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Cite this: DOI: 10.1039/c0xx00000x

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ARTICLE TYPE

Catalytic system for pyridine oxidation to N-oxides under mild conditions based on polyoxomolybdate

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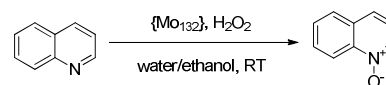
Received (in XXX, XXX) Xth XXXXXXXXXX 20XX, Accepted Xth XXXXXXXXXX 20XX

DOI: 10.1039/b000000x

A reusable and effective catalytic system has been developed for oxidation of pyridines catalyzed by Keplerate polyoxomolybdate ($\{Mo_{132}\}$) at room temperature. Pyridine compounds including quinoline and quinoline derivatives could be oxidized in high yields under mild conditions.

As a class of well-defined inorganic transition-metal oxide clusters, polyoxometalates (POMs) have been studied for many years. Due to their functional property with abundant compositions, POMs are commonly used in catalysis, medicine, imaging, sensing, and multifunctional materials [1]. Among them, catalysis is particularly one of important research field based on polyoxometalates. Because of green chemistry, hydrogen peroxide as a mild oxidant was used widely in catalytic oxidations. POMs, as effective catalysts for oxidation reaction with hydrogen peroxide have drawn wide attention in the past years, such as alcohol oxidation [2], sulfur compound oxidation [3] and olefin epoxidation [4]. In above catalytic systems, Keggin polyoxometalates with saturated, lacunary or transition-metal-substituted structures were mostly used as effective catalysts. Other structures of polyoxometalates have been reported less used for catalytic reactions. Recently, giant polyoxomolybdate with Keplerate structure $[(NH_4)_{42}[Mo^{VI}_{72}Mo^V_{60}O_{372}(CH_3COO)_{30}(H_2O)_{72}]]$ ($\{Mo_{132}\}$) was reported as effective catalyst for oxidation of olefins and sulfides [5]. The study explored the application of Keplerate-polyoxometalates and made title methodologies suitable for industrial goals.

On the other hand, as important and versatile synthetic intermediates, heterocyclic N-oxides of pyridines are used widely in fields of chemistry and biology. They can be used as protecting groups, auxiliary agents, oxidants, catalysts, surrogates for heterocyclic boronic acids and ligands in metal complexes [6]. Catalytic oxidations of pyridines to N-oxides using effective catalyst with hydrogen peroxide have received much attention in recent years [7]. Some reusable and mild catalytic systems for pyridine oxidation based on polyoxometalates with hydrogen peroxide have been developed [8]. In these systems, several pyridines were oxidized to corresponding N-oxides with high yields, and the catalyst could be reused after first reaction. However, there were some disadvantages for the procedures, such as long reaction time during oxidation of pyridine derivatives and



Scheme 1

high reaction temperature during oxidation of quinoline derivatives.


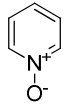

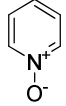

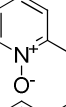

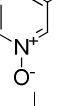

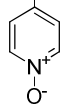

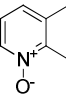

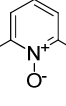

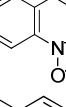

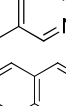

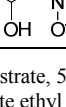
To expand applications of Keplerate polyoxomolybdate ($\{Mo_{132}\}$) in catalytic reactions and avoid the shortcomings in previous catalytic systems for pyridine oxidation, herein we develop an effective and reusable catalytic system for pyridine oxidation to N-oxides catalyzed by $\{Mo_{132}\}$. In this system, heterocyclic N-oxides were obtained in high yields by oxidation of pyridines in mixed solvent of water and ethanol at room temperature catalyzed by $\{Mo_{132}\}$ with aqueous hydrogen peroxide (see Scheme 1). Pyridine and its derivatives could be oxidized in high yields during short time at room temperature. Interestingly, quinoline and its derivatives also could be oxidized in high yields at room temperature, which could not be achieved in previous reported similar systems. In addition, the catalyst after reaction could be recovered and reused for several times without obvious loss in activity.

Table 1 summarizes the results of catalytic oxidation of different pyridine and its derivatives based on $\{Mo_{132}\}$ with hydrogen peroxide in the mixed solvent (water and ethyl alcohol). To obtain high yields of products, 5 equivalents of hydrogen peroxide were used in the system. Pyridine was successfully oxidized to pyridine N-oxide with 93% yield during six hours at room temperature (Table 1, entry 2). The control experiment was also carried out to reveal that the oxidation of pyridine was hardly processed without catalyst (<2 %, entry 1). Most of the substrates were successfully oxidized to the corresponding N-oxides in high yields. Selectivities to the products of N-oxides were $\geq 99\%$. It was found that 2-picoline, 3-picoline and 4-picoline were converted to the corresponding N-oxides in excellent yields without obvious differences during 6 h (entries 3-5). Di-substituted pyridine derivatives of 2, 6-lutidine and 2, 3-lutidine were also examined in this catalytic system. Compared to mono-substituted pyridines, longer reaction time was necessary during oxidation of di-substituted pyridines (entries 6 and 7).

Interestingly, high to excellent yields of corresponding N-oxides were obtained in this catalytic system at room temperature during oxidation of quinoline and its derivatives, containing quinoline, isoquinoline and 8-hydroxy-quinoline (Table 1, entries

8-10). The mixture solvent of water and ethyl alcohol played an

Table 1 Oxidation of pyridines to N-oxides with hydrogen peroxide catalyzed by $\{Mo_{132}\}^a$

Entry	Substrate	Product	Reaction time (h)	Yield ^b (%)
1 ^c			6	<2
2			6	93
3			6	94
4			6	92
5			6	90
6			10	86
7			10	85
8			24	84
9			24	90
10			24	89

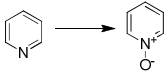
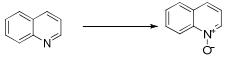
^a Reaction conditions: 1 mmol substrate, 5 mmol (30% aq.) H_2O_2 , 0.01 mmol catalyst, H_2O (3 ml), absolute ethyl alcohol (2 ml); Room temperature (298 K). ^b Isolated yields; Assignments of products were analyzed by 1H NMR and ^{13}C NMR. ^c Without catalyst.

important role in these reactions. Catalyst of $\{Mo_{132}\}$ was dissolved in aqueous phase containing water and hydrogen peroxide. However, substrates of quinoline and its derivatives were hydrophobic which resulted in an unsuccessful contact between the substrate and the catalyst. The addition of ethyl alcohol could be significantly improved the mass transfer in the medium. So, the oxidation of quinoline and its derivatives were successfully carried out in the mixed solvent at room temperature.

To manifest the superiority of this catalytic system, some similar previous systems catalyzed by polyoxometalates with hydrogen peroxide were listed with the described system in Table 2. As shown in the Table, for oxidation of pyridine, the shortest reaction time (6 h) and mild reaction temperature (298 K) were required in our system. For oxidation of quinoline, higher

reaction temperature was always necessary in previous systems to

Table 2 Catalytic activity in oxidation of pyridine and quinoline in different systems

Reaction	Reaction temperature (K)	Reaction time (h)	Yield (%)	System
	348	7	96	Ref. 8a
	298	12	91	Ref. 8b
	298	16	96	Ref. 8c
	298	6	93	This work ^a
	298	6	42	This work ^a
	348	7	82	Ref. 8a
	338	6	95	Ref. 8b
	298	24	29	Ref. 8b
	298	24	84	This work ^a
	298	24	39	This work ^a

^a Phosphomolybdic acid hydrate used as catalyst.

improve the catalytic activity. Only in our catalytic system, quinoline was oxidized to quinoline-N-oxide with high yield at room temperature. The catalytic activity of Keggin polyoxomolybdate of phosphomolybdic acid hydrate ($H_3PMo_{12}O_{40} \cdot xH_2O$) has also been checked for oxidation of pyridine and quinoline (listed in Table 2). Under same reaction conditions, only 42% and 39% yields of corresponding N-oxides were obtained when oxidation of pyridine and quinoline catalyzed by phosphomolybdic acid. Based on the above descriptions, we can see that our method is superior to the most of the previously reported methods.

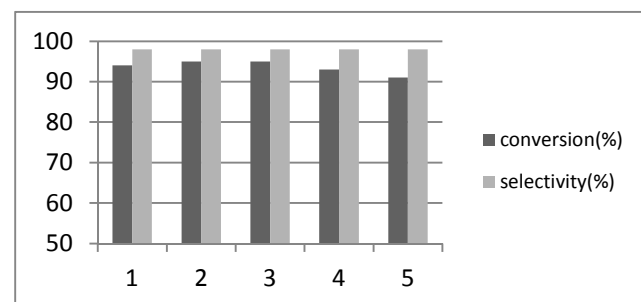


Figure 1 Recycling of the catalytic system for oxidation of 2-picoline

The catalyst could be reused in this catalytic system. During reaction, the catalyst dissolved in aqueous phase and catalyzed the oxidation of pyridines. After reaction, the organic product was separated from the aqueous phase by extraction. The catalyst was still remained in the aqueous solution after extraction, and the aqueous phase could be directly used for the next run. For oxidation of quinolines, part of catalyst could be precipitated from medium because of property of substrates and products. After reaction, filtration was carried out before extraction. The obtained catalyst could be added into the aqueous phase after washed and dried when used for next oxidation. The reuse performances of $\{Mo_{132}\}$ in the oxidation of 2-picoline are shown in Figure 1. After five consecutive reused, there was no significant loss of initial catalytic activity. The yield of N-oxide obtained with the recovered catalyst was nearly the same as that

of the first reaction, indicating that catalyst $\{\text{Mo}_{132}\}$ is a reusable and robust catalyst in the oxidation system.

The IR spectra of the catalyst before and after oxidation have been listed in supporting information (SI). As shown in Figure S1, there were obvious differences in the IR spectra between the fresh catalyst and the used catalyst, indicating that the structure of the catalyst after reaction has been changed. Several reports have proved that polyoxometalates are not stable in the presence of hydrogen peroxide. The spectrum of $\{\text{Mo}_{132}\}$ treated with H_2O_2 has also been listed in Figure S2, indicating that the structure of catalyst used in the system would change when reacted with H_2O_2 . Polyoxometalate catalysts would be transformed into peroxy species during reaction by hydrogen peroxide have been reported in the past years [1, 4 and 10]. In addition, the spectrum of precipitated solid during oxidation of quinoline was also listed in SI (Figure S3). The used catalyst and precipitated compound after oxidation of quinoline may all belongs to polyoxomolybdate species, which were produced after decomposition of $\{\text{Mo}_{132}\}$ by hydrogen peroxide. However, both of them have catalytic activity for oxidation. The ^1H NMR spectrum of fresh catalyst has been detected (shown in SI). The signals were consistent with the previous report [11]. The large signal at 4.79 ppm is due to solvent of water; the signal at 7.26 ppm is due to NH_4^+ ; the signal at 1.99 ppm is due to free ligand of acetate; the signals at 1.03 and 0.84 ppm are due to coordinated species of acetate. There were no obvious signals of acetate have been detected in the NMR of recovered catalyst. The results also indicate that the structure of recovered catalyst after reaction has been changed, which is consistent with IR spectra.

According to the experimental data and referencing the reported systems [10], we presumed a possible mechanism for pyridine oxidation in this system. When treated with hydrogen peroxide, $\{\text{Mo}_{132}\}$ will change to several polyoxomolybdate species. The species could become active peroxy molybdate species during reaction, which is active and responsible for the oxidation of pyridines. Exactly, the Keplerate polyoxomolybdate used in the system is a precatalyst. When the oxidation of substrates catalyzed by peroxy species finished, the catalyst would change back to the polyoxomolybdate species, which could be used for the next oxidation.

Conclusions

In conclusion, an effective, reusable and mild catalytic system for pyridine oxidation has been developed based on a Keplerate polyoxomolybdate. Pyridine and pyridine derivatives were efficiently oxidized to the corresponding N-oxides in high yields at room temperature during short time. Even some hydrophobic substrates were successfully oxidized to N-oxides with high yields at room temperature which required high reaction temperature in other reported catalytic systems. In addition, productions could be obtained simply, and the catalyst reused after reaction was retentive of catalytic performance.

Experimental

Preparation of catalyst
 $[(\text{NH}_4)_{42}[\text{Mo}^{\text{VI}}_{72}\text{Mo}^{\text{V}}_{60}\text{O}_{372}(\text{CH}_3\text{COO})_{30}(\text{H}_2\text{O})_{72}]\{\text{Mo}_{132}\}] [9]$:

Firstly, 5.6 g (4.5 mmol) of $(\text{NH}_4)_6\text{Mo}_7\text{O}_{24}\cdot 2\text{H}_2\text{O}$ and 12.5 g

(162 mmol) of $\text{CH}_3\text{COONH}_4$ were dissolved in 250 ml of water with stirring. 0.8 g (6.1 mmol) of $\text{N}_2\text{H}_4\text{H}_2\text{SO}_4$ was then added to the solution. The solution was then stirred for 10 min and the color changed to blue green. 83 mL of CH_3COOH (50%) was subsequently added. The deep green solution was kept at 293-298 K without further stirring for four days (color change to dark brown). The precipitated red-brown crystals were filtered through a glass frit (G2). The sample was washed with 90% ethanol, then with a 1:1 mixture of ethanol/diethyl ether and finally dried in air. The yield is about 3.2 g (about 50% yield based on molybdate). IR spectrum (KBr, cm^{-1}): 1624, 1540.9, 1401.8, 968.6, 937.0, 856.6, 794.8, 727.1, 631.6, 567.8, 512.8, 464.2, 438.5, 409.5.

Catalytic reaction

Catalyst (0.01 mmol), H_2O (3 ml), absolute ethyl alcohol (2 ml), substrate (1 mmol), and H_2O_2 (5 mmol, 30 % aq.) were charged in the reaction flask. The mixture was then stirred at room temperature (298 K) for 6-24 h. The reaction was detected by TLC. After reaction, the organic products were separated from the aqueous phase by extraction with dichloromethane. The combined organic layers were dried over anhydrous Na_2SO_4 , and the pure products were obtained by evaporation or column chromatography. The products were analyzed by ^1H NMR and ^{13}C NMR. The aqueous phase containing the catalyst was carried out for the next oxidation cycle.

Acknowledgements

This work was financially supported by the National Natural Science Foundation of China (Grant No. 21443007) and the Natural Science Foundation of Nanyang Normal University (No. QN2014015).

Notes and references

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 † Electronic Supplementary Information (ESI) available: [further experimental and characterization of oxidation products]. See DOI: 10.1039/b000000x/
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