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Pd/Mg–La mixed oxide catalyzed oxidative sp^2 C—H bond acylation with alcohols

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ABSTRACT

Pd/Mg–La mixed oxide is used as an efficient catalyst for the oxidative direct acylation of arene sp^2 C—H bonds with alcohols. TBHP was used for in situ oxidation of the alcohols to aldehydes which after coupling with 2-aryl pyridines forms aryl ketones. The catalyst is recovered and used for four cycles.

1. Introduction

One of the most important mission for synthetic chemists is the development of new, more efficient, environmentally benign, air and moisture stable direct transformations that allows reduced number of synthetic operations [1–3]. In this regard, direct conversion of C—H bonds into C—C bonds is highly attractive since they would increase the atom efficiency of the transformations [4,5].

The transition-metal-catalyzed C—H activation reactions have seen great progress [6–10] and many interesting results such as arene C—H bond cleavage to realize C—C [11–20] and C—X [21–27] bond formations have been reported. Scheuermann et al. and others [28,29] have reported the formation of C—C bonds directly from two different C—H bonds through a cross-dehydrogenative coupling reaction catalyzed by transition metals in the presence of oxidizing reagents. Remarkable selectivity in the C—C bond formation has been achieved with the C—H bonds adjacent to a heteroatom or an unsaturated C—C bond catalyzed by transition metals [30–35]. Recently, much effort has been put to realize the formation of arene—arene bonds through the oxidative coupling of two different aryl C—H bonds [29].

Aryl ketones have a wide range of applications in many areas such as pharmaceuticals, fragrances and dyes [36]. Aryl ketones are also used as building blocks in the synthesis of agrochemicals. Synthesis of aryl ketones is performed mainly by classical Friedel–Crafts acylation of aromatic compounds catalyzed by corrosive $AlCl_3$ or by the oxidation of the corresponding secondary alcohols by stoichiometric amounts of toxic oxidizing reagents such as chromium [37].

The direct incorporation of carbonyl functional groups into the aromatic motifs through the transition metal catalyzed C—H bond cleavage will be an attractive synthetic strategy since it will be more environmentally compatible, regioselective and complimentary to the classical Friedel–Crafts acylation. However, the transition metal catalyzed aryl C—H bond reactions with acyl C—H bond remains a highly challenging area.

Li et al. [38,39] and others [40–43] have reported the oxidative sp^2 C—H bond acylation of 2-phenylpyridine derivatives with aromatic and aliphatic aldehydes and alcohols [44] using $Pd(OAc)_2$ catalyst at a reaction temperature of 140 °C for 24 h under homogeneous conditions. Very recently, Wu et al. [45] have reported ortho-acylation of 2-aryl pyridine derivatives using arylmethyl amines as new acyl sources by using $PdCl_2$ as a homogeneous catalyst. On industrial perspective, heterogeneous catalytic process has advantage over homogeneous in view of its ease of handling, simple workup and recoverability. Earlier Figueras et al. reported the synthesis and use of highly basic Mg–La mixed oxide catalyst for various reactions like direct condensation of alcohols [46]

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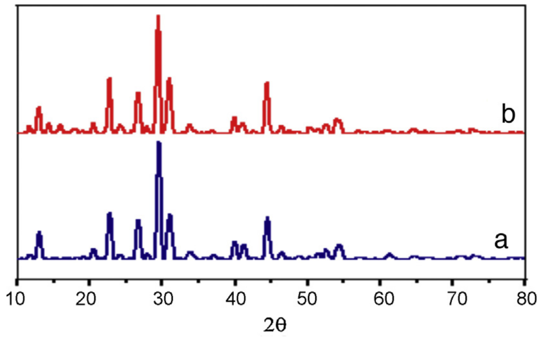
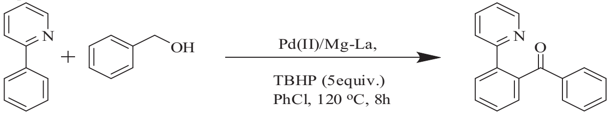


Fig. 1. XRD patterns of the Pd(II)/Mg–La mixed oxide: [a] fresh and [b] used catalysts.

and Michael addition reactions [47] under heterogeneous conditions. Moreover, we have demonstrated the catalytic activity of the Mg–La mixed oxide in the condensation of aldehydes and imines with ethyl diazoacetate using DMF as a solvent [48]. Very recently, we have explored the activity of Pd(0)/Mg–La mixed oxide catalyst towards the chemoselective hydrogenation of olefinic double bonds under heterogeneous conditions [49]. In continuation of our studies, we report the use of Pd(II)/Mg–La mixed oxide as a heterogeneous and reusable catalyst for the oxidative direct acylation of *sp*^{2} C—H bonds of 2-phenylpyridine derivatives with alcohols using TBHP as the oxidant.

Table 1

Optimization of reaction conditions[a].



Entry	Oxidant/equiv.	Solvent	Temperature (°C)	Yield (%)
1	TBHP/3 equiv.	DMSO	140	0
2	TBHP/3 equiv.	DMF	140	0
3	TBHP/3 equiv.	Chloro benzene	120	60
4	TBHP/5 equiv.	Chloro benzene	120	82
5	TBHP/3 equiv.	Water	100	55
6	TBHP/5 equiv.	Water	100	55
7	TBHP/3 equiv.	No solvent	100	60
8	$K_2S_2O_8$/3 equiv.	Chloro Benzene	120	0
9	H_2O_2/3 equiv.	Chloro Benzene	120	0
10	TBHP/5 equiv.	No solvent	120	70

[a] 0.2 mmol 2-phenylpyridine, 1 mmol benzyl alcohol, 30 mg Pd(II)/Mg–La catalyst.

2. Experimental

2.1. Materials and methods

All reagents were commercial grade materials and were used without further purification. All solvents were dried and distilled by standard methods as described in the literature. Thin layer chromatography was performed on pre-coated silica gel 60-F254 plates.

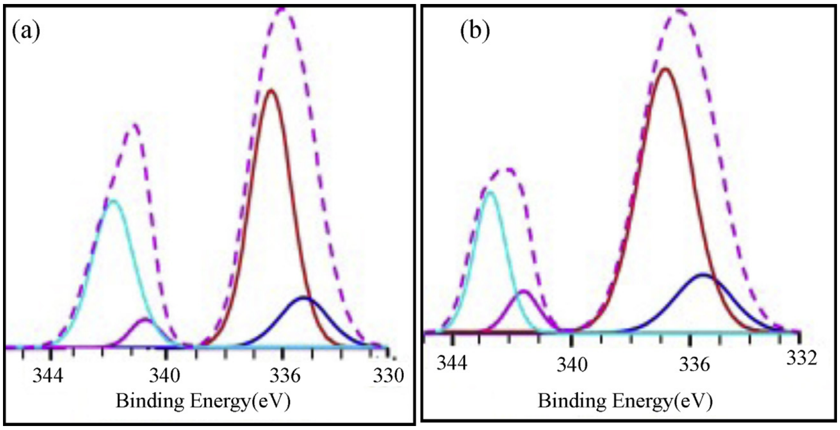


Fig. 2. The XPS spectra of (Pd 3d5/2, 3d3/2) [a] fresh and [b] used Pd(II)/Mg–La mixed oxide catalysts.

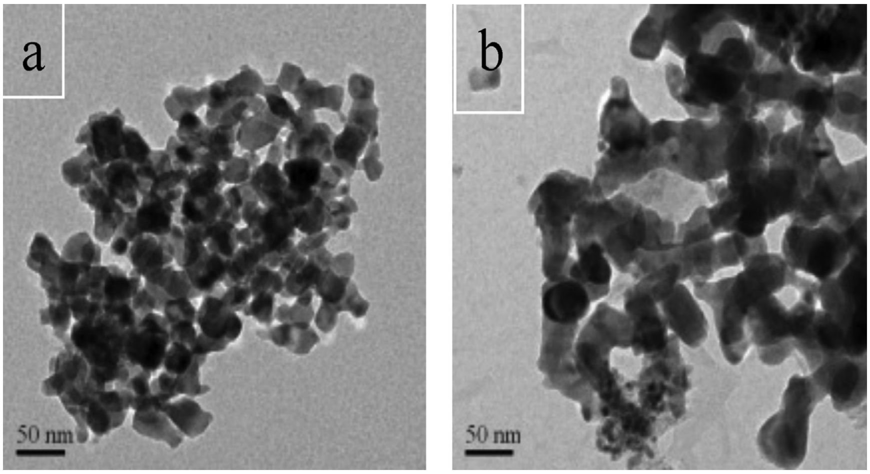
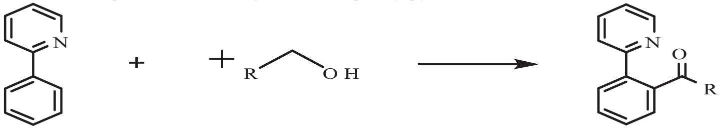
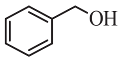
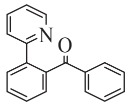
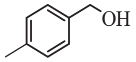
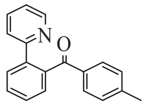
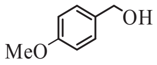
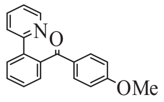
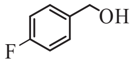
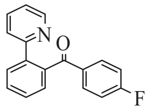
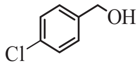
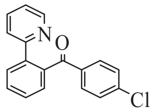
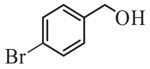
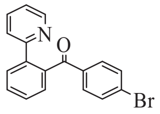
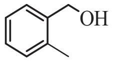
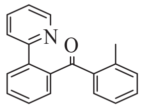
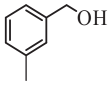
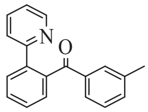
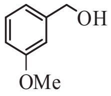
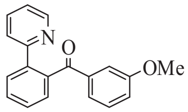
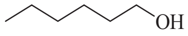
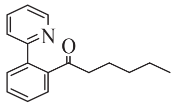
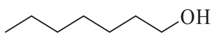
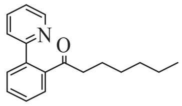
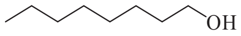
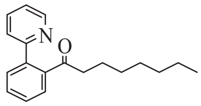
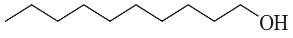
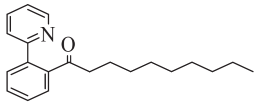


Fig. 3. TEM images of the Pd(II)/Mg–La mixed oxide: [a] fresh and [b] used catalyst (recovered after 4th cycle).

Table 2
Substrate scope of oxidative acylation of 2-phenylpyridine with different alcohols.



Entry	Alcohol	Product	Yield (%)
1			82
2			80
3			70
4			80
5			77
6			60
7			75
8			70
9			70
10			53
11			67
12			67
13			65

[a] Reaction conditions: 0.2 mmol 2-phenylpyridine, 1 mmol benzyl alcohol, 30 mg catalyst, 1 mmol TBHP (70% in water solution), chlorobenzene (0.5 mL), 120 °C, 8 h.

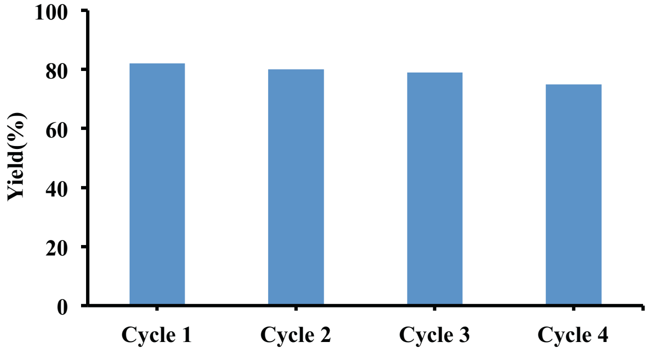


Fig. 4. Recyclability of catalyst.

The ^1H NMR and C NMR spectra were recorded on 200, 300 and 500 MHz spectrometer. Chemical shifts (δ) are reported in ppm, using TMS as an internal standard. XPS spectra were recorded on a KRATOS AXIS 165 equipped with Mg Kα radiation (1253.6 eV) at 75 W apparatus using Mg Kα anode and a hemi spherical analyzer. The C 1s line at 284.6 eV was used as an internal standard for the correction of binding energies. The X-ray diffraction (XRD) patterns of the fresh and used samples were obtained on a Rigaku Miniflex X-ray diffractometer using Ni filtered Cu Kα radiation (θ = 0.15406 nm) from 2θ = 10 to 80°, at a scan rate of 2° min^{-1}, with the beam voltage and beam current of 30 kV and 15 mA respectively.

2.2. Preparation of catalyst

Pd(II)/Mg–La catalyst was prepared following a modified procedure of the previous work reported by Figueras et al. [50] Mg–La mixed oxide was obtained by co-precipitation of Magnesium nitrate ($Mg(NO_3)_2{\cdot}6H_2O$) and Lanthanum nitrate ($La(NO_3)_3{\cdot}6H_2O$). A solution containing 0.386 mol magnesium nitrate ($Mg(NO_3)_2{\cdot}6H_2O$) and 0.129 mol lanthanum nitrate ($La(NO_3)_3{\cdot}6H_2O$) dissolved in 0.5 L water for an atomic ratio Mg/La = 3, was precipitated by using mixture of KOH (1 mol) and K_2CO_3 (0.26 mol) in 0.52 L of distilled water maintained at a constant pH 10. The solid was filtered, washed with distilled water, dried at 373 K and calcined at 923 K for 5 h. The Mg–La mixed oxide (1.5 g) was suspended in 150 mL of aqueous palladium (II) nitrate hydrate ($Pd\ (NO_3)_2{\cdot}xH_2O$) [0.345 g, 1.5 mmol] solution and stirred at 25 °C for 12 h under a nitrogen atmosphere. The solid was filtered, washed with distilled water, dried at 373 K and calcined at 923 K for 5 h. The BET-surface area of the calcined Pd/Mg–La sample is found to be 47.5 m^2 g^{-1} and the pore volume is 0.123 cc g^{-1}.

2.3. General procedure for the oxidative sp^2 C—H bond acylation with alcohols

In a typical reaction, a 10 mL oven-dried reaction vessel was charged with Pd/MgLa mixed oxide (30 mg), 2-phenylpyridine (29 mg, 0.2 mmol), benzyl alcohol (108 mg, 1 mmol), tert-butyl hydroperoxide (70% solution in water, ~129 mg, 1 mmol) and chlorobenzene (0.5 mL) were added. The resulting solution was stirred at 120 °C for 8 h in open air. The reaction was monitored by thin-layer chromatography (TLC). After cooling to room temperature, catalyst was separated by simple centrifugation. The filtrate was concentrated under reduced pressure and the residue was purified by column chromatography using silica gel and a mixture of hexane/ethyl acetate as eluents. All the products were confirmed by ^1H NMR and ^{13}C NMR spectroscopy. The recovered catalyst was used for the next cycle without any further purification.

3. Results and discussion

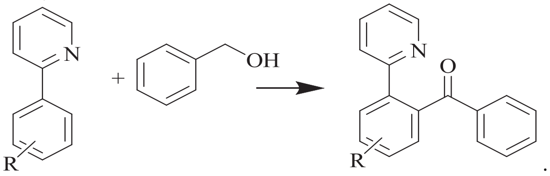
3.1. Catalyst characterization

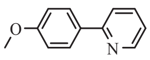
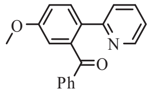
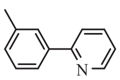
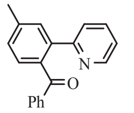
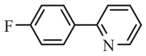
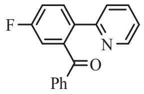
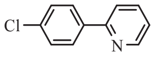
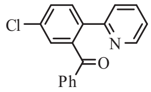
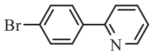
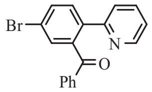
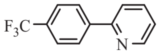
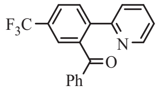
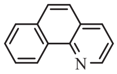
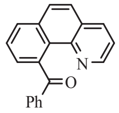
The XRD patterns of the fresh and used Pd/MgLa mixed oxide catalysts (Fig. 1) results revealed that the presence of both $La_2O_2(CO_3)$ and PdO phases. Diffraction lines appeared at 2θ = 29.55°, 22.84°, 13.1°, 30.82°, [ICDD # 23-0435] and their corresponding '*d*' values 0.302, 0.389, 0.675 and 0.289 nm is attributed to the lanthanum oxide carbonate phase. The diffraction peaks observed at 2θ = 31.70°, 45.54°, 27.33° [ICDD # 46-1211] and the '*d*' values of 0.282, 0.199, 0.326 nm is indicative of PdO phase.

The XPS analysis of the fresh and used (after 4th cycle) Pd(II)/MgLa mixed oxide catalyst is presented in Fig. 2. The PdO species are present on the surface which was confirmed by XPS signal appeared at binding energies 336.41 eV and 341.87 eV of Pd $3d_{5/2}$ and Pd $3d_{3/2}$ respectively over fresh catalyst and 336.87 eV and 342.75 eV of $3d_{5/2}$ and $3d_{3/2}$ over used catalyst.

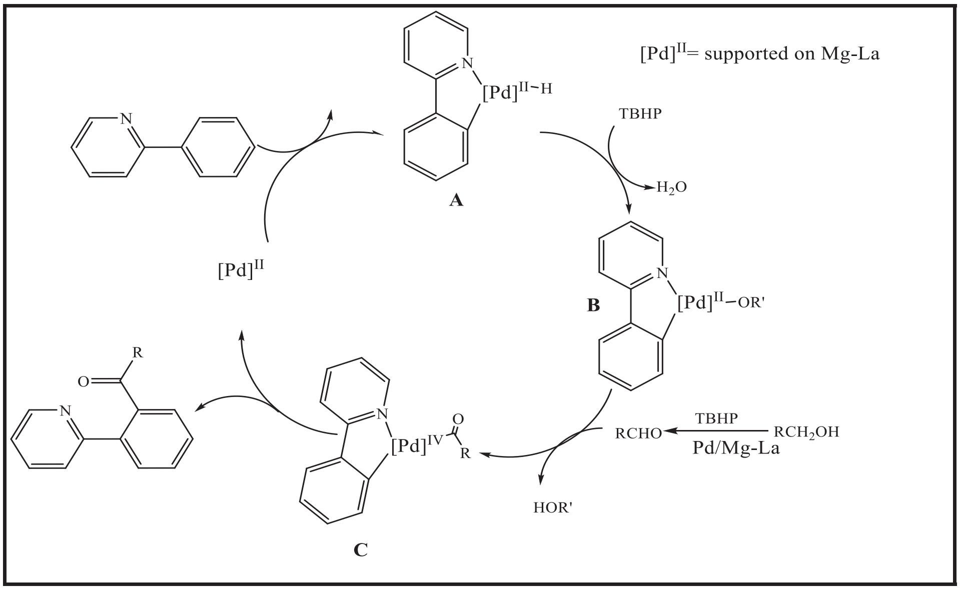
The transmission electron microscopic (TEM) pictures of the fresh and used (after 4th cycle) Pd/Mg–La mixed oxide catalysts

Table 3
Substrate scope of oxidative acylation of different 2-phenylpyridine derivatives with benzyl alcohol.



Entry	2-Arylpyridine	Product	Yield (%)
1			82
2			80
3			70
4			80
5			77
6			60
7			75

[a] Reaction conditions: 0.2 mmol 2-phenylpyridine, 1 mmol benzyl alcohol, 30 mg catalyst, 1 mmol TBHP (70% in water), chlorobenzene (0.5 mL) 120 °C, 8 h.



Scheme 1. Plausible reaction mechanism.

are reported in Fig. 3[a] and [b]. The Pd particle size was measured from TEM images (Fig. 3) and found to be 19.3 and 23.9 nm for fresh and used catalysts respectively.

3.2. *Catalytic activity of Pd/Mg–La mixed oxide catalyzed oxidative sp^2 C—H bond acylation with alcohols*

When polar solvents such as DMSO and DMF were used, surprisingly no product formation was observed. However, we are delighted to find that using chlorobenzene as the solvent at a temperature of 120 °C produced the desired product about 60% yield using 3 equiv. of 70% aqueous solution of TBHP (Table 1, entry 3). Upon increasing the amount of TBHP (5 equiv.) the yield of the product increased to 82% (Table 1, entry 4). The reaction gave 55% yield of the product using water (Table 1, entry 5). However, increasing the amount of TBHP from 3 to 5 equiv. did not show any effect on the product yield for the reaction carried in water (Table 1, entry 6). The reaction was also carried out under solvent free condition using 3 equiv. of TBHP and interestingly 60% yield of the product formation was observed (Table 1, entry 7). Next we studied the effect of different oxidizing agents on the acylation reaction. The reaction failed when $K_2S_2O_8$ and H_2O_2 were used as oxidizing agents. Therefore, among the various optimization studies performed, the most promising result obtained is shown in Table 1 entry 4.

A preliminary study on the catalytic activity of Pd/Mg–La mixed oxide for the oxidative acylation of 2-phenylpyridine and benzyl alcohol was performed using TBHP as the oxidant and the results are summarized in Table 1. Performing the reaction on various alcohols and 2-phenylpyridine under the optimized reaction condition produced yields ranged between 53 and 82% (Table 2). A lower yield of the desired product was obtained when sterically bulky ortho-substituted benzyl alcohol was used (Table 2, entry 7). To our delight, this reaction is not limited to benzyl alcohol and its derivatives. More challenging aliphatic alcohols such as 1-hexanol and 1-octanol were also reactive towards 2-phenylpyridines which resulted in 53% and 67% yields of the desired products respectively (Table 2, entry 10 and 12). It should be noted that the reaction gave the mono acylation product selectively in all cases. The results of 2-phenyl derivatives with benzyl alcohol are presented in Table 3. A series of functional groups including methyl, methoxy, chloro, fluoro, bromo, trifluoromethyl were tolerated under the optimal reaction conditions and the desired products were obtained in moderate to good yields. When benzo[*h*]quinoline was subjected to the procedure, a 54% yield of the acylation product was isolated (Table 3, entry7).

3.3. *Recyclability*

The recyclability of the catalyst was examined using 2-phenylpyridine and benzyl alcohol at 120 °C in TBHP under chlorobenzene as solvent and the results are shown in Fig. 4, which clearly illustrates that the catalyst can be used for four consecutive cycles with consistent yields and selectivity. In the recyclability studies, catalyst was recovered by simple centrifugation. The recovered catalyst was washed, air-dried and used directly for the next cycle without any further purification. The ICP-MS analysis showed that the Pd(II) content of fresh and used is 9.1% and 8.9% respectively. From this we can conclude that there no significant leaching of Pd.

3.4. *Plausible mechanism*

A proposed mechanism to rationalize this transformation is illustrated in Scheme 1. The reaction proceeds through the chelation-directed C—H activation of 2-phenylpyridine by active palladium catalyst to generate intermediate (A) Then the reaction of A with TBHP generates intermediate (B) which in turn reacts with the aldehyde which is produced from the oxidation of alcohol, forming the acyl intermediate (C). Finally, intermediate (C) undergoes reductive elimination to produce the coupling product and regenerates palladium catalyst for further reactions.

4. Conclusions

In conclusion, we have developed a simple and efficient method for the oxidative sp^2 C—H bond acylation of 2-phenylpyridine derivatives using alcohols and TBHP as the oxidizing agent and Pd/Mg–La mixed oxide as heterogeneous catalyst. The catalyst can be readily recovered and reused for four consecutive cycles with consistent activity and selectivity.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.molcata.2013.08.020.

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