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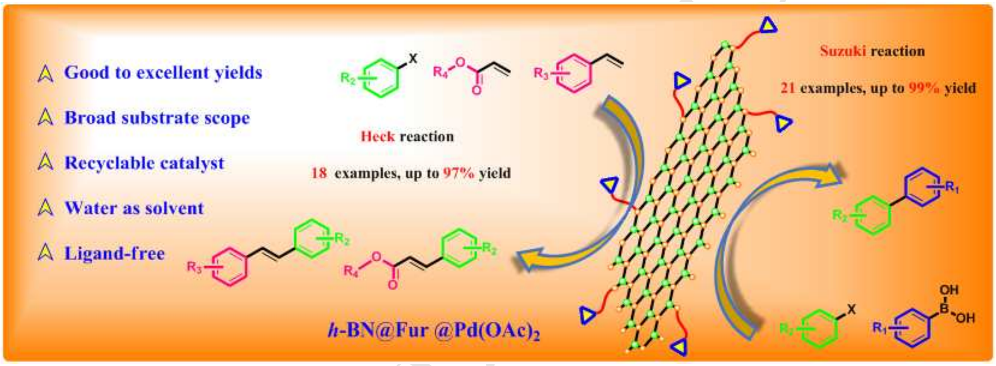

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ABSTRACT

A moisture- and air-stable palladium(II)-Schiff base complex supported on h-BN was simply prepared by using commercially available reagents. This nanomaterial was applied as an excellent and recyclable heterogeneous catalyst for the Suzuki and Heck cross-coupling reactions. And it has been characterized by FT-IR, XRD, SEM, XPS, TG and ICP-AES techniques. High yields, ligand-free, low reaction time, water as solvent, non-toxicity and recyclability of the catalyst are the main merits of these protocols. In addition, a series of pharmacologically relevant products were successfully synthesized using this catalyst. Above all, this work opens up an interesting and attractive avenue for the use of h-BN as an efficient support for heterogeneous catalysts.

1. Introduction

Transition-metal catalyzed cross-coupling reactions have been used as a powerful method in modern synthetic organic chemistry for the preparation of natural products, advanced materials, agrochemicals, pharmaceuticals, herbicides, biologically active compounds, polymers, UV screens, hydrocarbons and liquid crystal materials.[1] Among the various transition-metal catalyzed cross-coupling reactions, the Heck–Mizoroki[2] and Suzuki–Miyaura reactions[3] are the most important and highly effective protocols for the construction of carbon–carbon bonds.[4] In the past few years, numerous effective and selective homogeneous palladium catalytic systems have been developed for such reactions, but they have disadvantages such as tedious separation and contamination of the coupled products with Pd species.[5] Alternatively, metal catalysts anchored on a heterogeneous support have received tremendous attention recently in C–C cross-coupling.[6] Heterogeneous processes have advantages such as ease of separation of the product, reusability of the catalyst, better steric control of the reaction intermediate and so on.[7] Notably, although C-C cross-coupling reactions catalyzed by palladium-phosphine systems have achieved great success over the last decade,[8] however, phosphine ligands are often quite expensive, air-sensitive, and virulent, which limit their wide use in large-scale application. Besides, the preparation of most reported ligands seems rather laborious and time-consuming. Therefore, based on the concerns of economic and green chemistry, the development of mild, simple and efficient procedures, using heterogeneous phosphorus-free catalysts, is still a topic of considerable interest in organic synthesis and industry.

On the other hand, Schiff bases are an important class of organic ligands in coordination chemistry and have been extensively used as metal Schiff base complexes to catalyze organic reactions due to the advantages such as their cost-effective, ease of synthesis, availability and thermal and chemical stability.[9] However, the use of metal Schiff base complexes as catalyst in homogeneous solution suffers from deactivation because of formation of µ-oxo and dimeric peroxo- species, which have been demonstrated to be inactive in various reactions.[10] Moreover, difficulties in separation and reusability of homogeneous metal (particularly expensive metals) Schiff base complexes have limited the applications of these catalysts. For overcoming the aforementioned drawbacks, metal Schiff base complexes can be immobilized on suitable solid supports.

Hexagonal boron nitride (h-BN) is defined as material whose free charges are immobile in one spatial dimension, but mobile in another two. This property enables h-BN to have novel or

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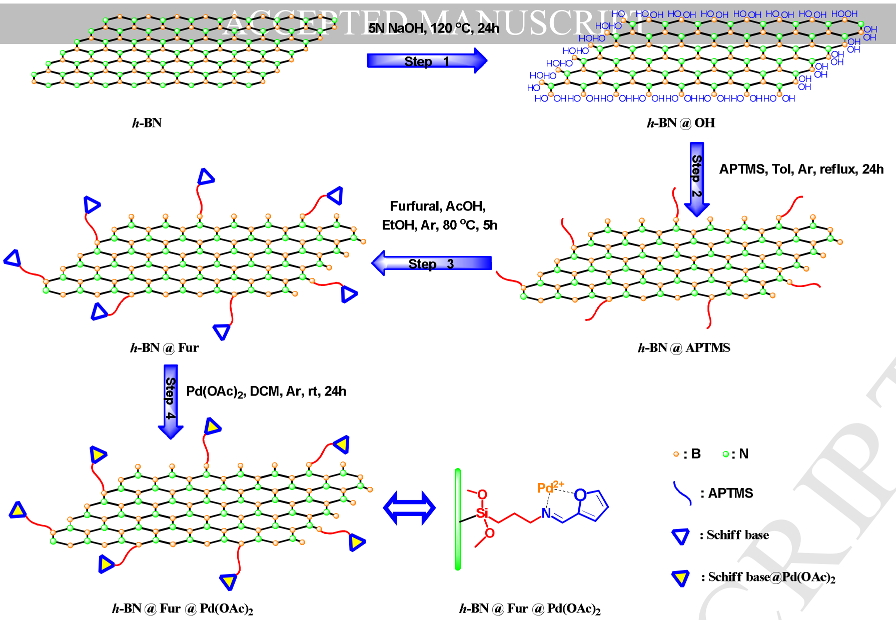


Scheme 1. The synthetic strategy for the synthesis of h-BN@Fur@Pd$(OAc)_2$.

superior functions, distinct from traditional bulk materials.[11] It is similar in many ways to graphene: it has a stacked sheet morphology, high thermal conductivity, and excellent mechanical strength.[12] However, it is an electrical insulator and is more chemically inert and temperature stable than graphene. Starting from reported applications, h-BN have been widely applied in hydrogen storage,[13] adsorption of pollutants,[14] drug delivery[15] and water cleanup.[16] In addition, h-BN can be used as very good catalyst supports because of their high surface area and insolubility in most solvents. For example, Pt/BN has been applied in deep oxidation of methanol and benzene.[17] Postole *et al.* studied the influence of the preparation methods of Pd/BN catalysts on the activity for methane oxidation.[18]

The introduction of metal nanoparticles into pristine h-BN has been widely reported during the past few years, and their application in organic synthesis have also been investigated.[19] However, these catalysts often show a broad size distribution and, in many cases, suffer from severe leaching phenomena. This is probably due to the lack of sufficient binding sites on the pristine h-BN surface and the only existent weak non-covalent interactions between pristine BN and metal nanoparticle. On the other hand, despite several studies on the morphology, properties and preparation of organic modified h-BN,[20] no metal has been immobilized onto functionalized boron nitride as a heterogeneous catalyst. Herein, we report the production of Pd catalyst based on Schiff-base modified h-BN, as a separable and recyclable catalyst for Suzuki and Heck coupling reactions. All these reactions were performed in water with high efficiency and excellent yields. To the best of our knowledge, this is the first report on the immobilization of palladium(II) on BN for catalytic application purpose. And, it's the first time to synthesize a BN-based heterogeneous catalyst for C-C coupling reactions.

2. Results and discussion

2.1 Catalyst preparation

As shown in Scheme 1, the immobilization of Pd(II) onto furfural-functionalized hexagonal boron nitride was performed in four steps. Firstly, pristine *h*-BN was treated with hydroxide anions, resulting in the formation of free hydroxyl group on the edge of BN sheets. Secondly, *h*-BN@OH reacted with amino propyl trimethoxy silane (APTMS) to synthesize amino-functionalized boron nitride. Thirdly, *h*-BN@Fur wasformed by the condensation of furfural with *h*-BN@APTMS. Ultimately, the complexation of $Pd(OAc)_2$ onto schiff base generate the heterogeneous Pd(II) catalyst.

2.2 Catalyst characterization

The synthesized nanocatalyst was characterized using several different microscopic and spectroscopic techniques including FT-IR, SEM, TGA, ICP, XRD and XPS analysis.

Scanning electron microscopy (SEM) has been used in order to shed light on the presence, distribution, and dimension of the prepared hybrid nanomaterials. As shown in **Fig. 1a-b**, no obvious morphology difference can been found between *h*-BN and *h*-BN@OH. They all exhibit schistose structures with smooth edge and flat surface. And it can be clearly seen that the size of palladium(II) loaded nanocatalyst is in range of 50-500 nm. Notably, after functionalization, the *h*-BN nanosheets still arranged in schistose structures and appeared more broken and aggregated (**Fig. 1c**).

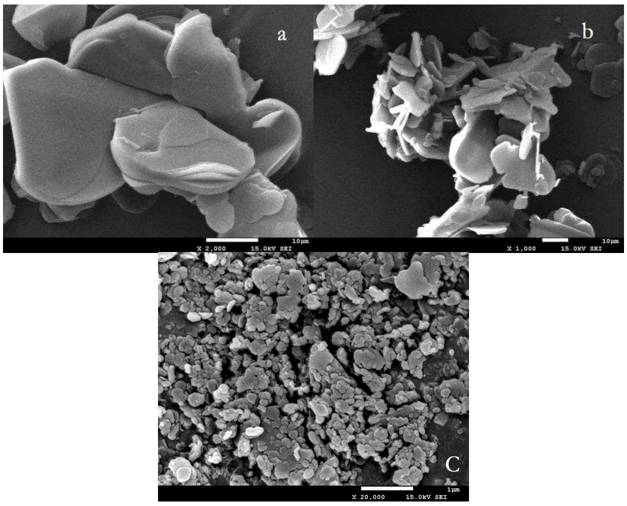


Figure 1. SEM of (a) pristine h-BN, (b) h-BN@OH and (c) h-BN@Fur@ Pd$(OAc)_2$.

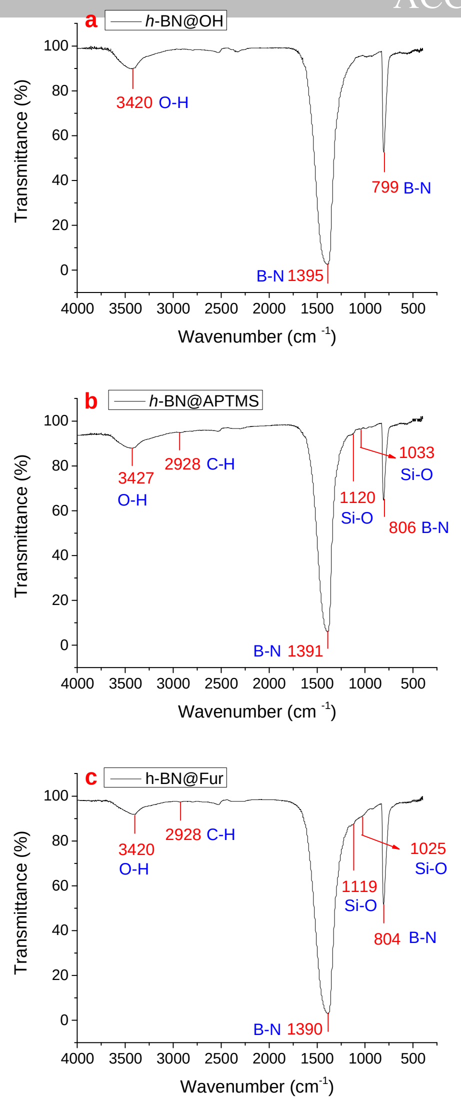


Figure 2. FT-IR spectra of (a) h-BN@OH, (b) h-BN@APTMS, (c) h-BN@ Fur.

Infra-red spectroscopy was used to characterize the organic components bound to the surface of *h*-BN (**Fig. 2**). The characteristic absorption band of B-N bonds was observed at 1395 cm^{-1} and 799 cm^{-1} (**Fig. 2 a**), which was slightly shifted to 1391 cm^{-1} and 806 cm^{-1} after the conjugations with APTMS (**Fig. 2 a vs b**). And all the functionalized *h*-BN showed a strong band at around 3420 cm^{-1}, which was attributed to the stretching vibrations of O-H bonds (**Fig. 2 a-b and c**). Comparison studies on *h*-BN@OH and *h*-BN@APTMS reveal additional strong bands at 1120 and 1033 cm^{-1} corresponding to characteristic absorption of Si-O bonds formed through the silylation process. Besides, for the *h*-BN@APTMS peak at 2928 cm^{-1} was assigned to stretching vibration of C-H bonds of the propyl-amine groups (**Fig. 2 b**). Unfortunately, the stretching vibrations of C=N bands, at near 1625 cm^{-1},[21] was concealed under the broad absorption peak of B-N bonds. But the condensation of *h*-BN@APTMS with furfural can be confirmed by other techniques.

For the quantitative analysis, the as-prepared *h*-BN@OH, *h*-BN@APTMS and *h*-BN@Fur were further observed via TGA, and these results are shown in **Fig. 3**. The experiments were performed at up to 760 °C in an N_2 atmosphere at a heating rate of 10 °C min^{-1}. Under these conditions, a weight loss of about 1.72% was observed for *h*-BN@OH, it should be ascribed to the removal of physically adsorbed solvents and surface hydroxyl groups. Besides, the weight loss of about 3.6% and 5.5% were observed for *h*-BN@APTMS and *h*-BN@Fur, respectively. These should be mainly attributed to the thermal degradation of organic components on the BN complex. Moreover, around 1.9% weight loss was observed when comparing these two samples. It suggests that furfural was successfully conjugated to *h*-BN@APTMS particles. In the curve of *h*-BN@Fur, the first step in the curve is associated with the loss of water molecules (below 200 °C). The second weight loss, starting at 200 °C disintegrates the supported organic parts with a calculated loss of 3.73%. Notably, the amount of palladium (1.7%) of *h*-BN@Fur@Pd(OAc)$_2$ was determined by inductively coupled plasma (ICP) analysis. In all, these results corroborate the FT-IR datas.

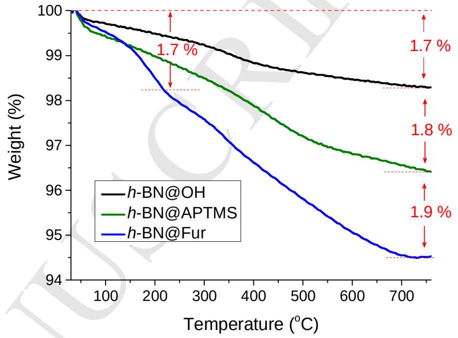


Figure 3. TGA thermograms of h-BN@OH, h-BN@APTMS and h-BN@Fur.

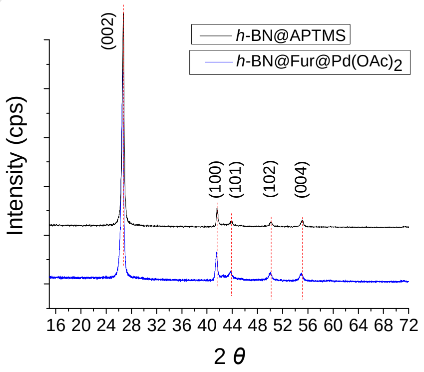


Figure 4. XRD patterns of h-BN@APTMS and h-BN@Fur@Pd(OAc)$_2$.

Fig. 4 shows the wide angle XRD patterns of *h*-BN@APTMS and *h*-BN@Fur@Pd(OAc)$_2$ nanomaterials. These two samples show the same diffraction peaks at 2θ = 26.7, 41.6, 43.9, 50.1 and 55.1, which correspond to the (002), (100), (101), (102) and (004) lattice planes of a typical hexagonal boron nitride structure (JCPDS no. 34-0421). It suggests that the crystal structure of the *h*-BN has not been compromised by the reaction. And in the process of the coordination between the *h*-BN@Fur and palladium ions, the formation of Pd nanoparticles was completely avoided. No characteristic peaks of palladium particles were found in the XRD pattern of *h*-BN@Fur@Pd(OAc)$_2$, which implies that all of the catalytic activity is attributed to divalent palladium. Moreover, no peaks corresponding to any other impurity were observed.

Detailed surface information of *h*-BN@APTMS and *h*-BN@Fur@Pd(OAc)$_2$ was collected by X-ray photoelectron spectroscopy (XPS) and the corresponding results are presented in **Fig. 5**. The new peaks of O 1s, C 1s and Si 2p can be assigned in **Fig. 5a**, indicating that (3-Aminopropyl)-trimethoxysilane

(APTMS) has successfully attached to the surface and edges of pristine BN particles. And the spectrum of the *h*-BN@Fur@Pd(OAc)$_2$ shows a large increase in the signal intensity of the O 1s and C 1s peaks, which is attributed to furfural covalently grafted to the h-BN@APTMS.

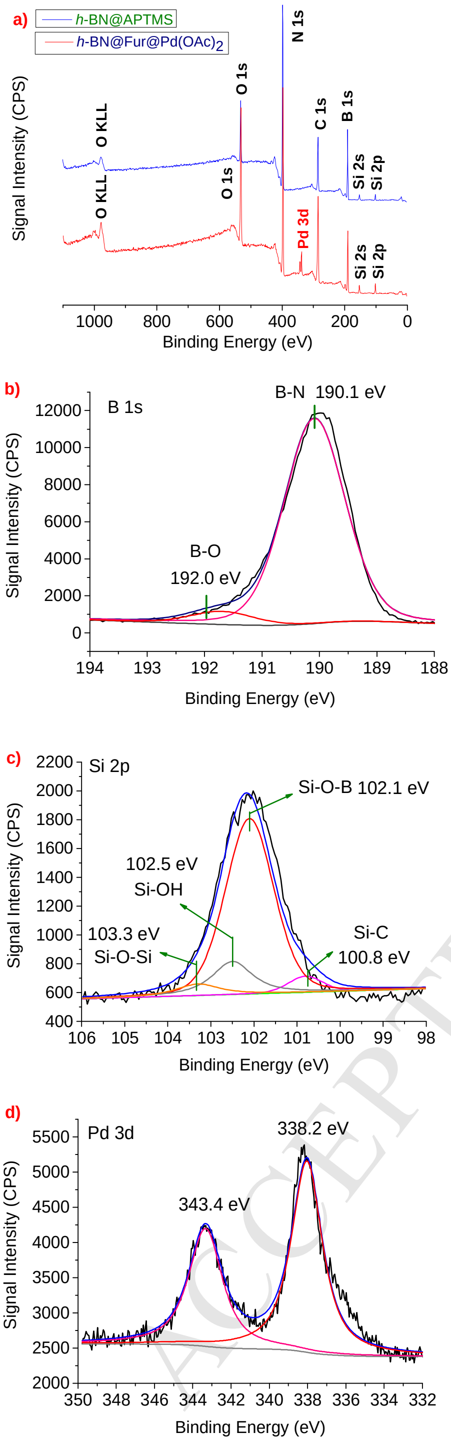


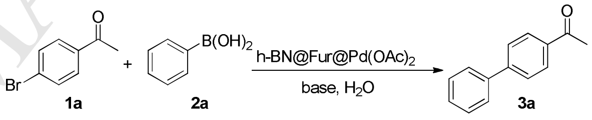
Figure 5. Full range XPS spectrum of h-BN@APTMS and h-BN@Fur@Pd(OAc)$_2$ (a), and the B 1s (b), Si 2p (c), Pd 3d (d) core level region XPS spectra of the h-BN@Fur@Pd(OAc)$_2$ nanocomposite.

The B 1s spectra of *h*-BN@Fur@Pd(OAc)$_2$ showed a strong binding energy peak for the B-N bond and a weak binding energy peak for the B-OH bond at 190.1 eV and 192.0 eV, respectively (**Fig. 5b**).[22] The B-OH peak resulted from the introduction of a hydroxyl group by the base treatment. In order to provide clearer evidence of chemical bonding between the BN particles and the silane curing agent, the Si 2p peak can be fitted by a curve with several component peaks (**Fig. 5c**). In the de-convoluted Si 2p spectra, the strong peak at the binding energy of 102.1 eV represents the bond between silicon and oxygen originating from the BN particles (B-O-Si), indicating that the surface curing agent and BN particles are connected through the hydroxyl groups. The peak at 103.3 eV is attributed to siloxane (Si-O-Si) resulting from the partial hydrolysis of the silane curing agent molecules during the silanization reaction. Moreover, the peak at 100.8 eV is attributed to Si-C bonding in the silane curing agent molecules. These results are in agreement with the reaction mechanism of silane, including the hydrolysis of -OCH$_3$, condensation to oligomers, hydrogen bonds between oligomer and hydroxyl groups on the substrate, and the formation of the covalent linkage between silane and the substrate. The peak at 102.5 eV is attributed to Si-OH bonding, indicating that some hydroxyl groups did not hydrolyze and a small amount of hydroxyl group remained.[23]

The XPS spectrum of the Pd 3d core level region for the *h*-BN@Sal@Pd(OAc)$_2$ nanocomposite displays main peaks at 338.2 and 343.4 eV which can be attributed to the binding energy of Pd 3d$_{5/2}$ and Pd 3d$_{3/2}$, respectively (**Fig. 5d**). These values correspond to the Pd(II) binding energies of Pd(OAc)$_2$.

2.3 Investigation of the catalytic activity of h-BN@Fur@Pd(OAc)₂ in the Suzuki reaction.

Table 1. Optimization of the Suzuki reaction between 4-bromoacetophenone and phenylboronic acid using h-BN@Fur@Pd(OAc)$_2$ as catalyst.[a]



Entry	Base	Pd (.equiv)	Temp (°C)	Yield[b] (%)
1	Cs_2CO_3	0.05	70	85
2	KOH	0.05	70	90
3	t-BuOK	0.05	70	87
4	K_2CO_3	0.05	70	97
5	Et_3N	0.05	70	88
6	$NaHCO_3$	0.05	70	89
7[c]	K_2CO_3	0.05	70	70
8[d]	K_2CO_3	0.05	70	85
9[e]	K_2CO_3	0.05	70	97
10	K_2CO_3	0.05	25	22
11	K_2CO_3	0.05	50	73
12	K_2CO_3	0.05	100	82
13	K_2CO_3	0.01	70	70
14	K_2CO_3	0.1	70	98
15	K_2CO_3	0.2	70	98
16[g]	K_2CO_3	0.05	70	N.R[f]
17[h]	K_2CO_3	0.05	70	N.R[f]
18[i]	K_2CO_3	0.05	70	N.R[f]
19[j]	K_2CO_3	0.05	70	N.R[f]
20[k]	K_2CO_3	0.05	70	96
21[l]	K_2CO_3	/	70	N.R[f]

[a] Reaction conditions: **1a** (1 mmol), **2a** (1.5 mmol), h-BN@Fur@Pd(OAc)$_2$ (0.05 mmol), base (1.5 mmol), H_2O (1 mL), Ar, 0.5h.

[b] Isolated yield.

[c] K_2CO_3 (0.5 mmol).

[d] K_2CO_3 (1.0 mmol).

[e] K_2CO_3 (2.0 mmol).

[f] N.R. = No reaction.

[g] h-BN@Fur@Pd$(OAc)_2$ was replaced by 300mg h-BN.

[h] h-BN@Fur@Pd$(OAc)_2$ was replaced by 300mg h-BN@OH.

[i] h-BN@Fur@Pd$(OAc)_2$ was replaced by 300mg h-BN@APTMS.

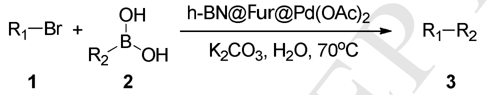
[j] h-BN@Fur@Pd$(OAc)_2$ was replaced by 300mg h-BN@Fur.

[k] h-BN@Fur@Pd$(OAc)_2$ was replaced by 11.3mg Pd$(OAc)_2$.

[l] No catalyst.

Cross-coupling reactions such as Suzuki and Heck reactions are powerful tools for the preparation of natural products, advanced materials and biologically active compounds. Therefore, h-BN@Fur@Pd$(OAc)_2$ was primarily used as a novel heterogeneous and highly reusable nanocatalyst in the Suzuki reaction. For this purpose, the coupling of 4-bromoacetophenone (**1a**) with phenylboronic acid (**2a**) was selected as a simple model reaction to optimize the reaction conditions, and the results are summarized in Table 1. First, a range of bases, such as Cs_2CO_3, KOH, t-BuOK, K_2CO_3, Et_3N and $NaHCO_3$, were used in this transformation, however, all of them were unsatisfactory except for K_2CO_3 (Table 1, entries 1-6). With respect to the amount of K_2CO_3, 1.5 equivalents was found to be adequate, as neither bigger nor smaller amount showed better yields (Table 1, entries 7-9). When the reaction was allowed to proceed in different temperatures, an optimal yield of 97% was obtained at 70 °C (Table 1, entries 4, 10-12). For the optimization of the amount of Pd used in the model reaction, less than 0.05 equivalent led to the incompletion of the reaction (Table 1, entry 13). And up to 0.1 or 0.2 equiv. of Pd did not increase the yield of **6a** significantly (Table 1, entries 14-15). Above all, aryl halides (**1**, 1 mmol) in the presence of a catalytic amount of h-BN@Fur@Pd$(OAc)_2$ (0.05 mmol) and K_2CO_3 (1.5 mmol) with phenylboronic acids (**2**, 1.5 mmol) in water at 70 °C was considered to be the ideal reaction conditions.

Table 2. Investigation of the substrate scope for Suzuki reaction catalyzed by h-BN@Fur@Pd$(OAc)_2$.[a]



Entry	R_1	R_2	Time (h)	Products	Yield[b] (%)
1	Ph	Ph	1	**3b**	85
2	Ph	2-CH_3-Ph	0.5	**3c**	90
3	Ph	3-CH_3-Ph	0.5	**3d**	89
4	Ph	3-OH-Ph	0.5	**3e**	81
5	Ph	4-OCH_3-Ph	0.5	**3f**	90
6	Ph	4-$C(CH_3)_3$-Ph	0.5	**3g**	90
7	Ph	3,5-$C(CH_3)_3$-Ph	0.5	**3h**	82
8	Ph	4-F-Ph	0.5	**3i**	79
9	Ph	3-CN-Ph	0.5	**3j**	83
10	Ph	1-naphthyl	0.5	**3k**	87
11	4-NH_2-Ph	Ph	3.5	**3l**	81
12	3-NH_2-Ph	Ph	2	**3m**	93
13	3-NH_2-4-CH_3-Ph	Ph	2	**3n**	82
14	4-OH-Ph	Ph	2	**3o**	99
15	2-OCH_3-Ph	Ph	3.5	**3p**	87
16	2-NH_2-5-pyridyl	Ph	9	**3q**	76
17	2-CHO-Ph	Ph	1.5	**3r**	85
18	3-NO_2-Ph	Ph	2.5	**3s**	85
19	3-$COCH_3$-Ph	Ph	5	**3t**	88

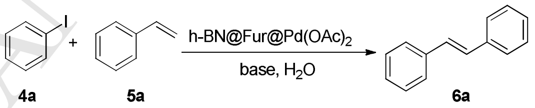
[a] Reaction conditions: **1** (1 mmol), **2** (1.5 mmol), h-BN@Fur@Pd$(OAc)_2$ (0.05 mmol), K_2CO_3 (1.5 mmol), H_2O (1 mL), Ar.

[b] Isolated yield.

After the optimization of the reaction conditions, we examined the catalytic activity of h-BN@Fur@Pd$(OAc)_2$ for various aryl halides and phenylboronic acids. As shown in Table 2, all the substrates including electron-donating or electron-withdrawing functional groups were successfully converted to the corresponding biphenyls in good to excellent yields. Besides, synthetically useful naphthyl and pyridyl were well tolerated in this transformation, giving **3k** and **3q** in good yields. Furthermore, the experimental procedure is very simple and convenient, and has the ability to tolerate a variety of different functional groups such as OH, OCH_3, CN, CHO, NO_2, NH_2 and halogen.

2.4 Investigation of the catalytic activity of h-BN@Fur@Pd(OAc)$_2$ in the Heck reactions.

Table 3. Optimization of the Heck reaction between iodobenzene and styrene using h-BN@Fur@Pd$(OAc)_2$ as catalyst.[a]



Entry	Base	Pd (.equiv)	Temp. (°C)	Yield [b] (%)
1	Cs_2CO_3	0.05	90	65
2	KOH	0.05	90	81
3	t-BuOK	0.05	90	84
4	K_2CO_3	0.05	90	91
5	Et_3N	0.05	90	70
6	$NaHCO_3$	0.05	90	72
7[c]	K_2CO_3	0.05	90	32
8[d]	K_2CO_3	0.05	90	73
9[e]	K_2CO_3	0.05	90	87
10	K_2CO_3	0.05	50	23
11	K_2CO_3	0.05	70	77
12	K_2CO_3	0.05	100	79
13	K_2CO_3	0.01	90	37
14	K_2CO_3	0.02	90	56
15	K_2CO_3	0.1	90	91
16[g]	K_2CO_3	0.05	90	N.R[f]
17[h]	K_2CO_3	0.05	90	N.R[f]
18[i]	K_2CO_3	0.05	90	N.R[f]
19[j]	K_2CO_3	0.05	90	N.R[f]
20[k]	K_2CO_3	0.05	90	92
21[l]	K_2CO_3	/	90	N.R[f]

[a] Reaction conditions: **4a** (1 mmol), **5a** (1.5 mmol), h-BN@Fur@Pd$(OAc)_2$ (0.05 mmol), base (2 mmol), H_2O (1 mL), 3.5h.

[b] Isolated yield.

[c] K_2CO_3 (0.5 mmol).

[d] K_2CO_3 (1.0 mmol).

[e] K_2CO_3 (3.0 mmol).

[f] N.R. = No reaction.

[g] h-BN@Fur@Pd(OAc)$_2$ was replaced by 300mg h-BN.

[h] h-BN@Fur@Pd(OAc)$_2$ was replaced by 300mg h-BN@OH.

[i] h-BN@Fur@Pd(OAc)$_2$ was replaced by 300mg h-BN@APTMS.

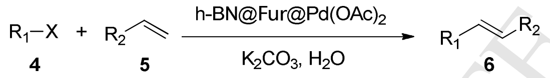
[j] h-BN@Fur@Pd(OAc)$_2$ was replaced by 300mg h-BN@Fur.

[k] h-BN@Fur@Pd(OAc)$_2$ was replaced by 11.3mg Pd(OAc)$_2$.

[l] No catalyst.

In order to extend the catalytic applications of h-BN@Fur@Pd(OAc)$_2$, it was then applied for another C-C cross coupling reaction. At the beginning of our investigation, experiments were carried out using iodobenzene (**4a**) and styrene (**5a**) as the model substrates. Among various bases examined, K_2CO_3 turned out to be the best choice, while others such as Cs_2CO_3, KOH, t-BuOK, Et_3N and $NaHCO_3$ were less effective (Table 3, entries 1-6). For the optimization of the amount of K_2CO_3 used in the model reaction, two equivalent was found to be adequate, as neither larger nor smaller amount showed better yields (Table 3, entries 7-9). Further investigation indicated that temperature was important for this transformation. An excellent yield has been obtained when the reaction was carried out at 90 °C (Table 3, entry 4). However, with the temperature increasing to 100 °C, the yield of **6a** dropped to 79% (Table 3, entry 12). Only 23% and 77% yields of **6a** were obtained when the reaction were conducted at 50 and 70 °C (Table 3, entries 10-11). Moreover, after extensive screenings, we were pleased to find that 0.05 mmol of Pd was enough to catalyze this reaction (Table 3, entries 4, 13-15). Therefore, as observed in this study, the optimized conditions for the synthesis of **6a** tend to be: iodobenzene (1 mmol), styrene (1.5 mmol), h-BN@Fur@ Pd(OAc)$_2$ (0.05 mmol) and K_2CO_3 (2.0 mmol) in water at 90 °C.

Table 4. Investigation of the substrate scope for Heck reaction catalyzed by h-BN@Fur@Pd(OAc)$_2$.[a]



Entry	R_1	X	R_2	Time (h)	Products	Yield[b] (%)
1	2-NH_2-Ph	I	Ph	5	**6b**	85
2	4-Cl-Ph	I	Ph	5	**6c**	90
3	2-CHO-Ph	Br	Ph	5	**6d**	84
4	4-CH_3CO-Ph	Br	Ph	5	**6e**	90
5	3-CHO-Ph	Br	Ph	5	**6f**	87
6	3-CH_3CO-Ph	Br	Ph	5	**6g**	85
7	3-NO_2-Ph	Br	Ph	5	**6h**	95
8[c]	Ph	I	$COOCH_3$	4	**6i**	95
9	Ph	I	$CONH_2$	4.5	**6j**	97
10	Ph	I	CN	5	**6k**	70
11	4-Cl-Ph	I	$COOC_2H_5$	2	**6l**	90
12	4-Cl-Ph	I	$COOC(CH_3)_3$	2	**6m**	91
13	3-OCH_3-Ph	I	$COOCH_3$	2.5	**6n**	95
14	2-NO_2-Ph	I	$COOCH_3$	2	**6o**	95
15	2-thienyl	I	COOCH3	4	**6p**	92

[a] Reaction conditions: **4** (1 mmol), **5** (1.5 mmol), h-BN@Fur@Pd(OAc)$_2$ (0.05 mmol) and K_2CO_3 (2 mmol) in water (1 mL) at 90°C.

[b] Isolated yield.

[c] 70 °C.

To further define the scope of this new catalyst for the Heck reaction, a wide range of aryl halides, styrenes and acrylates were reacted under the optimized conditions. And the results were summarized in Table 4. A host of aryl halides bearing either the electron-donating groups or electron-withdrawing groups were well tolerated during the course of the reaction, providing the desired compounds **6b-h** in good to excellent yields. Besides, in addition to stilbenes, the acrylate derivatives **6i-j** and **6l-p** could also be obtained in excellent yields. Notably, synthetically useful heterocyclic groups, such as thienyl (**6p**), were well tolerated in this transformation. What's more, a variety of functional groups such as carbonyl, ether, halogen, amino, nitro and aldehyde group were well-suited for this reaction.

2.5 Recycling of the catalyst

For practical applications of catalytic systems, the lifetime of the catalyst and its level of reusability are significant factors. To clarify this issue, the feasibility of recycling the Pd catalyst was then examined. After the reaction, the catalyst was simply separated by filtration and successively washed with water, dichlormethane and acetone. And in the recycling experiment, the recovered dry catalyst was recharged with a fresh substrate for the next run under the same reaction conditions. h-BN@Fur@Pd(OAc)$_2$ has been reused ten times in the reaction of 4-bromoacetophenone and phenylboronic acid without significant loss of its catalytic activity (**Fig. 6a**). Besides, the catalyst still remained catalytically active after being reused nine times in the reaction of 1-iodo-2-nitrobenzene and methyl acrylate. The Heck reaction at the 8th and 9th runs gave the desired product in 94% and 92% yields (**Fig. 6b**). Thus, it is reasonable to believe that the immobilized catalyst can be repeatedly used for large-scale production without a significant loss of its catalytic activity.

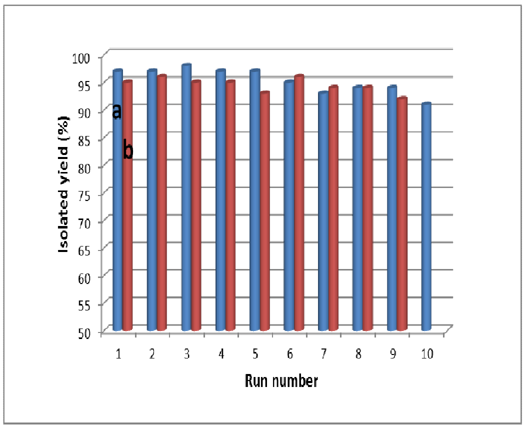
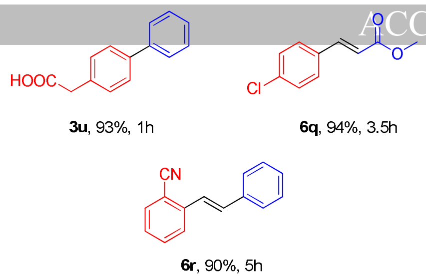


Figure 6. Reusability of h-BN@Fur@Pd(OAc)$_2$ for the synthesis of **3a** (a) and **6o** (b).

2.6 Synthesis of pharmacologically relevant compounds via Suzuki and Heck reactions

The synthesis of pharmacologically interesting compounds is one of the most important applications of C-C coupling reactions. Inspired by its high efficiency, excellent recyclability and wide scope of substrates, h-BN@Fur@Pd(OAc)$_2$ was utilized in the synthesis of pharmacologically important products through Suzuki and Heck reactions (**Fig. 7**).



3u, 93%, 1h

6q, 94%, 3.5h

6r, 90%, 5h

Figure 7. Pharmacologically relevant compounds synthesized by using h-BN @Fur@Pd(OAc)$_2$ as catalyst.

Felbinac **3u**, a non-steroidal anti-inflammatory drug (NSAID), was first launched in 1993 by Takeda and Wyeth Pharmaceuticals (now Pfizer) for the treatment of rheumatic and mild arthritic pain, sprains, strains and other soft tissue injuries.[24] Felbinac acts as a non-selective inhibitor of the enzyme cyclooxygenase (COX), and is characterized as non-selective because it inhibits both the cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2) isoenzymes. The Suzuki reaction of 4-bromophenylacetic acid with phenylboronic acid was smoothly conducted, using h-BN@Fur@Pd(OAc)$_2$ as catalyst under the optimized conditions, providing Felbinac in 93% yield. On the other hand, diverse derivatives of cinnamic acid possess various pharmacological activities. For example, Zhu *et al.* reported that compound **6q** showed strong antifungal activity by altering the permeability of fungal cell membrane.[25] And good antibacterial activity of compound **6r** had been exhibited by Davis and co-works.[26] These two compounds can be easily obtained in 94% and 90% yields *via* h-BN@Fur@Pd(OAc)$_2$ catalyzed Heck reactions.

3. Conclusion

In conclusion, a novel covalently immobilized palladium(II)-Schiff base complex on hexagonal boron nitride (h-BN@Fur@Pd(II)) has been synthesized. After its characterization using various methods, it was used as a new air- and moisture-stable catalyst for Suzuki and Heck C-C cross coupling reactions. A wide range of aryl halides were successfully coupled with aryl-boronic acids, styrenes and acrylates to generate high yields of the corresponding products in water. And a series of pharmacologically relevant products have been successfully synthesized using this catalyst. Furthermore, the catakyst can be separated easily by filtration and recycled at least nine runs without appreciable loss of its catalytic activity. The continued study on the broader scope of this catalyst to other reaction substrates and other types of chemical reactions will be on the way.

4. Experimental section

4.1 General

The *h*-BN powder (99.9%) was obtained from Micxy Regent Co. Ltd. (Chengdu, China). (3-Aminopropyl) trimethoxysilane (APTMS, 97%) was purchased from Aladdin Reagent Co.Ltd. (Shanghai, China). Sodium hydroxide (NaOH, 96%) was collected from Tianjin Ruijinte Chemicals Co. Ltd. (Tianjin, China). 2-furfuraldehyde (99.0%) was provided by Tianjin Bodi Chemicals Co. Ltd. (Tianjin, China). Palladous acetate (Pd(OAc)$_2$, 99.0%) was supplied by Xian Catalyst Chemicals Co. Ltd. (Xian, China). All other materials were commercially available and used without further purification. Thin layer chromatography (TLC) characterization was performed with precoated silica gel GF254 (0.2mm), while column chromatography characterization was performed with silica gel (100-200mesh). ^{1}H NMR spectra were recorded at 400 or 600 MHz and ^{13}C NMR spectra were recorded at 100 MHz. Fourier transform infrared (FT-IR) spectra were performed on a Nicolet 6700 FI-IR spectrometer (Nicolet), using KBr pellets. X-ray photoelectron spectroscopy (XPS) measurements were carried out on AXIS Ultra ^{DLD} spectrometer (KRATOS). X-ray diffractometer (XRD) spectra were recorded with EMPYREAN spectrometer (Panalytical). The morphologies of *h*-BN catalyst were observed by using scanning electron microscopy (SEM, JSM-7500F). Thermal gravitational analysis (TGA) was performed with a thermal analyzer (TGA/DSC2, METTLER TOLEDO) at rate of 10 °C/min under N_2 protection. The loading content of Pd was determinded by inductively coupled plasma optical emission spectroscopy (ICP-OES, SPECTRO ARCOS).

4.2 Preparation of the catalyst

Preparation of hydroxy functionalised h-BN (h-BN@ OH). First, *h*-BN (4 g) was dispersed in 5M sodium hydroxide solution (500 mL) at 120 °C for 24 h. Then the particles were filtered and washed with D.I. water (3 x 150 mL) to adjust the pH from basic to neutral. Finally, the obtained white solid (3.50 g) was dried under reduced pressure at 80 °C for 6 h, and stored in a desiccator at room temperature.

Preparation of amino functionalised h-BN (h-BN@ APTMS). The *h*-BN@OH particles (3 g) were dispersed in dry toluene (120 mL) and stirred at 25 °C for 20 mins. Then, to the resulting solution, 1.6 mL (3-Aminopropyl)trimethoxy-silane (APTMS) was added drop wise. And the mixture was stirred for 24 h at 120 °C under argon protection. The resulting particles (*h*-BN@APTMS) were filtered and wished several times with toluene. Finally, the obtained white solid (3.05 g) was dried under reduced pressure at 80 °C for 6 h.

Preparation of h-BN@Fur@Pd(OAc)$_2$. First, the prepared *h*-BN@APTMS particles (500 mg) were dispersed in 40 mL of absolute ethanol. Then 2-furfuraldehyde (218.3 mg, 2.27 mmol) and four drops of acetic acid were added into the suspension. After refluxing for 5 h. Pale brown solid was got by filtering the mixture and washing with methanol and DCM each for 3 times. Then, the particles were mixed with Pd(OAc)$_2$ (408 mg, 1.8 mmol) in DCM (50 mL) and stirred for 24 h under argon protection at room temperature. The resulting mixture was filtered and washed with DCM for 5 times to remove unreacted $Pd(OA_C)_2$. Finally, the brown solid (417 mg) was dried under vacuum at room temperature for 5 h.

4.3 General procedure for the Suzuki reaction

In a typical run, h-BN@Fur@Pd(OAc)$_2$ (0.05 mmol) was added to a mixture of arylboronic acid **1** (1.0 mmol), aryl bromide **2** (1.5 mmol) and K_2CO_3 (1.5 mmol) in water (1 mL). The resulting mixture was stirred at 70 °C under Ar protection, and the progress of the reaction was monitored by TLC. After completion of the reaction, ethyl acetate was added to the reaction mixture and the catalyst was separated. The organic phase was washed with water, dried over anhydrous Na_2SO_4 and the solvent was evaporated under reduced pressure. Finally, the residue was isolated by chromatography on a column of silica gel to afford the corresponding product **3**.

4.4 General procedure for the Heck reaction

A mixture of aryl halogen **4** (1.0 mmol), substituted alkene **5** (1.5 mmol), K_2CO_3 (2.0 mmol) and h-BN@Fur@Pd(OAc)$_2$ (0.05 mmol) was stirred in water at 90 °C (progress of the reaction was monitored using TLC). After completion of the reaction, the mixture was cooled to room temperature and then catalyst was separated and washed with ethyl acetate three times. Then the filtrate was diluted with water and extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulfate and the solvent was removed under vacuum. Finally, the crude residue was purified by flash chromatography on silica gel to give the final product **6**.

Supplementary Material

General reaction procedure for the synthesis of **3** and **6**, spectroscopic characterization data of new compounds.

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