

INFLUENCE OF BORIC ACID ON HYDROLYSIS RATE OF SALICYLIDENEANILINES

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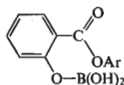
The catalytic effect of boric acid on hydrolysis rate of salicylideneanilines has been studied in aqueous-alcoholic buffers. It has been confirmed that the undissociated form of boric acid is the catalytically active component and that the association of boric acid is significant too. The mechanism of the hydrolysis catalyzed by boric acid has been studied in neutral and alkaline regions. It has been found that the formation of the complex with boric acid is very rapid. Its reaction with water or the decomposition of the adduct formed is the rate-determining step in neutral medium. The reaction rate in alkaline region is directly proportional to the undissociated Schiff's base concentration. The hydrolysis rate increase with increasing OH^- concentration is caused by reaction of the complex with hydroxyl ions.

When studying the influence of pH on the hydrolysis rate of the salicylideneanilines¹, we found that the reaction is faster in borax buffers than in phosphate buffers of the same pH. It is known that boric acid forms covalent adducts with hydroxy compounds which results in increasing the reactivity towards nucleophilic reagents in many cases². An especially marked tendency to the complex formation is encountered in such cases where the molecule contains a further atom with a free electron pair (electron donor) besides the hydroxyl group, so that a six-membered complex can be formed³. Such a complex would have the structure *Ia* in the case of salicylideneaniline derivatives (Scheme 1). The formation of nitrogen-boron bond increases the reactivity of the >C=N- bond towards the nucleophilic reagents, and thus the hydrolysis rate increase can be explained. Recently, Capon and Ghosh⁴ studied in detail the kinetics of hydrolysis of phenyl salicylate catalyzed by borax, where the complex structure as well as the proper hydrolysis mechanism should be analogous to those of salicylideneaniline hydrolysis. On the basis of these studies, the authors derived Eq. (1) for the reaction catalyzed by borax; $[\text{SH}]$ and $[\text{B}^-]$ are the concentrations of the

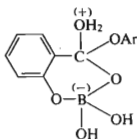
$$v = k'_2[\text{SH}][\text{B}^-] + k'_6[\text{SH}][\text{B}^-][\text{OH}^-] \quad (1)$$

substrate and boric acid anion respectively. According to the mechanism suggested by Capon and Ghosh, a complex of borate and phenyl salicylate is formed in the first equilibrium step and reacts with water or OH^- to give an intermediate which in turn decomposes to products. Tanner and Bruce³ studied in detail the complex formation between borax and organic hydroxy compounds and found that (in contrast to the opinion of Capon and Ghosh) the complexes are formed with boric acid and not with borax, and that the experimental data of Capon and Ghosh agree far better with the kinetical equation (2) where $[\text{BH}]$ is the boric acid concentration. According to these authors³, the ester *II* is formed in the first reversible step of the reaction of phenyl salicylate with boric acid; the ester reacts with water or hydroxyl ion (the oxygen-boron bond being formed simultaneously) to give the intermediates *IIIa* or *IIIb* respectively.

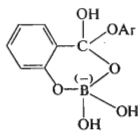
$$v = k_a''[\text{SH}][\text{BH}] + k_b''[\text{SH}][\text{BH}][\text{OH}^-] \quad (2)$$



II



IIIa



IIIb

In order to ascertain the mechanism of the borax catalyzed hydrolysis of salicylideneaniline, we have studied in detail the dependence of the hydrolysis rate on the concentrations of boric acid and borate as well as on pH in 22% ethanolic buffers at 22°C. The study has been extended by borax catalyzed hydrolysis of several salicylideneaniline derivatives.

EXPERIMENTAL

The salicylideneaniline derivatives described in our previous papers^{1,5} were used for kinetic measurements. The measurements were carried out in acetate, phosphate^{1,5} and borax aqueous-alcoholic buffers (22% by vol. ethanol). The borax buffers were prepared by mixing the solutions of borax and boric acid, borax and sodium hydroxide, boric acid and sodium hydroxide. Ionic strength was kept at 0.100 by addition of potassium chloride. Kinetic measurements were carried out with the use of a Unicam spectrophotometer SP 800 at 22°C in 3 and 4 cm cells. pH of the solutions was measured with a PHM 4c apparatus (Radiometer) using a glass electrode of the type B. The pH value of the borax buffer having the lowest total concentration ($c_B = 0.010$ mol/l) and component ratio acid : anion = 1 : 1 was taken to be pK_A of borax in 22% ethanolic buffer at 22°C.

RESULTS AND DISCUSSION

In all the cases the hydrolysis took a 1. order course with respect to salicylideneaniline concentration, and the respective aldehyde and amine were the only reaction products. The experimental rate constant increased with increasing borax buffer concentration (c_B) at constant pH (borax buffer concentration c_B is practically equal to boric acid concentration at pH 7.5). The relation between the rate constant k_{exp} and concentration was linear at the beginning, but increasingly deviated from linearity with increasing c_B (Fig. 2, curve 1). The deviation from linearity was greater at higher pH. If we change the borate concentration at roughly constant boric acid concentration in the range of pH 7.5–9, the experimental rate constant does not practically change at boric acid concentrations below 0.010 mol/l (Fig. 1, curve 2a). At higher boric acid concentrations, however, the rate constant gradually decreases with increasing borate concentration (Fig. 1, curves 6a, 8a–10a). If, on the contrary, the boric acid con-

centration is changed in the same pH range, the borate concentration being constant, k_{exp} increases with increasing boric acid concentration. The dependence found has the same course as in Fig. 2, curve 1. These results stand in accord with the conclusions of Tanner and Bruice, that the monomer boric acid is the catalytically active component. The reaction rate in this pH range 7.5–9 can be expressed by kinetic equation (3) where $[\text{SH}]$ and $[\text{BH}]$ stand for concentrations of salicylideneaniline and boric acid monomer respectively.

$$v = k_0[\text{SH}] + k_a[\text{SH}][\text{BH}] \quad (3)$$

The deviation of the dependence of k_{exp} on boric acid concentration from linearity (Fig. 2) can be explained by association of the boric acid monomer. This association is increased with increasing borax buffer concentration and with increasing pH. A detailed study of this association in aqueous solution was carried out by Ingri⁶ who arrived at the conclusion that equations (4) and (5) hold at borax buffer concentrations $c_B < 0.4$ mol/l, the respective dissociation constants values being $K_{13} = 10^{-7.29}$ (at 25°C in 0.1M-NaClO₄); $K_{13} = 10^{-6.84}$ (at 25°C in 3M-NaClO₄); $K_{23} = 10^{-15.44}$ (at 25°C in 3M-NaClO₄).

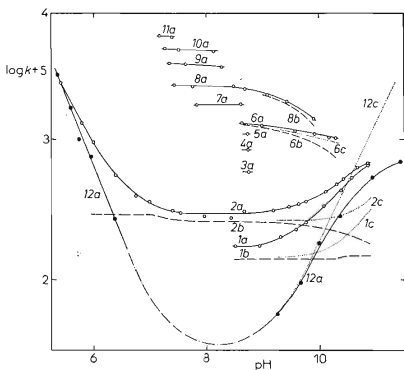
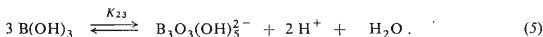
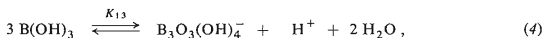


FIG. 1

Dependence of Logarithm of Rate Constants on pH for the Hydrolysis of 5-Methylsalicylideneaniline Catalyzed by Boric Acid (Curves 1–11) and Non-Catalyzed (Curve 12)

Concentration of boric acid: 1 0.005M, 2 0.010M, 3 0.020M, 4 0.030M, 5 0.040M, 6 0.050M, 7 0.070M, 8 0.100M, 9 0.150M, 10 0.200M, 11 0.250M. Curves a k_{exp} , b k_{bor} , c k'_{bor} . k in s^{-1} .

Martin and coworkers⁷ considered only the equation (4) when studying the catalytic effect of boric acid on intramolecular amination of esters (at low boric acid concentration and in weakly alkaline range pH 8–9). Using this equation, we have calculated the boric acid monomer concentration [BH] for the given c_B concentration and plotted the k_{exp} values against [BH] (Fig. 2, curve 2). As the value of the trimerisation equilibrium constant K_{13} in 22% ethanol is not known, we have used the value $K_{13} = 10^{-7.3}$ found by Ingri. As it can be seen from Fig. 2, curve 2, the dependence k_{exp} vs. monomer boric acid concentration [BH] thus calculated is linear practically in the whole range.

First of all, the influence of increasing OH^- ions concentration was studied at low boric acid concentrations in order to suppress the effect of boric acid association on the dependences studied as far as possible. At pH > 9 a gradual increase of the rate constant took place with increasing pH (Fig. 1, curves 1a, 2a). As the boric acid non-catalyzed reaction makes itself increasingly felt with increasing pH, it was necessary to subtract the rate constant of non-catalyzed reaction from experimental rate constant (Fig. 1, curve 12a). The rate constant k_{bor} thus calculated for the lowest boric acid concentrations (0.005 mol/l) appears to be practically pH-independent in the whole range measured up to pH 11 (Fig. 1, curve 1b). In experiments with higher boric acid concentration at pH 9, the identically computed k_{bor} values decrease with increasing pH, and the decrease is the greater the higher is the borax buffer concentration (Fig. 1, curves 2b, 6b, 8b). The increasing formation of boric

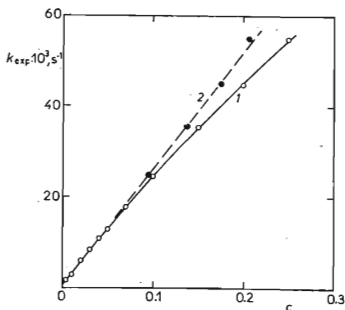


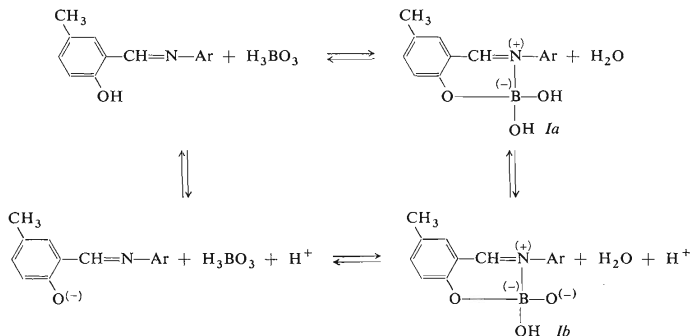
FIG. 2

Dependence of Experimental Rate Constant k_{exp} on Boric Acid Concentration at pH 7.5

1 Dependence of k_{exp} on boric acid concentration; 2 dependence of k_{exp} on monomer boric acid concentration [BH].

acid trimer is the reason for this decrease (resp. one of the reasons). We did not calculate the monomer boric acid concentration, because, in this pH range, the equilibrium (5) can make itself felt to a considerable extent in addition to equilibrium (4); the dissociation constant of equilibrium (5) in 22% ethanol will probably differ considerably from that measured in water.

Dissociation of salicylidene hydroxyl group begins to make itself felt considerably at $\text{pH} > 10$ (pK_A 10.84). Capon and Ghosh⁴ as well as Tanner and Bruce³ supposed that only the neutral form reacted in borax catalyzed hydrolysis of phenyl salicylate. Even though we can write the equations of complex formation from neutral Schiff's base as well as from anion (Scheme 1), the concentration of the complex *Ia* remains directly proportional to Schiff's base concentration at any pH value, and, consequently, the rate of the hydrolytic reaction going through this complex must be directly proportional too. The hydrolysis rate could depend on the anion concentration in such a case only, if complex *Ib* underwent hydrolysis.



SCHEME 1

This reaction is very improbable with respect to the negative charge on the complex. Tanner and Bruce³ analyzed in detail the experimental data⁴ and arrived at the conclusion that hydrolysis of such a complex was practically out of the question. On the basis of these considerations we assumed that, in our case too, the rate was directly proportional to the undissociated Schiff's base concentration in the whole pH range studied. Therefore, we eliminated the influence of salicylidene hydroxyl group dissociation by multiplication of the rate constants k_{bor} of the boric acid non-catalyzed reaction (Fig. 1, curves *b*) by the fraction S_T/S_H (S_T and S_H are the total and undissociated Schiff's base concentrations respectively) and thus obtained the rate constants k'_{bor} referring to undissociated Schiff's base concentration

(Fig. 1, curves 1c, 2c, 6c). From Fig. 1 it can be seen that the values of these rate constants increase with increasing OH^- ions concentration which is apparently caused, as in the phenyl salicylate hydrolysis, by the reaction of the complex *Ia* with OH^- ions. The overall kinetic equation (6) differs from Eq. (2) only by the expression for borax non-catalyzed reaction.

$$v = k_0[\text{SH}] + k_a[\text{SH}][\text{BH}] + k_b[\text{SH}][\text{BH}][\text{OH}^-] = (k_0 + k_{\text{bor}})[\text{SH}] \quad (6)$$

A relatively less steep increase eventually decrease of the dependence k'_{bor} on pH at higher boric acid concentrations is caused by an increased formation of boric acid trimer (Fig. 1, curves 2c, 6c). The independence of the calculated rate constant k_{bor} (Fig. 1, curve 1b) can then be explained by that the reaction with OH^- begins to make itself felt simultaneously with the decreasing concentration of the undissociated Schiff's base and that the both antagonistic effects cancel each other roughly.

We tried to prove the presence of complex *Ia* in some way. At pH about 9.8 and 10.3 the spectra of the Schiff's base were measured in the region 250–500 nm with and without the addition of boric acid. As hydrolysis takes place during the measurements, the extinctions found were extrapolated to zero time using the known rate constants. In the both cases the extrapolated spectra with and without boric acid addition were practically identical. Capon and Ghosh⁴ could not find any difference in spectra, too, even though it clearly followed from their kinetic data that most phenyl salicylate was transferred to the complex at higher boric acid concentrations. Tanner and Bruce³ suppose that the difference in spectra will appear in that case only when the non-complexed substance is present in the form of anion, because the spectrum of the undissociated substance does not substantially differ from that of the complex. We also tried to trace spectrophotometrically the initial reaction phase, when the equilibrium between the Schiff's base and complex was established. At this phase, the extinction decrease should be slower than in the subsequent stationary state. Although we were able to trace the reaction as early as 5 s after mixing the components, the time dependence of the logarithm of the absorbance was linear in the whole course.

This result points to that the equilibrium is established very rapidly, the second less probable interpretation being that the reaction of the Schiff's base eventually its anion with boric acid is the rate-determining step. In order to supply a basis for the decision between the two alternatives, we have studied the kinetics of boric acid catalyzed hydrolysis of salicylideneaniline derivatives. We expected that the influence of substituents would differ in the two abovementioned cases. The hydrolysis kinetics was followed in the pH range 7–8 at several concentrations of boric acid. In this pH range the dissociation of salicylideneaniline hydroxyl group is not significant, and the trimerization of boric acid at low concentration (up to about 0.04 mol/l) is insignificant, too. The k_a rate constants were read from the plot $\log k_{\text{exp}}$ vs boric acid concentration. In Fig. 3 $\log k_a$ is plotted against the Hammett σ constants, and, at the same time for the comparison, the analogous dependence of $\log k'$ (boric acid non-catalyzed reaction) of hydrolysis of protonated Schiff's base with

water (in acid region at pH 5.5) is given. It can be seen that the both dependences have very similar courses inclusive of the characteristic breaks. As the reaction of protonated Schiff's base with water or the decomposition of the adduct formed was the rate-determining step of the acid catalyzed reaction, we suppose that the boric acid catalyzed reaction has an analogous rate-determining step, too.

In the case of 4'-CH₃ and 3'-Cl substituted salicylideneanilines the dependence of the rate constant on pH (in the range 7.5–11.3) was measured in 0.01M-H₃BO₃. As in the case of the unsubstituted derivative, the constants of boric acid non-catalyzed reaction were subtracted from the experimental rate constants, and the constants k_{bor} thus obtained were plotted against pH (Fig. 4). The dependence of 4'-CH₃ substituted derivative (curve 1b) has a similar course to that of unsubstituted Schiff's base, whereas a far more marked decrease is encountered with 3'-Cl derivative (curve 2b). In accord to the mechanism suggested, this decrease can be explained by that the dissociation of Schiff's base will make itself felt kinetically at lower pH values than the reaction of the Schiff's base with OH⁻ ions will. In Fig. 4 the rate constants k'_{bor} referring to the undissociated Schiff's base are plotted against pH. It is interesting that the reaction of the complex with OH⁻ ion makes itself felt kinetically sooner in the case of 3'-Cl derivative (curve 2c) than in the case of 4'-CH₃ derivative (curve 1c), although chlorine in *meta*-position increases the reactivity of the complex towards nucleophilic reagents, and hence its selectivity should be lowered.

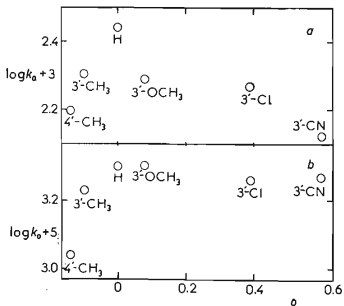


FIG. 3

Dependence of Logarithm of Rate Constants on Hammett σ Constants

a Neutral medium; b specific acid catalyzed hydrolysis at pH 5.5.

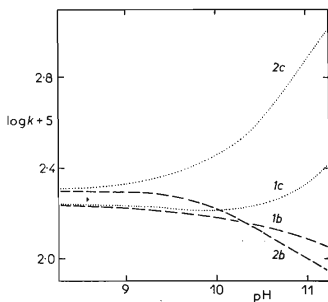


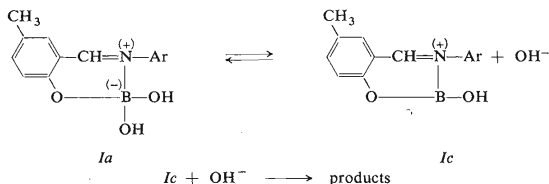
FIG. 4

Dependence of Logarithm of Rate Constants of the Hydrolysis of Salicylideneaniline Derivatives Catalyzed by Boric Acid on pH

1 For 5-methylsalicylidene-4'-methylaniline; 2 for 5-methylsalicylidene-3'-chloroaniline. Curves b k_{bor} , c k'_{bor} .

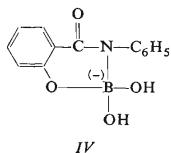
The comparison of the reactivities of complexes of the both derivatives, is, however, complicated by the fact that the rate-determining steps are obviously different in the two cases^{1,5}.

We supposed that the neutral complex *Ia* reacted with water in the region where the rate constant was independent of H^+ ions concentration. This possibility is kinetically indistinguishable from the second one where the neutral complex *Ia* dissociates in a preceding equilibrium step, and the positively charged complex *Ic* thus formed reacts with OH^- ion in a subsequent step (Scheme 2).



SCHEME 2

This would be an analogy to the hydrolysis of Schiff's bases in neutral region, where the protonated base reacts with hydroxyl ion, too⁸. Tanner and Bruice³ measured the extent of dissociation of the complex *IV* and found it to be 50% at pH 5.5. As



there is a positive charge at nitrogen atom in the complex *Ia*, we can presume that the 50% dissociation will take place at a still lower pH. Therefrom it follows that the concentration of the neutral complex *Ia* is practically constant, and the concentration of the positively charged complex *Ic* is directly proportional to the proton concentration in the pH range of the abovementioned measurements. The reactivity of the positively charged complex should be comparable with that of the protonated Schiff's base, because the both species are similar with respect to their stereochemical arrangement as well as the location of the positive charge. In the hydrolysis of the salicylideneaniline at $pH < 7$ the reaction of the protonated Schiff's base with water predominates kinetically (Fig. 1, curve 12a), so that the hydrolysis rate is directly proportional to the proton concentration. In the case of the boric acid catalyzed

reaction we failed in finding the dependence of the hydrolysis rate on the proton concentration even at pH 6 (Fig. 1, curve 2b). Therefore, we take this second mechanism to be not very likely.

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