2502 © *1984 The Chemical Society of Japan* *Bull. Chem. Soc. Jpn.*, *57*, *2502—2507 (1984)* [Vol. 57, No. 9

Hydrolysis of *N*-Salicylidene-2-methoxyethylamine. Intramolecular General Base Catalysis and Specific Effects of Boric Acid

Hiroaki Nagamatsu, Tadashi Okuyama,* and Takayuki Fueno
Faculty of Engineering Science, Osaka University, Toyonaka, Osaka 560

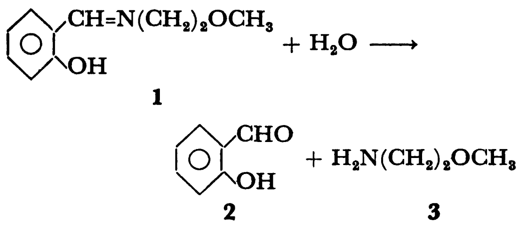
(Received March 8, 1984)

Hydrolysis of *N*-salicylidene-2-methoxyethylamine is kinetically investigated at 30 °C. Intramolecular general base catalysis by the *o*-O$^-$ substituent takes place in the neutral pH region. Nucleophilic catalysis by morpholine was also found to be operative. Added boric acid accelerates the hydrolysis above pH 5.5 while it decelerates the hydrolysis below pH 5.5. The hydrolysis rate as the function of the boric acid concentration follows a saturation curve in harmony with a reaction sequence involving a rapid equilibrium formation of a borate-substrate complex followed by its breakdown. The morpholine catalysis is inhibited by boric acid in accord with the slow reaction of morpholine with the complex. The water reaction of the complex is considered to involve a rearrangement of the complex and an intramolecular transfer of the boron-coordinated hydroxide ion to the iminium carbon.

Boric acid greatly accelerates the hydrolysis of *N*-salicylideneaniline.[1] We have found, however, that hydrolysis of a Schiff base derived from α-hydroxyisobutyrophenone is decelerated by boric acid in acidic solution although it is accelerated in alkaline solution.[2] These effects of boric acid on the hydrolysis of hydroxy Schiff base occur through a borate-substrate complex involving a boron–hydroxyl coordination. Possible mechanisms for this reaction were presented.[1,2]

Similar accelerative effects of boric acid were also found during hydrolyses of phenyl salicylate[3] and hydroxy thiocarboxylic *S*-esters.[4] It was concluded in the latter case that the catalysis takes place through a mechanism involving an intramolecular transfer of a boron-coordinated hydroxide ion within a borate-substrate complex.[4]

In the present investigation, hydrolysis of *N*-salicylidene-2-methoxyethylamine **1** is examined in the presence of boric acid as well as morpholine. Boric acid accelerates the hydrolysis above pH 5.5 while it decelerates the hydrolysis at lower pH. Nucleophilic catalysis of the hydrolysis by morpholine is retarded by added boric acid. A detailed mechanism of the borate action is presented.



(1)

Results

Hydrolysis in the Absence of Boric Acid. Hydrolysis of Schiff base **1** was carried out at 30 °C in aqueous solution of the constant ionic strength of 0.10 maintained with KCl. The reaction was monitored by the decrease in the absorption of **1** at 275 nm. An isosbestic point was always observed at about 262 nm. The final spectra of the reaction mixtures agreed with the spectrum of salicylaldehyde **2** (λ_{max} 255 nm). The time-dependent absorbance changes obeyed the pseudo-first-order kinetics.

The hydrolysis rates were first measured without any added boric acid in usual buffer solutions of formate, acetate, and tertiary amines as well as HCl solutions in the pH range 2—12. Buffer effects were observed only below pH 6. Logarithms of the rate constants k_0 extrapolated to zero buffer concentration are plotted against pH in Fig. 1.

The pH-rate profile is quite similar to those observed for the hydrolysis of *N*-salicylideneisopropylamine[5,6] and *N*-salicylideneaniline[7] and may be interpreted in the same way (Scheme 1). The rate-determining step changes with pH from formation (pH>3) to decay (pH<3) of an α-amino alcohol intermediate. A rate increase above pH 8 must be due to the contribution from a zwitterionic from (**1**±) of **1**. The profile can be described by Eq. 2 according to Scheme 1: Equation 2 may be derived by applying the steady-state approximation to the α-amino alcohol intermediate **I**

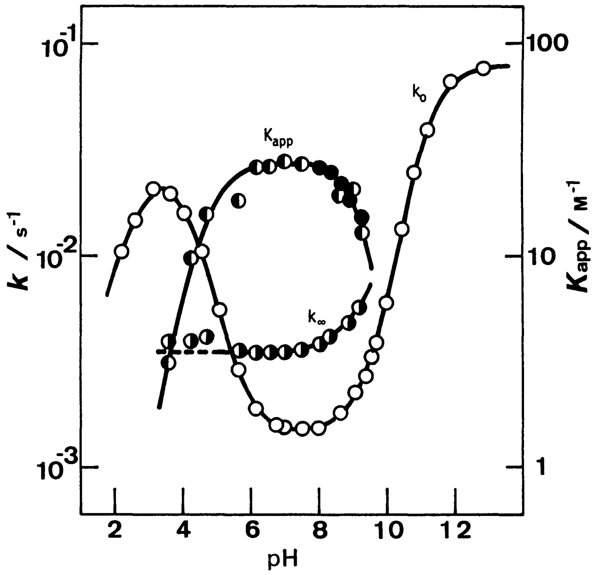
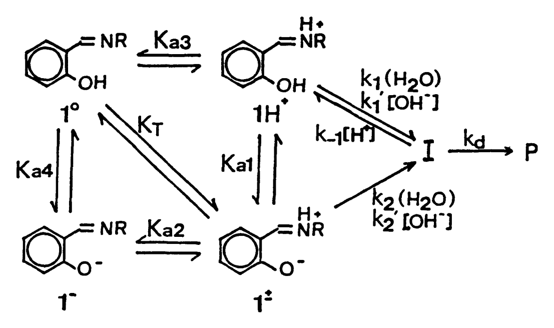


Fig. 1. pH dependences of hydrolysis rates and the equilibrium constant K_{app}. ○, k_0; ◑, k_∞; ◐, K_{app} obtained from the hydrolysis; ●, K_{app} obtained from the morpholine reaction. K_{app} refers to the right ordinate. For theoretical curves, see text.



Scheme 1.

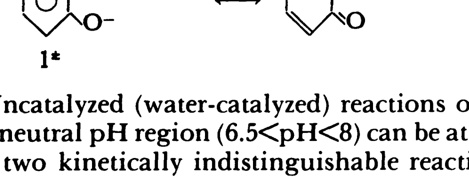
Table 1. Kinetic parameters for the hydrolysis of Schiff base **1** at 30 °C

k_1/s^{-1}	2.4×10^{-2}
k_2/s^{-1}	1.5×10^{-3}
$k_2'/\text{M}^{-1}\,\text{s}^{-1}$	3.7×10
$k_3/\text{M}^{-1}\,\text{s}^{-1}$	1.0×10^{3}
$k_4/\text{M}^{-1}\,\text{s}^{-1}$	1.6×10^{-1}
$k_\text{M}/\text{M}^{-1}\,\text{s}^{-1}$	2.7×10^{-2}
$(k_\text{d}/k_{-1})/\text{M}$	4.4×10^{-3}
$K_{\text{a}1}/\text{M}$ (p$K_{\text{a}1}$)	3.9×10^{-5} (4.4)
$K_{\text{a}2}/\text{M}$ (p$K_{\text{a}2}$)	7.0×10^{-12} (11.2)

in a usual way[5,6] with the correction for the additional equilibrium (K_T). Kinetic parameters (defined in Scheme 1) are summarized in Table 1.

$$k_0 = \frac{k_1[\text{H}^+]^2+(k_1'K_\text{w}+k_2K_{\text{a}1})[\text{H}^+]+k_2'K_{\text{a}1}K_\text{w}}{[\text{H}^+]^2+K_{\text{a}1}(1+1/K_\text{T})[\text{H}^+]+K_{\text{a}1}K_{\text{a}2}}\cdot \frac{k_\text{d}/k_{-1}}{(k_\text{d}/k_{-1}+[\text{H}^+])}. \tag{2}$$

The equilibrium constant K_T for the tautomerization $\mathbf{1}^{\circ}\rightleftharpoons\mathbf{1}^{\pm}$ is hard to determine, but it must be much greater than unity[9] in favor of zwitterion $\mathbf{1}^{\pm}$. The spectrum of **1** in aqueous solution at pH 4—11 has absorption maxima at 275 and 393 nm, which are characterstic of the iminium and phenolate functions, respectively.[8] The zwitterion $\mathbf{1}^{\pm}$ is stable owing to the contribution from the quinonoid resonance form.[9]



Uncatalyzed (water-catalyzed) reactions observed in the neutral pH region (6.5<pH<8) can be attributed to the two kinetically indistinguishable reactions: The hydroxide reaction on the protonated substrate $\mathbf{1}\text{H}^+$ ($k_1'K_\text{W}/K_{\text{a}1}$) and the water reaction of $\mathbf{1}^{\pm}$ (k_2). If the former reaction were the main contributor to k_0, k_1' should have been $4\times10^{6}\ \text{M}^{-1}\,\text{s}^{-1}$,[10] which is too large (17-fold) as compared with a similar value for the hydrolysis of *N*-(*o*-methoxybenzylidene)-2-methoxyethylamine **4**.[11] The latter reaction must be the predominant reaction here and $k_2=1.5\times10^{-3}\ \text{s}^{-1}$, which is about 1/10 of k_1 and is not unreasonable in magnitude. Similar conclusions were reached before for other *N*-salicylidene amines.[6,7]

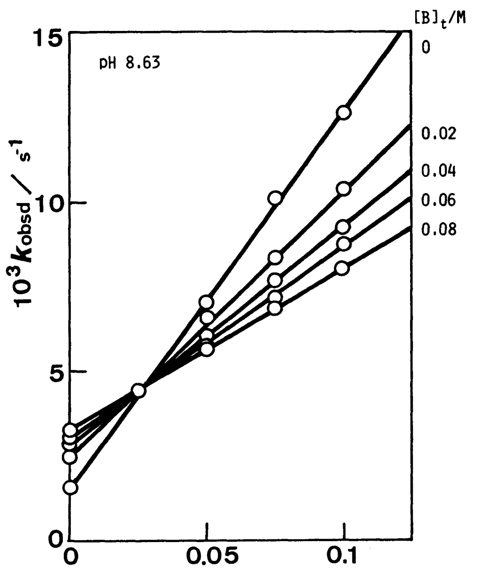


Fig. 2. Dependences of k_obsd on the concentration of morpholine $[\text{M}]_\text{t}$ at the concentrations of boric acid indicated.

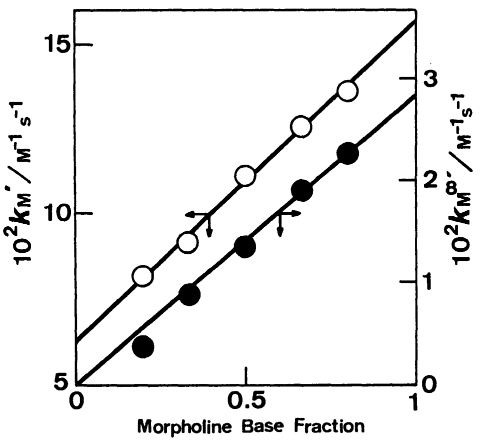


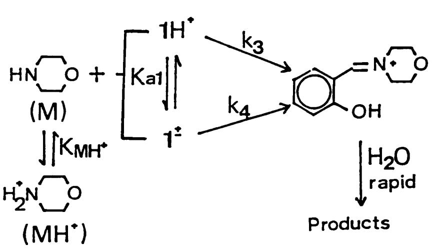
Fig. 3. Plots of k_M' (○) and $k_\text{M}^{\infty\prime}$ (●) against the base fraction of morpholine buffers.

The hydrolysis of **1** was remarkably accelerated by morpholine buffer at pH 8—9.3, although tertiary amines like 1,4-diazabicyclo[2.2.2]octane and *N*,*N*-dimethyl-2-hydroxyethylamine had no effects in this pH region. Furthermore, both UV spectra of the initial and final reaction solutions were respectively the same as those observed in other normal buffer solutions. Observed rate constants k_obsd increased linearly with total morpholine concentration $[\text{M}]_\text{t}$ (Eq. 3) as shown in Fig. 2.

$$k_\text{obsd} = k_0 + k_\text{M}'[\text{M}]_\text{t} \tag{3}$$

The observed catalytic constants k_M' are plotted against the base fraction of morpholine buffer in Fig. 3. The linear correlation gives the rate constants for base and conjugate acid dependences $k_\text{M}=0.16\ \text{M}^{-1}\,\text{s}^{-1}$ and $k_\text{MH}=0.063\ \text{M}^{-1}\,\text{s}^{-1}$.

$$k_\text{M}' = (k_\text{MH}[\text{MH}^+] + k_\text{M}[\text{M}])/[\text{M}]_\text{t} \tag{4}$$



Scheme 2.

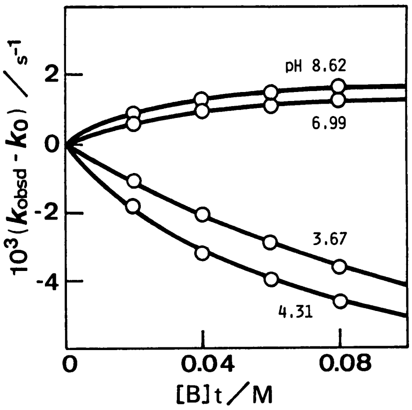


Fig. 4. Dependence of the hydrolysis rate of **1** on the boric acid concentration at pH indicated.

These accelerations must be due to the nucleophilic catalysis by morpholine. The reactive species of **1** in this nucleophilic reaction should be $1H^+$ and $1\pm$, and the rate constants k_{MH} and k_M correspond to $k_3K_{MH^+}/K_{a1}$ and k_4 according to Scheme 2, respectively. Calculated values of k_3 and k_4 are given in Table 1.

Hydrolysis in the Presence of Boric Acid. When a small amount of boric acid was added to the reaction mixture, the hydrolysis was accelerated at high pH while it was decelerated at low pH. Although the spectrum of the initial solution of the substrate showed a new absorption band at 350 nm, that of the product solution was the same as that observed in the absence of boric acid. Induction periods were not observed in any kinetic runs.

Hydrolysis rates were measured with varying concentrations of boric acid at constant pH maintained with a second buffer (when necessary). The rate increased at pH>5.5 but decreased at pH<5.5 with total borate concentration $[B]_t$ as shown in Fig. 4. These changes follow a saturation curve described by Eq. 5, as observed for the hydrolysis of an α-hydroxy Schiff base.[2)]

$$k_{obsd} = (k_0' + k_\infty K_{app}[B]_t)/(1 + K_{app}[B]_t) \tag{5}$$

Here, k_0' is the rate constant in the absence of boric acid and is usually equal to k_0 (negligible effects of the second buffer). The magnitude of k_∞ is greater at pH>5.5 but smaller at pH<5.5 than k_0. The curved rate dependence of Eq. 5 is consistent with a reaction sequence involving a rapid equilibrium formation of a borate-substrate complex followed by a slow breakdown of the complex to lead to the hydrolysis products.[2,12)] K_{app} and k_∞ stand for the equilibrium constant for the complexation and the rate constant for the breakdown of the complex, respectively. They were evaluated from a least-squares treatment of the linear relation between k_{obsd} and $(k_{obsd}-k_0')/[B]_t$ in the same way as before.[2)] The results are given in Table 2. In the pH range 4—6, where the hydrolysis is buffer-dependent, the "normal" buffer effects by boric acid must be taken into consideration. However, the general-base-catalytic acceleration by borate should be small enough to be neglected.[13)] The second buffer used to maintain pH constant affects only the k_0' term but not the borate term.

Table 2. KINETIC PARAMETERS FOR THE HYDROLYSIS OF **1** IN THE PRESENCE OF BORIC ACID AT 30 °C

pH[a)]	$10^3 k_\infty/s^{-1}$	K_{app}/M^{-1}
3.67[b)]	4.0±1.5	3.4±1.0
4.31[c)]	4.0±0.7	10.3±0.5
4.69[c)]	4.2±1.0	15.4±0.8
5.66[d)]	3.6±0.2	17.6±1.5
6.18[d)]	3.5±0.1	25.8±0.6
6.52[d)]	3.5±0.1	25.8±0.4
6.99[e)]	3.5±0.2	28.1±0.8
7.50[e)]	3.6±0.2	26.3±0.7
8.01[e)]	3.8±0.2	23.9±1.0
8.33[f)]	4.2±0.2	25.1±1.2
8.62[f)]	4.5±0.1	18.4±1.0
8.94[f)]	4.8±0.3	18.3±1.5
9.00[f)]	5.6±0.2	20.2±2.0
9.19[f)]	5.7±0.3	13.4±2.3
9.26[f)]	4.9±0.2	12.9±1.3

a) pH (±0.03) were maintained with a buffer of 0.05 M. b) Formate. c) Acetate. d) 2-(*N*-Morpholino)-ethanesulfonate. e) *N*-Methylmorpholine. f) 1,4-Diazabicyclo[2.2.2]octane.

The effects of added boric acid were found also in the morpholine-catalyzed hydrolysis. When the pH and the morpholine concentration $[M]_t$ were kept constant, the rates increased at low $[M]_t$ and, in contrast, decreased at high $[M]_t$ with increasing $[B]_t$ (Fig. 5). At pH 8.6 and $[M]_t$=0.025 M, the observed rate was almost constant with varying $[B]_t$. In an opposite sense, at constant pH and $[B]_t$, the rates increased linearly with $[M]_t$ and lines (for various $[B]_t$) cross at a certain $[M]_t$ (*e.g.*, $[M]_t$=0.025 M at pH 8.6) as shown in Fig. 2. That is, in the presence of both boric acid ($[B]_t$=constant) and morpholine, k_{obsd} is described by Eq. 6.

$$k_{obsd} = k_0{}^B + k_M{}^B[M]_t \tag{6}$$

The slopes of the plots of Fig. 2, $k_M{}^B$, decreased with increasing $[B]_t$ as shown in Fig. 6. The curved dependences of $k_M{}^B$ $[B]_t$ are described by Eq. 7 in the same way as Eq. 5.

$$k_M{}^B = (k_M + k_M{}^{\infty\prime} K_{app}[B]_t)/(1 + K_{app}[B]_t) \tag{7}$$

Kinetic parameters, $k_M{}^{\infty\prime}$ and K_{app}, obtained similarly are given in Table 3. Values of K_{app} obtained here agree well with those obtained in the absence of morpholine as shown with closed circles in Fig. 1.

The limiting rate constant $k_M{}^{\infty\prime}$ corresponds to that for the nucleophilic reaction of morpholine with the

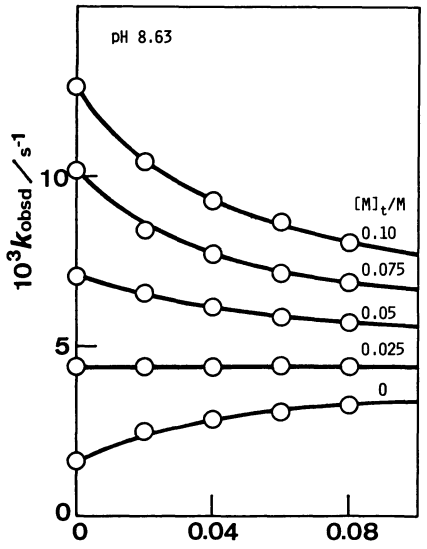


Fig. 5. Dependences of k_{obsd} on the concentration of boric acid at the concentrations of morpholine indicated.

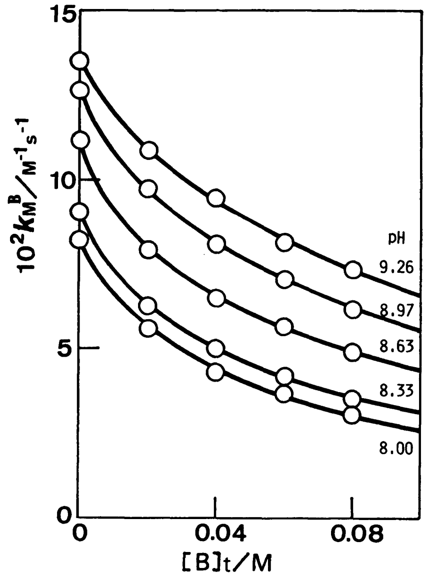


Fig. 6. Dependence of $k_M{}^B$ on the boric acid concentration at pH indicated.

borate-substrate complex. The values of $k_M{}^{\infty\prime}$ are proportional to the base fraction of morpholine buffer as seen in Fig. 3, the slope being $k_M{}^{\infty}=2.7\times10^{-2}\ M^{-1}\ s^{-1}$.

Discussion

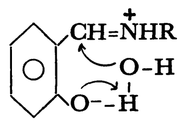
Catalysis of Hydrolysis. Hydrolysis of Schiff base **1** derived from salicylaldehyde **2** is somewhat complicated because of tautomerization of the neutral substrate $\mathbf{1}^0 \rightleftharpoons \mathbf{1}^\pm$. This occurs because the zwitterion $\mathbf{1}^\pm$ is stabilized by resonance with the quinonoid form. The increase in hydrolysis rate at alkaline pH is ascribed to the reaction of $\mathbf{1}^\pm$ with hydroxide ion.

The predominant reaction in the neutral pH region is the water reaction of $\mathbf{1}^\pm$ but not the hydroxide reaction of $\mathbf{1}H^+$ as described above. The same conclusion was reached from the lack of salt effects[7] and the substituent effect[6] observed in the hydrolysis of *N*-salicylidene amines. Failure in the observation of buffer effects in this pH region seems to be incompatible with the water reaction, which should be catalyzed by general bases, but to conform with the hydroxide reaction. However, an intramolecular general base catalysis by the *o*-O$^-$ group may make the external catalysis unnecessary.[14]

Table 3. Kinetic parameters obtained in the presence of both morpholine and boric acid

pH[a]	$10^2k_M{}^{\infty\prime}/M^{-1}\ s^{-1}$	K_{app}/M^{-1}
8.00	0.33±0.15	25.0±1.9
8.33	0.82±0.08	24.7±3.1
8.63	1.3±0.3	22.7±3.1
8.97	1.9±0.2	18.9±2.8
9.26	2.2±0.2	14.8±2.2

a) ±0.03.



Such an intramolecular catalysis was once considered to occur during the hydrolysis of Schiff bases derived from salicylaldehyde[15] and 3-hydroxy-4-pyridinecarbaldehyde,[16] but it was later disregarded by comparisons of the reactivities of *o*- and *p*-hydroxy as well as methoxy derivatives of *N*-benzylideneisopropylamine.[5] However, the comparisons made by the latter authors do not seem to be adequate. First of all, they attributed the predominant reaction in the neutral pH region to the hydroxide reaction of the protonated substrate and the rate constants for the hydroxide reactions of hydroxy and methoxy substrates were compared. As mentioned above, the main reaction is the water reaction of the zwitterion in the case of salicylidene derivatives.

Comparisons of rate constants for various nucleophilic reactions at iminium functions are given in Table 4. Nucleophilic reactions of *o*-methoxybenzylidene derivative **4**[11] are involved for the reference of the comparison. The rate constants are logarithmically plotted against pK_a of the conjugate acid of the nucleophiles in Fig. 7. Three points for $\mathbf{4}H^+$ fall on a straight line of slope (β) of 0.5. Two points (H_2O and morpholine) for $\mathbf{1}H^+$ fall also in the vicinity of the same line. Three points for zwitterion $\mathbf{1}^\pm$ can form a line of slope of about 0.35. However, the low sensitivity in relative nucleophilicity of less reactive substrate $\mathbf{1}^\pm$ (compared with $\mathbf{1}H^+$ or $\mathbf{4}H^+$) is not reasonable. These points may be rationalized as follows: Hypothetical nucleophilic reactivities of $\mathbf{1}^\pm$ would have formed a line of $\beta=0.5$ through a point for hydroxide ion but an intramolecular base-catalyzed acceleration of morpholine and water reactions by the *o*-O$^-$ group resulted in the positive deviations of these points (10- and 300-fold for morpholine and water) from the hypothetical line. Such deviations

TABLE 4. RATE CONSTANTS FOR NUCLEOPHILIC REACTIONS OF VARIOUS IMINIUM SPECIES ($k_{Nuc}/M^{-1}\,s^{-1}$) AT 30 °C

Nucleophile (pK_a)	**1**H$^+$	**4**H$^{+\,a)}$	**1**	**1B**
H_2O (−1.7)	4.3×10^{-4}	8.8×10^{-4}	2.7×10^{-5}	6.3×10^{-5}
Morpholine (8.6)	1.0×10^{3}	3.2×10^{2}	1.6×10^{-1}	2.7×10^{-2}
OH^- (15.7)		2.3×10^{5}	3.7×10	1.1×10^{2}

a) Ref. 11.

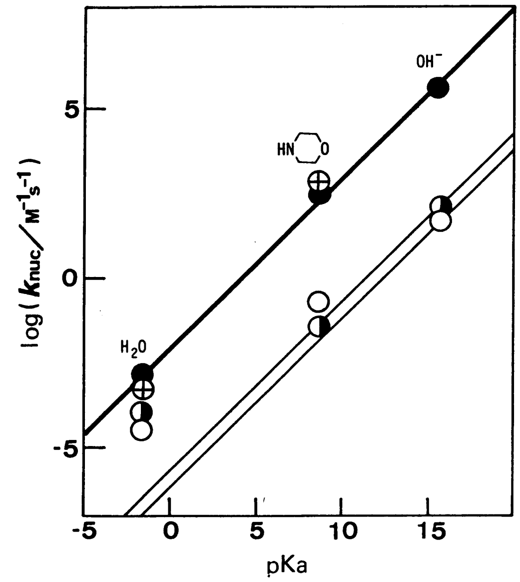
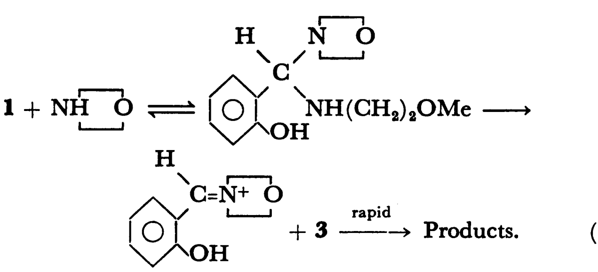


Fig. 7. Plot of $\log(k_{Nuc})$ against pK_a for various iminium species.
●, **4**H$^+$; ⊕, **1**H$^+$; ○, **1**$^\pm$; ◑, **1B**.

of water reactions of the zwitterion of other *N*-salicylidene amines seemed to be observed as compared with benzylidene analogues.[5,7)]

Nucleophilic catalysis of the Schiff base hydrolysis by morpholine is not unexpected since such catalysis of Schiff base formation is well known.[17)] This catalysis must take place through transimination to form *N*-salicylidenemorpholinium ion, which is hydrolyzed rapidly (Eq. 8):

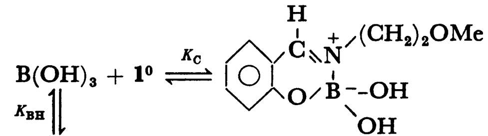


(8)

The rate-determining step of this reaction must be the initial nucleophilic reaction of morpholine with **1**. This is consistent with the observation that morpholine shows a nucleophilicity expected from the water and hydroxide reactions of **1**H$^+$ and **4**H$^+$ (Fig. 7), and is reasonable since a more basic amine is in general more readily released from a *gem*-diamine intermediate as observed during transiminations.[18)] Transimination reactions are subject to buffer catalysis[18—20)] and the morpholine reaction with **1**$^\pm$ may be facilitated by an internal catalysis by the salicylidene O^- group.

Effects of Boric Acid. The apparent equilibrium constants K_{app} for the complexation between **1** and boric acid show a bell-shaped change with pH as seen in Fig. 1. This change is described by Eq. 9, which is based on the assumption that the complex **1B** is formed from the neutral substrate **1**° (the fraction is $(K_{a1}/K_T)[H^+]/\{[H^+]^2+K_{a1}(1+1/K_T)[H^+]+K_{a1}K_{a2}\}$) and boric acid (the fraction of acid form is $[H^+]/(K_{BH}+[H^+])$) with the equilibrium constant K_C (Eq. 10).

$$K_{app}=\frac{(K_CK_{a1}/K_T)[H^+]^2}{\{[H^+]^2+K_{a1}(1+1/K_T)[H^+]+K_{a1}K_{a2}\}(K_{BH}+[H^+])} \tag{9}$$



1B

(10)

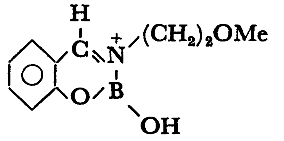
A probable structure of **1B** must involve a tetra-coordinated boron. Chelate complexes formed from polyols and boric acid involve a tetra-coordinated boron center.[21,22)] Complexes of a structure similar to **1B** were isolated as diacetates from the reaction of *N*-salicylidene amines with boric acid in acetic anhydride.[23)]

A theoretical curve for the bell-shaped plot of Fig. 1 is calculated with parameters given in Table 1 and $K_C/K_T=27\ M^{-1}$ according to Eq. 9, where K_T is assumed to be much geater than unity $(1+1/K_T\simeq1)$. If the K_T value is in the range of 10—60,[24)] $K_C=300—1600\ M^{-1}$. The formation constant K_C is much greater than those observed for the complexation of 1,2-diols and boric acid,[21,25)] but a similar value ($K_C=435\ M^{-1}$) was obtained for complexation between an α-hydroxy Schiff base and boric acid.[2)]

The limiting rate constant k_∞ refers to the breakdown of complex **1B** to give hydrolysis products. The values of k_∞ are essentially constant below pH 7.5, but increase at higher pH (Fig. 1). This pH dependence of k_∞ is accommodated by the reactions of **1B** with water and hydroxide ion (Eq. 11): $k_5=3.5\times10^{-3}\ s^{-1}$ and $k_5'=1.1\times10^2\ M^{-1}\,s^{-1}$.

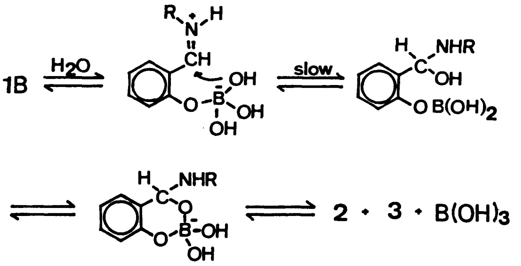
$$k_\infty=k_5+k_5'[OH^-] \tag{11}$$

A possible contribution from a cationic complex like **1B**$^+$ is unlikely,[26)] since such a reaction was not found in the morpholine reaction. The rate constant $k_M{}^\infty$ must be that for the nucleophilic reaction of morpholine with complex **1B**.



1B$^+$

Logarithms of the rate constants for the nucleophilic reactions on **1B** are plotted against pK_a for the corresponding nucleophiles with half-filled circles in Fig. 7. Points for hydroxide ion (k_5') and morpholine (k_M^∞) form a straight line of slope of 0.5, as found for the reaction with **4H$^+$** and **1H$^+$**. However, the point for water (k_5) deviates upward by 2.5 log unit from the line. This 300-fold deviation of the k_5 point suggests that this reaction is not a simple water attack on the iminium carbon of **1B**. This water reaction is not catalyzed by a general base. Furthermore, the anomaly occurs only with water but not with morpholine. Boronic group of **1B** must participate in the reaction. A possible mechanism is presented in Scheme 3. This mechanism involves a rapid (but unfavorable) rearrangement of **1B** to an open zwitterionic complex, within which a rate-determining, intramolecular transfer of the hydroxide ion occurs from the boron to the iminium carbon. Similar reaction mechanisms have been presented for the boric acid-dependent hydrolyses of an α-hydroxy Schiff base[2] and hydroxy thiocarboxylic *S*-ester.[4]



Scheme 3.

In conclusion, boric acid decelerates the hydrolysis of **1** in the low pH region where the reaction of **1H$^+$** predominates, while it accelerates the hydrolysis at higher pH where **1$^\pm$** is the reactive species. The reactivities of the iminium species are in the order: **1H$^+$**>**1B**>**1$^\pm$**. The water reaction of **1$^\pm$** is catalyzed by the internal O$^-$ group in the *ortho* position.

Experimental

Materials. Salicylaldehyde (**2**) and 2-methoxyethylamine (**3**) were commercially obtained and distilled under nitrogen. Salicylidene-2-methoxyethylamine (**1**) was prepared from **2** and **3** by the reaction of the two components at 0 °C for 1 h. After taken up with ether and dried over MgSO$_4$, the products were distilled: bp 142 °C (7 mmHg (1 mmHg≈133.322 Pa)). Other chemicals were obtained as before.[2] Glass-distilled water was used throughout.

Kinetic Measuremens. All the aqueous solutions containing appropriate amounts of boric acid and other buffers were prepared at room temperature and adjusted to an ionic strength of 0.1 with KCl. A stock solution of the substrate **1** was obtained as an acetonitrile solution of about 10^{-3} M. Reactions were started by adding 30 μl of the substrate stock solution from a microsyringe into a 3-ml buffer solution equilibrated at 30±0.1 °C in a stoppered quartz cuvette inserted in a water-jacketed cell holder. The reaction was followed by the decrease in the absorption at 275 nm on a Shimadzu UV 200 or 140 spectrophotometer. Pseudo-first-order rate constants were calculated by a modified Guggenheim method.[27] Values of the pH of buffer and reaction solutions were determined by a Hitachi-Horiba F7 pH meter.

References

1) J. Hoffmann and V. Štěrba, *Collect. Czech. Chem. Commun.*, **37**, 2043 (1972).

2) H. Matsuda, H. Nagamatsu, T. Okuyama, and T. Fueno, *Bull. Chem. Soc. Jpn*, **57**, 500 (1984).

3) B. Capon and B. Ch. Ghosh, *J. Chem. Soc., B*, 472 (1966).

4) T. Okuyama, H. Nagamatsu, and T. Fueno, *J. Org. Chem.*, **46**, 1336 (1981).

5) W. Bruyneel, J. J. Charette, and E. de Hoffmann, *J. Am. Chem. Soc.*, **88**, 3808 (1966).

6) R. Herscovitch, J. J. Charette, and E. de Hoffmann, *J. Am. Chem. Soc.*, **96**, 4954 (1974).

7) J. J. Charette and E. de Hoffmann, *J. Org. Chem.*, **44**, 2256 (1979).

8) The protonated and neutral forms of *N*-(*o*-methoxybenzylidene)-2-methoxyethylamine (**4**) have λ_{max} at 276 and 249 nm, respectively. The anionic form of **2** has λ_{max} at 377 nm while the neutral **2** has λ_{max} at 324 nm.

9) R. Herscovitoh, J. J. Charette, and E. de Hoffmann, *J. Am. Chem. Soc.*, **95**, 5135 (1973).

10) 1 M=1 mol dm^{-3}.

11) H. Nagamatsu, M. Kitano, T. Okuyama, and T. Fueno, unpublished results.

12) a) Borate associates by itself at higher concentrations[12b] and this association could be responsible for the diminishing activity of boric acid. To avoid this effect [B]$_t$ was kept low enough. b) N. Ingri, G. Lagerstrom, M. Frydman, and L. G. Sillen, *Acta Chem. Scand.*, **11**, 1034 (1957); N. Ingri, *ibid.*, **16**, 439 (1962); **17**, 573, 581 (1963).

13) Rate constant for general base catalysis by acetate (pK_a=4.6) is 1.6×10^{-1} M^{-1} s^{-1}. If the Brønsted β is assumed to be 0.3, the catalytic constant for borate (pK_a=9.2) is calculated to be 3 M^{-1} s^{-1} and the contribution from borate ([B]$_t$≤0.08 M) is estimated to be smaller than 10^{-4} s^{-1} at pH 6.

14) T. Okuyama, H. Shibuya, and T. Fueno, *J. Am. Chem. Soc.*, **104**, 730 (1982).

15) R. L. Reeves, *J. Org. Chem.*, **30**, 3129 (1965).

16) T. C. French, D. S. Auld, and T. C. Bruice, *Biochemistry*, **4**, 77 (1965).

17) E. H. Cordes and W. P. Jencks, *J. Am. Chem. Soc.*, **84**, 826 (1962).

18) K. Koehler, W. Sandstrom, and E. H. Cordes, *J. Am. Chem. Soc.*, **86**, 2413 (1964).

19) J. L. Hogg, D. A. Jencks, and W. P. Jencks, *J. Am. Chem. Soc.*, **99**, 4772 (1977).

20) H. Fischer, F. X. DeCandis, S. D. Ogden, and W. P. Jencks, *J. Am. Chem. Soc.*, **102**, 1340 (1980).

21) J. Böeseken, *Adv. Carbohyd. Chem.*, **4**, 189 (1949).

22) R. P. Oertel, *Inorg. Chem.*, **11**, 544 (1972).

23) S. M. Tripathi and J. P. Tandon, *J. Inorg. Nucl. Chem.*, **40**, 983 (1978).

24) H. Nagamatsu, T. Okuyama, and T. Fueno, *Bull. Chem. Soc. Jpn.*, **57**, 2508 (1984).

25) G. L. Roy, A. L. Laferriere, and J. O. Edwards, *J. Inorg. Nucl. Chem.*, **4**, 106 (1957).

26) An increasing tendency of k_∞ at low pH (<5) might be ascribed to the contribution from **1B$^+$**.

27) E. S. Swinbourne, *J. Chem. Soc.*, **1960**, 2371.