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ACID CATALYZED HYDROLYSIS OF SUBSTITUTED ANILINOMETHANESULFONATES

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Abstract: *Kinetic evidence from acid catalyzed hydrolysis is used to support an alternative mechanism for the formation and hydrolysis of anilinomethanesulfonates.*

The mechanism of the reactions of formation and hydrolysis of substituted anilinomethanesulfonates (RAMS) is of crucial importance due to the use of these compounds as pharmacological vectors for amine-containing drugs, as well as blocking groups is dye synthesis. For several years the mechanism for the formation of the RAMS has been supposed to proceed through a Schiff base intermediate. An alternative mechanism for the formation reaction in aqueous and 50% alcoholic neutral solutions has been proposed, postulating a SN2 rate determining step. We now report the results on the acid catalyzed hydrolysis of the same compounds, which do confirm the mechanism proposed formerly.

EXPERIMENTAL

The reactions kinetics were followed spectroscopically on a Varian-Techtron mod. 635 spectrophotometer. Temperature was maintained constant at ∓ 0.2°C by means of Masterline model 2095 thermostatic bath. pH measurements were done with an Orion mod. 801A pH-meter.

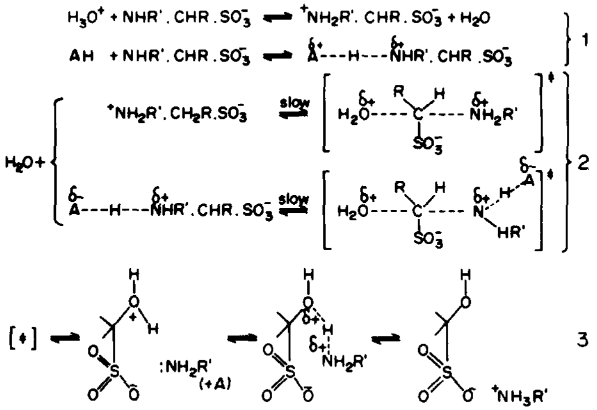
The substituted anilinomethanesulfonates were synthesized by the reaction of equimolar amounts of hydroxymethanesulfonate and the corresponding substituted aniline, and purified by the methods already described(1). pH's were mantained constant using cyanoacetic/cyanoacetate and acetic/acetate buffers.

The ionic strenght was regulated with 0.1M NaCl.

RESULTS AND DISCUSSION

All reactions proved to be first order in RAMS and show general and specific acid catalysis as can be seen from Figure 1, exemplified for m-ClAMS.

This values are in accordance with the mechanism proposed formerly(2,3), now extended for specific and general acid catalysis



where the rate determining step is the formation of the SN2 complex with most of the charge still on the N-atom. The expulsion of the amine group may be simultaneous with the formation of the sulfonate-quarternary amine ion-pair, assisted by a proton transfer from the hydroxyl and of the molecule through a six membered ring. This ion-pair is similar to the structure of the anilinium anilinomethanesulfonates used as characteristic derivatives for RAMS(4).

The ρ-values for the catalyzed reactions, i.e. -2.77 and -2.00 are quite similar to that found for the non-catalyzed (or water catalyzed) reaction (-2.30), and represents mainly the protonation of the RAMS in reaction (1). This reaction is followed by the SN2 rate determining step with a highly polar activated complex with most of the charge on the N-atom side of the complex. In this case, $k = K_1.k_2$ and $\rho = \rho_1 + \rho_2$. The ρ-value for the protonation of the RAMS might be somewhat lower than that for substituted anilines(5) (-3.4), due to the presence of the $-CH_2SO_3^-$ electron withdrawing group. On the other hand, the position of the charge on the activated complex makes the values of ρ_2 relatively small, as pratically no charge displacement occurs at the rate determination step. The value of k will depend mainly on the pK of the catalysing acid, whereas values for k_2 should be similar for early activated complexes(6). Thus, when comparing the dissociation constants of the used acids (55 for H_3O^+, 3×10^{-3} for cyanoacetic acid, and 10^{-14} for H_2O) it can be seen that, for small values of the α-Brønsted constant, the values for k_H and k_{AH} will differ in one order of magnitude, whereas the value for k_o (= $k_{n.c.} \times [H_2O]$) can, eventually, be smaller by about a factor

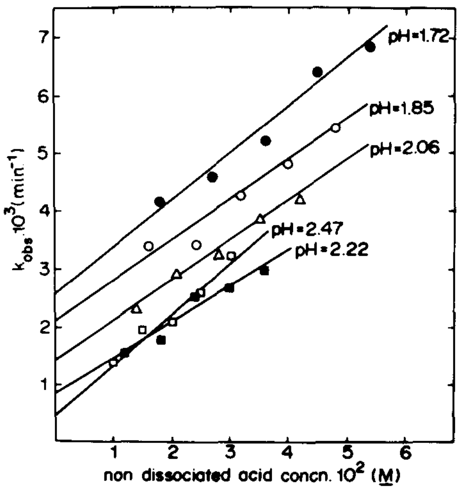


Figure 1. Observed rate constants for the acid catalyzed hydrolysis of m-ClAMS

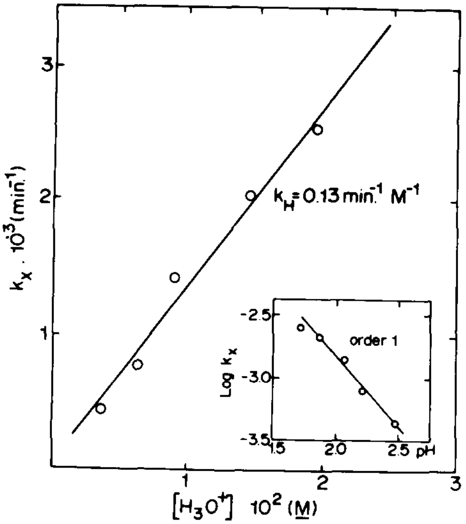


Figure 2. Specific acid catalysis rate constant determination for m-ClAMS

These results correspond to a general behaviour of k_{exptl} in the acid region

$$k_{exptl} = k_o + k_H [H^+] + k_{AH} [AH]$$

The values extrapolated of the lines in Figure 1, can be correlated as shown in Figure 2, which will give the values of k_H and k_{AH} for each compound as shown in Table I.

Table I. *General and specific acid catalysis rate constants for the hydrolysis of substituted anilinomethanesulfonates (RAMS)*

R	p-OMe	p-Me	H	p-Cl	m-Cl
$k_H(M^{-1}min^{-1})$	6.55	7.80	1.35	0.28	0.13
$k_{AH}(M^{-1}min^{-1})$	1.13	0.94	0.40	0.19	0.07

With the values from this table, Hammett plots can be drawn for k_H and k_{AH} rendering ρ-values of -2.77 and -2.00, respectively.

10^3, as can be seen qualitatively in Figure 3.

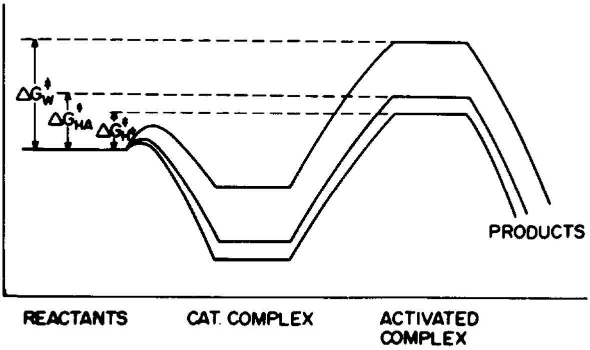


Figure 3. Free energy diagram for the RAMS hydrolysis reactions catalyzed by protons ($\Delta G_H^{\neq}$), weak acids ($\Delta G_{HA}^{\neq}$) and water ($\Delta G_w^{\neq}$)

In addition, no variation of the rate constant was found when changing the ionic strengh of the solution, meaning that an uncharge species must be participating at the rate determining step.

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