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FULL PAPER

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Ligand-free Mizoroki–heck reaction using reusable modified graphene oxide-supported Pd(0) nanoparticles

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Palladium nanoparticles supported on graphene oxide surfaces modified with metformin was found to be an effective and recyclable nanocatalyst in Mizoroki–Heck coupling reactions under aerobic conditions without requiring any phosphine or ligand coordination. Excellent product yields were achieved with a wide variety of substrates and the catalyst could be recycled seven times without any noticeable loss of its catalytic activity.

KEYWORDS
graphene oxide, heck, metformin, nanocatalyst, palladium

1 | INTRODUCTION

One of the important cross-coupling reactions is the Mizoroki–Heck reaction. In general, cross-coupling reactions are known as powerful synthesis approaches that enable formation of carbon–carbon bonds. This means that they can provide arylation, alkylation or vinylation of various alkenes through reaction with aryl, vinyl, benzyl or allyl halides in the presence of an appropriate base. Catalysis of these reactions is usually undertaken using homogeneous palladium complexes, in which Pd is coordinated to phosphine ligands to make the complexes water soluble. However, such homogeneous catalytic systems are not recoverable and need coordinated unstable and toxic ligands.[1–10] The ligands aim to activate and stabilize Pd against agglomeration and Pd black formation, in many homogeneous catalysts. Alternatively, heterogeneous Pd nanocatalysts should be developed, which can exhibit high activity, stability and recyclability, simultaneously. Recyclability is a considerable objective of nanomaterial research that would significantly impact chemical and pharmaceutical industries in the future.

The reason that this study has applied Pd to the Heck reaction is that Pd nanoparticles (NPs) have demonstrated high catalytic activity for this reaction.[11,12] Also, immobilization of Pd NPs on various solid supports has been studied by several researches for the preparation of active and stable catalytic systems for the Heck reaction. In this respect, carbon nanomaterials,[13] silica,[14] hydroxyapatite,[15] magnetic NPs,[16] molecular sieves,[17] metal–organic frameworks[18] and polymers[19,20] have been used to stabilize NPs.

One of the catalyst supports that should be evaluated for Pd stabilization and immobilization is graphene oxide (GO), which can be produced by oxidation of graphene. GO is one of the most large-scale cost-effective products of chemically modified graphene.[21,22] Moreover, it is superior to other carbon-based supports, e.g. carbon nanotubes and porous carbon, due to its higher surface-to-weight ratio, accessible surface area and controllability of its chemical composition.[23,24] These advantageous GO characteristics make it a more convenient catalyst support since surface chemistry of catalyst supports can play an important role in tuning catalytic activity and preventing leaching of supported metallic NPs. Furthermore, application of GO-supported Pd catalysts for the Heck reaction is motivated by their improved catalytic activities in oxygen reduction and Suzuki–Miyaura cross-coupling reactions.[25,26] Recently, we reported the preparation of Pd NPs that were incorporated into a metformin/GO nanocomposite (Pd/Met/GO) and Pd/Met/GO was found to be a novel recoverable heterogeneous catalyst in Suzuki–Miyaura reactions.[27] In the work reported herein, the catalytic activity of Pd/Met/GO was investigated in Mizoroki–Heck reactions.

2 | EXPERIMENTAL

2.1 | Preparation of GO

GO nanosheets were prepared from natural graphite powder using a modified Hummers method.[28]

2.2 | Synthesis of Pd(II)/met/GO and Pd(0)/met/GO

Met/GO was synthesized by the condensation reaction of GO and Met. Briefly, 50 mg of GO was dispersed in 50 ml of dimethylformamide (DMF). After ultrasonication for 1 h, the GO solution was cooled to 0 °C and then 6 mmol of EDC and 6 mmol of NHS were added. The mixture was stirred for 2 h at 0 °C. Then 10 mmol od Met was added and stirred at 100 °C for 24 h. The obtained Met/GO was separated by filtration and washed successively with acetone and water. Met/GO was dried in vacuum at 40 °C.

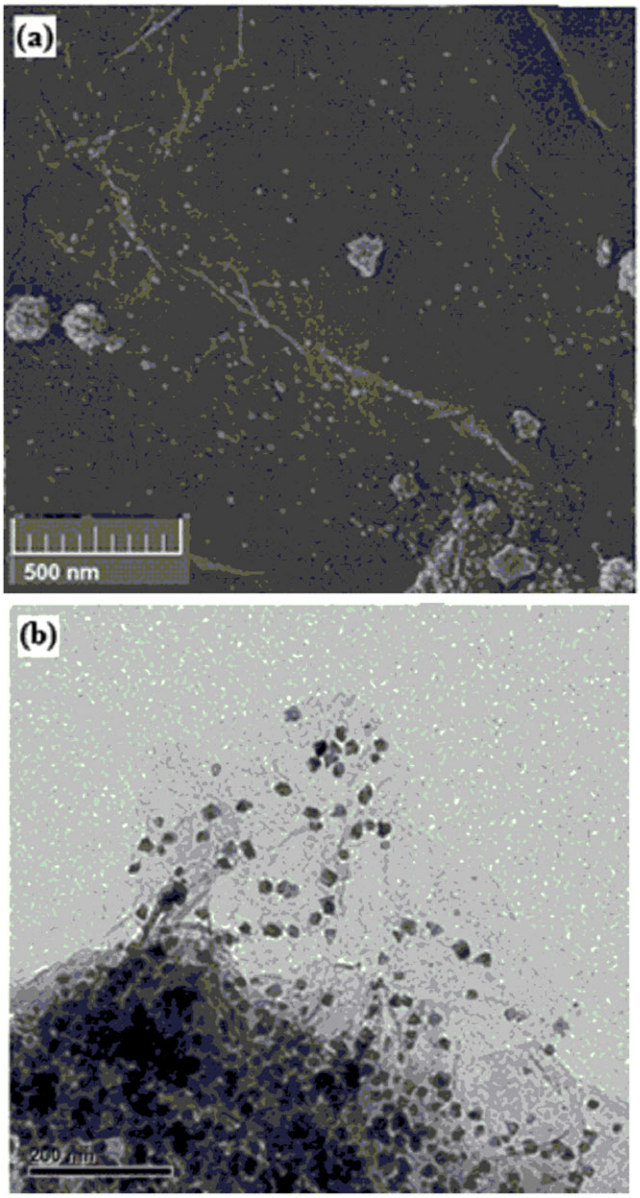


FIGURE 1 (a) FESEM and (b) TEM images of Pd/met/GO

For the preparation of Pd(II)/Met/GO and Pd(0)/Met/GO,[27] 50 mg of Met/GO was dispersed in 100 ml water. After the solution was sonicated for 15 min, 5 mg of $PdCl_2$ was added and the mixture was sonicated for 10 min. Then the solution was stirred overnight. After filtration, the solid was washed successively with water and acetone. The obtained Pd(II)/Met/GO was dried in vacuum at 40 °C. The reduction of Pd(II)/Met/GO using hydrazine hydrate was performed as follows: 30 mg of Pd(II)/Met/GO was dispersed in 50 ml of water, and then 90 μl of hydrazine hydrate (80%) was added. The pH of the mixture was adjusted to 10 with 25% ammonium hydroxide and the reaction was carried out at 95 °C for 2 h. The final product, Pd(0)/Met/GO, was washed with water and dried in vacuum at 50 °C. The concentration of Pd in Pd/Met/GO was 4.2 wt% (0.39 mmol g^{-1}), which was determined using inductively coupled plasma atomic emission spectrometry (ICP-AES).

2.3 | General procedure for Mizoroki–heck reactions

A mixture of aryl halide (1 mmol), olefin (1.2 mmol), triethylamine (2 mmol), DMF (3 ml) and Pd/Met/GO (10 mg, 0.1 mol%) was added into a round-bottomed flask and stirred at 110 °C in atmosphere for 1–12 h. After completion of the reaction, the reaction mixture was cooled to room temperature and the catalyst was recovered by centrifugation and washed with ethanol, and then dried under vacuum for reuse. The residual mixture was extracted with EtOAc (3 × 20 ml), and the combined organic layer was dried over $MgSO_4$. The solvent was

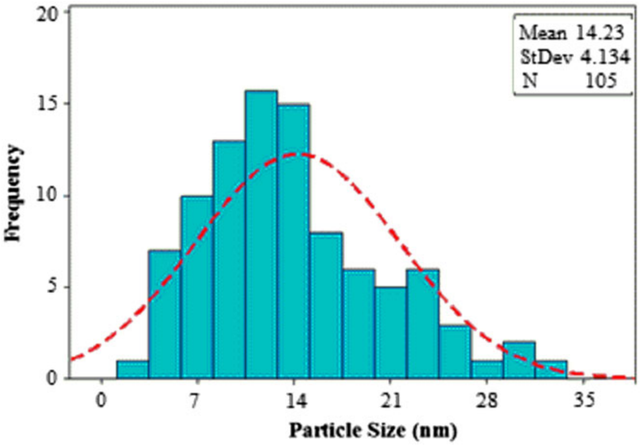
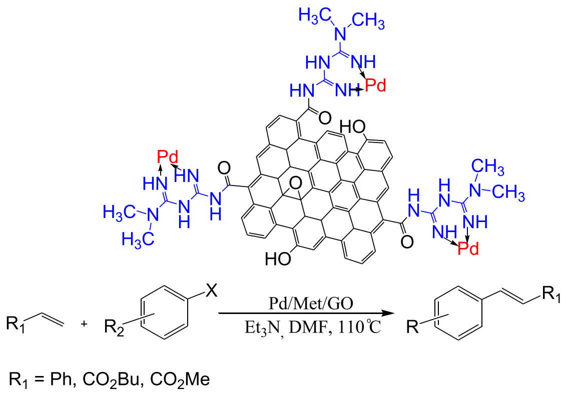


FIGURE 2 Size distribution of Pd NPs from TEM imaging of Pd/met/GO



SCHEME 1 Pd/met/GO as heterogeneous catalyst in heck coupling reactions

evaporated and the crude products were purified by column chromatography (hexane–acetone, 6:1).

3 | RESULTS AND DISCUSSION

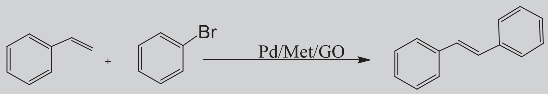
The main objective of our ongoing research programme is the development of new synthetic methodologies.[29] Therefore, the title catalyst was fabricated,[27] and its surface morphology was investigated using field-emission scanning electron microscopy (FESEM) and transmission electron microscopy (TEM). Figure 1(a) presents a FESEM image of Pd/Met/GO with large quantities of Pd NPs distributed on Met/GO surfaces. According to TEM analysis (Figure 1b), Pd is dispersed well on the surface of Met/GO. More importantly, the morphology results indicate that Met has a significant role in promoting the dispersibility of Pd/Met/GO and preventing aggregation of Pd NPs. Figure 2 shows the size distribution of the Pd NPs and reveals that their average size is about 14.23 nm.

To evaluate the catalytic activity of the synthesized Pd/Met/GO nanocomposite in heterogeneous catalysis, the Heck coupling reaction was considered (Scheme 1). As the first step of exploring the performance of the catalyst in Heck reactions, the conditions of coupling reaction between bromobenzene and styrene were optimized as a model reaction through choosing various amounts of catalyst and applying various solvents and bases (Table 1).

Among the examined bases, Et_3N displayed the highest level of effectiveness and the other bases were substantially less effective. In addition, evaluation of the effect of solvent on the Heck coupling reaction indicated that DMF is the best solvent choice (Table 1, entry 9).

After optimizing and identifying the most reliable set of conditions (Table 1, entry 9), the scope and generality of the developed protocol were investigated with respect to aryl halide structures and olefins using 0.1 mol% Pd/Met/GO, in the presence of 2 eq. of Et_3N in DMF at 110 °C. The obtained results are summarized in Table 2.

TABLE 1 Optimization of conditions for heck reaction of bromobenzene with styrene[a]

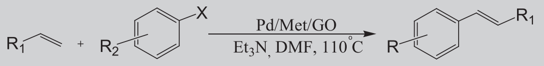


Entry	Solvent	Pd (mol%)	Base	Time (h)	Yield (%)[b]
1	EtOH–H_2O	0.1	K_2CO_3	6	50
2	Toluene	0.1	K_2CO_3	6	70
3	EtOH	0.1	K_2CO_3	8	35
4	MeOH	0.1	K_2CO_3	8	35
5	CH_2Cl_2	0.1	K_2CO_3	8	Trace
6	H_2O	0.1	K_2CO_3	12	45
7	CH_3CN	0.1	K_2CO_3	6	60
8	DMF	0.1	K_2CO_3	3	80
9	DMF	0.1	Et_3N	3	96
10	DMF	0.1	NaOAc	3	72
11	DMF	0.1	KOH	3	65
12	DMF	0.1	NaOH	3	60
13	DMF	0.2	Et_3N	3	96
14	DMF	0.05	Et_3N	6	75

[a] Reaction conditions: bromobenzene (1 mmol), styrene (1.2 mmol), Pd/Met/GO, solvent (3 ml), reflux.

[b] Isolated yield.

TABLE 2 Scope of heck–Mizoroki reaction



Entry	R_1	R_2	X	Time (h)	Yield (%)[b]	M.p. (°C)	
						Found	Reported
1	Ph	H	I	1	96	122–124	121–123[30]
2	Ph	H	Br	3	96	122–124	121–123[30]
3	Ph	H	Cl	24	75	122–124	121–123[30]
4	Ph	4-OMe	I	1	96	134–136	135–137[30]
5	Ph	4-OMe	Br	5	96	134–136	135–137[30]
6	Ph	4-Cl	I	2	96	37–39	38–40[31]
7	Ph	4-$COCH_3$	Br	8	85	142–145	142–145[32]
8	Ph	4-CH_3	I	1	96	118–120	117–119[32]
9	Ph	4-CH_3	Br	3	95	118–120	117–119[32]
10	Ph	4-CH_3	Cl	24	75	118–120	117–119[32]
11	CO_2Bu	H	I	1	96	—	
12	CO_2Bu	H	Br	2	90	—	
13	CO_2Me	H	I	1	90	—	
14	CO_2Me	H	Br	2	85	—	

[a] Reaction conditions: bromobenzene (1 mmol), olefin (1.2 mmol), Pd/Met/GO (10 mg, 0.1 mol%), Et_3N (2 mmol), DMF (3 ml).

[b] Isolated yield.

Phenyl iodide, phenyl bromide and phenyl chloride can react efficiently with styrene, under optimized conditions (Table 2, entries 1–3). Both electron-withdrawing and electron-releasing functional groups on styrene can give the corresponding *trans*-stilbene products in good yields (Table 2, entries 4–10). Olefins, such as methyl acrylate and or butyl acrylate, were very well tolerated under the optimum conditions (Table 2, entries 10–14).

Recyclability of a heterogeneous catalyst is essential for its large-scale application. Therefore, it was imperative to recycle and reuse Pd/Met/GO, in the reaction between bromobenzene and styrene under optimal conditions. With this purpose, when the reaction was completed, the reaction mixture was cooled to room temperature. Then, EtOAc was added to the reaction mixture and the catalyst was separated through centrifugation. The separated catalyst particles were then rinsed with water and ethanol and reused in further catalytic runs. The data for catalytic activity of the reused catalyst (Figure 3) indicate that the catalyst can be recycled seven times without any significant loss of its activity. The observed high level of catalytic activity can be attributed to the strong interaction between Pd NPs and the active sites of Met.

To determine heterogeneity of Pd/Met/GO, the hot filtration test was carried out with the Heck reaction between bromobenzene and styrene under the optimum conditions. After 60 min of reaction progress, 54% product yield was achieved, and then Pd/Met/GO was separated by centrifuging the reaction mixture. After separating the catalyst, the reaction was continued for another hour. However, no increase in yield of the target product was observed. This observation verified the heterogeneity of the catalyst. The amount of Pd leached into the reaction solution was determined using ICP-AES. The Pd content of Pd/Met/GO (after seven cycles) was determined to be 0.38 mmol g^{-1}, which means the Pd content had

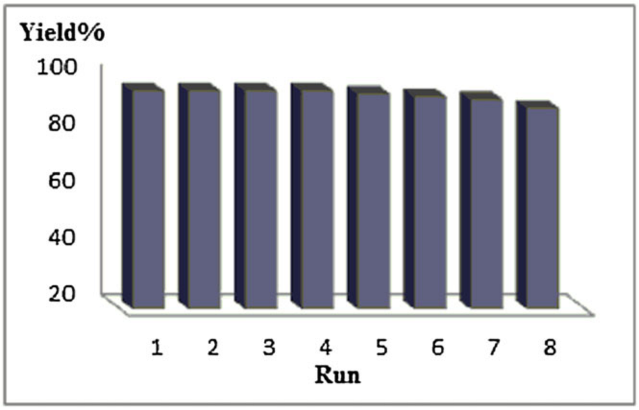


FIGURE 3 Recycling of Pd/met/GO for heck coupling reaction

decreased about 2% compared to the fresh form. The reason for such a small amount of Pd leaching from the NPs is due to the presence of the Met groups on GO surface.

4 | CONCLUSIONS

This study has evaluated the catalytic performance of Pd/Met/GO and verified its effectiveness in Mizoroki–Heck reactions of aryl halides with olefins and even less reactive aryl chlorides. This heterogeneous nanocatalyst has the following advantages: (a) simple preparation; (b) convenient separation from a reaction mixture by centrifugation; and (c) reusability for several reaction cycles with no significant loss of activity. The presence of Met stabilizes of the catalyst particles. The favourable results presented suggest new perspectives for employing such carbon-supported catalysts in other organic reactions.

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