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Catalytic synthesis of niacin from 3-methyl-pyridine and 30% H_2O_2 by Cu-based zeolite

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Abstract

Niacin is well known not only as vitamin B3 but also as an important chemical, and has wide applications in the fields of food, farming, medicine, pharmaceuticals, and industry. With the rapid development of human society, the requirement for niacin has been increasing constantly worldwide. Meanwhile, development of green routes to produce niacin under mild conditions has become particularly urgent to substitute the conventional reaction process with the consideration of energy conservation and emission reduction. Among various synthesis routes of niacin, selective oxidation of 3-methyl-pyridine and hydrogen peroxide (H_2O_2) in the liquid phase has become the focus of research due to its distinct advantages, such as mild reaction conditions, environmentally friendly reaction processes, and so on. Herein, zeolite-based catalysts have been first applied in the liquid phase synthesis of niacin from 3-methyl-pyridine and 30% H_2O_2 under mild reaction conditions. In addition, Cu-based 13X zeolite is found to show the highest catalytic performance, and optimal catalytic reaction systems have been established. This work provides a green and optional route for the synthesis of niacin.

Keywords: Zeolite, copper, niacin, 3-methyl-pyridine, H_2O_2

INTRODUCTION

Niacin (nicotinic acid) is well known as the essential vitamin B3 for all living cells. People are prone to



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getting symptoms if they lack niacin as the human body does not produce it. Therefore, niacin is widely used as an additive for food and feed production and in medical drugs. Additionally, niacin has important applications in pharmaceutical synthesis and the chemical industry^[1-7].

With the rapid development of human society, for example, the greatly increased demand for health, the global need for niacin has been increasing constantly. The conventional synthesis methods of niacin mainly include gas- (ammonia oxidation and air oxidation) and liquid-phase catalytic oxidation (inorganic acids as oxidants)^[7-12]. However, the gas-phase oxidation faces several challenges, including harsh reaction conditions, complex and multi-step reaction processes, and high energy consumption. On the other hand, the liquid-phase oxidation encounters issues such as a corrosive production environment and enormous post-treatment pressure. Therefore, development of green routes to synthesize niacin under mild conditions has become an urgent task. In 2016, the selective oxidation of 3-methyl-pyridine to niacin was reported using Ag/Mn₃O₄ spinel nanorods as catalysts and 50% H₂O₂ as an oxidant^[13]. On the one hand, this route offers several clear advantages, including mild reaction conditions, environmental friendliness, and fewer by-products. On the other hand, it sparks greater interest among researchers to develop new catalytic reaction systems considering economy and security, such as efficient non-noble metal-based catalysts, and low-concentrated H₂O₂.

Zeolite, an important crystalline material with unique and excellent physicochemical properties, is widely used in areas such as adsorption and separation, ion exchange, and catalysis^[14-26]. Herein, a series of zeolite-based catalysts had been prepared and applied in the liquid phase synthesis of niacin from 3-methyl-pyridine and 30% H₂O₂ under mild reaction conditions [Scheme 1]. Unexpectedly, it was found that non-noble metal-based zeolites presented high catalytic activity, and the highest niacin yield was achieved over Cu-based 13X zeolite. In addition, the optimal catalytic reaction systems had been established based on the Cu-based 13X zeolite catalyst, including solvent type, metal content of catalyst, molar ratio of substrate and H₂O₂, oxidant type, reaction temperature and time.

EXPERIMENTAL

Chemicals and raw materials

The chemicals and raw materials used in the work included the ones purchased from Macklin [cupric sulfate anhydrous, CuSO₄, 99%; copper nitrate trihydrate, Cu(NO₃)₂·3H₂O, 99%; cobalt nitrate hexahydrate, Co(NO₃)₂·6H₂O, 99%; copper acetate monohydrate, Cu(CH₃COO)₂·H₂O, 99%], the ones from Aladdin [iron nitrate nonahydrate, Fe(NO₃)₃·9H₂O, 98%; chromium nitrate nonahydrate, Cr(NO₃)₃·9H₂O, 99%; 50% hydrogen peroxide aqueous solution, 50% H₂O₂; 3-methyl-pyridine, 99%; sodium hypochlorite solution aqueous, NaClO, 6%~14%], the ones from Sinopharm [zinc nitrate hexahydrate, Zn(NO₃)₂·6H₂O, 99%; nickel nitrate hexahydrate, Ni(NO₃)₂·6H₂O, 99%; silver nitrate, AgNO₃, 99%; cuprous chloride, CuCl, 99%; acetonitrile, 99%; acetic acid, 99%; ethyl alcohol, 99%; acetone, 99%; tert-butyl hydroperoxide (TBHP) solution, 65%], the zeolites from Nankai University Catalyst Co LTD (Na-Y, Na-13X, Na-Beta, Na-4A, Na-MOR, Na-ZSM-5, TS-1), the one from Degussa (aerosil-200 fumed silica, SiO₂, 99.9%), the one from Chengdu Kelong Chemical Co LTD (30% hydrogen peroxide aqueous solution, 30% H₂O₂), and self-made deionized water. All the above chemicals and raw materials were applied directly in the catalyst preparation and catalytic reaction without further purification.

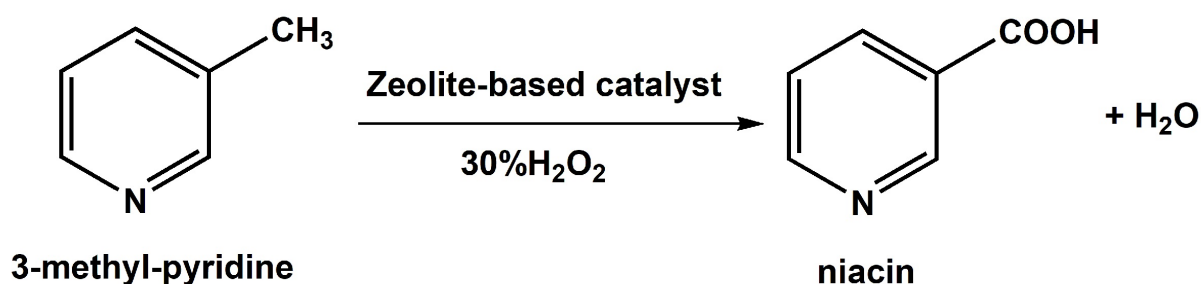
Preparation of catalysts

A series of zeolite-based catalysts with the same metal content [Table 1], were prepared using different types of metal salts and zeolites based on the reported method^[27], among which Cu/13X and Cu'/13X represented the catalysts prepared from cupric sulfate anhydrous and cuprous chloride, respectively. In addition, CuO_x/

Table 1. Catalytic synthesis of niacin from 3-methyl-pyridine and 30% H_2O_2 ^a

Entry	Catalyst	Conversion of 3-methyl-pyridine (%)	Selectivity (%)			Yield of niacin (%)
			Nicotinyl alcohol	Niacin	Others	
1	Zn/13X	62.4	57.2	12.8	30.0	8.0
2	Ag/13X	93.3	68.1	15.0	16.9	14.0
3	Cr/13X	60.5	46.3	27.0	26.7	16.3
4	Ni/13X	63.7	55.6	30.2	14.2	19.2
5	Co/13X	65.8	49.3	36.2	14.5	23.8
6	Fe/13X	71.3	41.4	35.1	23.5	25.0
7	Cu ⁺ /13X	81.5	3.8	54.1	42.1	44.1
8	Cu/13X	83.6	2.3	69.0	28.7	57.7
9	Cu/MOR	64.9	6.4	55.2	38.4	35.8
10	Cu/4A	67.1	6.8	53.7	39.5	36.0
11	Cu/ZSM-5	74.2	6.2	50.8	43.0	37.7
12	Cu/Beta	75.3	5.6	57.2	37.2	43.0
13	Cu/Y	80.1	5.4	61.6	33.0	49.3
14	CuSO ₄	74.1	3.3	65.9	30.8	48.8
15 ^b	Cu(NO ₃) ₂ ·3H ₂ O	75.4	3.3	61.8	34.9	46.6
16 ^c	Cu(CH ₃ COOH) ₂	74.3	3.1	65.0	31.9	48.3
17 ^d	13X	94.5	81.9	7.2	10.9	6.8
18	CuO _x /SiO ₂	90.1	6.1	35.2	58.7	31.7
19	TS-1	> 99.9	97.8	-	2.2	-
20	-	99.1	94.3	-	5.7	-

^aReaction condition: 1.0 g 3-methyl-pyridine, 100 mg catalyst, 10.0 mL MeCN, H_2O_2 /3-methyl-pyridine molar ratio of 13, 70 °C, 8 h. ^{b-d}22.0 mg CuSO₄, 39.0 mg Cu(NO₃)₂·3H₂O, and 43.0 mg Cu(CH₃COOH)₂ were used, respectively.

**Scheme 1.** Liquid-phase synthesis of niacin over zeolite-based catalyst.

SiO₂ was also prepared for comparison through the following process. Materials 0.846 g Cu(NO₃)₂·3H₂O, 2.0 g SiO₂ and 50.0 g were added into a 100 mL single-necked round bottom flask equipped with a condensing device, kept stirring for 9 h at ambient temperature, followed by rotary evaporation at 90 °C, drying at 100 °C overnight, and calcination at 550 °C for 6 h in air atmosphere.

Characterization

Powder X-ray diffraction (XRD) patterns were recorded on a Bruker D8A25 diffractometer equipped with Cu K α radiation ($\lambda = 1.54184 \text{ \AA}$) with a scanning speed of 10.0°/min. X-ray photoelectron spectroscopy (XPS) spectra were determined on a PerkinElmer PHI electron spectroscopy for chemical analysis (ESCA) system. Scanning electron microscopy (SEM) images were obtained on JEOL JSM-6510A and ThermoFisher Helios G4 CX, and energy dispersive X-ray spectroscopy (EDS) was performed using an

Oxford Instrument Ultim Max 100. The textural parameters were measured on a Quantachrome iQ-MP gas adsorption analyzer by physical adsorption/desorption of nitrogen at 77 K. Before the nitrogen adsorption, samples were dehydrated at 523 K for 14 h. The surface area was calculated via the Brunauer-Emmett-Teller (BET) equation. The pore volume was obtained from the adsorbed amount of nitrogen at a relative pressure of approximately 0.98.

Catalytic reaction

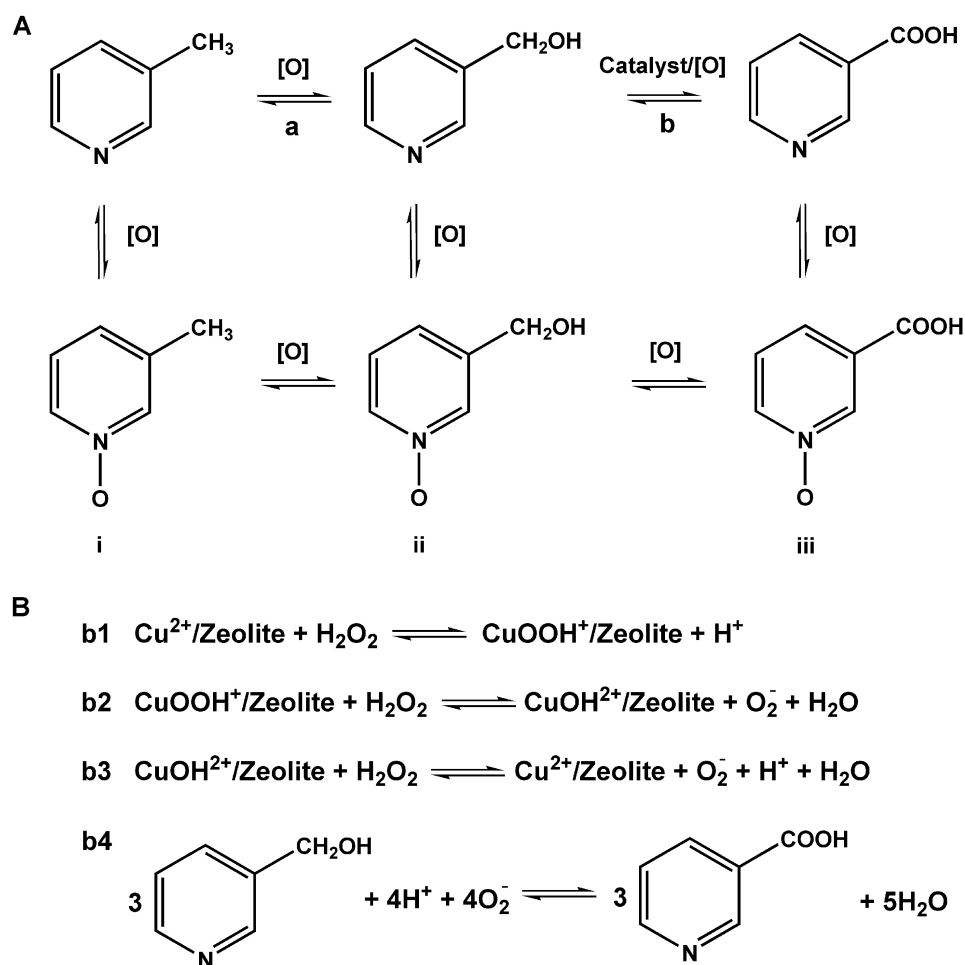
The catalytic reaction experiments were carried out under atmospheric pressure. Typically, 100 mg catalyst, 10 mL acetonitrile, and 10.7 mmol 3-methyl-pyridine were added successively into a 50 mL double-necked round-bottom flask equipped with a condensing device, and then the mixture was kept on stirring under a specific temperature for a period of time, during which aqueous solution of hydrogen peroxide was added into the mixture drop by drop. Subsequently, the reaction mixture was cooled to room temperature, and the liquid separated from the solid catalyst by centrifugation was analyzed by a liquid chromatography (LC, EClassical 3100 HPLC system, Dalian Elite Analytical Instruments CO LTD) equipped with a chromatographic column (O3100). The liquid chromatogram analysis results of 3-methyl-pyridine, niacin, and nicotiny alcohol were shown in [Supplementary Figures 1-3](#), respectively. In addition, an American Agilent 6224 time-of-flight liquid chromatography/mass spectrometry (TOF-LCMS) system was also applied to identify the products, and the analysis results were shown in [Supplementary Figure 4](#). Based on the above analysis, “others” in [Table 1](#) referred to the N-oxides of i and ii (entries 1 and 20) or the N-oxides of i, ii, and iii (entries 2~19) shown in [Scheme 2](#). The conversion of 3-methyl-pyridine, selectivity of niacin, and yield of niacin were calculated based on: conversion of 3-methyl-pyridine (mol%) = (moles of 3-methyl-pyridine reacted/total moles of 3-methyl-pyridine added) × 100%, selectivity of niacin (%) = (moles of niacin formed/total moles of products) × 100%, yield of niacin (%) = (moles of niacin formed/total moles of 3-methyl-pyridine added) × 100%.

RESULTS AND DISCUSSION

Catalytic performance evaluations were conducted over various samples for the conversion of 3-methyl-pyridine with 30% H_2O_2 to niacin under the same reaction condition, and the results were listed in [Table 1](#).

Entries 1~8 had compared the catalytic performance of various metal salt-based 13X zeolite catalysts. The yield of niacin over Zn/13X was merely 8.0%, which originated from low conversion of 3-methyl-pyridine (62.4%) and selectivity for niacin (12.8%). High conversion of 3-methyl-pyridine (93.3%) and quite low selectivity for niacin (15%) were obtained over Ag/13X. Although catalysts Cr/13X, Ni/13X, Co/13X, and Fe/13X showed distinctly increased selectivity for niacin ($\geq 27\%$), the yields of niacin were not higher than 25%. In contrast, Cu'/13X achieved 81.5% conversion of 3-methyl-pyridine and 54.1% selectivity for niacin, and the yield of niacin reached 44%, distinctly higher than the above catalysts. For comparison, 83.6% conversion of 3-methyl-pyridine and 69.0% selectivity for niacin were acquired over catalyst Cu/13X, with a niacin yield of about 58%, obviously higher than that obtained over Cu'/13X. The above results indicated the efficiency of copper species in the synthesis of niacin.

Entries 8~13 had compared the effect of zeolite support on the catalytic performance of various Cu/zeolite catalysts prepared by cupric sulfate and different types of zeolites. It was found that the selectivity for niacin over various Cu/zeolite catalysts was higher than 50%, while the yield of niacin obtained with Cu/MOR, Cu/4A, Cu/ZSM-5, Cu/Beta and Cu/Y (< 50%) was significantly lower than that achieved with Cu/13X. In addition, different metal salts, including CuSO_4 , $\text{Cu}(\text{NO}_3)_2 \cdot 3\text{H}_2\text{O}$, and $\text{Cu}(\text{CH}_3\text{COOH})_2$, had also been applied in the reaction directly (entries 14~16). It was found that these metal salts had shown similar conversion of 3-methyl-pyridine (74%~75%) and product distribution (about 62%~66% for niacin, 3% for



Scheme 2. (A) Main products and (B) possible mechanism in the liquid-phase oxidation of 3-methyl-pyridine with 30% H_2O_2 to niacin over Cu/zeolite catalyst.

nicotiny alcohol, and 30%~32% for others), with the niacin yield distinctly lower than that of Cu/13X. When 13X parent zeolite was used as a catalyst, nicotiny alcohol was the main product, and the selectivity for niacin was merely 7.2% (entry 17). In addition, when $\text{CuO}_x/\text{SiO}_2$ was applied in the reaction (entry 18), although 90.1% conversion of 3-methyl-pyridine was achieved, the yield for niacin was merely 31.7% due to its high selectivity for others (58.7%), implying its low catalytic activity for the reaction. The above results suggested the important roles of zeolite as support in the reaction, which influenced not only the conversion of 3-methyl-pyridine but also the distribution of products.

It was noteworthy that when TS-1 zeolite was applied in the reaction (entry 19), nearly all 3-methyl-pyridine was converted into nicotiny alcohol, and no niacin was detected, indicating that TS-1 did not work in the selected conditions of this reaction. Interestingly, a similar result was observed in a blank experiment without a catalyst (entry 20). The above results implied that nicotiny alcohol probably was an intermediate of the reaction. In order to prove this conjecture, a controlled experiment was particularly designed and conducted, in which the reaction proceeded under the system without a catalyst for the initial 4 h and then with a catalyst for the subsequent 2 h. [Supplementary Figure 5](#) showed the product distributions corresponding to the fourth hour without a catalyst and the sixth hour with a catalyst. It was obvious that nicotiny alcohol had been converted to niacin after the addition of a catalyst, which proved the above

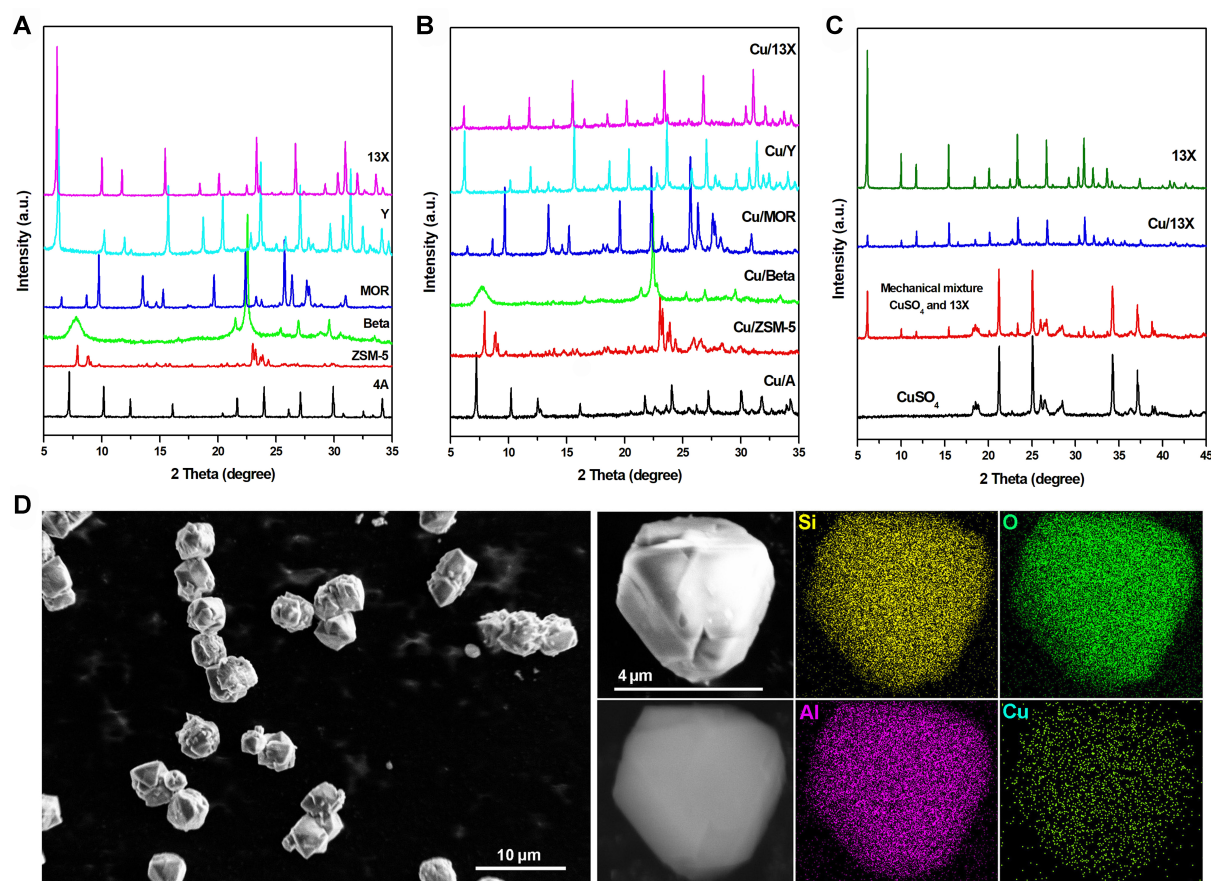


Figure 1. (A–C) Powder XRD patterns of parent zeolites, zeolite-based catalysts, CuSO_4 , mechanical mixture of CuSO_4 and 13X; (D) SEM and EDS of Cu/13X. XRD: X-ray diffraction; SEM: scanning electron microscopy; EDS: energy dispersive X-ray spectroscopy.

conjecture that nicotinyl alcohol was an intermediate of the reaction. The reusability tests of Cu/13X indicated that its catalytic activity did not decrease appreciably after reuse three times, implying its good chemical stability, and a slight decrease was ascribed to its tiny leaching of Cu^{2+} into the solution during the reaction. The XRD pattern and SEM image of the Cu/13X zeolite catalyst after reaction shown in [Supplementary Figure 6](#) indicated its good structure stability.

To explore the relationship between catalyst property and structure, various characterizations had been conducted over typical samples. The powder XRD patterns of selected samples were shown in [Figure 1](#) and [Supplementary Figure 7](#). Compared with the characteristic XRD patterns of parent zeolites, the counterparts of zeolite-based catalysts presented distinctly decreased XRD relative intensity, which was ascribed to the incorporation of copper species into the zeolites. Based on the XRD pattern of pure CuSO_4 phase shown in [Figure 1C](#), it was found that the peaks belonging to CuSO_4 were obviously observed in the pattern of CuSO_4 /13X mechanical mixture but were extremely weak and nearly invisible in the patterns of zeolite-based catalysts. It suggested that the copper species had been highly dispersed over the zeolite support. The SEM and EDS of Cu/13X zeolite catalyst were shown in [Figure 1D](#). It was observed that the particle size of Cu/13X zeolite catalyst was about 4.5 μm , and no obvious other phase was observed. The EDS images indicated that the distribution of various elements over the particle was highly uniform. This implied that the copper species had been highly dispersed over the 13X zeolite, consistent with the XRD analysis results.

Table 2. Textural parameters of Cu²⁺-exchanged zeolite catalysts

Catalyst	Surface area (m ² /g)	Pore volume (m ³ /g)
Cu/4A	243.3	0.1308
Cu/ZSM-5	327.5	0.1508
Cu/Beta	496.3	0.1844
Cu/MOR	388.5	0.2043
Cu/Y	779.8	0.1920
Cu/13X	746.2	0.3128
Cu'/13X	743.7	0.2446

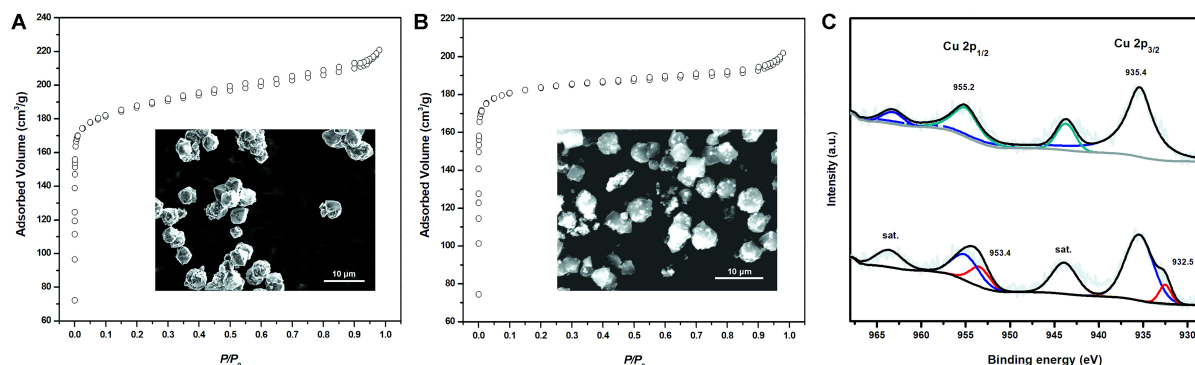


Figure 2. SEM images, N₂ adsorption-desorption isotherms, and XPS patterns of catalysts Cu/13X (A) and Cu'/13X (B); (C) top: Cu/13X, bottom: Cu'/13X. SEM: Scanning electron microscopy; XPS: X-ray photoelectron spectroscopy.

Particularly, based on the comparison of the SEM images [Figure 2], catalysts Cu/13X and Cu'/13X presented similar particle size and morphology, and no obvious difference was observed. In addition, the N₂ adsorption-desorption isotherms of the two catalysts were also shown in Figure 2, which corresponded to a typical microporous structure. The textural parameters of selected zeolite-based catalysts were listed in Table 2. It was found that catalysts Cu/Y (779.8 m²/g), Cu/13X (746.2 m²/g), and Cu'/13X (743.7 m²/g) exhibited distinctly higher surface area than other catalysts (< 500 m²/g), and the average pore volume of catalysts Cu/13X (0.3128 m³/g) and Cu'/13X (0.2446 m³/g) were slightly higher than that of Cu/Y (0.1920 m³/g). Based on the results of Tables 1 and 2, it was found that Cu/zeolites with relatively larger surface area and pore volume showed obviously higher catalytic performance for the conversion of 3-methyl-pyridine to niacin. It was ascribed to the positive effects for the diffusion and mass transfer of various molecules in the reaction system.

The chemical states of Cu/13X and Cu'/13X were also characterized by XPS analysis [Figure 2]. In the XPS pattern of Cu/13X, the peaks attributed to Cu2p_{3/2} at 934.8 eV and Cu2p_{1/2} at 954.7 eV were observed, corresponding to Cu²⁺ states^[28]. In the XPS pattern of Cu'/13X, peaks (Cu2p_{3/2} at 933.0 eV and Cu2p_{1/2} at 953.4 eV) for both Cu⁺ states and Cu²⁺ states were observed. This was ascribed to the partial conversion of Cu(I) to Cu(II) cations during the catalyst preparation process. Therefore, compared to catalyst Cu'/13X, the higher catalytic activity and selectivity to niacin displayed by Cu/13X was ascribed to its higher content of Cu(II) cations, based on the above reaction and characterization results. It also suggested the efficiency of Cu(II) cations as catalytic active sites in the conversion of 3-methyl-pyridine to niacin.

Based on the above results, the main steps in the reaction were shown in Scheme 2, including the first oxidation of 3-methyl-pyridine to nicotiny alcohol by hydrogen peroxide [Scheme 2A] and then the

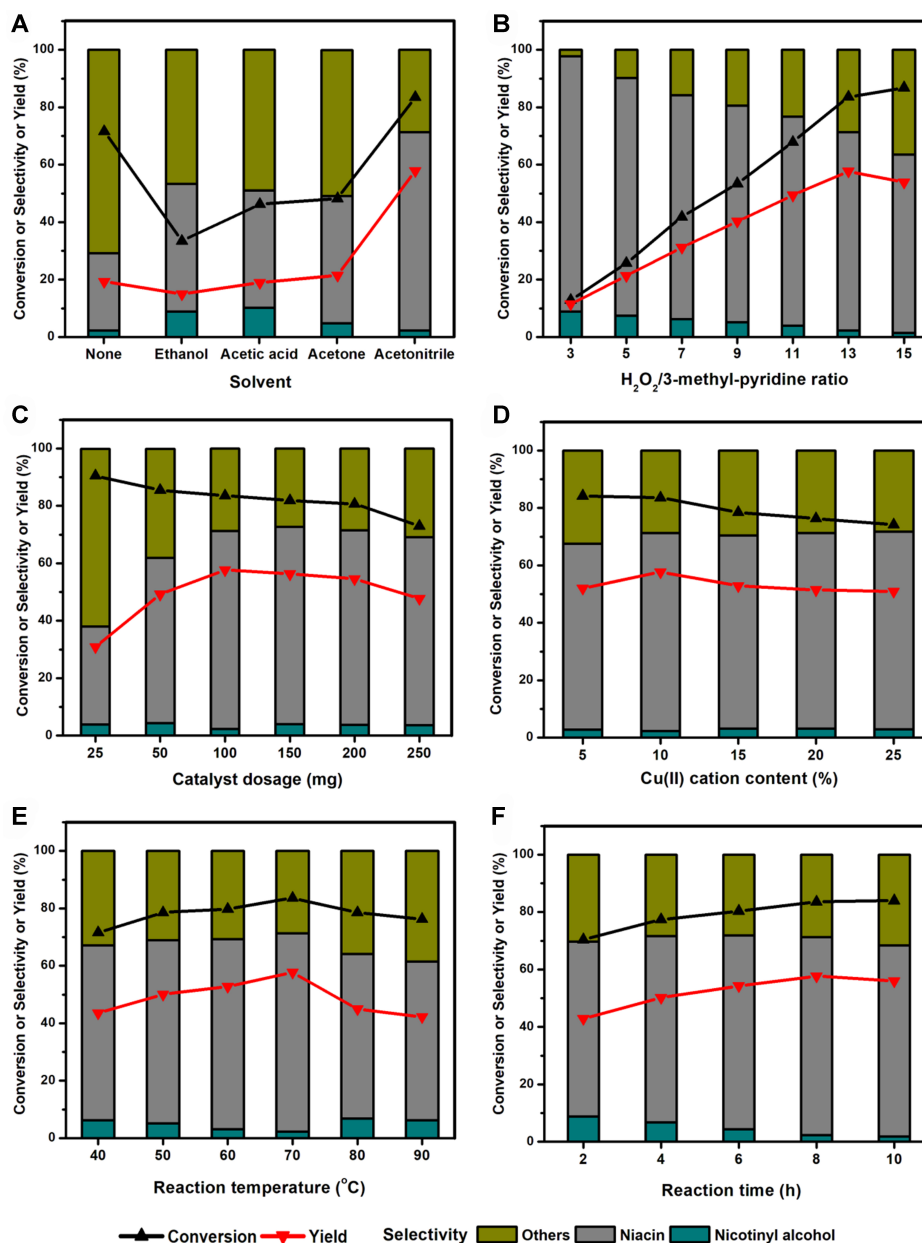


Figure 3. Effects of (A) solvent, (B) H₂O₂/3-methyl-pyridine ratio, (C) catalyst dosage, (D) metal content, (E) reaction temperature and (F) time.

oxidation of nicotiny alcohol to niacin by zeolite-based catalysts [Scheme 2B]. The excellent catalytic performance shown by Cu/13X for the synthesis of niacin was ascribed to the cooperative contribution of Cu(II) ions and zeolite support, where Cu²⁺ ions played an important role in activating H₂O₂ molecules while the zeolite stabilized various intermediate ions in the reaction system.

The effects of various parameters on the catalytic oxidation of 3-methyl-pyridine to niacin by using Cu/13X as a catalyst had been systematically studied, including the effects of solvent type, molar ratio of H₂O₂/3-methyl-pyridine, catalyst dosage, Cu(II) cation content of catalyst, reaction temperature, reaction time, and oxidant type, and the results were shown in Figure 3 and Table 3.

Table 3. Reaction results over 10%Cu/13X catalyst by using different oxidants^a

Oxidant	Conversion of 3-methyl-pyridine (mol%)	Selectivity (mol%)			Yield of niacin (%)
		Niacin	Nicotinyl alcohol	Others	
30% H_2O_2	83.6	69.0	2.3	28.7	57.7
50% H_2O_2	71.0	65.8	3.8	30.4	46.7
TBHP	33.7	58.8	20.8	20.4	19.8
NaClO	34.2	49.4	26.2	24.2	16.9
Air ^b	-	-	-	-	-
None	-	-	-	-	-

^aReaction conditions: 100 mg catalyst, 10 mL MeCN, 10.7 mmol 3-methyl-pyridine, 139.1 mmol H_2O_2 (or TBHP) or 278.2 mmol NaClO, 70 °C, 8h.

^bThe flow rate of air is 40 mL/min. TBHP: Tert-butyl hydroperoxide.

By using 10%Cu/13X as a catalyst, the effect of solvent type on the reaction was first explored [Figure 3A], including polar solvents ethanol, acetone, acetic acid, and acetonitrile. When no organic solvent was added into the reaction system, the reaction happened in the environment of water that was introduced by 30% H_2O_2 aqueous solution; although 71.5% 3-methyl-pyridine was converted, the yield of niacin was quite low (19.2%), and the by-product was the majority, including about 2.3% nicotinyl alcohol and 70.8% others. When using ethanol as a solvent, only 33.3% 3-methyl-pyridine was converted, and the selectivity for niacin was about 44.4%. When using acetone as a solvent, the conversion of 3-methyl-pyridine was increased to 48.1%, while a similar niacin selectivity (44.3%) with that in ethanol was obtained. When using acetic acid as a solvent, 46.1% 3-methyl-pyridine was converted, and the selectivity of niacin was about 40.8%. The highest niacin yield was achieved over 10%Cu/13X when acetonitrile was chosen as a solvent.

The effect of H_2O_2 /3-methyl-pyridine molar ratio on the reaction over 10%Cu/13X was shown in Figure 3B. With the increase of H_2O_2 /3-methyl-pyridine molar ratio from 3 to 13, the yield of niacin had increased distinctly from 11.5% to 57.7%, which corresponded to the sharply increased conversion of 3-methyl-pyridine from 12.9% to 86.8% and slightly decreased selectivity for niacin from 88.8% to 69.0%. Based on the product distribution data, a decrease in selectivity of niacin was accompanied by a gradual reduction in nicotinyl alcohol and an increase in other by-products. With the rise of H_2O_2 /3-methyl-pyridine molar ratio from 13 to 15, although the conversion of 3-methyl-pyridine had continuously increased from 83.6% to 86.8%, the yield of niacin had decreased from 57.7% to 53.9%. It was mainly ascribed to the sharply decreased selectivity of niacin from 69.0% to 62.1%.

Figure 3C had compared the effect of catalyst dosage on the reaction. It was found that with the increase of 10%Cu/13X catalyst dosage from 25 to 250 mg, the conversion had declined gradually from 90.5% to 73.0%, and the yield of niacin reached the maximum value when 100 mg catalyst was used. When the catalyst dosage of 10%Cu/13X increased from 25 to 100 mg, the yield of niacin grew gradually, which was led by the slightly decreased conversion from 90.5% to 83.6% and distinctly increased selectivity from 34.1% to 69.0%. If catalyst dosage was further increased from 100 to 250 mg, the yield showed a slight reduction, which was led by a distinct decline in conversion from 83.6% to 73.0% and a slight drop in selectivity from 69.0% to 65.4%. The phenomenon where the conversion of 3-methyl-pyridine decreased with increasing catalyst amount was ascribed to two main respects. First, the catalyst played the catalytic roles on both the forward and reverse reactions, which was assumed to be the primary reason when the catalyst dosage was relatively low. Second, partial decomposition of hydrogen peroxide induced by the elevated catalyst became the main reason when the catalyst dosage was relatively high.

By the same preparation process except different Cu(II) cation contents in theory, a series of Cu/13X catalysts had been prepared and applied in the reaction, and the results were shown in [Figure 3D](#). It was found that, as Cu(II) cation contents increased from 5% to 25%, the conversion had decreased slightly from 83.6% to 74.2%. First, this was attributed to the limited actual supporting amount of CuSO₄ over 13X zeolite; second, to the partial decomposition of hydrogen peroxide caused by the excessive Cu species over the catalyst. The highest yield of niacin was achieved over catalyst 10%Cu/13X.

[Figure 3E](#) had compared the effect of temperature on the reaction, which was positive when the temperature was lower than 70 °C but negative when higher than 70 °C. The phenomenon where the conversion of 3-methyl-pyridine decreases with increasing reaction temperature from 70 to 90 °C was mainly ascribed to the accelerated decomposition of hydrogen peroxide induced by the increased temperature. For example, the yield of niacin decreased greatly to 42.2% under a reaction temperature of 90 °C, corresponding to 76.3% conversion and 55.3% selectivity. The yield of niacin reached the maximum value of 57.7% under 70 °C, which was determined to be the optional reaction temperature.

[Figure 3F](#) demonstrated the effect of time on the reaction. As the reaction time extended from 2 to 8 h, both the conversion and selectivity improved gradually, corresponding to the yield rise from 42.9% to 57.7%. When the time was continuously prolonged to 10 h, it was found that the conversion had maintained at about 84%, but the by-products had increased distinctly, and the yield of niacin showed a slight decrease trend to 56%. It was probably due to the nearly complete consumption of H₂O₂ in 8 h, and the consequent reaction had accelerated the formation of by-products.

The effect of oxidant type on the reaction was shown in [Table 3](#). It was found that the yield of niacin had obviously decreased when 30% H₂O₂ was substituted by 50% H₂O₂ under the same reaction condition, mainly due to the obvious decrease in conversion and selectivity. TBHP and NaClO were unsuitable oxidants for the selective oxidation of 3-methyl-pyridine, and the yield of niacin was lower than 20%. When air was introduced into the reaction system as an oxidant, the reaction did not occur, consistent with the result that no oxidant was used, implying the ineffectiveness of air and the necessity of 30% H₂O₂ as an oxidant.

Based on the above results and demonstration, obvious advantages were displayed by Cu-based 13X zeolite catalysts in the liquid phase synthesis of niacin from 3-methyl-pyridine and hydrogen peroxide under mild reaction conditions compared with the reported work^[13], including simple and low cost of catalyst preparation processes, low concentration of hydrogen peroxide, high yield of niacin, and more [[Supplementary Table 1](#)]. It provided a green and optional route for the synthesis of niacin.

CONCLUSIONS

The Cu/13X zeolite catalyst has been prepared and applied in the selective oxidation of 3-methyl-pyridine and 30% H₂O₂ to synthesize niacin under mild conditions, demonstrating highly efficient catalysis activity and selectivity. This is mainly ascribed to the highly dispersed Cu(II) ions and their co-contribution with the zeolite support. The optimal reaction conditions indicate that this is a green reaction process for the synthesis of niacin with potential applications.

DECLARATIONS

Authors' contributions

Carried out the experiments, analyzed the data, and wrote the draft manuscript: Liu Z, Shuai J
Analyzed the data: Xu W, Lu X

Provided helpful discussion: Xia Q

Directed and supervised the project, analyzed the data, and wrote and revised the manuscript: Zhou D

Availability of data and materials

The data and materials supporting the findings of this study are available within the article and its [Supplementary Materials](#).

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Conflicts of interest

All authors declared that there are no conflicts of interest.

Ethical approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

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