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Novel cyclodextrin-modified h-BN@Pd(II) nanomaterial: An efficient and recoverable catalyst for ligand-free C-C cross-coupling reactions in water

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1 | INTRODUCTION

With the rapid development of the modern industry, environmental concerns are of increasing interests. Further development of catalytic system has been planned based on using advanced catalysts that can selectively catalyze the specific chemical reactions with a high reactivity, and also can be recycled through the simple separation and regeneration process.^[11] Not surprisingly, the use of heterogeneous catalysts appears to be a promising methodology for the development of environmentally friendly organic processes, because of their separability, reusability, as well as their unique activity that came from the interaction between the catalytic species and supports.^[2]

An environmentally friendly palladium(II) catalyst supported on cyclodextrin-modified h-BN was successfully prepared. The catalyst was characterized by FT-IR, SEM, TG, XRD and XPS, and the loading level of Pd in h-BN@ β -CD@Pd(II) was measured to be 0.088 mmol g⁻¹ by ICP. It exhibits excellent catalytic activity for the Suzuki and Heck reactions in water, and can be easily separated and consecutively reused for at least nine times. In addition, a series of pharmacologically interesting products were successfully synthesized using this catalyst to demonstrate its potential applications in pharmaceutical industries. Above all, this work opens up an interesting and attractive avenue for the use of cyclodextrin-functionalized h-BN as an efficient support for hydrophilic heterogeneous catalysts.

KEYWORDS

boron nitride, cross-coupling reaction, cyclodextrin, heterogeneous catalyst, water

On the other hand, biphenyls and acrylates constitute a class of key structural motifs present in numerous biologically important compounds, such as nifedipine, biphenylindanone A, losartan HIV-1 protease and taxol.^[3] They are also useful for the construction of structurally important compounds, such as triphenylamino-1,8naphthalimides, poly(9,9-dihexyl)-fluorene and (BTZ-CDT),^[4] benzothiadiazole-cyclopentadithiophene which are widely used in solar cells and electroluminescent materials.^[5] To the best of our knowledge, Suzuki and Heck cross-coupling reactions are the most common and powerful methods to form C-C bonds in the synthesis of these compounds.^[6,7] However, these reactions generally proceeds in the presence of homogeneous palladium catalyst, of which the recycling and separation are complicated and difficult and may also cause unacceptable palladium contamination of products. Furthermore, even though palladium-phosphine catalyzed Suzuki and Heck reactions have achieved great success over the last decade,^[8] the expensive, air-sensitive, and virulent phosphine ligands often limited their spreading in large-scale application. So, it is highly desirable to design a more efficient, stable and recoverable ligand-free heterogeneous palladium catalyst for C-C cross coupling reactions.

Boron nitride (BN) is the isoelectric and isostructural analog to graphite with alternating boron and nitrogen atoms in the structure.^[9–11] Within each layer, boron and nitrogen are connected by strong covalent bonds, while weaker van der Waals bonding stablizes the stacked neighbour layers. Recently, h-BN has attracted increasing attentions due to its high intrinsic thermal conductivity, excellent electrical insulation, and low dielectric constant.^[12] By utilizing its intrinsic thermal conductivity, h-BN was studied as an effective heat transferring medium between an electrical conductor made of CNTs/CNFs and an epoxy resin in shape memory polymer nanocomposites for Joule heating and infrared light induced shape recovery behaviors.^[13,14] Moreover, its strong mechanical and corrosion resistance, high stability against thermal shock, chemical attacks^[15] and oxidation^[16-18] make h-BN a promising catalyst support for all applications where stability is a concern.

In addition, from the viewpoint of green chemistry, it is preferable to use water to replace toxic organic solvents as the reaction medium. However, many developed heterogeneous catalytic systems suffer from the drawbacks of low catalytic activity and selectivity, and are not suitable for the reactions in aqueous media as most organic substrates have poor solubilities in water. These problems can be easily solved by introducing a water-soluble material onto the heterogeneous catalysts. For instance, β -cyclodextrin (β -CD), a kind of excipients, is such a material. It is composed of seven glucoside units and contains a hydrophobic internal cavity capable of hosting a wide range of inorganic and organic molecules to form the inclusion complexes.^[19] This hosting process has been shown enhanced fluorescence intensity when β -CD are bound with various substrates.^[20,21] Furthermore, β -CD is able to stabilize catalytically active nanoparticles via hydrophobic-hydrophobic interactions between metal nanoparticles and cyclodextrin.^[22,23] Based on this property, combinations of nanomaterials and cyclodextrins have been successfully employed in the analysis of pollutants^[24-26] environmental and in biosensing applications.^[27,28]

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.^[29] 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 surface of pristine h-BN, where the metal nanoparticles are bounded only by weak non-covalent interactions. On the other hand, despite several studies on the morphology, properties and preparation of organic modified h-BN,^[30] no metal has been immobilized onto organicfunctionalized boron nitride as a heterogeneous catalyst. Herein, we report the first production of Pd catalyst based on β-CD modified h-BN, as a separable and recyclable catalyst for Suzuki and Heck coupling reactions. All these reactions were performed in water and ligand-free conditions with high efficiency and excellent yields. To the best of our knowledge, this is the first report on the immobilization of palladium ion on BN for catalytic application purpose. And, this also is 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, to immobilize the Pd(II) onto β -CDfunctionalized hexagonal boron nitride, a four steps process was introduced. 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, β -cyclodextrin was attached to h-BN@APTMS *via* the carbonyldimidazole (CDI) promoted condensation reaction. Ultimately, the complexation of Pd(OAc)₂ onto β -CD generated 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 Figure 1a-b, no obvious morphology difference has been found between h-BN and h-BN@OH. They all exhibit schistose structures with smooth edges and flat surfaces. And it can be clearly seen that the size of palladium(II) loaded nanocatalyst is in ranges of 50–500 nm. Notably, after functionalization, the h-BN nanosheets still arranged in schistose structures but appeared to be broken and aggregated (Figure 1c).

Infra-red spectroscopy was used to characterize the organic components bound to the surface of h-BN (Figure 2). The characteristic absorption band of B-N bonds was observed at 1395 cm^{-1} and 799 cm^{-1} (Figure 2a), which



SCHEME 1 The synthetic strategy for the synthesis of h-BN@ β -CD@Pd(OAc)₂

was slightly shifted to 1391 cm⁻¹ and 806 cm⁻¹ after conjugating with APTMS (Figure 2a 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 (Figure 2a-b and d). Comparison studies on h-BN@OH and h-BN@APTMS revealed that the additional strong bands at 1120 and 1033 cm⁻¹ may correspond to the characteristic absorption of Si-O bonds formed through the silylation process. Besides, another h-BN@APTMS peak at 2928 cm⁻¹ could be assigned to the stretching vibration of C-H bonds of propyl-amine groups (Figure 2b). Moreover, the spectrum of β -CD (Figure 2c) displayed characteristic peaks at 1050 and 927 cm⁻¹ were also observed in spectrum of h-BN@ β -CD with little shift (Figure 2d). These results provided direct evidences of the conjugation of APTMS and β -CD on h-BN.

For the quantitative analysis, the as-prepared *h*-BN@OH, *h*-BN@APTMS, *h*-BN@ β -CD, and *h*-BN@ β -CD@Pd(OAc)₂ were further observed via TGA, and these results are shown in Figure 3. The experiments were performed at up to 800 °C in an N₂ 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 could be ascribed to the removal of physically adsorbed solvents and surface hydroxyl groups. Likewise, a weight loss of about 3.66% and 5.64% were observed for h-BN@APTMS and h-BN@ β -CD, respectively. These should be due to the thermal degradation of organic components on the BN complex. Moreover, around 1.98% weight loss was observed when comparing these two samples. It suggests that β -CD was successfully conjugated to

h-BN@APTMS particles. For the curve of *h*-BN@ β -CD@Pd(OAc)₂, 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 4.18%. The amount of palladium (0.94%) of *h*-BN@ β -CD@Pd(OAc)₂ was determined by inductively coupled plasma (ICP) analysis. The TGA curve and atomic absorption analysis also confirmed the successful supporting of Pd(OAc)₂ onto the functionalized *h*-BN. In all, these results further corroborated the FT-IR data.

Figure 4 shows the wide angle XRD patterns of *h*-BN@APTMS and *h*-BN@ β -CD@Pd(OAc)₂ nanomaterials. These two samples show the same diffraction peaks at $2\theta = 26.7$, 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@ β -CD 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@ β -CD@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@ β -CD@Pd(OAc)₂ was collected by X-ray photoelectron spectroscopy (XPS) and the corresponding results are presented in Figure 5. The new peaks of O 1 s, C 1 s and Si

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FIGURE 1 SEM of (a) pristine h-BN, (b) h-BN@OH and (c) h-BN@ $\beta\text{-}CD@Pd(OAc)_2$

2p seen in Figure 5a, indicated that (3-Aminopropyl) trimethoxysilane (APTMS) had been successfully attached to the surface and edges of pristine BN particles. And the



FIGURE 2 FT-IR spectra of (a) h-BN@OH, (b) h-BN@APTMS, (c) β -CD, (d) h-BN@ β -CD



FIGURE 3 TGA thermograms of h-BN@OH, h-BN@APTMS, h-BN@β-CD, and h-BN@β-CD@ Pd(OAc)₂

spectrum of the *h*-BN@ β -CD@Pd(OAc)₂ showed a large increase in the signal intensity of the O 1 s and C 1 s peaks. This could be attributed to covalently attachment of β -CD to the *h*-BN@APTMS.

The B 1 s spectra of h-BN@ β -CD@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 (Figure 5b).^[31] 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 (Figure 5c). In the de-convoluted Si 2p spectra, the strong peak at 102.1 eV of the binding energy represented the bond between silicon and oxygen originating from the BN particles (B-O-Si), indicating that the surface curing agent and BN particles were 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 could be attributed to Si-C bonding in the silane curing agent molecules. These results are in agreement with the reaction mechanism of



FIGURE 4 XRD patterns of h-BN@APTMS and h-BN@ β -CD@Pd(OAc)₂



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

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 then might be attributed to the Si-OH bonding, indicating that some hydroxyl groups were not hydrolyze and a small amount of hydroxyl group remained.^[32]

The XPS spectrum of the Pd 3d core level region for the h-BN@ β -CD@Pd(OAc)₂ nanocomposite displayed main peaks at 338.2 and 343.4 eV, which could be attributed to the binding energy of Pd 3d_{5/2} and Pd 3d_{3/2}, respectively (Figure 5d). These values correspond to the Pd(II) binding energies of Pd(OAc)₂.

2.3 | Investigation of the catalytic activity of h-BN@β-CD@Pd(OAc)₂ in the Suzuki reaction

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@ β -CD@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 Cs₂CO₃, KOH, t-BuOK, K₂CO₃, Et₃N and NaHCO₃, were used in this transformation. And the best yield was obtained in the presence of K₂CO₃ (Table 1, entries 1–6). With respect to the amount of K₂CO₃, 1.5 equivalents was found to be adequate, as neither larger nor smaller amount showed better vields (Table 1, entries 7-9). When the reaction was allowed to proceed in different temperatures, an optimal yield of 99% 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 3a significantly (Table 1, entries 14-15). Above all, aryl halides (1, 1 mmol) in the presence of a catalytic amount of h-BN@β-CD@Pd(OAc)₂ (0.05 mmol) and K₂CO₃ (1.5 mmol) with phenylboronic acids (2, 1.5 mmol) in water at 70 °C was considered to be the ideal reaction conditions.

After the optimization of the reaction conditions, we examined the catalytic activity of h-BN@ β -CD@Pd(OAc)₂ for various aryl halides and phenylboronic acids. As shown in Scheme 2, all the substrates including electron-donating or electron-withdrawing functional groups were successfully converted to the corresponding biphenyls in good to excellent

$Br + U = B(OH)_2 + B(OH)$						
Entry	Base	Pd (.Equiv)	Temp. (°C)	Yield ^b (%)		
1	Cs ₂ CO ₃	0.05	70	81		
2	КОН	0.05	70	90		
3	t-BuOK	0.05	70	87		
4	K ₂ CO ₃	0.05	70	99		
5	Et ₃ N	0.05	70	79		
6	NaHCO ₃	0.05	70	75		
7 ^c	K ₂ CO ₃	0.05	70	76		
8 ^d	K ₂ CO ₃	0.05	70	85		
9 ^e	K ₂ CO ₃	0.05	70	97		
10	K ₂ CO ₃	0.05	25	37		
11	K ₂ CO ₃	0.05	50	77		
12	K ₂ CO ₃	0.05	100	81		
13	K ₂ CO ₃	0.01	70	75		
14	K ₂ CO ₃	0.1	70	99		
15	K ₂ CO ₃	0.2	70	97		

TABLE 1 Optimization of the Suzuki reaction between 4-bromoacetophenone and phenylboronic acid using h-BN@ β -CD@Pd(OAc)2 as catalyst^a

^aReaction conditions: **1a** (1 mmol), **2a** (1.5 mmol), h-BN@β-CD@Pd(OAc)₂ (0.05 mmol), base (1.5 mmol), H₂O (1 mL), Ar, 0.5 h. ^b Isolated yield. ^c K₂CO₃ (0.5 mmol). ^d K₂CO₃ (1.0 mmol). ^e K₂CO₃ (2.0 mmol)



SCHEME 2 Investigation of the substrate scope for Suzuki reaction catalyzed by h-BN@ β -CD@Pd(OAc)₂. Reaction conditions: **1** (1 mmol), **2** (1.5 mmol), h-BN@ β -CD@Pd(OAc)₂ (0.05 mmol) and K₂CO₃ (1.5 mmol) in water (1 mL) at 70 °C

yields. Besides, synthetically useful naphthyl and pyridyl were well tolerated in this transformation, giving **3** \mathbf{k} and **3q** in good yields. Furthermore, the experimental procedure is very simple and convenient, and can tolerate a variety of different functional groups such as OH, OCH₃, CN, CHO, NO₂, NH₂ and halogen.

2.4 | Investigation of the catalytic activity of h-BN@ β -CD@Pd(OAc)₂ in the Heck reactions

In order to extend the catalytic applications of h-BN@ β -CD@Pd(OAc)₂, it was then applied to 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, K₂CO₃ turned out to be the best choice, while others such as Cs₂CO₃, KOH, t-BuOK, Et₃N and NaHCO₃ were less effective (Table 2, entries 1–6). For the optimal amount of K₂CO₃ used in the model reaction, two equivalent was found to be adequate, as neither larger nor smaller amount showed better yields (Table 2, 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 2, entry 4). However, when the temperature was increased to

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TABLE 2 Optimization of the Heck reaction between iodobenzeneand styrene using h-BN@ β -CD@Pd(OAc)2 as catalyst^a

h-BN@β-CD@Pd(OAc) ₂ base, H ₂ O					
4a Entry	Base	Pd (.Equiv)	Temp. (°C)	Vield ^b (%)	
1	Cs ₂ CO ₃	0.05	90	67	
2	KOH	0.05	90	83	
3	t-BuOK	0.05	90	80	
4	K ₂ CO ₃	0.05	90	93	
5	Et ₃ N	0.05	90	72	
6	NaHCO ₃	0.05	90	77	
7 ^c	K ₂ CO ₃	0.05	90	11	
8 ^d	K ₂ CO ₃	0.05	90	70	
9 ^e	K ₂ CO ₃	0.05	90	81	
10	K ₂ CO ₃	0.05	50	20	
11	K ₂ CO ₃	0.05	70	67	
12	K_2CO_3	0.05	100	83	
13	K ₂ CO ₃	0.01	90	60	
14	K ₂ CO ₃	0.02	90	75	
15	K ₂ CO ₃	0.1	90	93	

^aReaction conditions: **4a** (1 mmol), **5a** (1.5 mmol), h-BN@β-CD@Pd(OAc)₂ (0.05 mmol), base (2 mmol), H₂O (1 ml), 3.5 h. ^bIsolated yield. ^cK₂CO₃ (0.5 mmol). ^dK₂CO₃ (1.0 mmol). ^eK₂CO₃ (3.0 mmol)

100 °C, the yield of **6a** dropped to 83% (Table 2, entry 12). Only 20% and 67% yields of **6a** were obtained when the reaction were conducted at 50 and 70 °C (Table 2, entries 10–11). Moreover, after extensive screening, we were pleased to find that 0.05 mmol of Pd was enough to catalyze this reaction (Table 2, 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@ β -CD@Pd(OAc)₂ (0.05 mmol) and K₂CO₃ (2.0 mmol) in water at 90 °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 Scheme 3. 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 **6 1–p** could also be obtained in excellent yields. Notably, synthetically useful heterocyclic groups, such as thienyl (**6p**), were well tolerated in this transformation. Furthermore, a variety of functional groups such as carbonyl, ether, halogen, amino, nitro and aldehyde groups were well-suited for this reaction.



SCHEME 3 Investigation of the substrate scope for Heck reaction catalyzed by h-BN@ β -CD@Pd(OAc)₂. ^aReaction conditions: **4** (1 mmol), **5** (1.5 mmol), h-BN@ β -CD@ Pd(OAc)₂ (0.05 mmol) and K₂CO₃ (2 mmol) in water (1 ml) at 90 °C. ^bR₃ = I. ^cR₃ = Br. ^d70 °C

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@β-CD@Pd(OAc)₂ has been reused thirteen times in the reaction of 4-bromoacetophenone and phenylboronic acid without significant loss of its catalytic activity (Figure 6a). Similarly, the catalyst also remained to be catalytically active after being reused nine times in the reaction of 1-iodo-2-nitrobenzene



FIGURE 6 Reusability of h-BN@ β -CD@Pd(OAc)₂ for the synthesis of **3a** (a) and **60** (b)

and methyl acrylate. The Heck reaction in the 8th and 9th runs gave the desired product in 90% and 92% yields (Figure 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.

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.^[33] And the impressive ability of Pd catalysts to create C-C bonds provides many new avenues for designing medicinal candidates. Inspired by its high efficiency, excellent recyclability and wide scope of substrates, h-BN@ β -CD@Pd(OAc)₂ was utilized in the synthesis of three pharmacologically important products through Suzuki and Heck reactions (Figure 7).

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.^[34] Felbinac acts as a non-selective inhibitor of the enzyme cyclooxygenase (COX), and inhibits both 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@ β -CD@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.^[35] And good antibacterial activity of compound 6r had been exhibited by Davis and co-works.^[36] These two compounds can be easily obtained in 97% and 95% yields via h-BN@β-CD@Pd(OAc)₂ catalyzed Heck reactions.

2.7 | Large-scale experiments

Finally, considering the general application of this catalyst, we demonstrated the gram-scale progress, and two examples



FIGURE 7 Pharmacologically relevant compounds synthesized by using h-BN $@\beta$ -CD $@Pd(OAc)_2$ as catalyst



SCHEME 4 Large-scale reactions

of large-scale reactions with excellent yields of the products are shown in Scheme 4.

3 | CONCLUSIONS

In conclusion, we have introduced an efficient and simple method for the chemical modification of h-BN, as an excellent support for the Pd heterogeneous catalyst. It has been used as an excellent heterogeneous catalyst in the Suzuki and Heck C-C cross coupling reactions. Wide scope of substrates, good to excellent yields, low reaction time, water as solvent, ligandfree, non-toxicity and recyclability of the catalyst are the main merits of these protocols. In addition, this nanocatcalyst can be separated easily by filtration, and can be recycled for at least nine times without appreciable loss of its catalytic activity. Further studies for other applications of this novel nanomaterial are ongoing in our laboratory. We anticipate that this work would open up a new direction for the development of novel and green nanocatalysts using organic modified h-BN as the support.

4 | EXPERIMENTAL

4.1 | General

The h-BN powder (99.9%) was obtained from Micxy Regent Co. Ltd. (Chengdu, China). (3-Aminopropyl)trimethoxysilane (APTMS, 97%), 1,1-carbonyldiimidazole (CDI, 97%) were purchased from Aladdin Reagent Co.Ltd. (Shanghai, China). β -cyclodextrin (β -CD, 99.0%), was provided by Chengdu Kelong Chemicals Co. Ltd. (Chengdu, China). Sodium hydroxide (NaOH, 96%) was collected from Tianjin Ruijinte 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 (0.2 mm), while column chromatography characterization was performed with silica gel (100-200mesh). ¹H NMR spectra were recorded at 400 or 600 MHz and ¹³C NMR spectra were recorded at 100 MHz. -WILEY-Organometallic 9 of 11 Chemistry

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 N₂ 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**

4.2.1 | Preparation of hydroxy functionalised h-BN (h-BN@OH)

First, *h*-BN (4 g) was dispersed in 5 M 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.

4.2.2 | 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)trimethoxysilane (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.

4.2.3 | Preparation of 1,1carbonyldiimidazole-β-cyclodextrin complex (β-CD-CDI)

 β -cyclodextrin (1 g, 0.88 mmol) and 1,1-carbonyldiimidazole (1.16 g, 7.14 mmol) were dissolved into 14 mL *N*,*N*-dimethyl-formamide (DMF) and stirred with argon protection at room temperature for 2 h. The solution was then precipitated with cold diethylether and filtered. The resulted white solid (1.04 g) was rined with acetone for 6 times and dried with vacuum desiccator at room temperature for 2 h.

4.2.4 | Preparation of β-cyclodextrin conjugated h-BN (h-BN@β-CD)

The prepared *h*-BN@APTMS (1 g) was dispersed into dry DMF (60 ml) and stirred at room temperature for 1.5 h. Next, β -CD-CDI (0.45 g) was added into the above solution. And the mixture was further stirred in a two-neck flask with argon protection at room temperature for 7 h. The resulting particles (*h*-BN@ β -CD) were filtered and successively washed with DMF and DCM each for 5 times to remove unreacted chemicals. Finally, the particles (0.99 g) were dried under vacuum desiccator at room temperature for 6 h.

4.2.5 | Preparation of h-BN@β-CD@Pd(OAc)₂

h-BN@ β -CD (1.0 g) and Pd(OAc)₂ (664 mg, 2.9 mmol) was mixed in DCM (100 ml) at room temperature, and stirred for 12 h under argon protection. The resulting mixture was filtered and washed with DCM for 5 times to remove unreacted Pd(OAc)₂. Finally, the off-white solid (0.98 g) was dried under vacuum at room temperature for 5 h.

4.3 | General procedure for the Suzuki reaction

In a typical run, h-BN@ β -CD@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 K₂CO₃ (1.5 mmol) in water (1 ml). The resulting mixture was stirred at 70 °C under Ar, 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 Na₂SO₄ 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@ β -CD@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**.

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