CHEMISTRY
A EUROPEAN JOURNAL

DOI: 10.1002/chem.201101705

# Palladium Nanoparticles Encapsulated in a Metal–Organic Framework as Efficient Heterogeneous Catalysts for Direct C2 Arylation of Indoles

**Yuanbiao Huang, Zujin Lin, and Rong Cao***[a]

**Abstract:** Highly dispersed palladium nanoparticles (Pd NPs) encapsulated in the mesoporous cages of the metal–organic framework (MOF) MIL-101(Cr) have been prepared by using the wetness impregnation method. The Pd NPs were characterized by powder X-ray diffraction (PXRD), $N_2$ adsorption, transmission electron microscopy, inductively coupled plasma atomic emission spectroscopy (ICP-AES), and X-ray photoelectron spectroscopy (XPS). The particles size ((2.6±0.5) nm) of the obtained Pd NPs was in good agreement with the cage diameters (2.9 and 3.4 nm) of the MOF. The resulting Pd/MIL-101(Cr) catalyst exhibited extremely high catalytic activities in the direct C2 arylation of substituted indoles by using only 0.1 mol % of the Pd catalyst. Moreover, the catalyst is easily recoverable and can be reused several times without leaching into solution and loss of activity. The combination of the highly dispersible Pd NPs within the accessible mesoporous cages and the favorable adsorption of the aryl halides on MIL-101 are suspected to be the main reasons for the observed high activities of the Pd/MIL-101(Cr) catalyst in the direct C2 arylation of indoles.

**Keywords:** C−H activation · heterogeneous catalysis · indoles · metal–organic framework · nanoparticles · palladium

## Introduction

The C2-arylated indole substructure is one of the most important building blocks of biologically active and functional molecules.[1] Although palladium-catalyzed cross-coupling reactions provide an efficient approach to these compounds, such protocols require functionalized indoles and activated arenes.[1,2] From a sustainable chemistry viewpoint, direct transformation of a C−H bond into a C−C bond is an efficient and environmentally friendly way for the synthesis of such compounds. Recently, great efforts have been devoted to palladium-catalyzed direct C2−H arylations of indoles with activated arenes.[3–7] However, unfortunately the expensive palladium catalyst in such a homogeneous form can not be recovered and is difficult to separate from the products. Although heterogeneous palladium catalysts have been developed for their easy separation and feasibility of catalyst recycling, up to now, there are only few reports describing the direct C2−H arylation of indoles by using heterogeneous palladium catalysts.[8]

Today, metal nanoparticles show great potential application in catalysis because of a great ratio of atoms remaining at the large surface area and the density of the unsaturated surface coordination sites.[9] Unfortunately, these metallic nanoparticles are unstable with respect to agglomeration to the bulk. In most cases, this aggregation generally leads to the loss of the catalytic properties.[9a] Therefore, suitable stabilizers and/or supports for nanoparticle catalysts are generally required.

Metal–organic frameworks (MOFs) have been emerging as very promising functional materials for gas storage, separation, heterogeneous catalysis, sensing, and drug delivery due to their high surface area, porosity, and chemical tunability.[10,11] These unique features make MOFs very attractive in heterogeneous catalysis. However, the MOFs used for catalysis should have high thermal and chemical stability. Additionally, the catalytic active sites of the most MOFs are not easy accessible for substrates due to the lack of big pores.[11] So far, only a handful of MOF materials have been reported to be used as catalysts for organic catalysis[11] and even fewer of them as host matrices to support metal nanoparticles (NPs) as catalysts for heterogeneous catalysis.[11e,12–15] To the best of our knowledge, up to now, there are no reports of employing MOFs as supports for metal NPs in the direct C−H arylation of indoles.

MIL-101(Cr) ($Cr_3(F,OH)(H_2O)_2O[(O_2C)\text{-}C_6H_4\text{-}(CO_2)]_3{\cdot}n\,H_2O$ ($n\approx 25$), MIL = Matérial Institut Lavoisier), synthesized by Férey et al.,[16] is an excellent MOF material due to its extra high specific surface area, its pore volume, and its high thermal (up to 300 °C) and chemical stability to water and common organic solvents. It has two types of mesoporous cages (2.9 and 3.4 nm) accessible through microporous windows (1.2 and 1.4 nm). The combination of these outstanding features makes it an interesting candidate for adsorption[17] and catalysis.[12a–g,13h,18] The mesoporous

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Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.201101705.

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cages can be used to confine the metal nanoparticles and to restrict their growth, which are pertinent features for their applications in heterogeneous catalysis.[12a–g] Furthermore, the mesoporous cages and large microporous windows may allow the large reactant molecules to reach the active site in the pores and the large product molecules to leave from the active sites easily. Herein, we choose MIL-101(Cr) to support Pd NPs as a highly active catalyst for the direct C–H arylation of indoles.

## Results and Discussion

**Preparation and characterization of Pd NPs**: MIL-101(Cr) was synthesized according to the literature.[16] For completed removal of the unreacted terephthalic acid in the pores, the as synthesized blue-green samples were solvothermally treated with DMF, aqueous $NH_4F$ solution, and EtOH, respectively. The X-ray powder diffraction (PXRD) patterns of the resulting solid are coincident with the simulated ones, confirming the formation of MIL-101(Cr) (Figure 1). Nitrogen adsorption measurements showed a high specific surface area of the obtained porous material ($S_{BET}=3447.7\,m^2g^{-1}$, Figure 2), which is in agreement with the previously reported data.[16] The supported Pd NP catalyst, denoted as Pd/MIL-101(Cr), was prepared through solution infiltraion of activated MIL-101(Cr) with $Pd(NO_3)_2$ as precursor, followed by treatment with $H_2$ at 200°C for 4 h. PXRD patterns (Figure 1) show that the frameworks of MIL-101(Cr) do not change after the Pd loading (ca. 0.5 wt%). The characteristic peak of Pd (111) at $2\theta=40.1°$ is indistinguishable due to the low Pd loading amount and the small well-dispersed Pd NPs.[12] TEM images (Figure 3) of Pd/MIL-101(Cr) indicate that most of the dispersed Pd NPs are successfully encapsulated in the cages of the MIL-101(Cr), with a mean diameter of (2.6 ± 0.5) nm (Figure 3), based on TEM observation by using the Nano Mersurer 1.2 version software.[12a] However, although the impregnated MIL-101(Cr) samples containing palladium salts have been repeatedly washed till the filtrate became colorless, few nanoparticles still remain outside the pores due to the electrostatic interactions between the MIL-101(Cr) and palladium.[12e] The decrease in surface area and pore size indicate that the cavities of MIL-101(Cr) may be occupied by palladium NPs and/or blocked by palladium NPs that are located at the surface (Figure 2 and Table 1).[12] X-ray photoelectron spectroscopy (XPS) (Figure 4) and EDS data (Figure 3) indicate that $Pd^0$ and $Cr^{III}$ coexist in the Pd/MIL-101(Cr) materials. In the XPS traces, the $3d^{5/2}$ and $3d^{3/2}$ peaks of $Pd^0$ appear at 336.2 and 341.4 eV and no obvious peak of $Pd^{2+}$ is observed, which indicates that most of the palladium is in the reduced form.[12r]

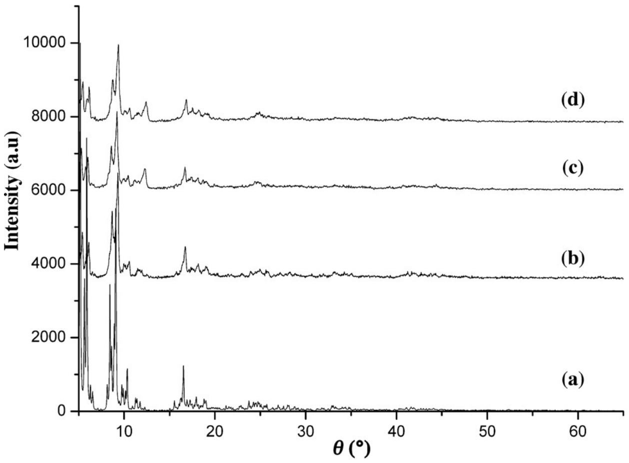


Figure 1. Powder XRD patterns of MIL-101 samples: a) MIL-101, simulated; b) MIL-101, activated; c) Pd/MIL-101, before reaction; d) Pd/MIL-101, after five runs of catalysis.

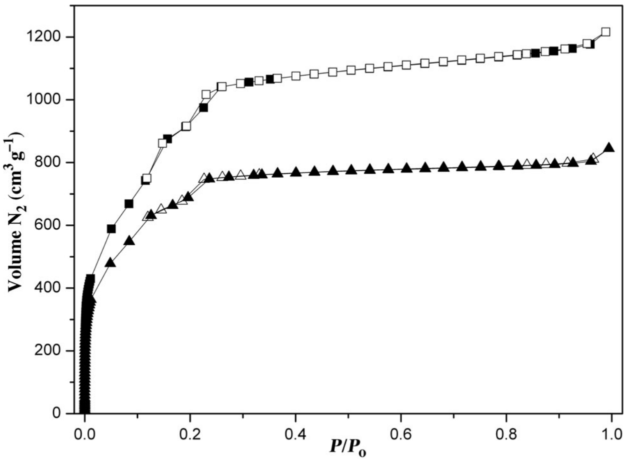


Figure 2. Nitrogen sorption isotherms at 77.3 K for MIL-101(Cr) (■ = adsorption, □ = desorption) and Pd/MIL-101(Cr) (▲ = adsorption, △ = desorption).

**Catalysis of C2-arylation of indoles**: It is well known that the activation of C–H bonds is very important for organic synthesis.[3–7] The C2–H arylation of *N*-methylindoles catalyzed by $Pd(OAc)_2$ in homogeneous catalysis is sensitive to the reaction conditions, such as solvent and/or base. Herein, *N*-methylindole and iodobenzene were employed as the substrates for the screening of optimized reaction conditions for direct C2–H arylation over Pd/MIL-101(Cr). It is noteworthy that almost no C3-arylation product is formed in the following cases. Our initial efforts towards the direct C2–H arylation of *N*-methylindoles in DMF were focused on the base (Table 2, entries 1–5). It should be noted that the reaction can not proceed without addition of a base (Table 2, entry 6). It became apparent that the organic base $NEt_3$ is not a suitable base for this reaction (Table 2, entry 1). A series of inorganic bases has been investigated. The coupling reactions gave moderate yields in the presence of KOAc and $Cs_2CO_3$ (Table 2, entries 3, 4). Interestingly, the results show that cesium acetate is the optimum reagent (85% yield, Table 2, entry 5), which indicates that both the cation ($Cs^+$) and anion ($OAc^-$) play an essential role.[3]

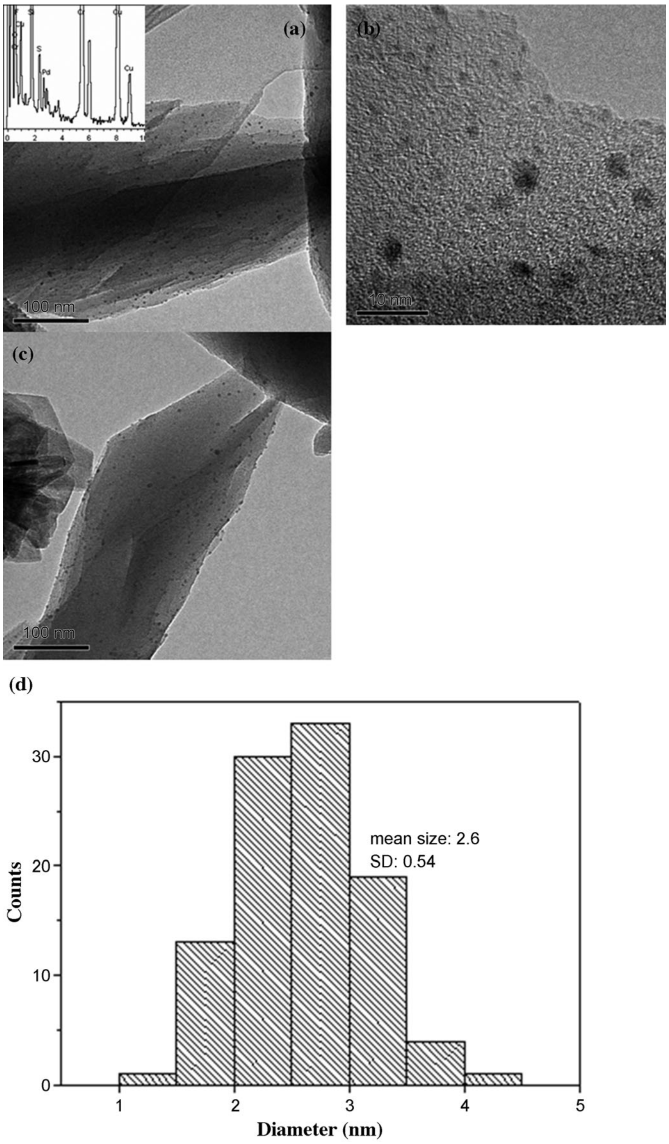


Figure 3. a,b) TEM and HRTEM images of Pd/MIL-101(Cr) (0.56 wt % Pd) before the reaction and c) after five catalytic cycles. d) Size distribution of Pd NPs. The inset of a) shows the energy-dispersive X-ray spectroscopy (EDS) pattern.

Table 1. Surface area measurements for MIL-101(Cr) and Pd/MIL-101(Cr) (0.56 wt % Pd).

| Sample | BET surface area [$m^2 g^{-1}$] | Langmuir surface [$m^2 g^{-1}$] | Pore volume [$cm^{-3} g^{-1}$] | Pore size [nm] |
|---|---|---|---|---|
| MIL-101(Cr) | 3447.7 | 5713.5 | 1.88 | 2.20 |
| Pd/MIL-101(Cr) | 2245.6 | 3800.9 | 1.31 | 2.18 |

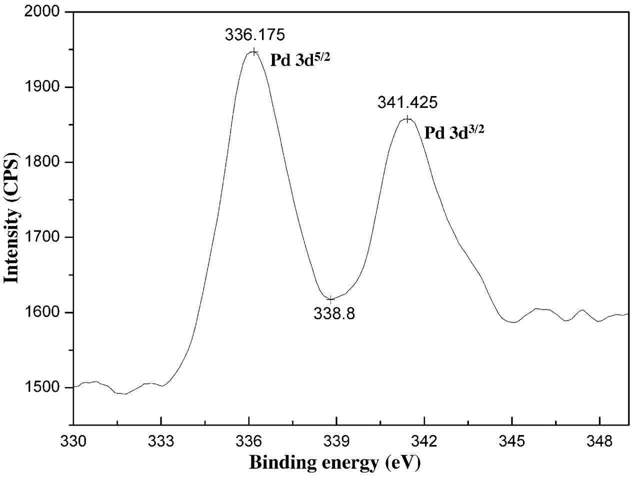
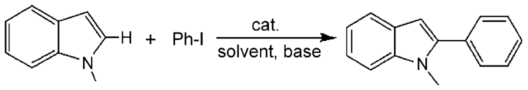


Figure 4. XPS spectrum of a Pd/MIL-101(Cr) sample.

Table 2. Optimization of direct arylation of *N*-methylindole with PhI.[a]



| Entry | Catalyst (Pd [mol %]) | Solvent (3 mL) | Base (2 mmol) | *T* [°C] | Yield [%][b] |
|---|---|---|---|---|---|
| 1 | Pd/MIL-101(Cr) (0.1) | DMF | $NEt_3$ | 120 | trace |
| 2 | Pd/MIL-101(Cr) (0.1) | DMF | $Na_2CO_3$ | 120 | 24 |
| 3 | Pd/MIL-101(Cr) (0.1) | DMF | KOAc[c] | 120 | 41 |
| 4 | Pd/MIL-101(Cr) (0.1) | DMF | $Cs_2CO_3$ | 120 | 38 |
| 5 | Pd/MIL-101(Cr) (0.1) | DMF | CsOAc | 120 | 85 |
| 6[d] | Pd/MIL-101(Cr) (0.1) | DMF | – | 120 | 0 |
| 7 | Pd/MIL-101(Cr) (0.1) | xylene | CsOAc | 120 | trace |
| 8 | Pd/MIL-101(Cr) (0.1) | NMP[e] | CsOAc | 120 | 37 |
| 9 | Pd/MIL-101(Cr) (0.1) | DMA[f] | CsOAc | 120 | 82 |
| 10 | Pd/MIL-101(Cr) (0.1) | DMF | CsOAc | 25 | trace |
| 11 | Pd/MIL-101(Cr) (0.1) | DMF | CsOAc | 75 | 26 |
| 12 | MIL-101(Cr) | DMF | CsOAc | 120 | 0 |
| 13 | Pd/MIL-101(Cr) (0.05) | DMF | CsOAc | 120 | 31 |
| 14 | Pd/MIL-101(Cr) (0.5) | DMF | CsOAc | 120 | 78 |
| 15 | Pd/MIL-101(Cr) (1) | DMF | CsOAc | 120 | 64 (18)[g] |
| 16 | Pd/MIL-101(Cr) (5) | DMF | CsOAc | 120 | 45 (32)[g] |
| 17 | Pd/MIL-101(Cr) (0.01) | DMF | CsOAc | 120 | 31 |
| 18[h] | Pd/MIL-101(Cr) (0.1) | DMF | CsOAc | 120 | trace |
| 19[i] | Pd/MIL-101(Cr) (0.1) | DMF | CsOAc | 120 | 21 |
| 20[j] | Pd/MIL-101(Cr) (0.1) | DMF | CsOAc | 120 | 22 |
| 21[k] | Pd/MIL-101(Cr) (0.1) | DMF | CsOAc | 120 | 57 |
| 22 | Pd/C (0.5) | DMF | CsOAc | 120 | trace (22)[g] |
| 23 | Pd/MIL-53(Al)-$NH_2$[l] (0.5) | DMF | CsOAc | 120 | 25 (11) |

[a] Conditions: *N*-methylindole (1 mmol), iodobenzene (1.2 mmol), $t=$ 24 h, under air. [b] Yield of isolated product based on *N*-methylindole. [c] Ac = acetate. [d] No base was added. [e] NMP = *N*-methyl-2-pyrrolidone. [f] DMA = dimethylacetamide. [g] Biphenyl was formed as byproduct. [h] $t=3$ h. [i] $t=6$ h. [j] The MIL-101(Cr) catalyst was removed after 6 h. The filtrate was kept on stirring for 24 h. [k] $t=12$ h. [l] Pd/MIL-53(Al)-$NH_2$ = Al(OH)[$H_2$N-BDC], $H_2$N-BDC = 2-aminoterephthalic acid.

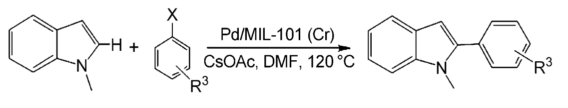
The influence of the solvents was then examined. Xylene was found to be ineffective in promoting the reaction (Table 2, entry 7). NMP was also less effective and gave moderate yield (Table 2, entry 8). It was found that the rate of the coupling reaction was significantly improved and the best yields were obtained in DMF or DMA (Table 2, entries 5 and 9). The temperature also affects the rate of the reaction. The substrates can not be activated at room temperature (Table 2, entry 10). At 75 °C only a low yield was obtained (Table 2, entry 11). To obtain good yields, a higher temperature (120 °C) was required (Table 2, entry 5), which is similar to the corresponding homogeneous reaction catalyzed by $Pd(OAc)_2$.[3]

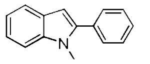
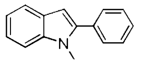
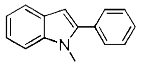
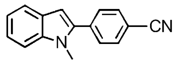
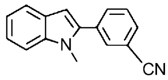
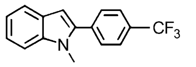
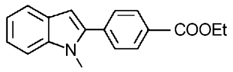
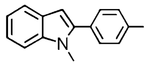
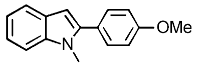
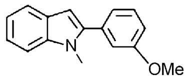
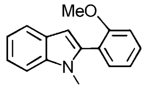
As shown in Table 2, the amount of catalyst is also very important for this reaction. The reaction does not take place in the presence of only MIL-101(Cr). The use of 0.05 mol% Pd catalyst gave only 31% yield (Table 2, entry 13). It is very interesting that *N*-methylindole can be activated effectively by only 0.1 mol% Pd catalyst, which gave a very high yield (86%, Table 2, entry 5). In contrast, higher catalyst loadings (up to 0.5 mol%) are generally required in the homogeneous catalyst system.[3–7] It should be noted that in most cases only traces of the byproduct biphenyl were obtained from the palladium-catalyzed Ullmann coupling reaction of iodobenzene.[3c,12a] However, increasing the amount of the catalyst (starting from 0.5 mol% Pd) led to a steady decrease of the yield of the desired product, but an increase of the yield of the byproduct biphenyl (Table 2, entries 14–16). This observation indicates that the Ullmann coupling reaction represents a key competitive process of the direct C2 arylation of *N*-methylindoles. Consequently, a decrease of the catalyst amount can favor the production of the desired product and suppress the formation of biphenyl, which requires a bimolecular transmetalation of the aryl–palladium species.[3c] The influence of the reaction time was also examined. Considering the slow diffusion of the reactants to reach accessible metal sites in the pores and the low catalyst loading, a long reaction time (about 24 h) was necessary to obtain good yields of the desired product. It is worthy noting that reactions catalyzed by $Pd(OAc)_2$ also need prolonged reaction time (24 h) to give good yields.[3]

For comparison, different supported palladium catalysts have been examined under the same conditions. A commercial Pd/C catalyst (5 wt% Pd) only gave traces of the C2-arylation product and 22% of the byproduct biphenyl (Table 2, entry 22). A low activity was also observed for our previous palladium-supported MIL-53(Al)-$NH_2$ catalyst (Table 2, entry 23), which exhibits high activity for the Suzuki reaction.[19] The high activity of Pd/MIL-101(Cr), as compared to Pd/C and Pd/MIL-53(Al)-$NH_2$, may be ascribed to the larger surface area and accessible mesoporous cages of MIL-101, which may ensure the high dispersion of the palladium active sites and facilitate the diffusion of the reactants and the large product molecules in the pores.[12a] Moreover, it can not be excluded that the enhanced surface Lewis acidity of MIL-101(Cr) may favor the adsorption of the aryl halides, and thus enhance the activity.[12a,b]

We next examined the scope of the reactions with a variety of substituted aryl halides (Table 3). Due to the high bond energy of the C–Br and C–Cl bonds, the activation of bromobenzene and chlorobenzene is difficult. Therefore, the reaction of bromobenzene/chlorobenzene with *N*-methylindole required harsh conditions and extended reaction time. Unfortunately, even at 150 °C after 48 h low yields were obtained for the reaction of bromobenzene/chlorobenzene with *N*-methylindole (Table 3, entries 2 and 3), which is similar to the $Pd(OAc)_2$-catalyzed reactions.[3–7] Interestingly, the reactions proceeded extraordinarily well with a variety of substituted iodobenzenes, bearing electron-withdrawing groups (CN, $CF_3$, and COOEt), with *N*-methylindole, giving excellent yields (Table 3, entries 4–7). Electron-rich functional groups in *para* and *meta* position to the iodine are also well tolerated in these reactions. Reactions between *N*-methylindole and a variety of iodobenzenes substituted with electron-donating groups (4-Me, 3-OMe, and 4-OMe) gave the C2-arylation products in good yields (Table 3, entries 8–10). Notably, the sterically hindered 2-iodoanisole, bearing an electron-donating group, also proceeded smoothly, affording the corresponding C2-arylation product in moderate yield (Table 3, entry 11). It should be noted that only traces of the C3-arylation product were obtained for the above-mentioned, substituted iodobenzenes, except for 2-iodoanisole (about 5% of the C3-arylation product were obtained, due to the sterically hindrance).[3]

Table 3. Direct arylation of *N*-methylindole with various aryl halides.[a]

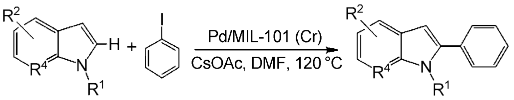


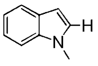
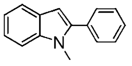
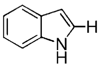
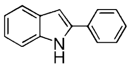
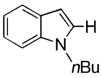
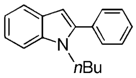
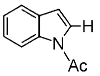
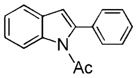
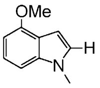
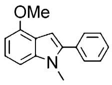
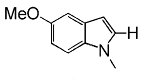
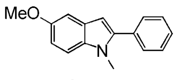
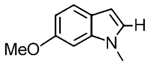
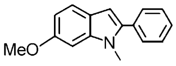
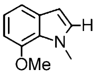
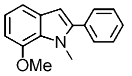
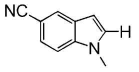
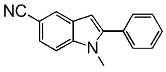
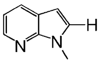
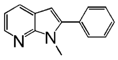
| Entry | X | $R^3$ | Product | Yield [%][b] |
|---|---|---|---|---|
| 1 | I | H |  | 85 |
| 2[c] | Br | H |  | 31 |
| 3[d] | Cl | H |  | 21 |
| 4 | I | 4-CN |  | 89 |
| 5 | I | 3-CN |  | 83 |
| 6 | I | $4-CF_3$ |  | 88 |
| 7 | I | 4-COOEt |  | 86 |
| 8 | I | 4-Me |  | 84 |
| 9 | I | 4-OMe |  | 74 |
| 10 | I | 3-OMe |  | 71 |
| 11[e] | I | 2-OMe |  | 49 |

[a] Conditions: *N*-methylindole (1 mmol), substituted iodobenzene (1.2 mmol), CsOAc (2 mmol), cat. (0.1 mol% Pd), DMF (3 mL), 120 °C, 24 h, under air. [b] Yield of isolated product. [c] Bromobenzene (2 mmol), 150 °C, 48 h. [d] Chlorobenzene (2 mmol),150 °C, 48 h. [e] 2-Methoxyl-iodobenzene (2 mmol), 5% of the C3-arylation product were obtained, based on GC-MS.

Subsequently, the influence of the substituent group at the indole on the direct arylation reactions was also examined. It was found that the process catalyzed by Pd NPs is able to transfer most aryl substituents on the indole to form the C2 regioisomer with excellent selectivity and in good yields (except for the free N–H indole; in this case about 4 % of the C3-arylation product were obtained). As shown in Table 4, the substituent on the indole nitrogen atom dramatically influences the reaction. The *N*-methylindole is more reactive than the free N–H indole (Table 4, entries 1 and 2). Interestingly, the use of *N*-(*n*-butyl)indole gave a higher yield than *N*-methylindole (Table 4, entry 3). In contrast, *N*-acetylindole was inactive in the reaction. The *N*-methylindole derivative, which contains an electron-rich substituent on the 5-position of the benzene segment (Table 4, entry 6) exhibited a higher yield than the derivative with an electron-withdrawing group (Table 4, entry 9). Notably, the substituents at the different positions of the benzene segment obviously affect the yield of the products (Table 4, entries 5–8). The *N*-methylindole derivatives, which contain a methoxy substituent at the 5- or 6-position of the benzene segment gave higher yields than the ones bearing the substituents at the 4- or 7-position. Interestingly, replacing the benzene ring of *N*-methylindole with a pyridine group did not affect the yield (Table 4, entry 10).

Table 4. Direct arylation of various indoles with PhI.[a]



| Entry | Indole | Product | Yield [%][b] |
|---|---|---|---|
| 1 |  |  | 85 |
| 2[c] |  |  | 18[c] |
| 3 |  |  | 91 |
| 4 |  |  | 0 |
| 5 |  |  | 67 |
| 6 |  |  | 84 |
| 7 |  |  | 85 |
| 8 |  |  | 71 |
| 9 |  |  | 78 |
| 10 |  |  | 81 |

[a] Conditions: indole (1 mmol), PhI (1.2 mmol), CsOAc (2 mmol), cat. (0.1 mol % Pd), DMF (3 mL), 120 °C, 24 h. [b] Yield of isolated product. [c] Crude yield based on GC-MS, about 4 % of the C3-arylation product were obtained.

It is known that one of the disadvantages of supported Pd catalysts is the leaching of palladium into solution, resulting in the contamination of the product with metal and the loss of the activity of the supported Pd catalysts.[20] For these reasons, leaching of the metal from the Pd/MIL-101(Cr) catalyst has been examined. After the workup, inductively coupled plasma atomic emission spectroscopy (ICP-AES) analysis showed that the amount of Pd leaching into the reaction mixture was very low (0.4 ppm), which satisfies specifications required by the pharmaceutical industry regarding the final purity of the products ($c$(Pd) < 2 ppm).[20] The result may be attributed to the fact that the escape of the nanoparticles from the mesoporous cages (2.9 and 3.4 nm) is difficult through the microporous windows (1.2 and 1.4 nm). There was also no detectable leaching of chromium to the reaction mixtures because of the high stability of MIL-101(Cr) ($c$(Cr) < 0.1 ppm for drinking water),[18a] so the support will not contaminate the environment. If the catalyst was removed after 20 % of conversion (after 6 h) and the resulting filtrate was monitored under identical reaction condition for another 24 h; no further conversion was detected (Table 2, entry 20). Advantages of the Pd/MIL-101(Cr) catalyst are the fact that the catalytic reactions can be conveniently carried out in air and that the separation of the catalyst can be achieved easily by centrifugation. After being recycled for five runs of the reaction of *N*-methylindole and iodobenzene, the Pd catalyst still exhibits a remarkable activity (the yield decreased only for 4 %) (Figure 5). The PXRD study showed that the crystalline structure of the catalyst is mostly retained after five catalytic cycles (Figure 1). The TEM image of the reused catalyst revealed that the size of the Pd NPs is very similar to that before the reaction (Figure 2). This may be ascribed to the fact that the Pd NPs are confined in the mesoporous cages and their growth is thus re-

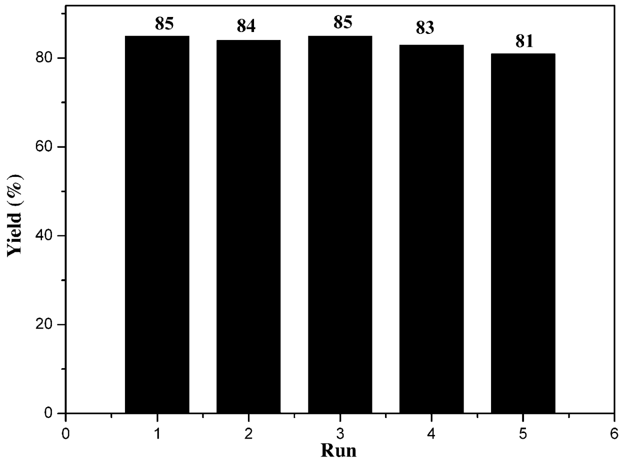


Figure 5. Catalytic activity of the recycle experimental of *N*-methylindole and iodobenzene at 120 °C for 24 h. Every experiment was repeated twice and the yields are the average of the two experiments. The error was within 3 %.

stricted. These results indicate that the reaction proceeds in a heterogeneous fashion.[12–15]

## Conclusion

In conclusion, we have developed a highly efficient heterogeneous catalyst system for the direct C2 arylation of indoles by using Pd NPs encapsulated in the mesoporous MOF MIL-101(Cr). The direct C2 arylation of indoles by using only 0.1 mol% Pd as catalyst afforded the desired products in good yields. Furthermore, the catalyst is easily recoverable and can be reused several times without leaching and loss of activity.

## Experimental Section

**Materials**: MIL-101(Cr)[16] and MIL-53(Al)-$NH_2$[21] were synthesized according to the literatures. The as synthesized MIL-101(Cr) was activated by solvothermal treatment with DMF (150 °C for 12 h), aqueous $NH_4F$ solution (0.1 M, 70 °C for 12 h), and EtOH (120 °C for 12 h), respectively. The obtained blue-green MIL-101(Cr) samples were dried at 150 °C under vacuum for 24 h. The obtained MIL-53(Al)-$NH_2$ was washed with DMF, followed by soaking in methanol at 70 °C for 24 h. The solid was finally dried overnight at 130 °C under vacuum. The catalysis substrates 5-cyano-*N*-methylindole, 4-methoxyl-*N*-methylindole, 5-methoxyl-*N*-methylindole, 6-methoxyl-*N*-methylindole, 7-methoxyl-*N*-methylindole, and 1-methyl-1*H*-pyrrolo[2,3-b]pyridine were synthesized according to the literatures.[3c] *N*-(*n*-Butyl)indole was synthesized by a similar method described in the literature[3c] by using indole and butyl bromide in the presence of NaH at 0 °C. All other reagents were commercial purchased and used as received.

**Catalyst preparation**: Pd/MIL-101(Cr) was prepared through a simple impregnation method. Typically, the activated MIL-101(Cr) powder (200 mg) was dispersed in deionized water (20 mL) and was subjected to ultrasonication for 30 min. A fresh aqueous solution of $Pd(NO_3)_2$ (10 mg, 10 mL) was slowly added dropwise to this solution under vigorous stirring for about 15 min. The suspension was then stirred at room temperature for further 24 h. The impregnated MIL-101(Cr) sample was washed with water till the filtrate became colorless and was dried under vacuum at 150 °C for 24 h. The as synthesized sample was treated in a stream of $H_2$ at 200 °C for 4 h to give Pd/MIL-101(Cr). The Pd loading on the MIL-101(Cr) was 0.56 wt% based on ICP-AES analysis. Pd/MIL-53(Al)-$NH_2$ was prepared by using an ion exchange method.[19] The Pd loading on the MIL-53(Al)-$NH_2$ was 0.97 wt% based on ICP-AES analysis.

**Typical catalysis experimental procedure**: Typically, *N*-methylindole (1 mmol), aryl halide (1.2 mmol), CsOAc (2 mmol), and the palladium catalyst (20 mg, 0.1 mol% Pd) were added to DMF (3 mL). The reaction mixture was stirred at 120 °C for 24 h. After cooling to room temperature, the solution was centrifuged and washed with ethyl acetate for three times. The organic phase was subsequently washed with water and brine and then dried over $Na_2SO_4$. The product was purified by silica gel chromatography (mixture of light petroleum and ethyl acetate as eluent). The identification was conducted by $^1H$ and $^{13}C$ NMR measurement.

For the measurement of the Pd leaching during the reaction, a hot-filtration experiment was run to investigate if the reaction proceeded in a heterogeneous or homogeneous fashion. After 6 h, the catalyst was separated by hot filtration and the filtrate was further treated under the same conditions for another 24 h. For the recyclability test, the catalyst was recovered from each of the reaction of *N*-methylindole with iodobenzene at 120 °C for 24 h, washed with water and ethanol several times, and then dried under vacuum at 150 °C for the next use.

## Acknowledgements

We acknowledge the financial support from 973 Program (2011CB932504, 2007CB815303), NSFC (2103128, 20731005 and 91022007), Fujian Key Laboratory of Nanomaterials (2006L2005), the Key Project from CAS and FJIRSM (SZD07002).

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Received: June 4, 2011