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Silver Nanoparticles Stabilized by Metal-Organic Framework (MIL-101(Cr)) as Efficient Catalyst for Imine Production from the Dehydrogenative Coupling of Alcohols and Amines

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In this paper, we present silver nanoparticles supported on metal-organic framework (Ag@MIL-101) as a catalyst for the one-pot tandem synthesis of imines from alcohols and amines. Ag@MIL-101 catalyst was fabricated using the liquid phase impregnation technique as an easy and effective method. The morphology and chemical structure of the prepared catalyst was systemically evaluated by inductively coupled plasma optical emission spectroscopy (ICP-OES), powder X-ray diffraction (P-XRD), X-ray photoelectron spectroscopy (XPS) and transmission electron microscopy (TEM). The highly crystalline feature of Ag metals on bifunctional MIL101(Cr) was revealed by TEM and HRTEM analyses. The Ag@MIL-101 catalyst was examined as catalyst for the synthesis of different imine derivatives. The catalytic performance of Ag@MIL-101 catalyst was monitored GC-MS and ¹H-NMR analyses for the dehydrogenative coupling of alcohols and amines. Furthermore, the effect of various factors such as the amount of catalyst, base, temperature and solvent was investigated to optimize the conditions for the best performance of the Ag@MIL-101 catalyst. Catalytic activity results showed that Ag@MIL-101 catalyst has a good catalytic activity with the TOF values in the range of 12.7-14.6 h⁻¹ in the synthesis of various imines.

Introduction

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Imines and their derivatives are of vital importance in various areas such as organic and biological chemistry due to serve as versatile intermediates for the synthesis of valuable nitrogen-containing biological active compounds (e.g. amides, amines, chiral amines, nitrones, oxaziridines, pyrrolines and hydroxyamines).¹⁻⁸ So, methodologies for their synthesis and conversion are of major importance in the fine chemical industry. Traditionally, the synthesis of imines is mainly relying on the condensation of highly reactive ketones or aldehydes with an amine over Lewis acid catalysts.⁹⁻¹¹ This methodology requires dehydration reagents, activated carbonyl compounds and higher reaction time. Recently, one-pot tandem reaction has been developed as a greener and more practical approach that promotes the use of easily accessible, green and inexpensive alcohols instead of reactive carbonyl

compounds as starting compounds.¹²⁻¹⁵ In the synthesis of imines from alcohols and amines via a one-pot tandem reaction, the alcohol is dehydrogenated in situ to the corresponding carbonyl compound as the byproduct. Later, the dehydogenative coupling reaction occurs between amine and carbonyl compound to form imine, amide, amine or other products.^{12,17,18} Nevertheless, the intrinsic self-coupling properties of the substrates and transformation into nitrile, amide, azo compound byproducts of primary amines remain the major challenges for this type of reaction¹¹. Although there are many efficient homogeneous catalysts devoloped for this transformation, they have the major disadvantages such as high cost of ligands, poor selectivity, recycling and competing hydrogen atom transfer reaction causing to a mixture of amine and imine products.^{7,19-25} In order to overcome these drawbacks, supported noble metal (e.g. Au²⁶, Pd¹⁴, Ag²⁷ and Pt¹⁵) catalysts have been efficiently used for the dehydrogenative coupling of alcohols and amines. Despite the great explorations in heterogeneous systems for this transformation, Ag based ones were really scarce in the literature. Actually, among the noble metals studied, Ag is advantageous for this transformation due to its low cost, unique optical properties, higher chemical stability and non-toxic nature²⁸. Furthermore, the strong oxidation ability of metallic Ag is known in the dehydrogenation reactions of alcohols under oxidant-free conditions; which is the ratedetermining step for tandem reaction in this study.²⁹⁻³¹

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Previous investigations on supported metal catalysts mainly focus on two properties of the catalyst: (i) particle size and morphology of the catalyst, (ii) synergistic effect between the acid-base sites of the support and a metal site. In particular, the synergistic effect between the support and the metal catalyst is important; because this effect could determine the catalytic behavior in the alcohol dehydrogenation step. Hence, the choice of support material is also very important as the metal. Because surface acid-base sites on the support material encourage the adsorption of substrate molecules to produce intermediate products which facilitate the reaction.³² For example, Mitsudome et. al. reported the hydrotalcite (HT) supported Ag nanoparticles (Ag/HT) as a heterogeneous catalyst system for the dehydrogenation of alcohols in the absence of oxidant.²⁹ Shimizu et. al. reported Ag/MgO, Ag/CeO₂ Ag/Al₂O₃ and Ag/TiO₂ catalysts as supported Ag cluster catalysts for oxidant-free dehydrogenation of benzyl alcohol and found that acid-base bifunctional supported Ag nanoparticles (Al₂O₃) showed much higher catalytic activity than basic (MgO and CeO₂) or acidic to neutral (SiO₂) ones.³⁰ In addition, Liu et. al. studied Ag nanoparticles supported on the surface of MgAl-MMO derived from MgAl-LDH precursor for the dehydrogenation reaction of benzyl alcohol and found that $Ag^{\delta+}$ site facilitates the breakage of α -C–H bond while $Mg^{\delta+}-O^{\delta-}$ sites of support accelerate the O-H bond cleavage.³¹

Metal-organic frameworks (MOFs) have been considered to be effective bifunctional support materials owing to their unique characteristics such as tunable pores, acid-base sites, large specific surface areas and chemical durability.^{33,34} The chemical properties of MOFs may effect the catalytic performances. Throughout catalytic process, the characteristic active sites in MOFs can play the roles of simplifying the electron/mass transfer or inhibiting the formation of intermediates by interacting with the substrates or cooperating with the metal active sites.33,35 For example, the unsaturated metal centers known as Lewis acid sites influences the electronic distribution of substrates or products, resulting in a considerable increase of selectivity or yield. On the other hand, the Lewis acid sites and the organic ligand linkers of MOFs can be functionalized with other various radical groups such as -NH2 or -SO₃H, so that leading the change of the surface chemical and physical properties, and thus regulating the reaction performances.³³ Further, the synergetic effect between the MOFs and metal-NPs, the reaction activity can also further enhanced. For instance, Zhang et al. [14] reported a Pd NPs and Lewis acide sites (Cr^{3+}) collaborative catalyst (Pd@MIL-101) for the synthesis of imines from cross-coupling of amines and alcohols. In this system, the Pd NPs showed high efficiency for the selective dehydrogenation to aldeyde of alcohol to facilitate the formation of the imine, while the Lewis acide sites in the MIL-101 showed high efficiency for the condensation of aldehyde with amine by preventing the over-oxidation of alcohol. In addition, more recently, various MOFs-based multifunctional catalytic systems (e.g. Pd/MIL-100(Fe),³⁶ Pd-Au@Mn(II)-MOF,¹⁷ and CdS@MIL-101³⁷) have been employed for the one-pot synthesis of imines from intrinsic selfcoupling of amines or cross-coupling of amines and alcohols.

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However, the poor conversion and selectivity of imines, low TOF values or more catalyst loading are the major drawbacks for these systems.

Therefore, in this study, we combined collaborative MIL-101(Cr) support and Ag nanoparticles as highly selective and effective heterogeneous catalyst and investigated the catalytic performance of the obtained Ag@MIL-101 catalyst for the one-pot tandem synthesis of imines from alcohols and amines. To the best of our knowledge, no research of applying Ag@MIL-101 catalyst to direct synthesis of imines from alcohols and amines has been reported. We found that the this new, efficient heterogeneous catalyst provides high efficiency and selectivity for this tandem reaction. Additionally, the catalyst can be reused five times without any loss of activity or selectivity.

Results and Discussion

Characterization of MIL-101(Cr) and Ag@MIL-101 catalyst

The loading of Ag supported on the MIL-101 material was determined as 1.51 wt% (theoretical metal loading is 2%) performed on the ICP-OES. This ICP-OES value was used to calculate the catalytic activity in turn-over frequency (TOF) for each substrate used in catalytic reactions.

Characteristic IR bands of the synthesized MIL-101 support material and Ag@MIL-101 catalyst are compared in Fig. 1. The bands at 3433 and 1625 cm⁻¹ corresponding to stretching (v) and bending (δ) vibrations are due to the adsorbed water on the surface of MIL-101, respectively. The band observed at 1402 cm⁻¹ is assigned to symmetric (O-C-O) vibrations of dicarboxylate, thus confirming the presence of terephthalic acid linker within the MIL-101 framework structure. The bands observed between 600 and 1600 cm⁻¹ are due to benzene ring, including stretching vibrations (C=C) at 1508 cm⁻¹ and deformation vibrations (C-H) at 1107, 1020, 749, and 663 cm⁻ ¹.³⁸⁻⁴² Peaks related to the mentioned bands were observed in the same regions in the Ag@MIL-101 catalyst. These results are considered as evidence that the MIL-101 host material was kept intact during the conversion of the Ag@MIL-101 catalyst.

The crystallinity of the host MIL-101 framework throughout the formation of Ag@MIL-101 catalyst was investigated by wide angle P-XRD analyses (Fig. 2). The wide angle P-XRD patterns of MIL-101 and Ag@MIL-101 catalyst showed the characteristic reflections of the host matrix MIL-101,43-45 which confirms the preservation of MIL-101 intact structure after silver (0) nanoparticles formation. Moreover, P-XRD pattern of Ag@MIL-101 sample shows Bragg peaks at 38.24°, 44.36°, 64.62° and 77.64°, attributable to (111), (200), (220) and (311) planes of a face-centered cubic (fcc) crystal structure of silver (JCPDS card number 04-0783).46,47

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Fig. 1. FTIR spectra of MIL-101 and Ag@MIL-101 catalyst in the range of 4000-400 cm⁻¹

The size, morphology and composition of Ag@MIL-101 catalyst were investigated by TEM, HRTEM and TEM-EDX analyses. Fig. 3 (ac) depicts the low resolution TEM image of Ag@MIL-101 catalyst and these images show that the large-sized silver agglomerates were not formed on the surface of MIL-101 crystals. According to the particle size analysis using the NIH image program⁴⁸ and counting more than 100 non-touching particles, the average particle size of the silver (0) nanoparticles in the Ag@MIL-101 catalyst were determined to be 2.43 ± 0.22 nm (Fig. 3 (d)). Fig. 3 (e) shows the EDX spectrum of Ag@MIL-101 catalyst from a selected region of a 100 nm scale TEM image. In the EDX spectrum, there are signals belonging to the Cr, C, O elements forming the structure of MIL-101 host material, as well as the Ag and Cu elements originating from the TEM sample carrier. The HRTEM image of Ag@MIL-101 catalyst given in Fig. 3(d) revealed that the highly crystalline feature of the resulting silver (0) nanoparticles in Ag@MIL-101 catalyst. The crystalline spacing distance was measured to be 0.235 nm, which agrees with the (111) lattice spacing of silver.49,50

The chemical nature of the silver (0) nanoparticles was further investigated by XPS analysis of Ag@MIL-101 catalyst. **Fig. 4** (a) and (b) shows the survey scan and Ag 3d core level XPS spectra of Ag@MIL-101 catalyst, respectively. The survey scan XPS spectrum of Ag@MIL-101 sample shows the presence of silver in addition to the MIL-101 framework elements (Cr, O, and C). In the Ag 3d core level XPS spectrum of Ag@MIL-101 catalyst, the signals at binding energies of 366.92 eV and 372.84 eV were corresponding to the

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 $3d_{5/2}$ and $3d_{3/2}$ orbits of Ag(0) (metallic silver).⁵¹⁻⁵⁴ As shown in Eig. 4 (b), Ag is mostly in the state of zero oxidation (366!929/372!84 eV), and there are also some types of Ag (I) (368.21 / 374.19 eV) that may be related to the un-reduced species and/or oxidized species of Ag.



Fig. 2. Wide angle P-XRD patterns of MIL-101 and Ag@MIL-101 catalyst (5.0 wt % Ag) in the range of 2θ = 5-80°.

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Fig. 3 (a-c) Low resolution TEM images in different scale, (d) associated particle size histogram, (e) related EDX spectrum and (f) HRTEM image in 5 nm scale of Ag@MIL-101 catalyst.

The catalytic efficiency of Ag@MIL-101 catalyst in the imine production from the coupling of alcohols and amines

In this study, we evaluated Ag@MIL-101 catalyzed one-pot synthesis of imines *via* dehydrogenative coupling of alcohols and amines. First, to achieve the maximum conversion and selectivity, reaction parameters were optimized. For this, the one-pot imine synthesis from *p*-toluidine and benzyl alcohol was chosen as the benchmark reaction. The optimization of temperature, the molar ratio of amine and alcohol, base and solvent was screened using this model reaction (**Table 1**). Meanwhile, before starting the activity studies, blank experiments were carried out without catalyst and imine formation was not observed (Table 1, entry 1). The results obtained are summarized in Table 1. The conversion and selectivity of the catalyst were monitored GC-MS and ¹H-NMR analyses for dehydrogenative coupling of alcohols and amines (see Supporting Material).

The synthesis of imines from amines and alcohols involves two consecutive reaction steps: *i*. dehydrogenation of alcohols to benzaldehyde which is catalyzed step; *ii*. imine formation from the condensation of benzaldehyde and amine, which is sometimes uncatalysed step.^{14,26,36,37,55} The one-pot tandem synthesis of imines from amines and alcohols is compelling. Because the required reaction conditions for the first aerobic alcohol oxidation step and the next anaerobic condensation step are substantially different from each other.¹⁷



Fig. 4 (a) Survey and (b) Ag 3d core level high resolution XPS spectra of Ag@MIL-101 catalyst

Therefore, we first performed a series of experiments to determine the reaction atmosphere. As shown in Table 1, when the imine synthesis from p-toluidine and benzyl alcohol was carried out in a sealed flask under an argon stream, conversion to the corresponding imine was not observed after 24 h because no dehydrogenation to benzaldehyde of alcohol could occur without oxygen (Table 1, entry 3). Conversely, when the reaction is carried out in an open flask under an argon stream, conversion to the corresponding imine was observed in good yield with high selectivity (Table 1, entry 2). Subsequently, the reaction was also performed in the air atmosphere condition and the formation of imine began to slow down (Table 1, entry 4). Actually, molecular oxygen plays an important role in the dehydogenation of benzyl alcohol. However, in the presence of excess oxygen, the amine can be oxidized, which causes the formation of the imine to slow down¹⁷. For understanding effect of the reaction atmosphere on the formation of imine, time-dependent experiments were performed and monitored by GC analysis (see Supporting Material).

Ag@MIL-101^a

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As expected, the results showed that imine formation slows under Air atm after 12 h compared to the Ar atm (**Fig. 5**(a)). Thus, we can say that the oxygen amount in the reaction medium is a very important factor for the one-pot tandem synthesis of imines. So, all further experiments were performed in an open flask under an argon stream.

On the other hand, in the absence of the base, no imine formation was observed (Table 1, entry 5). It is known that an alkaline environment is required for the dehydrogenation of benzyl alcohol. Therefore, the presence of Lewis acid sites in the MIL-101(Cr) framework can have a negative impact on the conversion of benzyl alcohol, which meaned the base is required to facilitate the conversion of benzyl alcohol.^{14,18,56} Thus, we evaluated the effect of various bases such as Na₃PO₄, Cs₂CO₃, KO^tBu and K₂CO₃. KO^tBu as the base was the best under the tested conditions. In contrast, using Na₃PO₄, Cs₂CO₃ and K₂CO₃ as a base the reaction was slower and imine formation very low (Table 1, entries 6-8). Subsequently, solvent screening was also performed; besides toluene, various solvents such as IPA, 1,4-dioxane and THF were evaluated. Because different solvents have different properties, which can influence the catalytic performance of catalyst. The optimization studies showed that the non-polar and aprotic toluene is proved to be the most convenient solvent for dehydogenative coupling of amines and alcohols (Table 1, entries 9-11).

The reaction temperature has a considerable impact for this transformation. When the reaction temperature was 60° C, the imine formation was low after 24 h, but the conversion was greatly increased when the temperature increased from 60 to 100° C (Table 1, entries 2, 12, 13, Fig. 5(b)). However, the imine formation exhibited no considerable progress when the reaction temperature was 120 °C (Table 1, entry 14). For this reason, 100 °C was chosen as the optimized reaction temperature.

	NH ₂	ОН					
Ent.	Cat.	Solv.	Alcohol/	Temp.	Base	Conv.	Sel.
			amine	(°C)		(%)	(%)
1		Toluono	ratio	100	KOtPu		
1 2	- 2.0% Ag@N4U	Toluono	1	100	KO BU	- 74	>00
2	101	Toluelle	1	100	KO-Bu	74	299
3 ^b	3.0%-Ag@MIL-	Toluene	1	100	KO ^t Bu	2	>99
4 ^c	3.0%-Ag@MIL- 101	Toluene	1	100	KO ^t Bu	62	>99
5	3.0%-Ag@MIL- 101	Toluene	1	100	-	2	>99
6	3.0%-Ag@MIL- 101	Toluene	1	100	Na_3PO_4	30	>99
7	3.0%-Ag@MIL- 101	Toluene	1	100	Cs ₂ CO ₃	22	>99
8	3.0%-Ag@MIL- 101	Toluene	1	100	K_2CO_3	12	>99
9	3.0%-Ag@MIL- 101	1,4- dioxane	1	100	KO ^t Bu	48	>99
10	3.0%-Ag@MIL- 101	THF	1	100	KO ^t Bu	3	>99
11	3.0%-Ag@MIL- 101	IPA	1	100	KO ^t Bu	4	>99
12	3.0%-Ag@MIL- 101	Toluene	1	60	KO ^t Bu	38	>99
13	3.0%-Ag@MIL- 101	Toluene	1	80	KO ^t Bu	54	>99
14	3.0%-Ag@MIL- 101	Toluene	1	120	KO ^t Bu	75	>99
15	3.0%-Ag@MIL- 101	Toluene	1.25	100	KO ^t Bu	81	>99
16 ^d	3.0%-Ag@MIL- 101	Toluene	1.5	100	KO ^t Bu	85	90
17 ^e	3.0%-Ag@MIL- 101	Toluene	1.25	100	KO ^t Bu	89	>99
18 ^f	3.0%-Ag@MIL- 101	Toluene	1.25	100	KO ^t Bu	99	>99
19	0.5%-Ag@MIL- 101	Toluene	1.25	100	KO ^t Bu	37	>99
20	1.0%-Ag@MIL- 101	Toluene	1.25	100	KO ^t Bu	48	>99
21	2.0%-Ag@MIL- 101	Toluene	1.25	100	KO ^t Bu	71	>99
22	4.0%-Ag@MIL- 101	Toluene	1.25	100	KO ^t Bu	91	>99
23	AgNO ₃	Toluene	1.25	100	KO ^t Bu	15	15
24	MII-101	Toluene	1 25	100	KOtBu	3	3

Table 1. Optimization of one-pot imine synthesis from alcohols and amines with DOL 10.1039/DOC 009/4A

^a Reaction conditions: Catalyst (5 mg), *p*-toluidine (0.5 mmol), benzyl alcohol (0.5 mmol), KO^tBu (0.10 mmol), Toluene (5 mL), 100 °C, 24 h, Open flask/Ar; ^bClosed system/Ar; ^c Air atm; ^d Benzyl benzoate formation was observed; ^e8 mg of catalyst; ^f10 mg of catalyst.

The effect of benzyl alcohol/*p*-toluidine ratios on the activity was also evaluated. When the molar ratio of benzyl alcohol and *p*-toluidine was 1:1, the imine formation was 74% and selectivity was >99% (Table 1, entry 14). The imine formation was 81% when the molar ratio was 1.25:1 and only traces of benzaldehyde as byproduct is formed (Table 1, entry 15). Further increase in molar ratio increased the conversion, but the selectivity of the imine decreased due to formation of benzaldehyde and benzyl benzoate (Table 1, entry 16).

To further increase imine formation, the catalyst amount was increased. As shown in Table 1, the imine formation increased with

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the increasing catalyst amount from 5 mg to 8 mg (*e.g.* 81 and 89% of imine are obtained, respectively, Table 1, entries 15 and 17). The maximum imine formation was obtained when the catalyst amount was 10 mg (*e.g.* 99% of imine are obtained Table 1, entry 18).

Furthermore, the Ag@MIL-101 catalysts with different Ag content were also tested in this study (e.g. 0.5%-Ag@MIL-101, 1%-Ag@MIL-101, 2%-Ag@MIL-101, 3.0%-Ag@MIL-101, 4.0%-Ag@MIL-101). As shown in entries 19-21 of Table 1, when the amount of Ag content decreases to 0.5%-Ag@MIL-101, 1%-Ag@MIL-101, 2%-Ag@MIL-101, the yield of the corresponding imine decreases to 37, 48 and 71%, respectively. Interestingly, when the amount of Ag content increases to 4%-Ag@MIL-101, the yield of the corresponding imine also decreases to 91% (Table 1, entry 22), which meaned the many Ag particles aggregated in the hole of the MIL-101. So, under the optimized condition, results of these reactions point to the optimal performance catalyst of 3.0%-Ag@MIL-101, providing about 99% formation of imine with 99% selectivity. We also tested AgNO3 and bare MIL-101 as the control catalysts (Table 1, entries 23-24). When using AgNO₃ as catalyst, the yield for the corresponding imine was only 15% and benzyl benzoate as over-oxidation product was the major by-product. When using MIL-101 as a catalyst, only a trace of imine was observed and there was no over-oxidation product.

As a result, the maximum conversion and selectivity of corresponding imine was reached to 99% in toluene by using 10 mg of 3.0%-Ag@MIL-101 catalyst in the presence of 0.5 mmol of ptoluidine, 0.625 mmol of benzyl alcohol and 0.010 mmol of KO^tBu at 100°C within 24 h (Table 1, entry 18). After determining the best reaction conditions, we tested the substrate scope and stability of this method. Therefore, under the optimized reaction conditions we evaluated one-pot imine synthesis from benzyl alcohol with various primary amines bearing as electron-donating or electronwithdrawing groups. The results obtained are given in Table 2. The reaction of aniline and benzyl alcohol gave the desired imine with high conversion yield and selectivity (99%, Table 2). Coupling of benzyl alcohol with amines bearing electron-donating substituents such as *p*-methyl and *p*-methoxy, produced the corresponding imines with 99% conversion, while the conversion of electronwithdrawing functional groups, including p-chloro and p-bromo, was slightly declined. Owing to the large steric effect, the conversion of 1-naphthylamine into its related imine is lower (84%, Table 2) than those of other *p*-substituted amines, but the selectivity of corresponding imine is still very high.

A comparison between the catalytic activities of the prepared Ag@MIL-101 catalyst and various reported catalyst systems (e.g. supported-noble, supported-non-noble and metal oxide) for the one-pot synthesis of imines was done, and the results are given in **Table S1**. According to the Table S1, 3.0%-Ag@MIL-101 catalyst showed excellent selectiviy and good catalytic performance with TOF values in the range between 12.7-14.6 h⁻¹ compared to the many reported heterogeneous catalysts.



Fig. 5. (a) Effect of the reaction atmosphere on the formation of imine (b) Effect of different reaction temperatures on the formation and selectivity of imine.



 Table 2. One-pot imine synthesis from various amines with benzyl alcohol over the Ag@MIL-101 catalyst.

^oThe reactions were carried out under the optimized conditions: Catalyst (10 mg), *p*-toluidine (0.5 mmol), benzyl alcohol (0.625 mmol), KO^tBu (0.10 mmol), Toluene (5 mL), 100 °C, 24 h, open system/Ar.

As mentioned above, the formation mechanism of imines from amines and alcohols involves initial dehydrogenation of alcohol to benzaldehyde, followed by condensation of benzaldehyde with amine. For understanding the competition between these two reactions, the time-dependent performance of the catalyst was monitored by GC analysis for dehydrogenation reactions to benzaldehyde of benzyl alcohol in both the absence and presence of *p*-toluidine, respectively (see Supporting Material). In the first 12 hours, the conversion to benzaldehyde of benzyl alcohol in the absence *p*-toluidine regularly increased and reached 84% after 24 hours. Interestingly, the presence of *p*-toluidine increased

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conversion of benzyl alcohol (99% after 24 hours). This increase in the yield of benzaldehyde is probably related to the weak basicity of the amine. Furthermore, as seen in **Fig. 6**, the condensation of benzaldehyde formed with *p*-toluidine proceeds very faster than the dehydrogenation of benzyl alcohol. The rate-determining step of this reaction is the dehydrogenation of alcohol to benzaldehyde. This observation is compatible with previous studies²⁶.

On the basis of the mentioned experimental results and previous reports, we proposed a possible reaction pathway. There are two types of active sites in Ag@MIL-101 catalyst that can catalyze onepot synthesis of imines. The one of the active sites is the Ag atom for the dehydrogenation of alcohol. To confirm the influence of Ag atom in the dehydrogenation step, we monitored the oxidation of benzyl alcohol using only MIL-101 as catalyst and did not observe considerable bezaldehyde yield (<5%). This result suggested that the benzyl alcohol is initially adsorbed on the Ag surface, forming a metal alkoxide and a metal hydride intermediate by breaking the O-H bond. Later, *via* a β -hydride elimination process, the benzyl alcohol is dehydrogenated forming forming a cationic intermediate (not detected in our system because its lifetime is not long enough) by removing a hydrogen from the reduced Ag sites. The cationic intermediate is transformed to benzaldehyde (verified by GC) by removing one more hydrogen from Ag-H sites (Fig. 7).14,57,58



Fig. 6. Conversion versus reaction time for dehydrogenation reactions to benzaldehyde of benzyl alcohol in both the absence and presence of *p*-toluidine.

It is known that after the benzaldehyde formed, the reaction can proceed in two possible pathways (**Scheme S1**): the resulting aldehyde can be reacted (*i*) with amine to form instable carbinolamine (α -amino alcohol) intermediate or (*ii*) with a water molecule to form gem-diol, which can be oxidized into carboxylic acid intermediate, however, the carboxylic acid intermediate was not detected in our system. Therefore, we predicted that the reaction pathway proceeds by forming an unstable carbinolamine intermediate. It loses water by acid-catalyzed pathways to form the corrresponding imine. In other words, the reaction between amine and benzaldehyde proceeds through the Lewis acid site the Cr³⁺ ion of MIL-101, forming a carbinolamine intermediate.^{14,59}

Consequently, in the possible reaction pathway for the condensation step, the carbonyl group in the Benzalden vde, Hormed by oxidation of benzyl alcohol, coordinates with this active site Cr³⁺ ion in the catalyst, which increases the electrophilicity of the carbonyl group. Then, as a result of the nucleophilic addition reaction to the carbonyl group of the related amine, an α -amino alcohol is formed (instable intermediate and not detected in our system). Finally, the formed α -amino alcohol is re-adsorbed on the acid sites, followed by dehydrated to obtain an imine product (Fig. 7). To confirm the influence of MIL-101 in the condensation step, we monitored the reaction between benzaldehyde with amine in both the presence and absence of MIL-101. In the absence of a catalyst, after 1.5 h the yield of corresponding imine was 88%, while in the presence of the MIL-101 the yield increased to 100% after 1.0 h. The results confirmed that MIL-101 promotes the condensation step and this is in agreement with the previous report¹⁴.

The reusability is an important performance parameter for heterogeneous catalysts. In this regard, we performed a reusability test for the Ag@MIL-101 catalyst under the optimized reaction conditions. The dehydrogenative coupling of benzyl alcohol and ptoluidine was also chosen as a model reaction for the reusability. After the first run, the catalyst is separated by centrifugation, washed with ethanol, ethyl acetate and deionized water, dried at 70 °C for 12 h under vacuum for further runs. Upon second use, the catalytic performance almost unchanged with a yield of 97%, showing the stability of catalyst under determined reaction conditions. After five cycles of reuse, the catalyst still indicated excellent catalytic performance with yields of 95-97% (Fig. 8). Ag@MIL-101 sample harvested from the fifth catalytic run was analyzed by P-XRD and TEM. The sum of their results showed that no obvious changes in crystallinity and morphology of AgNPs (Fig. S19-20). The slight decrease (~ 3-5%) in the activity of Ag@MIL-101 catalyst can be attributed to increase in the average size of AgNPs from 2.43 ± 0.22 nm to 3.75 ± 0.31 nm (Fig. S20). These results indicate that Ag@MIL-101 catalyst was stable under the current dehydrogenative coupling of benzyl alcohol and p-toluidine conditions and could be reused for multiple runs of the dehydrogenative coupling of alcohols and amines.

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MIL-101(Cr) Ag@MIL-101(Cr)

Fig. 7. Proposed catalytic mechanism for the one-pot imine synthesis.



Fig. 8. The reusability of Ag@MIL-101 catalyst for the one-pot imine synthesis from benzyl alcohol and p-toluidine.

Experimental

Materials

Silver nitrate (AgNO₃), chromium trinitrate nonahydrate (Cr(NO₃)₃·9H₂O), terephthalic acid (C₈H₆O₄), methanol (CH₃OH), acetone (CH₃COCH₃), sodium borohydride (NaBH₄) were supplied from Sigma-Aldrich[®]. Pure water, which is used for all catalytic studies and cleaning processes, was obtained with Human RO 180 brand water purifier. In addition, the glass and other materials needed in all studies were used by washing with a chromic acid cleaning solution, water and acetone and drying.

Characterization devices

FTIR spectra were taken on a Bio-Rad-Win-IR spectrophotometer carrying out KBr discs in between 4000 and 400 cm⁻¹. The amount of silver loading onto MIL-101(Cr) support was determined by

inductively coupled plasma optical emission spectroscopy (ICP-OES) by using Perkin Elmer DRC II model. The powder X-ray diffection (PA XRD) analyses were carried out on Rigaku Ultima-IV by using Cu-Ka radiation (wavelength 1.54 Å, 40 kV, 55 mA). TEM and HRTEM samples were prepared by dropping one drop of dilute suspension on copper coated carbon TEM grid and the solvent was then dried. TEM analysis was carried out on a JEOL JEM-200CX transmission electron microscope operating at 120 kV. HRTEM analyses were run on a JEOL JEM-2010F transmission electron microscope operating at 200 kV. The XPS analyses were performed on a Physical Electronics 5800 spectrometer equipped with a hemispherical analyzer and using monochromatic Al- K α radiation (1486.6 eV, the X-ray tube working at 15 kV and 350 W, and pass energy of 23.5 eV).

Synthesis and purification of MIL-101(Cr)

MIL-101 (Chromium (III) terephthalate; MIL: Materials of Institut Lavoisier) was prepared according to the methods given in the literature and purified from impurities. According to the synthesis protocol, Cr(NO₃)₃.9H₂O (2.0 g, 5 mmol), terephthalic acid (0.83 g, 5.0 mmol) and distilled water (20 mL) were kept until pH = 2.58 in sonication. Then, the mixture was taken into a Teflon coated autoclave and kept in the oven for 18 hours without mixing at a temperature of 493 K. At the end of this period, the cooled mixture was removed from the autoclave and the solid part was isolated by centrifugation for 10 min. at 5000 rpm. The solid was washed with water and methanol, respectively, taken into acetone and separated from acetone by centrifugation for 10 min. at 5000 rpm. The separated solid was sonicated in dimethylformamide for 10 min. and stirred overnight in an oil bath at 343 K. MIL-101 crystals from the mixture cooled to room temperature were again isolated by centrifugation (5000 rpm; 10 min), washed with methanol and acetone and dried at 323 K for 10 hours under vacuum at 10⁻¹ Torr. The synthesized MIL-101 was placed in the annealing furnace in the quartz bed, and was activated by removing the water and solvent molecules around the Cr(III) centers (10⁻³ Torr) by keeping them under vacuum from room temperature to 393 K for 2 hours and then for 3 hours at this temperature.

Synthesis of MIL-101(Cr) stabilized silver nanoparticles (Ag@MIL-101)

Silver (I) cations were introduced to MIL-101(Cr) support using a well-known liquid phase impregnation method in a 10 mL aqueous solution containing 200 mg MIL-101(Cr) and AgNO₃ (86 μ mol, 14.62 mg) for 3 hours at room temperature. Then 2.0 mL of aqueous NaBH₄ solution (1.36 mmol, 51.4 mg) was added to this solution to reduce Ag (I) cations and the final solution was stirred at room temperature for half an hour under air. The solid was then isolated by centrifugation (6000 rpm, 5 min), washed abundantly with water (3×20 mL) to remove nitrate ions and dried in the oven at 353 K, resulting in a powdered Ag@MIL-101 catalyst.

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General experimental procedure for one-pot synthesis of imines

In a typical procedure for one-pot synthesis of imines, a mixture of amine (0.5 mmol), benzyl alcohol (0.625 mmol), KO^tBu (0.10 mmol) and catalyst (10 mg) was refluxed with 5 mL of toluene at 100 °C for 24 h in open system under an argon atm. After cooling, ethyl acetate was added to dilute the reaction mixture and the catalyst was centrifuged from the solution. Then, solution filtered through a short pad of SiO₂ column. The filtrate was analyzed by GC–MS and NMR.

Reusability experiments

The dehydrogenative coupling of benzyl alcohol and *p*-toluidine was also chosen as a model reaction for reusability tests. After the completion of the first reaction, the catalyst was separated by centrifugation, washed with ethanol, ethyl acetate and deionized water, dried at 70 °C for 12 h under vacuum, and was used for the further runs.

Conclusions

In this study, we designed a novel, efficient and sustainable Agbased heterogeneous catalytic system for the one-pot synthesis of imines from alcohols and amines. The Ag@MIL-101 catalyst is prepared using the liquid phase impregnation method and characterized by ICP-OES, P-XRD, FT-IR, TEM, HRTEM, and XPS spectroscopies. The average particle size of the silver (0) nanoparticles in the obtained Ag@MIL-101 catalyst was calculated as 2.43 ± 0.22 nm. The catalyst showed high activity and selectivity in the one-pot synthesis of imines from alcohols and amines and can easily be recycled five times without loss of activity and selectivity. Furthermore, on the basis of the mentioned experimental results and previous reports, we examined a possible reaction pathway. High catalytic performance of the Ag@MIL-101 catalyst used in the one-pot synthesis of imines is achieved by synergistic cooperation between the silver (0) nanoparticles and MIL-101(Cr).

Conflicts of interest

There are no conflicts to declare.

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