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Iron exchanged molybdophosphoric acid as an efficient heterogeneous catalyst for the synthesis of quinoxalines

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ABSTRACT

An efficient iron exchanged molybdophosphoric acid catalyst is reported for the one pot tandem oxidative cyclization of α-hydroxy ketones with 1,2-diamines under aerobic conditions. The fresh and used catalysts were characterized by FT-infra red, X-ray diffraction and Raman spectroscopy. The characterization results reveal the presence of Keggin ion after the exchange of protons of MPA with iron for fresh and used catalysts. The preparation of the catalyst is simple and reusable with consistent activity. The catalyst has a practical advantage for the synthesis of quinoxalines. A plausible reaction mechanism is proposed for the synthesis of quinoxalines.

1. Introduction

Quinoxaline derivatives are an important class of nitrogen-containing heterocycles as they constitute useful intermediates in organic synthesis [1]. Quinoxalines plays an important role as a basic skeleton for the design of a number of antibiotics such as echinomycin, actinomycin and leromycin [2]. A number of synthetic strategies have been developed for the preparation of substituted quinoxalines. By far, the most common method is the condensation of an aryl 1,2-diamine with 1,2-dicarbonyl compounds refluxing in ethanol or acetic acid [3–5].

Alternative routes have been developed recently by using α-hydroxy ketones instead of 1,2-dicarbonyls [6–8]. The α-hydroxy ketones are oxidatively cyclized with diamines in the presence of transition metal catalysts to yield quinoxalines. Robinson and Taylor reported the synthesis of quinoxaline from hydroxy ketones using homogeneous $Pd(OAc)_2$, $RuCl_2(PPh_3)_2$ catalytic system [6]. These protocols require the stoichiometric amount of promoters or bases. Active manganese oxide in combination with molecular sieves [7] and $CuCl_2$ catalyzed synthesis of quinoxalines has been reported [8]. All these homogeneous methods are suffer from tedious workup and low recyclability of the catalyst. Very recently, a recyclable manganese oxide octahedral molecular sieves catalyzed synthesis of quinoxalines has been reported [9]. However, the preparation of this type of oxides required special methods. Thus development of novel and cheaper heterogeneous catalytic system remains an exciting challenge.

Keggin type heteropoly acids (HPAs) have many advantages that make them economical and environmentally attractive catalysts for both academic and industrial applications. They are useful as acid and oxidation catalysts for various reactions since their catalytic features can be varied at molecular level. Heteropolyoxometalates, particularly 12-molybdophosphoric acid (MPA) with Keggin structure, are widely used as homogeneous and heterogeneous catalysts for the oxidation of different organic molecules such as alcohols, alkanes and alkenes [10,11]. However these catalysts are highly soluble in polar solvents. Efforts are being made to overcome the solubility problem by converting them into their corresponding salts or exchanging their protons with different metal ions. We have been working on the development of metal exchanged heteropoly acid as catalyst for different applications [12–14].

In the present communication, we report environmentally friendly iron exchanged molybdophosphoric acid (FeMPA) as a highly effective heterogeneous catalyst for the synthesis of quinoxalines from hydroxy ketones and diamines. The advantage of present catalyst is that it does not require any additives or promoters. Furthermore, the preparation of the catalyst is very simple, inexpensive and reusable without any loss of activity.

2. Experimental

2.1. Preparation of FeMPA catalyst

Iron exchanged with the protons of MPA was obtained as a precipitate by adding 1.1 g of iron nitrate in aqueous solution to

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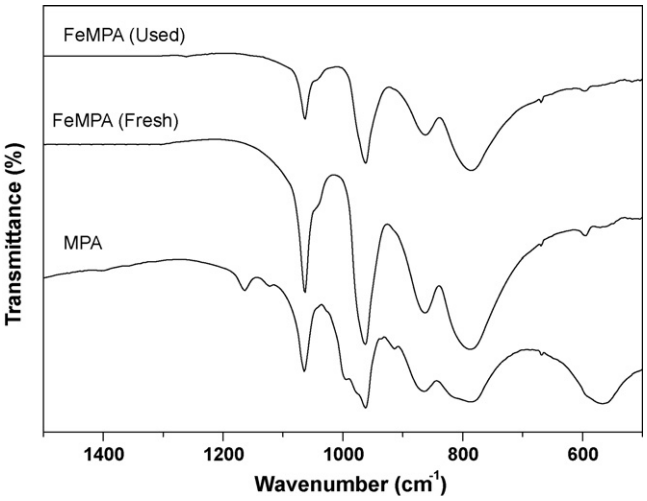


Fig. 1. FT-IR patterns of MPA and FeMPA catalysts.

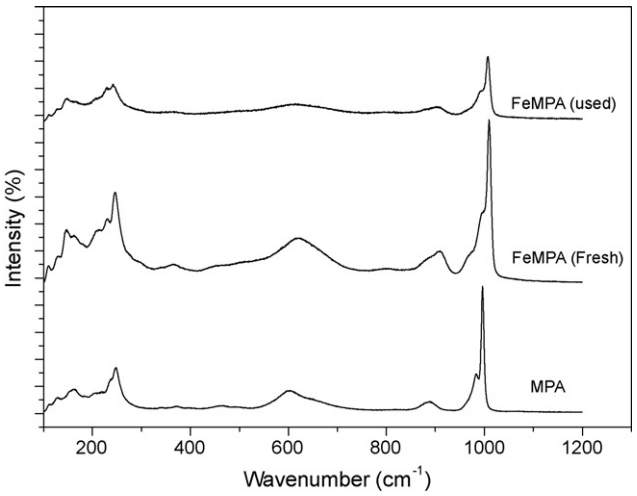


Fig. 3. Laser Raman spectra of MPA and FeMPA catalysts.

5 g of 12-molybdophosphoric acid dissolved in 25 mL of distilled water with constant stirring. The excess water was removed on a water bath and the resultant salt was dried in an oven at 120 °C for 12 h. Finally the catalyst was calcined in air at 300 °C for 2 h. The composition of the final catalyst determined by ICP mass is $Fe_{0.64}H_{0.36}PMo_{12}O_{40}$. This catalyst is denoted as FeMPA.

FT-IR spectra of catalysts were taken on a DIGILAB (USA) IR spectrometer by using KBr disc method. Powder X-ray diffraction (XRD) patterns of the catalysts were recorded on a Rigaku Miniflex (Rigaku Corporation, Japan) X-ray diffractometer using Ni filtered Cu Kα radiation (λ = 1.5406 Å) with a scan speed of 2° min^{-1} and a scan range of 2–80° at 30 kV and 15 mA.

The Raman spectra of the samples were collected with a Horiba-Jobin Yvon LabRam-HR spectrometer equipped with a confocal microscope, 2400/900 grooves/mm gratings, and a notch filter. The laser excitation at 532 nm (visible/green) was supplied by a Yag doubled diode pumped laser (20 mW). The scattered photons were directed and focused onto a single-stage monochromator and measured with a UV-sensitive air cooled CCD detector.

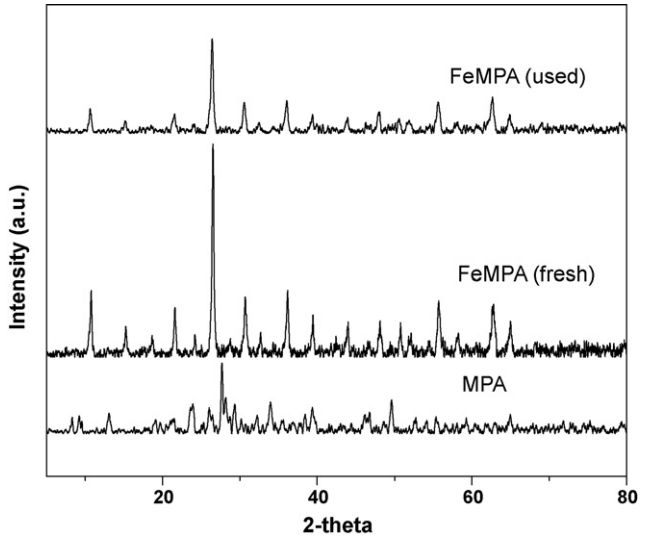


Fig. 2. XRD patterns of MPA and FeMPA catalysts.

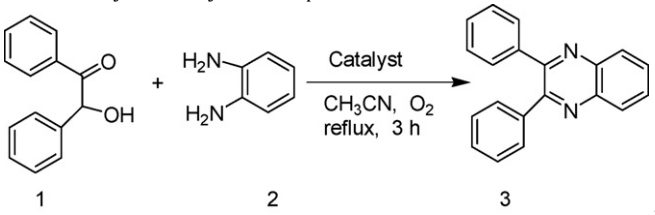
2.2. Catalytic reaction

About 1 mmol of hydroxyl ketone, 2 mmol of 1,2-diamine and 5 mL acetonitrile were taken in a 25 mL round bottom flask. The catalyst about 50 mg was added to the reaction mixture. The reaction mixture was stirred at 80 °C for a given reaction time under atmospheric pressure in the presence of molecular oxygen. The progress of the reaction was monitored by thin-layer chromatography (TLC). After completion of the reaction, the reaction mixture was cooled to room temperature and diluted with ethyl acetate. The resulting suspension was filtered and the filtrate was concentrated and purified by column chromatography to obtain the desired product. The identity and purity of the product was confirmed by ^{1}H NMR and ^{13}C NMR and the data were compared with the existing literature.

3. Results and discussion

The catalysts were characterized by FT-IR, XRD and Raman spectroscopy. The FT-IR spectra of pure MPA and FeMPA catalysts are shown in Fig. 1. The used catalyst spectrum was also presented in the same figure. The IR bands found in all the samples at 1064, 946, 864 cm^{-1} and a broad band at 785 cm^{-1} attributed to Keggin ion characteristic stretching vibrations of $P–O_d$, $Mo=O_t$, $Mo–O_b–Mo$ and $Mo–O_c–Mo$ bands, respectively [15]. The FT-IR analysis shows that the Keggin structure is intact after the exchange of Fe with the protons of 12-molybdophosphoric acid.

Table 1
Effect of catalyst for the synthesis of quinoxaline[a].



Entry	Catalyst	Yield (%)[b]
1	None	20
2	$FeCl_3$	30
3	$Fe(NO_3)_3$	25
4	MPA	50
5	FeMPA	97

[a] Reaction conditions: benzoin (1 mmol), 1,2-phenylenediamine (2 mmol), catalyst (50 mg), acetonitrile (5 mL) under reflux, 3 h.
[b] Isolated yield.

Table 2
Oxidative cyclization of different α-hydroxy ketones with substituted diamines over FeMPA catalyst[a].

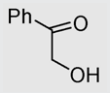
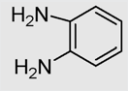
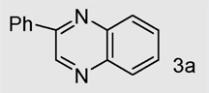
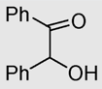
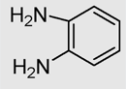
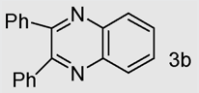
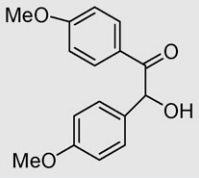
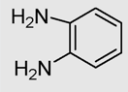
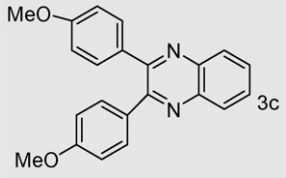
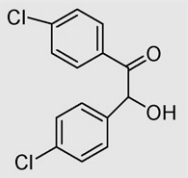
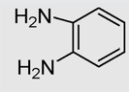
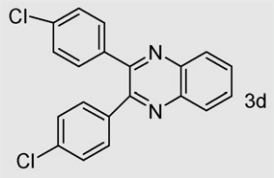
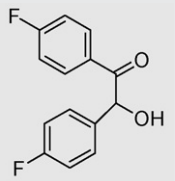
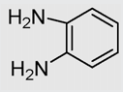
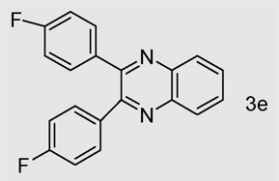
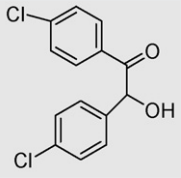
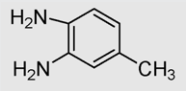
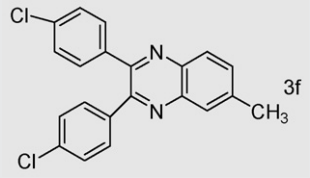
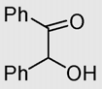
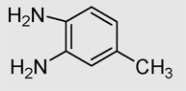
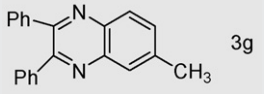
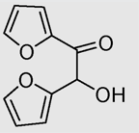
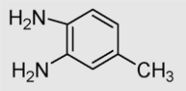
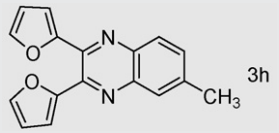
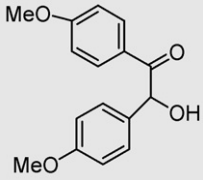
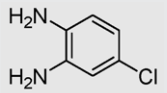
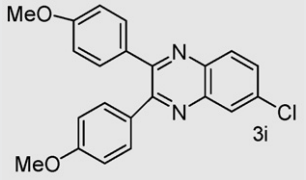
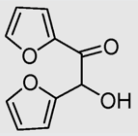
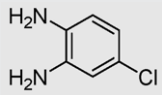
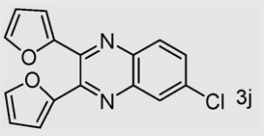
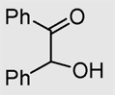
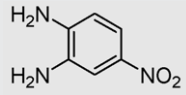
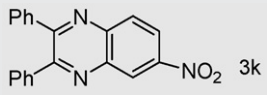
Entry	Hydroxy ketone	Diamine	Quinoxaline	Yield (%)[b]
1			 3a	99
2			 3b	95
3			 3c	60
4			 3d	91
5			 3e	89
6			 3f	90
7			 3g	96
8			 3h	92
9			 3i	50
10			 3j	87

Table 2 (*Continued*)

Entry	Hydroxy ketone	Diamine	Quinoxaline	Yield (%)[b]
11			 3k	49

[a] Reaction conditions: hydroxy ketone (1 mmol), 1,2-diamine (2 mmol), catalyst (50 mg), acetonitrile (5 mL) under reflux, 3 h.
[b] Isolated yield.

Fig. 2 shows the XRD patterns of fresh and used catalysts. The main characteristic peaks related of Keggin ion of MPA are found in all the samples. The exchange of Fe resulted in the enhanced crystalline nature with marginal shift in 2θ angles related to the cubic crystalline structure FeMPA. Similar observations are also reported for the Cs salts of MPA [16]. The XRD results are in support with FT-IR, which suggests the existence of Keggin ion structure for FeMPA catalyst.

Laser Raman spectra of the MPA, FeMPA fresh and used are presented in Fig. 3. The basic heteropoly molybdate MPA exhibit the characteristic bands of the Keggin structure with bands at 996, 983, 885, 600 and 248 cm^{-1} [17]. The strong band at 996 cm^{-1} with a shoulder at 983 cm^{-1} arise from the symmetric and asymmetric stretching modes of the Mo=O_t bond, respectively. The broad bands ~885 and ~600 cm^{-1} are from the asymmetric Mo–O_b–Mo and symmetric Mo–O_c–Mo stretching modes, respectively. The strong band at 248 cm^{-1} corresponds to Mo–O–Mo bending mode of the intact Keggin. Similar Raman bands have been observed when Fe was exchanged with the protons of MPA suggesting the Keggin structure in the modified catalyst also.

Initially the oxidative cyclization of benzoin with o-phenylenediamine was carried using MPA, Fe exchanged MPA and with different iron salts. The results are presented in Table 1. A blank reaction (without catalyst) was also carried out using benzoin and o-phenylenediamine in acetonitrile at reflux condition for 4 h under atmosphere of O_2 resulting in the formation of 2,3-diphenyl quinoxaline with about 20% yield. With the same substrates using a catalytic amount of MPA produced about 50% yield in 3 h. When the reaction was performed in the presence of iron exchanged molybdophosphoric acid, afforded the product in 97% yield. Different iron salts are also tested for this reaction. The iron salts are not very effective for the synthesis of quinoxalines. MPA which is known for its oxidizing ability (due to Mo) and acidity (due to protons) is not a very effective catalyst for this reaction. The iron salts like $FeCl_3$ which is a Lewis acid is also not an efficient catalyst. However, when Fe is exchanged with MPA results in a highly active catalyst for the oxidative cyclization of hydroxyl ketones with diamines.

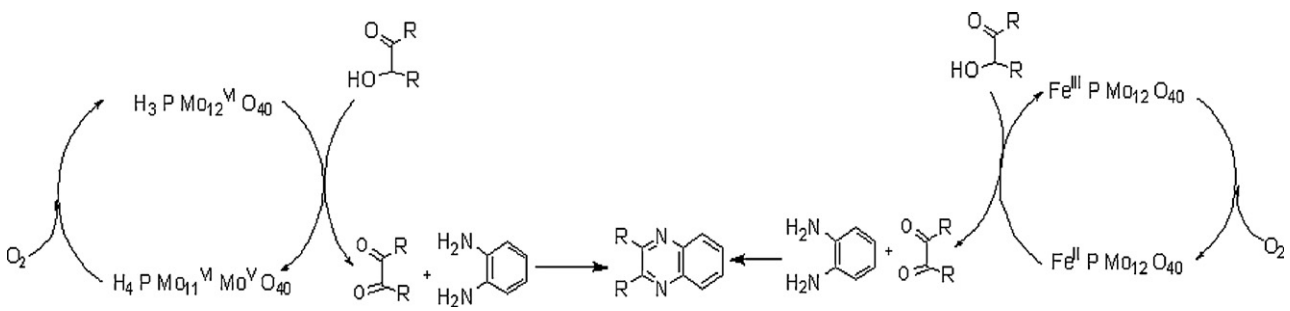
Encouraged by the efficiency of this protocol described above, the substrate scope was investigated further. The results obtained for the cyclization of different hydroxyl ketones and diamines are summarized in Table 2. Quinoxaline synthesis with 2-hydroxyacetophenone and benzoin with 1,2-phenylenediamine gave excellent yields (Table 2, entries 3a and 3b). With the presence of electron donating substituents in the amine part, increased yields were obtained. Low yields were obtained when electron-withdrawing substituents are present in amine. On the other hand, electron-donating substituents on the aromatic ring attached to hydroxyl ketones decreased the product yields and reverse trend observed with the electron withdrawing groups. Anisoin gave the lowest yield among all the studied hydroxyl ketone substrates (Table 2, entries 3c and 3i). The presence of electron donating OCH_3 group in the benzene ring may retard the nucleophilc attack on the in situ formed dicarbonyl leading to a lower yield. Heterocyclic substrate furoin with 4-methyl-1,2-phenylenediamine gave 92% yield (Table 2, entry 3h), indicating that electron donating methyl group in the diamines enhances its nucleophilicity. Over all the catalyst showed exceptionally high activity towards this reaction.

Table 3
Recycling results of FeMPA catalyst.

S. no.	No. of recycles	Yield (%)	Catalyst recovery (%)
1	0	95	–
2	1	93	94
3	2	90	92
4	3	87	90

After completion of the reaction, the catalyst was separated by simple filtration and washed several times with acetonitrile. Later the catalyst was dried in air oven at 120 °C for 1 h and reused. The recover of the catalyst with cycle is varied with in 90–94%. The results obtained by recycling the catalysts are summarized in Table 3. The yields of 2,3-diphenyl quinoxaline after four cycles were almost same without loss of catalytic activity (Table 3).

In order to know the stability of the catalyst FeMPA (used) is characterized by XRD, FT-IR and Raman spectroscopy. As shown in Figs. 1, 2 and 3 the IR, XRD and Raman patterns, respectively of the used catalyst are same as that of fresh catalyst. The XRD patterns of the used catalyst is similar to that of the fresh catalyst. This suggests that there are no structural changes during the reaction. The used catalyst characterization suggests the stability of Keggin ion for this reaction.



Scheme 1. Plausible reaction mechanism.

The role of the MPA and FeMPA catalyst is explained by the plausible mechanism as shown in Scheme 1. In this reaction the first step is the oxidation of α-hydroxy ketone to dicarbonyl followed by the cyclization of dicarbonyl with diamines. The oxidation reaction is facilitated by the catalyst and once the dicarbonyl forms it readily reacts with diamine to yield quinoxaline.

The MPA is also showed considerable activity for this reaction (Table 1). In this reaction α-hydroxy ketone undergoes oxidation to dicarbonyl over MPA, leading to reduction of Mo^{6+} to Mo^{5+} [18]. It is known that heteropoly anions are easily reducible chemical species. The oxidant oxygen reoxidizes the reduced Mo. In the case of iron exchanged MPA, apart from the participation of Mo, Fe also undergoes reduction from Fe^{III} to Fe^{II} by converting α-hydroxy ketone to dicarbonyl compound. It again reoxidized by the molecular oxygen. The presence of Fe in MPA facilitates the oxidation of α-hydroxy ketones on Fe, which is known for its oxidizing ability. The synergetic effect of both Fe and Mo might be the reason for high oxidation ability of the FeMPA catalyst.

4. Conclusions

The present FeMPA catalyst could act as an efficient heterogeneous catalyst for the single-pot synthesis of quinoxalines from hydroxy ketones and diamines. This reaction gave the corresponding quinoxalines in good to excellent yields. The use of FeMPA can provide alternative to toxic and precious metals. The present catalytic system is inexpensive, easy to handle, non-corrosive and environmentally benign. The catalyst was heterogeneous, easy to recover and reused with retention of its high catalytic activity.

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