

THE BASE CATALYZED RING-OPENING REACTION OF  
1-(N,N-DIMETHYL-CARBAMOYL)PYRIDINIUM CHLORIDE

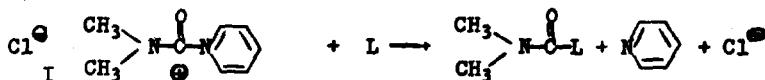
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1-(N,N-Dimethylcarbamoyl)pyridinium chloride, I, reacts directly with nucleophiles, L, over a wide pH range in water to yield pyridine and the dimethylcarbamoyl substitution product of L. This reaction is first order in I and first order in L. However, at pH values

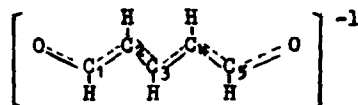


greater than 10, increasing amounts of an unstable intermediate, II, are formed. The rate of formation of II (which follows a pseudo first order rate law at constant pH to greater than 90% reaction), is identical to the rate of decomposition of I. The decomposition rate of II is at least 200 times smaller than the rate of formation of II, enabling the separation of the rate of formation of II from its rate of decomposition. The rate of formation and decomposition of II was followed spectrophotometrically at 4100 Å and 3400 Å. The following rate laws were obtained in carbonate and other buffers:

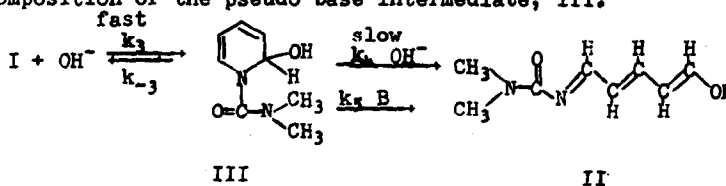
$$dII/dt = (I) [k_1(OH^-)^2 + k_2(OH^-)(CO_3^{2-})] \quad \text{pH 10-13} \quad (1)$$

$$-dII/dt = (II) \frac{(A + B(OH^-)^2)(OH^-)}{(1 + C(OH^-) + D(OH^-)^2)(1 + E(OH^-))} \text{pH 7-16.5} \quad (2)$$

The intermediate II decomposes by two major products paths, a and b, giving by path a which predominates at pH > 13.5 glutacondialdehyde and 1,1-dimethylurea, and giving by path b which predominates at pH 8-13 pyridine and dimethylamine. The course of decomposition of II was followed by proton magnetic resonance using a preparation of II, contaminated only with inorganic salts, dissolved in aqueous solutions of various pH. The methyl signals of II, dimethylamine, and 1,1-dimethylurea are well separated enabling product analysis: anionic II, -106 c.p.s.; neutral II, -104 c.p.s.; protonated dimethylamine, -89 c.p.s.; neutral dimethylamine, -62 c.p.s.; and 1,1-dimethylurea, -99 c.p.s. All signals are reported as displacements from t-butanol in water. The anionic glutacondialdehyde product,  $pK_a = 5.75^2$ , has a distinctive p.m.r. spectrum identical to that of authentic glutacondialdehyde, with a doublet at -440 c.p.s. (10 c.p.s. splitting) due to the aldehydic protons split by  $C_2H$  ( $C_4H$ ); a triplet at -382 c.p.s. (13 c.p.s. splitting) due to  $C_3H$  split by  $C_4H$  and  $C_2H$ ; and four signals at -278, -268, -264, and -254 c.p.s. due to  $C_2H$  ( $C_4H$ ) slit both by  $C_1H$  ( $C_5H$ ) and  $C_3H$ . The relative areas of these three groups of signals are 2:1:2.



The unstable intermediate II has a  $pK_0$  of -1.8 ( $\text{IIH}^+ \rightleftharpoons \text{II} + \text{H}^+$ ) and a  $pK_1$  of 12.0 ( $\text{II} \rightleftharpoons \text{II}^- + \text{H}^+$ ) as determined spectrophotometrically by extrapolating the absorbance of reacting solutions of various pH containing identical quantities of II to zero time.  $\text{IIH}^+$  has a  $\lambda_{\text{max}}$  at 3925 Å, II has a  $\lambda_{\text{max}}$  at 3350 Å, and  $\text{II}^-$  has a  $\lambda_{\text{max}}$  at 4110 Å. When II is placed in acid solutions in which the decomposition rate of II is greater by a factor of 100 or more than the decomposition rate<sup>1</sup> of I, I is not formed as would be expected if II were the pseudo base of I. The chemical and physical properties of II allow an assignment of a Schiff base structure. The kinetics of formation of II also support the assigned structure of II, since the pathway for formation of II requires two hydroxide ions, or one hydroxide ion and one general base group, consistent with a slow base catalyzed decomposition of the pseudo base intermediate, III.



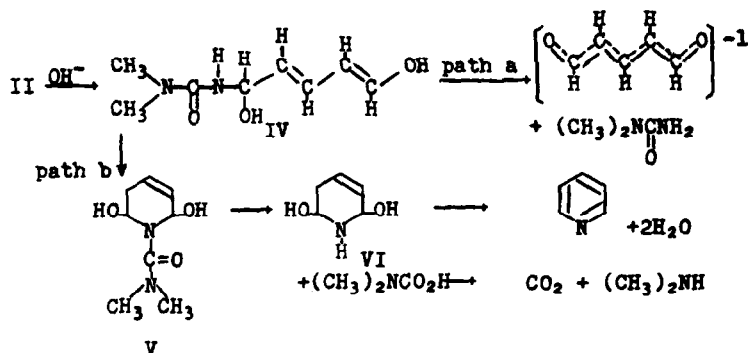
$$k_{\text{obs}} = \frac{k_3(\text{OH}^-)(k_4(\text{OH}^-) + k_5(\text{B}))}{k_{-3} + k_4(\text{OH}^-) + k_5(\text{B})} \sim \frac{k_3 k_4 (\text{OH}^-)^2 + k_3 k_5 (\text{OH}^-)(\text{B})}{k_{-3}}$$

The pH rate profile for the disappearance of II has a maximum at pH 11.8 and a minimum at pH 13.5 (Fig. 1). These

kinetics are consistent with a rate determining base catalyzed formation<sup>3</sup> of the carbinolamine derivative of the Schiff base, IV, over the pH range 7-11.8, a rate determining acid catalyzed decomposition of IV over the pH range 12-13.5, and a rate determining base catalyzed decomposition of IV at pH > 13.5. At constant ionic strength ( $\mu = 0.6$ ) and constant pH a 6-fold increase in carbonate buffer concentration gave identical rate constants to  $\pm 5\%$ , indicating no general catalysis. If II were decomposing to I at pH < 12 a general base reaction would be expected by the principal of microscopic reversibility. Such a reversal would lead to the observed pyridine and dimethylamine products since I decomposes to these products (at a rate greater than that for the decomposition of II over this pH range). The fact that the decomposition of II is not general catalyzed over this pH range indicates that II is not reverting to I.

The decomposition of II to glutacondialdehyde and 1,1-dimethylurea is an expected result. However, the decomposition of II to pyridine and dimethylamine by a pathway which bypasses I is an unexpected result. Therefore the formation of pyridine must arise from the carbinolamine IV, the formation of which is the slow step. It is suggested that IV decomposes at pH > 13.5 predominantly to glutacondialdehyde and 1,1-dimethylurea, and at lower pH the closed ring form of IV is formed (V) which hydrolyzes to dihydroxy-

tetrahydropyridine (VI) and dimethylcarbamic acid. These products would be expected to rapidly form the observed products. The formation of III and then I from V is not possible as this would be an unsymmetrical path from I to I or III to III.<sup>3</sup>



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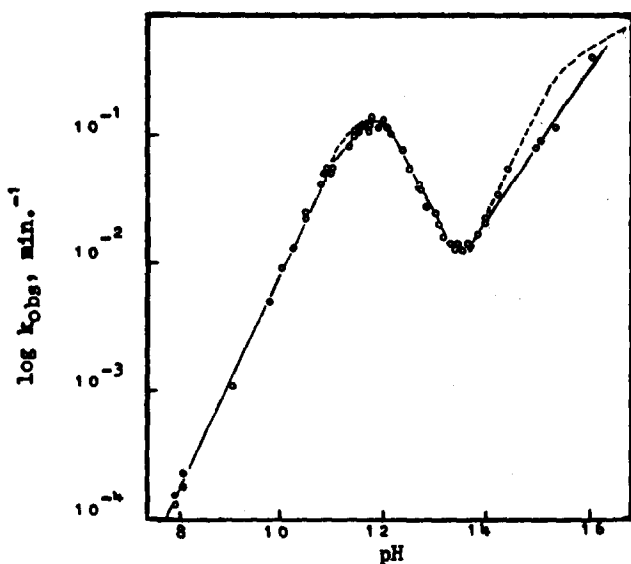


Figure 1 - Solid line, rate of decomposition of II. Dashed line, calculated rate.

$$k = \frac{82.6(1 + 10^{7.5} [\text{OH}^-]^2) [\text{OH}^-] / K_w}{(1 + 10^{2.4} [\text{OH}^-] + 10^{7.5} [\text{OH}^-]^2)(1 + K_1 / K_w [\text{OH}^-])}$$

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