

molecule head-groups and counter-ions are employed.

Experimental. The measurements were made at 31°C on a Varian A-60 spectrometer, equipped with a Hewlett Packard 202A audio oscillator and a Hewlett Packard 5512A electronic counter. The chemicals used in the reported measurements were of reagent grade except for cetyl pyridinium chloride which was of *purum* grade (m.p. 79–81°C) obtained from Kebo AB, Stockholm. The required magnetic volume susceptibility values were calculated from the data compiled by Foëx¹².

Acknowledgements. Drs Erik Forslind and Gunnar Aniansson are thanked for their kind interest in this investigation and for helpful discussions. The cost of the NMR-apparatus has been defrayed by a generous grant from the *Knut and Alice Wallenberg foundation*.

- Schneider, W. G., Bernstein, H. J. and Pople, J. A. *Can. J. Chem.* **35** (1957) 1487.
- Sata, N. and Sasaki, H. *Proc. 2:nd Intern. Congr. of Surface Activity*, Butterworths, London 1957, p. 340.
- McBain, M. E. L. and Hutchinson, E. *Solubilization*, Academic Press, New York 1955.
- Shinoda, K. and Hutchinson, E. *J. Phys. Chem.* **66** (1962) 577.
- Cf.* Pople, J. A., Schneider, W. G. and Bernstein, H. J. *High-resolution Nuclear Magnetic Resonance*, McGraw-Hill, New York, Toronto, London 1959, p. 199.
- Ref.⁵ p. 408.
- Cf.* Mukerjee, P. *J. Phys. Chem.* **66** (1962) 1733.
- Strauss, U. P. and Layton, L. H. *J. Phys. Chem.* **57** (1953) 352.
- Smith, M. B. and Alexander, A. E. *Proc. 2:nd Intern. Congr. of Surface Activity*, Butterworths, London 1957, p. 349.
- Snyder, L. R. *J. Phys. Chem.* **67** (1963) 234.
- Bohon, R. L. and Clausen, W. F. *J. Am. Chem. Soc.* **73** (1951) 1571.
- Foëx, G. *Constantes sélectionnées. Diamagnétisme et paramagnétisme*. Masson et Cie., Paris 1957.

Received May 16, 1963.

Kinetics of the Alkaline Hydrolysis of 3-Acetoxy-quinuclidine Hydrochloride and Methiodide

BERTIL HANSEN* and ARNE FLORMARK

*Research Institute of National Defence,
Department 1, Sundbyberg, Sweden*

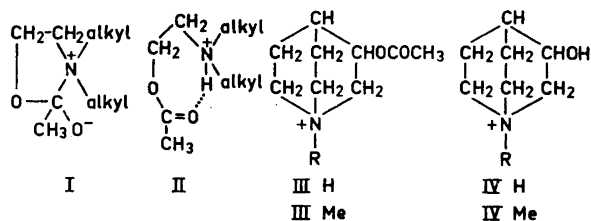
It has been observed that esters of the structure dialkyl-NR(CH₂)_nOCOCH₃, V, $n = 2$ or 3 , are 20–30 and 10 times, respectively, more rapidly hydrolyzed in alkaline solution when R=H than when R = alkyl¹. The pH-dependence of the reaction rate can be explained either as a first order reaction of the amine form of the ester where the rate determining step should be the formation of a cyclic intermediate, I, or a reaction with hydroxyl ions under catalysis by an intramolecular hydrogen bond, II. By varying the alkyl groups it was possible to show that the latter mechanism is the most likely one¹. In the present communication the rates of the alkaline hydrolysis of the hydrochloride, III H, and the methiodide, III Me, of 3-acetoxy-quinuclidine, are reported. In III H both intramolecular hydrogen bonding and the formation of an intermediate resembling I are impossible for steric reasons.

3-Quinuclidinol, prepared according to Sternbach's and Kaiser's method², was dissolved in ethanol and neutralized with HCl. The solvent was evaporated under vacuum at room temperature. The solid residue dissolved when refluxed for 1 h in acetyl chloride. After a further half hour the excess of acetyl chloride was evaporated. The residue, recrystallized from anhydrous ethanol/ligroin 3:7, was III H. (Found: C 52.4; H 7.70. Calc. for C₉H₁₆ClNO₂ (205.7): C 52.6; H 7.84).

3-Acetoxy-quinuclidine, prepared according to the method reported by Grob *et al.*³, was dissolved in acetone and excess methyl iodide was added. The crystals of III Me formed in 24 h were recrystallized from anhydrous ethanol/acetone 1:1. M.p. 165°. Grob *et al.*³ found m.p. 165–166°.

The kinetic experiments were carried out using a pH-stat and were run in 0.07 M

* Present address: AB Pharmacia, Uppsala, Sweden.



KClO₄ at 25°C¹. The reaction of III Me was followed until more than 50 % completion in runs at pH 10.30 and 10.60. Pseudo first-order rate constants, k_{obs} , were calculated according to Guggenheim's method and compared with k_{obs} for acetylcholine iodide determined at the same pH-values. Log k_{obs} for III Me was 0.27 ± 0.03 units lower than for acetylcholine. Lack of the substance III Me made it impossible to carry out the desirable measurements of the initial rate at lower pH. As the pH readings were somewhat uncertain, the k_{obs} -values were not used for calculation of the second order rate constant, k_2 . Instead, $\log k_2 = -0.10$ (k_2 in M⁻¹ sec⁻¹), for III Me was calculated from the above difference in $\log k_{\text{obs}}$ and $\log k_2 = 0.17$ for acetylcholine iodide in a solution of ionic strength $\mu = 0.07$ ¹.

The available amount of III H was sufficient for only one hydrolysis run. This was carried out as a measurement of the initial rate of NaOH consumption, first at pH 9.40 and then at 9.65 and 9.80. Both III H ($\text{p}K'_{\text{aIII}} = 9.10$) and the hydrolysis product IV H ($\text{p}K'_{\text{aIV}} = 9.90$) exist in an amine form and an ammonium form. Only the ammonium form of III H amounting to $1/(1 + K'_{\text{aIII}}/[\text{H}^+])$ of the total ester concentration was assumed to be hydrolyzed. Because of the protolytic equilibria of III H and IV H, one mole of hydrolyzed ester results not in one but in

$$1 + 1/(1 + K'_{\text{aIII}}/[\text{H}^+]) - 1/(1 + K'_{\text{aIV}}/[\text{H}^+])$$

equivalents of hydrogen ions. After correcting for these effects and the amount of ester consumed, the following values of $\log k_2$ for the reaction between the ammonium form of III H and hydroxyl ions were obtained: pH, $\log k_2$; 9.40, -0.04 ; 9.65, $+0.16$; 9.80, $+0.11$. Mean value $\log k_2 = 0.08 \pm 0.12$. The calculations were based on the concentration and not the activity of the hydroxyl ions¹.

The assumption that the amine form of III H is not responsible for the main part

of the hydrolysis is justified by the fact that $\log k_2$ is much higher than for ethyl acetate, $\log k_2 = -0.96$. The latter value may be considered an upper limit for $\log k_2$ of the amine form of III H¹.

The tertiary ester III H is hydrolyzed only about 50 per cent faster than the quaternary ester III Me. This difference is very small compared with the 20–30 times differences observed for the acyclic tertiary and quaternary ammonium compounds V. This shows that the catalytic effect of the ammonium group in V requires that this group must be able to come close to the carboxylic group.

The values $\text{p}K'_{\text{aIII}} = 9.10$ and $\text{p}K'_{\text{aIV}} = 9.90$ were determined from curves obtained by recording pH as a function of the amount of NaOH added to a solution of the hydrochlorides of III H and IV H. The value of $\text{p}K'_{\text{aIII}}$ is almost exactly the same as for the acyclic compound $\text{Et}_2\text{NHCH}_2\text{CH}_2\text{OCOCH}_3$, VI, $\text{p}K'_{\text{aVI}} = 9.09$ ¹. As the $\text{p}K'_{\text{a}}$ -values of quinuclidine, 10.58⁴, and of Et_2NEt , 10.53, are also almost identical it may be concluded that the effect of a 2-acetoxy group on $\text{p}K'_{\text{a}}$ of tertiary amine is the same in quinuclidine as in other amines¹.

It was possible to calculate from the titration curve of III H, allowing for a small NaOH-consumption due to hydrolysis, an equivalent weight of III H which within a few per cent agreed with the theoretical value.

- Hansen, B. *Acta Chem. Scand.* **16** (1962) 1927.
- Sternbach, L. H. and Kaiser, S. *J. Am. Chem. Soc.* **74** (1952) 2215.
- Grob, C. A., Kaiser, A. and Renk, E. *Helv. Chim. Acta* **40** (1957) 2170.
- Webster, B. M. *Rec. Trav. Chim.* **71** (1952) 1171.

Received May 15, 1963.