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Electroreductive Palladium-Catalysed Ullmann Reactions in Ionic Liquids: Scope and Mechanism

Laura Durán Pachón,[a] Cornelis J. Elsevier,[a] and Gadi Rothenberg[a,*]

[a] van 't Hoff Institute of Molecular Sciences, University of Amsterdam, Nieuwe Achtergracht 166, 1018 WV Amsterdam, The Netherlands
Fax: (+31)-20-525-5604; e-mail: gadi@science.uva.nl

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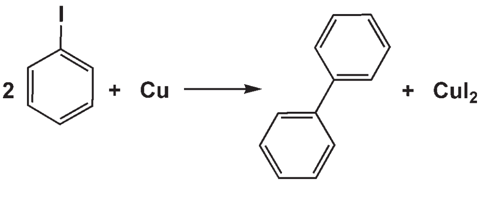
Abstract: A room-temperature catalytic alternative to the Ullmann reaction is presented, based on electroreductive homocoupling of haloarenes catalysed by palladium nanoparticles. The particles are generated *in situ* in an electrochemical cell, and electrons are used to close the catalytic cycle and provide the motivating force for the reaction. This system gives good yields using iodo- and bromoarenes, and requires only electric current and water as reagents. Using an ionic liquid solvent combines the advantages of excellent conductivity and cluster stabilising. The solvent is reusable at least five times. Kinetic experiments at different electrode potentials show that the two-electron oxidation of water closes the catalytic cycle by regenerating the Pd(0). A mechanism involving radical anion formation is proposed. The advantages and limitations of this new system for carbon-carbon homocoupling and cross-coupling are discussed.

Keywords: biaryls; C–C coupling; electrochemistry; green chemistry; heterogeneous catalysis; homogeneous catalysis; nanoparticles

Introduction

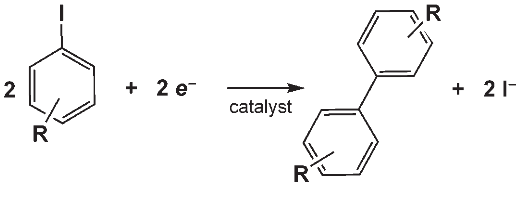
Symmetrical biaryls are important intermediates for synthesising agrochemicals, pharmaceuticals and natural products.[1] One of the simplest protocols to make them is the Ullmann reaction,[2] the thermal homocoupling of aryl iodides in the presence of copper metal. This reaction, although over a century old, is still used today despite two main disadvantages: First, it uses stoichiometric copper, generating stoichiometric amounts of CuI_2 waste [Eq. (1)]. Second, it only works with aryl iodides. This is a problem because chemicals react by their molarity, but are quantified by their mass, and aryl iodides are both expensive and wasteful in this respect.[3]



(1)

In the past five years, we have shown that heterogeneous Pd/C catalyses Ullmann-type reactions of aryl iodides, bromides, and chlorides. Two reaction pathways are possible: Reductive coupling, where Pd^{2+} is generated and reduced back to Pd(0) using an external reducing agent, and oxidative coupling, which starts with Pd^{2+} and needs an oxidising agent. Various reagents can be used for closing the reductive coupling cycle, including HCO_2^-,[4] H_2 gas,[5] Zn/H_2O,[6] and alcohols.[7] The two pathways can even be joined, giving a tandem system that converges on one product.[8] All of these examples, however, require an additional chemical reagent.

Using electrochemistry is an interesting alternative, because in principle the reductive coupling requires only two electrons for closing the catalytic cycle. Ullmann-type reactions using a combination of electrochemistry and Ni(0), Pd(0) or Co(0) complexes as well as sacrificial Mg anodes have been reported.[9,10] In this paper, we present a different approach that combines electrochemical reduction and palladium nanoparticle catalysts in an ionic liquid solvent[11] [Eq. (2)]. The catalytic cycle is closed by electrochemical regeneration of the Pd(0) species.



(2)

Results and Discussion

Palladium Cluster-Catalysed Electrosynthesis of Biphenyl

The initial experiments were run with iodobenzene. In a typical reaction, PhI was stirred in [octylmethylimidazolium]$^+$[BF$_4$]$^-$ in a specially constructed electrochemical cell (Figure 1, *left*) containing a Pd anode and a Pt cathode. Using an ionic liquid as solvent[12] has two main advantages: First, it is a good conductor of electricity; second, it can stabilise metal nanoparticles *via* an ion bilayer mechanism, avoiding additional electrolytes or stabilisers. This type of 'ligand-free' catalysis has gained considerable importance, as it avoids using expensive ligands and allows catalyst recycling.[13,14]

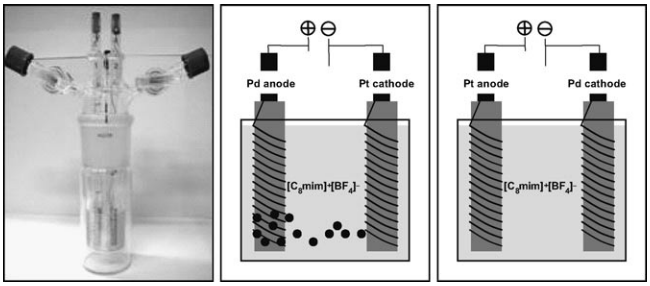


Figure 1. Photo of the two-electrode cell (*left*) and cartoons showing the generation of Pd clusters using a Pd anode and a Pt cathode (*middle*) and the reverse configuration (*right*).

The solution was kept at 25 °C under a constant current intensity of 10 mA (1.6 V) and the reaction progress was monitored by gas chromatography (GC). After 20 min, the reaction mixture turned from a light yellow solution to a dark brown suspension. However, no conversion was observed by GC analysis at this stage. The colour change reflects the anodic oxidation of Pd(0) to Pd^{2+} ions [Eq. (3)]. These are in turn re-

$$\mathrm{Pd(0)} \rightarrow \mathrm{Pd^{2+}} + 2\,e^- \quad E^0 = -0.83\ \mathrm{V} \tag{3}$$

duced to adatoms at the Pt cathode, and finally form stabilised Pd(0) nanoparticles (Figure 1, *middle*).[15] After 8 h, the PhI was totally consumed, giving 80 % biphenyl and 20 % benzene. Weighing the electrodes before and after the reaction showed a difference of ~2.5 mg in the Pd anode, equivalent to 0.1 mol % relative to the initial amount of PhI. This corresponds to a minimum TON of 1000 (assuming that all the 'missing' Pd participates in the catalysis).

To investigate the role of palladium nanoparticles in this system, we switched the current between the two electrodes, so that now the Pd electrode was the cathode and the Pt electrode was the anode (Figure 1, *right*). The rationale behind this experiment was that, in theory, the catalysis could occur on the cathode surface (Figure 2).[4] Direct electron transfer from a Pd(0) atom on the cathode surface to PhI would give a [PhI]$^{-\cdot}$ radical anion, that would then dissociate to Ph$^\cdot$ and I$^-$.[16] The constant supply of electrons to the cathode would ensure the electron transfer (Figure 2). However, we did not observe any reaction in this case, and no Pd nanoparticles formed. Thus, we conclude that, in our system, Pd nanoparticles are necessary for catalysing the homocoupling of aryl halides.

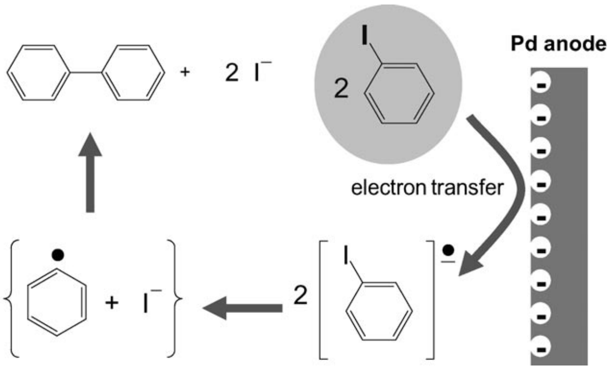
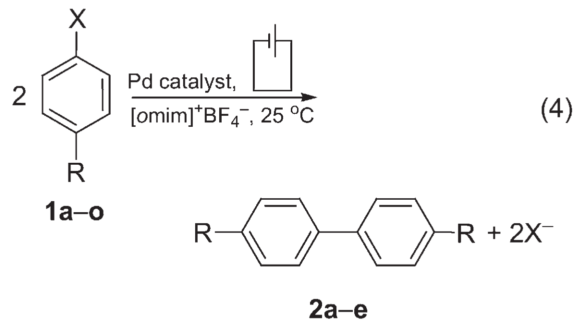


Figure 2. Testing the direct electron-transfer hypothesis, where the PhI radical anion forms directly at the Pd cathode (this experiment was done using the reverse configuration, *cf.* Figure 1, *right*).

To examine the scope of this catalytic system, we tested a variety of *p*-substituted haloarenes [Eq. (4) and Table 1]. Aryl iodides gave good yields (Table 1, entries 1–3) with the exception of the electron-donating iodoaniline. Aryl bromides were also active, but surprisingly less conversion was observed for the electron-withdrawing bromobenzotrifluoride. The corresponding chloride substrates showed little or no activity. The ionic liquid [*o*mim]$^+$[BF$_4$]$^-$ was recycled after the reaction and re-used as solvent five times without change in activity (see Experimental Section for details).

Mechanistic Studies

Palladium-catalysed systems have been described as an alternative to the stoichiometric Ullmann protocol with copper. The reaction mechanism, however, is still unclear. One proposal involves the formation of a radical anion through a single electron transfer (SET) process that give a [PhX]$^{-\cdot}$ radical anion that then dissociates, forming a Ph$^\cdot$ radical and ultimately the biaryl product.[4,17] To understand the mechanism in our system, we must first clarify what closes the cata-



(4)

1a–o

2a–e

1a R = H, X = I
1b R = NO_2, X = I
1c R = CH_3, X = I
1d R = NH_2, X = I
1e R = H, X = Br
1f R = NO_2, X = Br
1g R = CH_3, X = Br
1h R = OCH_3, X = Br
1i R =CN, X = Br
1j R = CF_3, X = Br
1k R = OH, X = Br
1m R = NO_2, X = Cl
1n R = CH_3, X = Cl
1o R = H, X = Cl

2a R = H
2b R = NO_2
2c R = CH_3
2d R = NH_2
2e R = OCH_3
2f R = CN
2g R = CF_3
2h R = OH

lytic cycle and what role do the Pd clusters play in this reaction.

First, we monitored the kinetics of the model reaction for PhI coupling (Figure 3). An induction period of almost 3 h was observed.[18–20] This induction period supports the involvement of palladium clusters in the cycle, because if the Pd(0) atoms or adatoms alone were responsible for the catalysis, there would not be such a long induction period.

After 3 h, the reaction rate increased from $k_1 = 0.0542\ \text{min}^{-1}$ ($R^2 = 0.979$) to $k_2 = 0.383\ \text{min}^{-1}$ ($R^2 = 0.999$, both R^2 values pertain to six observations in duplicate experiments). We think this is due to the "optimal particle size" formation during the induction period, as proposed by Finke and co-workers in the case of hydrogenation.[20] The unusual kinetic profile for such reactions, where an induction period was also found, was interpreted by Schmidt and Smirnov using the concept of a "cluster magic number".[20,21] We used transmission electron microscopy (TEM) to characterise the particle size at the end of the induction period. Spherical well-dispersed particles were observed (Figure 4, *left*) with a size distribution of 2.5 ± 0.5 nm. This corresponds to a 'magic number' of ~300 atoms.

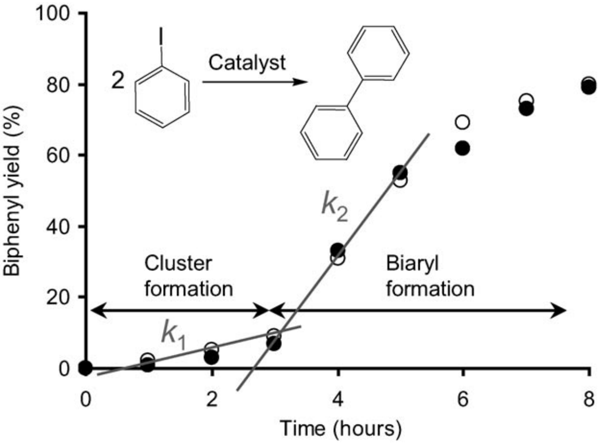


Figure 3. Time-resolved reaction profiles for the electroreductive Pd-catalysed coupling of PhI. Reaction conditions are as in Table 1. The '○' and '●' symbols represent duplicate experiments.

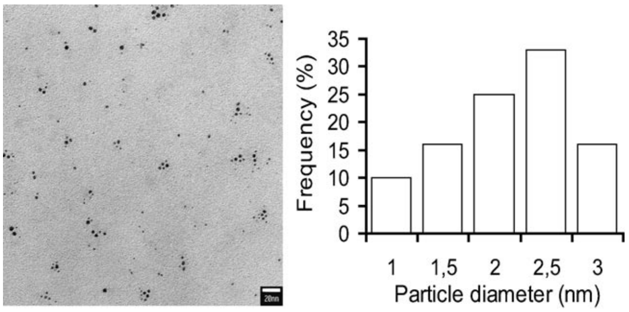


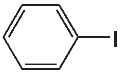
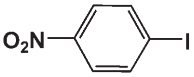
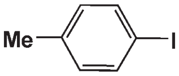
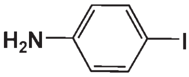
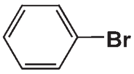
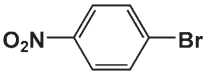
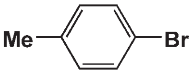
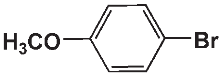
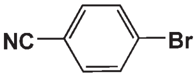
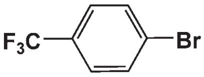
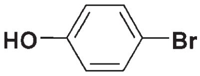
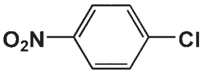
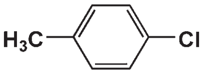
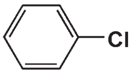
Figure 4. Transmission electron micrograph (*left*) and Pd cluster size distribution (*right*, based on 600 particles counted).

The TOF for these 2 h was $230\ \text{h}^{-1}$, more than double the average TOF during the entire reaction ($100\ \text{h}^{-1}$). This also fits well with the 'active cluster' concept. Another interesting point is the reaction order for this period. We fitted the kinetic data and the best R^2 value was obtained for a first-order reaction ($k_2 = 0.383\ \text{min}^{-1}$, $R^2 = 0.999$; *cf.* with $R^2 = 0.977$ for second-order). This agrees with a first-order rate-determining step, e.g., the dissociation of the $[PhX]^{-\cdot}$ radical anion.

An important mechanistic question is: "what closes the catalytic cycle?" We think that it is oxidation of water into dioxygen [Eq. (5)], recovering the Pd(0) catalyst and neutralising the halide anions in the media. A similar reaction was observed by Raynal et al. in their elegant Ni complex-catalysed electrosyn-

$$2\,H_2O \longrightarrow O_2 + 4H^+ + 4\,e^- \qquad E^0 = -1.23\ \text{V} \tag{5}$$

Table 1. Pd-catalysed electroreductive homocoupling of various haloarenes.[a]

Entry	Aryl halide	Conversion [%][b]	Yield [%][b]	TON[c]	Time [h]
1		99	80 (55)	800	8
2		99	82	820	8
3		83	76	760	9
4		56	35	350	9
5		99	75	750	14
6		74	61	610	20
7		83	59 (38)	590	24
8		80	65	650	24
9		78	61	610	24
10		20	14	140	24
11		5	4	40	24
12		5	3	30	24
13		<1	-	-	-
14		<1	-	-	-

[a] *Reaction conditions:* 20 mmol aryl halide, 50 mL [*o*mim]$^+$[BF$_4$]$^-$, 25 °C.

[b] Based on GC analysis, corrected for the presence of an internal standard. The numbers in parentheses represent isolated yields.

[c] Minimum TON based on the difference in weight in the Pd anode before and after the reaction. This electrode weight difference was independent from the reaction time.

thesis of biaryls in water.[22] Ionic liquids are notoriously hygroscopic, and a small water impurity would suffice for closing the cycle.[23] To test this hypothesis, we ran control experiments in the presence of one molar equivalent of water. The reaction was indeed faster (complete conversion after 6 h, *cf.* with 8 h for the 'dry' system). However, no difference in reactivity was found when more equivalents of water were added.

To obtain further evidence for the water oxidation, we performed a simple experiment varying the potential during the reaction (Figure 5). For the same model reaction, the applied potential (1.60 V) was decreased after a given time to below the potential necessary for water oxidation (1.23 V). Again, we observed an induction period of 3 h. Subsequently, the reaction rate increased, reaching ~30% conversion in 1 h. As expected, the same *k* value was found as before at this point ($k_3 = 0.383\ \text{min}^{-1}$, $R^2 = 0.999$ for four observations in duplicate experiments). After 4 h, the potential was decreased to 1.00 V for 3 h. GC analysis showed that almost no reaction occurred. After 7 h, we increased the potential back to 1.60 V and the reaction re-started immediately, reaching the

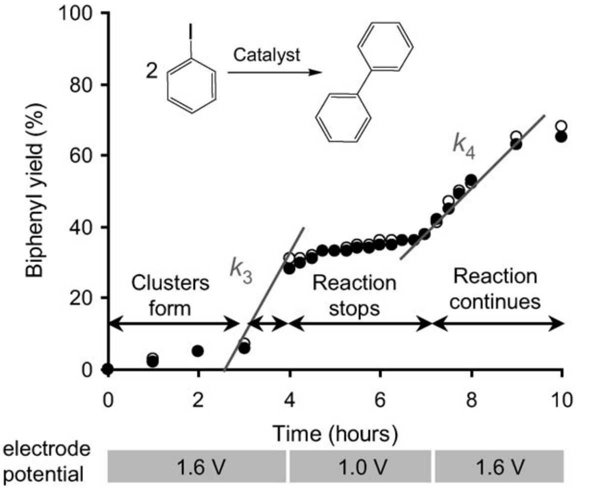


Figure 5. Time-resolved reaction profiles observed for the coupling of PhI to biphenyl using palladium clusters catalyst. Reaction conditions are as in Table 1. The '○' and '●' symbols represent duplicate experiments.

maximum conversion after ~10 h ($k_4 = 8.25 \times 10^{-3}$ min^{-1}, $R^2 = 0.920$ for 12 observations in duplicate experiments). This experiment shows that water oxidation indeed closes the cycle. Furthermore, the reaction can be controlled by simple variation of the potential.

From these studies we conclude that two processes take place in this system. First, the *in situ* formation of the palladium nanoparticles. Second, the Pd-catalysed electroreductive homocoupling of biaryls with a first-order rate-determining step. Based on this we propose a catalytic cycle (Figure 6) wherein a SET occurs from a Pd cluster to an ArX molecule, forming a $[ArX]^{-\cdot}$ radical anion and a positively charged Pd^+ cluster. In case of a single Pd atom, this would be unstable, but the charge on the cluster would be stabilised by the electron cloud of the neighbouring Pd(0) atoms. First-order dissociation of $[ArX]^{-\cdot}$ to $Ar^{\cdot}$ and X^- followed by coupling of two aryl radicals would give the biaryl product. Simultaneously, oxidation of water to dioxygen and $2H^+$ regenerates the Pd(0) clusters and closes the catalytic cycle.

Conclusions

We show that palladium nanoparticles generated *in situ* catalyse efficiently Ullmann-type reactions. To the best of our knowledge, this is the first time this reaction has been performed using electroreductive palladium catalysis. Room-temperature ionic liquids are good solvents for preparing and stabilising palladium nanoparticles. The kinetic data support a cycle involving the formation of a phenyl radical anion that coordinates on the surface of the palladium nanoparticles. The attractiveness of this system lies in the fact that only electrons and water are necessary for closing the catalytic cycle. However, any practical large-scale application would have to include recovery of the 'lost' palladium catalyst. Further investigations of this interesting system will be the subject of future research in our laboratory.

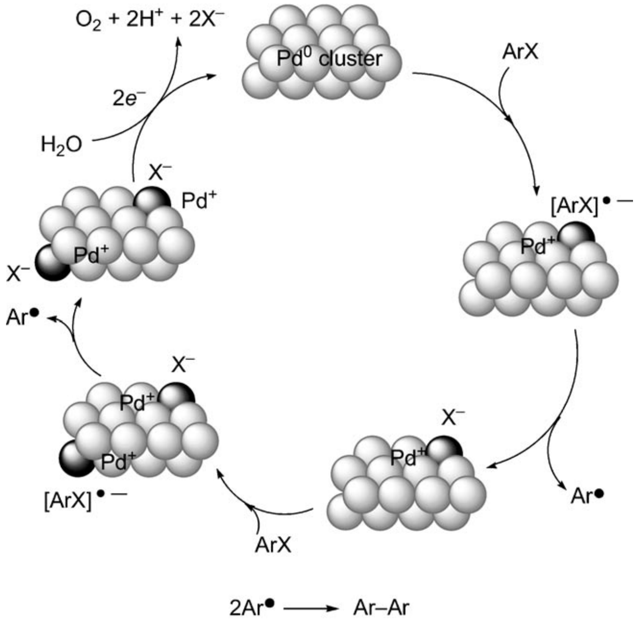


Figure 6. Proposed catalytic cycle for the electroreductive palladium-catalysed homocoupling of aryl halides. The dark grey spheres represent Pd^+ ions. This cycle shows for clarity two single electron transfers from the same cluster, but in principle these processes could also occur on different clusters.

Experimental Section

Materials and Instrumentation

^1H NMR spectra were recorded on a Varian Mercury vx300 instrument at 25 °C. GC analysis was performed on an Interscience GC-8000 gas chromatograph with a 100% dimethylpolysiloxane capillary column (DB-1, 30 m × 0.325 mm). GC conditions (pentadecane internal standard): isotherm at 105 °C (2 min); ramp at 30 °C min^{-1} to 280 °C; isotherm at 280 °C (5 min). Electrochemical experiments were done using a special home-made cell coupled to a dual current supply with a maximum output of 10 V/40 mA. The electrode surface areas were 1.5 cm^2 for the Pd electrode (wire, 99.9%) and 3.0 cm^2 for the Pt electrode (wire, 99.9%), respectively. A detailed technical description of this system has been published elsewhere.[24] The ionic liquid $[o\text{mim}]^+$ $[BF_4]^-$ was prepared following a published procedure and dried prior to use.[25] All other chemicals were purchased from commercial sources (>98% pure). The ionic liquid solvent was recycled following a published procedure.[26]

Procedure for Pd-Catalysed Electroreductive Ullmann Coupling

Example 1 – Biphenyl (2a) from iodobenzene (1a): The electrochemical cell was charged with PhI (4.09 g, 20.0 mmol) and 50 mL $[o\text{mim}]^+[BF_4]^-$. After stirring for 5 min, a constant current (10 mA, 1.6 V) was applied and the mixture was further stirred for 8 h at 25 °C. Reaction progress was monitored by GC. After 8 h, the product was extracted with ether (3 × 50 mL). The ether phases were combined and evaporated under vacuum to give the product as colourless crystalline platelets; yield: 0.81 g (55 mol% based on PhI); mp 71–73 °C (lit.,[27] 69–72 °C). The solvent was recycled by washing with aqueous $NaBF_4$. ^1H NMR (Me_4Si): $\delta = 7.36–7.42$ (m, 2H), 7.45–7.51 (m, 4H), 7.62–7.68 (m, 4H). Good agreement was found with the literature values.[14]

Example 2 – 4,4′-Dimethylbiphenyl (2c) from 1-bromo-4-methylbenzene (1g): The electrochemical cell was charged with $CH_3C_6H_4Br$ (3.50 gr, 20.0 mmol) and 50 mL $[o\text{mim}]^+[BF_4]^-$. The reaction was performed as above to give the product as light yellow crystalline needles; yield: 0.71 g (38 mol% based on $CH_3C_6H_4Br$); mp 118–121 °C (lit.,[28] 119–121 °C). The solvent was recycled by washing with aqueous $NaBF_4$. ^1H NMR (Me_4Si): $\delta = 2{,}51$ (m, 6H), 7.41–7.49 (m, 2H), 7.53–7.57 (m, 4H), 7.60–7.66 (m, 4H). Good agreement was found with the literature values.[28]

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