



# A convenient phosphine-free palladium-catalyzed direct arylation of thiazole under mild aerobic conditions



Xiao-Xi He, Yan-Fang Li, Ju Huang<sup>\*\*</sup>, Dong-Sheng Shen, Feng-Shou Liu<sup>\*</sup>

School of Chemistry and Chemical Engineering, Guangdong Pharmaceutical University, China

## ARTICLE INFO

### Article history:

Received 15 September 2015

Received in revised form

19 November 2015

Accepted 4 December 2015

Available online 12 December 2015

### Keywords:

Bulky aniline

Palladium complex

Thiazole

Direct arylation

Aerobic condition

## ABSTRACT

A series of bulky amine palladium complexes  $\{[(Ar-NH_2)_2PdCl_2]\}$  were synthesized and characterized. The catalytic activity of the palladium complexes was evaluated via the direct C–H arylation of thiazoles with aryl bromides in aerobic conditions at 80–100 °C. Under the optimal conditions, 0.5–0.05 mol% of the bulky palladium complexes were found to be very efficient and produced the desired cross-coupling products in high yields.

© 2015 Elsevier B.V. All rights reserved.

## 1. Introduction

With broad functional group tolerance and without the need for synthesis of organometallic coupling partners, palladium-catalyzed direct C–H bond arylation has become an important method for the formation of carbon–carbon bonds during the past decade [1]. Particularly, the direct arylation of thiazoles has received much attention [2–4] because such structural units are frequently found in pharmaceuticals, natural products, and functional organic materials [5]. The efficiency of this cross-coupling is greatly influenced by the choice of ligand, base, solvent and additives [6]. The ligand, which binds to the palladium to stabilize the catalytic intermediates, plays a pivotal role in the transformation process. Thus, considerable efforts have been directed toward the development of efficient ligands [7]. Noticeable advances have been achieved with bulky and electron-rich phosphine ligands, which have significantly enlarged the scope of direct arylation [2g,h,n,o]. However, except some well-known air-stable phosphine developed by Buchwald, most of these phosphine-based ligands are not readily available, and they are air-sensitive and toxic [8].

In contrast, the recent development of phosphine-free and

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

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

E-mail addresses: [xianghuangj@163.com](mailto:xianghuangj@163.com) (J. Huang), [fengshou2004@126.com](mailto:fengshou2004@126.com) (F.-S. Liu).

ligand-free catalysts has shown promise because they have the potential to overcome the disadvantages of catalytic instability and environmental concerns [7a–c]. Itami and coworkers were the first to report the palladium-catalyzed C4-selective arylation of thiazoles with arylboronic acids using 2,2'-bipyridyl (bipy) or 1,10-phenanthroline (phen) as the ligand [3h,r,s]. Subsequently, the Pd/bipy was successfully applied for the C5-selective arylation of thiazole with aryl iodides [3g]. Murai and coworkers highlighted that commercial  $[Pd(phen)_2](PF_6)_2$  can promote the one-pot multiple direct arylation of thiazole with aryl halides in the presence of 5 mol% catalyst loading [3f,i]. Recently, Doucet and Gök demonstrated the *N*-heterocyclic carbenes (NHCs) palladium catalysts have excellent performance in the preparation of arylthiazoles, even using the aryl bromides and chlorides as the coupling partners in a high reaction temperature (>130 °C) [3e,p]. However, there are still much room to explore an efficient phosphine-free palladium catalyst for the direct C–H arylation, especially with respect to the palladium loading (<0.1 mol%), the substrate scope of the method, and mild reaction temperature. Therefore, there is a need for readily available and efficient catalysts that can mediate the transformation under mild conditions.

Simple amines are highly efficient ligands for the Suzuki–Miyaura cross-coupling reaction, and they have a broad substrate scope [9]. Very recently, the use of dual Pd/Cu catalysts in conjunction with amine ligands enabled the direct arylation of 2'-deoxyadenosines with both aryl iodides and bromides [10].

Moreover, Bulky substituted pyridine developed by Tsuji also exhibited highly efficient in air oxidation of alcohols [11]. Inspired by the promising performance of the nitrogen based ligands, we hypothesized that sterically bulky primary anilines, which can stabilize the palladium active species, would be beneficial for the direct arylation. Herein, we report a general method for the synthesis of 5-arylthiazoles using aniline palladium complexes under mildly aerobic reaction conditions.

## 2. Results and discussion

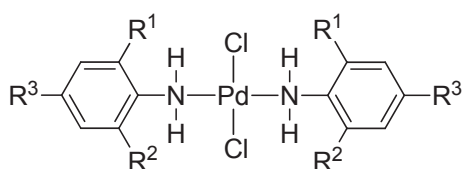
### 2.1. Synthesis and characterization of aniline palladium complexes

**L2-L5** can be readily synthesized via the *ortho*-alkylation of anilines with diphenylmethanol in one-step, according to the procedure proposed by Markó and Nolan [12]. Moreover, the reaction of substituted anilines with palladium chloride in DMAc produced the corresponding **C1–C5** in high yields (Scheme 1). These palladium complexes were characterized using NMR, MS, and elemental analysis. An advantage of these palladium complexes is that they are stable toward air and moisture, so that the preparation, purification and crystallization of the palladium complexes can be conveniently operated in open-air.

Crystals of **C2–C5** that were suitable for X-ray diffraction were grown from a solution of dichloromethane and methanol in aerobic conditions. As shown in Figs. 1–4, a slightly distorted square-planar coordination geometry was observed, in which the two aniline ligands are oriented *trans* to each other in the **C2–5**. The nitrogens, N(1) and N(2), and chlorines, Cl(1) and Cl(2) that are attached to palladium are all in the same plane. The solid state structure of these four palladium complexes revealed similar bond lengths. Nevertheless, it is deserved to note that the Pd–N bond lengths (2.056(3) Å) in **C2** were shorter than that of the typical Pd–N(sp<sup>3</sup>) single bond length (2.07–2.10 Å) and that of **C2–5**, indicating a slightly stronger interaction between the coordinated atoms and the palladium in **C2** [9b,i,13].

### 2.2. Direct arylation catalyzed by aniline palladium complexes

Initially, we chose 4-methylthiazole (**1a**) and 4-bromobenzonitrile (**2a**) as the model substrates in the presence of 0.5 mol% of the palladium complex (Table 1). To establish mild reaction conditions, the heteroarene and the aryl bromides were employed in equimolar quantities. The experiments were performed at a temperature of 80 °C for 24 h, using K<sub>2</sub>CO<sub>3</sub> as the base, DMAc as the solvent, and pivalic acid (PivOH) as the additive. As shown in Table 1, the precatalysts critically affected the efficiency of



- C1:** R<sup>1</sup>=*i*Pr, R<sup>2</sup>=*i*Pr, R<sup>3</sup>=H;  
**C2:** R<sup>1</sup>=Me, R<sup>2</sup>=CHPh<sub>2</sub>, R<sup>3</sup>=Me;  
**C3:** R<sup>1</sup>=CHPh<sub>2</sub>, R<sup>2</sup>=CHPh<sub>2</sub>, R<sup>3</sup>=Me;  
**C4:** R<sup>1</sup>=CHPh<sub>2</sub>, R<sup>2</sup>=CHPh<sub>2</sub>, R<sup>3</sup>=OMe;  
**C5:** R<sup>1</sup>=CHPh<sub>2</sub>, R<sup>2</sup>=CHPh<sub>2</sub>, R<sup>3</sup>=Cl;

Scheme 1. Structure of the aniline palladium complexes.

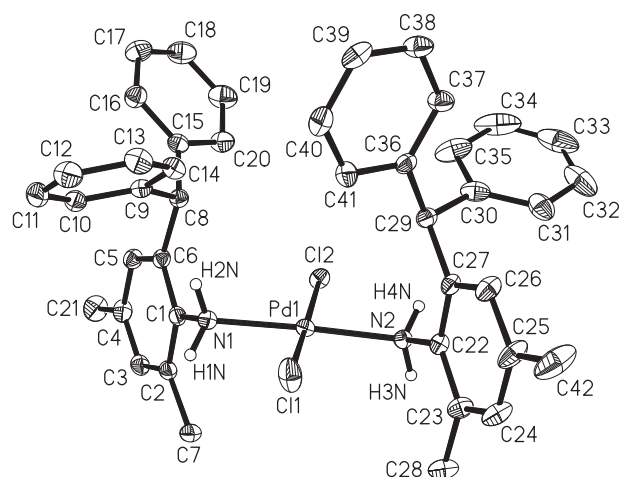


Fig. 1. Molecular structure of **C2** depicted with 30% thermal ellipsoids. Hydrogen atoms except on the amines and one half of the non-coordinated methanol molecule have been omitted for clarity. Selected bond distances (Å): Pd(1)–N(1) 2.056(3), Pd(1)–N(2) 2.056(3), Pd(1)–Cl(1) 2.2914(10), Pd(1)–Cl(2) 2.2938(9).

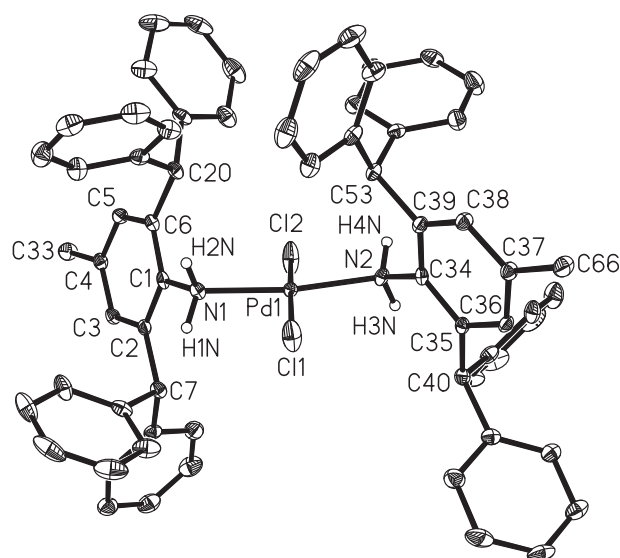


Fig. 2. Molecular structure of **C3** depicted with 30% thermal ellipsoids. Hydrogen atoms except on the amines and four non-coordinated dichloromethane molecules have been omitted for clarity. Selected bond distances (Å): Pd(1)–N(1) 2.073(4), Pd(1)–N(2) 2.072(4), Pd(1)–Cl(1) 2.2752(13), Pd(1)–Cl(2) 2.2764(13).

this reaction. Cy<sub>2</sub>NH/PdCl<sub>2</sub>, which was proved highly efficient in the Suzuki–Miyaura coupling [9a,b], showed promising results, and it provided the direct arylation product, **3aa**, in a 86% GC yield (Entry 1, Table 1). Meanwhile, **C1**, with 2,6-diisopropyl substituents on the aniline moiety, provided the coupling product, **3aa**, with almost the same efficiency as the Cy<sub>2</sub>NH/PdCl<sub>2</sub>. In contrast, the bulky benzhydryl group on the aniline moiety exhibited a profound effect on the activities. For example, **C2–C5** exhibited superior reactivity than **C1** and Cy<sub>2</sub>NH/PdCl<sub>2</sub> (Entries 3–6, Table 1). Reasonably, the use of bulky steric of the ligand, which can stabilize the palladium center and further facilitate the elimination rate, is essential for the direct arylation process [2i,14]. However, quite out of our expectation, in these aniline palladium complexes screened, **C2**, which is less bulky than **C3–C5**, was found to be the most active catalyst in the direct arylation. For example, the coupling reaction that employed **C2** as the precatalyst afforded the corresponding

Download English Version:

<https://daneshyari.com/en/article/1322986>

Download Persian Version:

<https://daneshyari.com/article/1322986>

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