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Preliminary communication

# First palladium-catalyzed Heck reactions with efficient colloidal catalyst systems [1]

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**Abstract**

For the first time it has been shown that palladium colloids are effective and active catalysts for the olefination of aryl bromides (Heck reaction). Worthy of note are the high activities of the catalyst system for activated aryl bromides under optimized reaction conditions, which are better than or comparable with "classical" palladium phosphine complexes. Addition of phosphines strongly retards the reaction rate of the colloid catalyst. Nevertheless, this type of catalyst is not suitable for the activation of non-activated substrates, especially technically interesting aryl chlorides.

*Keywords:* Palladium; Heck reaction; Colloids; Catalysis

The functionalization of aryl and vinyl halides by palladium-catalyzed reactions has evolved to be one of the most important uses of transition metals in organic synthesis (for reviews see Ref. [2]). In this respect the olefination of aryl and vinyl halides, the so-called Heck reaction (for reviews see Ref. [3]), offers unique possibilities for carbon–carbon bond formation. So far, the main topics of research concerning Heck reactions are the development of new synthetic applications, recently especially stereoselective protocols (for recent examples of enantioselective Heck and related reactions see Ref. [4]).

Catalyst efficiency, which is a key factor for practical applications, e.g. for the production of speciality organic chemicals like cinnamic acid derivatives, has been of only limited interest so far (the best catalyst activities (turn over number (TON) of 130000) for aryl bromides were previously described by Spencer [5] who used an in situ $Pd(OAc)_2/P(o\text{-Tolyl})_3$ catalyst system). While trying to overcome this problem we discovered phosphapalladacycles, a new class of catalysts for Heck [6] and Suzuki reactions [7] of technically interesting aryl bromides and aryl chlorides, which show superior total turn over numbers for aryl bromides up to 500.000 mol product/mol palladium compared with all previously known palladium catalysts (for the Heck reaction of 4-bromoacetophenone with styrene a TON of 490000 and a turn over frequency (TOF) of 7100 $h^{-1}$ (yield 49%) was observed with a phosphapalladacycle catalyst [8]). Despite the advantages of phosphapalladacycles, improvements in activation of aryl chlorides as well in catalyst turn over frequencies would generally have to be made for industrial applications.

Recently, palladium dispersions containing small metal particles (20–80 Å) have been of increasing scientific interest [9]. Concerning applications, they show superior catalytic properties for some organic reactions, e.g. hydrogenation and dehydrohalogenation, compared with the molecular complexes (for selected examples for catalysis see Ref. [10]) [11]. Thus, we were interested in studying the catalytic activity of palladium colloids for Heck reactions, although Crabtree and coworkers [11] showed that a colloid derived from $Pd(CF_3COCHCOCF_3)_2$ and polymethylhydrosiloxane (PHMS) was not active even for the coupling of phenyl iodide with styrene.

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$$[N(C_8H_{17})_4]Br + Na[B(C_2H_5)_3H] \longrightarrow [N(C_8H_{17})_4][B(C_2H_5)_3H] + NaBr$$

$$[N(C_8H_{17})_4][B(C_2H_5)_3H] + PdCl_2 \longrightarrow Pd_{colloid}[N(C_8H_{17})_4]Cl$$

Fig. 1. Preparation of the palladium colloids.

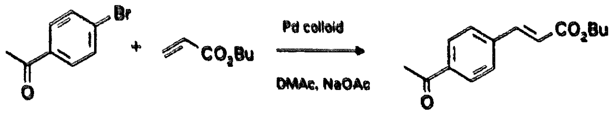
Among the different methods for preparing the palladium colloids we used the elegant synthesis developed by Bönnemann and coworkers [12] (Fig. 1).

In a two step procedure tetraoctyl ammonium bromide was suspended first in tetrahydrofuran and reacted with sodium triethyl boronate to give the corresponding ammonium boronate. The resulting solution was reacted afterwards with $PdCl_2$ to yield a dark brown solution of colloidal palladium stabilized by an excess of ammonium ions. After evaporation of the solvent the palladium particles were dissolved in dimethylacetamide to give a solution containing 0.05 mmol palladium $ml^{-1}$, which was used directly for Heck reactions.

Initial catalytic tests were performed with 4-bromoacetophenone and *n*-butyl acrylate as starting materials in dimethylacetamide as solvent and sodium acetate as base (Scheme 1).

Following standard procedures the reactions were not reproducible and sometimes gave only low conversions. (Standard reaction procedure: 19.9 g (100 mmol) of 4-bromoacetophenone and 25.6 g (200 mmol) of *n*-butyl acrylate were dissolved in 40 ml of dimethylacetamide. After addition of 10.0 g (120 mmol) of sodium acetate and 10 ml of dimethyl acetamide solution containing 0.5 mol% palladium colloid, the reaction mixture was heated to 140 °C.) We attributed this problem to the thermal instability of the active palladium colloids under reaction conditions (the palladium-catalyzed olefination of aryl bromides generally requires phosphine ligands for stabilization of the catalyst and not for activation!).

Therefore we tried a slow addition of the catalyst solution to the reaction mixture at temperatures of 130–140 °C, which resulted in a very efficient reaction. Surprisingly, the initial addition of 1.0 ml of catalyst solution (corresponding to 0.05 mol% catalyst) gave rise to a highly exothermic reaction. Thus, the reaction temperature of the solution rose from 140 up to 164 °C in the first 5 min! GC analysis of the mixture showed 97% conversion. This corresponds to a TOF of nearly 24000 mol product/mol palladium $h^{-1}$. This result is comparable with the fastest Heck reactions of activated aryl bromides reported in the literature so far [5,6].



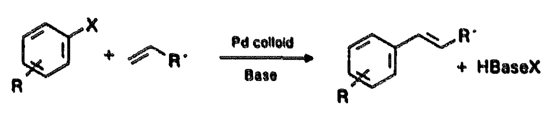
Scheme 1. Heck reaction of 4-bromoacetophenone with *n*-butyl acrylate.

In order to get this high reaction rate with palladium colloids, efficient stirring of the mixture, as well as a ceiling temperature above 135 °C, are important features of this method. Moreover, it is important to use a freshly prepared colloid because aging deactivates the palladium colloid to some extent. Interestingly, the addition of 4 equivalents of triphenylphosphine to the reaction strongly retarded the reaction rate. Thus, in the presence of 0.5 mol% palladium colloid catalyst and 2.0 mol% triphenylphosphine it takes 5 h to get 93% conversion of 4-bromoacetophenone (TOF 37 $h^{-1}$).

To compare the reactivity of the palladium colloid system with the "usual" palladium(0) phosphine complexes the reaction of 4-bromobenzaldehyde with styrene in the presence of 1.0 mol% $Pd(PPh_3)_4$ was tested under the above described reaction conditions. Although the phosphine stabilized palladium catalyst is quite active, conversion of above 95% was reached only after 7 h. Because of the catalytic properties of the palladium colloid, we were interested in expanding the reaction towards other aryl halides and olefins. A summary of the reactions performed is given in Table 1.

It soon became evident that colloidal palladium shows good activity only for activated aryl bromides, e.g. 4-bromoacetophenone, 4-bromobenzaldehyde. Reasonable reactivity was observed for 4-bromofluorobenzene, 4-acetoxy-bromobenzene, and 2-bromo-6-methoxynaphthalin (2-bromo-6-methoxynaphthalin was reacted with 1.2 equiv. of styrene to yield the corresponding stilbene in 60% yield). Deactivated aryl bromides and chlorides show only low activity, if any at all. In general, irreversible agglomeration of the metal which leads to deactivated palladium species is observed here. This problem can be attributed to the non-reductive reaction conditions for Heck reactions, contrary to hydrogenation methods where catalyst deactivation is a reversible process.

Table 1
Heck reactions with palladium colloid catalysts



| X | R | R' | Catalyst (mol%) | Temperature (°C) | Yield (%) |
|---|---|---|---|---|---|
| Br | 4-CHO | $CO_2Bu$ | 0.1 | 130 | 90 |
| Br | 4-F | Ph | 1 | 140 | 55 |
| Br | H | Ph | 1 | 140 | 13 |
| Br | $4\text{-}CH_3CO$ | $CO_2Bu$ | 0.05 | 140 | 97 |
| Br | $4\text{-}CH_3CO$ | CN | 0.2 | 140 | 93 |
| Br | 4-AcO | Ph | 1 | 140 | 30 |
| Br | 4-MeO | Ph | 1 | 130 | 9 |
| Cl | $4\text{-}NO_2$ | Ph | 1 | 140 | < 5 |
| Cl | 4-CN | $CO_2Bu$ | 1 | 130 | < 5 |
| Cl | $4\text{-}CH_3CO$ | Ph | 1 | 140 | < 5 |

The arylation of different olefins, such as *n*-butyl acrylate, styrene or acrylonitrile, has been tested. In the case of activated aryl bromides all olefins gave acceptable results. In order to get a good yield for acrylonitrile as olefin, a specific reaction procedure was used to overcome the problem of the low boiling point of the reaction mixture containing acrylonitrile. Thus, both the palladium catalyst and the olefin were added simultaneously to the mixture at 135–140°C. Moreover, the use of additional tetraalkyl ammonium salts led to improved results. (19.9 g (100 mmol) of 4-bromoacetophenone and 10.5 g of tetraethyl ammonium bromide were dissolved in 40 ml of dimethylacetamide. After addition of 10.0 g (120 mmol) of sodium acetate the reaction mixture was heated to 135–140°C. Then, simultaneously, 6.4 g (120 mmol) of acrylonitrile and 4 ml of dimethyl acetamide solution containing 0.2 mol% palladium colloid were added during 20 min. The conversion was above 96%. To isolate the product the resulting salts were filtered and the remaining mixture was distilled with an air cooled condenser.) The products derived from acrylonitrile were obtained, as expected, as 80:20 mixtures of E/Z-isomers.

In conclusion, we have been able to demonstrate for the first time that palladium colloids are effective catalysts for activated aryl bromides. Nevertheless, they show only moderate to little activity for deactivated aryl bromides or chlorides respectively. Thus, our investigations demonstrate that the often discussed involvement of colloids as catalytically active species in palladium-catalyzed coupling reactions, e.g. under the so-called Jeffrey conditions (see for example Ref. [13]), are not likely for deactivated aryl bromides and chlorides.

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