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# Abstract

## A highly efficient and recyclable $Fe_3O_4$ magnetic nanoparticles immobilized palladium catalyst for the direct C-2 arylation of indoles with arylboronic acids

**Lei Zhang,[a] Pinhua Li,[a] Can Liu,[a] Jin Yang,[a] Min Wang,[a] and Lei Wang*[a,b]**

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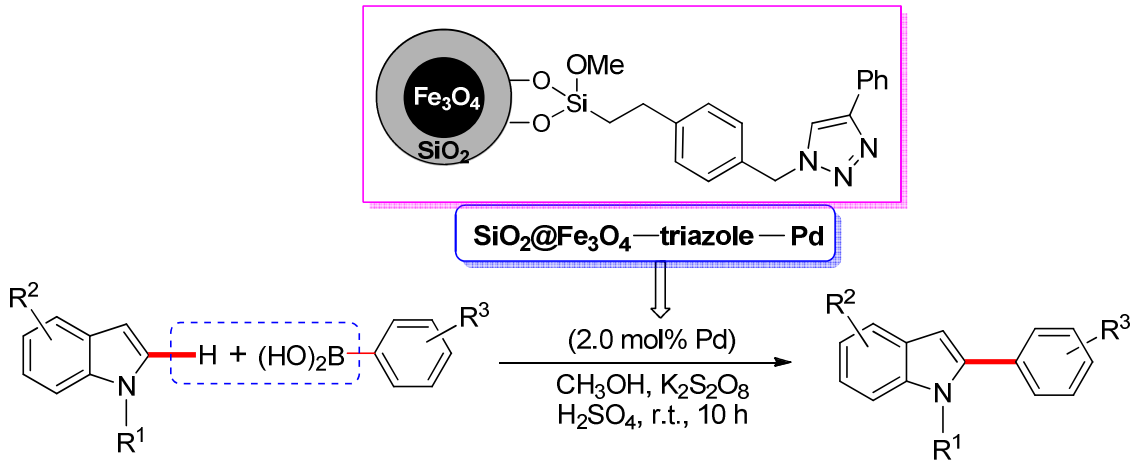


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Paper

# A highly efficient and recyclable $Fe_3O_4$ magnetic nanoparticles immobilized palladium catalyst for the direct C-2 arylation of indoles with arylboronic acids

**Lei Zhang,[a] Pinhua Li,[a] Can Liu,[a] Jin Yang,[a] Min Wang[a] and Lei Wang*[a,b]**

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**A highly efficient $Fe_3O_4$ magnetic nanoparticles (MNPs) immobilized palladium catalyst was prepared and applied in the direct C-2 arylation of indoles with arylboronic acids. The reactions generated the corresponding cross-coupling products in good yields. In addition, the supported catalyst with low loading (2.0 mol%) showed high stability, which could be recovered and reused for 8 times without significant loss of its activity.**

## Introduction

The indoles are one of the most important nitrogen-containing organic molecules, which are widely presented in natural products, materials, and bioactive compounds, such as antibiotics and anticancers.[1] Over the past decades, C-2 arylation of indoles received considerable attention due to C-2 arylated indoles are important building blocks for the natural products and pharmaceuticals.[2] For the synthesis of these compounds and their further functionalization, remarkable progress has been made by a numbers of organic chemists.[3] In 2005, a one–pot synthesis of indoles from *o*-haloanilines and alkenyl halides was reported by Barluenga,[3a] and a Pd-catalyzed tandem C–N/C–C coupling of *gem*-dihalovinyl with arylboronic acids for the synthesis of 2-arylated indoles was developed by Lautens.[3b] Then, a Au-catalyzed cross-coupling-cyclization reaction of terminal alkynes with 2-iodoaniline to form C-2 arylated indoles in excellent yields was described by our group,[3c] and a Pd-catalyzed synthesis of 2-arylindoles from ammonia and bromophenylacetylenes was report by Stradiotto.[3d] Recently, transition-metal-catalyzed C–H bond activation has contributed greatly to the construction of C–C bonds in organic synthesis.[4] Most importantly, the direct C-2 arylation of indoles has recently attracted significantly attention. Palladium-catalyzed cross-coupling reactions between functionalized indoles and activated arenes are an efficient and concise approach to 2-arylated indoles,[5] and significant achievements which have been accomplished are based on Pd-catalyzed direct C-2 arylation of indoles with a variety of coupling partners, such as aryl halides,[2h,6] hypervalent iodine arylating agents,[7] organoboranes,[8] organosilanes[9] and sodium sulfinates.[10] Although homogeneous palladium catalysts exhibit excellent activity, homogeneous catalysis suffers from the high expense, and it is worth noting that large amounts of palladium catalysts were used, which attendant brings a series of problems, such as catalyst separation and recycling, heavy metal contamination of the product purification, economic concern in large-scale syntheses could not be ignored. The supported catalysts have become extremely powerful tools in the development of modern methods for chemical synthesis, due to the increasing environmental concerns, and exploring environmentally friendly supported catalysts is becoming more and more important because they are fits for green methodologies and they have more advantages, such as the easier separation, recovery, reuse of the catalyst and the removal conveniently of the expensive and/or toxic heavy metal complexes from the reaction medium.[11]

More recently, magnetite $Fe_3O_4$ nanoparticles have been emerged widely for various areas, such as biotechnology, medical applications, environmental remediation.[12] Application of functionalized magnetic nanoparticles (MNPs) has been extensively explored in organic synthesis,[13] which have been considered as excellent and ideal supports with significant industrial potential for immobilization because the magnetic nanoparticles supported catalysts are readily available, chemically stable and can be prepared by simple methods.[14] Furthermore, these MNPs can be easily separated from the reaction medium by an external permanent magnet, which achieves simple separation of the catalysts without filtration. Recently, Rosario-Amorin and Heuzé have developed an efficient magnetic nanoparticle–supported metallodendritic Pd-catalyzed Suzuki C–C coupling reactions.[15] After that, Pericàs and his co-workers reported MacMillan-type organocatalysts used "click" strategy for the asymmetric Friedel-Crafts alkylation of *N*-substituted pyrroles with *α,β*-unsaturated aldehydes.[16] Meanwhile, Varma et al. have prepared $Fe_3O_4$-dopamine-Pd/Ru/Ni catalyst successfully and used in a variety of organic transformations.[17] Recently, we have developed a series of $Fe_3O_4$ magnetic nanoparticles immobilized catalysts and used in the organic transformations.[18] Following the research of our group, we focused our attention on developing

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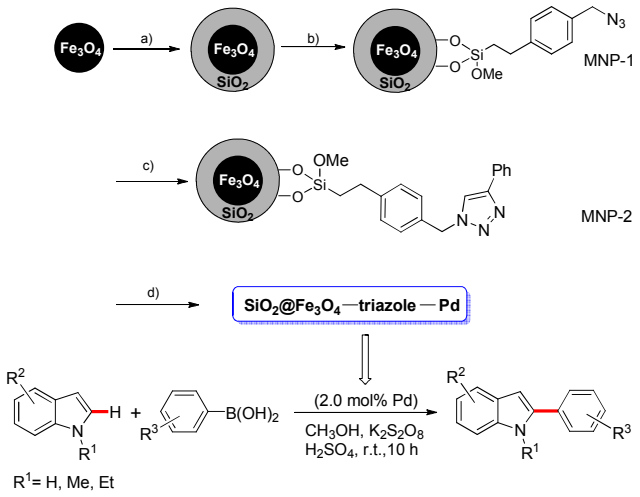
new MNPs supported palladium catalysts and their application in the organic reactions. Triazoles has been gained much attention for catalyst immobilization as a high stable linker and a chelator, and researchers have successively explored many their metal catalysts, such as Pd,[19] Au[20] and V.[21] Recently reports have been shown that 1,4-substituted 1,2,3-triazole could be used as a potentially mono-dentate ligand coordinating to Pd(II).[22] Inspired by its attractive features, herein we attempt to apply "click" chemistry concept, forming 1,2,3-triazole as a mono-dentate ligand to coordinate with $Pd^{II}$ and providing 1,2,3-triazole-$Pd^{II}$ complex immobilized on the $Fe_3O_4$ magnetic nanoparticles (MNPs). The results indicated that the MNPs-1,2,3-triazole-Pd catalyst exhibits high catalytic activity for the direct C-2 arylation of indoles with arylboronic acids (Scheme 1). More importantly, the supported catalyst could be recovered and reused well for 8 times without significant loss of its catalytic activity.




**Scheme 1** Preparation of magnetic nanoparticles-supported palladium catalyst and its application in C-2 arylation of indoles.

Reaction conditions: a) $Si(OEt)_4$, EtOH; b) (4-(azidomethyl)phenethyl)trimethoxysilane, toluene; c) phenylacetylene, $CuSO_4$, NaAsc, *tert*-butanol/$H_2O$; d) $Pd(OAc)_2$, THF.

## Results and discussion

The magnetic nanoparticles supported palladium catalyst was synthesized according to the procedure in Scheme 1. The silica-coated $Fe_3O_4$ ($SiO_2$@$Fe_3O_4$) was prepared according to the literature,[23] the prepared $Fe_3O_4$ nanoparticles, with an average diameter of 140 nm (Figure 1), were coated with a thin layer of silica using a sol-gel process to give silica-coated $Fe_3O_4$. TEM images of the $SiO_2$@$Fe_3O_4$ indicated the core-shell structure of the particles, and the silica coating, which has a uniform thickness of 20 nm (Figure 2). The azide could be anchored easily onto the surface of the $SiO_2$@$Fe_3O_4$ by using (4-(azidomethyl)phenethyl)trimethoxysilane at reflux temperature in toluene for 24 h, with a loading of 0.206 mmol of azide per gram, which was quantified via CHN microanalysis based on the carbon content determination. Immobilization of the triazole moieties was carried out by the ''click'' reaction of phenylacetylene with the azide functionalized magnetic core-shell nanoparticles in the presence of copper sulfate and sodium ascorbate in aqueous methanol solution for 24 h to form the triazole loaded magnetic nanoparticles, with a loading of 0.27 mmol of triazole per gram, which was quantified by CHN microanalysis on the basis of nitrogen content determination. The supported Pd catalyst was obtained by dissolving $Pd(OAc)_2$ in THF and treating it with the above triazole-functionalized $SiO_2$@$Fe_3O_4$, with a loading of 0.166 mmol of palladium per gram determined via inductively coupled plasma atomic emission spectrometry (ICP-AES). XRD measurements of the supported palladium catalysts exhibited diffraction peaks corresponding to the typical spinel maghemite structure and the diffraction peak of the layered amorphous silica was not obvious. There were also no peaks characteristic for palladium(0) nanoparticles observed, proving that the good dispersion of the palladium sites on the magnetic nanoparticles (Figure 3). However, there will be aggregated in some extent after several cycles (Figure 2, a *vs* b).

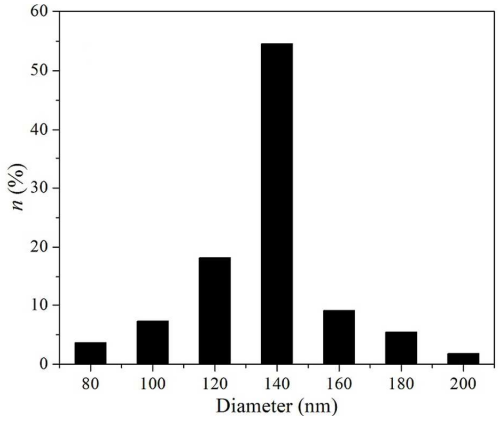



**Figure 1** The size of $SiO_2$@$Fe_3O_4$–triazole–Pd particles and their distribution

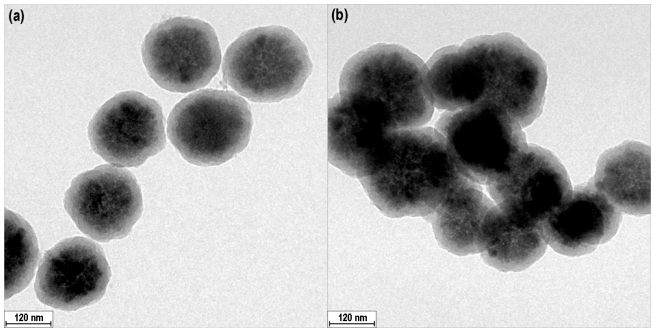



**Figure 2** TEM images of the catalysts: (a) $SiO_2$@$Fe_3O_4$–triazole–Pd catalyst; (b) recycled $SiO_2$@$Fe_3O_4$–triazole–Pd catalyst

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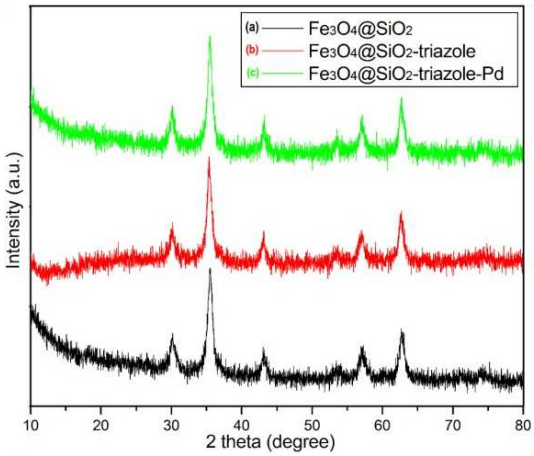
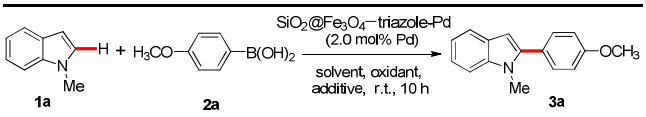



**Figure 3** XRD determinations of the supported catalysts

In order to evaluate the catalytic activity of obtained catalyst, a direct arylation of 1-methylindole (**1a**) with 4-methoxyphenylboronic acid (**2a**) was chosen as model reaction for our investigation, and the results were listed in Table 1. Initially, the influence of oxidant on the model reaction was explored using the MNPs-immobilized palladium catalyst ($SiO_2$@$Fe_3O_4$-triazole-Pd, containing 2.0 mol% Pd) in $CH_3OH$ with $CH_3CO_2H$ (0.5 equiv) as additive at room temperature (Table 1, entries 1–8).[7] Among the tested oxidants, $K_2S_2O_8$ exhibited the highest activity and 68% of desired product **3a** was obtained. $O_2$, TBHP, and TBPB were subsequently inferior, and **3a** was isolated in 39–56% yields. However, BQ, DDQ, $PhI(OAc)_2$ and $(NH_4)_2S_2O_8$ were found to be ineffective for this reaction. No desired product was formed in the absence of oxidant (Table 1, entry 9). Then the influence of the solvents on the reaction was examined, and a significant solvent effect was observed. Good yield was obtained with $CH_3OH$ (Table 1, entry 1). $C_2H_5OH$ and 1,4-dioxane was found to be inferior (Table 1, entries 10 and 11). No desired product **3a** was observed when the reaction was performed in DMSO, DMF, $CH_3CN$, $CH_2Cl_2$, THF, or toluene (Table 1, entries 12–17). The additive was also investigated and the results clearly indicated that 0.50 equiv of $H_2SO_4$ was the best one and gave the product **3a** in 81% yield (Table 1, entry 18). $CF_3CO_2H$, $CF_3SO_3H$ and PivOH shut down the reaction completely (Table 1, entries 19–21). Other organic acids, such as $PhCO_2H$, *o*-$NO_2PhCO_2H$, or *p*-$NO_2PhCO_2H$ were less effective (Table 1, entries 22–24). In the absence of any additive, only 30% yield of **3a** was obtained (Table 1, entry 25). The loading of the catalyst was also examined. As shown in Table 1, it was found that catalyst loading affected the reaction obviously. The use of 0.50 mol% Pd catalyst only gave **3a** in 20% yield. Increasing the amount of catalyst loading up to 1.0 mol%, 57% yield of **3a** was obtained. However, the yields of **3a** were not improved significantly upon increasing the amount of catalyst loading up to 3.0 mol%. Thus, 2.0 mol% of catalyst was the best choice (Table 1, entry 26). During further investigation of the reaction time, the model reaction was found to be completed in 10 h at room temperature (Table 1, entry 27).

**Table 1** Optimization of the cross-coupling between *N*-methyl indole and (4-methoxyphenyl)boronic acid[a]




| Entry | Solvent | Oxidant | Additive | Yield [%][b] |
|---|---|---|---|---|
| 1 | $CH_3OH$ | TBHP | $CH_3CO_2H$ | 42 |
| 2 | $CH_3OH$ | TBPB | $CH_3CO_2H$ | 39 |
| 3 | $CH_3OH$ | $O_2$ | $CH_3CO_2H$ | 56 |
| 4 | $CH_3OH$ | $K_2S_2O_8$ | $CH_3CO_2H$ | 68 |
| 5 | $CH_3OH$ | $PhI(OAc)_2$ | $CH_3CO_2H$ | trace |
| 6 | $CH_3OH$ | BQ | $CH_3CO_2H$ | NR |
| 7 | $CH_3OH$ | DDQ | $CH_3CO_2H$ | NR |
| 8 | $CH_3OH$ | $(NH_4)_2S_2O_8$ | $CH_3CO_2H$ | NR |
| 9 | $CH_3OH$ | — | $CH_3CO_2H$ | NR |
| 10 | $C_2H_5OH$ | $K_2S_2O_8$ | $CH_3CO_2H$ | 49 |
| 11 | 1,4-dioxane | $K_2S_2O_8$ | $CH_3CO_2H$ | 17 |
| 12 | DMSO | $K_2S_2O_8$ | $CH_3CO_2H$ | NR |
| 13 | DMF | $K_2S_2O_8$ | $CH_3CO_2H$ | NR |
| 14 | $CH_3CN$ | $K_2S_2O_8$ | $CH_3CO_2H$ | NR |
| 15 | $CH_2Cl_2$ | $K_2S_2O_8$ | $CH_3CO_2H$ | NR |
| 16 | THF | $K_2S_2O_8$ | $CH_3CO_2H$ | NR |
| 17 | Toluene | $K_2S_2O_8$ | $CH_3CO_2H$ | NR |
| ***18*** | ***$CH_3OH$*** | ***$K_2S_2O_8$*** | ***$H_2SO_4$*** | ***81*** |
| 19 | $CH_3OH$ | $K_2S_2O_8$ | $CF_3CO_2H$ | NR |
| 20 | $CH_3OH$ | $K_2S_2O_8$ | $CF_3SO_3H$ | NR |
| 21 | $CH_3OH$ | $K_2S_2O_8$ | PivOH | NR |
| 22 | $CH_3OH$ | $K_2S_2O_8$ | $PhCO_2H$ | 42 |
| 23 | $CH_3OH$ | $K_2S_2O_8$ | *o*-$NO_2PhCO_2H$ | 55 |
| 24 | $CH_3OH$ | $K_2S_2O_8$ | *p*-$NO_2PhCO_2H$ | 53 |
| 25 | $CH_3OH$ | $K_2S_2O_8$ | — | 30 |
| 26 | $CH_3OH$ | $K_2S_2O_8$ | $H_2SO_4$ | 20[c]<br>57[d]<br>81[e]<br>43[f] |
| 27 | $CH_3OH$ | $K_2S_2O_8$ | $H_2SO_4$ | 79[g]<br>81[h] |

[a] Reaction conditions: 1-methylindole (**1a**, 0.50 mmol), 4-methoxyphenylboronic acid (**2a**, 1.0 mmol), oxidant (1.0 mmol), additive (0.25 mmol), $SiO_2$@$Fe_3O_4$–triazole-Pd catalyst (60 mg, containing Pd 0.01 mmol, 2.0 mol%), in solvent (2.0 mL) at room temperature and stirred for 12 h. [b] Isolated yields. [c] 0.5 mol% of $SiO_2$@$Fe_3O_4$–Pd catalyst was used. [d] 1.0 mol% of $SiO_2$@$Fe_3O_4$–triazole-Pd catalyst was used. [e] 3.0 mol% of $SiO_2$@$Fe_3O_4$–triazole-Pd catalyst was used. [f] for 4 h. [g] for 8 h. [h] for 16 h. BQ = 1,4-benzoquinone; DDQ = 2,3-dichloro-5,6-dicyano-1,4-benzoquinone; TBHP = *tert*-butyl hydroperoxide; TBPB = *tert*-butyl peroxybenzoate; PivOH = pivalic acid.

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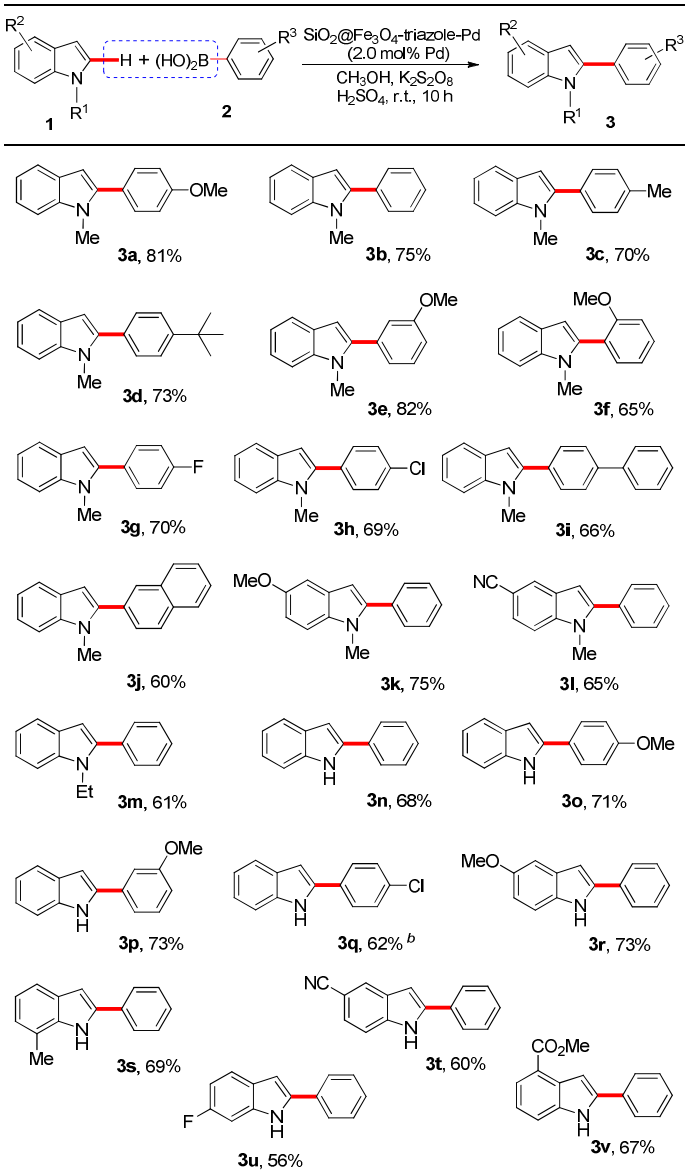
We next examined the versatility of this protocol, the $SiO_2$@$Fe_3O_4$–triazole-Pd catalyzed C-2 arylation of a variety of substituted indoles with different aryl boronic acids were investigated under the optimized reaction conditions and the results were summarized in Scheme 2. As shown in Scheme 2, good yields of the corresponding products were obtained in the reaction of 1-methylindole with different arylboronic acids in the most cases. The reaction of 1-methylindole (**1a**) with phenylboronic acid generated the corresponding product 1-methyl-2-phenylindole (**3b**) in 75% yield. It is worth noting that the substituted aryl boronic acids with both electron-rich and electron-poor groups, such as $CH_3$, $CH_3O$, *t*-Bu, biphenyl, F and Cl groups at the *para*- or *meta*-positions on the benzene rings tolerated the reaction with **1a** under the present reaction conditions, and generated the corresponding products in good to excellent yields (Scheme 2, **3a**, **3c–e**, and **3g–3i**, 66−82% yields). The steric effect was observed when arylboronic acid with *para*-, *meta*-, or *ortho*-methoxy on the benzene ring was used as one of the substrate to react with **1a** (Scheme 2, **3a** and **3e**, *vs* **3f**). It should be noted that the reaction of 1-methylindole with naphthalen-2-ylboronic acid underwent direct C-2 arylation to generate the corresponding product **3j** in 60% yield (Scheme 2, **3j**).

Finally, the substitution effect in the indole moiety was investigated under the standard reaction conditions. Indoles, which containing electron-donating groups, such as MeO or Me on the phenyl rings reacted smoothly with arylboronic acids and generated the corresponding direct C-2 arylation of indoles products (Scheme 2, **3k**, **3r**, **3s**). However, the product yields of the reactions of indoles containing electron-withdrawing groups, for instance, CN, F and $CO_2Me$ on the phenyl rings with arylboronic acids were slightly lower (Scheme 2, **3r** and **3s** *vs* **3t–3v**). In the case of the free N-H indole, it was found that it slightly less reactive than 1-methyl indole, giving the corresponding products in good yields (Scheme 2, **3a** *vs* **3o**; **3b** *vs* **3n**; **3e** *vs* **3p**; **3h** *vs* **3q**; **3k** *vs* **3r**; **3l** *vs* **3t**). When 1-ethyl indole was used instead of 1-methyl indole to react with phenylboronic acid under the recommended reaction conditions, 61% of **3m** was isolated (Scheme 2). However, when 1-(*n*-butyl)indole or 1-pivaloyl indole reacted with phenylboronic acid, no corresponding product was obtained, probably due to the steric hindrance.

In addition, the recovery and reuse of the developed magnetic nanoparticles supported palladium catalyst was examined, 4-methoxyphenylboronic acid and 1-methylindole were chosen as model substrates. After the reaction carried out under the optimized reaction conditions, the catalyst was washed with diethyl ether, ethanol and water respectively, dried in air and reused for the next reaction. It was found that the supported catalyst could be recycled and reused for 8 consecutive trials without significant loss of its catalytic activity (Table 2). Moreover, palladium leaching in $SiO_2$@$Fe_3O_4$-triazole-Pd catalyst was determined. ICP analysis of the reaction solution indicated that Pd contents were less than 0.20 ppm.

According to the literature[7,8a,8c,8d,24] and our observation, the possible reaction mechanism is via a Pd(0)/Pd(II) process. Initially, the Pd (II) catalyst reacts with C–H of indole in the C-2 position to form an Ar-Pd(II)-OAc intermediate, which is subsequently displaced by arylboronic acid to generate an aryl-palladium complex, Ar-Pd(II)-Ar'. Then, a reductive elimination of the formed Ar-Pd(II)-Ar' affords the coupling product and Pd(0) species, which is oxidized by $K_2S_2O_8$ to regenerate Pd(II), completing the catalytic cycle.




**Scheme 2** $Fe_3O_4$ magnetic nanoparticles immobilized palladium catalyzed C-2 arylation of indoles with arylboronic acids.

Reaction conditions: indole (0.50 mmol), arylboronic acid (1.0 mmol), $K_2S_2O_8$ (1.0 mmol), $H_2SO_4$ (0.25 mmol), $SiO_2$@$Fe_3O_4$–triazole-Pd catalyst (60 mg, containing Pd 0.01 mmol, 2.0 mol%), $CH_3OH$ (2.0 mL), room temperature, 12 h; isolated yields of the products.

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**Table 2** Recycling $SiO_2$@$Fe_3O_4$–triazole-Pd catalyst for the direct C-2 arylation of 1-methyl indole with (4-methoxyphenyl)boronic acid[a]


| Run | Yield (%)[b] | Run | Yield (%)[b] |
|---|---|---|---|
| 1 | 81 | 5 | 79 |
| 2 | 81 | 6 | 78 |
| 3 | 80 | 7 | 77 |
| 4 | 79 | 8 | 76 |

[a] Reaction conditions: 1-methylindole (**1a**, 0.50 mmol), 4-methoxyphenylboronic acid (**2a**, 1.0 mmol), $K_2S_2O_8$ (1.0 mmol), $H_2SO_4$ (0.25 mmol), $SiO_2$@$Fe_3O_4$–triazole-Pd catalyst (60 mg, containing Pd 0.01 mmol, 2.0 mol%), in $CH_3OH$ (2.0 mL) at room temperature and stirred for 12 h. [b] Isolated yields.

## Conclusions

In summary, we have successfully applied a recyclable MNPs–triazole–Pd catalyst in the direct C-2 arylation of indoles reactions. A variety of substituted indoles reacted with different aryl boronic acids in the presence of 2.0 mol% supported palladium catalyst, affording the corresponding products in good yields. It is important to note that the supported catalyst could be recovered and reused at least 8 times without significant loss of its activity. The operationally simple procedure for the catalyst preparation and recovery of the catalyst make it an ideal catalytic system for the direct C-2 arylation of indoles reaction.

## Experimental Section

### 1. General Remarks

The chemicals were purchased from commercial suppliers (Aldrich, USA and Shanghai Chemical Company, China) and were used without purification prior to use. All $^1$H NMR and $^{13}$C NMR spectra were recorded at 400 MHz and 100 MHz by a Bruker 400 MHz FT-NMR spectrometer, respectively. Chemical shift are given as δ value with reference to tetramethylsilane (TMS) as internal standard. The CHN analysis was performed on a Vario El III elementar. The Pd content was determined by a Jarrell-Ash 1100 ICP analysis. Transmission electron micrograph (TEM) images were obtained at JEOL-2010 transmission electronic microscopy. X-ray diffraction (XRD) measurements were carried out at room temperature using a Bruker D8 Advance X-ray powder diffractmeter. X-ray photoelectron spectroscopy (XPS) measurements were performed on a Perkin-Elmer PHI 5000C ESCA system. Products were purified by flash chromatography on 200–300 mesh silica gel, $SiO_2$.

### 2. Preparation of the magnetic nanoparticles supported palladium catalyst

#### 2.1 Synthesis of the magnetic nanoparticles ($Fe_3O_4$)

The magnetic microspheres were synthesized according to the literature.[23] $FeCl_3$·$6H_2O$ (5.4 g) was dissolved in 120 mL of ethylene glycol stirring for 1.0 h. Then 12.0 g of sodium acetate were added to the solution. After stirring for 1.0 h, the resultant solution was transferred into a Teflon-lined stainless-steel autoclave (200 mL). The autoclave was sealed and heated at 200 °C for 10 h, then cooled to room temperature. The magnetic microspheres were separated by using an external magnet, washed with ethanol and diethylether each for three times and dried under vacuum.

#### 2.2 Synthesis of the silica-coated magnetic nanoparticles ($SiO_2$@$Fe_3O_4$)

Generally, the magnetite particles (0.18 g) were treated with HCl aqueous solution (5.0 mL, 2.0 mol/L) under ultrasound for 3 min. And 2.0 mL of $NH_3$·$H_2O$ were added to a mixture of deionized water (15.0 mL) and ethanol (85.0 mL), the mixture was then sonicated for approximately 0.50 h. To this well dispersed magnetic nanoparticles solution, followed 1.0 g of $Si(OEt)_4$ was slowly added, the solution was stirred for 12 h at room temperature. Finally, the product was washed with deionized water until the solution was neutral, then washed with ethanol and diethylether each for three times and dried under vacuum.

#### 2.3 Synthesis of azide-functionalized $SiO_2$@$Fe_3O_4$

(4-(Azidomethyl)phenethyl)trimethoxysilane[19a] (0.494 g) dissolved in dry toluene (10.0 mL), were added to a suspension of $SiO_2$@$Fe_3O_4$ (2.0 g) in dry toluene (45.0 mL). Then the mixture was shaking for 24 h at 100 °C. The product was separated by using an external magnet, washed with toluene and $CH_2Cl_2$ three times to remove the un-immobilized species and dried under vacuum.

#### 2.4 Synthesis of triazole-functionalized magnetic nanoparticles ($SiO_2$@$Fe_3O_4$)

Azide-functionalized $SiO_2$@$Fe_3O_4$ (1.0 g) was dispersed in the MeOH/$H_2O$ (80 mL, v/v = 1/1). Then phenylacetylene (0.122 g, 1.2 mmol), $CuSO_4$•$5H_2O$ (0.013 g, 0.05 mmol), sodium ascorbate (0.033 g, 0.17 mmol) were added to the mixed solution. The reaction mixture was stirred at 60 °C for 24 h in air. Then the product ($SiO_2$@$Fe_3O_4$-triazole) was separated by using an external magnet and washed with methanol, deionized water, ethanol, ether each of three times to remove excess components. Finally, the product was dried under vacuum at 60 °C.

#### 2.5 Synthesis of $SiO_2$@$Fe_3O_4$-Pd

Palladium acetate (11.2 mg, 0.05 mmol) and THF (8.0 mL) were added to a sealable reaction tube. The solution was shaking at room temperature for 10 min, and then 1.0 g of the above triazole-functionalized magnetic nanoparticles ($SiO_2$@$Fe_3O_4$-triazole) was added. The mixture was shaking at room temperature for 5 h, then the catalyst was magnetically separated using external magnate, and the solid was washed with THF three times, and dried under vacuum at 50 °C for 3 h.

#### 2.6 Preparation of the TEM samples

First a small amount of the catalyst was dispersed in ethanol, ultrasonic dispersed about 15 minutes, allowing large particles precipitated for 3-5 minutes. Then take 3 drops of superficial

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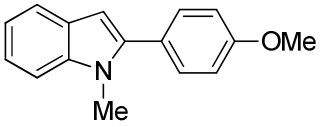
liquid on the copper grid. At last the sample dried at room temperature then observed by TEM.

### 2.7 Preparation of the XRD samples

The catalyst sample was placed in a mortar grinding for about 20 minutes. Then the sample powder was sprinkled on the glass slide as evenly as possible. After that the sample was dispersed evenly with ethanol, the sample dried at room temperature.

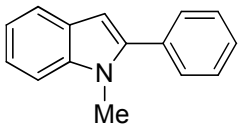
## 3. General procedure for the direct C-2 arylation of indoles

1-Methylindole (0.5 mmol), 4-methoxyphenylboronic acid (1.0 mmol), $K_2S_2O_8$ (1.0 mmol) and $SiO_2$@$Fe_3O_4$–Pd catalyst (60 mg, containing Pd 0.01 mmol) were added to a reaction tube. Anhydrous $CH_3OH$ (4.0 mL) was added, then $H_2SO_4$ (0.25 mmol) was added to the mixture. The resulting solution was then stirring for 10 h at room temperature. After the catalyst separated by magnetic, the catalyst was washed with diethyl ether, alcohol, water, diethyl ether each of three times, and used directly for the next run. The organic phase was evaporated under the reduced pressure and the product was purified by column chromatography on silica gel.



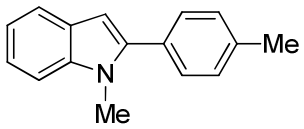

**3a: 2-(4-Methoxy-phenyl)-1-methyl-1*H*-indole**

White solid. m.p. 117.2–119.5 °C (lit.[7] m.p. 117–120 °C). $^1$H NMR (400 MHz, $CDCl_3$): δ 7.67 (1H, d, $J$ = 7.8 Hz), 7.48 (2H, d, $J$ = 8.5 Hz), 7.40 (1H, d, $J$ = 8.1 Hz), 7.30–7.27 (1H, m), 7.20–7.17 (1H, m), 7.05 (2H, d, $J$ = 8.5 Hz), 6.55 (1H, s), 3.91 (3H, s), 3.76 (3H, s); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 159.5, 141.4, 138.2, 130.6, 128.0, 125.3, 121.4,120.2, 119.7, 114.0, 109.5, 101.0, 55.3, 31.0. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{16}H_{16}NO$: 238.1232, Found: 238.1230.



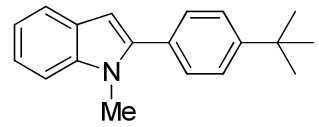

**3b: 1–Methyl–2–phenyl–1*H*–indole**

White solid. m.p. 101.2–102.5 °C (lit.[7] m.p. 99–102 °C). $^1$H NMR (400 MHz, $CDCl_3$): δ 7.70 (1H, d, $J$ = 7.8 Hz), 7.59–7.57 (2H, m), 7.54–7.51 (2H, m), 7.48–7.41 (2H, m), 7.34–7.30 (1H, m), 7.23–7.20 (1H, m), 6.64 (1H, s), 3.80 (3H, s); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 141.5, 138.3, 132.8, 129.4, 128.5, 128.0, 127.9, 127.8, 121.6, 120.5, 119.8, 109.6, 101.6, 31.1. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{15}H_{14}N$: 208.1126, Found: 208.1130.



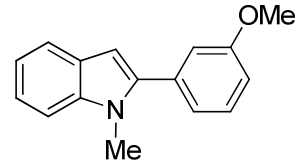

**3c: 1-Methyl-2-*p*-tolyl-1*H*-indole**

White solid. m.p. 97.4–99.5 °C (lit.[7] m.p. 96–98 °C). $^1$H NMR (400 MHz, $CDCl_3$): δ 7.71 (1H, d, $J$ = 7.8 Hz), 7.46 (2H, d, $J$ = 7.9 Hz), 7.42 (1H, d, $J$ = 8.1 Hz), 7.36–7.29 (3H, m), 7.24–7.20 (1H, m), 6.62 (1H, s), 3.80 (3H, s), 2.50 (3H, s); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 141.6, 138.3, 137.7, 129.9, 129.2, 129.1, 128.0, 121.5, 120.3, 119.8, 109.5, 101.3, 31.1, 21.2. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{16}H_{16}N$: 222.1283, Found: 222.1282.



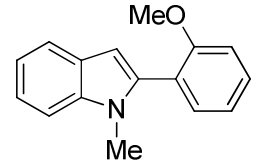

**3d: 2-(4-(*tert*-Butyl)phenyl)-1-methyl-1*H*-indole**

White solid. m.p. 114.3–115.5 °C (lit.[25] m.p. 115–116 °C).$^1$H NMR (400 MHz, $CDCl_3$): δ 7.65 (1H, d, $J$ = 7.8 Hz), 7.53–7.46 (4H, m), 7.38 (1H, d, $J$ = 8.2 Hz), 7.28–7.26 (1H, m), 7.17–7.14 (1H, m), 6.57 (1H, s), 3.78 (3H, s), 1.41 (9H, s); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 150.9, 141.7, 138.3, 129.9, 129.1, 128.0, 125.4, 121.5, 120.0, 119.8, 109.5, 101.4, 34.7, 31.3. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{19}H_{22}N$: 264.1752, Found: 264.1749.



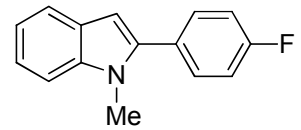

**3e: 2-(3-Methoxyphenyl)-1-methyl-1*H*-indole**

Colorless oil.[8a] $^1$H NMR (400 MHz, $CDCl_3$): δ 7.70 (1H, d, $J$ = 7.8 Hz), 7.46–7.41 (2H, m), 7.33–7.30 (1H, m), 7.23–7.20 (1H, m), 7.17–7.12 (2H, m), 6.64 (1H, s), 3.92 (3H, s), 3.81 (3H, s); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 159.5, 141.4, 138.4, 134.2, 129.5, 127.9, 121.8, 121.7, 120.5, 119.9, 115.1, 113.4, 109.6, 101.7, 55.3, 31.1. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{16}H_{16}NO$: 238.1232, Found: 238.1234.




**3f: 2-(2-Methoxyphenyl)-1-methyl-1*H*-indole**

Colorless oil.[26] $^1$H NMR (400 MHz, $CDCl_3$): δ 7.74 (1H, d, $J$ = 7.8 Hz), 7.54–7.44 (3H, m), 7.36–7.32 (1H, m), 7.25–7.21 (1H, m), 7.17–7.13 (1H, m), 7.09 (1H, d, $J$ = 8.3 Hz), 6.61 (1H, s), 3.89 (3H, s), 3.68 (3H, s); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 157.5, 138.5, 137.6, 132.5, 130.0, 127.9, 122.0, 121.2, 120.6, 120.4, 119.3, 110.8, 109.3, 101.7, 55.4, 30.6. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{16}H_{16}NO$: 238.1232, Found: 238.1235.




**3g: 2-(4-Fluorophenyl)-1-methyl-1*H*-indole**

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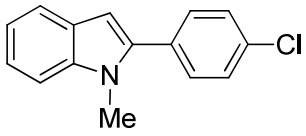
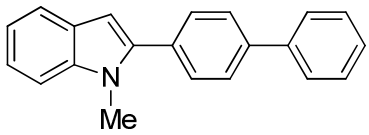
White solid. m.p. 119.7–121.3 °C (lit.[7] m.p. 119–122 °C). $^1$H NMR (400 MHz, $CDCl_3$): δ 7.68 (1H, d, $J$ = 7.8 Hz), 7.52–7.49 (2H, m), 7.40 (1H, d, $J$ = 8.2 Hz), 7.32–7.29 (1H, m), 7.23–7.18 (3H, m), 6.58 (1H, s), 3.75 (3H, s); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 162.6 (d, $J$ = 246.2 Hz), 140.4, 138.3, 131.1 (d, $J$ = 8.0 Hz), 128.9 (d, $J$ = 3.4 Hz), 127.9, 121.8, 120.5, 120.0, 115.5 (d, $J$ = 21.5 Hz), 109.6, 101.7, 31.0. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{15}H_{13}FN$: 226.1032, Found: 226.1029.



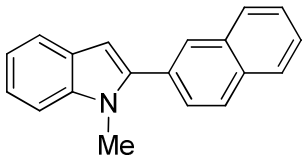

**3h: 2-(4-Chlorophenyl)-1-methyl-1*H*-indole**

White solid. m.p. 115.1–117.2 °C (lit.[7] m.p. 115–118 °C). $^1$H NMR (400 MHz, $CDCl_3$): δ 7.67 (1H, d, $J$ = 7.8 Hz), 7.48 (4H, s), 7.39 (1H, d, $J$ = 8.2 Hz), 7.32–7.28 (1H, m), 7.21–7.17 (1H, m), 6.60 (1H, s), 3.76 (3H, s); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 140.2, 138.5, 134.0, 131.3, 130.5, 128.7, 127.9, 121.9, 120.5, 120.0, 109.6, 102.0, 31.1. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{15}H_{13}{}^{35}ClN$: 242.0737, Found: 242.0741.



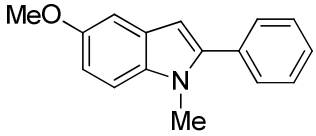

**3i: 2-([1,1'-Biphenyl]-4-yl)-1-methyl-1*H*-indole**

White solid. m.p. 153.7–155.3 °C. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.73–7.67 (5H, m), 7.62–7.60 (2H, m), 7.51–7.48 (2H, m), 7.41–7.39 (2H, m), 7.30–7.26 (2H, m), 7.19–7.15 (1H, m), 6.64 (1H, s), 3.82 (3H, s); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 141.2, 140.7, 140.6, 138.5, 131.8, 129.7, 128.9, 128.0, 127.5, 127.2, 127.1, 121.7, 120.5, 119.9, 109.6, 101.8, 31.3. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{21}H_{18}N$: 284.1439, Found: 284.1436.



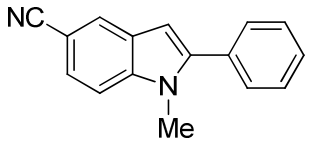

**3j: 1-Methyl-2-(naphthalen-2-yl)-1*H*-indole**

White solid. m.p. 151.0–152.4 °C (lit.[27] m.p. 152–153 °C). $^1$H NMR (400 MHz, $CDCl_3$): δ 8.01–7.93 (4H, m), 7.72–7.67 (2H, m), 7.58–7.56 (2H, m), 7.43 (1H, d, $J$ = 8.2 Hz), 7.34–7.30 (1H, m), 7.23–7.19 (1H, m), 6.71 (1H, s), 3.84 (3H, s); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 141.6, 138.6, 133.3, 132.8, 130.3, 128.3, 128.1, 128.0, 127.8, 127.2, 126.5, 126.4, 121.8, 120.5, 120.0, 109.6, 102.2, 31.3. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{19}H_{16}N$: 258.1283, Found: 258.1281.



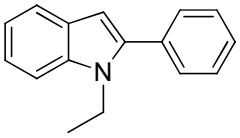

**3k: 5-Methoxy-1-methyl-2-phenyl-1*H*-indole**[8a]

White solid. m.p. 126.7–129.2 °C. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.57–7.50 (4H, m), 7.46–7.43 (1H, m), 7.31 (1H, d, $J$ = 8.8 Hz), 7.17–7.16 (1H, m), 6.99–6.96 (1H, m), 6.56 (1H, s), 3.99 (3H, s), 3.76 (3H, s); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 154.3, 142.1, 133.8, 132.9, 129.2, 128.4, 128.2, 127.7, 111.9, 110.3, 102.2, 101.3, 55.9, 31.2. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{16}H_{16}NO$: 238.1232, Found: 238.1236.



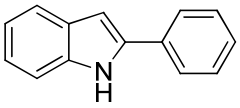

**3l: 1-Methyl-2-phenyl-1*H*-indole-5-carbonitrile**[8b]

White solid. m.p. 118.9–120.5 °C. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.98 (1H, s), 7.52–7.47 (6H, m), 7.42–7.40 (1H, m), 6.63 (1H, s), 3.79 (3H, s); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 143.9, 139.7, 131.6, 129.4, 128.7, 128.6, 127.7, 125.9, 124.6, 120.9, 110.4, 102.8, 102.3, 31.4. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{16}H_{13}N_2$: 233.1079, Found: 233.1076.



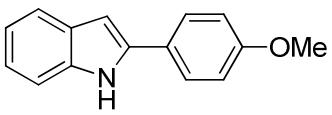

**3m: 1-Ethyl-2-phenyl-1*H*-indole**[28]

White solid. m.p. 85.6–87.0 °C. $^1$H NMR (400 MHz, $CDCl_3$): δ 7.67 (1H, d, $J$ = 7.8 Hz), 7.55–7.43 (6H, m), 7.29–7.25 (1H, m), 7.19–7.15 (1H, m), 6.56 (1H, s), 4.23 (2H, q, $J$ = 7.2 Hz), 1.36 (3H, t, $J$ = 7.2 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 141.1, 137.0, 133.2, 129.4, 128.5, 128.3, 127.9, 121.5, 120.6, 119.7, 109.9, 102.0, 38.7, 15.4. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{16}H_{16}N$: 222.1283, Found: 222.1288.




**3n: 2-Phenyl-1*H*-indole**

White solid. m.p. 186.5–187.6 °C (lit.[7] m.p. 188–189 °C). $^1$H NMR (400 MHz, $CDCl_3$): δ 8.37 (1H, br, s), 7.69–7.64 (3H, m), 7.48–7.41 (3H, m), 7.36–7.32 (1H, m), 7.23–7.19 (1H, m), 7.15–7.12 (1H, m), 6.85 (1H, s); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 137.9, 136.9, 132.4, 129.3, 129.0, 127.7, 125.2, 122.4, 120.7, 120.3, 110.9, 100.0. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{14}H_{12}N$: 194.0970, Found: 194.0971.



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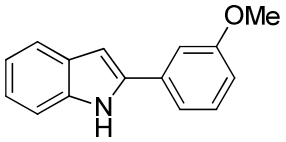
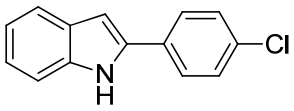
**3o: 2-(4-Methoxyphenyl)-1*H*-indole**

White solid. m.p. 226.6–228.4 °C (lit.[29] m.p. 228–229 °C). $^1$H NMR (400 MHz, $CDCl_3$): δ 8.26 (1H, br, s), 7.62–7.60 (3H, m), 7.40 (1H, d, $J$ = 7.8 Hz), 7.20–7.10 (2H, m), 6.99 (2H, d, $J$ = 8.2 Hz), 6.73 (1H, s), 3.87 (3H, s); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 159.4, 138.0, 136.7, 129.5, 126.5, 125.3, 121.9, 120.4, 120.2, 114.5, 110.7, 98.9, 55.4. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{15}H_{14}NO$: 224.1075, Found: 224.1074.



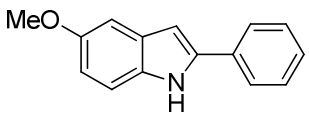

**3p: 2-(3-Methoxyphenyl)-1*H*-indole**

White solid. m.p. 137.2–148.5 °C (lit.[29] m.p. 136–137 °C). $^1$H NMR (400 MHz, $CDCl_3$): δ 8.36 (1H, br, s), 7.66 (1H, d, $J$ = 7.8 Hz), 7.42–7.36 (2H, m), 7.28–7.27 (1H, m), 7.23–7.21 (2H, m), 7.18–7.14 (1H, m), 6.92–6.90 (1H, m), 6.86 (1H, s), 3.90 (3H, s); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 160.1, 137.7, 136.8, 133.8, 130.0, 129.2, 122.4, 120.7, 120.2, 117.7, 113.1, 111.0, 110.9, 100.2, 55.3. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{15}H_{14}NO$: 224.1075, Found: 224.1078.



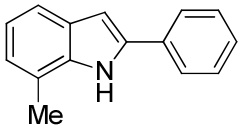

**3q: 2-(4-Chlorophenyl)-1*H*-indole**

White solid. m.p. 201.3–202.6 °C (lit.[29] m.p. 203–205 °C). $^1$H NMR (400 MHz, $CDCl_3$): δ 8.27 (1H, br, s), 7.65 (1H, d, $J$ = 7.8 Hz), 7.59 (2H, d, $J$ = 8.4 Hz), 7.43–7.40 (3H, m), 7.25–7.21 (1H, m), 7.17–7.13 (1H, m), 6.83 (1H, s); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 136.9, 136.7, 133.4, 130.9, 129.2, 129.1, 126.3, 122.7, 120.7, 120.5, 110.9, 100.5. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{14}H_{11}{}^{35}ClN$: 228.0580, Found: 228.0582.



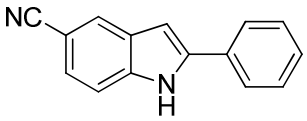

**3r: 5-Methoxy-2-phenyl-1*H*-indole**

White solid. m.p. 168.7–170.0 °C (lit.[7] m.p. 166–169 °C). $^1$H NMR (400 MHz, $CDCl_3$): δ 8.26 (1H, br, s), 7.67–7.65 (2H, m), 7.47–7.43 (2H, m), 7.35–7.29 (2H, m), 7.11 (1H, s), 6.89–6.86 (1H, m), 6.77 (1H, s), 3.88 (3H, s); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 154.6, 138.6, 132.5, 132.1, 129.8, 129.0, 127.6, 125.1, 112.6, 111.6, 102.4, 99.9, 55.9. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{15}H_{14}NO$: 224.1075, Found: 224.1077.



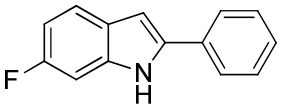

**3s: 7-Methyl-2-phenyl-1*H*-indole**

White solid. m.p. 116.2–117.9 °C (lit.[30] m.p. 116–117 °C). $^1$H NMR (400 MHz, $CDCl_3$): δ 8.35 (1H, br, s), 7.76–7.74 (2H, m), 7.57 (1H, d, $J$ = 7.8 Hz), 7.52–7.48 (2H, m), 7.41–7.37 (1H, m), 7.16–7.07 (2H, m), 6.91 (1H, s), 2.61 (3H, s); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 137.6, 136.4, 132.5, 128.9, 128.8, 127.5, 125.1, 122.9, 120.4, 120.0, 118.3, 100.5, 20.9. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{15}H_{14}N$: 208.1126, Found: 208.1127.



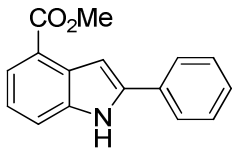

**3t: 2-Phenyl-1*H*-indole-5-carbonitrile**

White solid. m.p. 193.6–195.7 °C (lit.[31] m.p. 194–196 °C). $^1$H NMR (400 MHz, $CDCl_3$): δ 8.80 (1H, br, s), 7.98 (1H, s), 7.70–7.69 (2H, m), 7.51–7.38 (5H, m), 8.89 (1H, s); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 140.3, 138.5, 131.3, 129.2, 129.0, 128.6, 126.0, 125.4, 125.2, 120.7, 111.8, 103.4, 100.2. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{15}H_{11}N_2$: 219.0922, Found: 219.0921.




**3u: 6-Fluoro-2-phenyl-1*H*-indole**

White solid. m.p. 179.5–180.3 °C (lit.[32] m.p. 180–181 °C). $^1$H NMR (400 MHz, $CDCl_3$): δ 8.33 (1H, br, s), 7.65–7.64 (2H, m), 7.56 (1H, s), 7.46 (2H, s), 7.36–7.35 (1H, m), 7.11–7.08 (1H, m), 6.94–6.90 (1H, m), 6.81 (1H, s); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 160.1 (d, $J$ = 236.7 Hz), 138.4 (d, $J$ = 3.8 Hz), 136.8 (d, $J$ = 12.4 Hz), 132.1, 129.1, 127.7, 125.8, 125.0, 121.3 (d, $J$ = 10.0 Hz), 109.0 (d, $J$ = 24.3 Hz), 99.9, 97.3 (d, $J$ = 26.1 Hz). HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{14}H_{11}FN$: 212.0876, Found: 212.0879.




**3v: Methyl 2-phenyl-1*H*-indole-4-carboxylate**[26]

White solid. m.p. 208.7–210.1 °C. $^1$H NMR (400 MHz, $CDCl_3$): δ 8.90 (1H, br, s), 7.94 (1H, d, $J$ = 7.5 Hz), 7.74–7.72 (2H, m), 7.60–7.58 (1H, m), 7.52 (1H, s), 7.45–7.42 (2H, m), 7.37–7.33 (1H, m), 7.24–7.20 (1H, m), 4.04 (3H, s); $^{13}$C NMR (100 MHz, $CDCl_3$): δ 168.4, 140.1, 137.7, 131.9, 129.0, 128.9, 128.2, 125.5, 123.8, 121.3, 121.2, 115.8, 101.1, 51.8. HRMS (ESI) ([M+H]$^+$) Calcd. for $C_{16}H_{14}NO_2$: 252.1025, Found: 252.1024.

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