



## Review

## When cross-coupling partners meet indolylphosphines



Shun Man Wong, On Ying Yuen, Pui Ying Choy, Fuk Yee Kwong\*

State Key Laboratory of Chirosciences, Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, Hung Hom, Kowloon, Hong Kong

## Contents

1. Introduction .....	158
2. Suzuki–Miyaura coupling .....	159
2.1. Mesylates and tosylates as electrophiles .....	159
2.2. Halides as electrophiles .....	159
3. Sonogashira coupling .....	170
3.1. Mesylates and tosylates as electrophiles .....	170
3.2. Halides as electrophiles .....	170
4. Hiyama coupling .....	170
5. Coupling using organotitanium as nucleophiles .....	173
6. Cyanation .....	173
7. Direct C–H arylation .....	173
8. Buchwald–Hartwig amination .....	174
9. Borylation .....	178
10. C–O coupling .....	178
11. Carbonylation .....	183
12. Reduction .....	183
13. Conclusion .....	184
Acknowledgments .....	184
References .....	184

## ARTICLE INFO

## Article history:

Received 27 August 2014

Received in revised form 19 January 2015

Accepted 27 January 2015

Available online 7 February 2015

## Keywords:

Palladium

Indolylphosphines

Cross-coupling

Ligands

Catalysis

## ABSTRACT

Indolylphosphines have been successful as unique and efficient ligands for palladium-catalyzed cross-coupling reactions. This review summarizes the recent decade developments and applications of different coupling partners in these reactions that employ indolylphosphines as supporting ligands. The ligand structural motifs and their specific catalytic activity are discussed.

© 2015 Elsevier B.V. All rights reserved.

## 1. Introduction

Palladium-catalyzed cross-coupling has received significant attention in the synthetic organic community for the construction

of both aromatic carbon–carbon and carbon–heteroatom bonds. Straightforward, modular and convergent features of these methods enable scientists to assemble highly complex yet diverse molecules in a relatively simple way [1]. By connecting different electrophilic and nucleophilic fragments together in a cross-matching mode, numerous products can be readily obtained. For instance, Suzuki–Miyaura coupling, Heck reaction and Buchwald–Hartwig amination allow the construction of

\* Corresponding author. Tel.: +852 34008682.

E-mail address: [fuk-yee.kwong@polyu.edu.hk](mailto:fuk-yee.kwong@polyu.edu.hk) (F.Y. Kwong).

diversified biaryls, arylated olefins/dienes, and aromatic amines, respectively [2]. These well-known coupling protocols have been implemented in manufacturing pharmaceuticals, advanced materials, and fine chemicals since the last decade.

Before the late 1990s, aryl iodides, bromides and triflates were often employed as electrophilic partners in coupling reactions because of their relatively high reactivity. The more abundant and inexpensive, but more inert aryl chlorides, tosylates and mesylates were less frequently applied. Ligands have been well-recognized as the key for enhancing efficiency and scope of coupling reactions. Since late 1990s, chemists have established electron-rich and sterically bulky phosphines for activating inert aromatic carbon-halogen bonds. Beller [3], Buchwald [4], Fu [5], Hartwig [6] and other research groups [7] have contributed considerably to the area of phosphine developments and their applications in coupling reactions. Among various phosphine ligands developed, indolylphosphines in which these ligands embodied indole nucleus in the main ligand skeleton, are a unique class of ligand for these reactions. In fact, examples of indolylphosphine have been reported for catalytic reactions since mid 1990s [8]. The successful applications of indolylphosphines in cross-coupling reactions have been achieved since early 2000s [9].

The use of indole moiety as the main ligand skeleton has many advantages. It can be easily diversified and prepared from commercially accessible starting materials [10]. Recent ligand exploration showed that indolylphosphines are highly efficient toward various palladium-catalyzed coupling reactions, such as Suzuki–Miyaura coupling, Sonogashira coupling, Hiyama coupling, Buchwald–Hartwig amination, cyanation, C–H functionalization and borylation. (Table 1) [11,12]. It is significant to understand how the catalyst performs through varying the structure of ligands. Palladium complexes associated with imidazole- [13], carbazole- [14] and benzimidazole-based phosphines [15] give insight about the unique metal-ligand interaction in catalysis (Table 2).

## 2. Suzuki–Miyaura coupling

Palladium-catalyzed Suzuki–Miyaura cross-coupling was firstly disclosed in 1979 [16] and has become a widely used protocol for preparing unsymmetrical biaryls for pharmaceutical, material, and agricultural sciences [1,17]. This method has many advantages as the reaction conditions offer excellent functional group compatibility and the coupling partners (arylboronic acids) are of low toxicity as well as high commercial availability. Aryl iodides, bromides, and more recently chlorides [12,18], tosylates and mesylates [11] are applicable electrophiles this biaryl synthesis.

### 2.1. Mesylates and tosylates as electrophiles

Aryl mesylates and tosylates are considerably more inert in coupling reaction than the corresponding aryl triflates and nonaflates. Nevertheless aryl mesylates and tosylates are less expensive. Over the past decade, efforts have been undertaken by researchers to expand the feasibility of using these coupling partners in cross-coupling reactions. In 2008, the first Pd-catalyzed Suzuki–Miyaura coupling of mesylated arenes employing **CM-phos** (**L1a**) was reported [19]. Palladium complex ligated with **CM-phos** was effective to handle a wide range of deactivated, functionalized aryl, and heteroaryl mesylates (Table 3, entries 1–3). In addition to arylboronic acids, aryltrifluoroborate salts and pinacol boronate esters were applicable nucleophiles (Table 3, entries 4–5). Single crystal X-ray crystallographic data revealed the formation of a dimeric palladium complex with two acetate bridging groups when Pd(OAc)<sub>2</sub> was complexed with **CM-phos** (**L1a**) under a basic medium. The

palladacycle formation involved the C3-position of the indole ring (Fig. 1) [20].

This Pd(OAc)<sub>2</sub>/**CM-phos** catalyst system was found general to this reaction and the Pd loading down to 0.2 mol% could be achieved (Table 3, entries 6–8) [21]. Remarkably, an example of aryl tosylate coupling at room temperature was illustrated (Table 3, entry 8). Having the same Pd complex, the scope of this reaction was extended to various organotrifluoroborate salts [22]. The applicability of potassium aryl, heteroaryl, alkyl and vinyltrifluoroborate salts was demonstrated (Table 3, entries 9–12). In addition to mesylated arenes, this system also allowed the coupling of alkenyl electrophiles under mild reaction conditions [23]. A variety of alkenyl tosylates (Table 3, entries 13–15) and the first examples of mesylates (Table 3, entries 18–19), couple well with an array of aryl or alkylboronic acids. Moreover, the first successful tri-*ortho*-substituted product examples from alkenyl tosylates were shown (Table 3, entries 16–17).

### 2.2. Halides as electrophiles

Aryl halides are widely used electrophilic arene sources for coupling reactions. With easily accessible indolylphosphines **L2a–L2c** having N–P bound feature [24], a variety of aryl and alkenyl chlorides could be coupled well with arylboronic acids (Table 4, entries 1–3). Remarkable catalyst loading (down to 0.02 mol% Pd) was achieved for particular substrates (Table 4, entry 2).

Ligand diversification from a convergent synthesis is of high attractiveness. Recently, a one-pot assembly of indolyl phosphine, e.g. **Amidole-phos** (**L3**) was reported [25]. In addition to general coupling examples of arylboronic acids with aryl chlorides (Table 4, entries 4–6), a preliminary study showed that the coupling of alkylboronic acid with aryl chlorides was successful (Table 4, entry 7). The catalyst loading of 0.01 mol% Pd could be achieved (Table 4, entry 5).

The synthesis of tetra-*ortho*-substituted biaryls has been a long synthetic challenge. By employing catalyst system of Pd<sub>2</sub>(dba)<sub>3</sub> and **CPh α-Nadole-phos** (**L4b**), the tetra-*ortho*-substituted biaryl synthesis was accomplished (Table 4, entries 8–9) [26]. Another set of aryl chlorides was also examined by **CPh o-Andole-phos** (**L4c**), this reaction proceeded smoothly to give tri-*ortho*-substituted biaryls under a relatively low catalyst loading (Table 4, entries 10–11).

Previous studies found that **CM-phos** (**L1a**) was highly active toward mesylated and tosylated arenes. In fact, **CM-phos** (**L1a**) could also deal with the cross-coupling of aryl halides. An investigation revealed that the coupling of 2-chlorotoluene with phenylboronic acid gave moderate yield under catalyst loading of 0.001 mol% (Table 4, entry 12) [27].

Sarkar and co-workers reported a bidentate phosphine ligand **L5** for Pd-catalyzed Suzuki–Miyaura coupling of aryl, heteroaryl, and allyl chlorides with phenylboronic acid (Table 4, entries 13–15) [28]. Later, the same group developed an interesting ligand **L6a** for C–C bond coupling reaction (Table 4, entry 16) [29]. Study toward the ligand substituent effects toward the efficacy of this reaction was carried out. Some ligands with a monodentate characteristic were effective in Suzuki–Miyaura reaction. Single crystal X-ray crystallographic analyses for both Pd–**L5** and Pd–**L6a** complexes were reported (Table 5).

The Pd-catalyzed Suzuki coupling of aryl and heteroaryl chlorides with potassium aryl and heteroaryltrifluoroborates in water was recently disclosed (Table 4, entries 17–19) [30]. Remarkably, under the Pd(OAc)<sub>2</sub>/**CPCy Phendole-phos** (**L4a**) system, low catalyst loading (down to 0.005 mol% Pd) could be achieved (Table 4, entry 18).

Heo and co-workers reported an efficient synthesis of dibenzo[*a,c*]cyclohepten-5-ones via a sequential Suzuki coupling

Download English Version:

<https://daneshyari.com/en/article/1299364>

Download Persian Version:

<https://daneshyari.com/article/1299364>

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