



## UvA-DARE (Digital Academic Repository)

### Nanocatalysts: Properties and applications

Gaikwad, A.V.

**Publication date**  
2009

[Link to publication](#)

#### **Citation for published version (APA):**

Gaikwad, A. V. (2009). *Nanocatalysts: Properties and applications*. [Thesis, fully internal, Universiteit van Amsterdam].

#### **General rights**

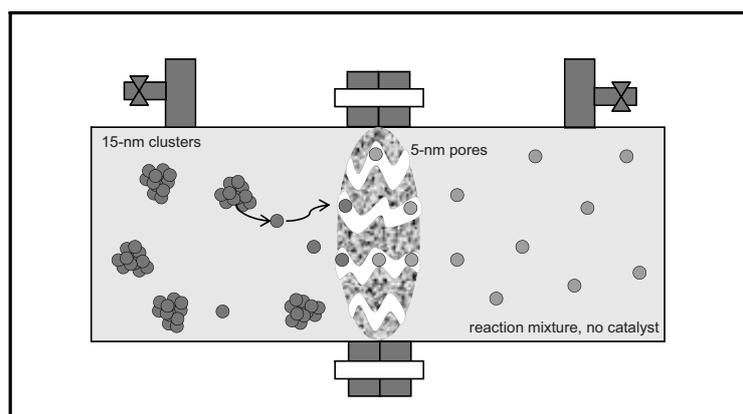
It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

#### **Disclaimer/Complaints regulations**

If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: <https://uba.uva.nl/en/contact>, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.

## Chapter 5

### *Detailed mechanistic studies of Pd nanoparticle-catalyzed cross-coupling reactions*



Part of this work is published as “Ion-leaching and Atom-leaching Mechanisms from Palladium Nanoparticles in Cross-coupling Reactions”, A. V. Gaikwad, A. Holuigue, M. B. Thathagar, J. E. ten Elshof and G. Rothenberg, *Chem. Eur. J.*, **2007**, *13*, 6908.

### Introduction

Palladium-catalysed cross-coupling is a versatile synthetic protocol used in producing drugs, agrochemicals and fragrances.<sup>[1-3]</sup> The main cross-coupling reactions in this family are the Heck, Suzuki-Miyaura, Negishi, and Stille couplings.<sup>[1]</sup> Traditionally, such reactions are catalysed by Pd<sup>II</sup>/Pd<sup>0</sup> complexes in the presence of phosphines, or other ligands.<sup>[4-6]</sup> These ligands are costly, and require careful separation from the final product. Moreover, many of them are air- and moisture-sensitive, making ‘ligand-free’ Pd catalysis using heterogeneous Pd/C<sup>[7]</sup> or Pd colloid suspensions an attractive alternative.<sup>[8-10]</sup> Nanocolloids are attracting considerable attention as C–C coupling catalysts.<sup>[10-12]</sup> They are not ‘classical heterogeneous catalysts’, but their dimensions (2–20 nm) are near those of the crystallites used in traditional gas/solid heterogeneous catalysis.<sup>[9, 12-14]</sup> Ligand-free Heck and Suzuki catalysis was reported using Pd salt precursors,<sup>[15]</sup> nanocluster suspensions<sup>[16, 17]</sup> and supported nanoclusters.<sup>[14]</sup> In the last case, different types of supports were used, including carbon,<sup>[13]</sup> (thiol-functionalised) silica,<sup>[18]</sup> zeolites,<sup>[19]</sup> resins,<sup>[20]</sup> polymer incorporated nanoparticles.<sup>[21]</sup> The primary aims of these studies were addressing the catalyst separation problem, and enabling reactions in diverse media, such as water, mixed solvents,<sup>[7]</sup> or ionic liquids.<sup>[22]</sup>

Interestingly, many of the so-called Pd-complex-catalysed coupling reactions, and especially those run at temperatures above 120 °C, were later shown to be actually catalysed by either Pd atoms or Pd clusters.<sup>[23]</sup> De Vries recently proposed a unifying mechanism for all high-temperature Heck reactions, showing evidence that regardless of the catalyst precursor type, the Pd is reduced at 120 °C to Pd(0), and forms colloids.<sup>[24]</sup> Similarly, our studies on more than 400 Heck reactions, using partial least squares (PLS) and artificial neural networks (ANNs) data mining methods,<sup>[25]</sup> showed that the reaction rate is indeed negatively correlated with the Pd precursor concentration, regardless of which precursor was used, with a clear cut-off point at 120 °C.<sup>[26]</sup>

Despite these important works, we still know very little about the mechanism of cluster catalysis in the liquid phase.<sup>[27]</sup> The main problem is the leaching of Pd atoms and/or ions from the clusters.<sup>[28]</sup> There has been much scientific argument about this point, especially regarding the actual catalytic species.<sup>[13, 29, 30]</sup> El-Sayed and co-workers and Bradely *et al.* reported that low co-ordination sites on the cluster catalyse the reaction.<sup>[31-34]</sup> Conversely, Schmidt and Mametova,<sup>[35]</sup> Arai and co-workers,<sup>[36]</sup> de Vries and co-workers and Reetz *et al.* suggested a homogeneous mechanism, where the Pd clusters act as

reservoir of active Pd atoms or ions.<sup>[15, 23, 24, 37, 38]</sup> Combining these two views, the mechanistic studies of Biffis *et al.* suggested that Pd<sup>II</sup> species leach into solution, catalyse the coupling reactions and then re-cluster.<sup>[39]</sup> Dupont and co-workers reported that aryl iodide attacks the cluster surface and forms the oxidative complex which then leaches into the solution and catalyses the reaction.<sup>[40]</sup> Richardson and Jones suggested very recently a simple way to entrap those soluble species.<sup>[41]</sup> All in all, these studies show that finding the true catalytic species is an important and relevant challenge.

In a recent preliminary communication, we presented the first direct and unambiguous test that proves that leached Pd species are the true catalysts in Pd cluster-catalysed C–C coupling reactions.<sup>[42]</sup> We did this using a special reactor, where the clusters and the reactants are physically separated by an alumina membrane.<sup>[43]</sup> This membrane allows Pd atoms and ions to pass, but not clusters. Here, we present a detailed study of the possible leaching pathways, and the species involved. We explore three hypotheses: First, that the leached species are Pd<sup>0</sup> atoms that re-form into clusters on the other side of the membrane. Second, that the leached species are Pd<sup>II</sup> ions; and third, that Pd forms an oxidative complex with the ArX substrate, that then transfers through the membrane. We test these hypotheses by monitoring Heck and Suzuki reaction profiles in our membrane reactor. Further experimental support is provided using <sup>1</sup>H and <sup>13</sup>C NMR spectroscopy, UV-visible spectroscopy, fast atomic bombardment mass spectrometry (FAB-MS) and transmission electron microscopy (TEM).

### Experimental Section.

**Materials and instrumentation.** *In situ* UV-visible measurements were performed using a Hewlett Packard 8453 spectrophotometer with a diode array detector. The recorded wavelength range was 190–1100 nm, at 1 nm resolution. <sup>1</sup>H and <sup>13</sup>C NMR were recorded on a Bruker AMX 300 spectrometer at 300.1 MHz and 75.2 MHz, respectively and on a Varian Inova 500 spectrometer at 499.8 MHz and 125.7 MHz, respectively. TEM images were obtained with a JEOL JEM-1200 EXII instrument, operated at an accelerating voltage of 120 kV. Samples were prepared by placing 150 μL of 1 mM Pd cluster suspension on carbon-coated copper grids. The solvent was then evaporated at 50 °C and 250 mm Hg. At least four images were taken for each sample. Inductive Coupled Plasma (ICP) measurements were performed on a Perkin Optima 3000 XL ICP instrument. Samples were first dried under vacuum at 65 °C and then digested using 6 ml of HCl and

2ml of HNO<sub>3</sub> and heated at 220 °C for 51 min. GC analysis was performed using an Interscience Trace GC-8000 gas chromatograph with a 100% dimethylpolysiloxane capillary column (VB-1, 30 m × 0.325 mm). GC/MS analysis was performed using a Hewlett-Packard 5890/5971 GC/MS equipped with a ZB-5 (zebron) column (15 m × 0.25 mm). All products are known compounds and were identified by comparison of their GC retention times to those of authentic samples and by MS analysis. GC conditions: isotherm at 80 °C (1 min); ramp at 30 °C min<sup>-1</sup> to 280 °C; isotherm at 280 °C (3 min). Fast Atom

in THF. Bombardment Mass Spectroscopy (FAB-MS) was carried out using JEOL JMS SX/SX 102A four-sector mass spectrometer. Samples were loaded in a matrix solution (3-nitrobenzyl alcohol) on to a stainless steel probe and bombarded with Xenon atoms with energy of 3 KeV. During the high resolution FAB-MS measurements a resolving power of 10,000 (10 % valley definition) was used. Chemicals were purchased from commercial firms (>99% pure). All solvents were degassed and dried using molecular sieves. Pd clusters were prepared according to the literature procedure.<sup>[10]</sup>

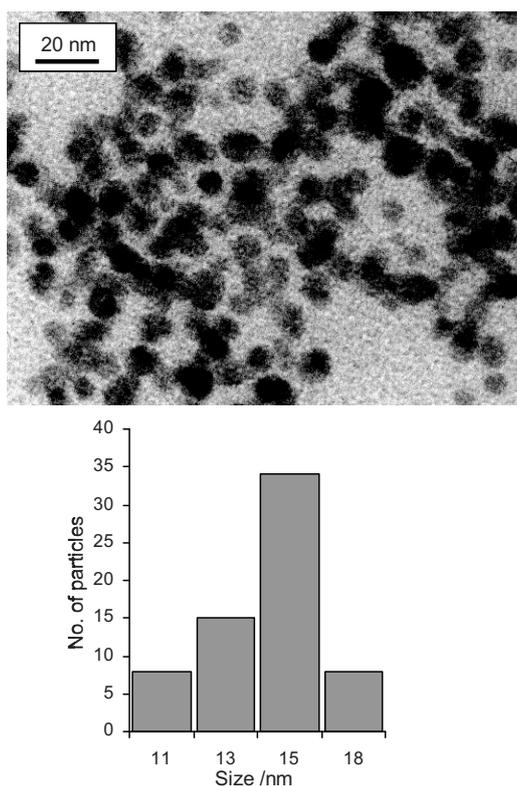
**Pd Cluster and Pd oxidative complex (with iodobenzene 2) transportation across membrane:** Membrane reactor was evacuated and refilled with N<sub>2</sub>. 70 ml DMF was placed into both sides (A and B) of membrane reactor. Then 30 ml of Pd clusters (10 mM in DMF) was added in side A and the solution was heated and stirred in the reactor at 100 °C for 144 h. 5 ml of sample was taken from B side after every 24 h. Above experiment was repeated using same amount of Pd clusters on A side and then 100 equivalents of iodobenzene **2** was added on both sides just to prevent the concentration gradients. 5 ml of sample was taken from B side after every 24 h. It is important to keep the reactor always under N<sub>2</sub>. All samples were then analyzed using ICP, <sup>13</sup>C NMR, TEM, UV-Vis spectrophotometer, and ES-MS. The experiments were carried out also

**Heck coupling of *n*-butylacrylate **1** and iodobenzene **2** with sample I and II:** A Schlenk-type vessel equipped with a rubber septum and a magnetic stirrer was evacuated and refilled with N<sub>2</sub>. Equal 1.5:1 mixtures of **1** (1.5 mmol, 0.19 g) and **2** (1.0 mmol, 0.2 g) in 25 mL DMF were placed into reactor. NaOAc (1.5.0 mmol, 0.21 g) was then added. 7 ml of solution was taken from side B of membrane reactor after 6 days and then added to the same reactor. The reactor was heated at 100 °C and the sample was taken after 72 and analyzed using GC (pentadecane internal standard). After each experiment, the membrane was washed (acetone, 4 × 10 mL) and extracted for 24 h with EtOH.

**Suzuki coupling of phenylboronic acid 4 with 4-iodotoluene 5:** Equal 1.5:1 mixtures of **4** (7.5 mmol, 1.1 g) and **5** (5 mmol, 1.1 g) in 50 mL DMF were placed on both sides of the membrane reactor. NaOAc (15 mmol, 2.07 g) was then added to side **B** and the Pd cluster suspension (10 ml, 10 mM, 2.0 mol%) to side **A**. The reactor was heated at 100 °C and the samples were taken from both the compartments and analyzed using GC (pentadecane internal standard).

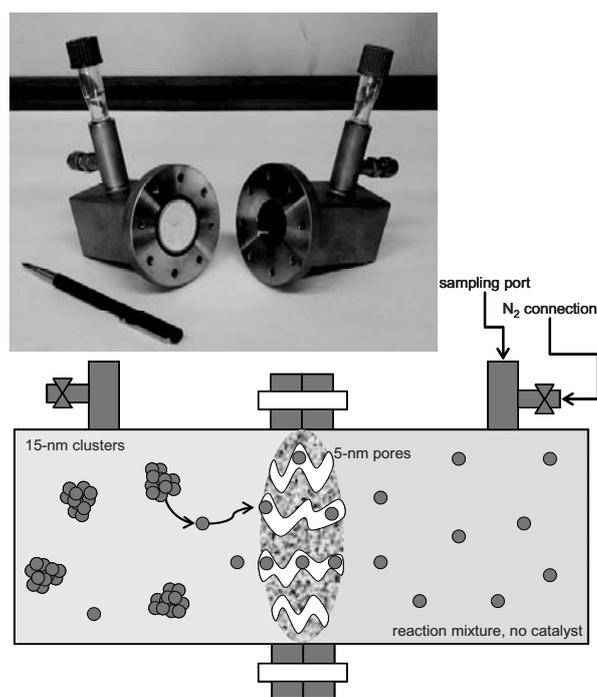
### Results and Discussion

Pd nanocolloids were synthesised by reducing Pd(OAc)<sub>2</sub> with tetraoctylammonium glycolate (TOAG), used both as reducing and stabilising agent.<sup>[31]</sup> This method gives clusters with an average size of 15 nm and a narrow particle size distribution (14 nm ± 3 nm, see Figure 1). No particles smaller than 11 nm were observed.



**Figure 1.** Transmission electron micrograph of Pd nanocolloids prior to the reaction (top) and corresponding size distribution, based on 62 particles counted (bottom).

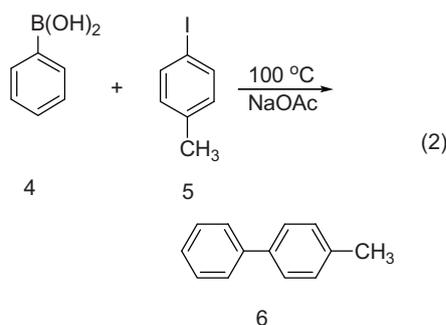
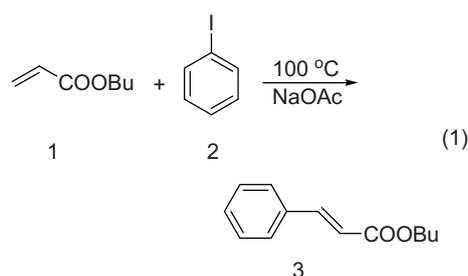
The coupling reactions were studied using a special membrane reactor, designed and built in-house.<sup>[44]</sup> This reactor consists of two stainless steel compartments separated by a membrane (henceforth referred to as ‘side A’ and ‘side B’, see Figure 2). Each compartment has a gas inlet and a sampling port. The alumina membrane was made by coating mesoporous  $\alpha$ -alumina with a layer of microporous  $\gamma$ -alumina.<sup>[43]</sup> This gives pores of *ca.* 5 nm in diameter (the pore size distribution of the membrane was determined by permoporometry<sup>[45, 46]</sup>). A few pores were larger than 5 nm, with a maximum size of 11 nm. However, due to the amorphous structure of the membrane, all the paths through it are tortuous wormholes, and no path consists of only maximum-size pores. Thus, this membrane also retains particles smaller than 11 nm (a detailed description of the reactor and the membrane is given elsewhere<sup>[42]</sup>).



**Figure 2.** Photo (top) and schematic (bottom) of the two-compartment membrane reactor.

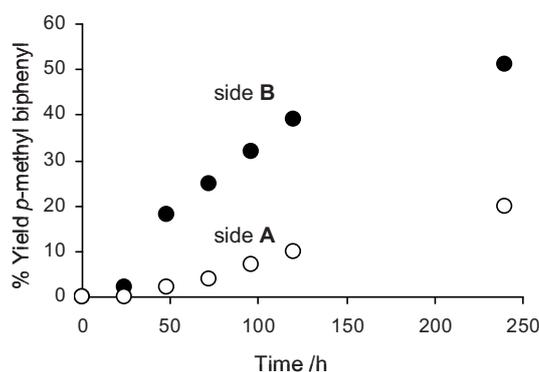
First, we studied the Heck coupling of *n*-butyl acrylate **1** with iodobenzene **2** to *n*-butyl cinnamate **3** in DMF (eq 1). Identical starting mixtures, with an acrylate:iodobenzene mole ratio of 1.5:1.0, were placed on both sides of the membrane, avoiding concentration

gradients. Then, 0.01 equiv of Pd clusters suspension was added to side **A** and 1.5 equiv NaOAc was added to side **B**. The base is necessary for closing the catalytic cycle. Since there is no base on side **A**, no product can form there. We then monitored the yield of *n*-butyl cinnamate on both sides **3** using GC. No reaction was observed for the first 5 h. This is because the leached Pd species from side **A** must first diffuse through the membrane to side **B**. After 120 h, the yield on side **B** was 88%, proving that some sort of Pd catalyst has diffused there. Another 4.9% was observed on side **A**. Control experiments confirmed that this product could not form on side **A** in the absence of a base (a detailed description of these experiments is given in our preliminary communication<sup>[42]</sup>). Importantly, the solubility of the base, NaOAc, is negligible (control experiments confirmed that the amount of solid NaOAc that dissolves in 100 mL DMF under the reaction conditions gives < 1.5% conversion). Thus, the product observed on side **A** must have diffused from side **B**. No Pd precipitation was observed on either side.



To determine whether this applies also to other coupling reactions, we examined also the Suzuki coupling between phenylboronic acid **4** and *p*-iodotoluene **5** (eq 2). Figure 3 shows the yield of *p*-methylbiphenyl **6** on sides **A** and **B**. Note that the Heck reaction requires a stoichiometric amount of base, while in the Suzuki reaction does not. The role of the base in the latter is more subtle – the base quaternises the boronic acid and thereby

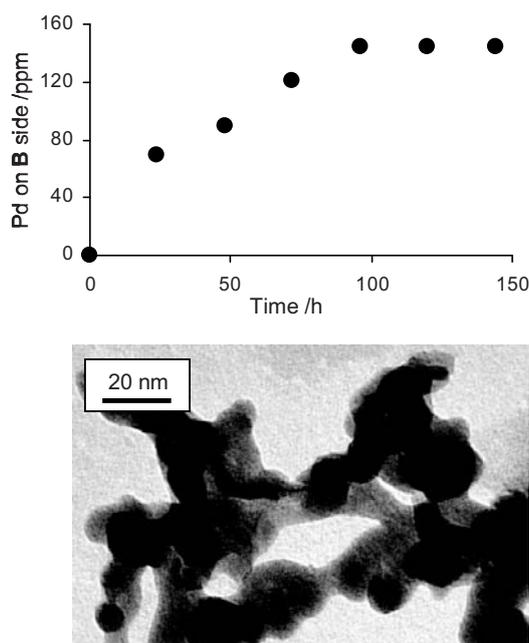
facilitates the transmetallation step. Because of this, the rates of product formation on sides **A** and **B** are much closer in the case of the Suzuki reaction. Nevertheless, in both cases the results show that leaching occurs (*cf.* with the studies of Hu and co-workers<sup>[47, 48]</sup>). However, these experiments do not give us precise information about the type and the amount of the catalytic Pd species on side **B**.



**Figure 3.** Reaction profile for the Suzuki coupling product, *p*-methylbiphenyl **6**. The product observed on side **A** has diffused from side **B**. Reaction conditions: 1.5 equiv phenylboronic acid; 1 equiv *p*-iodotoluene; 3 equiv NaOAc; 0.02 equiv Pd clusters suspension; DMF; 100 °C; N<sub>2</sub>.

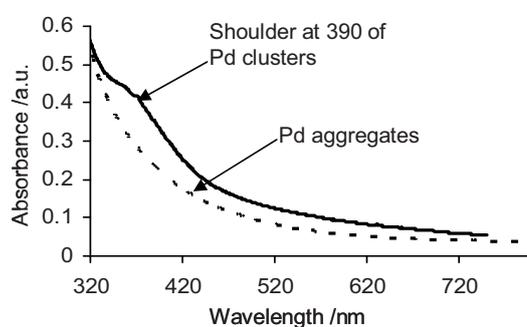
We then investigated whether Pd<sup>0</sup> atoms or small Pd<sup>0</sup> clusters leach through the membrane. First, we examined if the original Pd clusters fragment, forming smaller clusters (< 5 nm) that could then diffuse through the membrane.<sup>[49]</sup> In this experiment, a Pd cluster suspension in DMF was placed on side **A**, while pure DMF was placed on side **B**. The contents of both sides were stirred at 100 °C under nitrogen for 144 h. The Pd amount on side **B** was quantified periodically by inductive coupled plasma (ICP) analysis. After 144 h, the metal species on side **B** were analysed using TEM. Figure 4 shows the amount of Pd (ppm) transferred *vs.* time, as well as the TEM results after 144 h. Initially, the Pd transfer rate is high, reaching a plateau after 120 h. A total of 140 ppm Pd was found on side **B**, which is 20% of the Pd originally placed on side **A**. The TEM micrograph shows irregularly-shaped particles, and no spherical clusters. We do not know why these irregular shapes form. It may be because of the different stabiliser/reducing agent composition on

side **B**. This shows that smaller clusters do not first form on side **A** and then diffuse to side **B**. Moreover, it shows that Pd<sup>0</sup> species (*i.e.* Pd atoms) do transfer across the membrane – the experiments were performed under inert conditions and there was no oxidising agent present that could oxidise the Pd<sup>0</sup> to Pd<sup>II</sup>. The mixture on side **B** was also analysed using <sup>13</sup>C and <sup>1</sup>H NMR spectroscopy, showing the presence of tetraoctyl ammonium ions. These are stabilising ions that were released from the cluster surface on side **A** and diffused to side **B** due to the concentration gradient. Note that no precipitation of inactive Pd black was observed on either side. The Pd aggregates formed on side **B** retained some catalytic activity. Adding 2 ml (2.7 μmol Pd, 0.27 mol% relative to substrate) of the suspension from side **B** to 1.5:1 mixtures of **1** and **2** yielded 90% conversion to the Heck coupling product after 120 h. Although the reaction conditions differ from the original membrane experiment, the similar outcome supports the conclusion that Pd atoms leaching from these aggregates.



**Figure 4.** (top) Amount of Pd (ppm) transferred to side **B** vs. time. Reaction conditions: 30 ml Pd clusters (10 mM in DMF) on side **A**, pure DMF on side **B**, 100 °C, N<sub>2</sub> atmosphere; (bottom) micrograph of the Pd species on side **B** after 144 h.

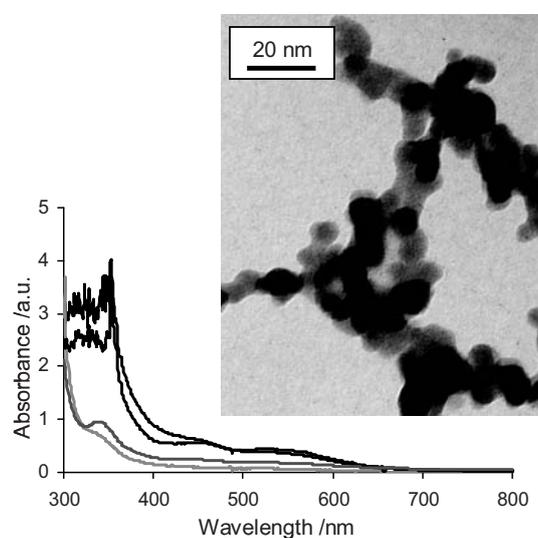
To rule out any possibility of Pd<sup>II</sup> transfer in this system, we also analysed after 144 h samples from both sides using UV-visible spectroscopy. Pd<sup>II</sup> ions show an absorption peak at 340–360 nm, while Pd clusters show a shoulder at 390 nm and Pd aggregates do not show any peak in UV-Visible region.<sup>[50]</sup> Figure 5 shows the UV-visible spectrum of the original cluster suspension that was added to side **A** as well that of the sample taken from side **B** after 144 h. The sample on side **B** shows no shoulder, supporting our hypothesis that Pd<sup>0</sup> atoms transfer through the membrane and not Pd<sup>II</sup> ions.



**Figure 5.** UV-visible absorption spectra of the original cluster suspension from side **A** (continuous curve) and the mixture on side **B** after 144 h (broken curve). Reaction conditions are same as in Figure 4.

We then examined whether Pd<sup>II</sup> ions can leach from the clusters as a result of oxidative addition, following the mechanisms originally put forward by Schmidt<sup>[35]</sup> and Arai and co-workers,<sup>[36]</sup> and recently reviewed by de Vries and co-workers.<sup>[24]</sup> They suggested that the aryl halide attacks the Pd cluster, extracting a Pd<sup>II</sup> ion as a complex into the solution. To check this hypothesis, we placed Pd clusters on side **A** together with 100 equivalents of iodobenzene in DMF, while on side **B** we placed only the same amount of iodobenzene in DMF, thus avoiding concentration gradient effects. Because of the sensitivity of the oxidative complexes to oxygen and water, extra care was taken in these experiments using a dry N<sub>2</sub> atmosphere and all solvents were freshly degassed and dried prior to the reaction. Samples were taken every 24 h from both sides. After 24 h, the typical black colour of the Pd clusters suspension changed to dark reddish on side **A**. One day later, this red colour also appeared on side **B**. Figure 6 shows the UV-visible

spectroscopy of the mixtures both sides after 144 h. We see absorption maxima at 320, 420, and 540 nm. These results agree with the observations of Dupont and co-workers.<sup>[40]</sup> The spectra match those of  $\text{PdX}_n^-$  salts. Examining the sample from side **B** with TEM, one sees some aggregation of Pd species (inset in Figure 6). Importantly, no spherical clusters are observed on side **B** in this case. If we compare figure 4 with the inset in figure 6, we see that the aggregate sizes are similar. Note that no complex formation was observed in control experiments using a 1:1 PhI:Pd ratio.

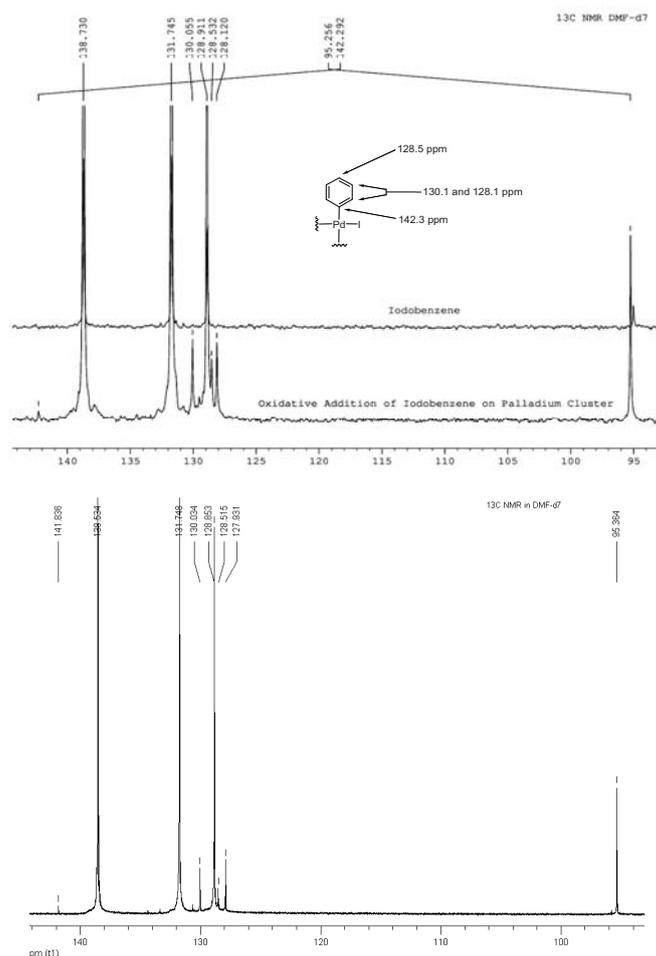


**Figure 6.** UV-visible spectra of oxidative complex formation on sides **A** and **B**. The blue, black, green and red curves pertain to concentrated and diluted samples from side **A** and **B**, respectively. The inset shows the TEM picture of the aggregates that form on side **B** after 144 h. Reaction conditions: 10 mM of 30 mL Pd clusters suspension on side **A**, 100 equivalents of iodobenzene on both sides, 100 °C,  $\text{N}_2$  atmosphere.

### **<sup>13</sup>C NMR and FAB-MS studies of the clusters and complexes in DMF**

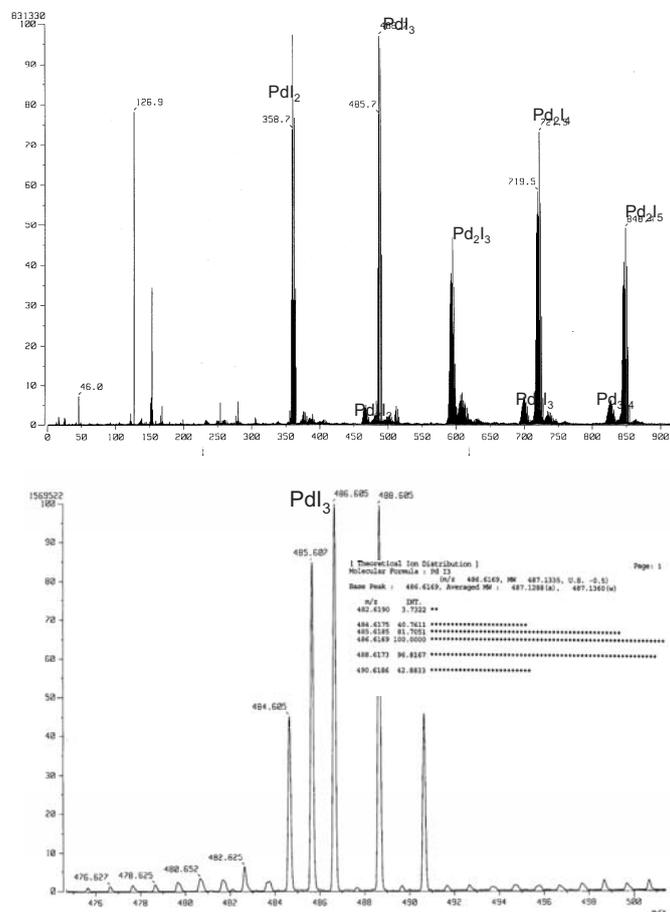
Figure 7 shows the  $^{13}\text{C}$  NMR spectrum of a mixture of Pd clusters and PhI in DMF (top), and the corresponding control sample without Pd (inset). Comparing this with the  $^{13}\text{C}$  NMR spectra of the reaction mixture from side **B** of the membrane reactor (bottom), we observe the same peaks as in the Pd-containing solution. We observed the signals at 127.9, 128.5, 130.0 and 141.8 ppm. The signal at 141.8 ppm is typical for Pd-bound C

atoms of arylpalladium compounds. These results are in agreement with the values reported by Reetz *et al.*<sup>[37]</sup>



**Figure 7.** (Top) <sup>13</sup>C NMR spectrum of a mixture of Pd clusters and PhI in DMF. The inset shows the corresponding control sample without Pd. (Bottom) <sup>13</sup>C NMR spectrum of the mixture from side **B** of the membrane reactor.

Furthermore, FAB-MS measurements showed polymeric species of oxidative complexes, in agreement with the observations of de Vries *et al.*<sup>[15]</sup> see figure 8).

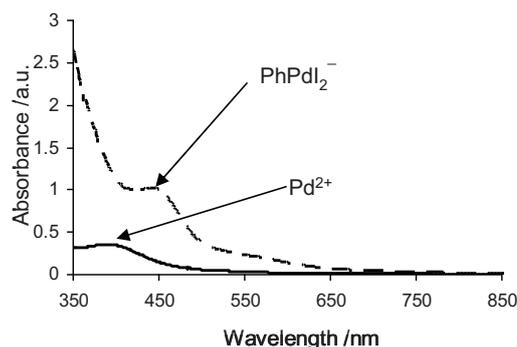


**Figure 8.** FAB-MS spectrum of the mixture from side **B** of the membrane reactor (top) and zoom-in view on the polymeric iodopalladium species (bottom).

### Oxidative complex formation in THF

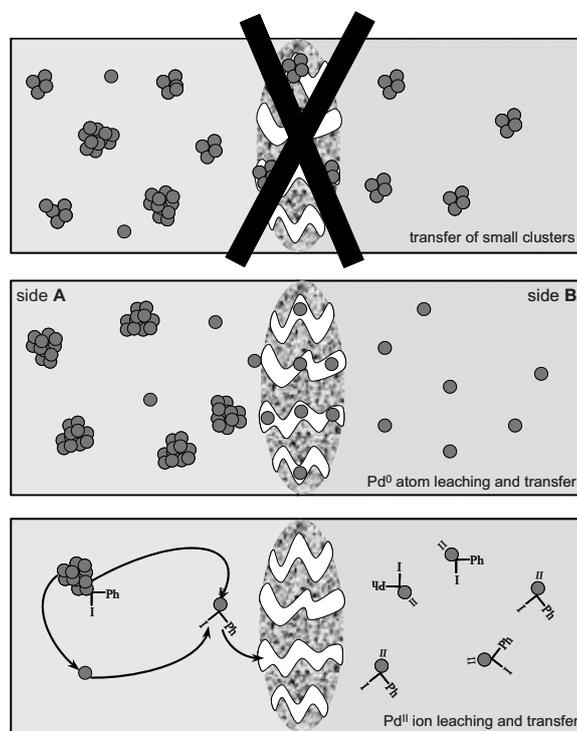
To rule out the possibility of formate reduction originating from the DMF solvent, we ran analogous experiments in THF. UV-visible spectroscopy confirmed that the same processes occur, regardless of the solvent. Interestingly, the complex formation and the Pd<sup>II</sup> leaching depends strongly on the solvent: In THF, we observed the Pd<sup>II</sup> complexes even when using a 1:1 PhI:Pd ratio. The typical black color of Pd colloids changed to brownish yellow. Figure 9 shows the UV-visible spectra of the sample in THF on side **B** after 144 h. We see an absorption peak around 450 nm, which can be attributed to the

(Ph)Pd(I)<sub>2</sub><sup>-</sup> complex. The oxidative complex with Pd is stable in both THF and DMF. To check the activity of this complex we ran Heck reaction using same sample in both solvents. In DMF this complex was active but in THF we didn't observe any reaction in the presence of NaOAc. In presence of triethylamine as a base the conversion was 70%.



**Figure 9.** UV-Visible absorption spectra of Pd(OAc)<sub>2</sub> in THF (continuous curve) and oxidative arylpalladium complex on side B (dotted curve). Reaction conditions: 10 mM of 30 mL Pd clusters suspension on side A, 1 equivalents of iodobenzene on both sides, 100 °C, N<sub>2</sub> atmosphere.

Based on these observations, we distinguish three different mechanisms by which a palladium species can transfer from side A to side B (Figure 10). In the first, the Pd<sup>0</sup> clusters may fragment, or decrease in size due to Pd atom leaching. The resulting small clusters could then transfer across the membrane (Figure 10, top). However, our results clearly show that this does not happen. No clusters are observed on side B in this case. Pd atom- or ion-leaching does result in smaller clusters (as we showed earlier for the Sonogashira cross-coupling<sup>[51]</sup>), but these clusters still cannot transfer through the membrane. In the second scenario, Pd<sup>0</sup> atoms leach from the clusters under non-oxidising conditions, and transfer as Pd<sup>0</sup> across the membrane (Figure 10, middle). Indeed, we observe this under carefully controlled reaction conditions where no formation of Pd<sup>II</sup> oxidative complexes is possible. Transferring “naked Pd<sup>0</sup>” atoms incurs a high energy penalty, and it may be that they form complex with a stabilising agent.



**Figure 10.** Suggested mechanisms for palladium transfer from side **A** to side **B**. Cluster fragmentation followed by small cluster transfer (top);  $\text{Pd}^0$  atom leaching and transfer under non-oxidising conditions (middle); Formation and subsequent transfer of  $\text{Pd}^{\text{II}}$  complexes (bottom).

The third mechanism pertains to the situation where an oxidative reagent, such as  $\text{PhI}$ , is present. This  $\text{PhI}$  can attack the cluster surface, forming  $\text{Pd}^{\text{II}}$  complexes that can then leach into solution and transfer across the membrane to side **B** (Figure 10, bottom). In this case, the aggregates observed on side **B** can come from two sources:  $\text{Pd}^0$  atoms (as in the previous scenario) and  $\{\text{aryl-Pd}^{\text{II}}\text{-X}\}$  complexes. The formation of the oxidative complex is solvent-dependent, and proceeds much better in THF than in DMF.<sup>[52]</sup> We cannot say whether the oxidative addition occurs on the cluster surface or on  $\text{Pd}^0$  atoms that are already in solution.

**Conclusion.**

Using a simple approach based on physical separation, we prove here that Pd atoms and ions do leach from Pd clusters under Heck and Suzuki coupling conditions. There are two leaching mechanisms, depending on the reaction conditions. In the absence of any oxidising agent, Pd<sup>0</sup> atoms leach from the clusters. Conversely, in the presence of PhI, Pd<sup>II</sup> complexes can form by oxidative addition, either on the cluster surface or through reaction with Pd<sup>0</sup> atoms that have already leached into solution. Both the Pd<sup>0</sup> atoms and the Pd<sup>II</sup> complexes can then enter the cross-coupling catalysis cycle. The remaining (smaller) Pd clusters are not the catalytically active species.

## References

- [1] F. Diederich, P. J. Stang, Wiley-VCH, Weinheim, **1997**.
- [2] M. Beller, *Vol. 1 and 2*, 2nd ed. (Eds.: M. Beller, C. Bolm), Wiley-VCH, Weinheim, **2004**.
- [3] J. G. de Vries, *Can. J. Chem.* **2001**, *79*, 1086.
- [4] A. Zapf, M. Beller, *Top. Catal.* **2002**, *19*, 101.
- [5] R. B. Bedford, C. S. J. Cazin, D. Holder, *Coord. Chem. Rev.* **2004**, *248*, 2283.
- [6] D. H. Valentine, J. H. Hillhouse, *Synthesis* **2003**, 2437.
- [7] S. Mukhopadhyay, G. Rothenberg, A. Joshi, M. Baidossi, Y. Sasson, *Adv. Synth. Catal.* **2002**, *344*, 348.
- [8] M. T. Reetz, J. G. de Vries, *Chem. Commun.* **2004**, 1559.
- [9] B. M. Choudary, S. Madhi, N. S. Chowdari, M. L. Kantam, B. Sreedhar, *J. Am. Chem. Soc.* **2002**, *124*, 14127.
- [10] M. B. Thathagar, J. Beckers, G. Rothenberg, *Green Chem.* **2004**, *6*, 215.
- [11] For a general overview on metal nanoclusters and their applications in catalysis see a) J. D. Aiken III, R. G. Finke, *J. Mol. Catal. A* **1999**, *145*, 1; b) J. S. Bradley, E. Hill, M. E. Leonowicz, H. Witzke, *J. Mol. Catal.* **1987**, *41*, 59; c) H. Bönemann, R. M. Richards, *Eur. J. Org. Chem.* **2001**, 2455.
- [12] a) R. L. Augustine, S. T. Oleary, *J. Mol. Catal. A: Chem.* **1995**, *95*, 277; b) A. Biffis, M. Zecca, M. Basato, *J. Mol. Catal. A: Chem.* **2001**, *173*, 249; c) S. S. Prockl, W. Kleist, M. A. Gruber, K. Köhler, *Angew. Chem.* **2004**, *116*, 1917; *Angew. Chem. Int. Ed.* **2004**, *43*, 1881.
- [13] K. Köhler, R. G. Heidenreich, J. G. E. Krauter, M. Pietsch, *Chem. a Eur. J.* **2002**, *8*, 622.
- [14] F. Y. Zhao, B. M. Bhanage, M. Shirai, M. Arai, *Chem. a Eur. J.* **2000**, *6*, 843.
- [15] A. H. M. de Vries, F. J. Parlevliet, L. Schmieder-van de Vondervoort, J. H. M. Mommers, H. J. W. Henderickx, M. A. M. Walet, J. G. de Vries, *Adv. Synth. Catal.* **2002**, *344*, 996.
- [16] K. Okamoto, R. Akiyama, H. Yoshida, T. Yoshida, S. Kobayashi, *J. Am. Chem. Soc.* **2005**, *127*, 2125.
- [17] E. H. Rahim, F. S. Kamounah, J. Frederiksen, J. B. Christensen, *Nano Lett.* **2001**, *1*, 499.
- [18] C. M. Crudden, M. Sateesh, R. Lewis, *J. Am. Chem. Soc.* **2005**, *127*, 10045.
- [19] A. Corma, H. Garcia, A. Leyva, A. Primo, *Appl. Catal. A: Gen.* **2003**, *247*, 41.
- [20] A. M. Caporusso, P. Innocenti, L. A. Aronica, G. Vitulli, R. Gallina, A. Biffis, M. Zecca, B. Corain, *J. Catal.* **2005**, *234*, 1.
- [21] H. Hagi, M. Sugiura, S. Kobayashi, *Org. Lett.* **2006**, *8*, 375.
- [22] C. C. Cassol, A. P. Umpierre, G. Machado, S. I. Wolke, J. Dupont, *J. Am. Chem. Soc.* **2005**, *127*, 3298.
- [23] A. H. M. de Vries, J. Mulders, J. H. M. Mommers, H. J. W. Henderickx, J. G. de Vries, *Org. Lett.* **2003**, *5*, 3285.
- [24] J. G. de Vries, *Dalton Trans.* **2006**, 421.
- [25] E. Burello, D. Farrusseng, G. Rothenberg, *Adv. Synth. Catal.* **2004**, *346*, 1844.
- [26] G. Rothenberg, J. A. Hageman, F. Clerc, H.-W. Frühauf, J. A. Westerhuis, *Chem. Ind. (CRC Press), Catal. Org. React.* **2006**, *115*, 261.
- [27] J. A. Widegren, R. G. Finke, *J. Mol. Catal. A: Chem.* **2003**, *198*, 317.
- [28] N. T. S. Phan, M. Van Der Sluys, C. W. Jones, *Adv. Synth. Catal.* **2006**, *348*, 609.
- [29] R. G. Finke, S. Özkaz, *Coord. Chem. Rev.* **2004**, *248*, 135.
- [30] A. S. Gruber, D. Pozebon, A. L. Monteiro, J. Dupont, *Tetrahedron Lett.* **2001**, *42*, 7345–7348.
- [31] J. S. Bradley, B. Tesche, W. Busser, M. Maase, M. T. Reetz, *J. Am. Chem. Soc.* **2000**, *122*, 4631.

- [32] R. Narayanan, M. A. El-Sayed, *J. Am. Chem. Soc.* **2003**, *125*, 8340.
- [33] R. Narayanan, M. A. El-Sayed, *J. Phys. Chem. B* **2003**, *107*, 12416.
- [34] J. Le Bars, U. Specht, J. S. Bradley, D. G. Blackmond, *Langmuir* **1999**, *15*, 7621.
- [35] A. F. Shmidt, L. V. Mametova, *Kin. Catal.* **1996**, *37*, 406.
- [36] B. M. Bhanage, M. Shirai, M. Arai, *J. Mol. Catal. A: Chem.* **1999**, *145*, 69.
- [37] M. T. Reetz, E. Westermann, *Angew. Chem. Int. Ed.* **2000**, *39*, 165.
- [38] M. B. Thathagar, J. Beckers, G. Rothenberg, *Adv. Synth. Catal.* **2003**, *345*, 979.
- [39] A. Biffis, M. Zecca, M. Basato, *Eur. J. Inorg. Chem.* **2001**, 1131.
- [40] C. S. Consorti, F. R. Flores, J. Dupont, *J. Am. Chem. Soc.* **2005**, *127*, 12054.
- [41] J. M. Richardson, C. W. Jones, *Adv. Synth. Catal.* **2006**, *348*, 1207.
- [42] M. B. Thathagar, J. E. ten Elshof, G. Rothenberg, *Angew. Chem. Int. Ed.* **2006**, *45*, 2886.
- [43] S. R. Chowdhury, J. E. ten Elshof, N. E. Benes, K. Keizer, *Desalination* **2002**, *144*, 41.
- [44] K. B. Jirage, J. C. Hulteen, C. R. Martin, *Science* **1997**, *278*, 655.
- [45] Permporometry is a characterization technique for determining pore size distributions in membranes. It is based on the controlled blocking of the pores by capillary condensation and the simultaneous measurement of the inert gas diffusion flux through the remaining open pores. When a condensable vapour (e.g., cyclohexane) is introduced at low vapour pressure, first a molecular adsorption layer (the so-called "t-layer") is formed on the inner surface of the pores. The pore size ( $d$ , in nm) is defined by  $d = 2(rK + t)$ , where  $rK$  is the Kelvin radius, and  $t$  is the layer thickness of the t-layer (~0.3 nm). For more details see a) A. Mey-Marom, M.G. Katz, *J. Membrane Sci.* **1986**, *27*, 119; b) M.G. Katz, G. Baruch, *Desalination* **1986**, *58*, 199.
- [46] N. Benes, A. Nijmeijer, H. Verweij, in *Recent Advances in Gas Separation by Microporous Ceramic Membranes* (Ed.: N. K. Kanellopoulos), Elsevier, Amsterdam, **2000**.
- [47] Y. B. Liu, C. Khemtong, J. Hu, *Chem. Comm.* **2004**, 398.
- [48] J. Hu, Y. B. Liu, *Langmuir* **2005**, *21*, 2121.
- [49] I. I. Moiseev, *J. Organomet. Chem.* **1995**, *488*, 183.
- [50] A. V. Gaikwad, G. Rothenberg, *Phys. Chem. Chem. Phys.* **2006**, *8*, 3669.
- [51] M. B. Thathagar, P. J. Kooyman, R. Boerleider, E. Jansen, C. J. Elsevier, G. Rothenberg, *Adv. Synth. Catal.* **2005**, *347*, 1965.
- [52] B. B. Crociani, S. Antonaroli, L. Canovese, P. Uguagliati, F. Visentin, *Eur. J. Inorg. Chem.* **2004**, 732.