

Inversion of Tertiary Amines in Aqueous Acid

By DONALD E. LEYDEN* and W. R. MORGAN

(Department of Chemistry, University of Georgia, Athens, Georgia 30601)

THE nitrogen inversion rate of amines in solution is usually too fast to be measured by n.m.r. techniques. Bottini and Roberts found that the nitrogen inversion of aziridines is in some cases sufficiently slow below -70° to be measured by n.m.r.¹ Saunders and Yamada introduced a technique which made the study of nitrogen inversion of certain tertiary amines in aqueous solution accessible by n.m.r.² The method is based upon the assumption that a protonated tertiary amine can not undergo inversion. By variation of the acidity of the aqueous solution of the amine, the fraction of the amine in solution which is protonated can be controlled. Because the rate of proton exchange is very fast, all amine molecules in the solution are rapidly converting between a protonated and deprotonated state. The overall effect is to reduce the averaged rate of inversion of each molecule to a value which can be measured using n.m.r.

Saunders and Yamada calculated the rate of inversion of *NN*-dibenzylmethylamine using the expression

$$1/\tau = k_{\text{inv}}[B]/([BH^+] + [B]) \quad (1)$$

where $[B]$ is the concentration of free amine, $[BH^+]$ is the concentration of the protonated amine, $1/\tau$ is the specific rate of nitrogen inversion, and k_{inv} is the inversion rate constant. The measurements are usually made in solutions which are sufficiently acidic that the approximation $[B] \ll [BH^+]$ is valid and equation 1 becomes

$$1/\tau = K_a k_{\text{inv}}/[H^+] \quad (2)$$

where K_a is the dissociation constant for the amine salt. According to Equation 2, a plot of $\log(1/\tau)$ against pH should yield a straight line with unit slope and an intercept of $\log(K_a k_{\text{inv}})$. For the case of three tertiary benzylamines including *NN*-dibenzylmethylamine, we have found that

the experimental results do not follow the predictions of equation 2 at low pH values.

In the case of *N*-benzyl-*N*-methylethanolamine, the plot of $\log(1/\tau)$ against pH is linear with a slope of unity above pH 3.5. Below pH 3.5 the slope approaches zero until at a pH of approximately 1.5 the slope again becomes positive. *NN*-Dibenzylmethylamine and *N*-benzyl-*N*-methyl-2-chloroethylamine show the same tendency. However, the pH range in which the latter compounds can be studied is more limited than in the case of *N*-benzyl-*N*-methylethanolamine.

We suggest that the explanation for this behaviour lies in the lifetime of the individual amine molecules capable of undergoing inversion. To be capable of inversion, the amine must be deprotonated and the hydrogen bond between the amine nitrogen atom and the hydrogen atom of a water molecule hydrogen-bonded to the amine must be broken. In the high-pH region, both the deprotonation and the breaking of the hydrogen bond are sufficiently rapid that the rate of nitrogen inversion is controlled by the equilibrium concentration of the free amine and the pH-dependence of the inversion follows equation 2. In the intermediate pH region, the rate of inversion is controlled by the rate of breaking of the amine-water hydrogen bond. The rate of this process is independent of pH, therefore the rate of inversion is independent of pH.³ In the lower pH region, the lifetime of the deprotonated, hydrogen-bonded amine depends upon the rate of reprotonation of the amine. This rate is directly proportional to the hydrogen ion concentration. In this region, the amine is frequently reprotonated before the hydrogen bond is broken. Therefore, the rate of inversion is pH-dependent but does not follow equation 2.

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¹ A. T. Bottini and J. D. Roberts, *J. Amer. Chem. Soc.*, 1956, **78**, 5126.

² M. Saunders and F. Yamada, *J. Amer. Chem. Soc.*, 1963, **85**, 1882.

³ E. Grunwald and E. K. Ralph, *tert.*, *J. Amer. Chem. Soc.*, 1967, **89**, 4405.