Kinetics of Base-Catalyzed Hydrolysis of Urea

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The hydrolysis of urea in both water and aqueous mineral acids has been thoroughly investigated[2]; in the latter solvent ureolysis is not directly subject to catalysis by hydrogen ion, and in both solvents the decomposition of urea produces cyanate and ammonium ions.

$$(NH_2)_2CO \longrightarrow CNO^- + NH_4^+ \qquad (1)$$

In acid solutions, cyanate is rapidly converted to ammonia and carbon dioxide.[3]

Although ureolysis in the presence of hydroxide ion has been the subject of several reports,[4] the kinetic laws pertaining to the reaction have not been unambiguously elucidated, nor the thermodynamic parameters determined. However, cyanate and ammonia are the products of the reaction, which, the data collected[4] suggest, does not proceed in a simple bimolecular process first order in each reactant. Because the ureolysis may have relevance as a model system for a study of the urease-catalyzed hydrolysis proceeding in this laboratory, it has been re-examined.

Experimental

Reagents. The urea, which was used without further purification, was of Analytical grade, as were the sodium hydroxide, hydrochloric acid, and sodium chloride employed. Nessler's reagent was prepared by the conventional procedure.

Method. Solutions of urea in sodium hydroxide of known molarity were prepared immediately before use. Aliquots (1 or 2 ml.) were sealed in Jena or Pyrex glass tubes which were then immersed in a constant (±0.03°) temperature bath at zero time and removed therefrom at measured intervals. Reaction was quenched by chilling the samples in iced water; they were then shattered under hydrochloric acid of such strength as to provide an acidic medium for the residual urea and the products of the ureolysis. After a time sufficient to allow conversion of any cyanate formed[4,5] to ammonium ion and carbon dioxide (during which period further hydrolysis of urea would be negligible[2,3]), the acid solution was diluted to a concentration convenient for treatment with Nessler's solution and subsequent measurement of the resulting color at 4100 Å. in a Unicam-SP600 spectrophotometer using cells of 1-cm. light path.

Results and Discussion

Pseudo-first-order rate constants were estimated graphically from the absorption measurements made as described above. Reaction was allowed to proceed in sodium hydroxide solutions ranging in concentration from 1 to 2 M for up to 70% of completion and no deviations from linearity were discerned in the pseudo-first-order plots. Re-formation of urea from its decomposition products in strong base was not found in this work nor by Warner.[4] A fourfold increase in the concentration of urea, from 0.1 to 0.4 M, caused a small drop in the experimental rate constant for hydrolysis in 2 M sodium hydroxide at 50.0° (0.97×10^{-6} sec.$^{-1}$ to 0.95×10^{-6} sec.$^{-1}$) which was within the limit of the combined errors of the analytical procedure used.

Hydrolysis of urea in 2 M hydroxide at 60° for twenty times the "half-time" of reaction yielded only 96% of the expected amount of ammonia; a white powder, probably a polymer formed from cyanate, was also found in the reaction vessels. For this reason, ureolysis was usually allowed to proceed to only 20–40% of completion.

A typical set of pseudo-first-order rate constants from reaction in base ranging in concentration from 1 to 2 M, at 60°, are listed in Table I. Although the errors are somewhat larger than those expected from kinetics measurements, this may be attributed to the analytical procedure used; Shaw,[2] who also employed Nesslerization for assay, found comparable errors in rate measurements of ureolysis. Usually, three separate experiments, performed in duplicates containing seven to ten samples each, were made at each temperature at which the reaction was investigated.

When the rate constants collected over the full range of base concentrations and temperatures studied (1–2 M, 33–70°) were plotted as a function of hydroxide ion concentration, a series of curves was obtained which indicated more rapid reaction at higher concentrations of base than simple first-order dependence on that solution parameter would allow. This effect could not be attributed to the difference in ionic strength between

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[2] W. H. R. Shaw and J. J. Bordeaux, *J. Am. Chem. Soc.*, **77**, 4729 (1955).

[3] A. R. Amell, *ibid.*, **78**, 6234 (1956).

[4] R. C. Warner, *J. Biol. Chem.*, **142**, 705 (1942).

[5] M. W. Lister, *Can. J. Chem.*, **33**, 426 (1955).

Table I: Pseudo-First-Order Rate Constants for Hydrolysis of 0.1 *M* Urea in Sodium Hydroxide at 60.0°

OH^-, *M*	k_{exptl},[a] sec.$^{-1}$ × 10^{-6}
1.0	1.02 ± 0.04
1.25	1.40 ± 0.03
1.50	1.79 ± 0.04
1.75	2.22 ± 0.13
2.0	2.69 ± 0.17

[a] Errors appended are standard deviations.

solutions at 1 and 2 *M* base, for adjustment of those at the former concentration to 2 *M* with sodium chloride caused no measurable alteration in the rate of hydrolysis at 50° ($k_{exptl} = 0.320 \times 10^{-6}$ sec.$^{-1}$ for each experiment).

If base-catalyzed ureolysis proceeds with both uni- and bimolecular participation of hydroxide ion, then

$$v = k_1[\text{urea}] + k_2[\text{urea}][OH^-] + k_3[\text{urea}][OH^-]^2 \quad (2)$$

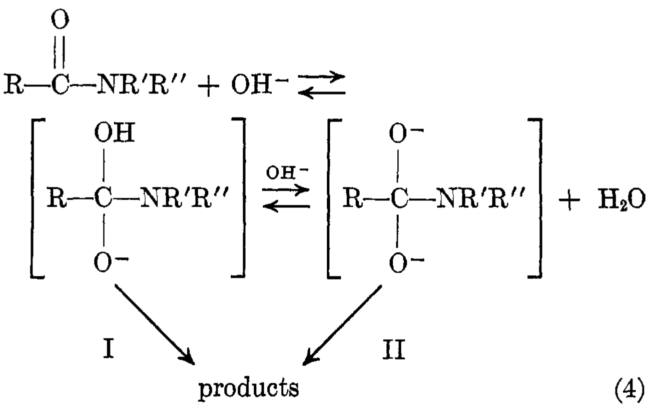
where v is the over-all velocity of reaction and k_1 is the specific rate constant for the hydrolysis in water, k_2 is that for reaction first order in both urea and hydroxide ion concentrations, and k_3 is that for reaction first order in substrate and second order with respect to base concentration. Consequently

$$(k_{exptl} - k_1)/[OH^-] = k_2 + k_3[OH^-] \quad (3)$$

where k_{exptl} is the experimentally determined pseudo-first-order rate constant for the base-catalyzed ureolysis.

When the left-hand side of eq. 3 was plotted as a function of hydroxide ion concentration, using values of k_{exptl} determined in this work and the data of Shaw and Bordeaux[2] for evaluation of k_1, straight lines of intercept k_2 and k_3 were calculated using least-squares procedures, and the results are collected in Table II.

Bieschler and Taft have shown[6] that the pseudo-first-order rate constants obtained for the hydrolysis of N-methylanilides of trifluoroacetic and other acids fit an equation analogous in form with that of (2), the term for the uncatalyzed reaction (k_1[amide]) being negligible in their systems. The equation was interpreted[6] with the reaction route described by



(4)

Table II: Evaluation of the Rate Constants k_2 and k_3

T, °C.	k_2,[a] l. mole^{-1} sec.$^{-1}$ × 10^{-7}	k_3,[a] l.^{2} mole^2 sec.$^{-1}$ × 10^{-7}
33.0	0.32 ± 0.02	0.19 ± 0.02
40.0	0.55 ± 0.08	0.47 ± 0.05
49.9	0.75 ± 0.06	2.01 ± 0.05
56.1	3.63 ± 0.36	2.74 ± 0.24
60.0	4.28 ± 0.30	4.14 ± 0.20
70.0	20.52 ± 3.72	7.42 ± 0.24

[a] Errors appended are standard deviations.

Supporting evidence for this mechanism was adduced from a variety of reactions.[6] More recently, Bender and Thomas[7] have reported ^{18}O-exchange studies which show that the initial step of eq. 4 must be represented by a rate, not a pre-equilibrium process for the anilides examined. It is also relevant to note that the hydrolysis of monochloroacetamide in sodium hydroxide has lately been shown[8] to proceed *via* both intermediates I and II.

Arrhenius energies of activation for the reactions uni- and bimolecular in base were estimated, using least-squares procedures, as 21.59 and 21.49 kcal./mole, respectively. The corresponding entropies of activation are −20.0 and −21.4 e.u. The pairs of thermodynamic parameters are almost identical, a situation similar to that obtaining for the hydrolysis of monochloroacetamide.[8] The Arrhenius energy of activation calculated from the experimental data of Warner,[4] which were available for only two temperatures, is in good agreement with those reported above. Furthermore, interpolation of data reported[4] previously at 66° in the Arrhenius plots for this work shows that there is close agreement between the rate constants found there and those of this study, even though entirely different methods of analysis were employed.

The route by which ureolysis in sodium hydroxide solution proceeds is described by eq. 4 in which R = NH_2 and R′ = R″ = H. For this reaction, little stabilization of either intermediate I or II would be ex-

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[7] M. L. Bender and R. J. Thomas, *ibid.*, **83**, 4183 (1961).

[8] F. Kezdy and A. Bruylants, *Bull. soc. chim. Belges*, **69**, 602 (1960).

pected; the large negative values of ΔS^* found verify that expectation. However, no definition of the rate-determining step(s) can be made at this time.

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Depolarization of Scattered Light by Optically Active Systems

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In the present note, we wish to draw attention to a complication arising in light scattering measurements on optically active systems. In particular, it will be shown that the value of the measured depolarization of the scattered light ($\rho_{u,m}$) depends on the dimensions of the light scattering cell; in order to obtain from $\rho_{u,m}$ the depolarization (ρ_u) characteristic for the system investigated, a correction for this artifact has to be applied. This is important in the interpretation[1] of measured depolarizations as well as in molecular weight determinations. In the latter case one needs the isotropic scattering (I_{is}) and this is obtained by multiplying the measured scattering (I_m) by a Cabannes factor, which for unpolarized incident light is given by

$$\frac{6 - 7\rho_u}{6 + 6\rho_u}$$

Let us consider the scattering by a solute molecule and let the solute be optically active. In general, the light scattered in any direction will have an electrical vector with components along all of three perpendicular axes; if the x axis is the direction of the incident beam and if we are observing along the y axis, then only the components along the x and z axes make contributions, I_x and I_z, to I_m.

Now, if the solution is optically active, both I_x and I_z when "leaving" the measuring cell will have rotated around the y axis by an angle α; the value of α depends on the distance traveled through the cell and on the specific rotation and concentration of the solute. Then the original I_x must be replaced by a new vector having the components $I_{x,x} = I_x \cos^2 \alpha$, and $I_{x,z} = I_x \sin^2 \alpha$; similarly, I_z has given rise to components $I_{z,z} = I_z \cos^2 \alpha$ and $I_{z,x} = I_z \sin^2 \alpha$. Consequently, the observed depolarization $\rho_{u,m}$ is given by

$$\rho_{u,m} = \frac{I_{x,x} + I_{z,x}}{I_{x,z} + I_{z,z}} = \frac{I_x \cos^2 \alpha + I_z \sin^2 \alpha}{I_x \sin^2 \alpha + I_z \cos^2 \alpha} = \frac{\rho_u + tg^2\alpha}{\rho_u tg^2\alpha + 1} \qquad (1)$$

So even if ρ_u is zero, $\rho_{u,m}$ will be finite, *viz.*, equal to $tg^2\alpha$.

To check the validity of eq. 1, we measured for two wave lengths, 5461 and 4358 Å., the depolarization in an aqueous sucrose solution of concentration 0.5 g./cm.^{3} at 23°. The instrument used was that described by Coumou[2]; in one set of experiments the center of the incident beam (beam width, 2 mm.) was at 3 mm. and in another at a 17-mm. distance from the side wall. By inserting the relevant α-values into eq. 1, ρ_u was calculated from $\rho_{u,m}$. The results are given in Table I. It is seen that ρ_u, unlike $\rho_{u,m}$, is within the experimental error independent of the distance traveled by the scattered light through the cell, as it should be.

Table I: Correction of Depolarization in Sucrose Solution

Wave length, Å.	Beam distance from side wall, mm.	$\rho_{u,m}$	α, deg.	ρ_u
5461	3	0.040	1.16	0.040
5461	17	0.052	6.60	0.039
4358	3	0.031	1.92	0.030
4358	17	0.066	10.88	0.029

Sucrose solutions are sometimes used for calibrating light scattering instruments.[3] Scattering of light by such solutions was studied by Maron and Lou[4] and by Stigter,[5] but these authors fail to mention the rotation effect discussed above. Both publications[4,5] compare τ_m, the turbidity derived from light scattering, with τ_{th}, the turbidity calculated from thermodynamic data. The latter quantity should be equal to τ_{is}, the turbidity for isotropic scattering. As τ_m is the total scattering, it must be converted into τ_{is} by applying the relation

$$\tau_{is} = \tau_m \times \frac{6 - 7\rho_u}{6 + 6\rho_u} \qquad (2)$$

For an easier comparison with the papers discussed, we use the symbol τ for a quantity loosely called

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