# N-Heterocyclic Carbene–Pd Polymers as Reusable Precatalysts for Cyanation and Ullmann Homocoupling of Aryl Halides: The Role of Solvent in Product Distribution

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A main-chain N-heterocyclic carbene (NHC) polymer with *N*-dodecyl-substituted groups was found to be a highly efficient precatalyst for cyanation of various aryl halides by using nontoxic cyanic source  $[K_4Fe(CN)_6]$  under relatively mild reaction conditions. Several aryl iodides, bromides, and activated chlorides were successfully converted to their corresponding benzonitrile derivatives without using additives (such as reducing agents or exogenous organic ligands) in good to excellent yields. Our investigations showed that changing the solvent from DMF to polyethylene glycol (PEG-200) resulted in dramatic decline of cyanation product formation to the benefit of the Ullmann homocoupling reaction. The catalyst could be reused four and five times with only slight loss of activity in cyanation and the Ullmann coupling, respectively.

## Introduction

Benzonitrile derivatives are very important building blocks because they can convert to various functional groups such as aldehyde, amides, carboxylic acids, and tetrazoles.<sup>[1]</sup> Moreover, organonitriles are directly present in various pharmaceutical products such as Fadrozole, Azoxystrobin, Letrozole and Citalopram or they participate in the synthesis of vital drugs such as HIV-1 protease inhibitor.<sup>[2]</sup>

On an industrial scale and on a laboratory scale these derivatives are usually synthesized by the Rosenmund–van Braun reaction from aryl halides<sup>[3]</sup> or by the Sandmeyer reaction.<sup>[4]</sup> Ammoxidation of toluene derivatives is another method for the ton-scale preparation of benzonitrile derivatives.<sup>[5]</sup> The major drawbacks of the mentioned methods include the release of stoichiometric amounts of heavy metal salts, employing elevated temperatures, low reactivity of aryl bromides and aryl chlorides, and restriction to nonfunctionalized heterocyclic starting materials.

Transition-metal-catalyzed cyanation is an alternative approach for the synthesis of benzonitrile derivatives. Cu, Ni, and Pd complexes are among the most popular catalysts for promoting this reaction.<sup>[6]</sup> Among them, Pd is definitely more reactive than Cu and tolerates various functional groups. Moreover, Pd is relatively less sensitive in contact with air and humidity and is significantly less toxic than Ni. The first Pd-cata-

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lyzed cyanation was reported in 1973 by Takagi et al. for the cyanation reaction of aryl bromides and iodides.<sup>[7]</sup> Since then, various methods have been reported that employ Pd for the development of the cyanation reaction.<sup>[8]</sup>

However, major concerns still exist for the cyanation reaction and these concerns need to be resolved. One concern is the use of a highly toxic source of cyanide such as NaCN<sup>[9]</sup> and KCN.<sup>[10]</sup> Although the toxicity issue of the cyanating agent could be circumvented to some extent by using Zn(CN)<sub>2</sub>,<sup>[11]</sup> which has a lower toxicity than the traditional sources of cyanide, there are associated economic issues. To address these issues, in 2004, Beller and co-workers introduced potassium hexacyanoferrate(II) [K<sub>4</sub>Fe(CN)<sub>6</sub>] as a nontoxic and inexpensive source of CN<sup>-,<sup>[12, 13]</sup> This reagent is commercially available in ton scale and does not need special precautions for its handling and storage.</sup>

Perhaps, the major drawback of Pd-catalyzed cyanation is the deactivation of the metal catalyst by dissolved cyanide ions in the reaction mixture. Therefore, compared to known coupling reactions (such as Suzuki, Heck, etc.), the catalyst activity and turnover number (TON) for cyanation reactions are often very low<sup>[14]</sup> and the reaction proceeds well in the presence of expensive ligands. In this context, despite the significant achievements in cyanation reactions of aryl, as well as heteroaryl halides, in most cases the employed catalysts are homogeneous and thus suffer from difficult separation from the reaction mixture and nonrecyclability. The lack of successful examples of reusable catalysts and also extensive catalyst deactivation in this reaction is mainly attributed to catalyst poisoning by cyanide ions and formation of inactive  $[Pd(CN)_4]^{2-1}$ and [(CN)<sub>3</sub>PdAr]<sup>2-</sup> species during the reaction.<sup>[15]</sup> Heterogeneous supported palladium catalysts may be an alternative for this reaction. Heterogeneous catalyst systems, which are conveniently recycled from the reaction media and have the potential to be integrated into flow reactors, are more attractive



and hold promise for use in large-scale productions. Therefore, a substantial volume of recent investigations have been directed towards the development of new and efficient cyanation protocols based on heterogeneous Pd catalysts.<sup>[16]</sup>

Although significant improvements have been achieved by using heterogeneous catalysts, the "lazy" kinetics of the cyanation reactions, extensive metal leaching, and limited substrate scope have remained to be major concerns of these methods and should be resolved. We respect the pioneering advances in this area, however, we believe that the development of a novel heterogeneous catalyst system that exhibits improved recyclability and durability and displays appropriated performance towards less-reactive aryl halides are still welcome.

Following the impressive discovery of Bielawski and coworkers on the synthesis of highly stable main-chain N-heterocyclic carbene (NHC)-based organometallic polymers<sup>[17]</sup> (NHC-MCOPs), we have recently prepared a set of self-supported NHC-Pd polymers based on various N-substituted bis(imidazolium) compounds (Scheme 1).<sup>[18]</sup> These materials demonstrated



 $\begin{array}{l} \label{eq:Scheme 1. Schematic procedure for the preparation of the NHC-Pd polymer catalyst: a) HCOOH, 110 °C, 36 h. b) (i) NaH (2.0 equiv.), PhCH_3, 110 °C; (ii) C_{12}H_{25}Br (6.0 equiv.), 25-110 °C, 4 h; (iii) DMF, 110 °C, 6 h; (iv) dioxane, 110 °C, then 75 °C. c) Pd(OAc)_2 in DMSO at 110 °C, 10 h. \end{array}$ 

outstanding catalytic activity in the Suzuki–Miyaura coupling reactions of aryl chlorides in water. In a separate in-depth mechanistic investigation it was also evident that the high catalytic performance of these NHC-Pd-MCOPs could likely be attributed to the in situ generation of an extremely low concentration of Pd nanoparticles within the framework of the polymers, which not only resulted in the generation of a highly active region containing trace amounts of Pd nanoparticles, but also prevented the agglomeration of these Pd nanoclusters.<sup>[18b]</sup>

Herein, we wish to disclose that a main-chain NHC–Pd polymer bearing an *N*-dodecyl substituent is also an efficient and highly recyclable catalyst system for the cyanation of various type of aryl halides with  $[K_4Fe(CN)_6]$  in DMF. Most interestingly, we detected that by changing the reaction solvent from DMF to polyethylene glycol (MW<sub>AV</sub>  $\approx$  200), the selectivity patterns of this reaction were remarkably shifted towards highly efficient formation of Ullmann homocoupling products, even in the

case of highly challenging substrates such as aryl chlorides and heteroaryl bromides.

## **Results and Discussion**

The route for the preparation of NHC polymer **3** is illustrated in Scheme 1 according to our previously reported procedure with slight modifications.<sup>[18b]</sup> The NHC precursors with an Nsubstituted dodecyl group were synthesized from the reaction between 1,2,4,5-tetraaminobenzene with freshly distilled formic acid, followed by the alkylation of the resulting benzobis(imidazole) **1** with 1-bromododecane. The obtained bis(imidazolium) bromides **2** were reacted with stoichiometric amounts of Pd(OAc)<sub>2</sub> in DMSO at 110 °C for 10 h.

Finally, the reaction mixture was cooled to room temperature then added to distilled water. The precipitated polymer was then collected by means of vacuum filtration and dried under vacuum at room temperature. Compounds 1 and 2 were characterized by <sup>1</sup>H NMR and <sup>13</sup>C NMR spectroscopy (see the Experimental Section). Gel permeation chromatography (GPC) showed that the average molecular weight (MW) of organometallic polymer **3** is approximately 85 000 Da (Scheme 1).

The efficiency of **3** was initially investigated for the cyanation of bromobenzene as a model substrate with  $[K_4Fe(CN)_6]$ . The data from the optimization reactions is shown in Table 1. Initially, the effect of the solvent was investigated in the reaction of bromobenzene with 0.6 mol% of catalyst **3**, 2 mmol of

Table 1. Screening of the NHC-Pd polymer (3)-catalyzed cyanation of bromobenzene using $[K_{4}Fe(CN)_{6}]$ .								
Br + [K₄Fe(CN) <sub>6</sub> ] → CN								
Entry	Solvent	Base	<i>t</i> [h]/ <i>T</i> [°C]	Yield [%] <sup>[a,b]</sup>				
1	H <sub>2</sub> O	K <sub>2</sub> CO <sub>3</sub>	12/95	-				
2	$H_2O + 1$ equiv. TBAB	K <sub>2</sub> CO <sub>3</sub>	12/95	-				
3	H <sub>2</sub> O/tbutanol (1:1)	K <sub>2</sub> CO <sub>3</sub>	12/95	15				
4	H <sub>2</sub> O/DMF (1:1)	K <sub>2</sub> CO <sub>3</sub>	12/95	29				
5	H <sub>2</sub> O/DMF (1:1)	K <sub>2</sub> CO <sub>3</sub>	24/95	35				
6	H <sub>2</sub> O/ethanol (1:1)	K <sub>2</sub> CO <sub>3</sub>	12/95	< 5				
7	DMSO	K <sub>2</sub> CO <sub>3</sub>	12/95	-				
8	DMF	K <sub>2</sub> CO <sub>3</sub>	12/95	91				
9	DMF	K <sub>2</sub> CO <sub>3</sub>	12/95	70 <sup>[c]</sup>				
10	DMF	K <sub>2</sub> CO <sub>3</sub>	12/110	86 (14) <sup>[d]</sup>				
11	DMF	K <sub>2</sub> CO <sub>3</sub>	12/RT	-				
12	DMF	K <sub>2</sub> CO <sub>3</sub>	24/60	-				
13	DMF	K <sub>2</sub> CO <sub>3</sub>	25/80	15				
14	DMF	K <sub>2</sub> CO <sub>3</sub>	12/95	26 <sup>[e]</sup>				
15	DMF	Et₃N	12/95	-				
16	DMF	Na <sub>2</sub> CO <sub>3</sub>	12/95	-				
17	DMF	CS <sub>2</sub> CO <sub>3</sub>	12/95	-				
18	DMF	K <sub>2</sub> CO <sub>3</sub>	12/95	15 <sup>[f]</sup>				
19	DMF	K <sub>2</sub> CO <sub>3</sub>	12/95	48 <sup>[g]</sup>				
[a] Reaction conditions: Catalyst (0.6 mol%), bromobenzene (1 mmol),								

 $[K_4Fe(CN)_6]$  (0.7 mmol), base (2 mmol), and solvent (2 mL) under Ar atmosphere unless otherwise stated. [b] Yields refer to GC (gas chromatography) results. [c] 0.5 mmol of  $[K_4Fe(CN)_6]$  was used. [d] 14% of homocoupling byproduct was observed. [e] 1 mmol of  $K_2CO_3$  was used. [f] The amount of catalyst was 0.2 mol%. [g] The amount of catalyst was 0.4 mol%.



 $K_2CO_3$ , and 0.7 equivalents of  $[K_4Fe(CN)_6]$  as the cyanide source at 95 °C. The results indicate that the best yields of benzonitrile were obtained in DMF rather than other organic or aqueous/ organic solvent mixtures (Table 1, entries 1–8).

It has been reported that [K<sub>4</sub>Fe(CN)<sub>6</sub>] is able to transfer all of the six  $\mathsf{CN}^{\scriptscriptstyle-}$  ions during the cyanation reaction.  $^{\scriptscriptstyle[12]}$  However, our investigations showed that the optimum amount of [K<sub>4</sub>Fe(CN)<sub>6</sub>] is 0.7 mmol per one mmol of bromobenzene and reducing this value to 0.5 mmol significantly reduces the yield of benzonitrile to 70% (Table 1, entry 9). Increasing the reaction temperature to 110 °C had a negative effect on the reaction selectivity. Under these conditions, a considerable amount of the competitive Ullmann homocoupling byproduct ( $\approx$  14%) was observed (Table 1, entry 10). Notably, the reaction did not proceed well at lower temperature even after 24 h (Table 1, entries 11-13). To get better insight into the optimal reaction conditions, the impact of various bases, as well as the amount of base, was also studied because these two parameters are known to be crucial in coupling reactions. Our investigations revealed that the highest yield was obtained when the cyanation reaction was carried out using  $K_2CO_3$  as a base (Table 1, entry 8 vs. 15–17). In the presence of  $K_2CO_3$ , a further decrease in the amount of base to 1 mmol significantly decreased the conversion of bromobenzene, giving a disappointing yield  $(\approx 26\%)$  of the cyanation product after 12 h (Table 1, entry 14). In addition, decreasing the catalyst loading to 0.4 and 0.2 mol% afforded the desired product in much lower yields of 48 and 15%, respectively, under otherwise the same reaction conditions (Table 1, entries 18, 19). After the screening of different parameters, the optimized conditions were found to be those in which the [K<sub>4</sub>Fe(CN)<sub>6</sub>] and catalyst loading are 0.7 equivalents and 0.6 mol%, respectively, in DMF (2 mL) at 95 °C (Table 1, entry 8).

With the optimal reaction conditions in hand, the performance and substrate scope of the presented NHC–Pd polymer **3** were investigated with various aryl halides (Table 2). As shown in Table 2, various aryl iodides with electron-withdrawing and electron-donating groups converted to their benzonitrile derivatives with good to excellent yields (Table 2, entries 1–4). For example, the less-reactive 4-iodoanisole converted into 4-methoxybenzonitrile in almost quantitative yield after 10 h (Table 2, entry 4).

The same trends were also observed for substituted aryl bromides with both electron-withdrawing and electron-donating functionalities. Notably, the highly efficient cyanation of 2-bromotoluene, as a model for challenging 2-substituted aryl bromides, afforded 2-cyanotoluene in excellent yield under similar reactions conditions (Table 2, entry 7). Similarly, this catalyst system was amenable to the efficient cyanation of highly deactivated aryl bromides, but a high loading of 0.8 mol% and longer reaction time were required to give excellent yields of the corresponding product (Table 2, entry 10). By comparison with cyanation coupling reactions catalyzed by most of the existing Pd catalysts, which employ highly expensive exogenous phosphine ligands (such as  $tBu_3P$ ), the presented results strongly confirm the high catalytic activity of **3** in the cyanation reaction.

Table 2. Cyanation of aryl halides with $[K_4Fe(CN)_6]$ using NHC-Pd polymer         3 under the optimized reaction conditions.         X         R         +         [K_4Fe(CN)_6]         R							
Entry	R	х	<b>3</b> [mol%]/ <i>t</i> [h]	Yield [%] <sup>[a,b,c]</sup>			
1	4-NO <sub>2</sub>		0.5/3	94 (90)			
2	Н	I	0.5/5	99 (92)			
3	4-CH <sub>3</sub>	I	0.5/8	99			
4	4-OCH <sub>3</sub>	I	0.5/10	99			
5	4-Cl	Br	0.5/10	88			
6	Н	Br	0.6/12	91 (88)			
7	2-CH <sub>3</sub>	Br	0.6/16	91			
8	4-NO <sub>2</sub>	Br	0.5/10	95 (89)			
9	4-Ph	Br	0.5/10	(85)			
10	4-OCH <sub>3</sub>	Br	0.8/15	87			
11	Н	Br	0.6/12	N.R.			
12	4-NO <sub>2</sub>	CI	1/24	61 (58) <sup>[d]</sup>			
13	Н	Cl	1/24	N.R. <sup>[e]</sup>			
[a] Reaction conditions: NHC-Pd polymer <b>3</b> , K <sub>2</sub> CO <sub>3</sub> (2 equiv.), DMF (2 mL)							

at 95 °C [b] Yields refer to GC results. [c] The data in parenthesis refer to isolated yields. [d] 1 equiv. TBAB was added. [e] Reaction conditions: 1 equiv. TBAB at 105 °C.

For the purpose of comparison, a commercially available Pd/ C catalyst (1 wt% Pd) was also tested under the same reaction conditions (Table 2, entry 11) and no cyanation product was obtained using this catalyst in the reaction of bromobenzene with  $[K_4Fe(CN)_6]$  within 24 h. The much higher activity of **3**, as compared to Pd/C and our previously developed IL@SBA-15-Pd<sup>[16]</sup> may be attributed to the presence of the NHC ligand and container-like structure of the NHC–Pd polymer,<sup>[18b]</sup> which ensures appropriate dispersion of highly active (possibly ultrasmall) Pd nanoparticles and facilitates the cyanation reaction.

Encouraged by these results, we then set up experiments to study the performance of **3** in the cyanation of even more challenging aryl chlorides under the described reaction conditions. It was found that 4-nitrobenzonitrile was produced with a good yield of 61% when 4-chloronitrobenzene was heated for 24 h at 95 °C in the presence of **3** (1 mol%) and  $nBu_4N^+Br^-$  (TBAB, 1 equiv.) under otherwise optimized reaction conditions. This yield is superior to that obtained from other existing heterogeneous Pd catalysts (Table 2, entry 12).<sup>[19]</sup> In this regard, the addition of TBAB enhanced the yield significantly, presumably owing to the stabilization effect of the in situ generated Pd nanoparticles.<sup>[18b, 20]</sup> Unfortunately, our attempts to use this method in its present form in the cyanation of chlorobenzene itself were unsuccessful even when higher temperatures or a higher loading of catalyst were applied (Table 2, entry 13).

Despite the high catalytic activity of NHC-Pd polymer **3** for the synthesis of benzonitrile derivatives under relatively mild conditions, our preliminary investigation showed that the cyanation reaction of heteroaryl halides such as bromo- or iodothiophene and pyridine was unsuccessful under the described conditions. Therefore, to find an alternative and more-appropriate reaction media for the cyanation of heteroaryl halides we focused our attempts on performing this reaction in other reactions solvents.



In this regard, polyethylene glycols (PEGs) with a wide range of molecular weight are known to be cheap, biodegradable, safe, and nonvolatile (high boiling) nonionic solvents. PEGs are capable of creating suitable reaction media in several metalcatalyzed C--C as well as C--heteroatom bond-forming reactions.<sup>[21]</sup> These solvents are also able to stabilize metal nanoparticles, demonstrating the strong potential of such solvent systems in establishing highly durable metal nanoparticlesbased catalyst systems. For these reasons, we next decided to study the impact of PEG-200 as a solvent in the cyanation of aryl halides in the presence of 3. To do this, we chose bromobenzene as a model substrate for the cyanation reaction in PEG-200 (2 mL) under otherwise optimal reaction conditions as demonstrated in entry 8 of Table 1, to deduce whether the excellent conversion obtained in DMF could be repeated in PEG-200. Surprisingly, we found that under the new reaction conditions, the yield of benzonitrile dramatically decreased to the benefit of the Ullmann homocoupling reaction of bromobenzene, affording an excellent biphenyl yield of  $\approx$  89% (Scheme 2).



**Scheme 2.** Results of the cyanation reaction of bromobenzene with PEG-200 as solvent.

This surprisingly different behavior between DMF and PEG-200 prompted us to further investigate whether PEG-200 could be employed as solvent system in the Ullmann coupling of various aryl halides by using **3** as catalyst.

With this initial interesting data in hand, we next proceeded to set up appropriate experiments for the Ullmann homocoupling reactions because symmetrical biaryls are also very promising synthetic units in organic transformations.[22] This reaction is generally performed at very high temperature (over 200°C) by using copper as a catalyst.<sup>[23]</sup> Unfortunately, at elevated temperatures, the scope of reaction is strongly limited to thermostable starting materials. However, our preliminary investigations showed that the present reaction can proceed even at 75 °C with high efficiency in the presence of 0.5 mol% of the catalyst. To illustrate the general applicability of NHC-Pd polymer 3, the present protocol was then subsequently extended to the Ullmann coupling of a series of substituted aryl halides. Table 3 summarizes the results of this investigation. The protocol was amenable to the homocoupling of various types of substituted aryl halides (I, Br, CI) as well as sterically hindered substrates.

To extend the application of NHC-Pd polymer **3**, the Ullmann homocoupling reactions of extremely challenging heteroaryl substrates were also investigated under the presented mild re-



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[a] Reaction conditions: NHC–Pd polymer **3** (0.5 mol %),  $K_2CO_3$  (2 equiv.), PEG (2 mL), 12 h at 75 °C. [b] Yields refer to isolated pure products. [c] 20 mol % KI was added at 90 °C for 24 h.



action conditions with PEG as a green reaction media. Based on our findings, various heteroaryl halides, comprising pyridine and thiophene rings, converted to their corresponding Ullmann product with excellent yields under very mild thermal conditions (Table 4).

The exact role of PEG in the process is not clear at this stage. However, a plausible explanation for this phenomenon is the trapping (or scavenging) of  $CN^-$  ions by formation of hydrogen bonds with PEG. In other words, it is most likely that the cyanide ions are entrapped among the solvent molecules. The most dominant reaction under these conditions is the Ullmann homocoupling. A schematic illustration for the scavenging of  $CN^-$  ions in the PEG media and the formation of the reaction core is shown in Scheme 3.

Recycling experiments were performed for both cyanation and homocoupling reactions by using bromobenzene as the substrate under the optimized reaction conditions. For cyanation, after reaction termination the products were extracted with organic solvent and the catalyst/solvent (DMF or PEG) mixture was recharged with starting materials. As shown in



Scheme 3. Proposed model describing the deactivation of  $CN^-$  ions in the PEG media by formation of a hydrogen bond to the solvent in favor of the homocoupling reaction inside the reaction core.

Table 5.         Recycling experiments for Ullmann homocoupling and cyanation           of bromobenzene using NHC-Pd polymer 3 as catalyst.								
Cyanation	Reaction runs GC yield [%]	1st 90	2nd 89	3rd 72	4th 72			
Ullmann homocoupling	Reaction runs Isolated yield [%]	1st 92	2nd 91	3rd 87	4th 84	5th 77		

Table 5, the catalyst could be reused at least in four successive reaction runs with only a slight decrease in the yields of benzonitrile. Table 5 summarizes the results of the recycling experiments for cyanation and the Ullmann homocoupling reaction of bromobenzene.

In the case of the Pd-catalyzed cyanation reaction the catalyst could be deactivated by  $CN^-$  ions and forms inactive  $[Pd(CN)_4]^{2-}$  and  $[(CN)_3PdAr]^{2-}$  species during the reaction.<sup>[15]</sup> In our recycling experiment for the cyanation reaction the first and second reaction runs gave constant yields of benzonitrile. However, for the third and fourth recycling experiment the yield was reduced to 72%. The fact that the yields of both coupling reactions for the reused polymer go down linearly in each step suggests that organometallic polymer **3** is gradually decomposing under the described reaction conditions, thus it is very unlikely that it functions as a truly heterogeneous catalyst.

To investigate whether the real catalytic species are naked Pd nanoparticles or robustly-bound NHC-Pd, an independent mercury poisoning test (Hg/Pd = 400:1) was set up for the coupling reaction of bromobenzene with  $[K_4Fe(CN)_6]$  to give benzonitrile under the otherwise standard reaction conditions. To do this, an excess amount of Hg<sup>0</sup> (Hg/Pd = 400:1) was added to the reaction mixture. It was found that benzonitrile was still

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obtained in 86% yields (determined by GC analysis), which is to some extent lower than the same reaction in the absence of mercury (Table 2, entry 6). Although the mercury poisoning experiment could not solely prove the formation of nanoparticles during the reaction, the weak mercury positive test accompanied with the observed changes in the molecularweight profile of the recovered NHC-Pd polymer 3 after the recycling experiment, as evidenced by GPC of the recovered catalyst, provides reasonable evidence that this polymer could be the source of the active Pd species in the form of either Pd nanoparticles or fragmented NHC-Pd complexes. Although, we were not able to detect the formation of Pd nanoparticles by direct TEM investigation, the above-mentioned observations clearly demonstrate that our NHC-Pd polymer might be indeed a source of a trace amount of (non-observable) Pd nanoparticles, which in turn could actually catalyze the titled reactions. These results are also in agreement with our recent studies of using the same organometallic polymer catalyst systems in the Suzuki-Miyaura coupling reaction.[18b] These features are schematically demonstrated in Scheme 4.





## Conclusions

We have demonstrated that a NHC-Pd polymer 3 bearing an N-dodecyl group is a highly efficient and recoverable precatalyst for the cyanation of aryl halides (I, Br, and CI) with [K<sub>4</sub>Fe(CN)<sub>6</sub>] in DMF under relatively mild conditions. We also found that by changing the reaction solvent from DMF to poly(ethylene glycol) (MW\_{AV}  $\approx$  200), the selectivity patterns of this reaction were remarkably shifted toward highly efficient formation of Ullmann homocoupling products even in the case of highly challenging substrates such as aryl chlorides and heteroaryl bromides. A model highlighting the possible role of PEG in attaining the high degree of selectivity towards the Ullmann coupling reaction was also described. The catalyst exhibited high tolerance to CN<sup>-</sup> ions during the cyanation reaction. The catalyst was successfully recycled and reused for four and five successive runs in cyanation and the Ullmann homocoupling reaction of bromobenzene, respectively, with only slight decrease in activity. Our studies on the recovered catalyst from the cyanation reaction demonstrated that this polymer could be the source of the production of active Pd species in the form of either Pd nanoparticles or fragmented NHC-Pd com-



plexes. Work is underway to expand the application of this catalyst system in other important chemical transformations.

# **Experimental Section**

#### Synthesis of benzo-bis(imidazole) (1)

1,2,4,5-Benzenetetraamine tetrahydrochloride (284 mg, 1.00 mmol) was poured into a round-bottomed flask charged with a magnetic stir bar. Formic acid (88–99%, 15 mL) was added and the flask was fitted with an air-jacketed condenser. The reaction was performed in an oil bath at 100 °C for 36 h. The reaction mixture was then allowed to cool, decanted into ice-cold water (equal volume to formic acid) and neutralized with K<sub>2</sub>CO<sub>3</sub>. Neutralization caused precipitation of the product, which was collected by vacuum filtration, washed with cold water, and dried under vacuum in the presence of P<sub>2</sub>O<sub>5</sub>. The desired product was obtained as a light brown solid. <sup>1</sup>H NMR (250 MHz, [D<sub>6</sub>]DMSO):  $\delta$  = 7.65 (s, 2 H), 8.15 ppm (s, 2 H); <sup>13</sup>C NMR (250 MHz, [D<sub>6</sub>]DMSO):  $\delta$  = 99.7, 135.4, 143.0 ppm.

#### Synthesis of tetradodecyl benzo-bis(imidazolium) bromide (2)

In a well-dried two-necked 100 mL Schlenk flask, bis(imidazole) (475 mg, 3.00 mmol) was added to a solution of NaH (245 mg, 60 wt%, 6.10 mmol) in toluene (15 mL) under an argon atmosphere. The resulting solution was heated to 110 °C for 1 h. After cooling the solution to RT, 1-bromododecane (4.8 mL, 20.00 mmol) was added through a syringe. The suspension was placed in an oil bath at 110°C for 1 h, then dry DMF (10 mL) was added through a syringe and the reaction was maintained at 110  $^\circ$ C for 12 h, then 60°C for 8 h. Upon completion, the suspension was allowed to cool. The concentrated suspension in vacuum was added to 2:1 CH<sub>2</sub>Cl<sub>2</sub>/MeOH. After removal of insoluble NaBr, ethyl acetate was added to the resultant oil until precipitation of the product occurred. The solids were collected by vacuum filtration and dried under vacuum over  $P_2O_5$  to give 2.31 g (77%) of the product as a light pink powder. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>):  $\delta = 10.08$  (s, 2 H), 9.53 (s, 2 H), 4.93 (t, J=6.35 Hz, 8 H), 1.98 (p, 8 H), 1.25-1.35 (m, 80 H), 0.90 ppm (t, J=6.9 Hz, 12 H),  $^{13}$ C NMR (250 MHz, CDCl<sub>3</sub>):  $\delta =$ 14.1, 22.6, 26.5, 29.1, 29.3, 29.4, 29.5, 29.6, 29.6, 31,9, 49.0, 100.7, 129.7, 144.9 ppm.

#### Typical procedure for preparation of NHC-polymer 3

Bis(imidazolium) bromide 2 (1.0 mmol) was dissolved in DMSO (5 mL, ca. 0.2 M) and Pd(OAc)<sub>2</sub> (1.0 equiv., 112 mg), was added in one portion. The solution was placed in a preheated oil bath at 110 °C and stirred in air for 5–10 h. The reaction mixtures typically darkened in color (to orange-brown) as the reaction progressed. The cooled reaction mixture was added to H<sub>2</sub>O. The resulting precipitated polymer was collected by vacuum filtration and dried under vacuum.

#### General procedure for the cyanation reaction using NHCpolymer 3

A mixture of aryl halide (1.0 mmol), finely powdered [K<sub>4</sub>Fe(CN)<sub>6</sub>]·3 H<sub>2</sub>O (0.7 mmol), K<sub>2</sub>CO<sub>3</sub> (2 mmol), and NHC-Pd polymer 3 (0.5-1 mol%) in DMF was stirred vigorously under an argon atmosphere at 95 °C. The reaction progress was monitored by GC analysis. After completion of the reaction the mixture was allowed to cool to RT and then small portion of distilled water was added to the mixture followed by extraction with *n*-hexane or diisopropyl ether. The upper organic phase was separated and washed several times with water dried over  $\mathsf{MgSO}_4$  and then the solvent was evaporated under reduced pressure. Pure products were obtained after recrystallization or purification by column chromatography on silica with *n*-hexane/ethyl acetate as eluent.

#### General procedure for the Ullmann homocoupling reaction using NHC-polymer 3

Aryl or heteroaryl halides (1 mmol), catalyst 3 (0.5 mol%), K<sub>2</sub>CO<sub>3</sub> (2 mmol), and PEG-200 (2 mL) were placed in a glass flask. The reaction was heated at 75 °C with vigorous stirring for 12 h. The reaction progress was monitored by TLC, and after completion of the reaction, the mixture was allowed to cool to RT and then small portion of distilled water was added to the mixture followed by extraction with n-hexane or diisopropyl ether. The upper organic phase was separated and dried over MgSO<sub>4</sub> and the solvent was evaporated under reduced pressure. Pure products were obtained after recrystallization or purification by column chromatography on silica with *n*-hexane/ethyl acetate as eluent.

#### **Recycling experiments**

All recycling experiments were performed on a 5 mmol scale of bromobenzene to facilitate easy recovery of the catalysts. As an example, after the first use of the catalyst 3 in the Ullmann homocoupling of bromobenzene to yield 92% of biphenyl (isolated yield as described above), the catalyst was separated by centrifugation and thoroughly washed with deionized water and EtOH and dried at 40 °C under vacuum. The recovered materials were then successfully used in the same way for five reaction cycles.

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**Keywords:** coupling reactions · cyanation · polyethylene glycol · polymers · Ullmann reaction

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