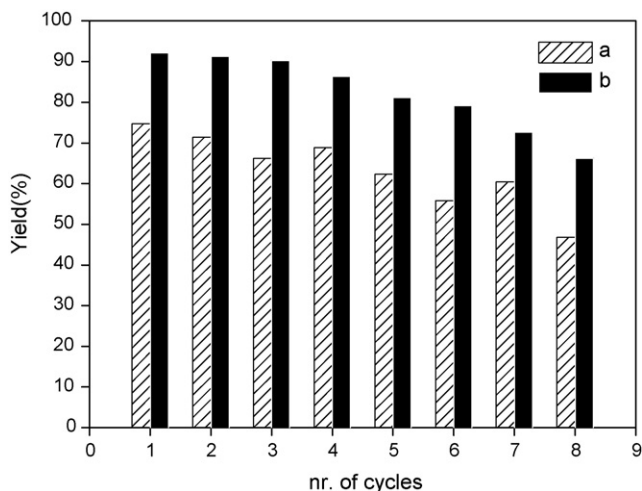


Fig. 2. Recycling of Pd(OAc)₂-[bmim][PF₆]-H₂O catalytic system. Reaction conditions: PhB(OH)₂ (2 mmol), K₂CO₃ (4 mmol), Pd(OAc)₂ (3.6 mol%), [bmim][PF₆]/H₂O = 3/3 g, 60 °C (external), 3 h. (a) Without the use of ethyl 2-bromoacetate. (b) 1 mmol ethyl 2-bromoacetate was added.

reaction under the same reaction conditions in moderate yields (Table 1, 14–16).

The reusability of the catalytic system was tested in the homocoupling reaction of phenylboronic acid using K₂CO₃ as the base in the presence of 3.6 mol% Pd(OAc)₂ and 1 mmol ethyl 2-bromoacetate at 60 °C for 3 h. Since the ionic liquids were insoluble in diethyl ether, the products were easily isolated by simple extraction with diethyl ether. The rest of the ionic liquid and catalyst was recovered and reused in the recycle without further generation or addition of Pd(OAc)₂ or ionic liquid (Fig. 2). We first examined the Pd(OAc)₂-H₂O-[bmim][PF₆] catalytic system in the absence of ethyl 2-bromoacetate (Fig. 2a). The catalytic system could be recycled eight times with only a small decrease in activity although the yields were not high. After the addition of ethyl 2-bromoacetate in every cycle, the yield of the homocoupling reaction was promoted markedly and the highly efficient recyclability of the catalytic system was obtained (Fig. 2b).

In conclusion, we have developed a novel recyclable method for the synthesis of symmetrical biaryls using the Pd(OAc)₂ as the catalyst in water and [bmim][PF₆] under mild reaction conditions. The additive of ethyl 2-bromoacetate promoted the homocoupling reaction significantly and the reaction allows a large range of substrates to form the symmetrical biaryls in high efficiency. The method has the advantage of rapid reaction time, use of nontoxic and nonflammable solvent, and facile separation of the products.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.molcata.2007.03.031.

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