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# Palladium on Ionic Liquid Derived Nanofibrillated Mesoporous Carbon: A Recyclable Catalyst for the Ullmann Homocoupling Reactions of Aryl Halides in Water

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Palladium nanoparticles supported on nanofibrillated mesoporous carbon (Pd@IFMC) were found to be highly active in heterogeneous catalysis for the Ullmann homocoupling of a broad range of aryl chlorides, bromides and iodides in aqueous medium without the need to any chemical co-reducing agents. The catalysts could be recovered and reused several times without significant loss of activity.

The aryl-aryl coupling reaction has become arguably one of the most important synthetic transformations for constructing biaryl units, which constitute a wide range of pharmaceuticals, natural products, and conducting polymers.<sup>[1]</sup> Of the aryl-aryl bond forming reactions, the Ullmann homocoupling of aryl halides has been widely used for the preparation of symmetrical biaryls over the past century.<sup>[2]</sup> However, this reaction has typically been performed at very high reaction temperatures (over 200 °C) with stoichiometric copper, which renders these methods impractical in the synthesis of biaryls bearing thermosensitive functional groups. Although considerable improvements have been made in recent years with varied Pd, Cu, and Ni-based catalysts,<sup>[1a,2b,3]</sup> these are mostly homogeneous procedures and require an excess of co-reductant, thereby suffering from limited utility in practical processes because of challenges associated with their separation, recovery, and product contamination. As a result, the use of heterogeneous catalysis is often favored for many chemical reactions to minimize the problems associated with homogeneous systems and improve the economic and environmental features of the processes. Despite these premises, very few heterogeneous and recyclable catalyst systems have been explored for the Ullmann homocoupling of aryl halides<sup>[4–8]</sup> and most of them are applicable only to the coupling of aryl iodides and bromides. Moreover, to the best of our knowledge, there have been no reports of Ullmann homocoupling of extremely challenging heteroaryl substrates by using heterogeneous palladium catalysts under

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mild reaction conditions in aqueous media. From practical and sustainable standpoints, the use of high performance recoverable catalysts, which can be applied in low concentrations for the activation of aryl chlorides and heteroaryl halides is preferable. Therefore, the quest for alternative heterogeneous catalysts for efficient Ullmann homocoupling of aryl and heteroaryl halides in water as the most environmentally benign solvent remains a great challenge. We have recently shown that a novel ionic liquid derived nanofibrillated mesoporous carbon (IFMC) displays excellent electrochemical<sup>[9]</sup> and chemical properties and can be used as a support for the activation and stabilization of Pd nanoclusters (Pd@IFMC) in the aerobic oxidation of a wide range of alcohols in water at low temperature.<sup>[10]</sup> Based on X-ray photoelectron spectroscopy (XPS) and electron tomography analyses, it was also evident that the high catalytic performance and stability of Pd@IFMC owed most likely to the presence of nitrogen functionalities on the surface of pristine IFMC and also the unique fibrous structure of the materials (Figure 1, inset), which not only resulted in a good distribution of small Pd nanoclusters but also suppressed their dissolution and agglomeration.<sup>[10]</sup>



**Figure 1.** TEM micrograph of Pd@IFMC (scale bar = 100 nm). A good distribution of Pd nanoparticles can be clearly observed. Inset: Electron tomogram accompanied with a 3D-reconstructed tomogram of IFMC.

In addition, the catalyst exhibited much improved catalytic performance in aqueous solution compared to Pd@CMK-3 and the commercial Pd@C catalyst in the aerobic oxidation of alcohols. Developing on this, we herein demonstrate that the synergism between the nitrogen functionalities and supported Pd nanoclusters in Pd@IFMC with appropriate palladium content

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Figure 2. a) TEM micrograph of a single nanofiber of Pd@IFMC, b) 3D TEM reconstruction of a cross-section of Pd@IFMC to show exact Pd NPs distributions, and c) 3D TEM reconstruction of Pd@IFMC.

(Figures 1 and 2) can be utilized as an efficient and recyclable catalyst for the Ullmann homocoupling of a variety of aryl halides without need for a co-reducing agent.

IFMC was synthesized through a two-stage carbonization of 1-methyl-3-phenethyl-1H-imidazolium hydrogen sulfate (MPIHS) in the presence of SBA-15 as hard template, following our previously reported procedure.<sup>[10, 11]</sup> The supported Pd catalyst (Pd@IFMC) was then prepared by simple impregnation of well-dispersed IFMC with Pd(OAc)<sub>2</sub> as the Pd precursor in THF, followed by treatment with a solution of hydrazine hydrate. The process of preparing Pd@IFMC was monitored by N<sub>2</sub> adsorption-desorption XPS and TEM analysis. N<sub>2</sub> sorption analysis showed that the isotherm shape of the pristine IFMC was preserved after modification, evidencing that the supported Pd nanoparticles (NPs) did not block or alter the mesopore structure. However, as expected, the pore diameter, surface area, and pore volume of Pd@IFMC decreased slightly, indicating that Pd NPs were incorporated into the interior nanospaces of the pristine IFMC. The (high-resolution) TEM, electron tomography, and 3D-reconstructed images of the materials revealed an almost monomodal distribution of Pd NPs, with particle sizes typically of 4-5 nm (Figures 1 and 2, and S5 Supporting Information).

As shown in Figure 2a and c, the Pd NPs in Pd@IFMC are supported not only on the external surface of the carbon materials, they are also well-distributed inside the mesopores. Although a relatively high Pd concentration of 2.5% was used, no evidence of Pd NPs agglomeration was observed. This excellent Pd NPs distribution is believed to be related to the high porosity and surface area as well as the fibrillar structure of the support. Pd XPS of the catalyst revealed a doublet peak corresponding to Pd  $3d_{5/2}$  and Pd  $3d_{3/2}$  at  $335.2\pm0.2$  and





Figure 3. XPS of Pd@IFMC in the Pd region.

 $340.3\pm0.2~eV$  respectively, which is attributed to Pd in the metallic (Pd^0) state (Figure 3 and S5, Supporting Information).

On the other hand, the high-resolution N1s scan indicated the presence of both pyrrolic ( $401.0 \pm 0.2 \text{ eV}$ ) and pyridinic ( $399.2 \pm 0.2 \text{ eV}$ ) nitrogen in the materials (Figure S6, Supporting Information).<sup>[12]</sup> First, we began our investigation on the Ullmann coupling reaction of 4-methoxyl iodobenzene by using Pd@IFMC (0.1 mmol palladium on 1 g of IFMC) in the presence of Et<sub>3</sub>N (3 equiv.) in water at 80°C. Under these conditions, we found that the coupling reaction proceeded well, affording the promising moderate yields of 63% of the corresponding biaryl with a high selectivity of >99% (Table 1, entry 1). This result directed our attention towards applying the interesting physicochemical properties of IFMC and well-distributed Pd NPs in its pore structure to enhance the Ullmann coupling reaction of varied aryl halides, without the need for co-reductant through

Table 1. Optimization of the Ullmann reaction.								
MeO								
Entry	Catalyst	Base	<i>t</i> [h]	Yield [%]				
1	Pd@IFMC	Et₃N	18	63				
2	Pd@IFMC	K <sub>2</sub> CO <sub>3</sub>	18	75				
3	Pd@IFMC	Et <sub>3</sub> N:K <sub>2</sub> CO <sub>3</sub>	18	90				
4	Pd@IFMC	NaOAc	18	83				
5	Pd@IFMC	Cs <sub>2</sub> CO <sub>3</sub>	18	99				
6	Pd@IFMC	KOH	18	52				
7	Pd@IFMC	Cs <sub>2</sub> CO <sub>3</sub>	18	70 <sup>[a]</sup>				
8	Pd@IFMC	Cs <sub>2</sub> CO <sub>3</sub>	18	89 <sup>[b]</sup>				
9	Pd/CMK-3	Cs <sub>2</sub> CO <sub>3</sub>	24	37 <sup>[c]</sup>				
10	Pd/C	Cs <sub>2</sub> CO <sub>3</sub>	24	38 <sup>[c]</sup>				
11	Pd@IFMC	-	18	n.d.				
12	IFMC	Cs <sub>2</sub> CO <sub>3</sub>	24	n.d.				
13	CMK-3	Cs <sub>2</sub> CO <sub>3</sub>	24	n.d.				
14	Pd@IFMC	Cs <sub>2</sub> CO <sub>3</sub>	18	25 <sup>[d]</sup>				
[a] 0.2 mol% catalyst. [b] $T = 70$ °C. [c] Considerable amounts ( $\approx 10-15$ %) of deiodination byproduct (anisole) were formed. [d] Under oxygen atmosphere.								

a cooperative pathway. Various bases such as K<sub>2</sub>CO<sub>3</sub>, K<sub>2</sub>CO<sub>3</sub>/ Et<sub>3</sub>N, NaOAc, Cs<sub>2</sub>CO<sub>3</sub>, and KOH, were also screened for their effect on the reaction. The best results in term of biaryl yields and product selectivity were obtained in the presence of Cs<sub>2</sub>CO<sub>3</sub> at 80 °C in water (entries 2–6). Furthermore, well-known Pd@CMK-3 and commercial Pd/C, a widely employed catalyst in C-C coupling reactions, were also tested under the optimized reaction conditions (entry 5) for comparative purposes. The observed conversions of 4-methoxy iodobenzene in both cases were remarkably inferior, with considerable formation of deiodination byproduct (>10%) (entries 9 and 10). Notably, base-free reactions and those using either the pristine IFMC or CMK-3 gave no conversion in the present system under the same reaction conditions (entries 11-13). These data confirmed that the high catalytic performance of Pd@IFMC (regarding both selectivity and activity) most likely originated from the synergism between the chemical functionalities on the IFMC and Pd NPs, which highlighted the decisive role of both metal and IFMC in catalyzing Ullmann coupling reaction efficiently. To gain better insight into the activity of the present catalyst system in the Ullmann coupling reaction, we then examined the catalytic properties of Pd@IFMC in an O2-saturated reaction system. Interestingly, the coupling reaction of 4-methoxy iodobenzene declined substantially under otherwise identical reaction conditions, as compared to the same reaction under an inert (Ar) atmosphere (entries 14 vs. 5).

To illustrate the general applicability of Pd@IFMC, the protocol was extended to the Ullmann coupling of a series of substituted bromoarenes and chloroarenes. The results of this investigation are summarized in Table 2. The protocol was applicable to the homocoupling of various types of substituted bromo- and chloroarenes bearing either electron-donating or electron-withdrawing groups, affording the corresponding biaryl units in excellent yields and selectivities (Table 2, entries 2-12). The coupling reactions of chloroarenes with an electron-withdrawing group are often accompanied with the production of byproduct arising from hydrodechlorination.<sup>[13]</sup> However, it was proved that Pd@IFMC exhibited excellent catalytic activity and selectivity for the Ullmann coupling of these substrates and no hydrodechlorination products were observed under the investigated conditions (Table 2, entries 10 and 11). In addition, to the best of our knowledge, there has been only one example of employing homogeneous Pd NPs in the Ullmann coupling reaction of heteroaryl bromides in the presence of stoichiometric amounts of co-reductant (propionaldehyde) and excess of tetrabutylammonium acetate.<sup>[14]</sup> Notably, by employing Pd@IFMC, 2-bromothiophene and 3-bromopyridine underwent the Ullmann coupling with high selectivities, although somewhat lower yields of the corresponding biaryls were obtained by using these extremely challenging substrates (Table 2, entries 13, 14). Therefore, the present catalytic system could be considered as the first example of Ullmann homocoupling of heteroaryl halides in water in the absence of co-reductant.

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The stability, durability, and reusability of the heterogeneous catalyst are important. Therefore, the recycling performance of Pd@IFMC was studied in the Ullmann reaction of 4-iodoanisole in water. Once the reaction was completed in the first run, the catalyst was recovered by simple filtration, followed by washing with excess of EtOAc and dried under vacuum. The recovered catalyst was then reused directly for the next run. As shown in Figure 4, the catalytic activity remained almost con-

Table 2. Ullmann coupling of various aryl halides using Pd@IFMC.									
	$R \xrightarrow{\qquad X \qquad Pd@IFMC (Y mol\%)}_{\begin{tabular}{c} Cs_2CO_3 (3 equiv.) \\ water, 80 \ ^{\circ}C \\ \end{tabular}} R$								
Entry	R	х	Y [mol%]	<i>t</i> [h]	Yield [%] <sup>[a]</sup>				
1	OMe	I	0.3	18	99				
2	Н	Br	0.7	20	96				
3	Et	Br	1	24	97				
4	CN	Br	0.7	15	98				
5	Cl	Br	0.7	24	90				
6	NO <sub>2</sub>	Br	0.7	15	97				
7	MeO	Br	1	24	96				
8	Н	Cl	1.5	24	92				
9	CH₃	Cl	1.5	24	90				
10	NO <sub>2</sub>	Cl	1.5	24	97				
11	CN	Cl	1.5	24	96				
12	MeO	Cl	1.5	24	85				
13	⟨ <sub>s</sub> ∖_ı	Br	1	24	58				
14		Зr	1	24	78				
[a] Isolat	[a] Isolated yields.								

possib



Figure 4. Recyclability of the Ullmann reaction of 4-iodoanisole in water with Pd@IFMC.

stant over 5 reaction cycles in water. After the 5th reaction cycle, the total Pd loading in the recovered Pd@IFMC was 0.08 mmolg<sup>-1</sup>, approximately 80% of the original value in the pristine Pd@IFMC. As the amount of Pd residue in the final product was very low at less than 5 ppb, as measured by inductively coupled plasma atomic emission spectroscopy, the possibility that trace Pd was lost from the catalyst during the

recovery and recycling (e.g., during the filtration and washing stages) could not be completely excluded.

At this point, one critical question arose: how could Pd@IFMC catalyze Ullmann coupling reactions of aryl halides in the absence of a co-reductant? One explanation could be that IFMC acts as both the catalyst support and the electron source (reducing agent), a feature demonstrated previously only for polyaniline nanofiber.<sup>[8]</sup> Another explanation could be the presence of heteroatom dopants in IFMC, particularly as other carbonaceous materials such as CMK-3 and activated carbon did not display similar features.

This hypothesis is confirmed to some extent by the significant suppression of the yield of coupled product by employing a sample of the catalyst with approximately half of the IFMC content with respect to the catalyst used in this study.<sup>[10]</sup> However, it remains unclear which type of functional groups at the surface of IFMC and also which nitrogen-bonding configuration play the key role in the present Ullmann coupling protocol. Work focused on more detailed studies of the exact reaction mechanism of this process to clarify the synergism between IFMC and supported Pd NPs in the Ullmann homocoupling reaction is currently ongoing in our laboratory.

In conclusion, we demonstrated that palladium nanoparticles supported on ionic liquid derived nanofibrillated mesoporous carbon (Pd@IFMC) are highly active in catalyzing the Ullmann homocoupling of a range of aryl chlorides, bromides, and iodides and, in particular, heteroaryl bromides in aqueous medium (water) without need for any chemical and stoichiometric co-reducing agents. The catalysts could be recovered and reused several times without significant loss of activity.

### **Experimental Section**

#### Preparation and analysis of IFMC

IFMC was prepared through the carbonization of MPIHS by using ordered mesoporous silica SBA-15 as a template according to the reported procedure.<sup>[10]</sup> At first, to deposit MPIHS into the surfactant-free SBA-15 channels, a dry acetonitrile solution of the ionic liquid (1 mL of MPIHS in 25 mL of acetonitrile) was added dropwise to a suspension of SBA-15 in acetonitrile. After 24 h of stirring at RT, the solvent was removed under reduced pressure. The resulting powdery material was impregnated with an aqueous solution of sulfuric acid (4 g  $H_2O$ , 0.14 g  $H_2SO_4$ ) and placed at 100 °C in a vacuum-drying oven for 6 h. Consequently, the oven temperature was increased to 160 °C and maintained for 6 h at that temperature to afford a dark brown powder. MPIHS 1 (0.4 mL) was incorporated again into mesoporous silica hosts by the same procedure. After that, the ionic liquid was carbonized at 900 °C for 3 h under a flow of Ar. IFMC was then obtained by dissolving the silica framework in NaOH aqueous solution for 24 h. The resulting carbon material was filtered, washed several times with deionized water and ethanol, and dried under vacuum.

#### Preparation and analysis of Pd@IFMC

Synthesis of the Pd@IFMC was performed by reduction of  $Pd(OAc)_2$  with hydrazine hydrate in absolute THF (Acros Organics). A suspension of IFMC (50 mg) in absolute degassed THF (40 mL) was soni-

cated for 30 min. Pd(OAc)<sub>2</sub> (0.018 mmol) was then dissolved in THF (15 mL) and added to the IFMC suspension. To load Pd NPs onto IFMC, hydrazine hydrate (10  $\mu$ L) was added to the suspension under vigorous stirring. After vigorous stirring at RT for 1 h, one drop of 30% hydrogen peroxide was added. Pd@IFMC was afforded after filtration, washed several times with THF, and dried at 40 °C under vacuum overnight. The total palladium content in Pd@IFMC was estimated to be 0.1 mmolg<sup>-1</sup> through the Pd measurement of an acid-washed (HNO<sub>3</sub>, 65%, 6 mL) solution obtained from a 100 mg sample of the catalysts by inductively coupled plasma atomic emission spectroscopy.

# General procedure for the Ullmann coupling reaction in water

Aryl halides (1 mmol), catalyst (0.3–1.5 mol%),  $Cs_2CO_3$  (3 mmol), and water (3 mL) were placed in a glass flask. The catalytic reaction was performed at 80 °C with vigorous stirring (see Table 2 for reaction times). The reaction was monitored by TLC. After completion of the reaction, the products were separated by organic extraction and were then purified by recrystallization.

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**Keywords:** C–C coupling · carbon · heterogeneous catalyst · mesoporous materials · palladium nanoparticles

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