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# Mechanism insight and scope of PEPPSI-catalyzed cross-coupling reaction between triarylbismuth and arylbromide

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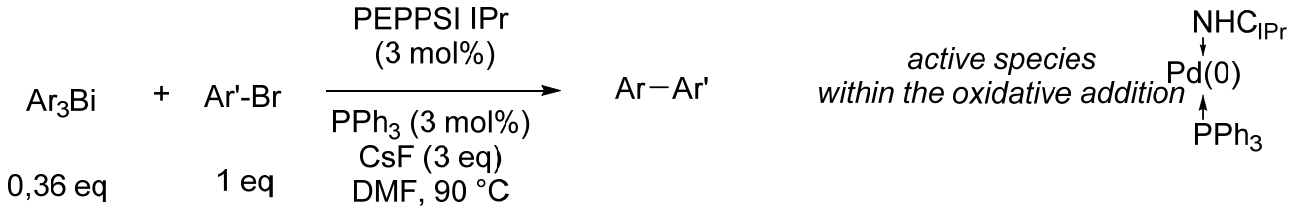
Graphical abstract



**Highlights**

- Cross coupling of $Ar_3Bi$ and Ar-Br are catalysed by NHC-Pd-($PPh_3$).
- $Ar_3Bi$ plays a dual role: aryl tranfert reagent and reducing agent.
- The active species is *in-situ* obtained by reactions from PEPPSI, $Ar_3Bi$ and $PPh_3$.
- A Lewis base is compulsory for the activation of aryltransfert.
- Phenol, amine, carboxylic acid are compatible with the reaction conditions.

**ABSTRACT :**

In this paper we report the first cross-coupling reaction of $Ar_3Bi$ with Ar'X mediated by Pd-NHC complexes by keeping the ability of $Ar_3Bi$ to transfer the three aryl moieties. Investigations were carried out in order to minimize the quantity of the side product Ar-Ar coming from the conversion of $Ar_3Bi$. The results showed that PEPPSI IPr was a good catalyst precursor. Efforts were focussed on the rule of each additive such as $PPh_3$ and the base. It was notably found that the presence of $PPh_3$ (ratio PEPPSI IPr/$PPh_3$: 1/1) was essential to keep the process efficient. Therefore NHC-Pd-$PPh_3$ has been assumed as being the catalytic species. Under the optimized reaction conditions the concomitant formation of the undesired biaryl side product was restricted to its inherent formation consecutive to the reduction of the catalyst precursor to Pd°. In a last study, the scope and the limitation of the new catalytic methodology were examined and a large range of unsymmetrical biaryl compounds Ar-Ar' bearing various substituents from strongly electron-donating to electron-withdrawing ones have been prepared and fully characterized.

**Keywords :**

PEPPSI • Triarylbismuth • Biaryl • Cross-coupling • Homogenous catalysis

## 1. Introduction

Since the pioneer work of Barton and Coll. published in 1987,[1] triarylbismuths ($Ar_3Bi$) have reached a great interest as aryl transfer reagents for transition metal-catalyzed reaction.[2] Most of the common palladium-catalyzed reactions carried out with common nucleophilic organometallic species such as arylboronic acids are also observed with symmetric triarylbismuths ($Ar_3Bi$): cross coupling with aryl-, heteroaromatic-, ethylenic-, benzylic-, allyl-, propargyl-, halides or triflates even with acyl chlorides.[2b] Conjugated addition may also be performed either under palladium-[3a-b] or rhodium-calalysis.[3c-d] Arylation on heteroatoms such as oxygen[4], nitrogen[5] can also be performed with ArBi(III) under a copper catalysis involving an *in-situ* oxidation of ArBi(III) into ArBi(V). Only one aryl group is transferred during the process. Arylation of sulphur[6] has been recently described and this reaction is atom efficient.

$Ar_3Bi$ are air- and moisture-stable and easily accessible from Grignard reagents[7] or Gosmini organozinc reagents.[8] Also triarylbismuth(III) reagents and the corresponding inorganic product $BiX_3$ are not considered as toxic so far, at least less toxic than other heavy metals and corresponding by-product such as $Ar_3SnX$.[9] Furthermore most of palladium-catalyzed cross-coupling reactions allowed the use of subequimolar quantities of $Ar_3Bi$ as far as all the three aryl groups are effectively transferred within the catalytic process. All these features led to award the title of green reagents to these nucleophilic organometallic compounds.

Many palladium complexes have been proposed as (pre)catalyst for C-C bond formation using $Ar_3Bi$. $Pd(PPh_3]_4$,[10] $PdCl_2/PPh_3$,[11] $[Pd_2Cl_2(\mu Cl)_2(PR_3)_2]$,[12] $Pd(OAc)_2$,[13] $Pd(OAc)_2(Cy_2NH)_2$,[14] $Pd_2(dba)_2$,[15] have been used within an homogeneous catalytic system whilst palladium(II) bipyridyl complexe anchored on nanosized mesoporous silica gel MCM-41,[16] palladium(II) supported on phosphine linked polystyrene resin,[17] or Pd/charcoal,[18] have been employed in the case of heterogeneous catalysis. It is important to notice that some of homogeneous catalytic systems are air-sensitive and that the heterogeneous conditions can seem more convenient and economic from an industrial point of view. However none of them cannot prevent from the unwanted biaryles Ar-Ar formation coming from the slow decomposition of $Ar_3Bi$ mediated by Pd(II) catalyst. [19] This main drawback has an impact on yields and on the easiness of the cross-coupling products purification.

Rao has disclosed in a preliminary study a way to inhibit this reaction using a unsymmetrical arylbismuth reagent.[20] Its structure exhibits a nitrogen lone pair chelating the bismuth atoms

*via* its 5f empty orbitals. As observed for most of stable nucleophilic arylorganometallic species, chelation favors the aryl transferred within the transmetalation elementary step of the proposed catalytic cycle.[21] However this specific structure cannot be considered anymore as green as symmetrical $Ar_3Bi$ reagents, not only because its preparation is not trivial but mainly because only one of the groups beared by the Bi atom can be transferred. That may explain why Rao ande co-workers then focused their activities on $Ar_3Bi$ to make them attractive reagents. It was notably found that additives such as Lewis bases ($PO_4^{3-}$, $CO_3^{2-}$, $F^-$) allow to minimize the dimerization but without its complete inhibition. Therefore further investigations must be carried out to propose standard experimental conditions that inhibit as much as possible the decomposition of $Ar_3Bi$ into the dimer Ar-Ar.

## 2. Experimental

### a. Palladium cross coupling procedure

Under inert atmosphere ($N_2$), in a 25 mL round bottom flask, $Ar_3Bi$ (0.208 mmol; 0.35 eq.), CsF (0.24 g: 1.8 mmol; 3 eq.), $PPh_3$ (0.004 g: 0.018 mmol; 3 mol%), the aryl bromide (0.60 mmol; 1 eq.) was added to DMF (5 mL). The solution was warmed to 90 °C *prior* addition of PEPPSI IPr (0.012 g: 0.018 mmol; 3 mol%). The reaction was monitored by GC/MS to follow the total consumption of the aryl bromide. Cooled to room temperature (RT), the reaction mixture was diluted by addition of diethyl ether (20 mL) and aqueous HCl 6M (30 mL). After decantation, the aqueous solution was extracted with diethylether (2 × 20 mL). The collected organic phases were then washed with HCl 6N (2 × 25 mL), water (25 mL) and brine (25 mL) *prior* drying over $MgSO_4$. After concentration under reduced pressure, the resulting crude product was subjected to purification by column chromatography leading after concentration under reduced pressure to the title compound.

### b. Analytical data

Analytical data of all isolated compounds can be found in the on-line version (supplementary material). Compounds were fully characterized by 1D and 2D NMR allowing full assignments of the signals when possible.

## 3. Results and discussion

### a. General consideration – catalytic system of choice

All the palladium-catalyzed cross-coupling procedures involving $Ar_3Bi$ suffer from the parallel reaction giving access to the undesired dimer Ar-Ar side product. In order to facilitate the purification and increase the yield, the kinetic rate ratio cross-coupling / dimerization must be improved: either by favoring the cross-coupling reaction or by disfavoring the side reaction. Some catalytic cycles have been proposed for the cross-coupling reaction: a less probable one based on a Pd(II)/Pd(IV) couple[22] compared to the classical one based on a Pd(0)/Pd(II) catalytic system[20] depicted in Scheme 1 that has been better considered for our purpose.

A catalytic cycle has also been proposed for the Ar decomposition into Ar-Ar conducted in protic solvents. (Scheme 2) [19]

Both catalytic cycles showed metathesis steps (step 2 from Scheme 1; steps 1 and 2 from Scheme 2) and a reductive elimination step (step 3 from Scheme 1; step 3 from Scheme 2). The main difference is that the desired cross-coupling catalytic cycle contains a Pd(0) oxidative addition into a C-Br bond (step 1 from Scheme 1). To discriminate the kinetics between the two reactions, this step must be favored. Recent literature shows that NHCs ligands exhibit this step. [23] In order to keep the easiness of the experimental procedure a precatalyst must be used, *i.e*. a Pd(II) complex that must be *in-situ* reduced to a Pd(0) complex giving access to the active species. We therefore drew our attention onto Pd(II)/NHC complexes, easily prepared or available such as **1**[24] and **2.** [25] We also focused our attention on PEPPSI catalysts developped by Organ[26] which are known to be robust against oxygen and likely to be *in-situ* reduced. (Scheme 3).

Complexes described in Scheme 3 have therefore been tested as precatalysts (firstly with a loading of 10 mol%) in a typical cross-coupling reaction between *p*-$Tol_3Bi$ and *p*-bromoacetophenone. At this stage Lewis base, temperature and solvent have been kept as those described by Rao: CsF (6 eq), DMF, 90 °C.[27] Catalysts efficiency have been compared regarding to Rao's classical catalytic system ($Pd(OAc)_2$ + 4 $PPh_3$) on the basis of the GC/MS analysis of every single crude product mixture: conversion ratio, reaction time for total consumption of the reagent and cross-coupled product/dimer ratio, in our case **3q** / *p*$Tol_2$. Results are given in Table 1:

Results clearly indicated that *bis*-NHC complexes **1** and **2** (Table 1: entries 2 and 3) are not efficient as really low conversions were observed after a few hours at 90 °C as it was also observed for PEPPSI IPENT (Table 1: entry 6). However less bulky PEPPSI catalysts showed an interesting reactivity as total conversion was observed. Both PEPPSI IPr and PEPPSI SPr gave interesting results compared to $Pd(OAc)_2$/2 $PPh_3$ (Table 1: entries 4 and 5 *vs* entry 1), but the most common one gave shorter reaction time (Table 1: entries 4 vs 5). PEPPSI IPr has therefore been kept as precatalyst for the following optimization procedure.

### b. triphenylphosphine – quantities and rule

Triphenylphosphine was found essential in each assay yielding good results. (Table 2: entries 1-4 *vs* 5). Variation on the PEPPSI IPr/$PPh_3$ ratio has been carried out with 10 mol% of catalyst. Results are given Table 2.

It is worth noting that the loading of $PPh_3$ must be at least equal to those of PEPPSI IPr and that no improvement was observed with an excess of phosphine. Without triphenylphosphine no reaction was observed even the dimer formation. Furthermore a ratio $PPh_3$/PEPPSI 4 /1, 2/1 or 1/1 gave similar kinetics. It is commonly stated that 2 equivalents of $PPh_3$ are required to reduce 1 equivalent of Pd(II) to Pd(0). Therefore the hypothesis that $PPh_3$ could reduced Pd(II) to Pd(0) is not consistent with the results (Table 2: entry 2 *vs* entry 3). $PPh_3$ may therefore act as ligand. However Organ usually involved an $(NHC)_1Pd(0)$ species as active species.[28] At this stage two oxidative addition mechanisms can be involved: an associative one and a dissociative one.

Organ usually involved a dissociative mechanism when the initial Pd(0) complex NHC-Pd(0)-Pyr loose the weak ligand 3-chloropyridine.[29] In this hypothesis, the active species would be a NHC-Pd(0) complex. However this mechanism is not consistent with the crucial rule of $PPh_3$. The first hypothesis would be that a dissociative mechanism will lead to NHC-Pd(0) and that in the presence of $Ar_3Bi$ this last complex will not be stable enough as it have been already demonstrated with $Pd(PPh_3)_4$.[30] Therefore this NHC-Pd(0) species requires to be stabilized by an ancillary ligand such as $PPh_3$ *via* a pool effect (Scheme 4). In the hypothesis of a NHC-Pd(0) active species an excess of $PPh_3$ regarding to PEPPSI will decrease the kinetic rate of the coupling reaction as the concentration of the NHC-Pd(0) species will decrease: this fact was not observed.

The second hypothesis would involve an associative mechanism with an active species bearing a phosphine ligand: NHC-Pd(0)-$PPh_3$. (see scheme 4) Associative mechanism with NHC ligand has already been demonstrated by Jutand and coll. using a $NHC_2Pd(0)$ complex.[31] It is worth to notice that they demonstrated that with really bulky NHC ligands, the mechanism is dissociative with a lower kinetic rate. Based on this hypothesis, the complex NHC-Pd(II)$Cl_2$-$PPh_3$ **4** has been prepared by metathesis of PEPPSI with 1 equivalent of $PPh_3$. $^1H$ and $^{31}P$ NMR data are consistent with those already described for this complex.[32] Then this complex has been used in the test cross-coupling reaction described above and led to similar results (product ratio and kinetic) with those already obtained with PEPPSI/$PPh_3$ in a 1/1 ratio. These results are consistent with an associative mechanism with NHC-Pd(0)-$PPh_3$ as active species. In our hypothesis, the 3-chloropyridine/triphenylphosphine exchange will take place prior to the reduction.

### c. PEPPSI Reduction

Once the rule of $PPh_3$ assigned as acting as a ligand, the question of how the precatalyst Pd(II) (PEPPSI) is reduced to Pd(0) active species within the reactive mixture became crucial. Similarly to what occurs for many Pd-catalyzed cross-coupling reactions using nucleophilic organometallic reagents,[33] we believe that triarylbismuth reduce the Pd(II) precatalyst into Pd(0) active species. Such a process would involve two consecutive metatheses on Pd(II) followed by a reductive elimination step, yielding the Pd(0) species and the dimer Ar-Ar in the same quantities. (Scheme 5) The –Cl / -*p*Tol exchange on Pd may be similar to those described by Jain and coll. as really fast and efficient.[22] Effectively, a kinetic study carried out by GC/MS with internal standard shows that Ar-Ar is produced in little quantities (<3 mol%) within 5 min using a 3 mol% loading of PEPPSI.

Therefore the dual role of $Ar_3Bi$ played on the cross-coupling reaction (reagent and reductive agent) led us to readjust its quantities regarding to the loading of PEPPSI (x mol), the quantities of arylbromide (1 equivalent) and the number of aryl transferred within each process. Keeping in mind that the 3 aryl groups will be effectively transferred, it came on that the quantity of $Ar_3Bi$ must be equal to [1/3 + 2/3 x mol%]. The following optimization has been carried out with this relationship.

### d. Loading

At this stage, the loading must be reduced *(i)* to decrease the financial and toxicological impact of the procedure, *(ii)* to reduce the quantity of $Ar_3Bi$ used and *(iii)* to minimize the inherent concomitant formation of Ar-Ar within the Pd(II)/Pd(0) reduction process. Results are given in Table 3.

Total consumption of the *p*-bromoacetophenone was observed until at least 3 mol% of catalyst was used within 1 h. It is worth noticing that the quantities of dimer decrease with the loading of catalyst. This observation is in full agreement with the reduction of PEPPSI by $Ar_3Bi$ previously mentioned.

### e. Lewis base

In a recent work devoted to the cross-coupling reaction of 2,6-dichloropyridazine with $Ar_3Bi$ under Pd(0)/$PPh_3$ catalysis, influence of the base (CsF, $CsCO_3$, $K_2CO_3$) was examined.[34] It was notably found that the cross-coupling reaction occurred efficiently without any additives but their beneficial influence was evidenced with $Ar_3Bi$ bearing electron withdrawing group (-CN, -$CO_2$R, -Ac, -$CF_3$) or in the cross-coupling involving triheteroarylbismuths.

At this stage of our study, we decided to focus again on their behaviours. Thus the Lewis base optimization has been carried out using various inorganic compounds ($K_2CO_3$, $Cs_2CO_3$, $K_3PO_3$, TBAF, CsF). The results given in Table 4 are pretty similar for most of the Lewis bases used but slightly better with CsF. Its quantity has been decreased from 6 eq to 3 eq. With a less important quantity, dimerization mainly took place and reaction occurred only very slowly without Lewis base.

These new optimized conditions yield 96 % of isolated cross-coupling product **3q** after only 1 h at 90 °C. The purification was made easier due to the really low quantity of dimer side-product (3 % GC yield).

### f. Scope and limitation – variation of the aryl moieties on both reagents

At this stage, variations on both reagents, triarylbismuth and arylbromide, have been performed in order to extend the scope and to define limitations of our methodology.

Reactions have been monitored by GC/MS analysis mainly in order to determine the time required for total consumption of the arylbromide. All results are given in Table 5. Runs have been carried out on a 1 mmol scale of the arylbromide.

First of all, it is important to mention that the GC/MS analysis of every single crude product showed that only two products can be observed (> 0.5 %): the coupling product and the dimer coming from the triarylbismuth used. In any case, neither the reduction nor the dimerization of the aryl bromide was observed not even the protonation of the triarylbismuth even with acidic compounds engaged.

Usually the desired compound was obtained with a GC yield over 95 % leading to high yields. Most common substituents (from strongly donating substituent such as -$NH_2$ to strongly electron-withdrawing (–$CF_3$ or –$NO_2$) can be introduced to the biaryl moiety. Basically two pathways can be forecasted, depending on the way of introducing the substituents either *via* the arylbromides or *via* $Ar_3Bi$. However the way to prepare unsymmetrical biaryl products must be driven by the following rule: it is better to introduce electron-donating substituent *via* an aryl transfer from $Ar_3Bi$ and electron-withdrawing group *via* the arylbromide. For instance, in order to access to biaryl compounds bearing an electron-donating group on one aryl moiety and an electron-withdrawing substituents on the other one, *i.e.* **3a**, **3b**, **3d**, **3e**, **3f**, yields turn to 90 % using electron-donating substituted $Ar_3Bi$ to 0 % using electron-withdrawing substituted $Ar_3Bi$. (entries 2, 4, 7, 10, 12 *vs* entries 1, 3, 8, 9, 11). Particularly triarylbismuths bearing strongly electron-withdrawing group such as methyl carboxylate or formyl group were found particularly poorly reactive whilst in one of our recent work devoted to the cross-coupling of 3-chloro-6-iodopyridazine with [*p*-$(CO_2Me)C_6H_4]_3Bi$ under Pd(0)/$PPh_3$ catalysis, led to moderate yields (60 %).[34] Furthermore it is worth noticing that the reaction time is driven by the electron properties of the substituents beared by the aryl moiety of the $Ar_3Bi$. Electron-donating (*p*-OMe, *p*-Me) or neutral (H, *p*-F) substitutents on $Ar_3Bi$ led to short reaction time (1 h : entries 2, 4, 7, 10, 12, 15, 16, 19, 20, 27-29, 32, 35-36), and the reaction time goes longer when the electron-withdrawing properties of the $Ar_3Bi$ substituent increase (*m*-OMe: 1 h30, entries 6, 31, 34; *m*-$CF_3$ : 5 - 6 h, entries 11,14). This seems to indicate that the rate determining step should be the Br/Ar exchange on Pd complex. (step 2 from Scheme 1)

These experimental observations are consistent with the proposed catalytic cycle (Scheme 1 completed by Scheme 5). In one hand, electron-donating substituents on $Ar_3Bi$ enhanced the aryl transfer (for the Pd(0) formation: Scheme 5, and for the cross-coupling reaction: scheme

1 step 2). In the other hand, electron-withdrawing substituents on the aryl halide favoured the oxidative addition (Scheme 1 step 1).

The acidity of arylbromide reagent is a second restriction to be considered. Indead the use of really basic ligand such as NHC (pKa NHC·HCl/NHC is given around 22 in DMSO)[35] could give rise to the decomposition of the active species in the presence of appropriate acids. In the standard conditions, *p*-bromophenol and *p*-bromobenzoic acid do not give access to the coupling product. But good improvements have been enabled by addition of carbonate prior to the introduction of PEPPSI to the reagent solution. With *p*-bromobenzoic acid, this slight modification was very beneficial since the product was obtained in 72 % yields (entry 23). However this modification could not be used for each acidic reagent. With *p*-bromophenol the upgraded yield remained low (entry 24: 22 %) and even lower with 4-hydroxymethylbromobenzene (entry 25). With less acidic compound such as *p*-bromoaniline (entry 26) and p-bromoacetophenone (entries 27, 28) excellent yields were obtained again. All these results (entries 23 - 28) are consistent with the pKa order.[36]

The case of the introduction of a methyl group at the *ortho* position of the biaryl moiety is tricky: this group cannot be introduce using *tris*-(*o*-tolyl)bismuth. In this case (entry 21, Table 5), no reaction was observed whatsoever: neither the formation of the desired product **3l**, nor the dimer formation which indicated that Pd(II) reduction did not occur. Similarly *tris*-(*o*-tolyl)bismuth did not dimerize in protic solvent in the presence of palladium catalyst[19] indicating that *o*-Tol substituent does not transfer from Bi to Pd. However, the switching of the two aryl moieties from the two starting materials (entry 22, Table 5) gave the desired product **3l**, with a moderate yield (entry 22 Table 5).

To finish, it could be noticed that the Pd catalysis is chemoselective and complementary from the Cu catalysis as no *N*-arylation was observed on the amino group (entry 26).[5]

## 4. Conclusions

In this paper, we have disclosed a new and efficient procedure for the cross-coupling reaction of $Ar_3Bi$ with aryl bromides mediated for the first time by Pd-NHC.

After optimisation of various parameters (loading, ratio of reagent/catalyst and ancillary ligand) a wide variety of unsymmetrical biaryl compounds bearing electron-withdrawing substituents as well as electron-donating substituents has been prepared.

Studies based on monitoring kinetic profiles led us to propose a mechanism insight where triphenylphosphine acts as ancillary ligand and where PEPPSI was reduced by the triarylbismuth. Therefore this green organometallic play a dual role within our conditions: reactant and reductive agent.

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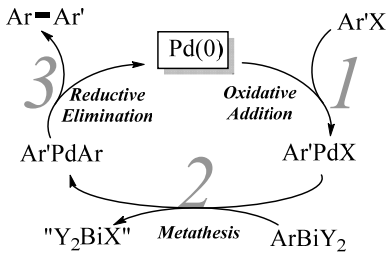
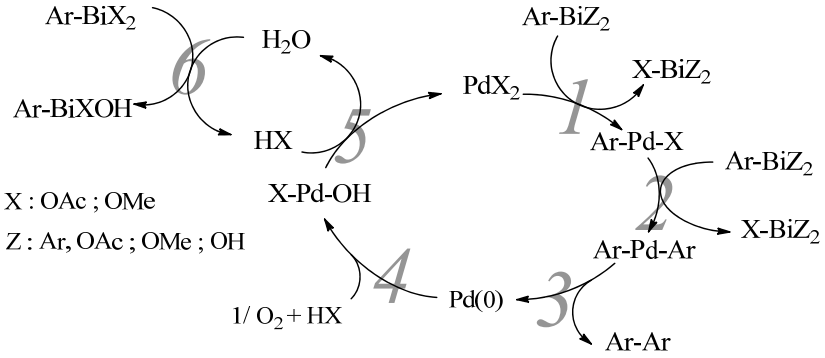
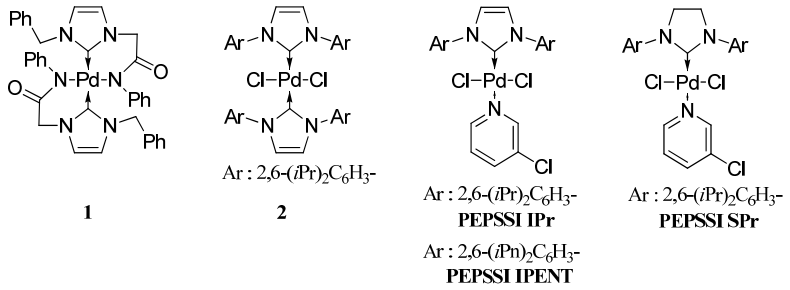


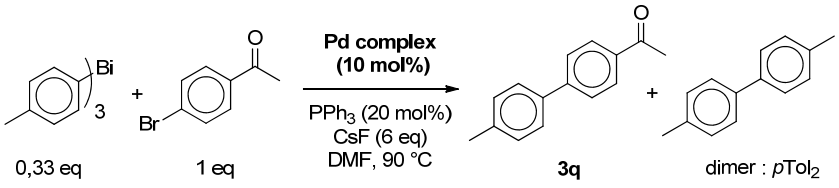

**Scheme 1.** Proposed mechanism cycle for the cross-coupling reaction.

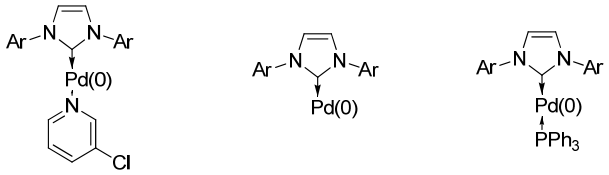



**Scheme 2.** Proposed mechanism cycle for the decomposition of $Ar_3Bi$ into Ar-Ar.

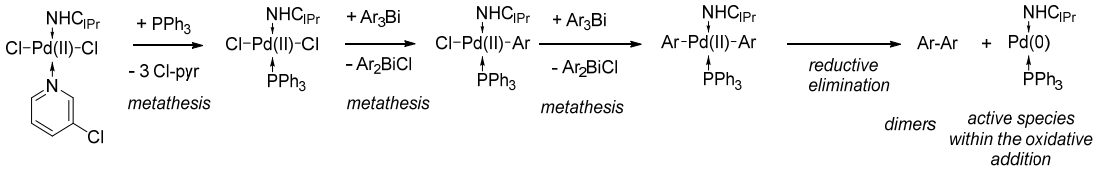



**Scheme 3.** List of NHC palladium precatalysts tested.






**Scheme 4.** Possible active species in the oxidative addition.



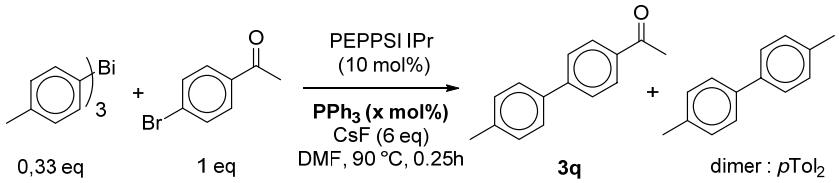

**Scheme 5.** Postulated pathway for the *in-situ* preparation of active Pd(0) catalyst from PEPPSI, $PPh_3$ and $Ar_3Bi$.

**Table 1.** Complexes activity on the cross-coupling reaction

| Entry | Pd Complex | Reaction time (h) | Conversion ratio (%) [b] | **3q** / *p*Tol$_2$ [c] |
|---|---|---|---|---|
| 1 | Pd(OAc)$_2$ / 2 PPh$_3$ [a] | 1.5 h | 100 % | 85 / 15 |
| 2 | **1** | 48 h | 2 % | 80 / 20 |
| 3 | **2** | 8 h | 25 % | 85 / 15 |
| 4 | PEPPSI IPr | 0.25 h | 100 % | 88 / 12 |
| 5 | PEPPSI SPr | 8 h | 100 % | 85 / 15 |
| 6 | PEPPSI IPENT | 48 h | 0 % | - |

[a] therefore 40 mol% of PPh$_3$ was used; [b] conversion ratio given as the percentage of reacted Ar-Br (1 mmol; [c] measured after integration of the assigned signal on GC/MS analysis relatively to internal standards.

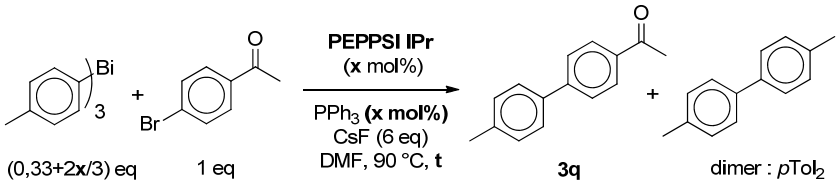
**Table 2.** Variation of the PPh$_3$ loading




| Entry | Loading of PPh$_3$ (x mol%) | Conversion ratio (%) [a] | **3q** / *p*Tol$_2$ [b] |
|---|---|---|---|
| 1 | 40 | 100 % | 85 / 15 |
| 2 | 20 | 100 % | 80 / 20 |
| 3 | 10 | 100 % | 85 / 15 |
| 4 | 5 | 10 % | 85 / 15 |
| 5 | 0 | 0 % | - |

[a] conversion ratio given as the percentage of reacted Ar-Br (1 mmol); [b] measured after integration of the assigned signals on GC/MS analysis relatively to internal standards.

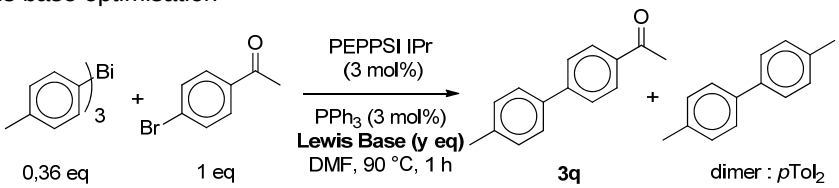
**Table 3.** Optimization of the loading of PEPPSI




| Entry | Loading of PEPPSI IPr (mol%) [a] | Reaction time (h)[b] | Conversion ratio (%) [c] | **3q** / $p$Tol$_2$ [d] |
|---|---|---|---|---|
| 1 | 10 | 0.25 h | 100 % | 85 / 15 |
| 2 | 5 | 0.25 h | 100 % | 91 / 9 |
| 3 | 4 | 0.33 h | 100% | 93 / 7 |
| 4 | 3 | 0.75 h | 100 % | 96 / 4 |
| 5 | 2 | 2.5 h | 95 % | 98 / 2 |
| 6 | 1 | 8 h | 85 % | > 98 / < 2 |
| 7 | 0 | 8 h | 0 % | - |

[a] Loading of catalyst is given in mol% relatively to the quantity of arylbromide (1 mmol); [b] reaction time is given once no change on the reaction profile was observed by GC/MS; [c]: conversion ratio given as the percentage of reacted Ar-Br; [d] measured after integration of the assigned signals on GC/MS analysis relatively to internal standards.

**Table 4.** Lewis base optimisation

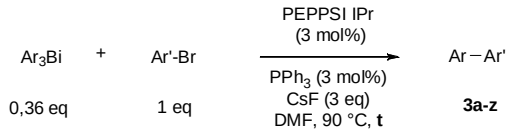


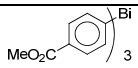
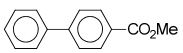
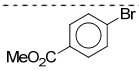
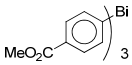
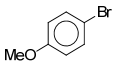
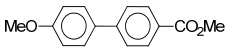
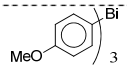
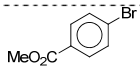
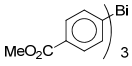
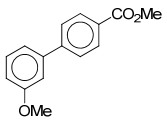
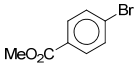
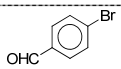
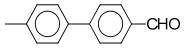
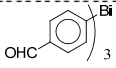
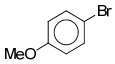
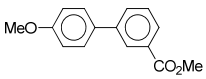
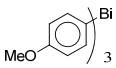
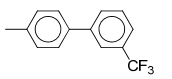
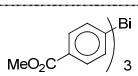
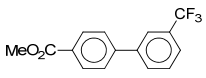

| Entry | Lewis Base | Quantity (y eq) | Conversion ratio (%) [a] | **3q** / $p$Tol$_2$ [b] |
|---|---|---|---|---|
| 1 | $K_2CO_3$ | 6 | 95 % | 80 / 20 |
| 2 | $Cs_2CO_3$ | 6 | 97 % | 82 / 17 |
| 3 | $K_3PO_4$ | 6 | 89% | 91 / 9 |
| 4 | CsF | 6 | 100 % | 96 / 4 |
| 5 | CsF | 3 | 100 % | 97 / 3 |
| 6 | CsF | 1.5 | 100 % | < 5 / > 95 |
| 7 | TBAF | 3 | 100 % | 97 / 3 |
| 8 | TBAF | 1.5 | 100 % | 5 / 95 |
| 9 | - | 0 | 25 % | < 5 / > 95 |

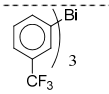
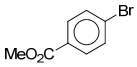
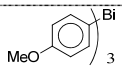
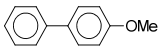
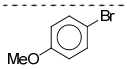
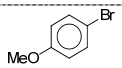
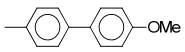
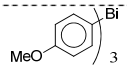
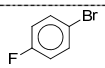
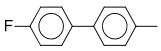
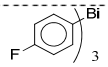
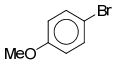
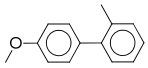
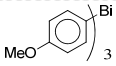
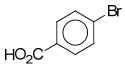
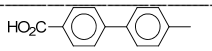
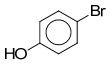
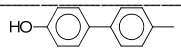
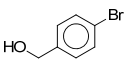
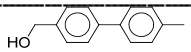
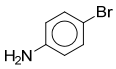
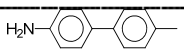
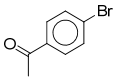
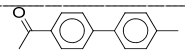
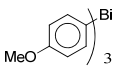
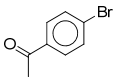
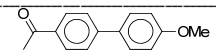
[a]: conversion ratio given as the percentage of reacted Ar-Br (1 mmol); [b] measured by GC/MS after integration of the assigned signals after GC/MS analysis relatively to internal

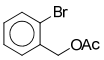
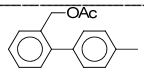
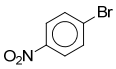
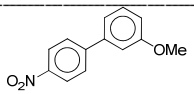
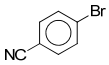
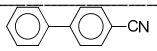
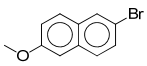
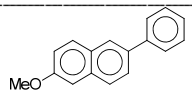
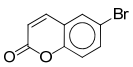
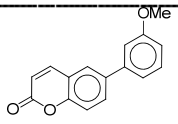
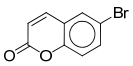
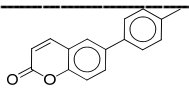
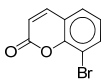
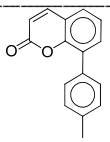
standards.

**Table 5.** Variation on both aryl moieties from $Ar_3Bi$ and Ar'-Br




| Entry | Reagents | | Coupling Product **3** | Reaction time (h) [a] | Yield *(GC yield)*[b] |
|---|---|---|---|---|---|
| | $Ar_3Bi$ | Ar'-Br | | | |
| 1 |  |  |  | 8 h | 0 % (7 %) |
| 2 |  |  | **3a** | 1 h | 95 % (97 %) |
| 3 |  |  |  | 8 h | 0 % (24 %) |
| 4 |  |  | **3b** | 1 h | 91 % (96 %) |
| 5 |  |  |  | 8 h | 0 % (15 %) |
| 6 |  |  | **3c** | 1.5 h | 88 % (95 %) |
| 7 |  |  |  | 1 h | 86 % (95 %) |
| 8 |  |  | **3d** | 8 h | 0 % (15 %) |
| 9 |  |  |  | 8 h | 0 % (7 %) |
| 10 |  |  | **3e** | 1 h | 90 % (95 %) |
| 11 |  |  |  | 5.5 h | 69 % [d] (96 %) |
| 12 |  |  | **3f** | 1 h | 91 % (96 %) |
| 13 |  |  |  | 8 h | 0 % (14 %) |

| | | | | | |
|---|---|---|---|---|---|
| 14 |  |  | **3g** | 5 h | 64 % (78 %) |
| 15 |  |  |  **3h** | 1 h | 97 % (98 %) |
| 16 |  |  | | 1 h | 91 % (95 %) |
| 17 |  |  |  **3i** | 1 h | 94 % (96 %) |
| 18 |  |  | | 1 h | 92 % (95 %) |
| 19 |  |  |  **3k** | 1 h | 90 %[d] (98 %) |
| 20 |  |  | | 1 h | 85 %[d] (97 %) |
| 21 |  |  |  **3l** | 8 h | 0 % (0 %) |
| 22 |  |  | | 13 h | 45 % (55 %) |
| 23 |  |  |  **3m** | 1 h | 72 %[c] (95 %)[c] |
| 24 |  |  |  **3n** | 1 h | 22 %[c] (49 %)[c] |
| 25 |  |  |  **3o** | 4 h | 24 %[c] (26 %)[c] |
| 26 |  |  |  **3p** | 1 h | 88 % (94 %) |
| 27 |  |  |  **3q** | 1 h | 96 % (98 %) |
| 28 |  |  |  **3r** | 1 h | 95 % (97 %) |
| 29 |  |  |  **3s** | 1 h | 85 % (93 %) |

| | | | | | |
|---|---|---|---|---|---|
| 30 |  |  |  **3t** | 1.5 h | 77 % (85 %) |
| 31 |  |  |  **3u** | 1.25 h | 86 % (91 %) |
| 32 |  |  |  **3v** | 1 h | 94 % (96 %) |
| 33 |  |  |  **3w** | 1 h | 91 % (95 %) |
| 34 |  |  |  **3x** | 1.25 h | 71 % (85 %) |
| 35 |  |  |  **3y** | 1 h | 81 % |
| 36 |  |  |  **3z** | 1.25 h | 19 % (39 %) |

[a] reaction time are given once no change in the reaction profile was observed by GC/MS; [b] yields are given for isolated product. Eventually GC yields are given between bracket; [c] results obtained with addition of 3 eq of $K_2CO_3$; [d] isolated yield lower from GC yield to a close polarity of expected product and Ar-Ar byproduct.