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Short communication

Ag_1Pd_1-rGO nanocomposite as recyclable catalyst for CDC reactions of 2-arylpyridines with aldehydes

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ABSTRACT

Ag_1Pd_1 nanoparticle-reduced graphene oxide (Ag_1Pd_1-rGO) nanocomposite was used as an efficient catalyst for the synthesis of aromatic ketones via cross dehydrogenative coupling (CDC) reactions of 2-arylpyridines with aldehydes. The catalyst can be reused for 5 cycles without significantly losing its catalytic activity. On the basis of the obtained experimental evidence, we proposed a possible mechanism for the heterogeneous catalysis. We find that the supported catalysts exhibit a set of benefits, including extraordinarily catalytic activity, high reusability and remarkable tolerance of a variety of substrates.

1. Introduction

A major theme in organic synthetic community is to develop ecologically and economically advantageous reactions which have the ability to transform simple precursors to multifunctional compounds or natural products [1]. Due to the abundance of C−H bonds in the starting substrates, direct and efficient conversion of these C−H bonds to C−C bonds is of significant importance [2–5]. Indeed, the past decade has witnessed the rapid development in C−H activation capable of leading to arene-arene or arene-alkane linkages [6]. The reported C−H activation strategies oftentimes relies on directing-group assisted C−H bond functionalization [7] or dehydrogenative cross-coupling [8,9]. In both strategies, catalyst, functionalized partner, and oxidant should be screened carefully to proceed the C−H bond cleavage and subsequent C−C bond formation effectively [10,11].

Aromatic ketones are an important class of chemicals which have widespread applications in the synthesis of pharmaceuticals, fragrance, dye and agrochemical industries [12]. The classical synthesis of aryl ketones is based on the use of Friedel-Crafts acylation of aromatics in the presence of solid acids, such as acid-treated metal oxides and heteropoly acids [13]. In comparison, the direct introduction of carbonyl functionality into aromatic motifs via C−H bond cleavage is more eco-friendly alternative. In fact, the synthesis of such compounds has achieved considerable advances via directed C−H bond activation [14]. A typical strategy is by use of direct acylation of 2-phenyl pyridines with a variety of potential acyl sources, such as aldehydes [15], alcohols [16], toluenes [17], α-oxocarboxylic acids [18], α-diketones [19], benzylamines [20] and alkenes/alkynes [21,22]. The reactions are commonly carried out in the presence of transition metal salts as homogenous catalysts, including $Pd(OAc)_2$ [15,17,19,22], $PdCl_2$ [16,20,21], $Pd(PhCN)_2Cl_2$ [18]. While the use of such homogeneous catalysts usually offers high selectivity and efficiency, the unrecyclable nature of the metal salts tremendously increases the economic cost in the practical use [23]. In addition, utilization of homogeneous catalysts definitely complicates the step of product purification and sometimes can lead to environmental concerns, especially for the case of needing for toxic phosphine compounds as ligands [24].

The use of Pd nanoparticles for C−H bond activation is expected to provide an alternative pathway to address the aforementioned issues [25]. In addition to catalyzing C−C coupling [26,27] and alkene hydrogenation [28], Pd nanoparticles have proven to possess comparable catalytic activity to palladium salts in C−H bond functionization. For example, the use of $Pd/\gamma\text{-}Al_2O_3$ (3 wt%) as catalyst led to the reaction of 2-phenylpyridine with benzaldehyde with a yield up to 88% in the presence of *tert*-butyl peroxybenzoate as oxidant [29]. However, this reaction applied unsuccessfully to aliphatic aldehydes, and the recyclability of the catalyst was not good. We reason that the catalytic performance of Pd nanoparticles in the C−H bond activation allows to be further improved by doping another component in the Pd lattice to form alloy nanoparticles in which a synergistic effect between the constituting elements appears [30]. By making use of Ag_1Pd_1 alloy nanoparticles on reduced graphene oxide (rGO) as catalysts, here we

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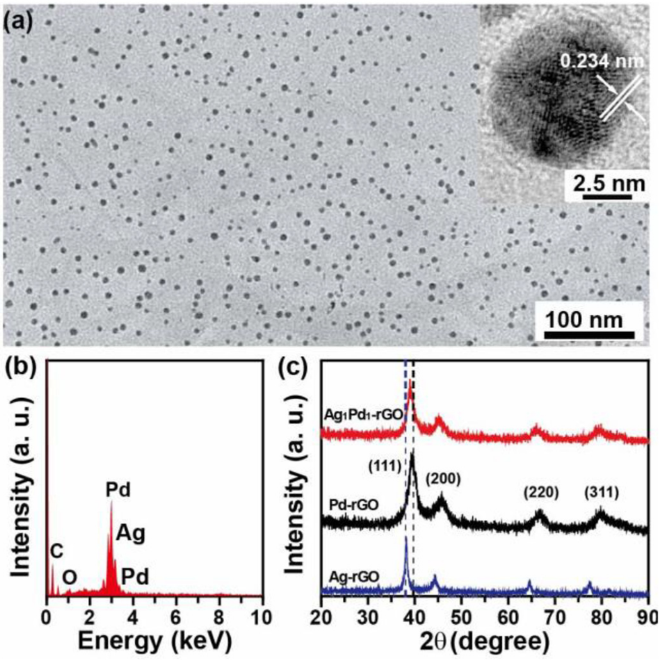


Fig. 1. (a and b) TEM and EDS profile of as-prepared Ag_1Pd_1-rGO nanocomposites, inset in a showing HRTEM image of an Ag_1Pd_1 nanoparticle on rGO. (c) XRD comparison of as-prepared Ag_1Pd_1-rGO, Pd-rGO and Ag-rGO nanocomposites.

report a cooperative effect between the elements of Ag and Pd in cross dehydrogenative coupling reactions of 2-arylpyridines with aldehydes. We find a negligible loss in the catalytic activity of the supported catalyst after 5 successive catalytic cycles. We demonstrate that the heterogeneous catalysts not only have extraordinarily catalytic activity, high reusability, but also remarkable tolerance of a variety of substrates. By combining our experimental evidence with previous findings, we propose a possible mechanism accounting for the heterogeneous catalysis process.

2. Results and discussion

2.1. Characterization of the catalysts

We first synthesized Ag_xPd_y-rGO (x/y = 1/1, 1/3 and 3/1) as well as Ag-rGO (or Pd-rGO) via our reported method (see supporting materials, Fig. S1) [31]. Transmission electron microscopy (TEM) showed that the surface of rGO was homogeneously decorated with Ag_1Pd_1 nanoparticles with an average diameter of 6 nm (Fig. 1a). The high-resolution TEM (HRTEM) image (inset in Fig. 1a) reveals high crystallinity of the loaded nanoparticles, and the *d*-spacing of the lattice fringes (0.234 nm) is in accordance with the lattice parameter of the AgPd alloy [32]. Energy dispersive X-ray spectroscopy (EDS, Fig. 1b) suggested that the atomic ratio of Ag-to-Pd in the alloy nanoparticles is about 1.24/1 that closely matches to the value obtained by inductively coupled plasma optical emission spectrometry (ICP-OES, $m_{Ag}/m_{Pd} = 17.7\%/13.9\%$, $n_{Ag}/n_{Pd} = 1.26/1$). X-ray power diffraction measurement (Fig. 1c) confirmed that the nanoparticles are alloy instead of a mixture of isolated Ag and Pd segments due to the presence of obvious peak shift in the diffraction patterns [33]. Meanwhile, the strong diffraction profiles implied the high crystalline nature of the as-prepared alloy nanoparticles. The character of Ag (0) and Pd (0) in the nanoparticles was further evidenced by X-ray photoelectron spectroscopy (XPS, Fig. S2c). The binding energies for Ag $3d_{3/2}$ (373.6 eV), $3d_{5/2}$ (367.6 eV) and Pd $3d_{3/2}$ (340.2 eV), $3d_{5/2}$ (334.9 eV) are in good agreement with those 3d binding energies for bulk pure Ag and Pd metals, respectively [34]. Other alloy nanoparticles and pure metal nanoparticles were characterized by a similar way before catalytic studies.

2.2. Optimization of the reaction conditions

We carried out catalyst screening for sp^2 C—H bond acylation of 2-phenylpyridine (**1a**) and benzaldehyde (**2a**) in the presence of *tert*-butyl hydroperoxide (TBHP) as an oxidant. We found the use of $Pd(OAc)_2$ (10 mol%) and $Pd(PPh_3)_4$ (3 mol%) offered a yield of 39% and 47%, respectively, after keeping the reaction at 110 °C for 18 h (Table 1, entries 1 and 2). A control experiment showed that indeed no reaction took place in the absence of catalyst (Table 1, entry 3). When replacing $Pd(OAc)_2$ and $Pd(PPh_3)_4$ with heteroneous catalysts of Pd-rGO, a comparable yield was obtained (Table 1, entry 4). To our delight, the yield was substantially elevated to 87% when Ag_1Pd_1-rGO (10 mg, 2.6 mol% Pd) was employed as a heterogeneous catalyst (Table 1, entry 5). The inability of Ag-rGO toward the C—H bond activation (Table 1, entry 6), together with the low catalytic activity of the Pd-rGO, implied a synergistic effect between the Ag and Pd atoms in the acylation of 2-phenylpyridine. The inferior catalytic performance of Ag_1Pd_3-rGO and Ag_3Pd_1-rGO in the model reaction suggested that the synergistic effect is highly dependent on the composition of the alloy nanoparticles (Table 1, entries 7 and 8). On a separate note, the application of commercialized Pd/C as catalyst led to a yield of 5% (Table 1, entry 22), indicating that ordinary Pd^0 heterocatalysts are likely to be ineffective for the cross-dehydrogenative coupling reactions.

Reaction conditions: **1a** (0.5 mmol), **2a** (0.75 mmol), catalyst Ag_1Pd_1-rGO (10 mg), and TBHP (0.75 mmol), 110 °C, 18 h under an air atmosphere. Yields of isolated product are listed.

Besides the nature of the catalyst, other reaction parameters, including the amount of catalyst, solvent, oxidant, temperature and atmosphere, also exert a profound impact on the yield. The reaction conditions were optimized as follows: 10 mg of catalyst Ag_1Pd_1-rGO (2.6 mol% Pd), toluene as solvent, TBHP as oxidant, 110 °C under air atmosphere (Table 1, entries 9–21).

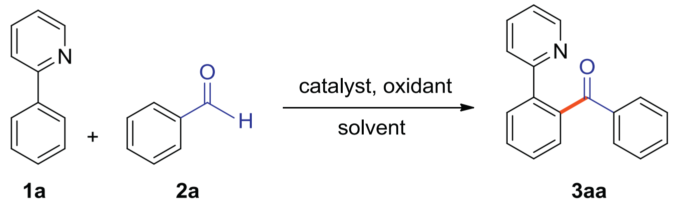
2.3. Synthesis of aromatic ketones

Under the optimized reaction conditions, the scope of the acylation reaction of substituted 2-arylpyridines and various benzaldehyde derives was examined (Scheme 1). A variety of benzaldehydes with electron-withdrawing and electron-donating groups, including methyl, methoxy, chlorine and trifluoromethyl, are suitable for this reaction, and the corresponding products (**3a**(**a–h**)) were obtained in good to moderate yields. In general, the reactivity of the electron-withdrawing group-substituted benzaldehydes is higher than that of the electron-withdrawing precursors. This may attribute to the difference in the activity of the substituted benzoyl radicals in situ formed in the reactions. Notably, the yields of 4-, 3-, 2-methoxy-substituted benzaldehydes were decreased in turn, which should be a result of a gradual increase in the steric effect. In addition, various arylpyridines bearing substituents on the benzene rings were also examined, and the results suggested that the functional groups, including electron-donating and -withdrawing ones, were tolerated (**3**(**b–h**)**a**). The CDC reaction was also applicable to other substrates, such as 7,8-benzoquinoline and 1-phenyl-pyrazole (scheme 1, **3ia**, **3ic**, **3if**, **3ja** and **3jc**), to afford corresponding compounds in good yields. To our delight, good yields were obtained as aliphatic aldehydes were used in the Ag_1Pd_1-rGO catalyzed C—H bond acylation reaction (scheme 1, **3ak**, **3al**, **3bl** and **3il**).

It is worth noting that scale-up reaction (15 times) of 2-phenylpyridine (**1a**) with benzaldehyde (**2a**) afforded a yield of 79%, showing the potential utility of the as-prepared catalyst in practical chemical industry.

We also investigated the possibility of using benzyl alcohol and toluene as potential acylation agent under the same conditions (TBHP:

Table 1
Optimization of reaction conditions for the AgPd-rGO-catalyzed C—H acylation.[a]



Entry	Catalyst	Solvent	Oxidant	Temp (°C)	Yield[b] (%)
1	$Pd(OAc)_2$[c]	Toluene	TBHP	110	39
2	$Pd(PPh_3)_4$[d]	Toluene	TBHP	110	47
3	–	Toluene	TBHP	110	NR
4	Pd-rGO	Toluene	TBHP	110	44
5	Ag_1Pd_1-rGO	Toluene	TBHP	110	87
6	Ag-rGO	Toluene	TBHP	110	NR
7	Ag_1Pd_3-rGO	Toluene	TBHP	110	48
8	Ag_3Pd_1-rGO	Toluene	TBHP	110	31
9	Ag_1Pd_1[e]	Toluene	TBHP	110	59
10	Ag_1Pd_1-rGO[f]	Toluene	TBHP	110	30
11	Ag_1Pd_1-rGO[g]	Toluene	TBHP	110	86
12	Ag_1Pd_1-rGO	DMSO	TBHP	110	Trace
13	Ag_1Pd_1-rGO	PhCl	TBHP	110	80
14	Ag_1Pd_1-rGO	Toluene	TBHP[h]	110	41
15	Ag_1Pd_1-rGO	Toluene	DTBP	110	75
16	Ag_1Pd_1-rGO	Toluene	IBX[i]	110	NR
17[j]	Ag_1Pd_1-rGO	Toluene	O_2	110	NR
18[k]	Ag_1Pd_1-rGO	Toluene	TBHP	110	63
19[j]	Ag_1Pd_1-rGO	Toluene	TBHP	110	74
20	Ag_1Pd_1-rGO	Toluene	TBHP	120	79
21	Ag_1Pd_1-rGO	Toluene	TBHP	100	70
22[l]	5% Pd/C	Toluene	TBHP	110	5

[a] Reaction conditions: **1a** (0.5 mmol), **2a** (0.75 mmol), catalyst (10 mg), and oxidant (0.75 mmol), 110 °C, 18 h under an air atmosphere.
[b] Yields were determined by GC through use of dodecane as an internal standard.
[c] 10 mol%.
[d] 3 mol%.
[e] Pure Ag_1Pd_1 (3 mg).
[f] Catalyst: 5 mg.
[g] Catalyst: 20 mg.
[h] 0.5 mmol TBHP.
[i] 2-iodoxybenzoic acid.
[j] O_2 balloon.
[k] Under argon.
[l] 30 mg.

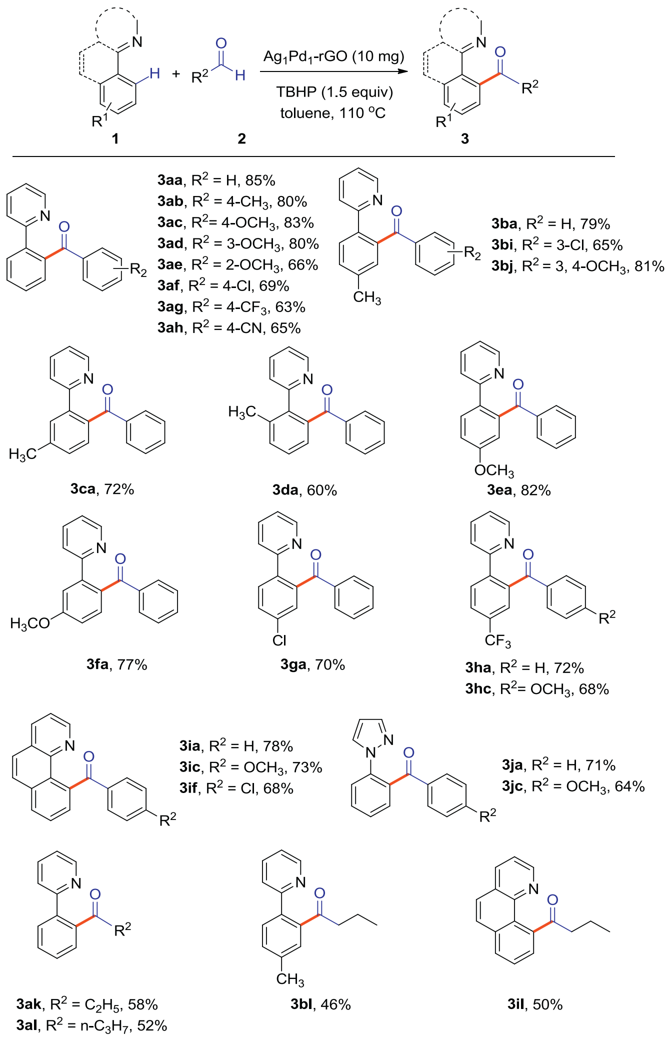
5equiv). However, the obtained yields of **3aa** were estimated to be only 37% and less than 10%, respectively. The lower yields were likely due to the poor ability of experimental conditions to complete both oxidation and coupling in a short time.

2.4. Recyclability of the catalyst

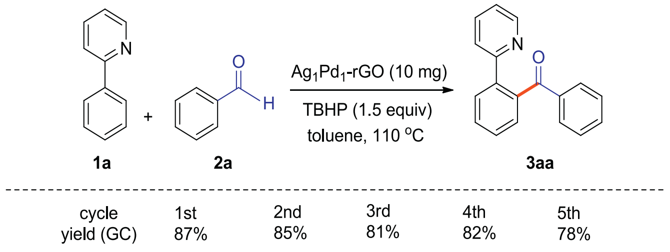
By use of the reaction of 2-phenylpyridine **1a** and benzaldehyde **2a** (Scheme 2) as a model system, we examined the recyclability of the catalyst. We discovered that the catalyst can be reused at least for five cycles with only 9% decline in the activity. The retention of the high catalytic activity of the catalyst is likely due to a marginable increase in the size of Ag_1Pd_1, as evidenced by TEM of the used Ag_1Pd_1-rGO catalyst (Fig. S2a). Besides, no obvious loss and aggregation of the supported Ag_1Pd_1 nanoparticles should make contribution of the maintained high catalytic activity as well. Comparative XRD analysis suggested no change in the crystallinity of these nanoparticles after catalytic use (Fig. S2b). However, XPS measurement (Fig. S2c and d) implied the oxidation of the surface Ag and Pd atoms to Ag(I) and Pd(II) after the catalytic use, respectively.

2.5. Plausible reaction mechanism

To gain more insight into the mechanism of Ag_1Pd_1-rGO catalyzed CDC reaction of 2-phenylpyridine with aldehyde, several control experiments were carried out, as shown in supporting materials. First, the effects of the directing group on the efficiency of the CDC reaction was investigated, the results suggest that the presence of a 2-pyridyl moiety in the starting compound is essential for the C—H bond activation process. Second, a deuterium-labeling experiment was carried out. The kinetic isotope effect (KIE) value of 1.2 was observed from the parallel reactions of **1a** and **1a**-d_5 respectively. The results indicated that the C—H cleavage of 2-phenylpyridine is not involved in the rate determining step. Furthermore, the desired acylation product (**3aa**) could not be obtained when radical inhibitor 2,2,6,6- tetramethyl piperidine-N-oxide (TEMPO, 2 equiv) was added to the standard reaction. This observation suggests a possible radical acylation process. Combing previous findings and our experimental evidence, we proposed a plausible mechanism as illustrated in Scheme 3. Initially, the surface Pd atoms of the alloy nanoparticles chelate with the nitrogen atom of 2-phenylpyridine. The surface Pd atoms are then oxidized into Pd^{II} upon heating at 110 °C in the presence of TBHP and air. The in-situ formed Pd^{II} species play an important role in the activation of the *ortho* C—H



Scheme 1. Scope of the Ag$_1$Pd$_1$-rGO-catalyzed C—H acylation. Reaction conditions: **1a** (0.5 mmol), **2a** (0.75 mmol), catalyst Ag$_1$Pd$_1$-rGO (10 mg), and TBHP (0.75 mmol), 110 °C, 18 h under an air atmosphere. Yields of isolated product are listed.

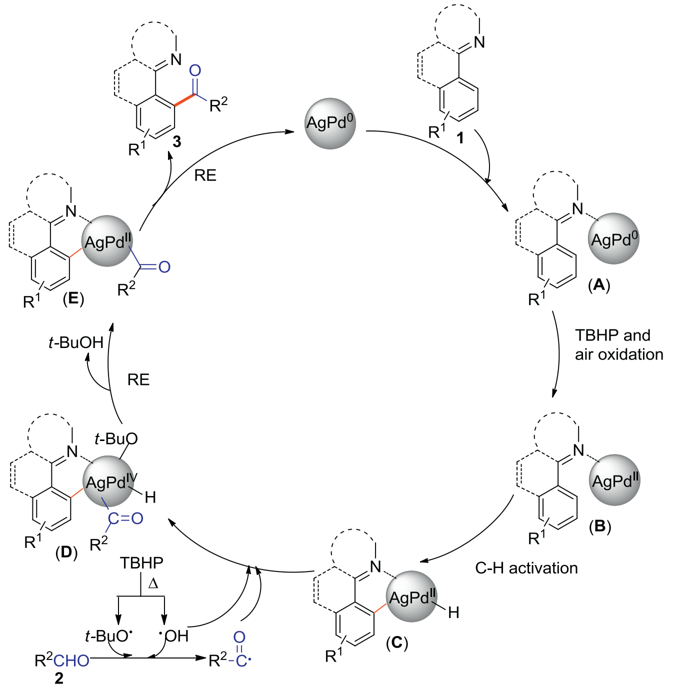


Scheme 2. Recyclability of the Ag$_1$Pd$_1$-rGO during the acylation of **1a** and **2a**.

bond through a chelate-directed effect to afford a palladacycle intermediate **C** [35]. Thereafter, the reaction of TBHP with benzaldehyde provides *t*-BuO radicals and acyl radicals; meanwhile, the two types of the radicals can react with intermediate **C** to form a Pd^{IV} complex **D**. The outcome of the reaction gives rise to *t*-BuOH, accompanying with the formation of intermediate **E**. Finally, the target product **3** is afforded through the reductive elimination of intermediate **E**, together with the regeneration of Pd^0 to continue the catalytic cycle.

3. Conclusions

In summary, we demonstrate that Pd-based alloy nanoparticles anchored on rGO can be used as recyclable catalyst for the direct aryl C—H acylation to efficient synthesis of aromatic ketones. We find a synergetic effect from the constituent atoms toward the C—H bond acylation reactions, and a possible mechanism was proposed. This work suggests that alloying of Pd and other transition metals represents a new strategy to develop high-performance and recyclable nanoparticles toward direct aryl C—H functionalization with great potential practical applications.



Scheme 3. Plausible mechanism for the Ag$_1$Pd$_1$-rGO catalyzed C—H acylation.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.catcom.2018.05.007.

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