

A New Reaction Route for the Synthesis of 5-Ethyl-2-methylpyridine

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Introduction

5-Ethyl-2-methylpyridine (MEP) is produced by liquid phase reaction of paraldehyde (para) at 200–300 °C and 12–13 MPa according to Montecatini-Edison process [1]. MEP is used as the starting material in the synthesis of nicotinic acid and nicotinamide. This study focuses on the definition of a new reaction route for MEP formation using acetaldehyde ammonia trimer (AAT) (Figure 1). AAT is a cyclic molecule that is characterized by the presence of three nitrogen atoms. The use of AAT allows an improvement in the reaction management due to direct insertion of nitrogen. Compared to conventional synthesis, the new route avoids addition of ammonia and enables savings in the downstream processes.

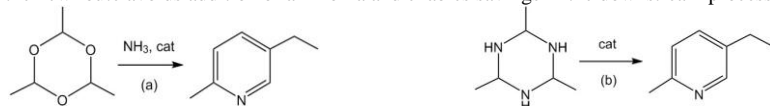


Figure 1. Reaction scheme of (a) para to MEP and (b) AAT to MEP

The aim of this work is to provide the first principle assessment of the reaction and to investigate the effect of different catalysts on MEP yield. The most important parameters for the reaction using AAT are defined and compared with the reaction of para. Finally, a first kinetic study is provided to explain the differences between the two reactions.

Materials and Methods

All experiments were performed in a 250 ml autoclave. The aqueous mixture of catalyst (100 ml) is charged into the reactor, which is then heated up to reaction temperature. Next, 100 ml of methanol solution containing AAT or para is fed using a HPLC pump [2]. The autoclave is kept at constant temperature and stirred for 2 h. The products are analyzed by GC and NMR. For the kinetic study, the reaction was monitored by *in-situ* Raman spectroscopy.

Results and Discussion

AAT reacts to form MEP using various ammonium salts as catalyst. To limit the acidity of catalytic solutions, salts are dissolved in an aqueous ammonia solution in 1:1 molar ratio. The yield is between 50–60 % and increases with decreasing pH of the catalytic solution (Table 1). To understand the role of catalyst, reaction was carried in the absence of ammonium source using acetic acid. The yield reached with acetic acid is close to ammonium acetate, indicating that the reaction goes through a similar mechanism. This confirms that the catalytic species is the acid (H⁺) and the nitrogen contained in trimer is fixed in the pyridine ring.

Table 1. Catalyst screening (Trimer solution 5%, trimer: catalyst (1:1) ratio, T= 200 °C)

Catalyst	NH ₄ HSO ₄	NH ₄ Cl	NH ₄ NO ₃	NH ₄ H ₂ PO ₄	NH ₄ F	NH ₄ OAc	AcOH
Yield[%]	49.3	53.6	55.8	56.4	56.8	58.9	58.7

Initial screening of parametric sensitivity made by experimental design methods revealed that the most important parameters are temperature, concentration of trimer and catalyst quantity. Experiments were performed using trimer or para and results are shown in Figure 2. Initial reactant concentration has a negative effect on the yield due to larger by-product formation. These by-products are mainly oligomers containing nitrogen. Temperature screening revealed an optimal temperature at 200 °C. Increasing the amount of catalyst linearly increases the yield until a threshold is reached. The results for trimer and para are almost identical for reactant concentration and temperature. However, the trend with different catalyst concentration is slightly different due to stoichiometric effect of ammonia in reaction mixture. The direct use of acetic acid as catalyst is possible, but more attention must be paid to the reaction conditions, since high yields can only be achieved in a limited pH range (Figure 2c).

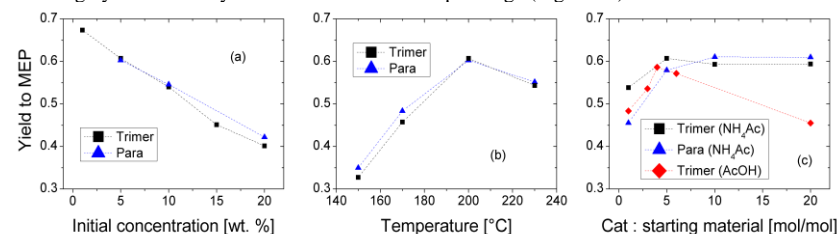


Figure 2. Effect of (a) AAT/para concentration, (b) temperature and (c) catalyst on yield

The greatest difference between the two systems is revealed by the kinetic investigation. Raman analysis revealed the time that is required to reach the completion of each reaction. Conversion of trimer to MEP is much faster, whereas para requires more than double the time to be completely consumed (Table 2).

Table 2. Time required for full conversion [s]

Initial conc. [wt. %]	2	5	10	20
Trimer	400	300	250	200
Para	1000	800	600	500

Significance

These results open the way to the definition of a new reaction scheme for a process producing MEP. The production can take place in two steps: An initial step consisting of formation of AAT from acetaldehyde and ammonia; and, secondly, a consecutive reaction of AAT to MEP in the absence of ammonia. Thanks to the faster reaction of trimer compared to para, the second reactor could be smaller than the conventionally used reactor in MEP production. Furthermore, significant savings in operation costs could be achieved by the different ammonia management, which allows for a reduction of compression costs for the recycle streams.

References

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