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ORIGINAL ARTICLE

MOF-253 immobilized Pd and Cu as recyclable and efficient green catalysts for Sonogashira reaction

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Abstract MOF-253·Pd(OAc)$_2$ and MOF-253·CuI were prepared, characterized, and evaluated firstly as heterogeneous co-catalysts, which showed high catalytic activity in Sonogashira coupling reaction of various substituted (hetero)aryl halides with terminal alkynes at 70–120 °C, and afforded the corresponding products in 45–99% yields with high TON (~2722 for Pd). The best result was achieved with an extremely low Pd (0.036 mol%) and Cu (0.397 mol%) loading. Moreover, the catalysts can be reused at least five times without significantly reducing the activity. Besides, Hg(0) and PVP-poisoning experiments confirmed that the present catalysts were efficient and heterogeneous catalysts in this coupling reaction.

1. Introduction

The Sonogashira reaction is one of the most efficient and straightforward methods for the construction of carbon (sp^2)-carbon (sp) bonds via palladium/copper co-catalyzed coupling of aryl, heteroaryl, and vinyl halides or triflates with terminal alkynes in the presence of amine as the base (Sonogashira, 2002), which was firstly reported in 1975 (Sonogashira et al., 1975). Because of the broad application of alkynes in various agrochemicals, natural products, pharmaceuticals, and versatile material intermediates, the reaction has still been received extensive attention for the synthesis of substituted alkynes (Danilkina et al., 2015; Frigoli et al., 2005; Mansour, 2016; Platonova et al., 2014; Wagner and Comins, 2006). In addition, the di-substituted acetylenes can contribute to being further converted into other functional groups (Chinchilla and Nájera, 2007). Although the significant progress has been achieved in this transformation, by utilizing catalytic palladium combined with CuI as a co-catalyst under homogenous conditions (Chinchilla and Nájera, 2011), they inherently suffer from some problems, such as non-reusability and metal residues, *etc*., which cause to the low economic efficiency of catalysts and narrow application range of products, particularly in the preparation of pharmaceutical chemicals and optoelectronic devices. Many efforts have been made to develop heterogeneous catalysts to overcome the mentioned drawbacks (Arpad, 2011; Shi, 2013). For these purposes, different solid supports, such as polymers (Gholinejad et al., 2015; Navalon et al., 2013; Steel and Teasdale, 2004), magnesium oxide (Gholinejad et al., 2018a, b), silica (Bedford et al., 2005; Dehbanipour et al., 2017), graphene (Gholinejad et al., 2017; Wang et al., 2017), resins (Bakherad et al., 2014; Ciriminna et al., 2013; Sengupta et al., 2014) and naturally occurring polysaccharides (Gholinejad et al., 2016a,b), have been used to anchor palladium or copper species. Visible-light-mediated Son-

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gashira coupling reactions have also been reported under homogeneous or heterogeneous conditions (Li et al., 2019a,b; Protti et al., 2005; Song et al., 2018; Zhou and Zhao, 2022). However, there is still space for improvement in this field, such as catalyst preparation, low efficiency of recyclable and loss of actives of the catalysts. Copper-free palladium-catalyzed Sonogashira reactions have also been reported in recent years (Ciriminna et al., 2013; Dissanayake et al., 2019; Gao et al., 2010; Gholinejad et al., 2018a,b; Handa et al., 2015; Handa et al., 2019; Gholinejad et al., 2016a,b; Yu et al., 2016), but it has been proved by some groups in many cases that the cross-coupling reaction could be accelerated in the presence of copper under oxygen-free conditions to prevent the formation of diyne as homo-coupling products (Beccalli et al., 2014; Bellina and Lessi, 2012; Lamblin et al., 2010; Mas-Marzá et al., 2003; Tan et al., 2013).

Metal-organic frameworks (MOFs) are a unique class of porous and crystalline materials composed of metal cations (or metal clusters) and organic linkers. The employment of MOFs as heterogeneous catalysis is one of the best promising applications (Dhakshinamoorthy et al., 2015; Jiao et al., 2018; Lee et al., 2009; Li et al., 2019a,b; Liu et al., 2014; Xu et al., 2019), which is attributed to the large surface areas, good thermal stability and potential metal active sites (Castillo-Blas and Gandara, 2018; Liu et al., 2010; Wen et al., 2018). Among them, (Al(OH)(bpydc)) (bpydc = 2,2′-bipyridine-5,5′-dicarboxylate) is one of the well-studied MOFs, which was firstly reported in 2010 by Yaghi et al. and denominated the structure as "MOF-253" (Bloch et al., 2010). After then, because of possessing open N,N'-chelating sites in its structure, MOF-253 has been investigated as an excellent carrier-immobilized metal heterogeneous catalyst in several organic conversions (Chen et al., 2015; Deng et al., 2018; Deng et al., 2019; Liu et al., 2012; Long et al., 2012; Van Zeeland et al., 2016; Wang et al., 2012). Nonetheless, there is no report with MOF-253 immobilized Cu and Pd as the co-catalysts for Sonogashira carbon–carbon coupling reactions.

In continuation to develop environmentally friendly protocols for transition-metal catalyzed carbon-heteroatom bonds formation (Li et al., 2016; Ma et al., 2018; Wang et al., 2018; Zhou et al., 2015), in this paper, the aim is to study the direct coupling reaction of (hetero)aryl halides with terminal alkynes by using MOF-253·xPd(OAc)$_2$ and MOF-253·yCuI (x or y, molar ratio of Pd(OAc)$_2$ or CuI to bpy) as the heterogeneous bimetallic catalysts system.

2. Experimental section

2.1. General methods

All reagents were purchased from Adamas-*beta* and used as received unless otherwise noted. Anhydrous DMSO (99.7+%, extra dry, over molecular sieves) was purchased from Acros. All the reactions were carried out in N$_2$ atmosphere under magnetic stirring. ^{1}H NMR and ^{13}C NMR were recorded on a Bruker Avance III HD 400 instrument using TMS as the internal standard and DMSO or CDCl$_3$ as the solvent. Mass spectra were recorded on a GC–MS (Agilent 7890A/5975C) instrument in EI mode. AAS was obtained on the AA-7003 instrument of Beijing East-West Instrumental Analysis. Inductively coupled plasma-mass spectrometry (ICP-MS) was obtained on an Agilent 720 instrument, and the elemental analysis (C, H, N) was measured by Thermo Fisher Flash 2000 instrument. Powder X-ray diffraction (XRD) was measured by a Bruker D8 ADVANCE instrument. Fourier transform infrared spectroscopy (FT-IR) spectra was determined by a Bruker Vertex70 FTIR spectrometer (wavenumber range 500–4000 cm^{-1}). X-ray photoelectron spectroscopy (XPS) was collected using a Kratos AMICUS spectrometer (Shimadzu, JP). N$_2$ adsorption/desorption experiments were detected using a Brunauer-Emmett-Teller (BET) instrument. Column chromatography was performed with silica gel (200-–300 mesh) purchased from Qingdao Haiyang Chemical Co., Ltd.

2.2. General procedure for MOF-253·Pd(OAc)$_2$/MOF-253·CuI-catalyzed the coupling reaction of (hetero)aryl halides with terminal alkynes

To a 25 mL of Schlenk tube were added MOF-253·Pd(OAc)$_2$ (Pd 0.036 mol%), MOF-253·CuI (Cu 0.397 mol%), (hetero) aryl halide (0.50 mmol), K$_2$CO$_3$ (1.0 mmol) and DMSO (2.0 mL), then the mixture was vacuumed three times to replace with N$_2$. The terminal alkyne (0.55 mmol) was added under N$_2$ atmosphere, and finally, the reaction tube was sealed and reacted in the preheated IKA reaction module at 70–120 °C for 12–24 h. The reaction mixture was cooled to room temperature and extracted with ethyl acetate (20 mL × 3). The combined organic phase was washed with water and brine, dried over anhydrous Na$_2$SO$_4$, and concentrated in *vacuo*. The residue was purified by flash column chromatography on silica gel (ethyl acetate/ petroleum ether as the eluent) to afford the target products **3a-3au** and **4a-4c**.

2.3. Recycling of the catalysts MOF-253·Pd(OAc)$_2$ and MOF-253·CuI

After completion of the first run, the reaction mixture was cooled to room temperature, and extracted with petroleum ether. The remaining petroleum ether in the reaction tube was steamed under reduced pressure at 80 °C. And then, the reaction liquid containing the catalyst was re-added with substrate, partial solvent (0.5 mL), and base (2.0 Equiv.) to start a new cycle. This process was then repeated 5 times.

2.4. Hg (0) and PVP poisoning experiment

At the beginning of the reaction, to a 25 mL of Schlenk tube was added MOF-253·Pd(OAc)$_2$ (Pd 0.036 mol%), MOF-253·CuI (Cu 0.397 mol%), and Hg(0) (56 mg) or PVP-60000 (112 mg). The mixture was stirred at room temperature for 30 min, then added to other required materials under standard conditions, reacted under optimal conditions, cooled at room temperature, and worked up to obtain the isolated yield.

2.5. Metal leaching test of catalyst MOF-253·Pd(OAc)$_2$ and MOF-253·CuI

After completion of the reaction, the reaction mixture was subjected to hot filtration under vacuum. The solid was washed with DMSO, and the liquid phase was analyzed by AAS.

3. Results and discussion

The synthetic method for the preparation of MOF-253 immobilized Pd and Cu catalysts is shown in Fig. 1. Oxidation of commercially available 5,5′-dimethyl-2,2′-bipyridine with H$_2$SO$_4$/K$_2$Cr$_2$O$_7$ catalytic system provided 2,2′-bipyridine-5,5′-dicarboxylic acid. Followed by the hydrothermal method with AlCl$_3$·6H$_2$O and acetic acid to afford MOF-253 (Wang et al.

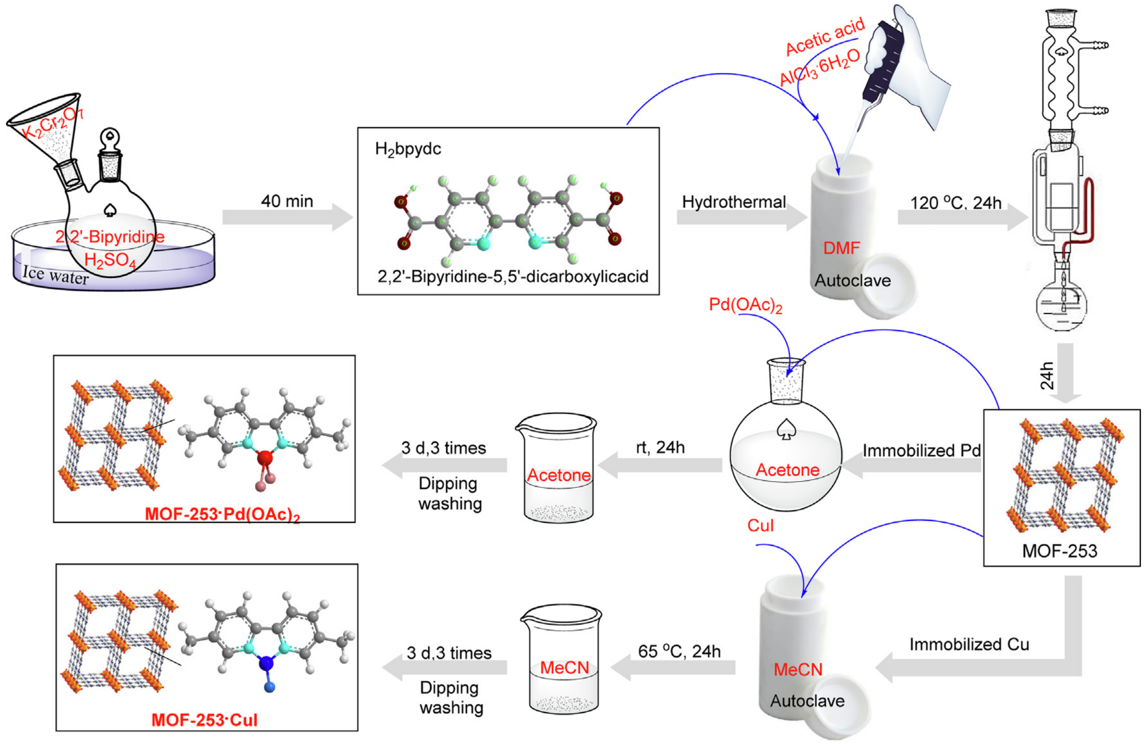


Fig. 1 Catalyst preparation process (Bloch et al., 2010; Wang et al. 2012).

2012). In MOF-253, the 2,2′-bipyridyl (bpy) moiety does not coordinate with any metal ion and thus provides a platform for coordination chelation of the metal center. Therefore, the activated MOF-253 was immersed in the acetone solution of $Pd(OAc)_2$ or in the acetonitrile solution of CuI to obtain MOF-253·x$Pd(OAc)_2$ and MOF-253·yCuI, respectively. The structures of MOF-253, MOF-253·x$Pd(OAc)_2$ ($x = 0.02$) and MOF-253·yCuI ($y = 0.54$) were characterized by XRD, FT-IR and BET analysis, which were matched with the reported literature (Figure S1-S3) (Wang et al. 2012), and the content of Pd and Cu were determined by ICP-MS and elemental analysis (Table 1). The intermolecular interactions between MOF-253 and $Pd(OAc)_2$ or CuI were investigated by XPS, and the results were illustrated in Fig. 2. Compared to MOF-253, the binding energy of the N 1s peak of MOF-253·CuI and MOF-253·$Pd(OAc)_2$ were shifted toward higher binding energy with the value of 0.8 eV and 1.4 eV, respectively, which indicated the existence of intermolecular coordination interaction between bpy unit of MOF-253 and CuI or $Pd(OAc)_2$, resulting in a decrease in the electron density of N atoms.

With the MOF-253 immobilized Pd and Cu solid catalysts prepared, 4-iodoanisole and phenylacetylene were selected as model substrates to optimize the Sonogashira coupling reaction conditions. Since the catalyst load greatly affects the economic benefits of the catalysts, the amount of the catalyst was firstly studied, and the results are shown in Fig. 3. When 0.073 mol% of MOF-253·$Pd(OAc)_2$ in combination with 2.416 mol% of MOF-253·CuI (molar ratio of Cu to Pd was 33:1) were used as co-catalyst, Cs_2CO_3 as the base in DMSO at 80 °C, a good isolated yield (91%) of the target product (**3a**) was obtained after 12 h (entry 1). Fixed the molar content of Pd at 0.073 mol% and continuously reduced the molar content of Cu to 0.397 mol%, the yield reduced from 96% to 90% (entries 2 and 3), and the best molar ratio of Cu: Pd was 11:1. Besides, it was considered that the amounts of catalysts used were more than the actual demand, decreased the amount of the catalysts by half while maintaining the same ratio of Cu: Pd (11:1), an excellent yield of 90% was also obtained (entry 4 vs 2). The yield was significantly reduced to 48%, when 0.036% of MOF-253·$Pd(OAc)_2$ was used alone with the same other reaction conditions (entry 5). Finally, the reaction car-

Table 1 The content of Pd, Cu, C, H, and N of samples.

Sample	Cu (wt%)[a]	Pd (wt%)[a]	C (wt%)[b]	H (wt%)[b]	N (wt%)[b]	Value of x and y
MOF-253·x$Pd(OAc)_2$	—	0.75	43.38	3.12	8.82	0.02
MOF-253·yCuI	8.41	—	34.79	2.39	6.87	0.54

[a] Measured by ICP-MS.
[b] Measured by element analysis.

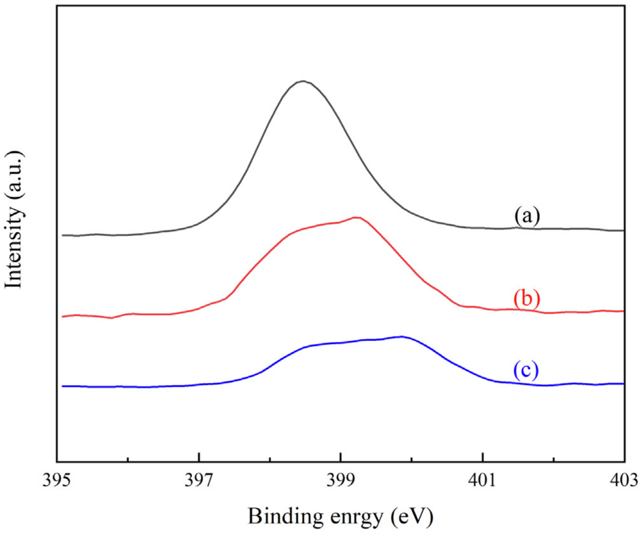


Fig. 2 XPS spectra of the N 1s region for (a) MOF-253, (b) MOF-253·CuI and (c) MOF-253·Pd$(OAc)_2$.

ried out in the absence of palladium was used as a comparison, and only trace of the target product was detected (entry 6).

In order to test the effect of alkalis and solvents, Cu:Pd (11:1) with the smaller amounts of catalysts, instead of the highest yield one, was chosen as the starting catalyst system (entry 4 in Fig. 3 and entry 1 in Table 2). As shown in Table 2, various bases were examined, including K_2CO_3, Et_3N, DABCO and *t*-BuOK, and the K_2CO_3 provided the best efficiency with a yield of 92% (entries 2–6). The control experiment indicated that the coupling reaction did not occur without a base (entry 7).

The reaction carried out in DMSO was faster than in DMF, H_2O, EtOH/H_2O, CH_3CN or 1,4-dioxane (entries 8–12). When raised the reaction temperature from 80 °C to 90 °C only slightly increased the yield (entry 13). Surprisingly, the yield increased to 98% when the reaction temperature was reduced to 70 °C, but further lowering the temperature to 60 °C resulted in a dramatic decrease in the yield (entries 14 and 15). In the absence of MOF-253, the addition of Pd$(OAc)_2$ and CuI only provided 50% yield (entry 14). Thus, the optimal coupling reaction conditions between 4 and iodoanisole and phenylacetylene are MOF-253·Pd$(OAc)_2$ (0.036 mol %), MOF-253·CuI (0.397 mol%) and K_2CO_3 (2.0 equiv.) under N_2 atmosphere in DMSO (2.0 mL) at 70 °C for 12 h. By calculating turnover number (TON) and turnover frequency (TOF) values, 0.036 mol% of Pd catalyst produced an extremely high TON of 2722 (entry 14), which was much higher than calculated values in other literatures (Ciriminna et al., 2013; Protti et al., 2005).

After successfully establishing optimized reaction conditions (entry 14 in Table 2), the substrate tolerances for various aryl iodides and different terminal alkynes were evaluated. The results are summarized in Table 3. The coupling reaction proceeded well for most aryl iodides and aryl alkynes, and furnished the desired products in good to quantity yields upon isolation. It is worth noting that the electronic nature of the *para*-substituents on aryl iodides has almost no effect on catalytic efficiency. For example, *para*-substituents aryl iodides with an electron-neutral group (**3a**), an electron-donating group such as OMe (**3b**), or electron-withdrawing groups such as Ph, F, COOH, CN or NO_2 (**3i**, **3j**, **3k**, **3m** and **3p**), provided the corresponding products in 92–98% yield. Steric hindrance has a certain effect on the reaction. 99% yield was obtained when 1-iodo-3,5-dimethylbenzene was reacted with phenylacetylene (**3c**), but the yield of *ortho*-substituted aryl iodides

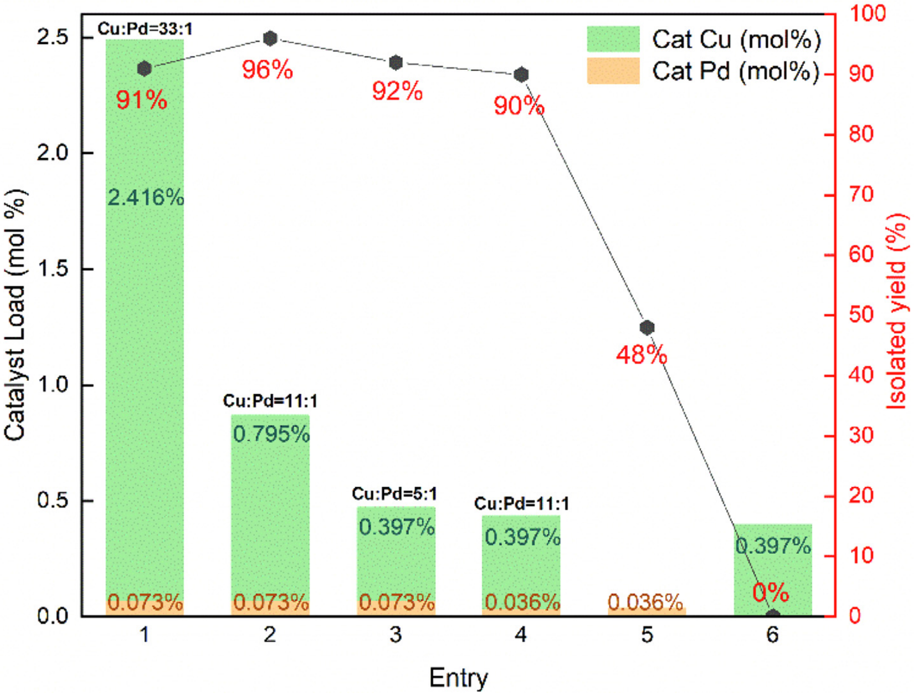
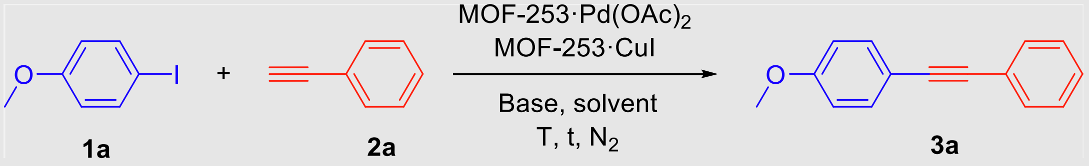


Fig. 3 Effect of MOF-253 immobilized catalyst loading on the coupling reaction of 4-iodoanisole and phenylacetylene.

Table 2 Optimization of coupling conditions of 4-iodoanisole and phenylacetylene catalyzed by MOF-253·Pd(OAc)$_2$ and MOF-253·CuI.[a]



Entry	Base	Solvent	Temp. (°C)	Yield (%)[b]	TON[c]	TOF (h^{-1})[c]
1	Cs_2CO_3	DMSO	80	90	2500	208
2	K_2CO_3	DMSO	80	92	2556	213
3	Et_3N	DMSO	80	47	1306	109
4	DABCO	DMSO	80	66	1833	153
5	K_3PO_4	DMSO	80	86	2389	199
6	*t*-BuOK	DMSO	80	trace	—	—
7	—	DMSO	80	—	0	0
8	K_2CO_3	DMF	80	53	1472	123
9	K_2CO_3	H_2O	80	13	361	30
10	K_2CO_3	EtOH/H_2O (1/1)	80	trace	—	—
11	K_2CO_3	CH_3CN	80	36	1000	83
12	K_2CO_3	Dioxane	80	20	556	46
13	K_2CO_3	DMSO	90	93	2583	215
14	K_2CO_3	DMSO	70	98, 50[d]	2722	227
15	K_2CO_3	DMSO	60	55	1528	127

[a] Reaction conditions: **1a** (0.5 mmol), **2a** (0.55 mmol), MOF-253·Pd(OAc)$_2$ (0.036 mol%), MOF-253·CuI (0.397 mol%), base (1.0 mmol), solvent (2.0 mL), 12 h, N_2 atmosphere.

[b] Isolated yield.

[c] For Pd catalyst.

[d] Pd(OAc)$_2$ (Pd 0.036 mol %), CuI (Cu 0.397 mol%).

(Me, *i*-Pr, OMe and NH_2) decreased approximately to 65–90% (**3d-3g**). The reaction of methyl 5-iodosalicylate with phenylacetylene proceeded relatively slowly, thus yielding a final yield of 68% (**3h**). The adaptation range of the substituted aryl terminal alkynes was tested, bearing different functional groups such as NH_2, F and *n*-C_5H_{11}. Among them, the reaction of 1-iodo-3,5-dimethylbenzene with 4-pentylphenylacetylene only provided the 76% yield caused by the incomplete conversion of aryl iodide (**3o**), while the other cases could be offered excellent yields of 87%-98% (**3l-3n**, **3p**, **3r**, **3s** and **3w**). Interestingly, heteroaryl iodides were very amenable under the standard reaction conditions, which showed the desired products in 93–98% yield (**3q-3w**).

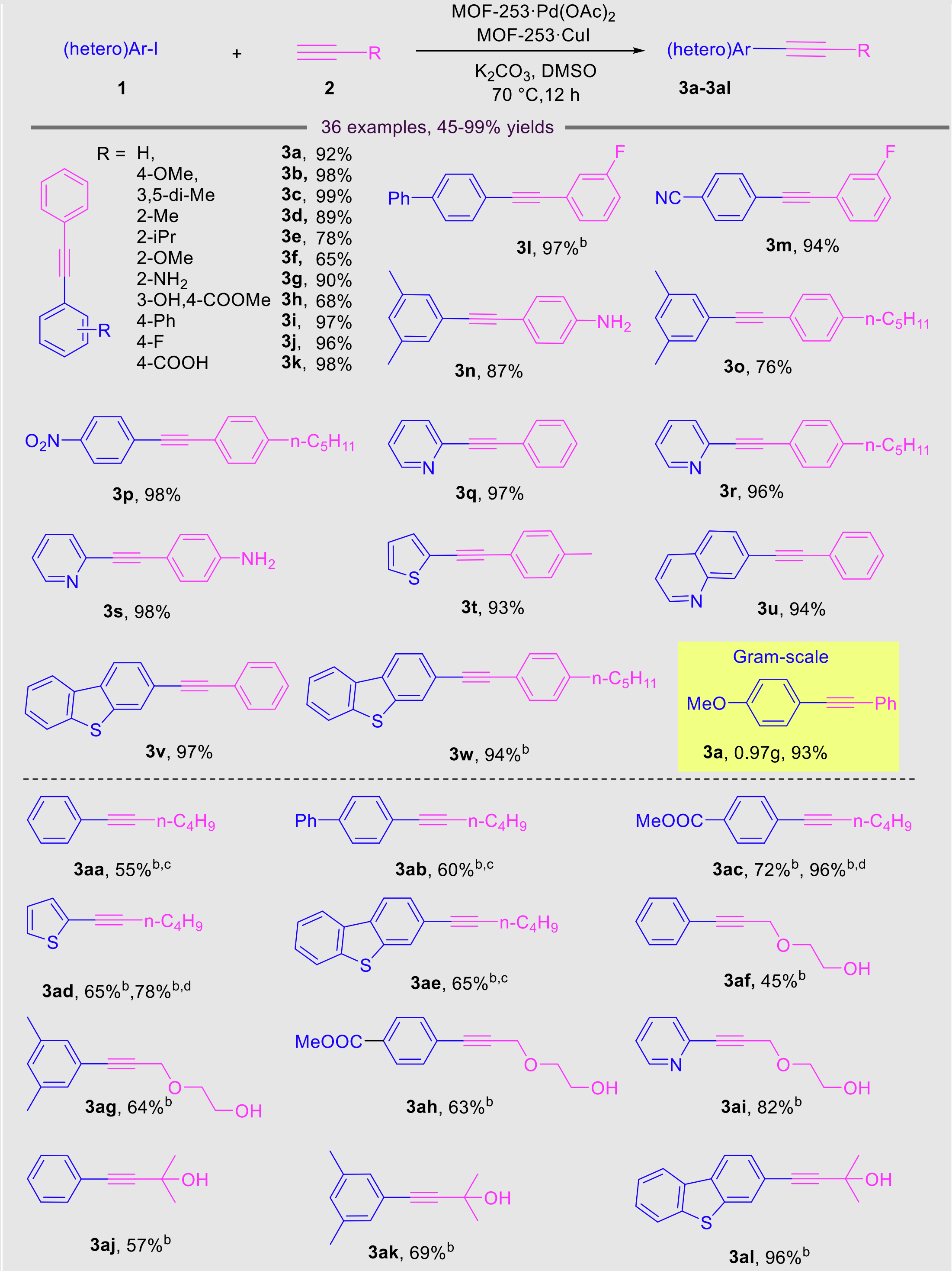
Due to the lower reactivity than aryl alkynes, alkynylation of aliphatic alkynes required prolonging the reaction time and/or elevating the temperature, and afforded relatively lower yields. For example, the reaction of 1-hexyne with aryl iodides gave moderate yields of 55%-72% (**3aa-3ae**). But the reaction of methyl 4-iodobenzoate and 2-iodothiophene with 1-hexyne can be significantly improved by raising the reaction temperature (**3ac** and **3ad**). The same results were observed in the reactions between 2-(prop-2-yn-1-yloxy)ethan-1-ol or 2-methylbut-3-yn-2-ol with electron-donating or electron-withdrawing substituted aryl iodides (**3af-3ah**, **3aj** and **3ak**). The reactions involving of 2-iodopyridine and 2-iodo dibenzothiophene once again proved that they were perfect reaction substrates, and excellent yield of 82% and 96% were obtained, respectively (**3ai** and **3al**).

To further verified the scalability and practicality of this present catalytic system, a scale-up reaction was carried out by taking 5.0 mmol of **1a** and 5.5 mmol **2a** under the standard conditions, and the expected product **3a** was generated in 93% yield (Table 3).

The catalytic system was also suitable for the reaction of different substituents of aryl bromides and phenylacetylene without changing other conditions, and only reacted at 80 °C for 24 h and achieved excellent yields of 94–98% (Table 4, **3am-3aq** and **3q**). For 5-bromobenzo[*b*]thiophene and 5-bromobenzo[*d*][1,3-dioxane], moderate yields of 62% and 68% were also obtained with the addition of 1.0 equivalent of tetrabutylammonium iodide (TBAI) and elevated temperature to 100 °C (**3ar** and **3as**). The coupling of 4-chloronitrobenzene with phenylacetylenes occurred with poor conversion under optimized reaction conditions. Nevertheless, further higher temperature (120 °C) and the additive (2.0 equiv. of TBAB) were required, and 68%-91% yields were obtained (**3ap-3au**).

Finally, the catalytic system was also applied to more complex drug-like substrates under the optimal conditions. As shown in Fig. 4, ethisterone, ethinylestradiol and norgestrel showed good efficiency, and estradiol had the best reactivity with a yield of 96% (**4b**). Meanwhile, 68% and 83% yields

Table 3 Coupling reaction of (hetero)aryl iodides with aryl and aliphatic terminal alkynes.[a]

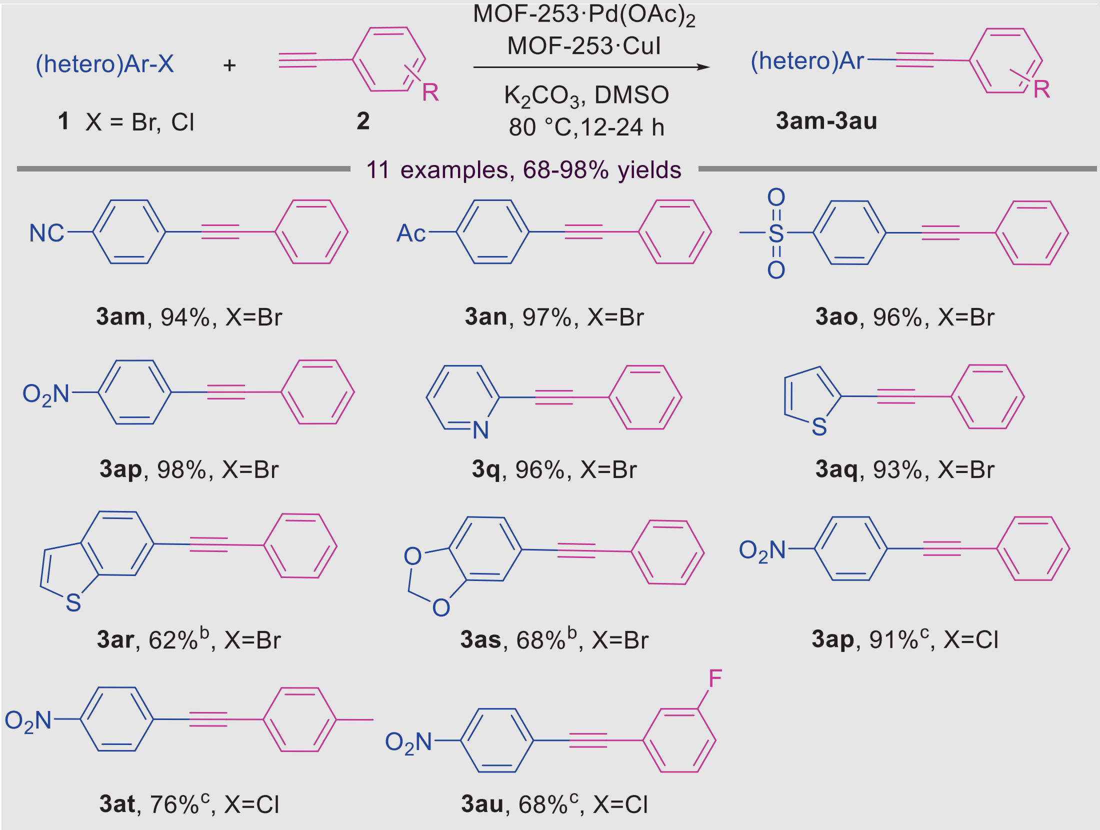


[a] Reaction conditions: **1** (0.5 mmol), **2** (0.55 mmol), MOF-253·Pd(OAc)$_2$ (0.036 mol%), MOF-253·CuI (0.397 mol%), K_2CO_3 (1.0 mmol), DMSO (2.0 mL), 70 °C, 12 h, N_2 atmosphere; isolated yield; [b] 24 h; [c] 100 °C; [d] 90 °C.

were obtained for ethisterone and norgestrel, respectively (**4a** and **4c**).

The recoverability and reusability are important features of heterogeneous catalysts. Based on this, a recycling experiment with coupling reaction of 4-iodoanisole and phenylacetylene under the standard conditions was conducted to check the recyclability of the catalytic system. The catalysts of MOF-253·Pd(OAc)$_2$ and MOF-253·CuI are fine powdery solids, and only 0.0026 g and 0.0015 g were used in the present experiment, respectively. In order to avoid the loss of catalyst

Table 4 Coupling reactions of aryl bromides and aryl chlorides with aryl terminal alkynes.[a]



[a] Reaction conditions: **1** (0.5 mmol), **2** (0.55 mmol), MOF-253·Pd(OAc)$_2$ (0.036 mol%), MOF-253·CuI (0.397 mol%), K_2CO_3 (1.0 mmol), DMSO (2.0 mL), 80 °C, 24 h, N_2 atmosphere, isolated yield; [b] 100 °C, 1.0 equiv. TBAI; [c] 120 °C, 2.0 equiv. TBAB.

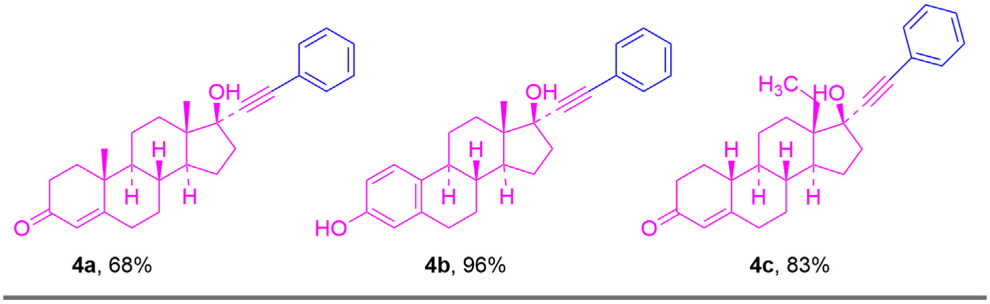


Fig. 4 Coupling reactions of ethisterone, ethinylestradiol and norgestrel with iodobenzene. Reaction conditions: iodobenzene (0.5 mmol), ethisterone, ethinylestradiol and norgestrel (0.55 mmol), MOF-253·Pd(OAc)$_2$ (0.036 mol%), MOF-253·CuI (0.397 mol%), K_2CO_3 (1.0 mmol), DMSO (2.0 mL), 100 °C, 24 h, N_2 atmosphere; isolated yield.

caused in the separation process, after each reaction was completed, the reaction mixture was carefully extracted with petroleum ether several times, and the residual petroleum ether in the Schlenk tube was evaporated under reduced pressure at 80 °C. Then, the substances, partial solvent and base were re-added to the reaction tube and started a new cycle. The catalyst can be recycled at least five times without an obvious decrease in yield (Fig. 5).

To evaluate the catalytic effect of leached ions. The coupling reaction of 4-iodoanisole and phenylacetylene was subjected to a hot filtration test under optimized reaction conditions (Fig. 6d). After 1 h, the catalyst was separated by filtration at the reaction temperature, and the remaining mixture with another 2.0 equiv. K_2CO_3 was further stirred for 2 h, 3 h, 6 h, 9 h and 12 h, respectively. It was pointed out that the yield of desired product was not increased and stopped

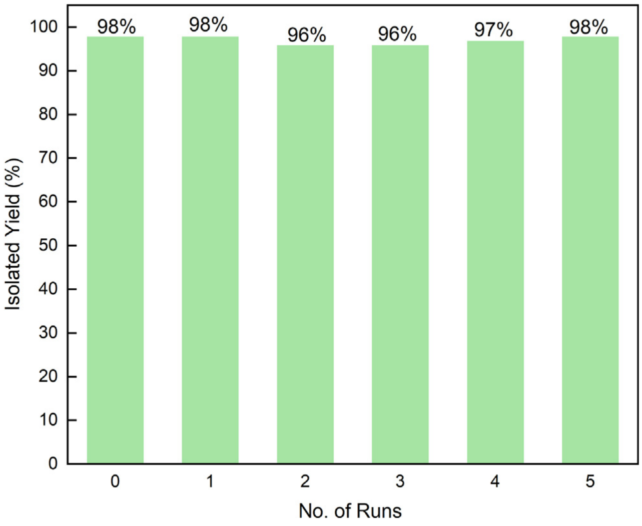


Fig. 5 Reusability of MOF-253·Pd(OAc)$_2$ and MOF-253·CuI for coupling reaction between 4-iodoanisole and phenylacetylene under the standard conditions.

completely at 27% isolated yield after the removal of the catalyst, which indicated that the catalyst was a good heterogeneous catalyst for this type of reaction, and the reaction only occurred over the solid catalyst rather than in the solution.

To further confirm the heterogeneous nature of the present catalytic system, the mercury-poisoning experiment was conducted with addition of excess Hg(0) to the reaction mixture as catalyst poison (1600-fold molar ratio relative to Pd). As shown in Fig. 6c, the reaction rate was slightly suppressed, but the final yield of 95% can still be achieved. It is well known that Hg(0) can poison heterogeneous catalysts always by fusing or adsorbing metal on the metal surface, which has been reported in many kinds of literature (Chernyshev et al., 2019; Gholinejad et al., 2016a,b; Richardson and Jones, 2006; Xie et al., 2018; Yu et al., 2005). However, different from common heterogeneous porous materials supported metal catalysts, in our catalytic system, MOF-253 immobilized Pd(OAc)$_2$ or CuI were formed by the strong coordination between bpy and Pd or Cu, this proposal was consistent with the aforementioned higher binding energy of N 1s peak of the XPS spectrum. As we know, Hg(0) has no poisoning effect on homogeneous or ligand-protected Pd species, and due to the strong coordination between ligand with Pd/Cu, we reasonably believe that it was also fit to MOF-253·Pd(OAc)$_2$ and MOF-253·CuI catalyst system. In addition, poly(vinyl pyridine) (PVP)-poisoning experiment was also carried out, which is another catalyst balancer and scavenger for soluble molecules Pd and soluble Pd(0) nanoparticles (Chernyshev et al., 2019; Gholinejad et al., 2016a,b; Richardson and Jones, 2006; Xie et al., 2018; Yu et al., 2005). Similar to the yield of standard conditions, 93% yield was obtained in the presence of PVP, which can be further confirmed the heterogeneous nature of our present co-catalyst (Fig. 6b).

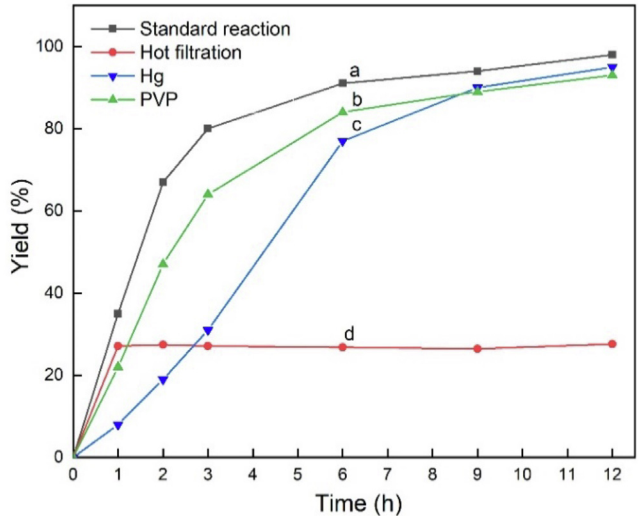


Fig. 6 MOF-253·Pd(OAc)$_2$ (Pd 0.036 mol%) and MOF-253·CuI (Cu 0.397 mol%) catalyzed the reaction of 4-iodoanisole with phenylacetylene: (a) reaction under optimized reaction conditions; (b) reaction in the presence of an excess amount of PVP; (c) reaction in the presence of an excess amount of Hg(0); (d) reaction under hot filtration conditions.

In addition, the investigation was also performed to check the metal leaching of the catalyst for the model reaction. The liquid reaction solution was collected by hot filtration after the completion of the reaction and analyzed by AAS analysis. Only low than 0.18% of Pd and 0.19% of Cu content was detected in the reaction solution. The result proved again that the MOF-253 immobilized catalyst in this experiment was an excellent green solid catalyst.

Finally, we compared the activity of our catalysts with other reported palladium catalysts in the Sonogashira reaction (Table S1). It can be seen that the present catalysts exhibited a higher efficiency with higher yields, lower Pd loading and broad substrate scopes than other reported methods.

In general, the mechanism of Cu/Pd-co-catalyzed Sonogashira reaction is believed to take place through two catalytic cycles (Pd-cycle and Cu-cycle) and *trans*-metalation process. Considering the two metals both attached to the independent MOF, the traditional *trans*-metalation process would occur difficultly in the present process. In addition, we observed that 48% yield was still obtained~~,~~ when 0.036% of MOF-253·Pd (OAc)$_2$ was used alone under the same reaction conditions (entry 5 in Fig. 3). Therefore, all the results indicated that the Pd-cycle was the primary catalytic cycle for the present reaction. And the existence of MOF-253·CuI merely improved the reaction and conversion rate by promoting the formation of alkyne anions, which did not form an independent cycle process.

Based on these results, the reaction mechanism for this transformation was proposed and shown in Fig. 7. MOF-253·Pd(OAc)$_2$ undergoes an oxidative addition reaction with an aryl halide to form an intermediate palladium complex (**A**). MOF-253·CuI reacts with terminal alkyne to form MOF-253·CuI π-alkyne complex (**C**), thus making the alkyne proton more acidic for more accessible abstraction (Camacho et al., 2017; Chinchilla and Nájera, 2007). Alkyne deprotonation by the K_2CO_3 would give the corresponding potassium acetylide (**D**), followed by a substitution reaction with complex (**A**) to form (**B**). Finally, reductive elimination reaction of (**B**) to provide the product and regenerate palladium catalyst.

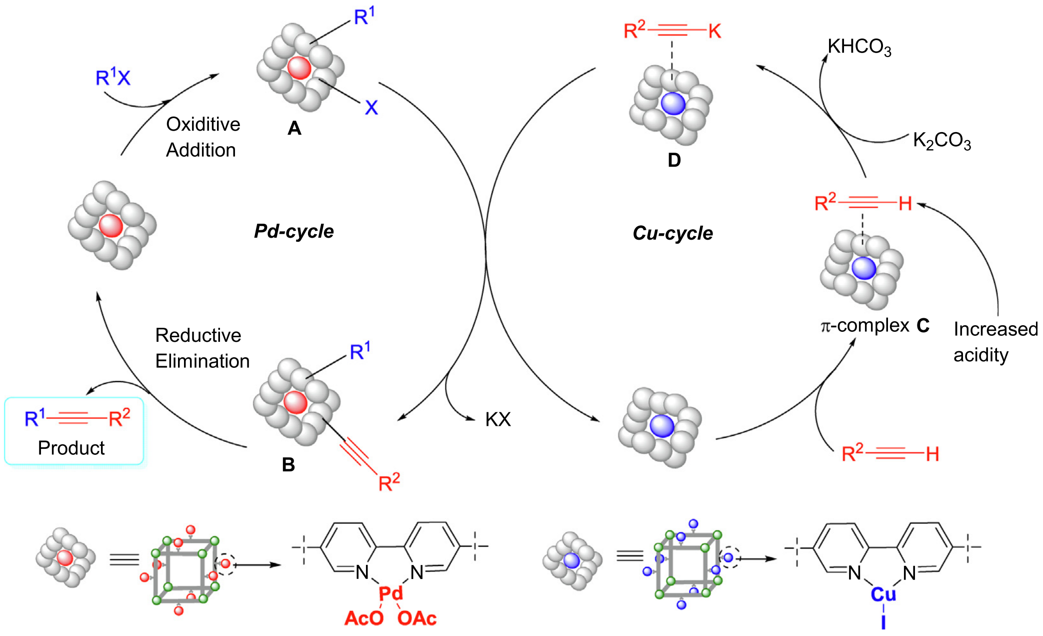


Fig. 7 Plausible reaction mechanism.

4. Conclusion

In summary, two MOF-253 immobilized Pd and Cu catalysts were synthesized and evaluated as the heterogeneous co-catalyst for the Sonogashira reaction between (hetero)aryl halides with terminal alkynes. In this catalytic system, various (hetero)aryl iodides, bromides and chlorides can be coupled with aryl/aliphatic terminal alkynes smoothly, and provided the corresponding products in the range of 45–99% yields at 70–120 °C with low Pd loading (0.036 mol%) and high TON. The co-catalysts could be reused at least 5 times without significantly reducing activity. The thermal filtration testing, Hg(0) and PVP poisoning experiments demonstrated that the MOF-253 immobilized catalyst was a high-quality green heterogeneous catalytic system in this reaction. Further studies of other types of immobilized MOF catalytic reactions are currently underway in our laboratory and will be reported as appropriate.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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