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COMMUNICATION

N-heterocyclic carbene based MOFs catalyst for Sonogashira cross-coupling reaction

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The post-synthetic modification of azolium containing MOFs generated a new heterogeneous *N*-heterocyclic carbene catalyst (1-Pd), which is very active for Sonogashira cross coupling reaction.

Shortcomings of homogeneous catalysts in industry are circumvented by employing their heterogeneous counterparts. Thus efficient recycling, easy separation, and improved handling and process control are some of the advantages of heterogeneous catalysts over their corresponding homogeneous counterparts.[1] Many diverse and efficient strategies have been established for construction of metal-organic frameworks (MOFs) for catalysis at the molecular level.[2] Catalysis in MOFs can occur by utilization of the unsaturated metal coordination sites,[3] immobilization of transition metal nanoparticles inside the pores,[4] employing ligand chelated metal complexes[5] as the linkers[6] and post-synthetic modification (PSM).[7] MOFs can undergo PSM both at their metal nodes and organic linkers thereby augmenting the quality of parent MOFs by incorporation of multiple functional units into them. Functionalized organic ligands are used for MOF synthesis in order to post-synthetically modify the linker in the framework. One good example of such linker is a *N*-heterocyclic carbene (NHC) precursor-containing ligand.

NHCs are not only NHC-to-metal σ → d donors, but also metal-to-NHC d → π* and NHC-to-metal π → d donations contribute to their metal bond.[8] Notably, MOFs based on azolium linkers generate pockets that are suitable for binding anionic guests and unmasking the protons of the azolium moieties makes them readily available for tethering catalytically active metal complexes.[9] Different synthetic routes have been applied for metalation of azolium-based MOFs.[10] Pre-formed NHC complexes or metalloligands have been used as linkers for MOFs[6] and concomitant generation of NHC complexes during MOFs synthesis.[11] More so, PSM of frameworks containing azolium-based linkers has been employed.[12, 13]

One of the most vital and widely employed sp^2-sp bond formation reactions in organic synthesis is the Sonogashira cross-coupling reaction that involves the coupling of vinyl or aryl halides with terminal acetylenes. This coupling reaction has been effectively utilized over the years in the synthesis of natural products, pharmaceuticals, biologically active molecules, heterocycles, herbicides, dendrimers and conjugated polymers or nanostructures.[14] Some reported works on employing MOF as catalyst for this application involved Cu(I)-MOF,[15] Pd(II)-MOF,[16] and Pd nanoparticle[17] as active sites. Pd sites have been reported as stable and efficient catalytic sites for this cross-coupling reaction.[18]

NHC is important in organometallic chemistry for the synthesis of efficient homogeneous and heterogeneous catalysts. Most of the NHC catalyst for Sonogashira cross-coupling reaction are homogeneous in nature.[19] Heterogenization of the NHC catalyst has been successfully obtained by supporting the NHC on inert solid materials such as carbon polymorphs, metal oxides, mesoporous solids and polymers.[20] Notwithstanding that MOF bridges both heterogeneous and homogeneous catalysts together, it also allows multiple catalytic sites to be created in close proximity that generally cannot be used simultaneously in solution.[21] Surprisingly, no attention has been directed towards supporting NHC on MOFs for Sonogashira cross-coupling reaction. In this communication, we hereby report the first successful NHC based MOFs catalyst for Sonogashira cross-coupling reactions.

Synthesis of the azolium ligand, 1,3-bis(4-carboxyphenyl) imidazolium chloride ($H_2L^+Cl^-$) was achieved in two steps following reported literature procedures.[22, 23] Compound **1** was synthesized according to a procedure reported in the literature[23] by solvothermal reaction of $H_2L^+Cl^-$ and $Zn(NO_3)_2.6H_2O$ with a metal/ligand ratio of 4:1 in DMF at 120 °C for 48 h. After the

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synthesis of **1**, we investigated whether the imidazolium moieties are still available for PSM in order to generate NHCs by digesting the framework with aqueous 5% HCl solution. The resulting residue was washed with water (3 x 10 mL), dried in vacuum at 90 °C overnight and analyzed in DMSO-d_6 for ^{1}H and ^{13}C NMR spectroscopy (Fig. S3 and Fig. S4). The ^{1}H-NMR spectrum showed that the imidazolium proton in **1** remained intact and no additional peaks was observed from the spectrum when compared with the spectrum of the ligand (Fig. S1 and Fig. S2). Furthermore, the FT-IR spectrum (Fig. S7) of **1** showed the characteristic band at 1172 cm^{-1} for C-H group of the C2 position of the imidazolium ring.[24]

Having realized that the carbene proton is still intact, we proceeded to post-synthetically modify the frameworks in order to generate NHCs by reacting **1** with $Pd(OAc)_2$ in THF under inert atmosphere. The crystalline nature of the frameworks was maintained after PSM as presented in the identical PXRD patterns (Fig. S5) of the as-synthesized and modified MOFs (**1**-Pd). Therefore, the structure of **1** can tolerate such a post-modification conditions without the collapse of the framework. The thermogravimetric analysis of **1** and **1**-Pd are presented in Fig. S6, which also indicate that **1** retained its thermal stability after modification. At the temperature range of 65.9-150 °C, a weight loss of 2.59% is observed corresponding to the loss of lattice water molecules. The weight losses of 2.63 and 8.69, at temperature ranges of 171.6-206.1 and 226.5-254.5 °C correspond to the release of the remaining water molecules and DMF respectively. The frameworks, **1** and **1**-Pd, collapse beyond 400 °C.

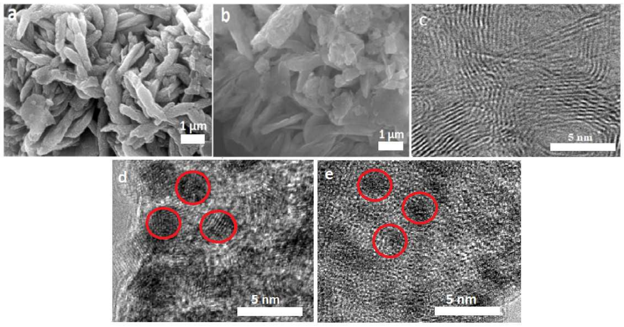

Fig. 1 FE-SEM images (a) **1**, (b) **1**-Pd and HR-TEM images (c) **1**, (d) **1**-Pd before catalysis, (e) **1**-Pd after the fourth catalytic cycle

The morphology of the frameworks was investigated by field emission scanning electron microscopy (FE-SEM) as shown in Fig. 1 (a) and (b). The FE-SEM image of **1** was composed of relatively uniform rod-like particles of average length 2.70-3.75 µm. The modified framework showed no significant change in length and morphology. In order to have a closer observation on the morphology and to evaluate the level of possible aggregation of the Pd during PSM, high-resolution transmission electron microscopy (HR-TEM) images Fig. 1 (c) and (d), of **1** and **1**-Pd samples were provided respectively. A judicious comparative observation of the TEM images shows the existence of black dots (Fig. 1 (d)) of dimensions 2.46-2.50 nm that are easily distinguished from the surrounding gray regions of **1**. A close examination of HR-TEM image of the modified framework ascribed that the black dots were distributed uniformly throughout the sample. Therefore, the Pd coordinated in the **1** framework could be in the form of NHC-Pd(II), some of them are highlighted using red circles. Also, the loading of Pd in the framework was confirmed by PXRD. The PXRD result of the modified MOF showed two peaks of Pd at 40.02 and 46.40 2θ/degrees, which were not observed in **1** (Fig. S5).[25] In addition, the energy dispersive X-ray spectroscopy (EDS) mapping (Fig. S8) confirms the existence of Pd in the modified frameworks. Zn, C and O are also present in the EDS mapping. The drastic decrease in absorption of C-H band (1184 cm^{-1}) of the carbenic group in the FT-IR spectrum of the modified framework supports the coordination of the Pd to the **1** (Fig. S7).[24] Also, as can be observed in Fig. S7, the formation of the frameworks resulted to the shift in the spectrum of **1** and **1**-Pd.

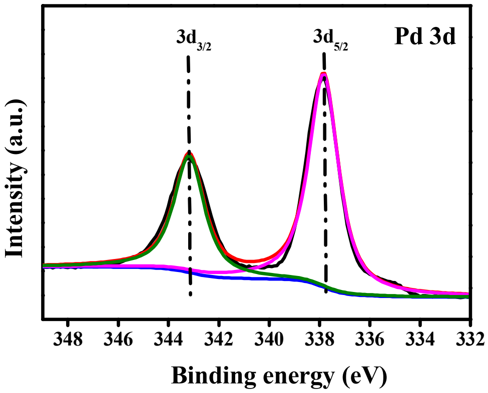

Fig. 2 XPS analysis of **1**-Pd, the curve-fitted Pd 3d spectrum.

Having realized that Pd is tethered in the framework, we repeated the digestion test on the modified framework to ascertain the actual position of the anchored Pd on the NHC structure. ^{1}H-NMR spectrum in Fig. S9 shows two signals in upfield region at δ = 7.42 and 6.95 ppm, which were absent in the ligand (Fig. S1) as well as digested **1** (Fig. S3). These two chemical shifts are the aromatic protons of the azolium ligand containing NHC-Pd coordination[26] and these peaks appearing in the downfield region may be due to the Pd-to-NHC d → π* donation. Integration of the ^{1}H-NMR demonstrates that 12.55% of the carbenic protons in the $H_2L^+Cl^-$ were deprotonated. Furthermore, in the ^{13}C-NMR spectrum (Fig. S10) of digested sample, a new signal in upfield region at δ = 206.94 ppm corresponds to carbene carbon coordinated to Pd, thereby confirming that the Pd is anchored on the carbene carbon generating Pd-NHC.[27] Additional prove for the presence and composition of Pd was obtained by performing inductively coupled plasma mass spectrometry (ICP-MS), which shows that 10.88% of Pd(II) tether to the carbene and this result is in agreement with the ^{1}H-NMR result. The Brunauer–Emmett–Teller (BET) surface area of **1** and **1**-Pd are 102.02 and 88.36 m^2/g respectively as presented in Table S1.

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We employed X-ray photoelectron spectra (XPS) to provide valuable information on the oxidation state of the anchored Pd (Fig. 2). Two peaks related to Pd $3d_{5/2}$ and $3d_{3/2}$ are centered at the binding energies of 337.9 and 343.2 eV, respectively. These binding energies are characteristic for divalent Pd cations,[16, 28] and are also consistent with the values reported for homogeneous Pd(II)–NHC complexes.[29] No peaks were observed around 335 and 340 eV, corresponding to the $3d_{5/2}$ and $3d_{3/2}$ levels of Pd(0),[30] which confirms that there are no Pd(0) nanoparticles in the framework. Furthermore, no trace of $Pd(OAc)_2$ was identified since the $3d_{5/2}$ level of binding energy peak at 338.7eV, that is characteristic of $Pd(OAc)_2$ was absent.[13]

Sonogashira cross-coupling reactions were performed for various substituted aryl halides and terminal alkynes to examine the catalytic activity for **1**-Pd. The representative data are summarized in Table 1. The coupling reactions were carried out with substituted aryl halide, substituted phenyl acetylene, Cs_2CO_3, **1**-Pd in DMF at 100°C under air atmosphere for 12 h to produce the corresponding products. Under these reaction conditions, **1**-Pd catalyse the reactions of 2-bromopyridine with substituted phenylacetylene to generate excellent corresponding yields (Table 1, entries 1-3). Apparently, lower yields were obtained for 2-bromopyridine with an *ortho*-substituted electron-donating group (Table 1, entries 9 and 10) when compared with yields obtained in Table 1 entries 1 and 2. Good yields were observed for substituted iodobenzene (Table 1, entries 4-8). The yield was somewhat low when tested on 2-chlorobenzene (Table 1, entry 11). On the other hand, the aryl halide with electron-withdrawing substituents like nitro, entry 12, and acetyl, entry 13, gave excellent yields. Furthermore, $Pd(OAc)_2$ as a catalyst was also used but the obtained yield was low, thus $Pd(OAc)_2$ was not just grafted on the framework, rather NHC-Pd was generated as an active site of **1**-Pd. As can be observed in the ^{1}H NMR spectra of the Sonogashira coupling products (see supporting Information), no homocoupled product of the alkyne reagent was formed during the coupling reaction. As shown in entry 16, the activity of the catalyst was not changed significantly after the fourth catalytic cycle. **1**-Pd was simply recovered by filtration, washed twice with DMF and subsequently used in the successive runs. The PXRD patterns of the recovered solid after four catalytic cycles revealed that the structural integrity of the catalyst was retained (Fig. S5). Furthermore, after four catalytic cycles, the TEM and XPS measurements showed no aggregation of the black dots, Fig. 1 (e) and that Pd maintained the oxidation state of +2, Fig. S11, respectively.

We employed dynamic light scattering (DLS) technique to check whether Pd(0) was formed after the catalytic reaction. A blank sample comprising 2-bromopyridine, phenylacetylene, and Cs_2CO_3 in DMF was heated to 100 °C for 12 h. From the DLS spectrum of the blank (Fig. S12), we observed a peak with particle size of about 1000 nm. The filtrates from Table 1, entries 2, 5, and 7 were also analyzed using DLS (Fig. S12), which showed only the same peak with same particle size, 1000 nm, (no extra peaks were identified) as the blank. Under the same reaction conditions, the DLS of the reaction mixtures before catalysis, without Cs_2CO_3, and without Cs_2CO_3 and **1**-Pd was analysed respectively (Fig. S12). For these three analyses, particle sizes less than 1 nm were identified, showing no formation of nanoparticles.[31] Therefore, It can be deduced that the peak with particle size of about 1000 nm may be attributed to the formation of inorganic micron-sized particles from the Cs_2CO_3 and no Pd(0) nanoparticle was formed after the catalytic reaction. The heterogeneous character of the catalyst was examined by heating a mixture of the catalyst and the base at the reaction temperature for 12 h followed by filtration. To the hot filtrate, 2-bromopyridine, phenylacetylene, and more base was added, followed by heating at reaction temperature for another 12 h, but no product was detected. Furthermore, no trace of Pd was detected in the ICP analysis result of the filtrate. The ICP of **1**-Pd after four catalytic runs showed no appreciable change in the Pd content. These results show the heterogeneous catalytic behaviour of **1**-Pd.

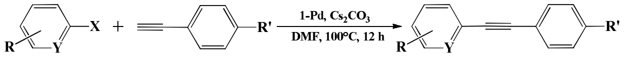

Table 1 Sonogashira cross-coupling reaction of different substrates with **1**-Pd

Entry	R	X	Y	R’	Yield (%)[b]
1	H	Br	N	4-OCH_3	84.6
2	H	Br	N	4-$C(CH_3)_3$	94.0
3	H	Br	N	H	98.0
4	4-CH_2CH_3	I	H	H	93.3
5	4-CH_2CH_3	I	H	4-OCH_3	87.7
6	4-CH_2CH_3	I	H	4-$C(CH_3)_3$	90.0
7	4-OCH_3	I	H	H	91.0
8	4-OCH_3	I	H	4-$C(CH_3)_3$	67.7
9	2-CH_3	Br	H	4-OCH_3	77.8
10	2-CH_3	Br	H	4-$C(CH_3)_3$	73.4
11	H	Cl	N	4-$C(CH_3)_3$	62.0
12	4-NO_2	I	H	H	>99
13	4-$COCH_3$	I	H	H	>99
14[c]	H	Br	N	4-$CH(CH_3)_3$	93.6
15[d]	H	Br	N	4-$CH(CH_3)_3$	93.1
16[e]	H	Br	N	4-$CH(CH_3)_3$	92.4
17[f]	H	Br	N	4-$CH(CH_3)_3$	36.0

[a] Reaction conditions: aryl halide (0.92 mmol), phenylacetylene (1.1 mmol), Cs_2CO_3 (1.84 mmol), catalyst (0.003 mmol based on Pd) in 6 mL DMF heated at 100 °C under air atmosphere for 12 h. [b] Isolated yield, [c] Second catalytic cycle, [d] Third catalytic cycle, [e] Fourth catalytic cycle, [f] Catalyzed by $Pd(OAc)_2$

To the best of our knowledge, **1**-Pd has the highest reported TON value of 300 among Pd(II)-MOF catalysts used in Sonogashira cross-coupling reaction.[16, 28, 32] This high value may be attributed to the efficient Pd-NHCs active site that has been reported as among the most stable and active Pd complexes to promote cross-coupling reactions.[33] From the proposed mechanism below, an electron-donating group attached to the aryl halide makes the displacement of the halide by the deprotonated terminal alkyne difficult (Table 1, entries 4 and 7). Furthermore, in this catalytic process, the base,

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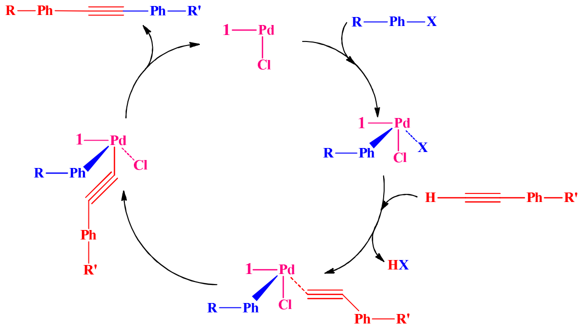
Cs_2CO_3, abstracts the acetylenic proton of the terminal alkyne, thereby enhancing the coordination of the acetylene ligand to the metal and the liberation of HX. The pH of series of the Sonogashira coupling reactions' mixture was analyzed before and after the reactions. The observed pH of the reaction mixtures dropped from the range 9.22-9.37 to 8.83-8.90 before and after the reaction respectively. This was attributed to the liberation of HX.



Scheme 1 The plausible catalytic cycle for Sonogashira coupling using **1**-Pd.

In summary, we synthesized a bent aromatic azolium ligand which was employed to construct **1**. The carbene protons in the **1** were still intact, thus the framework was post-synthetically modified in order to design a new heterogeneous NHCs catalyst (**1**-Pd) that is highly active (with low catalyst loading) for Sonogashira cross-coupling reaction for various substituted aryl halides with terminal alkynes. **1**-Pd presents a high density and uniform distribution of the active site, NHCs-Pd, in the framework and retains its catalytic activity for at least four cycles without losing its structural integrity. Optimization of the reaction conditions of **1**-Pd for the Sonogashira cross-coupling reaction, as well as extension of their applications to other Pd-catalyzed cross coupling reactions are still in progress.

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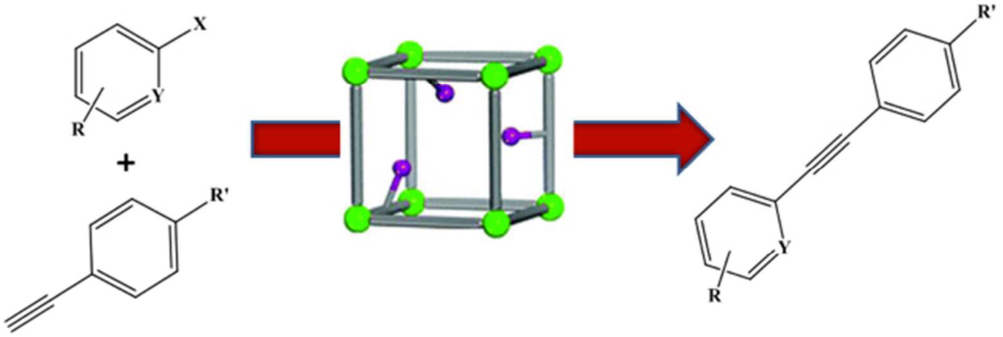

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