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# Self-Assembled Poly(imidazole-palladium): Highly Active, Reusable Catalyst at Parts per Million to Parts per Billion Levels

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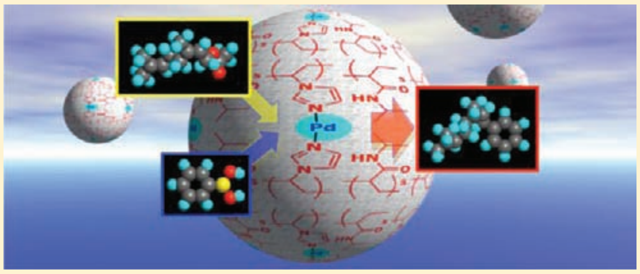
Supporting Information



**ABSTRACT:** Metalloenzymes are essential proteins with vital activity that promote high-efficiency enzymatic reactions. To ensure catalytic activity, stability, and reusability for safe, nontoxic, sustainable chemistry, and green organic synthesis, it is important to develop metalloenzyme-inspired polymer-supported metal catalysts. Here, we present a highly active, reusable, self-assembled catalyst of poly(imidazole-acrylamide) and palladium species inspired by metalloenzymes and apply our convolution methodology to the preparation of polymeric metal catalysts. Thus, a metalloenzyme-inspired polymeric imidazole Pd catalyst (MEPI-Pd) was readily prepared by the coordinative convolution of $(NH_4)_2PdCl_4$ and poly[(*N*-vinylimidazole)-*co*-(*N*-isopropylacrylamide)$_5$] in a methanol–water solution at 80 °C for 30 min. SEM observation revealed that MEPI-Pd has a globular-aggregated, self-assembled structure. TEM observation and XPS and EDX analyses indicated that $PdCl_2$ and Pd(0) nanoparticles were uniformly dispersed in MEPI-Pd. MEPI-Pd was utilized for the allylic arylation/alkenylation/vinylation of allylic esters and carbonates with aryl/alkenylboronic acids, vinylboronic acid esters, and tetraaryl borates. Even 0.8–40 mol ppm Pd of MEPI-Pd efficiently promoted allylic arylation/alkenylation/vinylation in alcohol and/or water with a catalytic turnover number (TON) of 20 000–1 250 000. Furthermore, MEPI-Pd efficiently promoted the Suzuki–Miyaura reaction of a variety of inactivated aryl chlorides as well as aryl bromides and iodides in water with a TON of up to 3 570 000. MEPI-Pd was reused for the allylic arylation and Suzuki–Miyaura reaction of an aryl chloride without loss of catalytic activity.

## INTRODUCTION

Metalloenzymes are supramolecular metal–organic hybrids of polypeptides and metal ions, which are essential proteins with vital activity to promote high-efficiency enzymatic reactions.[1,2] The high catalytic activity of metalloenzymes is attributable to (1) regulation of the molecular orientation between substrates, reactants, and the metalloenzyme; (2) cooperative catalysis of functional groups in the metalloenzyme; and (3) regulation of the reaction field in the metalloenzyme. To go even further and also ensure catalytic activity, stability, and reusability for safe, nontoxic, sustainable chemistry, and green organic synthesis, the development of polymer-supported metal catalysts is of particular interest.[3,4]

Metalloenzymes show the importance of amphipathic imidazole units in themselves. Imidazole units in histidine coordinate to metal species to provide their catalytic site, the supramolecular tertiary structure of proteins, and their Lewis basicity. Imidazole units themselves also play a role in building the quaternary structure of proteins through ionic interaction and hydrogen-bond formation; thus, polymeric imidazole ligands are widely used as the building blocks of artificial metal–organic self-assembled supramolecules for functional materials including catalysts.[5] We focused on one metalloprotein, urease, where the bond formation between imidazoles and nickel species is important for creating catalytic sites and stabilization of polypeptides.[6] Therefore, we considered that some insoluble self-assembled catalysts of polymeric imidazole amphiphiles and platinum group metal species should offer high catalytic activity as metalloenzymes, but with much higher reusability; that is, metalloenzyme-inspired polymeric metal catalysts.

We have reported convoluted polymeric metal catalysts for organic transformation reactions, in which a soluble linear polymer having multiple ligand groups is noncovalently cross-linked with transition metals via coordinative or ionic complexation.[7] We envisaged how the application of our concept to the preparation of metalloenzyme-inspired polymeric imidazole platinum group metal catalysts could overcome the issues, providing highly active, reusable, heterogeneous, self-assembled catalysts. Here, we report the full details of the development of a novel polymeric imidazole-acrylamide palladium catalyst.[8] The catalyst was utilized for the allylic arylation/alkenylation/vinylation of allylic esters and carbonates with aryl/alkenylboronic acids, vinylboronic acid esters, and tetraaryl borates. Even 0.8–40 mol ppm Pd of the catalyst efficiently promoted the allylic arylation/alkenylation/vinylation in alcohol and/or water with a catalytic turnover number

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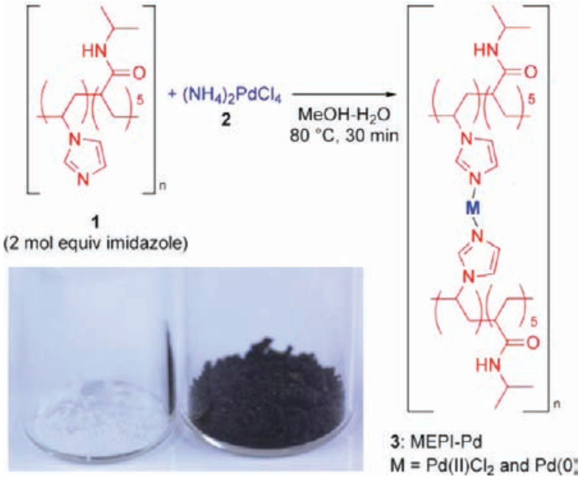
(TON) of 20 000–1 250 000. This time, we found that the catalyst efficiently drove the Suzuki–Miyaura reaction of a variety of inactivated aryl chlorides as well as aryl bromides and iodides in water with a TON of up to 3 570 000. The catalyst was reused for the allylic arylation and Suzuki–Miyaura reaction of an aryl chloride without loss of catalytic activity. We found that our molecular convolution methodology provided the globular-aggregated, self-assembled structure of the catalyst.

## RESULTS AND DISCUSSION

**Preparation of Metalloenzyme-Inspired Polymeric Imidazole Pd Catalyst (MEPI-Pd).** A novel metalloenzyme-inspired polymeric imidazole Pd catalyst (MEPI-Pd) was readily prepared from an amphiphilic acrylamide-imidazole polymer and Pd(II) species. Thus, when the coordinative convolution of poly[(*N*-vinylimidazole)-*co*-(*N*-isopropylacrylamide)$_5$][9] (**1**; 2 mol equiv imidazole) and $(NH_4)_2PdCl_4$ (**2**; 1 mol equiv Pd) was performed in a methanol/water solution at 80 °C for 30 min, MEPI-Pd **3** was precipitated out as a brown powder at a yield of 92% (Scheme 1). While polymer **1** was soluble in water, methanol, DMF, THF, $CH_2Cl_2$, MEPI-Pd **3** was hardly soluble in water, methanol, DMF, EtOAc, $CH_2Cl_2$, and hexane.

**Scheme 1. Preparation of Metalloenzyme-Inspired Polymeric Imidazole Pd Catalyst (MEPI-Pd) 3 and Photo Images of 1 (left) and MEPI-Pd 3 (right)**



Low-resolution SEM observation (×1800) showed a lump of **3** with a width of 50 $\mu$m. As shown in Figures 1 and 2, SEM images revealed that the precipitates formed a globular-aggregated, self-assembled structure similar to the quaternary structure of proteins. The globules ranged from 100 to 1000 nm in diameter and aggregated to construct a mesoporous suprastructure. EDX/SEM mapping images and an EDS/SEM image showed that both Pd (green dots) and Cl (red dots) species were uniformly dispersed in the polymeric material (Figure 1). C–N stretching absorption of **1** and **3** in IR was observed at 1548 and 1530 cm$^{-1}$, respectively. These results suggest that polymeric imidazole units coordinate to palladium species. XPS analysis of the Pd3d$_{5/2}$ showed a major peak at 336 eV and a minor peak at 334 eV, which were assigned as Pd(II) as a major species and Pd(0) as a minor species, respectively (Figure 2). TEM and high-resolution TEM observation revealed the formation of palladium nanoparticles having a diameter of 4.9 ± 2.5 nm. Palladium nanoparticles could be prepared by reduction using MeOH as a reducing agent. These results indicate that MEPI-Pd **3** is a metal–organic composite of the polymeric imidazole **1**, $PdCl_2$, and Pd(0) species including palladium nanoparticles, in which palladium species are well-dispersed in the composite. The palladium complexes should act as cross-linkers between the polymeric imidazoles **1** through Pd–imidazole coordination, and the imidazole units in **1** could stabilize the Pd nanoparticles as Lewis bases. Elemental analysis and ICP-AES analysis of the palladium supported the structure shown in Scheme 1.

**Allylic Arylation/Alkenylation/Vinylation of Allylic Acetates and Carbonates with Tetraarylborates, Aryl/Alkenylboronic Acid, and Vinylboronic Acid Esters.** Since an insoluble metal–polymer composite MEPI-Pd **3** was readily prepared and characterized, its catalytic activity and reusability were examined for allylic arylation/alkenylation/vinylation of allylic esters with tetraarylborates, aryl/alkenylboronic acid, and vinylboronic acid esters. While there are numerous reports on aryl–aryl coupling with aryl boron reagents (Suzuki–Miyaura reaction), little attention has been paid to the more challenging allyl–aryl coupling (allylic arylation), which often requires relatively high reaction temperature with a large amount (1–10 mol %) of catalyst.[10–12] We previously reported the allylic arylation of allylic esters and tetraaryl borates using a microchannel reactor with a PA-TAP-Pd catalytic membrane.[13] However, both the reactivity and substrate generality were insufficient. The results suggested that the newly developed catalysts should be applied to the allylic arylation to provide high catalytic activity and reusability as well as high substrate tolerance.

The allylic arylation of cinnamyl acetate (**4a**) and sodium tetraphenylborate (**5a**) using 40 mol ppm Pd (0.004 mol % Pd) of MEPI-Pd **3** was selected for the examination of catalytic activity and reusability (Scheme 2). Thus, when the reaction of **4a** and **5a** was carried out in *i*-PrOH–$H_2O$ with 40 mol ppm Pd (0.004 mol % Pd) of MEPI-Pd **3** at 50 °C, the reaction proceeded smoothly to quantitatively give 1,3-diphenylpropene (**6a**) in 4 h. The turnover number and frequency were 25 000 and 6250 h$^{-1}$, respectively, which are the highest numbers for allylic arylation. In contrast, the reaction without catalysts or with the polymer **1** did not proceed. Moreover, MEPI-Pd **3** was reused five times without any loss of catalytic activity to quantitatively give **6a**. The coupling reaction with the reused (fifth) catalyst provided no leaching of Pd species in the reaction mixture (ICP-AES analysis; detection limit 5 ppb Pd; >99.5% of Pd was retained in **3**). SEM, TEM, and HR-TEM observation and XPS analysis of fresh MEPI-Pd **3** and reused MEPI-Pd indicated that the catalyst was undamaged and unchanged under the reaction conditions (Figure 2). XPS analysis of the Pd3d$_{5/2}$ showed a major peak at 336 eV and a minor peak at 334 eV, which were assigned as Pd(II) as a major species and Pd(0) as a minor species, respectively. The proportion is similar to that of the fresh MEPI-Pd (Figure 2, bottom vs top). HR-TEM showed that the mean diameter of the palladium nanoparticles in the fresh and reused (fifth) catalyst was 4.9 ± 2.5 and 4.8 ± 2.4 nm, respectively. Pd(0) species were intact and did not aggregate during the recycling reactions.

Since the catalytic activity and reusability were satisfactory, a variety of allylic acetates with tetraarylborates were utilized for the allylic arylation with 40 mol ppm Pd of MEPI-Pd **3** (Table

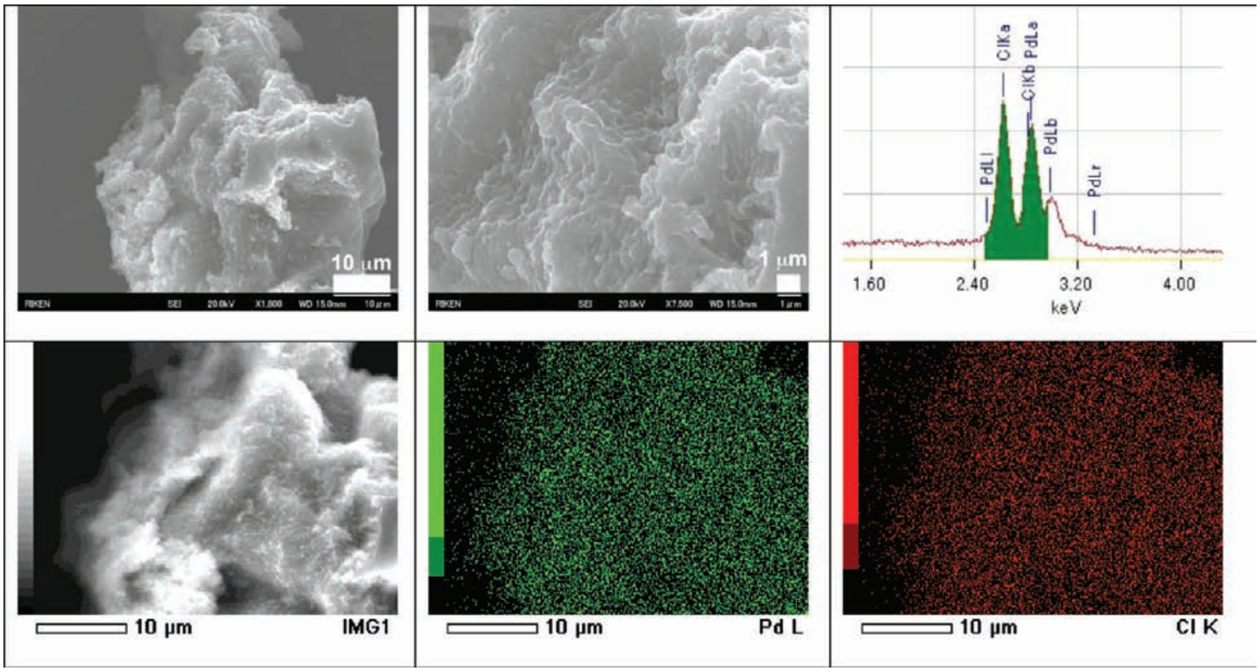


**Figure 1.** SEM and EDX/SEM images of MEPI-Pd **3**: (top left) low-resolution SEM image (bar scale 10 $\mu$m), (top center) SEM image (bar scale 1 $\mu$m), (top right) EDX image, (bottom left) SEM image for elemental mapping, (bottom center) mapping image of Pd (green dots), and (bottom right) mapping image of Cl (red dots) (bar scale 10 $\mu$m).

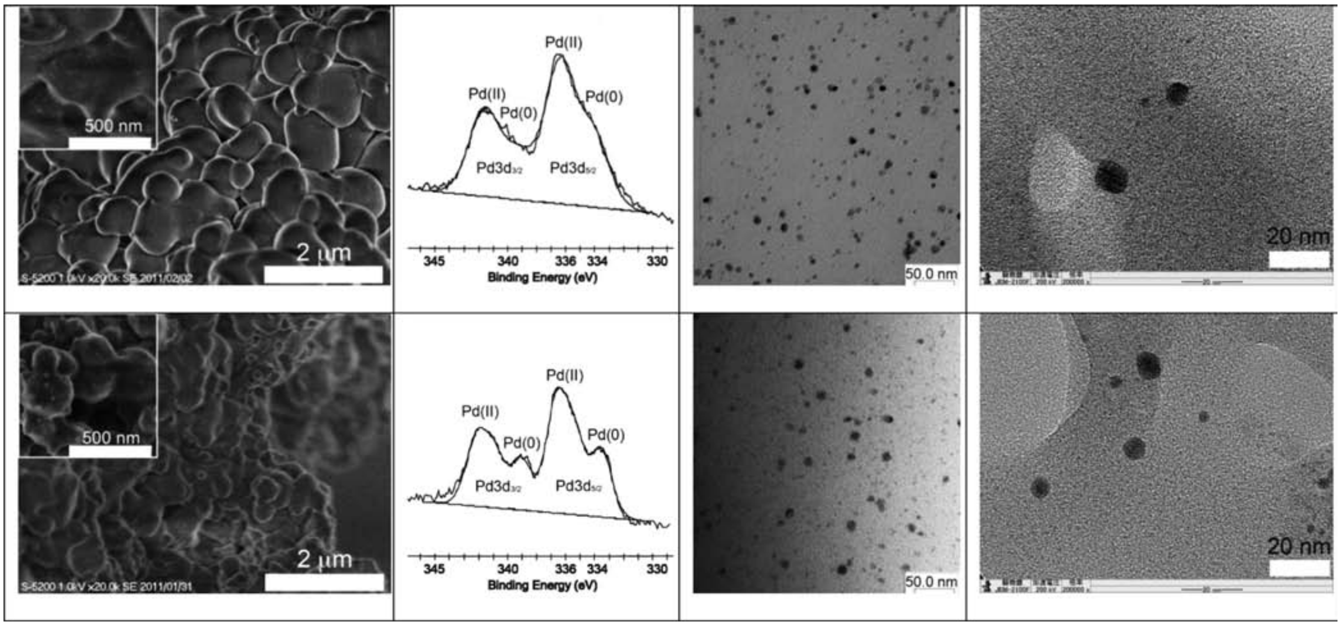
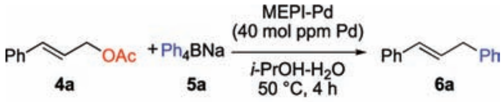


**Figure 2.** HR-SEM, XPS, TEM (90 kV), and HR-TEM (200 kV) images (from left to right) of MEPI-Pd **3** before use (top) and after the fifth reuse (bottom).

1). Thus, the reaction of **4a** and **5a** in *i*-PrOH−$H_2O$ or in water without using any organic solvents proceeded smoothly to give **6a** at a yield of 99% and 98%, respectively (entries 1 and 2). The reaction of phenyl vinyl carbinol ester **4b** gave **6a** at a yield of 96% (entry 3). Electron donating and withdrawing group substituted cinnamyl esters **4c−g** with substituted tetraaryl borates **5a−d** were efficiently converted to the corresponding products **6b−i** at a yield of 93−98% (entries 4−11).

It is interesting to note that the methyl-, ethyl-, and hexylvinyl carbinol esters **4h−k** underwent palladium-catalyzed (40 mol ppm Pd of the catalyst) allyl−aryl coupling with substituted tetraaryl borates **5a−d** to quantitatively yield the corresponding coupling products **6j−p** (entries 12−19). The reaction of alkyl vinyl carbinol esters must proceed via the corresponding $\pi$-allylpalladium intermediate bearing the $\beta$-sp$^3$-hydride, which often suffers from $\beta$-hydride elimination under palladium-catalyzed conditions to give undesirable 1,3-dienes.[11] However, no trace of 1,3-dienes was observed in the reactions. This palladium-catalyzed (40 mol ppm Pd of the catalyst) reaction of **4i** was also performed in water without using any organic solvents to quantitatively give **6k** (entry 14).

**Scheme 2. Recycling of MEPI-Pd for Allylic Arylation of 4a with 5a**



1st use: 99%
2nd use: 99%
3rd use: 99%
4th use: 99%
5th use: 99%
6th use: 99%

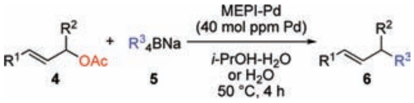
(No leaching of Pd (ICP-AES))

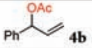
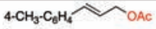
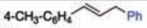
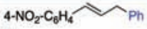
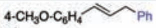
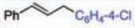
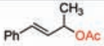
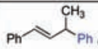
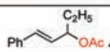
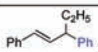
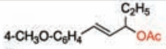
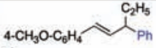
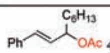
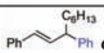
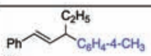
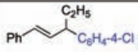
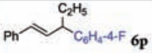
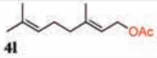
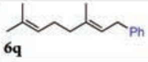
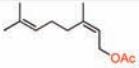
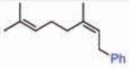
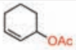
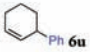
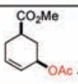
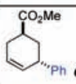
Furthermore, the coupling of aliphatic 2-alkenyl acetates is more challenging than that of cinnamyl acetates in terms of reactivity. However, geranyl acetate (**4l**), neryl acetate (**4m**), prenyl acetate (**4n**), and 2-hexenyl acetate (**4o**) efficiently led to the corresponding phenylated compounds **6q**–**t** at a yield of 96–98% (entries 20–24). Isomerization was not observed in the reactions, and water was used as a reaction solvent (entry 24). Alicyclic acetates **4p** and **4q** were readily converted to the corresponding products **6u** and **6v** at a yield of 96% (entries 25 and 26); the reaction of *cis*-**4q** proceeded via net inversion to give *trans*-5-methoxycarbonyl-3-phenyl-1-cyclohexene (**6v**) as a single diastereomer (entry 26).

Since MEPI-Pd readily drove the allylic arylation of allylic acetates, here we decided to apply the MEPI-Pd-catalyzed system to the allylic arylation of allylic carbonates (Table 2). Thus, the reaction of methyl cinnamyl carbonate (**7a**) and **5a** was performed with 40 mol ppm Pd (0.004 mol % Pd) of MEPI-Pd **3** in aqueous *i*-PrOH at 50 °C for 4 h to afford **6a** at a yield of 97% (entry 1), where the turnover number and frequency of **3** were also 24 250 and 6060 $h^{-1}$, respectively. The reaction rate of the cinnamyl acetate **4a** and carbonate **7a** was similar (Table 1, entry 1 vs Table 2, entry 1). The reaction of phenyl vinyl carbinol carbonate **7b** gave **6a** at a yield of 97% (entry 2). It is also noteworthy that the allylic arylation of methyl-, ethyl-, and hexylvinyl carbinol carbonates **7c**–**f** also proceeded smoothly to quantitatively give the corresponding coupling products **6j**–**m** (entries 3–6). In these reactions as well, no trace of 1,3-dienes was observed. A 2-alkenyl carbonate, methyl neryl carbonate (**7g**), was readily converted to the phenylated product **6r** at a yield of 98%. These results indicated that a variety of allylic carbonates undergo the allylic arylation with 40 mol ppm Pd of MEPI-Pd under mild conditions.

The insoluble self-assembled catalyst MEPI-Pd **3** efficiently promoted allylic substitution with aryl/alkenylboronic acids, which are versatile and readily available boron reagents (Table 3). Thus, the allylic phenylation of **4a** with phenylboronic acid (**8a**) with methanolic or aqueous KF solution at 70 °C proceeded smoothly to quantitatively yield **6a** (entries 1 and 2). Substituted arylboronic acids **8b**–**d** readily underwent allylic arylation under similar conditions to give **6h**,**w**,**x** at a yield of 98% (entries 3–5). The alkyl vinyl carbinol esters **4i**,**k**, neryl acetate (**4m**), and cyclohexenyl acetate (**4p**) were converted to the corresponding alkenes **6k**,**m**,**r**,**u** at 97–99% yield (entries 6–9). Allylic alkenylation, the allyl–alkenyl coupling reaction, of allylic acetates with alkenylboronic acids is more challenging in terms of reactivity as well as isomerization of olefins compared to allylic arylation.[14] However, the reaction of **4a** with (*E*)-1-pentenylboronic acid (**8e**) proceeded smoothly with 40 mol ppm Pd of MEPI-Pd under similar conditions to give (1*E*,4*E*)-1-phenyloctadiene (**9a**) at a yield of 98%, where no

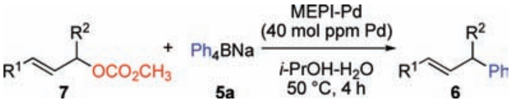
**Table 1. Allylic Arylation of Allylic Acetates with Tetraarylborates**[a]

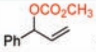
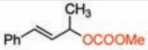
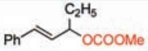
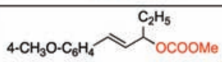
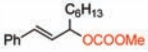
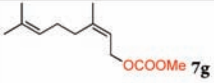


| Entry | 4 | $R^3$ 5 | 6 | Yield (%) |
|---|---|---|---|---|
| 1 | **4a** | Ph **5a** | **6a** | 99 |
| 2[b] | **4a** | **5a** | **6a** | 98 |
| 3 |  **4b** | **5a** | **6a** | 96 |
| 4 |  **4c** | **5a** |  **6b** | 97 |
| 5 |  **4d** | **5a** |  **6c** | 93 |
| 6 |  **4e** | **5a** |  **6d** | 96 |
| 7 |  **4f** | **5a** |  **6e** | 98 |
| 8 |  **4g** | **5a** |  **6f** | 98 |
| 9 | **4a** | 4-$CH_3C_6H_4$ **5b** |  **6g** | 98 |
| 10 | **4a** | 4-$ClC_6H_4$ **5c** |  **6h** | 96 |
| 11 | **4a** | 4-$FC_6H_4$ **5d** |  **6i** | 98 |
| 12 |  **4h** | **5a** |  **6j** | 98 |
| 13 |  **4i** | **5a** |  **6k** | 99 |
| 14[b] | **4i** | **5a** | **6k** | 99 |
| 15 |  **4j** | **5a** |  **6l** | 98 |
| 16 |  **4k** | **5a** |  **6m** | 97 |
| 17 | **4i** | **5b** |  **6n** | 98 |
| 18 | **4i** | **5c** |  **6o** | 96 |
| 19 | **4i** | **5d** |  **6p** | 98 |
| 20 |  **4l** | **5a** |  **6q** | 96 |
| 21 |  **4m** | **5a** |  **6r** | 97 |
| 22 |  **4n** | **5a** |  **6s** | 98 |
| 23 |  **4o** | **5a** |  **6t** | 97 |
| 24[c] | **4m** | **5a** | **6r** | 97 |
| 25 |  **4p** | **5a** |  **6u** | 96 |
| 26 |  **4q** | **5a** |  **6v** | 96 |

[a] Conditions: **4** (0.5 mmol), **5** (1 mmol), MEPI-Pd **3** (20 nmol), *i*-PrOH–$H_2O$ (0.75 mL each) or $H_2O$ (1.5 mL), 50 °C, 4 h. [b] The reaction was carried out in water for 8 h. [c] The reaction was carried out in water for 24 h.

**Table 2. Allylic Arylation of Allylic Carbonates with 5a**$^{a}$



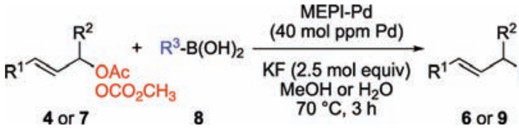
| Entry | 7 | 6 | Yield (%) |
|---|---|---|---|
| 1 |  **7a** | **6a** | 97 |
| 2 |  **7b** | **6a** | 97 |
| 3 |  **7c** | **6j** | 96 |
| 4 |  **7d** | **6k** | 97 |
| 5 |  **7e** | **6l** | 98 |
| 6 |  **7f** | **6m** | 98 |
| 7 |  **7g** | **6r** | 98 |

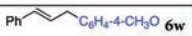
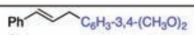
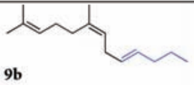
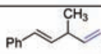
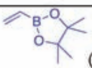
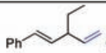
$^{a}$Conditions: **7** (0.5 mmol), **5a** (1 mmol), MEPI-Pd **3** (20 nmol), *i*-PrOH−$H_2O$ (0.75 mL each), 50 °C, 4 h.

isomerization was observed (entry 10). Neryl acetate (**4m**) was also cross-coupled with the alkenylboronic acid **8e** to afford the triene **9b** at a yield of 98% (entry 11). Furthermore, the allylic vinylation proceeded smoothly under similar conditions. Thus, the allylic vinylation of **4a,h,i** with dibutyl vinylboronate (**8f**) and vinylboronic acid pinacol ester (**8g**) yielded the corresponding *exo*-dienes **9c−e** at 95%, 95%, and 92% yield without the formation of isomers (entries 12−14). The catalytic system was also applied to the reaction of allylic carbonates. Cinnamyl carbonate (**7a**), phenyl vinyl carbinol carbonate (**7b**), and neryl carbonate (**7g**) underwent arylation under similar conditions to afford the corresponding phenylated products **6a** and **6r** at a yield of 98% (entries 15−17). In the reaction of **7g** with **5a**, a hot filtration test was conducted to prove that the insoluble catalyst promotes the reaction under heterogeneous conditions (Figure 3).[15] The reaction of **7g** with **5a** was performed under identical conditions as that in Table 3, entry 17. After 2 h, MEPI-Pd **3** was subjected to membrane filtration ($\phi$ = 0.45 $\mu$m) at 70 °C, and the resulting filtrate was stirred at 70 °C for an additional 2 h. As shown in Figure 3, GC analysis showed the yield of **6r** after the filtration. The results indicate that the reaction proceeded under heterogeneous conditions. Moreover, as shown in Figure 2, ICP-AES analysis proved that there was no leaching of Pd in the reaction mixture (detection limit 5 ppb Pd; >99.5% of Pd was retained in **3**). Ultimately, MEPI-Pd promoted the reaction under heterogeneous conditions without leaching of Pd species.

Since MEPI-Pd **3** promoted efficient allylic arylation and alkenylation without leaching of Pd under heterogeneous conditions, 0.8 mol ppm Pd of MEPI-Pd was used for the reaction of **4a** and **5a** (Scheme 3). We found that the desired coupling product **6a** was quantitatively obtained in 12 h at 50 °C, in which the TON and the turnover frequency (TOF) were more than 1 million (1 250 000) and 104 000 h$^{-1}$, respectively. To the best of our knowledge, this is the highest TON and TOF for allylic arylation.

**Table 3. Allylic Arylation/Alkenylation of Allylic Acetates or Allylic Carbonates with Arylboronic/Alkenylboronic Acid Derivatives**$^{a}$



| Entry | 4 or 7 | R$^3$ 8 | 6 or 9 | Yield (%) |
|---|---|---|---|---|
| 1 | **4a** | Ph **8a** | **6a** | 97 |
| 2$^{b}$ | **4a** | **8a** | **6a** | 99 |
| 3 | **4a** | 4-ClC$_6$H$_4$ **8b** | **6h** | 98 |
| 4 | **4a** | 4-OCH$_3$C$_6$H$_4$ **8c** |  **6w** | 98 |
| 5 | **4a** | 3,4-(OCH$_3$)$_2$C$_6$H$_3$ **8d** |  **6x** | 98 |
| 6 | **4i** | **8a** | **6k** | 99 |
| 7 | **4k** | **8a** | **6m** | 99 |
| 8 | **4m** | **8a** | **6r** | 98 |
| 9 | **4p** | **8a** | **6u** | 97 |
| 10 | **4a** | (*E*)-  **8e** |  **9a** | 98 |
| 11 | **4m** | **8e** |  **9b** | 98 |
| 12 | **4a** |  (**8f**) |  **9c** | 95 |
| 13 | **4h** | **8f** |  **9d** | 95 |
| 14 | **4i** |  (**8g**) |  **9e** | 92 |
| 15 | **7a** | **8a** | **6a** | 98 |
| 16 | **7b** | **8a** | **6a** | 98 |
| 17 | **7g** | **8a** | **6r** | 98 |

$^{a}$Conditions: **4** or **7** (0.5 mmol), **8** (0.6 mmol), **3** (20 nmol), MeOH (1.5 mL), 70 °C, 3 h. $^{b}$The reaction was carried out in water for 60 h.

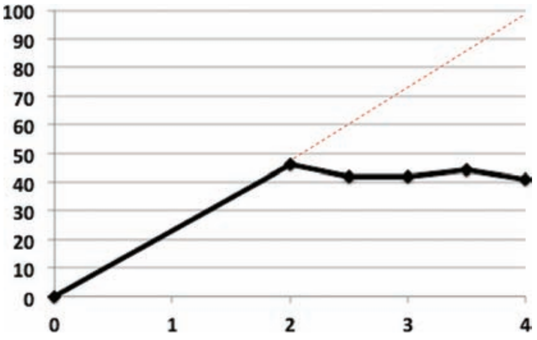
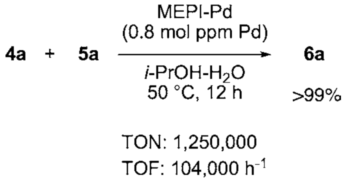


**Figure 3.** Hot filtration test of allylic arylation of **7g** with **5a** (vs Table 3, entry 17).

**Plausible Catalytic Pathway.** The plausible reaction pathway is as follows (Figure 4).[12] The oxidative addition of an allylic acetate (carbonate) to Pd(0) species **A** proceeds to

**Scheme 3. Allylic Arylation of 4a with 5a Catalyzed by 0.8 mol ppm Pd of MEPI-Pd 3**



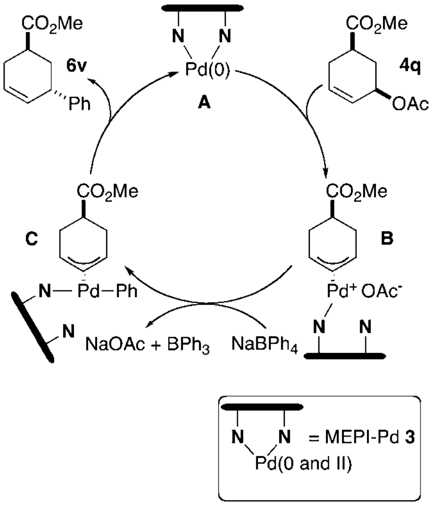


**Figure 4.** Plausible catalytic cycle of allylic arylation of **4q** with **5a**.

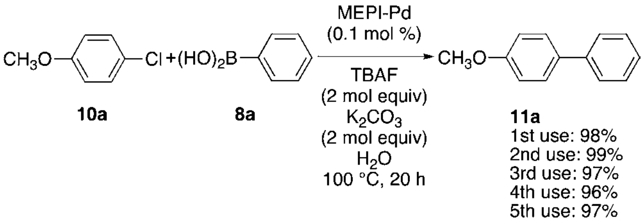
give the $\pi$-allylpalladium intermediate **B**, which undergoes transmetalation to afford the $\pi$-allyl(aryl)palladium intermediate **C**. Reductive elimination provides the corresponding product and the regeneration of **A**. In the reaction of *cis*-**4q** with **5a**, *trans*-**6v** was yielded as a single diastereomer. This result suggests that the oxidative addition proceeds via inversion to give *trans*-**B** and the transmetalation proceeds via retention to afford *trans*-**6v**.

The ability of the imidazole ligand to coordinate with the palladium species is categorized as "moderate" in the HSAB theory[16] and is lower than that of phosphine ligands. One of the imidazole ligands should readily dissociate from the palladium species in the catalytic route from **A** to **B** to efficiently promote the catalytic reaction. Since the catalyst **3** was prepared as the most thermodynamically stable form and the imidazole ligands were connected by the main-chain polymer backbone, the imidazole ligand readily associated with the palladium species in the catalytic route from **C** to **A** to stabilize the catalyst. We believe that the efficient dissociation–transformation–association process in the catalytic reaction overcomes the issues of low catalytic activity and reusability to provide a highly active and reusable heterogeneous catalytic system.

**The Suzuki–Miyaura Reaction of Aryl Chlorides, Bromides, and Iodides.** The Suzuki–Miyaura cross-coupling is among the most important reactions for synthetic organic chemistry and process chemistry which is applied to the preparation of pharmaceutical compounds, solar cells, organic conductors, and a variety of functional materials.[17] One contemporary topic is the development of highly active and reusable solid-phase catalysts for the Suzuki–Miyaura reaction of aryl chlorides, versatile and readily available substrates, but inactivated in water (on water) under atmospheric conditions.[18,19] Although polymer-supported alkyl phosphine ligands have been used, they generally are readily decomposed (oxidized) under atmospheric conditions. The progress of heterogeneous catalysts for this purpose is still in the development stage in terms of both high catalytic activity and reusability. Since MEPI-Pd **3** demonstrated its high catalytic activity and reusability for the allylic arylation, the big challenge for us was its application to the Suzuki–Miyaura reaction of aryl chlorides as well as aryl bromides and iodides in water (on water) under aerobic conditions with high catalytic activity and reusability.

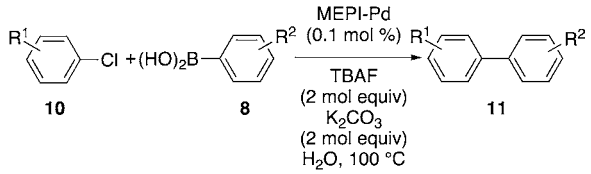
As shown in Scheme 4, when the Suzuki–Miyaura reaction of a less reactive and more electron-rich aryl chloride, 4-chloroanisole (**10a**), with phenylboronic acid (**8a**) was carried out with 0.1 mol % Pd of MEPI-Pd **3** at 100 °C for 20 h under aerobic and aqueous conditions, the reaction proceeded smoothly to afford 4-methoxybiphenyl (**11a**) at a yield of 98%. The insoluble catalyst was readily recovered by filtration and reused four times to give **11a** at a yield of 99% (second use), 97% (third use), 96% (fourth use), and 97% (fifth use). The reaction proceeded under air, which generally oxidizes alkylphosphine ligands and deactivates alkylphosphine Pd catalysts. ICP-AES analysis of the reaction mixture in the fifth reaction showed no detection of Pd species (detection limit 5 ppb Pd; >99.95% of Pd were retained in **3**).

**Scheme 4. Suzuki–Miyaura Reaction of an Electron-Rich Aryl Chloride 10a with 8a in Water**



Since catalytic activity and reusability were also satisfactory, the Suzuki–Miyaura reaction of a variety of aryl chlorides was investigated (Table 4). Thus, the reaction of **10a** with **8a** afforded **11a** at a yield of 98% (entry 1). The coupling of the electron-rich 4-chlorotoluene (**10b**) also proceeded smoothly under similar conditions to give 4-methylbiphenyl (**11b**) in 93% yield (entry 2). The electron-poor 4-chloroacetophenone (**10c**) and 4-chlorobenzonitrile (**10d**) were readily converted to the corresponding biaryl products **11c** and **11d** in 90% and 95% yield, respectively (entries 3 and 4). Phenol and aniline moieties did not disturb the coupling; the reaction of 4-chlorophenol (**10e**) and 4-chloroaniline (**10f**) gave the desired biaryls **11e** and **11f** in 94% and 95% yield, respectively (entries 5 and 6). The cross-coupling of aryl chlorides **10a–f** with 4-tolylboronic acid (**8h**) was carried out under similar conditions to afford the corresponding 4-methylbiaryl products **11g–l** in 89–94% yield (entries 7–12). The electron-rich boronic acid **8c** was coupled with aryl chlorides **10b–f** to give the corresponding 4-methoxybiaryl compounds and **11g,m–p** in 88–94% yield (entries 13–17). An electron-sufficient 3,4-dimethoxyphenylboronic acid (**8d**), an *o*-substituted 2-tolylboronic acid (**8i**), and a bulky 2-naphthylboronic acid (**8j**) were also reacted with aryl chlorides **10c,e,b** to give the corresponding couplings **11q–s** in 89–92% yield (entries 18–20).

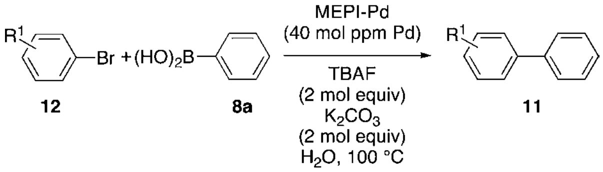
Table 4. Suzuki–Miyaura Reaction of Aryl Chlorides[a]



| entry | $R^1$ **10** | $R^2$ **8** | time (h) | **11** | yield (%) |
|---|---|---|---|---|---|
| 1 | 4-$OCH_3$ **10a** | H **8a** | 20 | **11a** | 98 |
| 2 | 4-$CH_3$ **10b** | **8a** | 10 | **11b** | 93 |
| 3 | 4-$COCH_3$ **10c** | **8a** | 9 | **11c** | 90 |
| 4 | 4-CN **10d** | **8a** | 9 | **11d** | 95 |
| 5 | 4-OH **10e** | **8a** | 9 | **11e** | 94 |
| 6 | 4-$NH_2$ **10f** | **8a** | 9 | **11f** | 95 |
| 7 | 4-$OCH_3$ **10a** | 4-$CH_3$ **8h** | 12 | **11g** | 92 |
| 8 | 4-$CH_3$ **10b** | **8h** | 12 | **11h** | 91 |
| 9 | 4-$COCH_3$ **10c** | **8h** | 12 | **11i** | 89 |
| 10 | 4-CN **10d** | **8h** | 8 | **11j** | 93 |
| 11 | 4-OH **10e** | **8h** | 8 | **11k** | 94 |
| 12 | 4-$NH_2$ **10f** | **8h** | 8 | **11l** | 94 |
| 13 | 4-$CH_3$ **10b** | 4-$CH_3O$ **8c** | 8 | **11g** | 91 |
| 14 | 4-$COCH_3$ **10c** | **8c** | 8 | **11m** | 88 |
| 15 | 4-CN **10d** | **8c** | 8 | **11n** | 94 |
| 16 | 4-OH **10e** | **8c** | 8 | **11o** | 93 |
| 17 | 4-$NH_2$ **10f** | **8c** | 8 | **11p** | 92 |
| 18 | 4-$COCH_3$ **10c** | 3,4-$(CH_3O)_2$ **8d** | 12 | **11q** | 92 |
| 19 | 4-OH **10e** | 2-$CH_3$ **8i** | 12 | **11r** | 90 |
| 20 | 4-$CH_3$ **10b** | 2-naph$B(OH)_2$ (**8j**) | 12 | **11s** | 89 |

[a]Conditions: **10** (0.5 mmol), **8** (0.6 mmol), **3** (500 nmol), TBAF (1.0 mmol), $K_2CO_3$ (1.0 mmol), $H_2O$ (1.5 mL), 100 °C.

Table 5. Suzuki–Miyaura Reaction of Aryl Bromides[a]



| entry | $R^1$ **12** | time (h) | **11** | yield (%) |
|---|---|---|---|---|
| 1 | 4-$OCH_3$ **12a** | 3 | **11a** | 97 |
| 2 | 4-$CH_3$ **12b** | 2.5 | **11b** | 98 |
| 3 | 4-CN **12c** | 2 | **11d** | 98 |
| 4 | 3-$NH_2$ **12d** | 2 | **11t** | 97 |
| 5 | 4-$C_4H_9$ **12e** | 2.5 | **11u** | 98 |

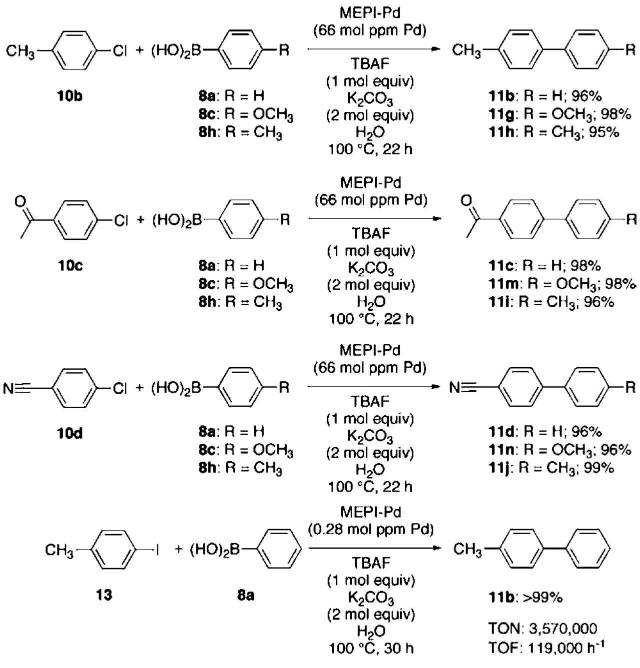
[a]Conditions: **12** (0.5 mmol), **8a** (0.6 mmol), **3** (20 nmol), TBAF (1.0 mmol), $K_2CO_3$ (1.0 mmol), $H_2O$ (1.5 mL), 100 °C.

Clearly, the Suzuki–Miyaura coupling of aryl bromides proceeded more efficiently (Table 5). Thus, the reaction of an electron-sufficient 4-bromoanisole (**12a**) was carried out with 40 mol ppm Pd of MEPI-Pd **3** under aqueous and aerobic conditions to quantitatively give 4-methoxybiphenyl (**11a**) (entry 1). Methyl-, nitrile-, amino-, and *n*-butyl-substituted aryl bromides were readily reacted with **8a** under similar conditions to quantitatively give the corresponding biaryl compounds, in which TON and TOF were up to 25 000 and 12 500 $h^{-1}$, respectively (entries 2–5).

To exhibit the highest catalytic activity for the heterogeneous catalyst-promoted Suzuki–Miyaura coupling, the reaction of aryl chlorides and iodide was demonstrated (Scheme 5). We found that the reaction of an inactivated, less reactive 4-chlorotoluene (**10b**) with **8a** was carried out with 66 mol ppm Pd of MEPI-Pd **3** under otherwise similar conditions to give 4-methylbiphenyl (**11b**) at a yield of 96% (TON 15 000). The reaction of 4-chloroacetophenole (**10c**) and 4-chlorobenzophenone (**10d**) with **8a** also proceeded with 66 mol ppm Pd of MEPI-Pd to give the corresponding biaryls **11c** and **11d** in 98% and 96% yield, respectively. Moreover, the coupling of 4-iodotoluene (**13**) with **8a** proceeded with 0.28 mol ppm Pd (280 ppb, 0.000 028 mol %) of MEPI-Pd **3** to quantitatively give the cross-coupling product **11b**, whereas the same reaction did not proceed without the catalysts. The TON and TOF in this reaction were 3 570 000 and 119 000 $h^{-1}$, respectively, which are, as far as we know, the highest TON and TOF for the heterogeneous catalyst-promoted Suzuki–Miyaura coupling.

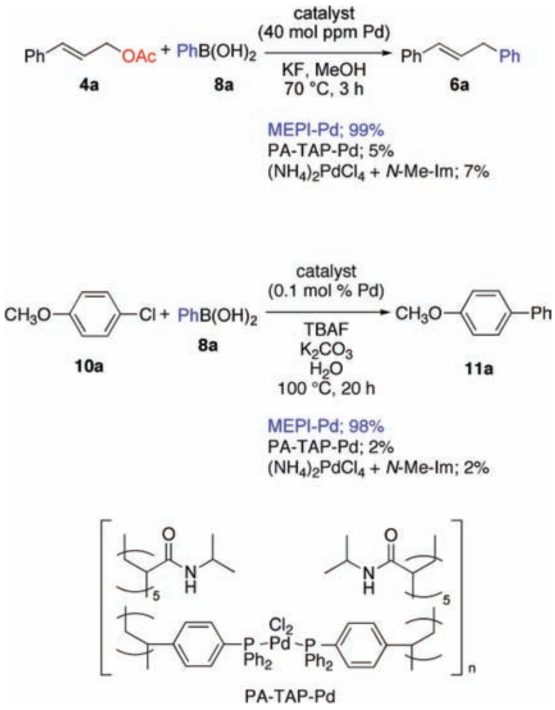
Scheme 6 shows the effect of the imidazole unit and the polymeric backbone in the allylic arylation and the Suzuki–Miyaura coupling of an aryl chloride. Thus, MEPI-Pd (40 mol ppm Pd) drove the allylic arylation of **4a** with **8a** to afford **6a**

Scheme 5. Suzuki−Miyaura Reaction with High TON and TOF in Water



(without catalysts: no reaction)

Scheme 6. MEPI-Pd vs PA-TAP-Pd and [$(NH_4)_2PdCl_4$ + *N*-Me-imdazole]



quantitatively, whereas the homogeneous counterpart [$(NH_4)_2PdCl_4$ + *N*-Me-imdazole] and PA-TAP-Pd[13] gave **6a** in 5% and 7% yield, respectively, under similar conditions. Moreover, MEPI-Pd promoted the Suzuki−Miyaura coupling of **10a** with **8a** efficiently to afford **11a** at a yield of 98%, while [$(NH_4)_2PdCl_4$ + *N*-Me-imdazole] and PA-TAP-Pd did not drive the reaction. These results indicate that the cooperative effect of the imidazole unit and the amphiphilic polymer backbone provide extremely high catalytic activity. It should be emphasized that the concept for the preparation of metalloenzyme-inspired polymeric metal catalysts will be important for designing highly active and reusable catalysts.

## ■ CONCLUSIONS

We developed a highly active, reusable, self-assembled catalyst of poly(imidazole-acrylamide) and palladium species inspired by metalloenzymes and applied our convolution methodology to the preparation of polymeric metal catalysts. The metalloenzyme-inspired polymeric imidazole Pd catalyst (MEPI-Pd) was readily prepared by the coordinative convolution of $(NH_4)_2PdCl_4$ and poly[(*N*-vinylimidazole)-*co*-(*N*-isopropylacrylamide)$_5$] in a methanol/water solution. MEPI-Pd (0.8−40 mol ppm Pd) promoted the allylic arylation/alkenylation of allylic acetates and carbonates with tetraarylborates, arylboronic acid, and alkenyl boron reagents in alcohol and/or water with a catalytic TON of 20 000−1 250 000. Moreover, MEPI-Pd efficiently drove the Suzuki−Miyaura reaction of a variety of inactivated aryl chlorides as well as aryl bromides and iodides with aryl boron reagents in water with a TON of up to 3 570 000. MEPI-Pd was reused for the allylic arylation and Suzuki−Miyaura reaction of an aryl chloride without loss of catalytic activity. We found that our molecular convolution methodology provided the globular-aggregated, self-assembled structure of MEPI-Pd.

## ■ ASSOCIATED CONTENT

### Ⓢ Supporting Information

Experimental details, compound data, and NMR charts. This material is available free of charge via the Internet at http://pubs.acs.org.

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### Notes

The authors declare no competing financial interest.

## ■ ACKNOWLEDGMENTS

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