



## Application of a dimeric P,C-palladacycle complex as a catalyst in Suzuki and Heck cross-coupling reactions

Kazem Karami\*, Mahdiyeh Ghasemi, Nasrin Haghghat Naeini

Department of Chemistry, Isfahan University of Technology, Isfahan 84156/83111, Iran

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### ABSTRACT

In this Letter the dimeric palladacycle  $[\text{Pd}(\mu\text{-Cl})(\text{P}(\text{OPh})_2(\text{OC}_6\text{H}_4))_2]$  containing a phosphorus donor atom is prepared and its catalytic activity was tested in the Suzuki reaction of phenylboronic acid at room temperature, and the Heck reaction of styrene at 130 °C with aryl halides of varying electron density. All reactions were monitored by GC and generally gave high yields of coupled products.

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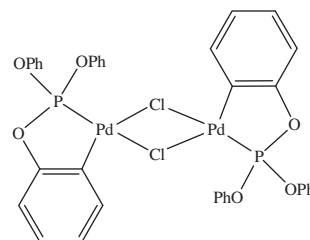
Cyclopalladated complexes are very important materials in organometallic chemistry.<sup>1,2</sup> Palladacycles have gained significant interest due to their applications in organic synthesis,<sup>3–5</sup> materials science,<sup>6</sup> photochemistry,<sup>7</sup> and in the pharmaceutical industry.<sup>8,9</sup> These thermally and air-stable complexes with low toxicity are used as catalysts in Suzuki,<sup>10,11</sup> Sonogashira,<sup>12</sup> Heck,<sup>13,14</sup> and Stille reactions.<sup>15,16</sup> Suzuki and Heck reactions are important methods for carbon–carbon bond formation, that involve a Pd(0)–Pd(II) catalytic cycle.<sup>17–19</sup> Among existing catalysts for these reactions, the preferred classes of catalyst are usually palladacycles containing a metalated carbon and a coordinating donor atom (P, N, S).<sup>20–22</sup> By changing the ligands on the transition metal atom, the catalyst properties can be altered. Bulky electron-rich phosphines tend to increase the reaction performance and they also act as catalysts themselves.<sup>23–25</sup>

Various aryl halides can be used in these reactions. Since the bond strengths of C–Cl and C–Br are stronger than C–I (bond dissociation energies for phenyl halides: Cl: 96 kcal/mol; Br: 81 kcal/mol; I: 65 kcal/mol), their reactivity decreases in the order ArI > ArBr > ArCl.<sup>26,19,27,28</sup> As aryl chlorides are cheaper, more readily available and practical, they are considered as the best substrates for coupling reactions in comparison with their bromide or iodide analogs.<sup>29</sup>

The palladacycle  $[\text{Pd}(\mu\text{-Cl})(\text{P}(\text{OPh})_2(\text{OC}_6\text{H}_4))_2]$  was reported by Albinati et al.<sup>30</sup> This dimeric complex contains mixed phosphorus–carbon (P–C) donors and is shown in Scheme 1. In this Letter, the catalytic activity of this complex was investigated in homogeneous Heck and Suzuki reactions.

Our initial investigation started with the cross-coupling reaction of phenylboronic acid and bromobenzene as a Suzuki model system. There are various related heterocycles that have been used for room temperature Suzuki reactions.<sup>31–34</sup> The reaction was carried out in the presence of 0.5 mol % of the catalyst in THF/water (2:1) at room temperature. The effect of various bases on the coupling reaction was studied (Table 1, entries 1–5) and Et<sub>3</sub>N was found to be the most effective. Using Et<sub>3</sub>N as the base, other substrates were examined (Table 1, entries 6–16). Solvents, such as acetonitrile (CH<sub>3</sub>CN), *N,N*-dimethylformamide (DMF), acetone, and toluene were not effective (Table 1, entries 8, 9, 10, and 12). The conversion of bromobenzene was low when THF was used as the solvent (Table 1, entry 6). Also, the conversion of bromobenzene was reduced with a THF/water ratio of 1:1 rather than a ratio of 2:1 (Table 1, entry 7).

The conversion was found to decrease on increasing the reaction temperature; the reasons for this are not clear (Table 1, entries 13 and 14). The highest yield was obtained at room temperature. The color of the suspension turned black within a few minutes due to the conversion of Pd(II) into the more active Pd(0)



Scheme 1. The dimeric palladacycle used in this work.

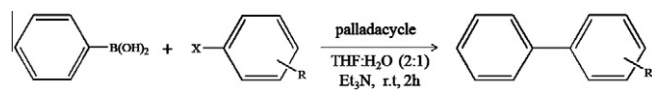
\* Corresponding author. Tel.: +98 3113912351; fax: +98 3113912350.

E-mail address: [karami@cc.iut.ac.ir](mailto:karami@cc.iut.ac.ir) (K. Karami).

**Table 1**  
Optimization of the reaction conditions for the Suzuki reaction of bromobenzene with phenylboronic acid<sup>a</sup>

Entry	Solvent	Base	Temp (°C)	Time (h)	Yield (%)
1	THF:H <sub>2</sub> O (2:1)	K <sub>3</sub> PO <sub>4</sub> ·3H <sub>2</sub> O	rt	2	29
2	THF:H <sub>2</sub> O (2:1)	Na <sub>2</sub> CO <sub>3</sub>	rt	2	73
3	THF:H <sub>2</sub> O (2:1)	Et <sub>3</sub> N	rt	2	85
4	THF:H <sub>2</sub> O (2:1)	K <sub>2</sub> CO <sub>3</sub>	rt	2	81
5	THF:H <sub>2</sub> O (2:1)	KOH	rt	2	83
6	THF	Et <sub>3</sub> N	rt	2	17
7	THF:H <sub>2</sub> O (1:1)	Et <sub>3</sub> N	rt	2	59
8	CH <sub>3</sub> CN	Et <sub>3</sub> N	rt	2	>15
9	DMF	Et <sub>3</sub> N	rt	2	<10
10	Acetone	Et <sub>3</sub> N	rt	2	10
11	MeOH	Et <sub>3</sub> N	rt	2	66
12	Toluene	Et <sub>3</sub> N	rt	2	<10
13	THF:H <sub>2</sub> O (2:1)	Et <sub>3</sub> N	50	2	77
14	THF:H <sub>2</sub> O (2:1)	Et <sub>3</sub> N	70	2	62
15	THF:H <sub>2</sub> O (2:1)	Et <sub>3</sub> N	rt	3.5	60
16	THF:H <sub>2</sub> O (2:1)	Et <sub>3</sub> N	rt	1	22

<sup>a</sup> Reaction conditions: bromobenzene (0.5 mmol), phenylboronic acid (0.55 mmol), base (1 mmol), solvent (4 ml), [Pd(μ-C1)(P(OPh)<sub>2</sub>(OC<sub>6</sub>H<sub>4</sub>))<sub>2</sub>] (0.005 mmol).

**Table 2**  
Suzuki reactions of various aryl halides with phenylboronic acid using 0.5 mol % of the Pd catalyst<sup>a</sup>

Entry	Ar-X	Product	Yield <sup>b</sup> (%)
1			47
2			97
3			71
4			85
5			97
6			98
7			60
8			60

**Table 2 (continued)**

Entry	Ar-X	Product	Yield <sup>b</sup> (%)
9			39
10			84
11			90
12			90
13			100

<sup>a</sup> Reaction conditions: derivatives of aryl halides (0.5 mmol), phenylboronic acid (0.55 mmol), Et<sub>3</sub>N (1 mmol), THF:H<sub>2</sub>O (2:1), (4 ml), Pd catalyst (0.005 mmol), rt, 2 h.

<sup>b</sup> Determined by GC.

**Table 3**

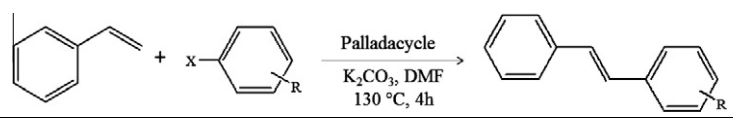
Optimization of the reaction conditions for the Heck reaction of bromobenzene with styrene<sup>a</sup>


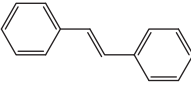
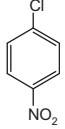
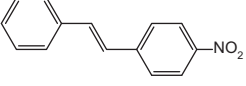
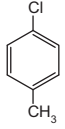
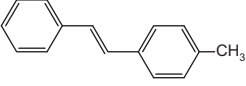
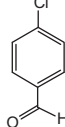
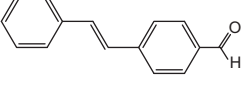

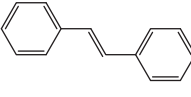
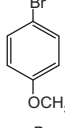
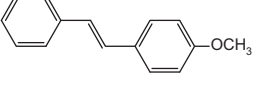
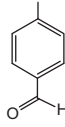
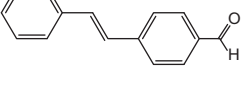

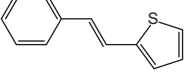

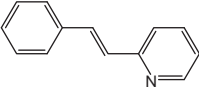
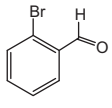
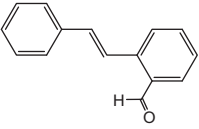

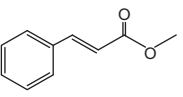
Entry	Solvent	Base	Temp (°C)	Time (h)	Yield (%)
1	THF:H <sub>2</sub> O (2:1)	Et <sub>3</sub> N	rt	2	Trace
2	THF:H <sub>2</sub> O (2:1)	K <sub>2</sub> CO <sub>3</sub>	rt	2	Trace
3	DMF	K <sub>2</sub> CO <sub>3</sub>	rt	5	Trace
4	DMF	K <sub>2</sub> CO <sub>3</sub>	130	3	86
5	DMF	K <sub>2</sub> CO <sub>3</sub>	130	4	92

<sup>a</sup> Reaction conditions: bromobenzene (0.5 mmol), phenylboronic acid (0.55 mmol), base (1 mmol), solvent (4 ml), [Pd(μ-C1)(P(OPh)<sub>2</sub>(OC<sub>6</sub>H<sub>4</sub>))<sub>2</sub>] (0.01 mmol).

catalyst.<sup>35</sup> As the catalyst is thermally stable and not sensitive to oxygen or moisture, the reactions were carried out under air. Increasing the reaction time did not lead to a higher conversion of bromobenzene (Table 1, entry 15). The best conversion of 85% for this reaction was attained at room temperature over 2 h (Table 1, entry 3). We applied the optimized conditions to the Suzuki cross-coupling reactions of different aryl halides with phenylboronic acid. The results are summarized in Table 2.

The catalytic activity of the palladacycle was also studied in the Heck reaction of bromobenzene with styrene using the optimized Suzuki reaction conditions (Table 3, entry 1). As satisfactory yields were not obtained, we tried to improve the conditions. Bases are used for the regeneration of the catalyst by removing HX and leaving the active Pd complex in the final stage of the catalytic cycle in the Heck reaction, according to the well-established mechanism.<sup>36,37</sup> The yield of the Heck reaction of bromobenzene with styrene at room temperature was negligible, and only a trace amount of the product was obtained (Table 3, entries 1–3). Moreover, a high temperature appears to be essential for the Heck reaction to take place (Table 3, entries 4 and 5). The best results for the Heck reaction of bromobenzene with styrene were obtained by using 0.01 mmol of the Pd catalyst in DMF as the solvent and K<sub>2</sub>CO<sub>3</sub> as the base at 130 °C for up to 3.5 h.

**Table 4**Heck reactions of various aryl halides with phenylboronic acid using 1 mol % of the Pd catalyst<sup>a</sup>


Entry	Ar-X	Product	Yield <sup>b</sup> (%)
1			52
2			95
3			44
4			85
5			92
6			75
7			100
8			89
9			25
10			95
11 <sup>c</sup>			30

<sup>a</sup> Reaction conditions: aryl halide (0.5 mmol), styrene (0.6 mmol), K<sub>2</sub>CO<sub>3</sub> (1 mmol), DMF (4 ml), Pd catalyst (0.01 mmol), 130 °C, 4 h.<sup>b</sup> Determined by GC.<sup>c</sup> Reaction was carried out with methyl acrylate instead of styrene.

The optimized conditions were applied to Heck reactions between styrene and various aryl halides (Table 4). As expected, aryl halides with electron-withdrawing substituents in *para* positions reacted smoothly; aryl halides with electron-donating substituents were less reactive. Deactivated electron-rich aryl chlorides also participated in these reactions but were poor substrates. The activated electron-deficient substrate, 4-chlorobenzaldehyde and

4-chloronitrobenzene reacted to give relatively high yields of the expected products (Table 2, entry 2 and Table 4, entries 2 and 4).

In conclusion, we have successfully employed a dimeric palladacycle complex as an efficient catalyst for the Suzuki and Heck cross-coupling reactions of various aryl halides. In the Suzuki reactions the corresponding products were obtained in yields in the range 39–100%, and those of the Heck reactions were

25–100%, depending on the substituent present on the aromatic ring of the aryl halide. The advantage of these methods is that the Suzuki reactions of aryl halides with phenylboronic acid were performed at room temperature and that the Heck reaction worked well in air, thus simplifying the work-up.

### Acknowledgment

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