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Preparation of Nicotinic Acid from Oxidation of 3-Picoline with Oxygen Under Catalysis of T(*o*-Cl)PPMn

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Abstract The oxidation of 3-picoline to nicotinic acid took place efficiently in an ethanol solution with O_2 as the oxidant under the catalysis of T(*o*-Cl)PPMn at 40—150 °C and 0.5—3.0 MPa oxygen pressure. The influences of temperature, oxygen pressure, reaction time, concentration of 3-picoline, concentration of sodium hydroxide, and concentration of T(*o*-Cl)PPMn catalyst, *etc.* on the production of nicotinic acid were investigated. The results show that T(*o*-Cl)PPMn presented excellent catalytic activity in the oxidation of 3-picoline to nicotinic acid and the yield of nicotinic acid varied greatly with the reaction temperature, oxygen pressure, T(*o*-Cl)PPMn concentration, *etc.*

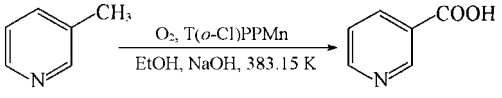
Keywords Nicotinic acid; 3-Picoline; Metalloporphyrin; Oxidation

1 Introduction

Nicotinic acid and its derivatives are very important fine chemicals and pharmic intermediates and can be widely used in the fields of food, feed, photoelectric materials, daily-use chemicals, and medical treatment[1]. Human cells require nicotinic acid for the synthesis of the co-enzymes used by dehydrogenase in tissue respiration. It can be used for the production of medicine, which can cure diseases such as coronary heart disease *etc.* and its deficiency cause pellagra[2,3]. It is estimated that the world demand of nicotinic acid and its derivatives is about 40000 tons every year.

The industrial production of nicotinic acid is mainly from ammoxidation of 3-picoline or the oxidation of 2-methyl-5-ethylpyridine or 3-picoline with nitric acid under high temperature and pressure[4,5]. It is reported that the yield of nicotinic acid can achieve 58.9% from the gas phase oxidation of 3-picoline with oxygen catalyzed by $Cr_{0.5}Al_{0.5}VO_4$ at 330 °C[6]. Electrochemical method for oxidation of 3-picoline to nicotinic acid with a yield of 70% was also described[7]. However, most of the above processes required high temperature and pressure or produced by-products, which contaminated the environment and increased the cost of production.

Metalloporphyrins as the mimic enzyme catalysts, which are consistent with our modern requirement of "green chemistry", have been widely studied in the recent years. T(*o*-Cl)PPMn is one of the metalloporphyrin catalysts that has good catalyzing activity[8—10]. However, most of the previous researches focused on the selective oxidation of alkane or aromatic alkane to get alcohol, aldehyde, and acid with molecular oxygen as oxidant under the catalysis of metalloporphyrins. Oxidation of the heterocyclic compounds with oxygen under the catalysis of metalloporphyrins was scarcely described. Our laboratory used oxygen to oxidize 3-picoline dissolved in ethanol in alkaline environment to prepare the nicotinic acid catalyzed by T(*o*-Cl)PPMn at 40—150 °C and 0.5—3.0 MPa oxygen pressure, which has a good yield(Scheme 1).



Scheme 1 Oxidation of 3-picoline to get nicotinic acid with oxygen under the catalysis of T(*o*-Cl)PPMn

2 Experimental

2.1 Materials and Facilities

All reagents and materials were analytically pure and chromatogram pure. Pyrrole was redistilled before use. Others were used as received. HPLC(Japan Spectroscopic Co.) was used to analyze the reaction

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mixture. FTIR spectrometer(Thermo Nicolet Company, USA) was used to characterize the catalyst.

2.2 Preparation of T(*o*-Cl)PPMn Catalyst

Synthesis of T(*o*-Cl)PPMn catalyst was performed *via* reported methods with slight modifications[11,12]. Acetic acid(30 mL), acetic anhydride(10 mL), and chloroacetic acid(2 g) were mixed in a three-necked flask and heated up under magnetic agitation. When the circumfluence appeared in the mixture, nitrobenzene(10 mL), pyrrole(20 mmol), and 2-chlorobenzaldehyde(20 mmol) were added to the mixture from the dropping funnel in 10 min. The reaction mixture was continuously heated to circumfluence and agitated for 1 h. After the completion of the reaction, when the temperature of the mixture decreased, methanol(30 mL) was added. The mixture was filtrated and the blue solid was acquired after it was placed quietly at room temperature for 24 h. The desired compound T(*o*-Cl)PP was separated from the blue solid mixture by column chromatography. The T(*o*-Cl)PP(0.2 mmol) and manganese acetate(1.0 mmol) were dissolved in DMF(5 mL). The mixture was heated to circumfluence and agitated. The reaction was monitored by TLC; it took 15 min for the reaction to end. The desired compound T(*o*-Cl)PPMn was separated from the reaction mixture by column chromatography with chloroform as the elution solvent. The bottle green crystal T(*o*-Cl)PPMn could be acquired after the chloroform was evaporated and it was kept in a desiccator.

2.3 Characterization of Catalyst

The desired compound was characterized by ^{1}H NMR, mass spectroscopy, elemental analysis, and absorption spectroscopic techniques. The data are consistent with the literatures. The IR spectrum of the T(*o*-Cl)PPMn catalyst is shown in Fig.1.

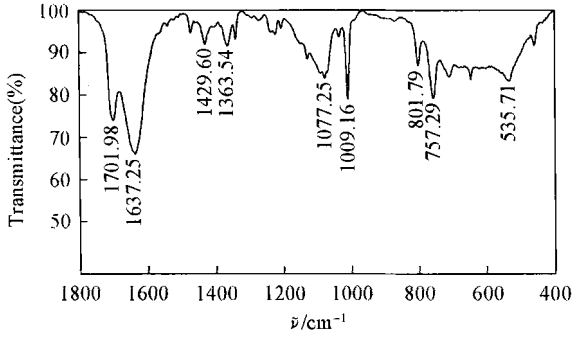

Fig.1 IR spectrum of T(*o*-Cl)PPMn catalyst

2.4 Oxidation of 3-Picoline to Nicotinic Acid by Oxygen Catalyzed by T(*o*-Cl)PPMn

Oxidation of 3-picoline with oxygen was carried out under the catalysis of T(*o*-Cl)PPMn in basic environment. The reaction was performed in an autoclave using ethanol as a solvent and stirred by magnetic force. After completion of the reaction, the autoclave was depressurized and 0.5 mL sample was taken from the contents and analyzed by HPLC after diluting the sample for 100 times in ethanol with toluene as the internal standard.

3 Results and Discussion

3.1 Effect of Reaction Temperature on the Production of Nicotinic Acid

The oxidation of 3-picoline to nicotinic acid is exothermic and high temperature is not favorable to the production of nicotinic acid. However, the reaction did not occur at a very low temperature. The reaction temperature was varied in different reaction mixtures for catalyzing the oxidation of 3-picoline to nicotinic acid, keeping other experimental conditions constant(Fig.2). From Fig.2, it can be seen that the yield of nicotinic acid increased as the reaction temperature increased from 40 to110 °C. The best temperature for the production of nicotinic acid is 110 °C. The reaction hardly occurred when the temperature was below 40 °C. However, the production of nicotinic acid decreased as the temperature was above 120 °C. The most probable reason to these observations is that there was more solid, which had been formed from ethanol and sodium hydroxide, in the reaction mixture as the reaction temperature increased. The solid reduced the solvent and deactivated the catalyst. Thus, the yield of nicotinic acid decreased when the reaction temperature became very high[13]. Rising temperature makes the cleavage of the C—H bond become easier

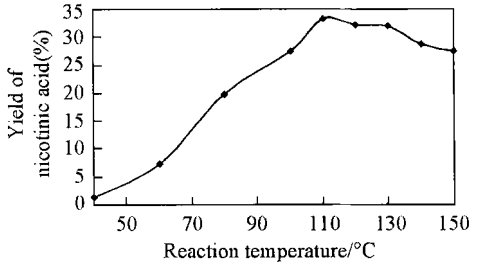

Fig.2 Effect of reaction temperature on the yield of nicotinic acid

Reaction conditions: 0.17 mol/L 3-picoline; 1.25 mol/L sodium hydroxide; oxygen pressure 1.5 MPa; 2×10^{-5} mol/L T(*o*-Cl)PPMn; reaction time 8 h.