

## SOME REACTIONS OF PYRIDINIUM YLIDS (1)

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Kröhnke (2) has reported that piperidine-catalyzed condensation of 1-methylpyridinium bromide with benzaldehyde in ethanol at reflux occurs at the 1-methyl group to give 1-(2-hydroxy-2-phenylethyl)pyridinium bromide in greater than 80% yield. The reaction proceeds via N-ylid A. The specificity of this reaction is interesting in light of the fact that N-ylid B, which has been invoked as an intermediate in studies (3) of base-catalyzed deuterium exchange of the ring  $\alpha$ -protons of 1-methylpyridinium salts, forms considerably faster than N-ylid A (Table I) under the conditions of the Kröhnke reaction.

TABLE I

Deuterium Exchange Studies with 1-Methylpyridinium Iodide

Solvent	Substrate Conc.	Base	Temp.	Protons	% Exchange <sup>a</sup>	Time, min.
CH <sub>3</sub> CH <sub>2</sub> OD	0.31 <u>M</u>	0.19 <u>M</u> piperidine	78°	ring $\alpha$	44	6.5
				methyl	51	169
CH <sub>3</sub> OD	0.66 <u>M</u>	1.0 <u>M</u> piperidine	ca. 23°	ring $\alpha$	50	1,260
				methyl	≤3	11,500
CH <sub>3</sub> OD	0.7 <u>M</u>	0.08 <u>M</u> NaOCH <sub>3</sub>	35°	ring $\alpha$	50	4.4
				methyl	48	1,240

<sup>a</sup> % Exchange relative to exchange at infinite time, determined by integration over the various proton resonances. The integral of the N-methyl resonance was corrected for overlap with the solvent C<sup>13</sup>-H satellite.

We have studied the condensation of 1-methylpyridinium iodide with benzaldehyde in some detail. Several processes are involved in this condensation. The major features of the reaction scheme are summarized in Figure 1. Our reaction conditions consisted of 0.19 M piperidine, 1.01 M benzaldehyde, and

0.31 M 1-methylpyridinium iodide in ethanol at 78°. The rate constants are pseudo first-order rate constants for reactions of the pyridinium species at fixed concentrations of piperidine and benzaldehyde. From failure to detect by NMR the presence of N-ylids A and B in the basic solutions during the exchange studies, it follows that  $k_1 \gg k_{-1}$  and  $k_2 \gg k_{-2}$ . That  $k_2 > k_1$  is known from the deuterium exchange studies.

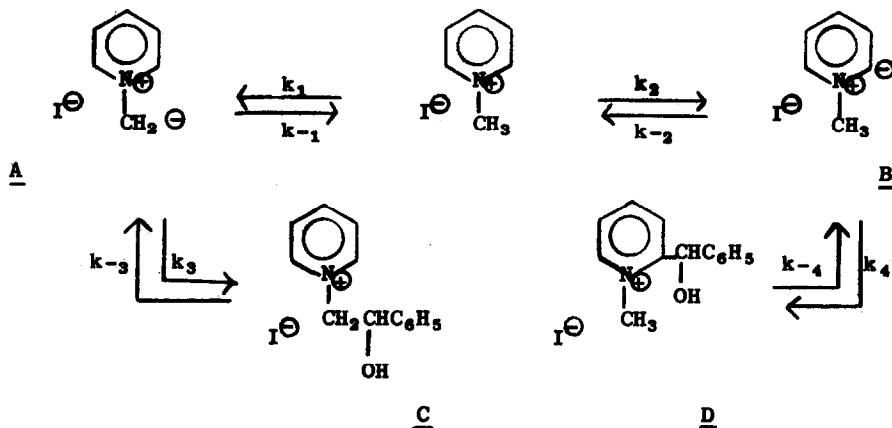


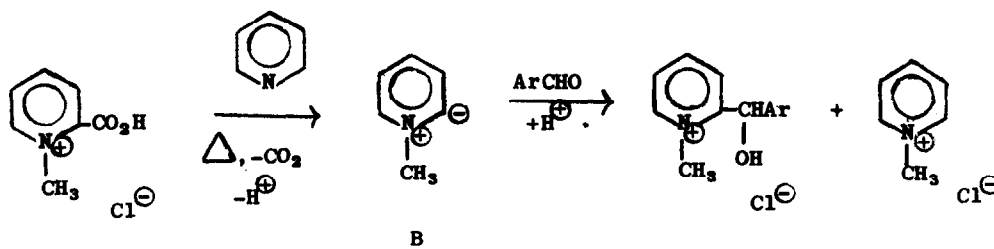
Fig. 1

The effective rate of cleavage of C must be small relative to the rate of formation of C since C is formed in good yield; on this basis  $k_{-3}$  may be neglected relative to  $k_3$ . Under our reaction conditions the pseudo first-order rate constant,  $k_C = k_1 k_3 / (k_{-1} + k_3)$ , for formation of 1-(2-hydroxy-2-phenylethyl)pyridinium iodide, C, was found to be  $6 \times 10^{-6} \text{ sec.}^{-1}$  at 11% conversion. The product C (4), m.p. 256-258° dec., was positively identified by its infrared and NMR spectra and elemental analysis. Under the reaction conditions but with benzaldehyde omitted authentic 2-( $\alpha$ -hydroxybenzyl)-1-methylpyridinium iodide was found to cleave to methylpyridinium iodide with  $k_{-4} \approx 3 \times 10^{-6} \text{ sec.}^{-1}$ . During the course of the condensation reaction NMR analysis revealed no trace of D.

Since formation of C is faster than cleavage of D, the possibility is excluded that D is formed faster than C and is slowly converted through back reactions to C. Instead, C is formed faster than D, even though B is formed

faster than A. Therefore, the rate ratio of product formation to reprotonation is greater for ylid A than for ylid B. One of the contributing factors to the lower rate ratio for ylid B may be steric hindrance to condensation at the ring  $\alpha$ -position offered by the methyl group.

Under the proper conditions ylid B can be caused to condense with aromatic aldehydes. Decarboxylation of homarine hydrochloride at 114° in excess benzaldehyde (with no other solvent) was complete in 15-20 min., and a mixture of 83% 2-( $\alpha$ -hydroxybenzyl)-1-methylpyridinium chloride and 17% 1-methylpyridinium chloride was obtained in quantitative yield. The very large excess of benzaldehyde and the low concentration of proton sources allow trapping (5,6) of the intermediate ylid by benzaldehyde. Pyridine serves as a catalyst for the reaction by ionizing the carboxyl group, thus facilitating the decarboxylation. With one equivalent of pyridine the decarboxylation is complete within 1.5 hr. at 80°.



- Ia, Ar = C<sub>6</sub>H<sub>5</sub>  
 b, Ar = 4-CH<sub>3</sub>OC<sub>6</sub>H<sub>4</sub>  
 c, Ar = 3,4-Cl<sub>2</sub>C<sub>6</sub>H<sub>3</sub>  
 d, Ar = 2,4-Cl<sub>2</sub>C<sub>6</sub>H<sub>3</sub>  
 e, Ar = 4-O<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>

The reaction proceeds with other aldehydes (Table II). Independent synthesis and NMR spectra confirm the structure assignments. Nitrobenzene was used as solvent when solid aldehydes were employed. As expected, the yield of condensation product generally increases with the electrophilicity of the aldehyde employed (direct comparison of the yields requires correction for different reaction conditions). This new method for synthesis of 2-(aryl-hydroxymethyl)-1-methylpyridinium halides offers the advantages of simplicity, generality, and good yields.

TABLE II

Condensation of Ylid B with Aromatic Aldehydes, 2 hr. at 80°

ArCHO Ar	Mole ratio, Aldehyde/homarine·HCl <sup>a</sup>	Solvent	Product	% Yield <sup>e</sup>	Product m.p.
C <sub>6</sub> H <sub>5</sub>	14.7	-----	Ia <sup>c</sup>	84	171-172° dec.
4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>	12.5	-----	Ib <sup>d</sup>	32	-----
3,4-Cl <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	6.8	C <sub>6</sub> H <sub>5</sub> NO <sub>2</sub> <sup>b</sup>	Ic <sup>c</sup>	80	199-200° dec.
2,4-Cl <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	6.9	C <sub>6</sub> H <sub>5</sub> NO <sub>2</sub> <sup>b</sup>	Id <sup>c</sup>	90	195-196°
4-O <sub>2</sub> NC <sub>6</sub> H <sub>4</sub>	6.5	C <sub>6</sub> H <sub>5</sub> NO <sub>2</sub> <sup>b</sup>	Ie <sup>c</sup>	92	209-210° dec.

<sup>a</sup> 1 equiv. of pyridine based on homarine·HCl. <sup>b</sup> 30 ml. of C<sub>6</sub>H<sub>5</sub>NO<sub>2</sub> per 10 mmoles of homarine·HCl. <sup>c</sup> Reference 4. <sup>d</sup> Not isolated. <sup>e</sup> Determined by NMR integration over the N-CH<sub>3</sub> resonances. In each case the combined yield of pyridinium salts was quantitative.

#### References

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