JOURNAL OF CATALYSIS 6, 26–34 (1966)

Catalytic Formation of Pyridine Bases from Crotonaldehyde and Ammonia

J. D. BUTLER

From the Department of Chemistry, University of Aston, Birmingham, England

Received September 23, 1965

Thermodynamic and kinetic data are presented for the formation of pyridine bases by reaction between crotonaldehyde and ammonia in the vapor phase at atmospheric pressure. It is shown that low yields of pyridines are obtained because thermal cracking of crotonaldehyde occurs preferentially. Results obtained with acidic and basic catalysts are reported. The presence of water vapor is shown to favor the formation of 5-ethyl-2-picoline. Routes to the various pyridines are discussed in the light of available evidence.

Introduction

The passage of aliphatic aldehydes and ammonia in the vapor phase over an alumina catalyst was shown by Chichibabin to produce low yields of pyridine bases (*1–4*). Reaction between crotonaldehyde and ammonia gave 3-ethyl-4-picoline, 5-ethyl-2-picoline, 2-picoline, 4-picoline, 2-*n*-propyl pyridine, 4-*n*-propylpyridine, and 2-propenylpyridine. A study by Frank and Seven (*5*) has shown that in the liquid phase, under pressure, 5-ethyl-2-picoline and 3-picoline are the major products. Mechanistically, the formation of these pyridines is believed to proceed through aldol or Michael additions (*6*) between two molecules of crotonaldehyde.

It is known that the presence of excess ammonium salts in liquid-phase reactions, and high pressures, are beneficial for the production of pyridines, but whether this is due to a thermodynamic or a catalytic effect has not been established. Surprisingly few examples of base-catalyzed reactions, excluding ammonia, have been reported (*7, 8*).

The object of this investigation was to compare the behavior of alumina impregnated with MoO_3, an acidic catalyst, with alumina impregnated with CaO, a basic catalyst, on the vapor-phase reaction between crotonaldehyde and ammonia. Aldol condensations are base-catalyzed in the liquid phase (*9*), proceeding by way of a carbanion mechanism, and since pyridines are formed by aldol condensations it was thought that a basic catalyst would also encourage such reactions in the vapor phase. It is shown in this paper that a basic contact catalyst can be used and that with anhydrous reactants very little resinification occurs on the catalyst bed at temperatures greater than 300°. It is also shown that in the vapor phase the presence of water vapor with the reactants exerts a profound effect on the reaction.

Preliminary experiments with basic catalysts prepared by impregnating alumina with potassium hydroxide showed that considerably more high-boiling nitrogenous-tar material was present in the reaction products than when alumina impregnated with calcium oxide was used. Furthermore, comparison of these catalysts indicated that the calcium oxide catalysts gave significantly better yields of pyridine bases and so the latter was selected for a detailed study. In the absence of a catalyst only tars were produced.

Experimental

Apparatus. A Pyrex glass converter 1-inch ID electrically heated furnace and temperature controller were similar to that described previously (*10*). A DCL micropump fitted with dual plungers was used for

pumping crotonaldehyde and, when required, aqueous ammonia, independently to the reactor.

Materials. Crotonaldehyde (Hopkin and Williams) was redistilled before use, b.p. 102° and was pure by gas-liquid chromatography. Anhydrous ammonia was obtained from an ICI cylinder of liquid ammonia. Aqueous ammonia was prepared by dilution of analytical grade 0.880 g/cc ammonia solution to give 15% ammonia by weight.

Catalysts. Granules, 1.5–3.0 mm, of ACTAL alumina (containing $\sim$ 3% SO_3) were treated with a current of hydrogen at 500° for 4 hr before impregnation.

(a) The Al_2O_3–MoO_3 catalyst was prepared by impregnating this alumina with a solution of ammonium molybdate, followed by heating to decompose the ammonium salt. Analysis gave 8.6% MoO_3 by weight.

(b) The Al_2O_3–CaO catalyst was obtained by impregnating alumina with a solution of calcium nitrate followed by heating in a current of air to decompose the nitrate. Analysis gave 19.7%. CaO by weight.

Procedure. Crotonaldehyde was pumped by the micropump to the top of the reactor at a rate of 35 ml/hr. Anhydrous gaseous ammonia was metered by a capillary flow meter and mixed with crotonaldehyde vapor above the catalyst bed. When aqueous ammonia was required it was pumped independently to the converter and vaporized before passing into the reactor. Contact times are quoted at 20° and are defined as the ratio of catalyst volume (ml) to the flow rate (ml/sec). They were varied by changing the amount of catalyst in the reactor.

Products from the converter were condensed in traps cooled by ice water and acetone–solid CO_2 mixtures. At the end of a run (each run was of about 1.5 molar scale based on crotonaldehyde fed) the condensate was acidified with hydrochloric acid to convert bases to water-soluble base-hydrochlorides. The lower aqueous layer was separated from the upper oily layer of neutral products. The aqueous layer was made strongly alkaline by addition of solid potassium hydroxide and the bases liberated were separated as an upper layer. This basic layer was dried over solid potassium hydroxide and distilled at 10 mm Hg. The fraction boiling between 30° and 102° was collected and analyzed. A viscous tar residue was left in the distillation flask.

Tricrotonylidene tetramine tetrahydrate (mol. wt. 296) was isolated by boiling an aqueous extract of the tar residue, m.p. 65.5°, molecular weight in benzene 299. Recrystallization from benzene gave the anhydrous material m.p. 102° ($C_{12}H_{24}N_4$ requires C, 64.3; H, 10.7; N, 25.0%. Found C, 64.04; H, 11.10; N, 24.80%).

Analysis. (a) Gas-liquid chromatography. Analyses were done on an Aerograph Auto-Prep model A-700 on a 5-ft × 3/16-inch column of HMDS treated Chromosorb P (60–80 mesh) impregnated with 20% SE 30. A column temperature of 80° and hydrogen carrier-gas flow rate of 60 ml/min was used. The column was calibrated with authentic samples of pyridines. This column would not separate 3-picoline, 4-picoline, and 2,4-lutidine, but infrared analysis of this fraction obtained from the chromatographed products showed that the peak was due to 4-picoline; neither 3-picoline nor 2,4-lutidine were present.

(b) Infrared spectroscopy. The products separated by gas-liquid chromatography and characterized by their retention times, were confirmed by infrared analysis using a Perkin-Elmer model 237 spectrophotometer.

(c) Chemical analysis of tricrotonylidene tetramine was carried out by Dr. Weiler and Dr. Strauss, Oxford.

Results and Discussion

Reactions with Anhydrous Ammonia

The influence of acidic and basic catalysts on the reaction as well as anhydrous and aqueous ammonia is summarized in Table 1. From the recovery of liquid products it can be seen that at least half of the crotonaldehyde consumed is converted into gaseous products. Crotonaldehyde is known (*11*) to crack thermally above 200° to give propene, carbon monoxide, ethylene, and methane

$$CH_3CH{=}CHCHO \rightarrow CH_3CH{=}CH_2 + CO$$

$$CH_3CH{=}CH_2 + H_2 \rightarrow CH_4 + C_2H_4$$

TABLE 1
CONVERSION OF CROTONALDEHYDE TO LIQUID NEUTRAL AND BASIC PRODUCTS AT 350°

Catalyst:	Al_2O_3–CaO	Al_2O_3–CaO	Al_2O_3–CaO	Al_2O_3–MoO_3	Al_2O_3–MoO_3[a]
Contact time (sec):	3.5	3.2	4.2	4.3	3.8
Dilution:	None	Steam	Benzene	None	Steam
	Wt (g) product per mole of crotonaldehyde consumed				
	Liquid Products				
Neutrals	10.0	0.8	—	18.5	5.6
Total bases	32.2	55.5	22.9	26.8	29.0
Pyridine bases	18.7	16.6	10.3	19.2	9.7
Tar residue	13.3	38.2	12.2	7.1	13.2
	Moles of pyridinic product × 100 per mole of crotonaldehyde consumed				
3-Ethyl-4-picoline	3.8	0.1	4.6	4.4	0.1
2-*n*-Propylpyridine	0.6	0.0	0.4	2.2	0.1
5-Ethyl-2-picoline	3.5	13.6	2.0	4.1	5.0
4-*n*-Propylpyridine	0.2	0.0	0.2	1.3	0.1
4-Picoline	5.4	1.0	0.9	3.9	2.2
2-Picoline	4.2	1.2	0.8	3.7	1.3

[a] Resinification on catalyst bed.

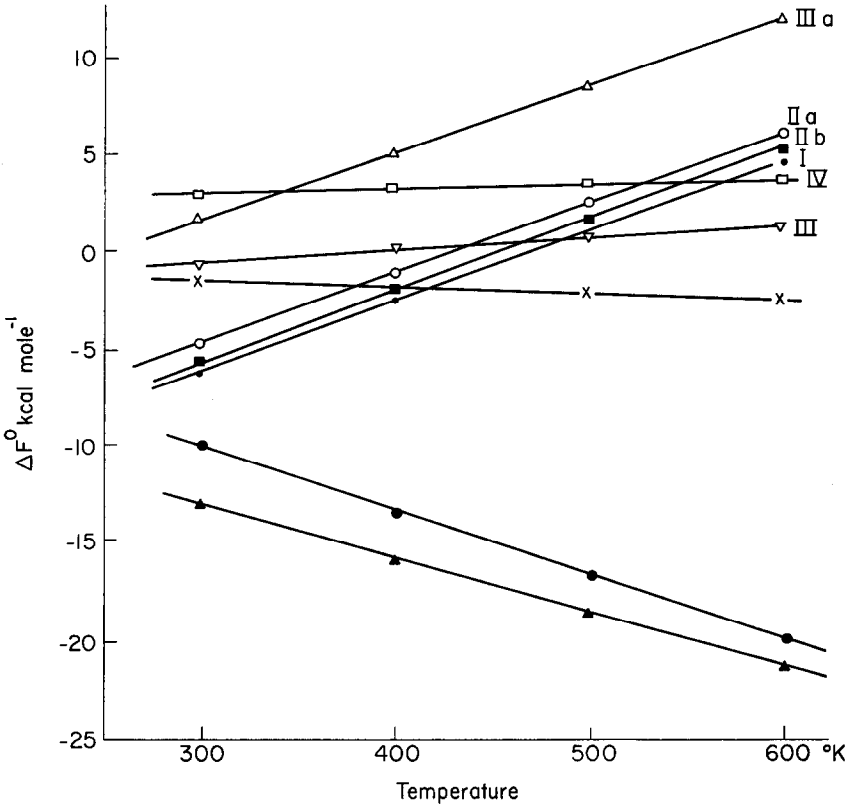


FIG. 1. Plots of $\triangle F^\circ$ as a function of temperature for the formation of intermediates (I), (IIa), (IIb), (IIIa), (III), (IV), and reactions

$CH_3CH{=}CHCHO + H_2O \rightarrow 2CH_3CHO$, ×;

$CH_3CH{=}CHCHO \rightarrow CH_3CH{=}CH_2 + CO$, ●;

$CH_3CHO \rightarrow CH_4 + CO$, ▲.

At 600°K $\Delta F°$ for the former process is ~ -20 kcal mole^{-1} (*12*) and evidence of the latter process was obtained because a high intensity $m/e = 16$ (attributable to CH_4^+) was found in the mass spectrum of the gaseous products when crotonaldehyde alone was passed over the basic catalyst at 350°. This feature of the reaction represents the greatest loss of crotonaldehyde which is not converted into pyridinic products.

In reality the decomposition of crotonaldehyde is probably more complex than outlined, since the formation of 2- and 4-picoline is generally assumed to be due to the decomposition of crotonaldehyde into acetaldehyde which gives rise to picolines by 3–2 synthesis from crotonaldehyde and acetaldehyde. The results given in Fig. 2 show that picolines are formed even at low contact times. The presence of tricrotonylidene tetramine was confirmed in the products at 250° and indicates that condensation occurs with the elimination of water at this temperature. This reaction is unavoidable since it will occur during the initial mixing of vapors above the catalyst bed. It can be shown (*12*), using group contribution methods, and available data (*13*) that the reaction

$$CH_3CH{=}CHCHO + H_2O \rightarrow 2CH_3CHO$$

is thermodynamically feasible (Fig. 1). The formation of acetaldehyde was confirmed; it was one of the products recovered from the aqueous condensate when crotonaldehyde and water vapor were passed over the basic catalyst at 350°. The concentration of acetaldehyde present in the reaction zone is probably lowered by the thermal decomposition which also occurs at operating temperatures (Fig. 1).

The formation of 2- and 4-picoline from crotonaldehyde and acetaldehyde as well as 5-ethyl-2-picoline and 3-ethyl-4-picoline from two molecules of crotonaldehyde can come about by different orientations of the reactants (*6*). Figure 2 shows that reaction favors the formation of pyridines with the

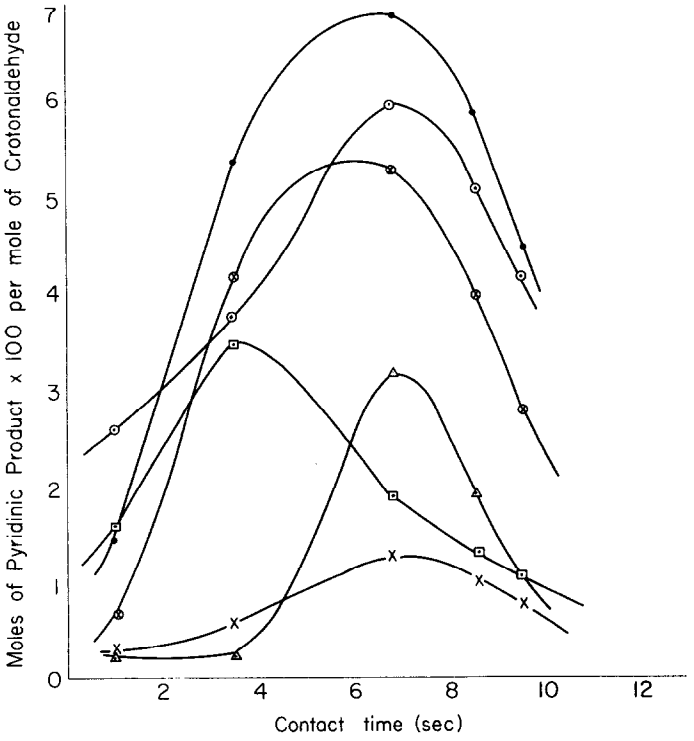
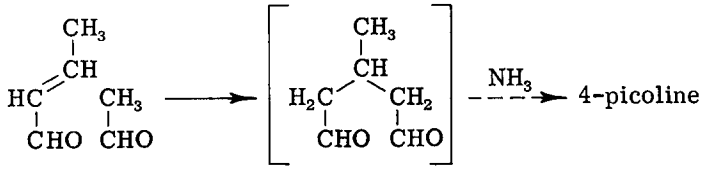


FIG. 2. Conversion of crotonaldehyde to pyridinic products over Al_2O_3–CaO at 350°C; mole ratio crotonaldehyde to ammonia 1:2; as a function of contact time: ⊗, 3-ethyl-4-picoline; △, 2-*n*-propylpyridine; ⊡, 5-ethyl-2-picoline; ×, 4-*n*-propylpyridine; •, 4-picoline; ⊙, 2-picoline.

methyl group in the 4-position. Yields of 4-picoline and 3-ethyl-4-picoline are significantly higher than 2-picoline and 5-ethyl-2-picoline.

Mechanism 1. The 4-methylpyridines can be formed by Michael additions across the olefinic double bond [reaction (1)]



(I) (1)

The route to 3-ethyl-4-picoline must involve dimerization between suitably orientated crotonaldehyde molecules so that the required substitution pattern is observed after cyclization. The absence of lutidines in the pyridinic products clearly shows that addition at the β position to the CHO groups of both molecules is unimportant in the formation of bases. Undoubtedly, addition docs occur at both β positions during reaction, but in this case cyclization can take place without inclusion of nitrogen in the ring and *o*-xylene is the ultimate product.

The possibility of isomerization of crotonaldehyde to give β,γ-unsaturated aldehyde

$$CH_3\ CH{=}CH{\cdot}CHO \rightleftharpoons CH_2{=}CH\ CH_2CHO \quad (2)$$

followed by Michael addition (3)

(3)

is also unlikely. β,γ-Unsaturated aldehydes are relatively difficult to synthesize and rearrange preferentially to the α,β-unsaturated form, particularly in the presence of basic reagents. The basic catalyst as well as ammonia will ensure that equilibrium lies far to the left.

The required substitution pattern in the final product can only be achieved in two ways:

Mechanism 2. (i) Dimerization by addition at the α position of one, to the β position of the other crotonaldehyde molecule, with proton migration to the β position: [reaction(4)].

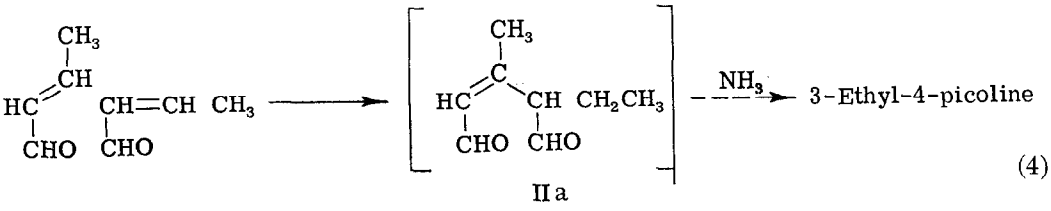
(ii) Dimerization by addition at the α position of one, to the β position of the other crotonaldehyde molecule, with proton migration to the α position [reaction (5)].

Chemically, route (ii) is more favorable because of the increased activity of the α position over the β position towards proton acceptance, as is usual in base-catalyzed Michael additions occurring through a carbanion mechanism.

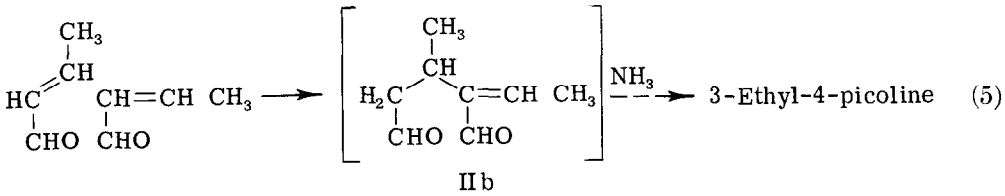
By analogy with the liquid-phase reaction the scheme for the formation of 5-ethyl-2-picoline probably involves the saturation of the double bond of crotonaldehyde by ammonia. Evidence is presented later that water vapor facilitates reaction (6). Figure 1 shows that once 3-aminobutanal has been formed $\Delta F°$ for the formation of the intermediate postulated (III), is only marginally positive.

Mechanism 3. Condensation of 3-aminobutanal [reaction (7)].

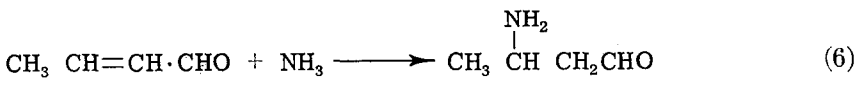
An alternative route for the first stage of the cyclization leading to 5-ethyl-2-picoline would require elimination of water between the aldehyde group of one 3-aminobutanal molecule and the amino group of the other molecule. An estimate of the $\Delta F°$ value of



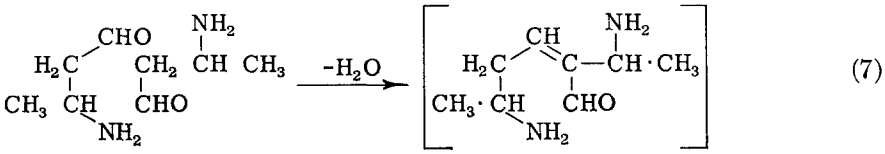
IIa (4)



IIb (5)



IIIa (6)



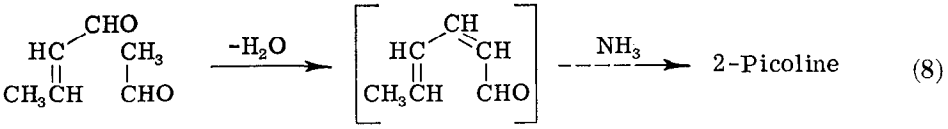
III (7)

this process gives a value of ~13 kcal/mole and this compares unfavorably with the route shown, where $\Delta F^\circ \sim 1$ kcal/mole.

It is also apparent that thermodynamically double-bond saturation by ammonia is less likely than formation of intermediates (I) and (IIa) or (IIb). Consequently, other things being equal, the yields of 5-ethyl-2-picoline would be expected to be low. Furthermore, the reaction becomes more improbable as the temperature is increased. The results given in Fig. 3 are consistent with this, in that the best yields of 5-ethyl-2-picoline are obtained at the lowest temperatures employed.

The formation of 2-picoline, on the other hand, does not show the same temperature dependence as 5-ethyl-2-picoline, Fig. 3. It appears, on this evidence that 3-aminobutanal is not important in the formation of 2-picoline. In this case aldol condensation between crotonaldehyde and acetaldehyde is thermodynamically more favorable than the saturation of the double bond by ammonia (Fig. 1).

Mechanism 4. Aldol condensation between crotonaldehyde and acetaldehyde (8):



IV (8)

It can be seen from Fig. 2 that the yields of pyridines are critically dependent upon the contact time. The distribution of prod-

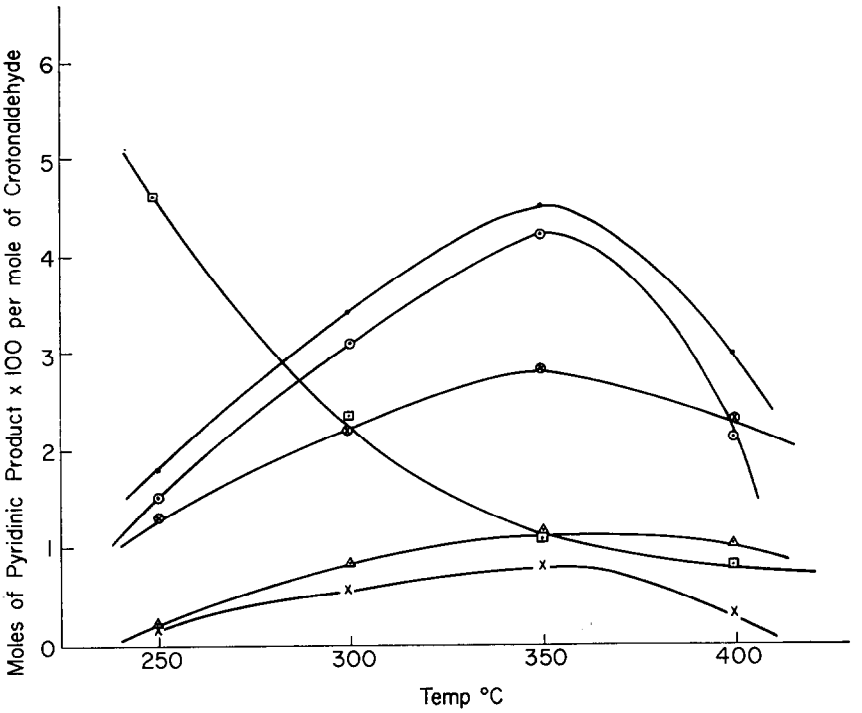


FIG. 3. Conversion of crotonaldehyde to pyridinic products over Al_2O_3–CaO; mole ratio crotonaldehyde to ammonia 1:2; contact time ~6 sec; as a function of temperature: ⊗, 3-ethyl-4-picoline; △, 2-*n*-propylpyridine; ⊡, 5-ethyl-2-picoline; ×, 4-*n*-propylpyridine; •, 4-picoline; ⊙, 2-picoline.

ucts is complex, particularly with reference to 5-ethyl-2-picoline and 2-*n*-propylpyridine. The shape of these curves suggests that either 5-ethyl-2-picoline is an intermediate which is isomerizing or degrading under reaction conditions or that the likelihood of its formation becomes progressively less as the contact time is increased.

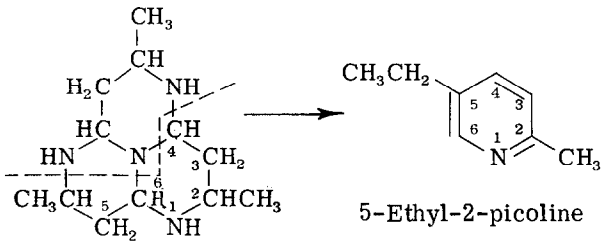
A sample of pure 5-ethyl-2-picoline was shown to be unchanged by passage through the reactor at 350° in the presence of anhydrous ammonia at a contact time of 6 sec. This establishes 5-ethyl-2-picoline as a stable product and leads to the conclusion that long contact times favor the cleavage of the crotonaldehyde molecule. This is reflected in the appearance of 2-*n*-propylpyridine from one molecule of crotonaldehyde and two molecules of acetaldehyde (2–2–1 synthesis).

Despite the overall improvement in conversion to basic products in the presence of the basic catalyst the pyridinic content is low and comparable to that obtained with the acidic catalyst. Both types of catalyst appear to influence the critical cyclization step to about the same extent. The basic catalyst prevented resinification on the catalyst bed, the high-boiling nitrogenous bases were easily desorbed from the alkaline catalyst surface and appeared in the condensate from the reactor. The basic catalyst also minimized the formation of liquid neutral products. These have been identified by Huntenburg (*14*) and beyond confirmation of acetonitrile, benzene, toluene, *o*- and *p*-xylene, benzonitrile, *o*- and *p*-toluonitrile have not been investigated further in this work.

Reactions with Aqueous Ammonia

When aqueous ammonia was fed to the reactor so that steam acted as a diluent 5-ethyl-2-picoline was the main pyridinic product, and it is evident that water vapor besides acting as a diluent changes the specificity of the reaction for the production

of pyridines. Dilution with benzene (mole ratio of crotonaldehyde to benzene 1:4) gave low yields of bases because there was less opportunity for aldehyde molecules to react with each other. Under these conditions the formation of 5-ethyl-2-picoline was suppressed and 3-ethyl-4-picoline was the favored product. This is understandable because the water vapor formed by the reaction will have less influence on the reaction when the inert diluent is present. For reactions carried out at 350° over Al_2O_3–CaO catalyst with aqueous ammonia and at 250° when anhydrous ammonia was used, where in both cases 5-ethyl-2-picoline was the main pyridinic product, it was possible to isolate tricrotonylidene tetramine from the tar residue remaining after distillation at 10 mm Hg. Attempts to isolate this compound from the tar residues of the other experiments carried out with anhydrous reactants at 350° were unsuccessful. The fact that tricrotonylidene tetramine could be isolated when 5-ethyl-2-picoline was the major product shows that significant amounts of tricrotonylidene tetramine are associated with the highest yields of 5-ethyl-2-picoline.



Tricrotonylidene tetramine

5-Ethyl-2-picoline

The structure and properties of tricrotonylidene tetramine have been studied by Delépine (*15*). Reaction between crotonaldehyde and ammonia to give tricrotonylidene tetramine was shown to occur by addition of ammonia across the olefinic double bond. Comparing the results given in Table 1 and Figs. 2 and 3 it appears that water vapor facilitates the latter process so that tricrotonylidene tetramine and 5-ethyl-2-picoline are the main products. It is evident that once ammonia has saturated the double bond to give 3-aminobutanal (IIIa), either two or three molecules can participate in condensation reactions to give 5-ethyl-2-picoline or tricrotonylidene tetramine, respectively.

Besides 5-ethyl-2-picoline formation by condensation of two molecules of 3-aminobutanal, it is also possible that this pyridine is formed from tricrotonylidene tetramine which is behaving as an intermediate. Delépine has shown that on heating tricrotonylidene tetramine above 160° ammonia is lost and 10% yields of 5-ethyl-2-picoline are obtained. Presumably, rupture occurs at the nitrogen–carbon bonds and the resulting fragment cyclizes to give the pyridine

Acknowledgments

We are indebted to Dr. M. Williams for the analyses of the catalyst samples, to Dr. R. H. Perett and Dr. A. V. Golton for gas chromatographic and infrared spectrophotometric analyses, and to Dr. A. W. P. Jarvie for helpful discussions. We also gratefully acknowledge the samples of pure pyridines given by Midland Tar Distillers Co., Ltd.

References

1. Chichibabin, A. E., and Oparina, M. P., *J. Prakt. Chem.* **107**, 145 (1924).
2. Chichibabin, A. E., *Bull. Soc. Chim. France* **3**, 762 (1936).
3. Chichibabin, A. E., *Bull. Soc. Chim. France* **4**, 1826 (1937).
4. Chichibabin, A. E., *Bull. Soc. Chim. France* **4**, 1831 (1937).
5. Frank, R. L., and Seven, R. P., *J. Am. Chem. Soc.* **71**, 2629 (1949).
6. Brody, F., and Ruby, P. R., *in* "Pyridine and Derivatives" (E. Klinsberg, ed.), Part 1, Chap. 2. Interscience, New York, 1960.

7. HANCOX, N. C., *Australian J. Chem.* **6**, 143 (1953).
8. STRAIN, H. H., *J. Am. Chem. Soc.* **54**, 1221 (1932).
9. BELL, R. P., *J. Chem. Soc.*, p. 1637 (1937).
10. BUTLER, J. D., AND WESTON, B. G., *J. Catalysis* **2**, 8 (1963).
11. HUGUENY, C., DE MOURGUES, L., TRAMBOUZE, Y., AND PRETTRE, M., *Bull. Soc. Chim. France* **2**, 497 (1965).
12. JANZ, G. J., "Estimation of Thermodynamic Properties of Organic Compounds." Academic Press, New York, 1958.
13. KOBE, K. A., AND CRAWFORD, H. R., *Petroleum Refiner* **37**, 125 (1958).
14. HUNTENBURG, W., *J. Prakt. Chem.* **145**, 23 (1936).
15. DELÉPINE, M., *Compt. Rend.* **216**, 785 (1943).