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Coordination Chemistry Reviews 251 (2007) 1281–1293
COORDINATION CHEMISTRY REVIEWS
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Review

Monomolecular, nanosized and heterogenized palladium catalysts for the Heck reaction

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Received 30 September 2006; accepted 17 November 2006
Available online 29 November 2006

Contents

Abstract

The review comprises discussion concerning transformations of soluble and insoluble palladium catalysts during the Heck reaction. Special attention is paid to two essential stages of the Heck reaction: reduction of Pd(II) in precursor to Pd(0) and oxidative addition of the main substrate, aryl halide, to Pd(0) in a form of monomolecular or nanosized Pd(0) colloid. It was shown that both, soluble and insoluble, palladium precursors form at the presence of the tetrabutyl ammonium salt soluble Pd(II) complexes of general formula $[Bu_4N]_2[PdPh_xX_{4-x}]$. Formation of these soluble complexes explains the change of Pd(0) nanoparticles size during the Heck reaction. Additionally the Heck reaction can proceed on the surface of Pd(0) nanoparticles (stabilized colloids).

Keywords: Heck reaction; Palladium; Nanoparticles; Pd(0) colloid; Heterogenized palladium catalyst

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1. Introduction

The extraordinary catalytic properties of palladium in C–C bond formation reactions are still intensively studied although they have been well known for many years [1–14].

The palladium catalyzed coupling based on aryl halides (mainly bromo- and iodoarenes) appears presently as a well-developed methodology, broadly used in advanced organic synthesis. The mechanisms of C–C bond formation processes such as the Heck reaction (HR) [5–9], alkoxycarbonylation [10,11], Miyaura and Suzuki [12], Sonogashira [13] and Stille [14] coupling, shown in Scheme 1, contain two common stages:

(a) formation of reactive Pd(0) species usually by reduction *in situ* of the Pd(II) precursors and,
(b) activation of substrate, usually aryl halide (ArX), via its oxidative addition to Pd(0) leading to a reactive intermediate of the type [ArPd(II)X].

Among such reactions, a special position is occupied by reactions of aryl halides that can be transformed into carboxylic acids or esters in a one-stage carbonylation process (Scheme 2a) [10,11,15–20].

Olefination of aryl halides, the so-called Heck reaction (HR) [5–9,21] is another palladium catalyzed process leading to functionalized (arylated) olefins (Scheme 2b). This reaction discov-

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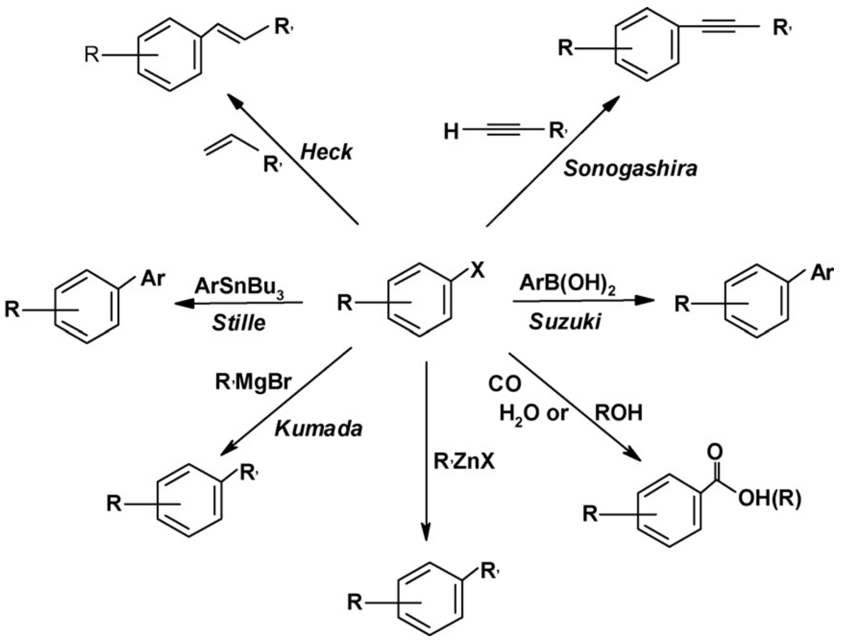
doi:10.1016/j.ccr.2006.11.013



Scheme 1. C–C bond formation reactions (HR [5–9], Miyaura and Suzuki [12], Sonogashira [13], Stille [14]).

ered independently by Heck and Mizoroki [22,23] belongs to one of the most important organic reactions catalyzed by palladium complexes and produces chemicals that are applied in advanced synthesis of pharmaceuticals and natural products. Coupling of boron-derivatives with aryl halides, so-called Suzuki reaction [12], which leads to biphenyl compounds, is the third very important reaction catalyzed by palladium complexes (Scheme 2c).

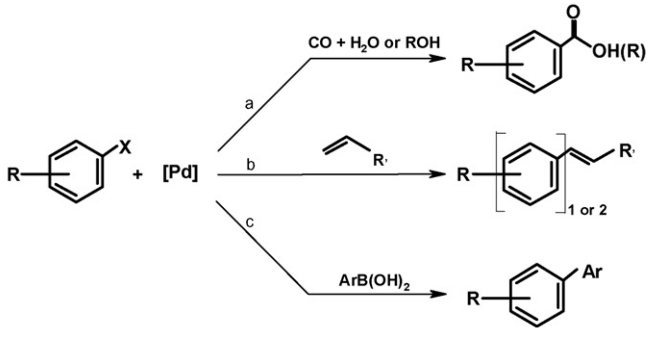
All these reactions (Scheme 2) are usually catalyzed in solution by palladium homogeneous catalysts generated *in situ* from different palladium precursors. They maybe either monomolecular Pd(0) or Pd(II) complexes, Pd(0) nanoparticles as Pd(0) colloids stabilized on polymer (i.e. polyvinylpyrrolidone, PVP) or Pd(0)/Pd(II) species heterogenized on inorganic supports such as silica, alumina or magnesium oxides.

Phosphane-free palladium catalyst precursors presented in Scheme 3 are divided into three structurally different groups:

(i) monomolecular Pd(0) or Pd(II) complexes: $Pd(dba)_2$, $Pd(PR_3)_{3,4}$, $Pd(OAc)_2$, $PdCl_2(PhCN)_2$, $PdCl_2(cod)$ soluble and homogeneous in reaction mixture;

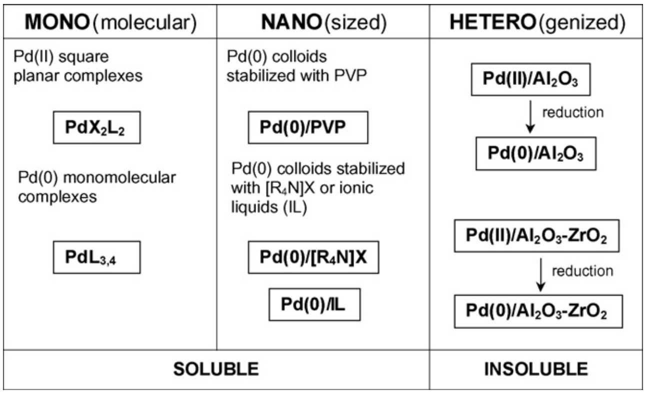
(ii) nanosized Pd(0) colloids supported on PVP or other polymers: soluble, but forming a solution not really homogeneous;

(iii) heterogeneous or heterogenized (supported) palladium catalysts: insoluble in the reaction mixture.



Scheme 2. Palladium catalyzed C–C bond formation reactions: (a) hydroxy/methoxycarbonylation; (b) HR; (c) Suzuki reaction.

In recent years many excellent reviews [6–8,24–26] and original papers have been published and in many cases they discuss or touch upon problems of true homogenity or real heterogenity of catalytic systems used in the C–C cross-coupling reactions. This subject seems to be essential for understanding the reaction mechanism and function of Pd catalysts. Although in this article we will discuss only “phosphane-free” catalytic processes, phosphorus ligands (P-ligands) are often used as stabilizers of the monomolecular structure of the Pd precursors [3,6]. There are phosphines, phosphites (mono- or polydentate), phosphinites [21,34,82], P-ligands forming palladacycles [27–30] and pincer type ligands [31–33] used for this purpose. Some of these systems are very active and can also be used for chloroaryls [3].



Scheme 3. Pd-catalyst precursors.

The essential specificity of the Pd precursors which play the same function in catalytic systems, is their different solubility in a liquid phase before the catalytic reaction starts (Scheme 3). Consequently catalytic precursors can be divided into two groups. In the first group there are Pd(II) and Pd(0) monomolecular complexes as well as Pd(0)/PVP colloids that are soluble in the reaction mixture, although Pd(0) colloids solutions cannot be considered as truly homogeneous because of possible sedimentation of nanoparticles as larger aggregates. In the second group are heterogeneous Pd(II)/Pd(0) precursors although insoluble at the beginning of catalytic reaction but which may undergo structural changes caused by oxidative addition of aryl halide. This process may lead to the appearance of soluble palladium species formed not necessarily by simple leaching process but by the formation of [ArPd(II)X] intermediates on the surface. These intermediates can be transferred to the solution as Pd(II) soluble complexes and therefore such system can be considered as hetero/homo system [26,35–37].

Finally, all the palladium catalyst precursors shown in Scheme 3 may undergo chemical decomposition or, in a case of Pd(II) precursors, reduction *in situ* at HR conditions (120–160 °C) to form Pd(0) colloids as was recently discussed by de Vries [26].

The formation of Pd(0) colloids is particularly plausible in “phosphane-free” systems (phosphines normally stabilize Pd(0) monomolecular species of Pd(0)$L_{3,4}$ type) although it was concluded from kinetic studies of HR catalyzed by palladacycle that a Pd(0) colloid was also formed in this case [26,38,39]. In some catalytic systems containing homogeneous Pd(II) precursors, Pd(0) colloids formation was proven by TEM studies [40,41,83].

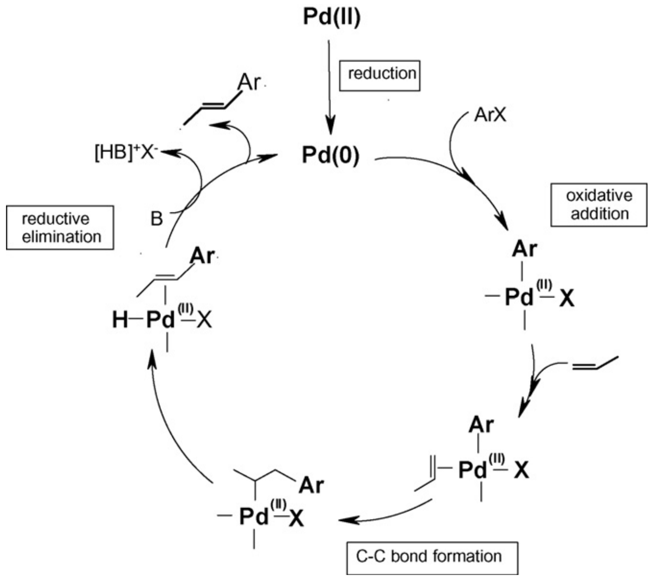
Evidence of Pd(0) colloid formation does not necessarily suggest its dominating role as the catalytically active species; however there is no doubt that the participation of Pd(0) colloids in C–C bond formation reactions (mainly in HR) is very important. The contribution of Pd(0) nanoparticles in HR may be considered in two ways. First, as catalytic activation of ArX substrate realized on the surface of a Pd(0) nanoparticle (colloid). Next, activated ArX as [ArPd(II)X] (still on the surface of colloid) interacts with an approaching olefinic substrate and the final product is transferred to the solution, whereas Pd(II) reduced *in situ* remains as a Pd(0) atom attached to the bulk of colloid. In this approach Pd(0) as a colloid acts as heterogeneous catalyst [57]. The second pathway allows transportation of [ArPd(II)X] species originally attached to the surface of the nanoparticles to the solution, usually as $[\mathrm{Pd(II)ArX_3}]^{2-}$ soluble complexes. These forms of palladium were found when ionic liquids were used as reaction media [42,43,83]. In catalytic cycles such intermediate forms of Pd(II) can again be reduced *in situ* to Pd(0) monomolecular or colloidal forms that may next aggregate to “palladium black” [8,26,35]. In active catalytic systems it is in fact not important which Pd species is the most active one, however estimation of contribution of different forms of palladium is needed for a precise description of the HR mechanism. Some problems appear with heterogeneous (or heterogenized) catalysts which are expected to be rather stable and easily separated from organic products. Efficient separation is important not only because of the high price of palladium but also because of the very low limit of palladium content permissible in the reaction products, especially for the pharmaceutical industry. The conversion of insoluble forms of heterogenized Pd(0) into soluble species need not be considered as lost palladium since the Pd(II) complex can be reduced again to Pd(0) nanoparticles or readsorbed on the support.

Understanding of the mechanistic function of different forms of Pd in catalytic process is important for construction of new active catalysts and for improving the reaction yield and/or selectivity. These problems will be discussed in this review.

2. Mechanism of the Heck reaction (HR)

In the traditional mechanism of the Heck reaction (Scheme 4) the process starts from reduction of Pd(II) precursor and formation of Pd(0)$L_{3,4}$ or coordinatively unsaturated labile Pd(0)L_2 complexes. Since typical strong reducing agents are, in most cases, not present in the reaction mixture, the palladium reduction is postulated but not explained in detail. In phosphane containing systems hard nucleophiles such as hydroxide or alkoxide anions, water or acetate ion [6] and amines [44,45] are considered as reducing agents. In phosphane-free systems amine, used a base or olefinic substrates of HR, can participate in the reduction of Pd(II) [6]. The possibility of Pd(II) reduction by quaternary ammonium salts or phosphonium salts was also postulated, however not fully proven experimentally [46].

The oxidative addition of aryl halide to a Pd(0) complex is a key step in HR as well as other reactions with aryl halides used as substrates. Activation of ArX via oxidative addition produces a Pd(II) complex with aryl and halide ligands coordinated to the metal which next reacts with olefin forming an π-olefin complex (Scheme 4). The olefin bonded to palladium undergoes a migratory insertion forming a new C–C bond, followed by β-hydride elimination and removal of the final product, arylated olefin from the coordination sphere of palladium. Palladium remains after



Scheme 4. HR mechanism, a general view [6,8,26].

this stage in the form of a hydrido complex and is converted back to the initial form by reaction with a base acting as HX acceptor (Scheme 4).

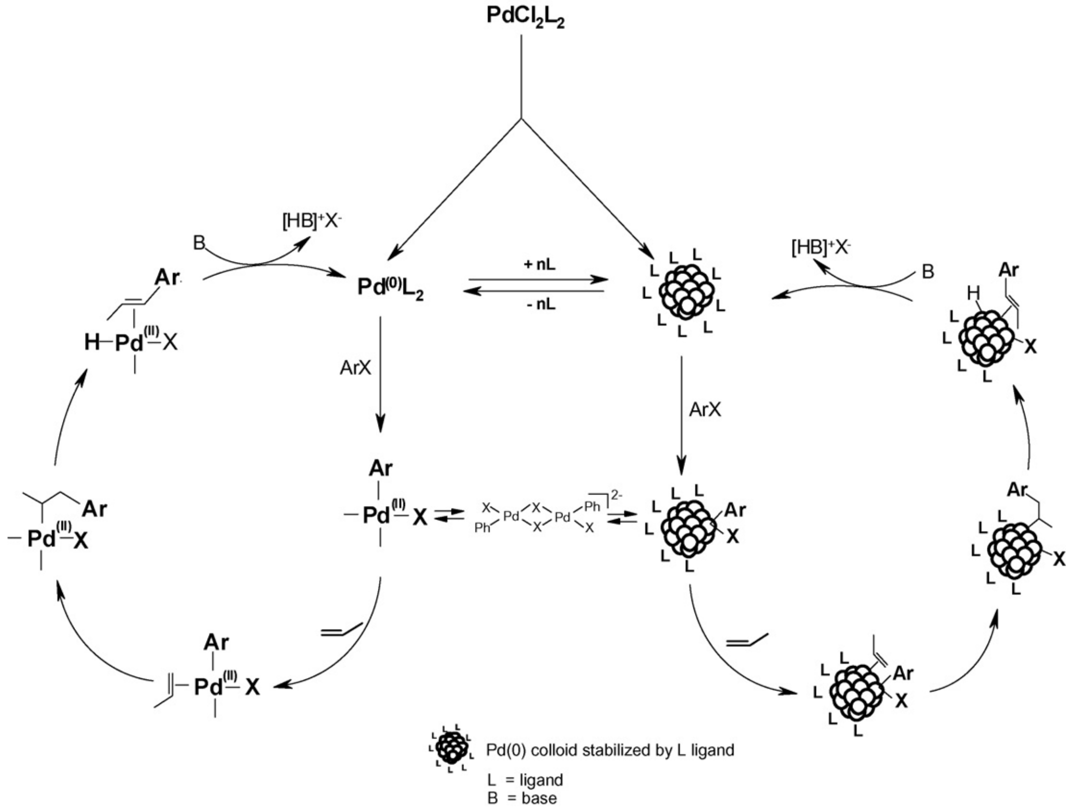
There are also alternative mechanisms proposed by Amatore and Jutand for phosphane-assisted HR [47–49] and by de Vries for phosphane-free system and iodobenzene as a substrate [26]. In both these mechanisms the formation of anionic Pd(0) species is considered at the beginning of catalytic cycle. The mechanism of Amatore and Jutand is constructed for $Pd(OAc)_2(PPh_3)_2$ as catalyst precursor and it starts with the formation of a Pd(0) anionic complex $[Pd(0)(PPh_3)_2(OAc)]^-$. Reduction of Pd(II) to Pd(0) is accompanied by the formation of $OPPh_3$. Oxidative addition of ArX to Pd(0) anionic complex produces a pentacoordinated Pd(II) aryl complex of formula $[ArPdX(OAc)(PPh_3)_2]^-$ which then reacts with olefin. Insertion of olefin into Pd–C(Ar) bond followed by β-hydride elimination leads to the formation of the HR product (arylated olefin) and a hydrido complex of palladium, $HPd(OAc)(PPh_3)_2$ (in a traditional mechanism the formation of $HPdXL_2$ is considered at this stage).

The reaction mechanism of HR with $Pd(OAc)_2$ catalyst in phosphane-free system was recently proposed [26]. Besides soluble palladium complexes the presence of Pd(0) colloid in this reaction was also considered, as very probable because of the deficiency of potential ligands. The catalysis in phosphane-free system starts with Pd(0) anionic complex $[(H_2O)Pd(OAc)]^-$, which activates aryl iodide via oxidative addition forming the anionic intermediate $[PhPdI_2]^-$. The same species was detected also as a product of oxidative addition of PhI to Pd(0) colloid stabilized with NaI [26]. Next, olefin coordinates to $[PhPdI_2]^-$ and a new C–C bond is formed in a migratory insertion step. After β-hydride elimination the catalytic cycle is closed by formation of arylated olefin and underligated $[PdI]^-$. The possible transformation of this species to anionic monomeric or dimeric forms ($PdI_3{}^-$, $Pd_2I_6{}^{2-}$) [50] or to Pd(0) colloid is proposed [26].

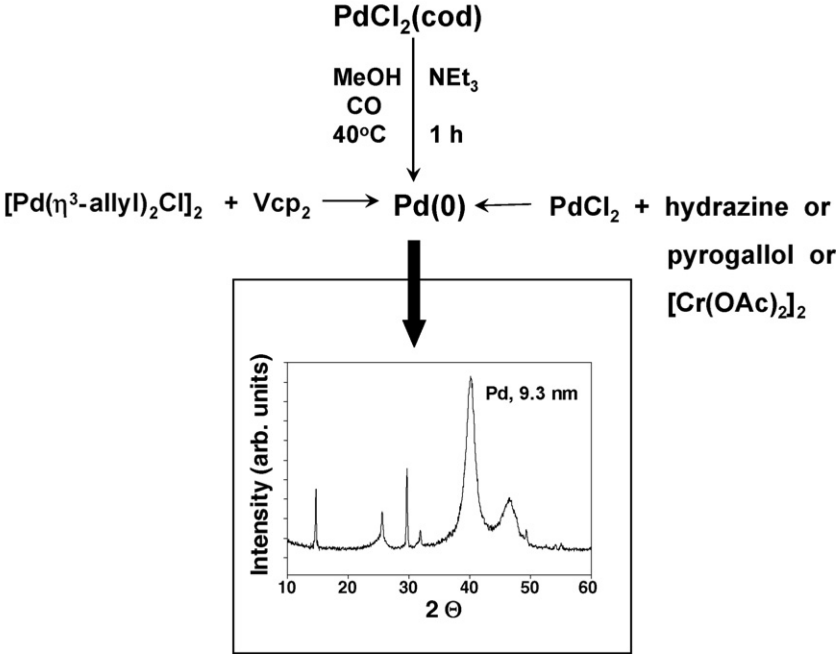
It can be expected that the HR with aryl bromides instead of aryl iodides can also proceed but more slowly, because oxidative addition is slower in this case [26]. Consequently a larger fraction of palladium can exist in the form of Pd(0) colloid or palladium black. Our studies of HR with bromobenzene were performed mainly in $[Bu_4N]Br$ medium which has an important influence on both—stabilization of Pd(0) colloid and solubilization of palladium [43]. Using Pd(0) colloids and phosphane-free Pd(II) precursors we have observed formation of Pd(II) anionic complexes of the type $[Bu_4N]_2[PdPh_xX_{4-x}]$ [43]. During the catalytic process several cycles of palladium reduction and oxidation (via oxidative addition) occur. From those studies we concluded that both forms, Pd(0) colloid and soluble Pd(II) complexes, participate in HR as catalysts (Scheme 5). Consequently bromobenzene, a substrate of HR, is activated via oxidative addition on the surface of a Pd(0) colloid (considered as nanoparticles) and in the coordination sphere of a monomolecular complex $Pd(0)L_x$ ($x = 2$–4).

2.1. Reduction of Pd(II) to Pd(0) species

According to the HR mechanism (Schemes 4 and 5) Pd(0) monomolecular complexes of type $Pd(0)L_{2-4}$ or Pd(0) colloids are considered as active forms of the catalyst. Although the HR



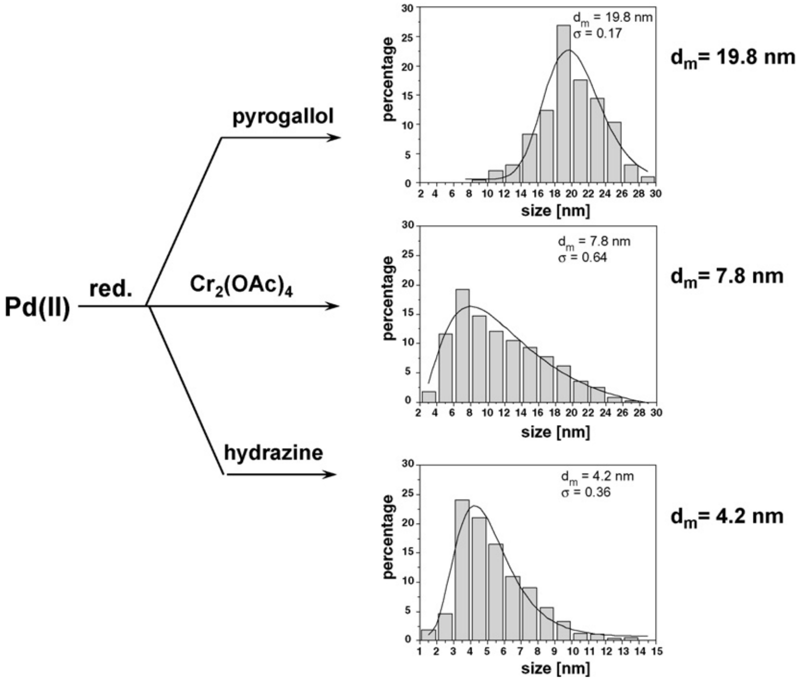
Scheme 5. Mechanism of HR catalyzed by palladium soluble complexes and Pd(0) colloid.



Scheme 6. Syntheses of Pd(0) colloid [20,58,84].

mixture does not contain any strong reducing agents, reduction of Pd(II) to Pd(0) observed very often and especially in phosphane-free systems, is not well explained. $Pd(OAc)_2$, a very popular precursor of the HR catalyst, undergoes decomposition during heating with formation of Pd(0), methane, ethane and CO_2 [51,52]. Amines, used as bases in HR, can also reduce Pd(II) to Pd(0) [6,44,45]. The formation of Pd(0) nanoparticles under HR conditions was noted for many phosphane-free precursors [42,53–57].

Our studies on the carbonylation of iodobenzene have demonstrated the formation of Pd(0) nanoparticles in reactions of $PdCl_2$(cod) as the catalyst precursor with NEt_3 and CO in MeOH [20]. Under these conditions cyclooctadiene is removed from coordination sphere as a cyclooctene-carboxylic acid derivative (2-methoxy-5-cyclooctene carboxylic acid methyl ester). Depending on the reaction conditions, nanoparticles of 2.5–5.6 nm size were obtained and this procedure can also be applied for the preparation of Pd(0) colloid stabilized on



Scheme 7. The size of Pd(0) nanoparticles depending on the kind of reducing agent used [58].

PVP [20]. Other reducing agents used successfully for this purpose are Vcp_2 [84], hydrazine, pyrogallol or $[Cr(OAc)_2]_2$ [58] (Scheme 6).

The size of the nanoparticles and their morphology are dependent on the method of preparation. For example reduction of $PdCl_2$ with pyrogallol gave large nanoparticles of 19.8 nm diameter, whereas reduction with hydrazine produced nanoparticles of 4.2 nm under the same conditions [58].

It is obvious that the catalytic activity of Pd(0) nanoparticles depends on their size [59–61]. Such dependence was demonstrated for methoxycarbonylation of iodobenzene where nanoparticles of 2.9–17.4 nm of diameter were tested [58] (Scheme 7). The results showed that not only the size of the nanoparticles but also their morphology are important for the final result. Both these parameters are dependent on the method of preparation, temperature and a kind of reducing agent used [58].

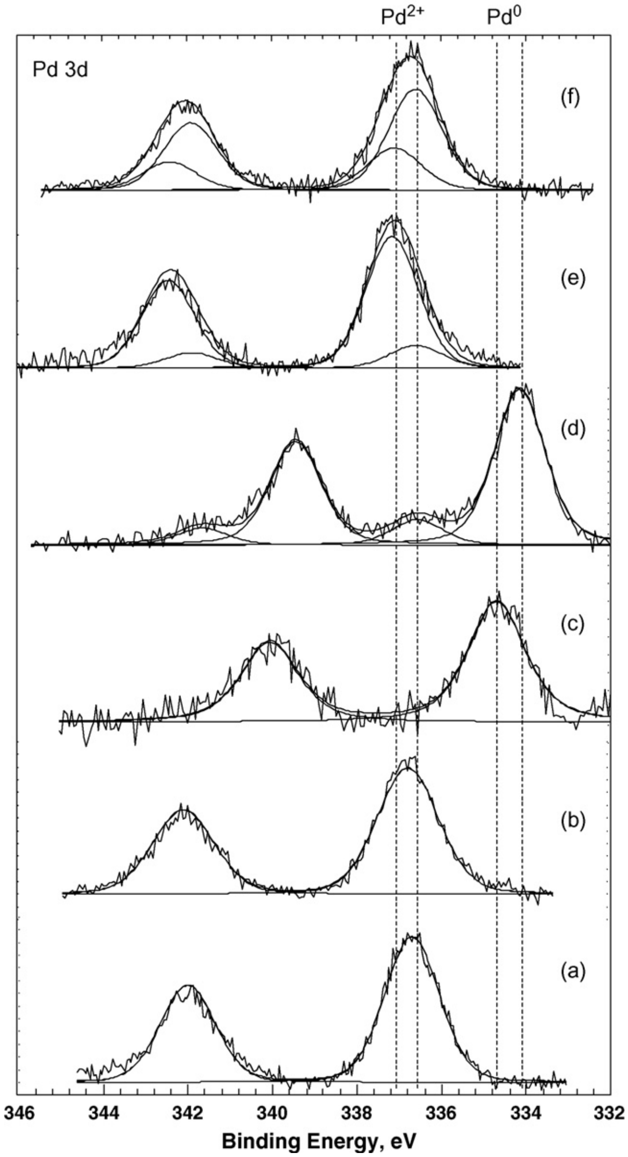
A series of experiments with $PdCl_2(PhCN)_2$ catalyst precursor have shown that Pd(II) can be reduced to Pd(0) in the presence of different sodium salts used as bases in HR, like $NaHCO_3$, NaOAc, $NaHCO_2$ [62].

Total reduction to Pd(0) was observed when $PdCl_2(PhCN)_2$ was heated with $NaHCO_2$, however under the same conditions no reduction was observed in the presence of NaOAc or $NaHCO_3$. In contrast when $PdCl_2(PhCN)_2$ was heated with NaOAc or $NaHCO_3$ in the presence of $[Bu_4N]Br$ 84.0% and 50.8% of Pd(0) was found respectively using XPS measurements [62] (Scheme 8).

Direct evidence of reduction of Pd(II) supported on Al_2O_3 (Pd/Al_2O_3) was also obtained from XPS measurements [62]. Both catalysts, $Pd(0)/Al_2O_3$ and $Pd(II)/Al_2O_3$ after being used in HR showed the same XPS spectrum with two lines with BE 334.4 and 339.7 eV, only slightly shifted to lower values compared to initial $Pd(0)/Al_2O_3$. Only trace amounts of Pd(II) (BE 337.3, 342.6 eV) were found in these samples. Thus, under HR conditions most of the palladium was reduced to Pd(0) even in the absence of typical reducing agents.

The participation of Pd(0) nanoparticles as catalysts in the HR reaction can be proposed on the basis of kinetic measurements [38]. It had already been observed some years ago that HR can be performed in the presence of a very small amount of palladium catalyst, called "homeopathic dose" [6]. Further, it has recently been demonstrated that $Pd(OAc)_2$ as well as palladacycle exhibit a non-linear dependence of the reaction yield on catalyst concentration and the optimal concentration corresponding to the highest yield of HR is between 0.01 and 0.1 mol% [38]. It was recommended that the palladium concentration should be kept below 0.1 mol%. However it was also pointed out that the substrate to catalyst ratio, not only concentration, is a very important parameter providing the highest yield of HR products [26,63].

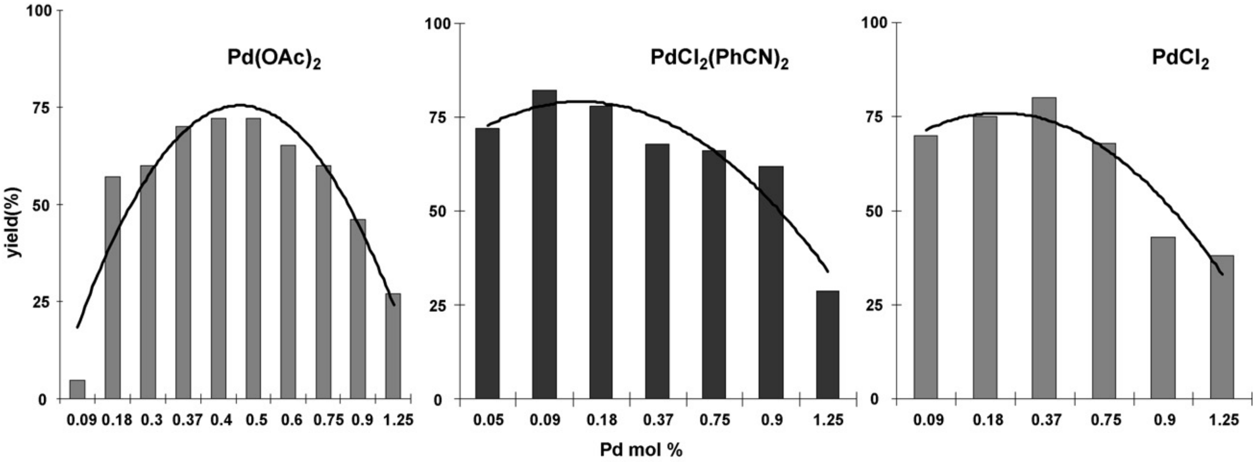
Another interpretation of the kinetic results was provided by Schmidt and Smirnov [64] who proposed that the size of the nanoparticles is dependent on the initial concentration of the Pd(II) precursor. That approach is based on the assumption of the existence of stable metal clusters (containing "magic" number of metal atoms) characterized by different degree of surface shell saturation of colloidal particles relative to full-shell clusters.



Scheme 8. XPS spectra of the Pd 3d region: (a) $PdCl_2(PhCN)_2$; (b) $PdCl_2(PhCN)_2$ + NaOAc; (c) $PdCl_2(PhCN)_2$ + $NaHCO_2$; (d) $PdCl_2(PhCN)_2$ + $[Bu_4N]Br$ + NaOAc; (e) $PdCl_2(PhCN)_2$ + $[Bu_4N]Br$ + $NaHCO_2$; (f) $PdCl_2(PhCN)_2$ + $[Bu_4N]Br$ [62].

A non-linear dependence of the HR yield on palladium concentration was observed for simple Pd(II) compounds, $PdCl_2(PhCN)_2$, $Pd(OAc)_2$ and $PdCl_2$ used as catalyst precursors in $[Bu_4N]Br$ in the absence of any base [65] (Scheme 9).

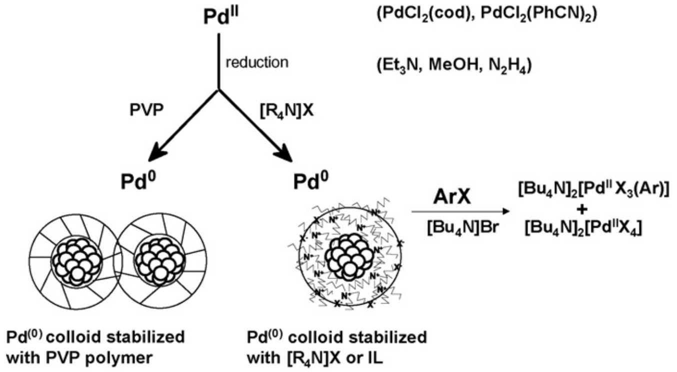
The highest product (butyl cinnamate) yields were obtained with different concentrations of each of the three catalyst precursors used in the reaction of bromobenzene with butyl acrylate. In the reaction catalyzed by $PdCl_2$ a maximum yield of 70% was achieved for a Pd concentration from 0.09 to 0.4 mol%, whereas with $PdCl_2(PhCN)_2$ the best range of concentrations was 0.05–0.4 mol%. A relatively high concentration, ca. 0.4–0.5 mol% was appropriate when $Pd(OAc)_2$ was used as precursor [65], while $Pd(OAc)_2$ gave very good results even at the concentration 0.01–0.1 mol% for reaction in NMP (NMP = 1-methyl-2-pyrrolidone) with NaOAc used as a base [38]. As



Scheme 9. Effect of Pd-catalyst precursor concentration on the yield of HR products in reaction of bromobenzene with butyl acrylate [65].

can be seen in Scheme 9 an increase of Pd concentration over 0.9 mol% caused a decrease in the HR yield in all three systems. Although the presence of Pd(0) colloids readily explains the non-linear dependence of the HR yield on palladium concentration, the formation of dimeric or polymeric species of Pd(II) should also be considered. In fact, in experiments performed with $PdCl_2$, $Pd(OAc)_2$ and $PdCl_2(PhCN)_2$ in $[Bu_4N]Br$ as reaction medium, aggregation of nanoparticles should diminish [83,85]. In addition the presence of $[Bu_4N]Br$ facilitates solubilization of nanoparticles and formation of anionic complexes of the type $[Bu_4N]_2[PdPh_xX_{4-x}]$ [43]. Metal colloids are thermodynamically unstable and exhibit a tendency to aggregate [59–61]. To prevent aggregation different stabilizing agents are used such as polymers (e.g. polyvinylpyrrolidone, PVP) (Scheme 10).

Pd(0) colloids formed *in situ* can be efficiently stabilized not only by PVP but also by tetraalkylammonium salts and ionic liquids as demonstrated in the methoxycarbonylation of iodobenzene [16,17,19]. Good results were obtained in these media with both precursors—$PdCl_2(cod)$ (forming a Pd(0) colloid *in situ*) as well as with the Pd(0) colloid earlier synthesized in a separate reaction and supported on PVP (Scheme 11). The very low yield of benzoic acid methyl ester obtained only in methanol, in the absence of any ionic liquid, can be explained by aggregation of unprotected palladium nanoparticles to palladium black, usually much less active.



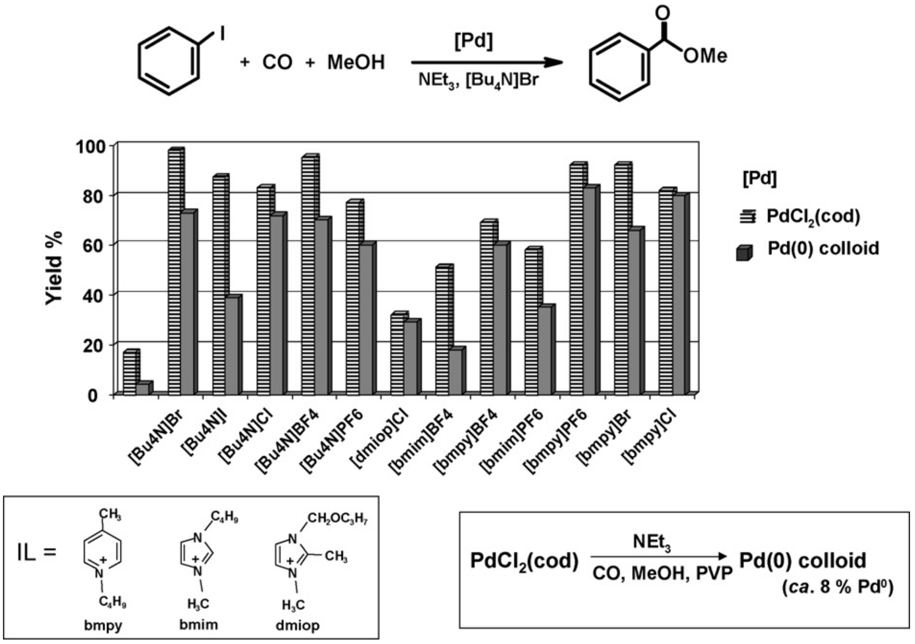
Scheme 10. Formation and stabilization of Pd(0) colloid in phosphorus-free systems.

2.2. *Oxidative addition of aryl halide to palladium(0) species*

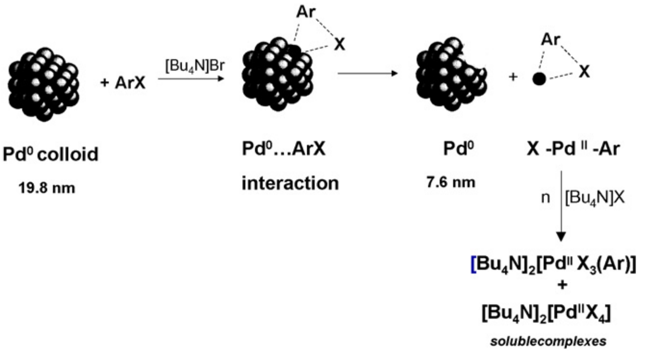
The oxidative addition of aryl halide to Pd(0) (in a monomolecular complex or in a colloid) is a key stage of the HR as well as other reactions catalyzed by palladium with aryl halides as substrates (Schemes 4 and 5). In reactions catalyzed by Pd(0) nanoparticles the product of oxidative addition containing the [X–Pd(II)–Ar] core can be attached to the surface of colloid or can be removed from the surface and transferred to the solution as a soluble Pd(II) monomolecular complex. The second pathway is facilitated by the presence of tetraalkylammonium salt (i.e. $[Bu_4N]Br$) which causes transformation of an aryl complex of Pd(II) coordinatively unsaturated to the anionic $[Bu_4N]_2[PdPh_xX_{4-x}]$ (Scheme 12).

A significant decrease of the size of the Pd(0) nanoparticles after their reaction with aryl halides, especially in the presence of tetraalkylammonium salts, confirmed the scheme mentioned above. Starting from a Pd(0) colloid containing nanoparticles of relatively large size (19.8 nm) it was possible to observe a size decrease to 18.1 and 17.5 nm in reactions with PhBr and PhI respectively. More significant dispersion, to 11.7 nm and even 7.6 nm was found when the Pd(0) colloid reacted with PhBr + $[Bu_4N]I$ and PhI + $[Bu_4N]Br$ respectively (Scheme 13) [43].

Oxidation of Pd(0) to the Pd(II) in reaction with PhBr was confirmed by XPS spectra, where the peak at BE 335.1 eV characteristic for Pd(0) disappeared and a signal at a higher BE value, at 336.9 eV appeared. A very similar peak position (BE 337.0 eV) was found for the product of Pd(0) colloid reaction with PhBr and $[Bu_4N]Br$ and this BE value is very close to that found for $[Bu_4N]_2[PdBr_4]$ (BE 337.06 eV). This observation supports the conclusion that Pd(0) was oxidized via oxidative addition to Pd(II) which was subsequently stabilized in the form of $[PdBr_4]^{2-}$ [43].



Scheme 11. Carbonylation of iodobenzene catalyzed by $PdCl_2$(cod) and Pd(0) colloid—effect of $[Bu_4N]X$ salts and ionic liquids (IL) [19,20].



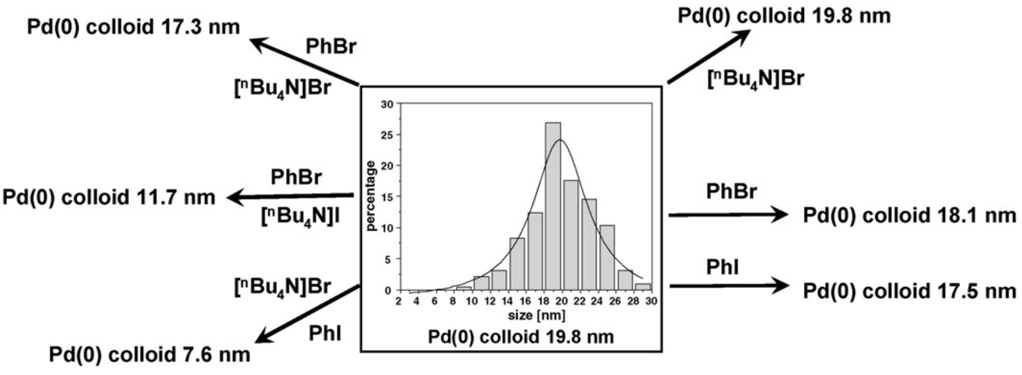
Scheme 12. Changes of Pd(0) colloid size as a consequence of oxidative addition of Ar–X at the presence of $[Bu_4N]Br$ salt [43].

Similar experiments with PhI and $[Bu_4N]Br$ were performed with the Pd/Al_2O_3 heterogeneous catalyst. In this case a decrease in size of the supported nanoparticles size from 6.3 to 5.5 nm was also observed, by XRD method, after heating the Pd/Al_2O_3 with PhI which confirms the formation of [Ph–Pd(II)–I] type species. A further decrease of nanoparticles size to 5.2 nm was found when Pd/Al_2O_3 was heated with PhI and $[Bu_4N]Br$. Under such conditions the formation of $[Bu_4N]_2[PdPh_xX_{4-x}]$ or $[Bu_4N]_2[PdX_4]$ species was noted by the presence of a new band appearing at 450 and 520 nm in UV–vis spectrum of the solution [62].

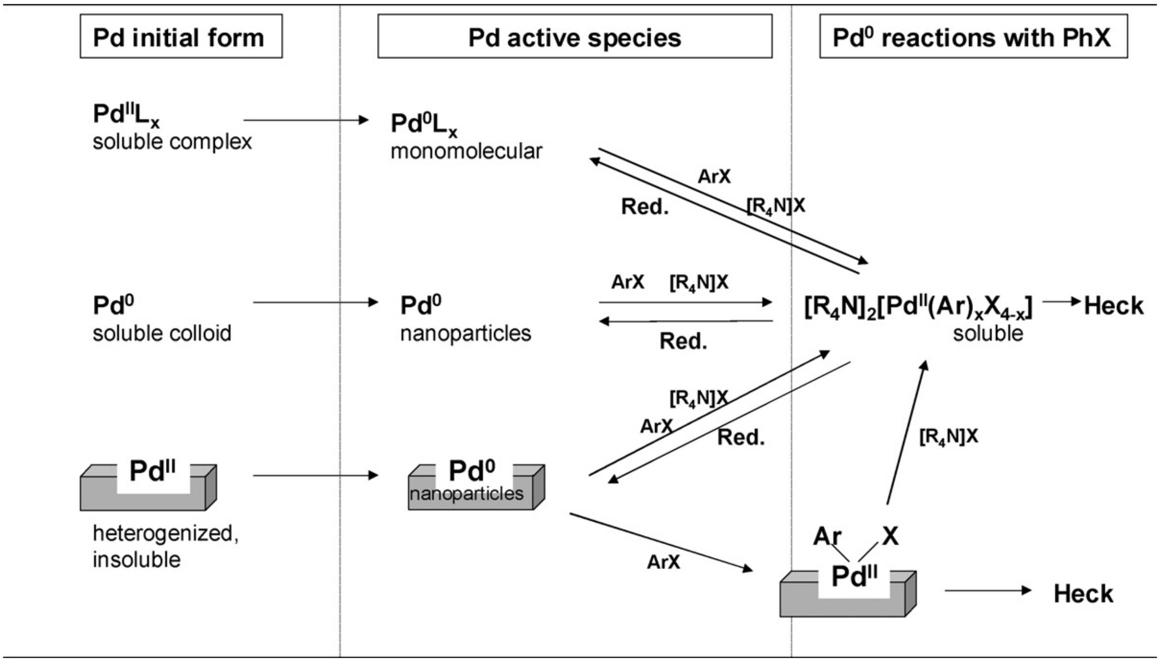
3. Transformations of soluble and insoluble catalysts in the Heck reaction

On the basis of the discussion above it is evident that in each catalytic system containing the phosphane-free Pd(II) complex or the Pd(0) colloid or $Pd(II)/Al_2O_3$ supported catalyst, the same soluble species of type $[Bu_4N]_2[PdPh_xX_{4-x}]$ is formed in the presence of PhX and $[Bu_4N]Br$ (Scheme 14).

As a consequence almost identical catalytic results were obtained in all three systems with monomolecular homogeneous, nanosized (colloidal) and heterogenized (or heterogeneous) catalyst precursors, as illustrated in Scheme 15.



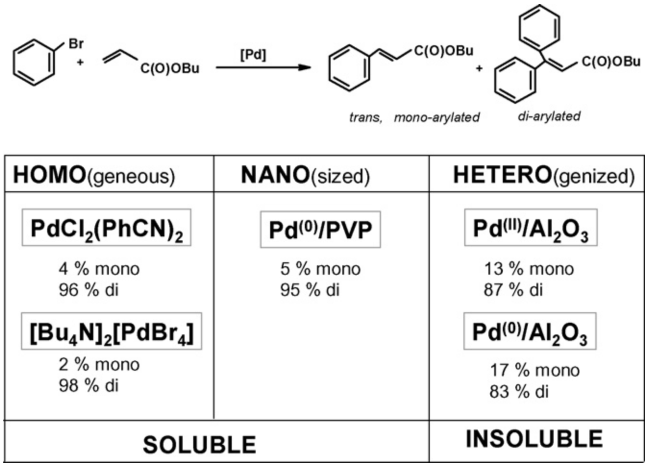
Scheme 13. Changes of the Pd(0) nanoparticles size at the presence of HR components [43].



Scheme 14. Transformations of palladium catalyst precursors during catalytic reactions at the presence of $[R_4N]X$ ammonium salts.

Five different Pd precursors were used, $PdCl_2(PhCN)_2$, $[Bu_4N]_2[PdBr_4]$, Pd(0)/PVP, Pd(0)/Al_2O_3 and Pd(II)/Al_2O_3, and in all cases the diarylated product was formed as a main product (83–98%) with 2–17% of the monoarylated species.

The positive effect of tetraalkylammonium salts in C–C cross-coupling reactions was discovered by Jeffery [66–68] who reported an enhancement of the HR rate and reaction selectivity. In so-called optimized Jeffery conditions $MeNCy_2$ was used as a base together with Et_4NCl [69]. There are many examples of the successful application of a tetraalkylammonium salt as co-catalyst in HR or as reaction medium [41,70,71,86]. The additional advantage of performing the catalytic reaction in the ammonium salt or in an ionic liquid is the easy separation of catalyst from the reaction products. However in some systems efficient separation is complicated by the transfer of palladium from ionic liquid to organic phase.



HOMO(geneous)	NANO(sized)	HETERO(genized)
$PdCl_2(PhCN)_2$ 4 % mono 96 % di	$Pd^{(0)}$/PVP 5 % mono 95 % di	$Pd^{(II)}/Al_2O_3$ 13 % mono 87 % di
$[Bu_4N]_2[PdBr_4]$ 2 % mono 98 % di		$Pd^{(0)}/Al_2O_3$ 17 % mono 83 % di
SOLUBLE		INSOLUBLE

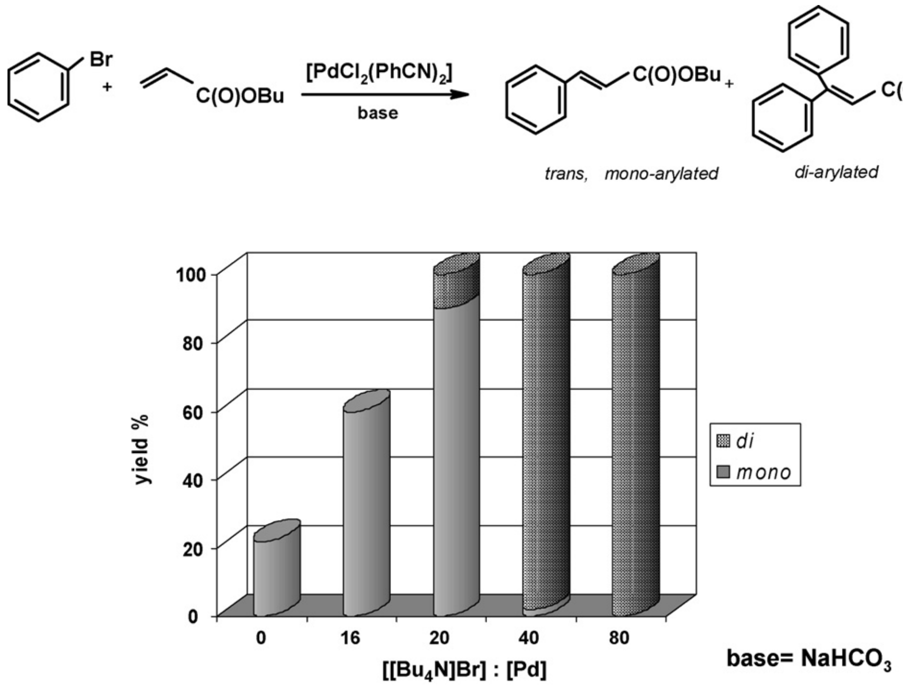
Scheme 15. Catalytic results of HR performed in $[Bu_4N]Br$ with structurally different catalyst precursors.

The influence of $[Bu_4N]Br$ on the selectivity of the HR reaction was studied in the system with $PdCl_2(PhCN)_2$ catalyst precursor [65]. In the reaction performed without any tetraalkylammonium salt only 20% of monoarylated product was obtained, whereas at 20-fold excess of salt over palladium 90% of monoarylated and 10% of diarylated were obtained. Further increase of salt favored the diarylated species such that at 40-fold excess of salt over palladium, the product was principally the diarylated species (98%) (Scheme 16).

The same tendency was also observed when other bases were used, namely Bu_3N or $Cs_2(CO_3)$. In both cases replacement of dimethylformamide (DMF) by $[Bu_4N]Br$ led to the increase of total conversion of butyl acrylate and increase of the yield of diarylated product [65] (Scheme 17).

In addition to these catalytically active soluble complexes, the HR can be also realized on the surface of Pd(0) nanoparticles or on the surface of a Pd(0)/Al_2O_3 heterogeneous catalyst [57]. The problem of participation of heterogeneous and soluble forms of palladium in HR has attracted significant interest. This is mainly because the heterogeneous catalyst can be easily separated from the organic species, i.e. both, products and eventually unreacted substrates. Many studies of the heterogenized Pd catalysts demonstrated significant leaching of palladium from the support and formation of soluble Pd(II) complexes [35,37,72–76,87]. In some systems, analyses of Pd content in solution during the catalytic process indicated redeposition of dissolved palladium species on the support at the end of catalytic process.

Such cases were reported by Köhler who concluded that the solid catalyst (Pd/MO_x) acts as a reservoir for molecular palla-

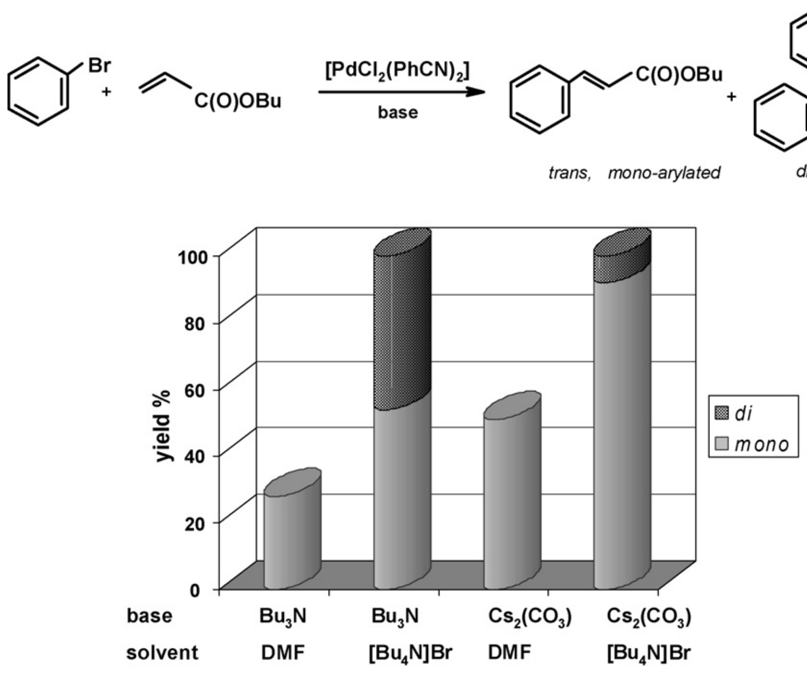


Scheme 16. Effect of $[Bu_4N]Br$ concentration on the yield of HR [65].

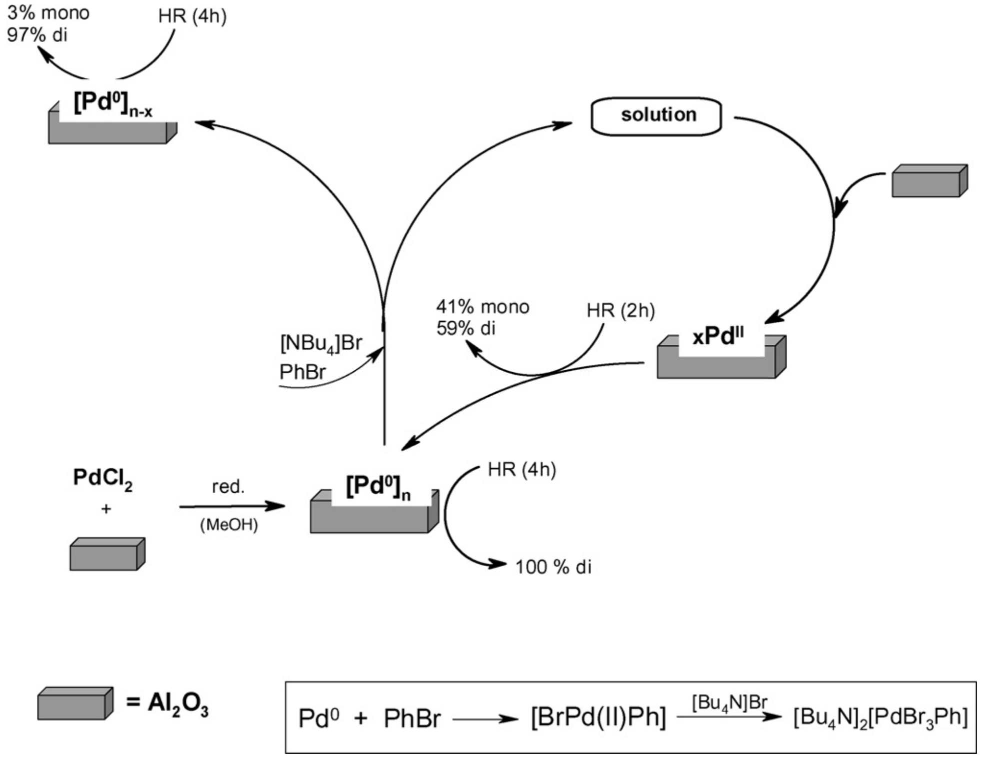
dium species appearing in solution, however, practically all the palladium is deposited back on the support after the catalytic process [74–76].

The reversible transfer of palladium species between support and solution during HR catalyzed by Pd/C and Pd/SiO_2 was reported [77–79]. When Pd/SiO_2 was used as a catalyst in NMP medium palladium leaching was observed and explained by interaction of NMP and NEt_3 with Pd(0) [77]. This process was easier for Pd(0) then for Pd(II). When the reaction was performed in a homogeneous system with $Pd(NH_3)_4Cl_2$ precursor with addition of different supports, palladium was found on the supports at the end of catalytic process. The amount of palladium on the support was much higher on carbon (89–100%) than on SiO_2 (63%) after the same reaction time (60 min) [77].

On the other hand there are also examples of heterogenized Pd systems in which leaching was described as negligible. Such observations have been made for Pd/MgLaO, Pd/C and Pd(II) bis-carbene complex immobilized on clay [80,81,88]. A sil-



Scheme 17. Effect of bases and solvents on the yield of HR [65].



Scheme 18. Effect of solubilization of heterogeneous Pd(0)/Al_2O_3 catalyst precursor in $[Bu_4N]Br$ medium [62].

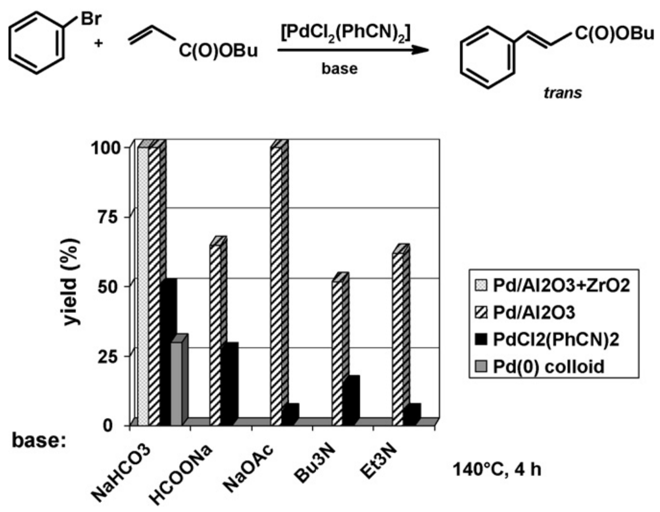
ica anchored palladium prepared by applying inorganic–organic support catalyzed highly selective HR and small amounts of Pd species present in solution do not promote the reaction [89].

Detailed studies of palladium leaching were performed with the Pd(II)/Al_2O_3 catalyst active in HR producing 100% of the diarylated product after 4 h [62]. First, the sample of Pd(0)/Al_2O_3 was heated for 1 h with $[Bu_4N]Br$ and bromobenzene. Next, the solid Pd/Al_2O_3 was separated from the solution and used again in a new HR experiment showing almost the same activity as in the first (up to 99% of diarylated product was obtained). After separation of Pd/Al_2O_3 from the solution which was supposed to contain soluble palladium species of the type $[Bu_4N]_2[PdBr_{4-x}Ph_x]$, a fresh portion of Al_2O_3 was added. After 24 h the material obtained was used as HR catalyst and produced after 2 h almost equimolar amounts of monoarylated and diarylated products [62] (Scheme 18) at 100% conversion. This experiment confirmed leaching of palladium from the support in the presence of PhBr and $[Bu_4N]Br$ as a result of oxidative addition according to the reaction:

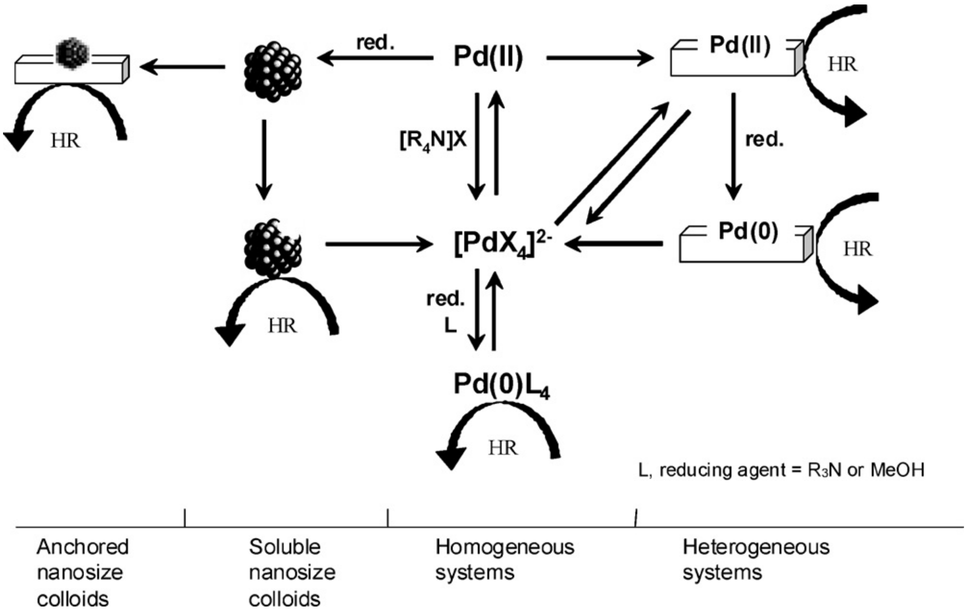
$$[Pd/Al_2O_3] + PhBr + [Bu_4N]Br \rightarrow [Bu_4N]_2[PdBr_{4-x}Ph_x] + [Al_2O_3].$$

Soluble palladium(II) anionic species can be readsorbed on Al_2O_3, however a part of soluble palladium species before being readsorbed can also form Pd(0) colloid. Therefore it was important to confirm that Pd(0) colloid can be attached to Al_2O_3. In fact the catalyst obtained by impregnation of Pd/PVP colloid (containing ca. 0.05 wt% of Pd) on Al_2O_3 produced 100% of diarylated product after 4 h confirming the high catalytic activity of the alumina supported Pd(0) colloid [62].

The results of HR performed under the same conditions (in DMF solution without $[Bu_4N]Br$) with different palladium catalyst precursors, such as: supported Pd(II)/Al_2O_3, Pd(II)/Al_2O_3 + ZrO_2, Pd(0)/PVP colloid and soluble $PdCl_2(PhCN)_2$ are shown in Scheme 19. Most interesting are the very high catalytic activities of supported catalyst precursors, remarkably higher than that of homogeneous $PdCl_2(PhCN)_2$. This suggests an important contribution of cat-



Scheme 19. Yield of HR in DMF with different Pd-catalyst precursors. In reactions with Pd/Al_2O_3 and $NaHCO_3$ and with Pd/Al_2O_3 + ZrO_2 and $NaHCO_3$ 40% and 22% of diarylated product were obtained.



Scheme 20. Transformations of Pd-catalyst precursors during HR.

alytic process occurring on the catalyst surface and not only in solution (see also Scheme 5).

4. Conclusions

Transformations of palladium catalysts during HR are summarized in Scheme 20. In reactions catalyzed by the Pd(II) soluble complex the active Pd(0) species may be formed as soluble monomolecular complexes or as Pd(0) colloids. The reverse process, of Pd(0) colloid (or Pd(0) supported precursors) solubilization as a result of oxidative addition of aryl halide, is also observed and it is facilitated by the presence of tetraalkylammonium salts or ionic liquids in HR mixture. The HR occurs on the surface of Pd(0) colloid supported on polymer or on an inorganic support. During the reaction some amounts of palladium are leached from the support in the form of Pd(II) soluble complexes, products of oxidative addition of aryl halide which are also catalytically active. Soluble palladium complexes of the type $[R_4N]_2[PdAr_xX_y]$ $(x+y=4)$ as well as Pd(0) colloid catalyze HR in homogeneous system or are readsorbed on the support forming a heterogeneous catalyst. To properly understand the HR mechanism it is important to consider different transformations of palladium precursors between solution and support.

Finally one may conclude that in HR as well as in other C–C bond coupling reactions that are using aryl halides as substrates, it is impossible to exclude both homogeneous and heterogeneous routes of catalytic process occurring independently on the kind of homo- or heterogeneous, Pd(0) or Pd(II) species used as precursors.

Acknowledgement

Financial support with grant PBZ-KBN-116/T09/2004 is gratefully acknowledged.

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