



## Zeolite catalysed synthesis of 5-ethyl-2-methylpyridine under high pressure

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### ABSTRACT

Simple and selective single-step synthesis of 5-ethyl-2-methylpyridine (EMP) under high pressure (auto-geneous pressure) conditions is achieved with high conversion and high selectivity over zeolites. The catalyst can be reused many times without significant loss of activity.

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### 1. Introduction

Pyridine bases are industrially important compounds. Pyridine, 2-picoline and 5-ethyl-2-methylpyridine (EMP) are in strong demand, whereas 3-picoline and 4-picoline have a limited market. All these bases can be produced from acetaldehyde. Industrially, large amounts of EMP are used as starting material for the production of nicotinic acid and its derivatives and 2-methyl-5-vinylpyridine (MVP), these chemical transformations involving the alkyl groups bound to the pyridine ring [1].

The condensation of acetaldehyde or paraldehyde with ammonia to form EMP has been described by a number of investigators [2–4] but low yields have been obtained due to the formation of pyridine derivatives having high boiling points and large amounts of tar. The tarry by-products are most likely the result of polymerization of acetaldehyde or its reaction with the substituted pyridines formed.

Later it is found that the excess of ammonia might increase the ratio of EMP to pyridine derivatives having high boiling points and tar. Various methods have been developed and reported for the synthesis of EMP such as paraldehyde and ammonia in the presence of ammonium salts as catalysts [5–7] and the continuous process using acetaldehyde and ammonia in the presence of ammonium acetate and ammonium salts of other organic acids, sodium

acetate, sodium carbonate, sodium fluoride and other metal halides as catalysts [8–10]. Frank and Seven have widely investigated this reaction and were able to obtain high yields of single products in certain instances by the use of an excess of aqueous ammonia. However, these investigators were able to obtain an improved yield of EMP by their method only when a derivative of acetaldehyde such as acetal or paraldehyde was employed and their yield under the same conditions using acetaldehyde was much lower (34%) [11]. All the processes for the production of EMP are carried out in the liquid phase under pressure with paraldehyde and ammonia in the presence of an ammonium salt as catalyst. This synthesis is essentially based on the studies carried out by Farbwerke Höchst [12] and Frank et al. [4]. Although the reaction has been widely studied [13,14], the yields were always low for instances if acetaldehyde is fed instead of paraldehyde [8–10] and if the reaction takes place in liquid ammonia [15] or in benzene [16]. The variations observed in the different plants are presumably due to the nature of the ammonium salt employed and to the technical solutions used in the different phases of the process. While in the patent literature the use of various salts as catalysts is reported, ammonium acetate and some fluorides particularly ammonium fluoride, difluorides are the most interesting catalysts [17,18]. These latter two show a catalytic activity even higher than that of ammonium acetate. However, in actual operation, they can cause corrosion.

Shimizu et al. [19] reported the aminocyclization of acetaldehyde and ammonia over modified zeolite catalysts. The main products were pyridine and picolines. The yield of pyridine was 68% over silylated ZSM-5 and 60% over Pb-ZSM-5. Kulkarni and co-workers [20–22] reported 61.5% yield of pyridine and 16.8% 3-picoline over W-ZSM-5 in the reaction of acetaldehyde, formaldehyde and ammonia under atmospheric pressure. In this paper, we

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report the formation of EMP using acetaldehyde and ammonia as reactants and zeolite as a catalyst under high pressure (autogeneous pressure) conditions.

However, most of the above methods are suffering from one or more of the following disadvantages such as long reaction times, vigorous reaction conditions, occurrence of side reactions, homogeneous catalysts, separation of catalyst and selectivity of product. Nevertheless, there is still a great demand for solid acid catalysts and selective synthesis of EMP under mild conditions.

The use of heterogeneous catalysts in various areas of the organic synthesis has now reached significant levels not only for the possibility to perform environmentally benign synthesis but also for the good yields frequently, accompanied by excellent selectivities that can be achieved. Zeolites are uniform microporous crystalline materials [23,24] and have been investigated extensively and used as solid catalysts in the field of petrochemistry. Zeolites are also known to catalyze various synthetic organic transformations much more effectively and selectively than Lewis acid catalysts. In view of this, we have developed a process for the synthesis of EMP with high selectivity and high conversion of acetaldehyde using zeolite catalysts under high pressure conditions.

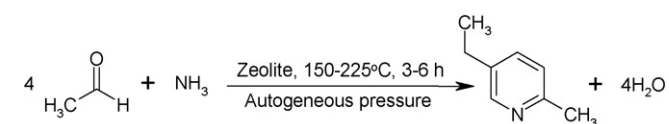
## 2. Experimental

All the reactions are carried out in a Parr autoclave (600 mL capacity, 20 cm height and 6.3 cm inner diameter) in the temperature range of 150–225 °C under constant stirring (90–100 rpm) at the respective autogeneous pressure. The reactants acetaldehyde (0.1 mol), 25% aqueous ammonia (0.5 mol), 2 g of catalyst and 200 mL of solvent (methanol) are loaded into an autoclave. At room temperature the autoclave is sealed and then the temperature is increased (150–225 °C) under stirring. Stirring is maintained for required time (3–6 h). After completion of the reaction, the autoclave is cooled to room temperature and the pressure is released slowly. The catalyst is filtered out and the solid is washed with methanol. The solvent is evaporated under reduced pressure. The aqueous layer is separated and the organic products were extracted with dichloromethane from the organic layer. The organic extract is dried over anhydrous sodium sulfate and solvent is evaporated under reduced pressure. The products are analyzed by GC using a 10% SE-30 column. The products are purified by column chromatography over silica gel (finer than 200 mesh) using 2–8% of ethyl acetate and hexane as eluent. All the products are characterized by <sup>1</sup>H NMR, mass and IR. HZSM-5 (Si/Al = 40, 150, 280), HY (Si/Al = 5.2) and Hβ (Si/Al = 15), H-mordenite (Si/Al = 12.5) are obtained from Sud-Chemie, India. HMCM-41 (Si/Al = 30) is synthesized in our laboratory using a reported procedure [25]. All the chemicals are obtained from Aldrich.

## 3. Results and discussion

We have synthesized 5-ethyl-2-methylpyridine using acetaldehyde and ammonia (25% aqueous) using zeolites as catalysts under autogeneous pressure at 150–225 °C (Scheme 1).

We have investigated the use of various zeolites, K10-montmorillonite, SiO<sub>2</sub> and SiO<sub>2</sub>-Al<sub>2</sub>O<sub>3</sub> as catalysts for the cyclization of acetaldehyde and aqueous ammonia (Table 1). H-



Scheme 1. Synthesis of EMP over zeolite catalysts under high pressure.

Table 1  
Variation of catalyst.<sup>a</sup>

S. No.	Catalyst	Conversion of acetaldehyde <sup>b</sup> (%)	Selectivity <sup>c</sup> (%)	
			EMP	Others <sup>d</sup>
1	H-beta	92.7	93.6	6.4
2	H-beta <sup>e</sup>	91.3	90.2	9.8
3	H-beta <sup>f</sup>	91.5	92.8	7.2
4	HX	81.8	46.5	53.5
5	HY	92.1	80.1	19.9
6	HZSM-5(40)	94.9	83.9	16.1
7	HZSM-5(150)	79.7	48.0	52.0
8	HZSM-5(280)	68.4	44.2	55.8
9	H-mordenite	93.6	79.6	20.4
10	HMCM-41	66.3	62.7	37.3
11	SiO <sub>2</sub> -Al <sub>2</sub> O <sub>3</sub>	93.0	77.4	22.6
12	SiO <sub>2</sub>	75.1	77.2	22.8
13	K10-montmorillonite	64.1	82.9	17.1
14	No catalyst	65.5	31.5	68.5

<sup>a</sup> Reaction temperature = 200 °C, reaction time = 6 h, mole ratio = 1:5 (35% aq. acetaldehyde:25% aq. ammonia), autogeneous pressure = 35 bar, solvent = methanol (200 mL).

<sup>b</sup> Isolated combined yields.

<sup>c</sup> Based on GC yields.

<sup>d</sup> Main by-products are imine, pyridine and picolines.

<sup>e</sup> Catalyst used for the second cycle.

<sup>f</sup> Catalyst used for the third cycle.

beta, HY, HZSM-5(40) and K10-montmorillonite show better results compared to other catalysts (S. No. 1, 5, 6 and 13). By considering the high conversion of acetaldehyde and selectivity to EMP, H-beta is found to be best catalyst. It is interesting to note that with the increase in the Si/Al ratio of HZSM-5 the conversion of acetaldehyde and selectivity to EMP are decreased (S. No. 6–8). This phenomenon can be explained by the decrease in Brønsted acid sites due to the increase in the Si/Al ratio [26]. In the absence of catalyst the conversion of acetaldehyde and selectivity to EMP are only 65% and 31%, respectively (S. No. 14). This observation clearly indicates the influence of a catalyst. Interestingly, if carried out in vapour phase conditions (400–500 °C), the reaction gives 2-methyl and 4-methylpyridines in varying amounts depending on experimental conditions; formation of EMP is observed in negligible amounts [27,28]. However, when the same reaction is carried out in an autoclave under high pressure, the system yields EMP with very high selectivity and yield. It indicates that the products formed are dependent on whether the reaction is carried out in an autoclave or in the fixed-bed flow system. In the presence of redox molecular sieves methanol can be transformed into formaldehyde. In our experiments, we have not used redox molecular sieves, so the formation of formaldehyde is negligible and methanol acts as a solvent. The solvent may also react with ammonia to a little extent depending on experimental conditions (e.g. when acetone is used as solvent). When tested for three cycles, the catalyst showed consistent activity (S. No. 2 and 3).

The reaction is carried out over H-beta in the temperature range of 100–225 °C. The conversion of acetaldehyde is increased from 50.4% to 98.9% with increase in reaction temperature from 100 to 225 °C (Table 2). Even though the conversion of acetaldehyde is high (98.9%) at 225 °C, the selectivity to EMP is very low (S. No. 4). From the above results, we can conclude that 200 °C is the optimum reaction temperature for highest conversion as well as highest selectivity to EMP. At higher temperature the selectivity to EMP is decreased as a result of dealkylation.

We found that the high selectivity to EMP can be achieved by maintaining a low concentration of acetaldehyde in the reaction mixture. In other words, an excess amount of ammonia is necessary for the reaction over that theoretically required. To establish the optimum conditions, we have studied the mole ratio of acetalde-

**Table 2**  
Effect of reaction temperature.<sup>a</sup>

S. No.	Temperature (°C)	Autogeneous pressure (bar)	Conversion of acetaldehyde <sup>b</sup> (%)	Selectivity <sup>c</sup> (%)	
				EMP	Others <sup>d</sup>
1	100	02	50.4	41.5	58.5
2	150	10	53.9	78.2	21.8
3	200	35	92.7	93.6	6.4
4	225	60	98.9	47.8	52.2

<sup>a</sup> Reaction time = 6 h, catalyst = H-beta, mole ratio = 1:5 (35% aq. acetaldehyde:25% aq. ammonia), solvent = methanol (200 mL).

<sup>b</sup> Isolated combined yields.

<sup>c</sup> Based on GC yields.

<sup>d</sup> Main by-products are imine, pyridine and picolines.

**Table 3**  
Effect of mole ratio of reactants.<sup>a</sup>

S. No.	Mole ratio (acetaldehyde:ammonia)	Conversion of acetaldehyde <sup>b</sup> (%)	Selectivity <sup>c</sup> (%)	
			EMP	Others <sup>d</sup>
1	1:0.25	99.8	16.3	83.7
2	1:0.5	90.6	46.4	53.6
3	1:1	99.5	54.5	45.5
4	1:3	95.1	62.4	37.6
5	1:5	92.7	93.6	6.4
6	1:7	90.2	46.7	53.3

<sup>a</sup> Reaction temperature = 200 °C, reaction time = 6 h, catalyst = H-beta, autogeneous pressure = 35 bar, solvent = methanol (200 mL).

<sup>b</sup> Isolated combined yields.

<sup>c</sup> Based on GC yields.

<sup>d</sup> Main by-products are imine, pyridine and picolines.

hyde to ammonia from 1:0.25 to 1:7. The increase in the amount of ammonia resulted in the increase in the selectivity to EMP from 16.3% to 92.7% (Table 3). It is observed that the selectivity to EMP at an acetaldehyde: ammonia mole ratio of 1:5 is very high (S. No. 2 and 5), whereas the selectivity to EMP is drastically dropped at a mole ratio of 1:7. The excess ammonia present in the reaction medium converts all acetaldehyde molecules to imine, which is the key intermediate for the formation of EMP. Moreover, the excess ammonia avoids the polymerization of acetaldehyde and formation of other products. It is interesting to note that the more excess ammonia has shown a negative effect (S. No. 5 and 6). The excess ammonia after the optimum level may cause over-dilution of the reaction mixture, reducing the active collisions between the reactant molecules.

The solvent effect on the reaction is found to be very significant. Among the solvents methanol, ethanol, acetonitrile, isopropanol and acetone the best yields are obtained with methanol (Table 4, S. No.1). Even though the conversion is high (99%) in the case of acetone, the selectivity to EMP is very poor (25.7%) (S. No. 5). This is due to the formation of various side products besides acetone. The

**Table 4**  
Effect of solvent.<sup>a</sup>

S. No.	Solvent	Autogeneous pressure (bar)	Conversion of acetaldehyde <sup>b</sup> (%)	Selectivity <sup>c</sup> (%)	
				EMP	Others <sup>d</sup>
1	Methanol	35	92.7	93.6	6.4
2	Ethanol	30	97.7	53.3	46.7
3	Acetonitrile	20	98.1	59.8	40.2
4	Isopropanol	28	85.5	48.0	52.0
5	Acetone	28	99.0	25.7	74.3

<sup>a</sup> Reaction temperature = 200 °C, reaction time = 6 h, catalyst = H-beta, mole ratio = 1:5 (35% aq. acetaldehyde:25% aq. ammonia), solvent = 200 mL.

<sup>b</sup> Isolated combined yields.

<sup>c</sup> Based on GC yields.

<sup>d</sup> Main by-products are imine, pyridine and picolines.

**Table 5**  
Effect of amount of catalyst.<sup>a</sup>

S. No.	Weight of catalyst (g)	Conversion of acetaldehyde <sup>b</sup> (%)	Selectivity <sup>c</sup> (%)	
			EMP	Others <sup>d</sup>
1	1	80.5	81.9	18.1
2	2	92.7	93.6	6.4
3	4	85.8	44.6	55.4
4	6	80.8	56.7	43.3

<sup>a</sup> Reaction temperature = 200 °C, reaction time = 6 h, mole ratio = 1:5 (35% aq. acetaldehyde:25% aq. ammonia), autogeneous pressure = 35 bar, solvent = methanol (200 mL).

<sup>b</sup> Isolated combined yields.

<sup>c</sup> Based on GC yields.

<sup>d</sup> Main by-products are imines, pyridine and picolines.

**Table 6**  
Variation of reaction time.<sup>a</sup>

S. No.	Reaction time (h)	Conversion of acetaldehyde <sup>b</sup> (%)	Selectivity <sup>c</sup> (%)	
			EMP	Others <sup>d</sup>
1	2	88.6	52.2	47.8
2	3	95.1	88.1	11.9
3	6	92.7	93.6	6.4
4	12	99.0	53.0	47.0

<sup>a</sup> Reaction temperature = 200 °C, mole ratio = 1:5 (35% aq. acetaldehyde:25% aq. ammonia), autogeneous pressure = 35 bar, solvent = methanol (200 mL), catalyst = H-beta (2 g).

<sup>b</sup> Isolated combined yields.

<sup>c</sup> Based on GC yields.

<sup>d</sup> Main by-products are imine, pyridine and picolines.

effect of amount of the catalyst has also been studied. The reaction has been carried out using 1, 2, 4 and 6 g of catalyst. Among all these, 2 g of catalyst has shown the best results (Table 5). The conversion of acetaldehyde and selectivity to EMP are decreased with the increase in the amount of catalyst (S. No. 3 and 4). It is observed that the excess amount (4 and 6 g) of catalyst is favoring the formation of side products.

In order to optimize the experimental conditions the reaction has been studied for various time periods (Table 6). At 2 h reaction time the conversion of acetaldehyde and selectivity to EMP are low, whereas at 6 h reaction time, maximum conversion and selectivity have been achieved (S. No. 3). At 12 h, the conversion is high and the selectivity to EMP is very low (S. No. 4).

#### 4. Conclusion

The present study demonstrates the development of the direct conversion of acetaldehyde and ammonia into 5-ethyl-2-methylpyridine under high pressure. Moreover it demonstrates the novelty of zeolite catalysts exercising a unique activity in the synthesis of EMP. The catalyst can be reused without any loss of activity. Inexpensive and environmentally friendly catalysts and commercially available reactants make our method valuable from a preparative point of view.

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#### References

- [1] A. Nenz, M. Pieroni, *Hydrocarbon Process.* 47 (1968) 139.
- [2] Chichibabin, *Bull. Soc. Chim.* 4 (1937) 1831.
- [3] Graf, *J. Prakt. Chem.* 150 (1938) 153.

- [4] R.L. Frank, J.R. Blegen, R.J. Dearborn, R.L. Myers, F.E. Woodward, J. Am. Chem. Soc. 68 (1946) 1368.
- [5] US Patent No. 2844583 (1958).
- [6] British Patent No. 749718 (1953).
- [7] British Patent No. 742268 (1953).
- [8] US Patent No. 2935513 (1960).
- [9] US Patent No. 3846435 (1974).
- [10] US Patent No. 2717897 (1955).
- [11] R.L. Frank, R.P. Seven, J. Am. Chem. Soc. 71 (1949) 2629.
- [12] F. Hochst, et al. German Patent 349184 (1922).
- [13] H. Maier-Bode, J. Altpeter, Das Pyridin und Seine Derivate, Verlag von Wilhelm Knapp, Halle, Saale, 1934.
- [14] E. Klingsberg, Pyridine and its Derivatives, Part One, Interscience, New York, 1960.
- [15] Japan Patent 6781 (1963).
- [16] Japan Patent 18387 (1963).
- [17] U.S. Patent 2,615,022 (1952).
- [18] U.S. Patent 2,745,833 (1956).
- [19] S. Shimizu, N. Abe, A. Iguchi, M. Dohba, H. Sato, K. Hirose, Micropor. Mesopor. Mater 21 (1998) 447.
- [20] R. Ramachandra Rao, S.J. Kulkarni, M. Subrahmanyam, A.V. Rama Rao, React. Kinet. Catal. Lett. 56 (2) (1995) 301.
- [21] S.J. Kulkarni, R. Ramachandra Rao, M. Subrahmanyam, A.V. Rama Rao, React. Kinet. Catal. Lett. 56 (2) (1995) 291.
- [22] A.V. Rama Rao, S.J. Kulkarni, R. Ramachandra Rao, M. Subrahmanyam, Appl. Catal. A 111 (1994) L101.
- [23] D.W. Breck, Zeolite Molecular Sieves, Wiley, New York, 1974.
- [24] A. Dyer, An Introduction to Zeolite Molecular Sieves, J. Wiley & Sons, Chichester, 1988.
- [25] A. Ortalm, J. Rathousky, G. Schulz-Ekloff, A. Zukal, Micropor. Mater. 6 (1996) 171.
- [26] N. Narender, P. Srinivasu, S.J. Kulkarni, K.V. Raghavan, J. Catal. 202 (2001) 430.
- [27] C.H. McAteer, E.F.V. Scriven, Heterocyclic Synthesis in Fine Chemical through Heterogeneous Catalysis, vol. 275, Wiley-VCH, Weinheim, 2001.
- [28] J.R. Calvin, R.D. Davis, C.H. McAteer, Appl. Catal. A 285 (2005) 1.