Kinetics of the Proton-Transfer Reactions of Some *ortho*-Hydroxy Derivatives of Azo and Azomethine Compounds in Dioxane-Water Medium*

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The kinetics of the proton-transfer reactions between hydroxide ion and *o*-hydroxy azo and *o*-hydroxy azomethine compounds having a strong O–H···N or an O–H···π intramolecular hydrogen-bond are studied in 50% (v/v) dioxane-water by means of temperature-jump method. The forward and the backward rate constant k_f and k_r for the overall reactions $OH^- + HA \underset{k_r}{\overset{k_f}{\rightleftharpoons}} H_2O + A^-$ are evaluated to be in the range between 4.4×10^4 and $6.1\times10^8\ M^{-1}\ s^{-1}$ and between 1.5×10^3 and $6.2\times10^4\ s^{-1}$ respectively. The values of the k_f for the azomethines are by several orders of magnitude higher than those of the corresponding azo compounds. The values of k_f and k_r in dioxane-water are found to be smaller than those in aqueous medium.

Eigen and coworkers have extensively investigated the kinetics of the proton-transfer reactions in aqueous media using chemical relaxation methods.[1-3] The protolytic reactions between so-called "normal" Brønsted acids and bases which can readily form hydrogen-bonded structure with solvent water molecules proceed almost diffusion-controlled. Thus the characteristic recombination rate constants k_f between hydrogen ion and normal bases are reported to be in the order of $10^{11}\ M^{-1}\ s^{-1}$ and those between hydroxide ion and normal acids almost $10^{10}\ M^{-1}\ s^{-1}$. The differences are attributed to the higher mobility of the hydrogen ion in aqueous solution.

Considerable decrease in the recombination rate constants k_f is observed, however, because of the following factors on the side of Brønsted acids and/or bases;[1-3] (1) the charge type, the size, and the shape of the reactants, (2) the liquid structure of the solvent water around the reacting species, (3) existence of the intramolecular hydrogen-bond at the periphery of the reaction site, and (4) intramolecular electronic rearrangement and/or the conformational orientation that activate the donor groups as CH acids and pseudo acids.[4]

The proton-transfer reactions in aqueous solutions between some *o*-hydroxy azo compounds and hydroxide ion have been reported in detail.[1-3),5),6] It was noted that the slowness of the recombination reaction would reflect the strength of the intramolecular hydrogen-bond. Eyring *et al.* reported the kinetics on the proton transfer between hydroxide ion and a number of Brønsted acids.[6-9] They suggested on the basis of the kinetic data the following order of the relative strength for intramolecular hydrogen-bonds:

O–H···N>O–H···O>N–H···N>N–H···O,

which is similar to that proposed by Freedman.[10]

Eigen pointed out that hydroxide ion can hardly approach the proton in the hydrogen-bridged structure of the Brønsted acid molecule and suggested a detailed mechanism involving pre-equilibrium between two states of the proton in Brønsted acids.[3]

Only a few attempts, however, have so far been made for the kinetic studies on the proton-transfer reactions in mixed solvents[11] as compared with equilibrium studies.[12] With respect to the reaction mechanism, the extensive kinetic studies are needed. Nevertheless, there prevail many complicated situations.

The dioxane–water medium has often been used for the determination of the acid dissociation constants and/or the complex formation constants of water-insoluble Brønsted acids. 1,4-Dioxane, a typical water-miscible dipolar aprotic solvent, can cover the wide range of the dielectric constant of the medium by mixing with water. These characteristics are convenient also in the fast proton-transfer reactions to evaluate the solvent effects such as electrostatic effects *etc.* In the present study we report the proton-transfer reactions between hydroxide ion and five *o*-hydroxy azo and four *o*-hydroxy azomethine compounds in 50% (v/v) dioxane–water system.

In general *o*-hydroxy azomethines are known to be weaker as acids than the corresponding azo derivatives.[13] Since *o*-hydroxy azomethines are only sparingly soluble and gradually hydrolyzed in water, it was difficult to measure the reaction rate in aqueous solutions.[14] Furthermore *o*-hydroxy azomethines are often unstable even in the mixed solvent containing water, so that we used a stopped-flow-temperature-jump technique.

It should be noted that the rate constants k_f and k_r obtained for the proton transfer in the mixed solvent are always lower than those in aqueous system. This tendency could not generally be observed in the reactions between "normal" acids and bases.[1]

Experimental

Materials. *Reagents*: All chemicals used were of analytical grade, unless otherwise specified. Water was deionized and distilled. Dioxane was distilled and the water content was determined to be 2.97 mg/ml by Karl Fischer titration. 10^{-3} M stock solutions of azomethines were prepared by dissolving in dioxane. The solutions were kept only for three weeks at room temperature.

o-Hydroxy Azo and o-Hydroxy Azomethine Compounds: The compounds used here are: Tropaeolin-O (I; TPO), 4-(2-pyridylazo)resorcinol (II; PAR), 1-(2-pyridylazo)-2-naphthol (III; PAN), *N*-salicylidene-2-aminopyridine (IV; SAP), *N*-(2-pyridylmethylene)-*o*-aminophenol (V; PMA), *N*-(2-hydroxy-1-naphthylidene)-2-aminopyridine (VI; NAP), *N*-salicylidene-2-aminothiazole (VII; SAT), 4-(2-thiazolylazo)-resorcinol (VIII; TAR), and 1-(2-thiazolylazo)-2-naphthol

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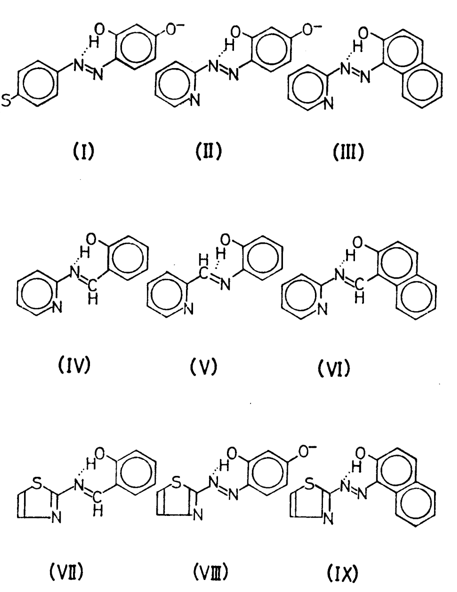


Fig. 1.

(IX; TAN). (See Fig. 1.)

The azo compounds (Dojindo) were purified by repeated recrystallization from 99.5% ethanol or ethanol–water. The azomethine compounds were prepared by condensation of aldehydes with amines, and recrystallized from 99.5% ethanol. As for the compound V, it was necessary to purify sufficiently the starting materials to prepare the pure crystalline compound.[15] Found: C, 72.8; H, 5.0; N, 13.9%. Calcd. for PMA, $C_{12}H_{10}N_2O$: C, 72.7; H, 5.1; N, 14.1%.

Measurements. *pH in the Mixed Solvents*: The analytical concentration C_H of the solvated proton in 50%(v/v) dioxane-water was determined titrimetrically. The pH* of the solution was measured with Hitachi-Horiba pH-meters, Model-P and Model M-7. For the potentiometric titrations of perchloric acid in the mixed solvent the ionic strength was adjusted with pure sodium perchlorate.[16] All measurements were carried out in nitrogen atmosphere.

Assuming the complete dissociation for the perchloric acid in the mixed solvent,[17] we used the following relation derived by Van Uitert and Haas[18] between the pH-meter readings (pH*) and $-\log C_H$ $(=pC_H)$:

$$\log U_H = pC_H - pH^*,$$

where the function $\log U_H$ contains the term of activity coefficients γ_H's of the solvated proton and the liquid junction potential ΔE_j:[17]

$$-\log U_H = -\log \gamma^s_H \cdot \gamma^m_H + \Delta E_j.$$

The medium effect term γ^m_H depends on the solvent composition and the interionic attraction term γ^s_H varies with the ionic strength. The plot of pH* *vs.* pC_H gave an excellent linear relationship both in the acid and the alkaline region. The values of $\log U_H$ are thus evaluated in the range of pH*=3—12 at 25.0±0.1 °C to be −0.14±0.02 (μ=0.1) and +0.05±0.02 (μ=0.01).

Spectrophotometric Measurements of the Acid-Base Equilibria in the Mixed Solvent: The acid dissociation constants were determined spectrophotometrically with a Hitachi recording spectrophotometer Model EPS-3T. As for the Schiff bases, we used a Union Giken rapid-mixing apparatus Model MX-7 to avoid undesired hydrolysis. In the spectrophotometric measurements, potassium nitrate was used for the adjustment of the ionic strength to avoid the undesired behavior of the $NaClO_4$ as often observed on the wall of the optical cell in the case of the mixed solvents.

Kinetics of the Proton-Transfer Reactions: All measurements were carried out with a Union Giken co-axial-cable temperature-jump apparatus Model RA-105 equipped with a rapid-mixing device Model MX-7. The dead time of the mixer was about 5 ms. A temperature-rise of about 7 °C was attained within 2 μs (μ=0.1) by discharging a 0.0204 F capacitor, a co-axial cable of 200 m long, charged to 30 kV. The reaction was followed on the storage screen of an oscilloscope at the absorption maximum of the conjugated base of the Brønsted acid. All measurements were made at 25±0.1 °C.

Results

Equilibria of the Reaction. The potentiometric titrations were carried out at 25 °C and μ=0.1 and 0.01. The apparent ionic product K^c_w of water in dioxane–water medium was measured using the value of $\log U_H$ as mentioned above. A mixture of 2 V ml of the perchloric acid containing equal volume of water and dioxane was titrated with v ml of 0.1 M aqueous NaOH and v ml of dioxane in order to maintain the solvent composition at 50%(v/v). According to the fundamental theory of the acid-base equilibrium $C_H - C_{OH} = (VC^\circ_H - VC^\circ_{OH})/2(v+V)$. Before the end point, $C_H \simeq VC^\circ_H(v_e - v)/2v_e(v+V)$ and after the end point, $C_{OH} \simeq VC^\circ_H(v - v_e)/2v_e(v+V)$, where C°_H and C°_{OH} denote the analytical concentrations of $HClO_4$ and NaOH added, respectively. The values of K^c_w are calculated to be $K^c_w = C_H \cdot C_{OH} = 4.23 \times 10^{-16}$ M^2 at μ=0.1 and 2.09×10^{-16} M^2 at μ=0.01.[19]

Since compounds IV, V, and VI are readily hydrolyzed in the mixed solvent in a few minutes, the absorption spectra were rapidly scanned immediately after mixing the solutions thermostated beforehand at 25±0.1 °C. The absorption spectra of PMA are shown in Fig. 2. The slow hydrolysis reaction did *not* affect the spectrophotometric measurement of pK^c_a as revealed by a definite isosbestic point. The stoichiometric

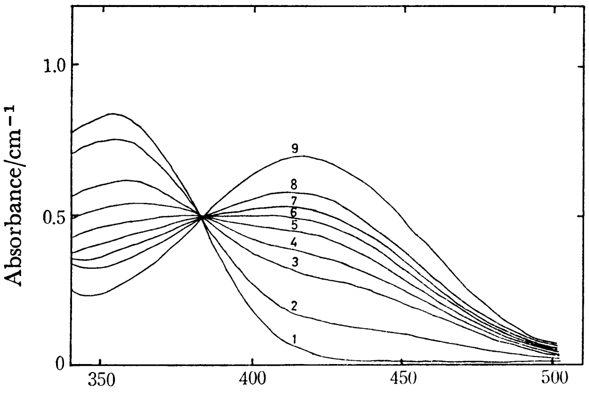
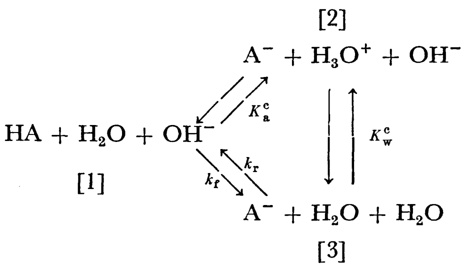


Fig. 2. Absorption spectra of *N*-(2-pyridylmethylene)-*o*-aminophenol (PMA; V) at various pH* values in 50%-(v/v) dioxane–water.
C°_{HA} (after mixing) = 1.279×10^{-4} M.
pH*: (1) about 6, (2) 8.82, (3) 10.71, (4) 11.21, (5) 11.45, (6) 11.88, (7) 12.09, (8) 12.30, (9) 0.1 M NaOH, at 25±0.1 °C, and μ=0.01 (KNO_3).

relation of the reactants is shown in the Scheme 1:



Scheme 1.

$$K_a^c = [H][A]/[HA] \quad (1)$$

$$K_b^c = k_f/k_r = [A]/[HA][OH] \quad (2)$$

$$K_w^c = [H][OH], \quad (3)$$

where [ ] represent the concentration, and charges are omitted. From Eqs. 1, 2, and 3 the following relationship is obtained:

$$K_a^c = (k_f/k_r)[H][OH] = K_b^c \cdot K_w^c. \quad (4)$$

The acid dissociation constants K_a^c's obtained spectrophotometrically are summarized in Table 1. As for PAR, the value of pK_a^c has so far been reported by several authors.[15,20]

In the present study it was found that the values of pK_a^c of the Brønsted acids increase with increasing dioxane content in the medium. The linear relationship between pK_a^c of weak acids such as acetic acid and the mole fraction of dioxane has been pointed out by Van Uitert and Haas[18] and Harned and Owen.[22] However the systematic kinetic study is needed in order to obtain the more useful information on the proton-transfer reactions in mixed solvents.

The equilibrium constant K_b^c and the rate constants for the reaction [1]⇌[3] were evaluated from the data of the temperature-jump study:

$$\tau^{-1} = k_f(\bar{C}_{OH} + \bar{C}_{HA}) + k_r. \quad (5)$$

Kinetics. Figure 3 shows a typical relaxation signal for SAT. The linear dependences of the reciprocal relaxation time on the sum of the equilibrium concentrations of the hydroxide ion and the Brønsted acid are given in Fig. 4. Serious deviation from the linear dependence of the observed τ^{-1} for the compound V at higher concentrations would be ascribed to the rising time of the temperature at μ=0.01 comparable to the relaxation time of the reaction. The measure-

Table 1. Acid dissociation constants K_a^c determined from the spectrophotometric data at 25 °C

Brønsted acid	pK_a^c(= −log K_a^c)[a] in water	pK_a^c(= −log K_a^c)[a] in 50% (v/v) dioxane-water
TPO	12.20	14.25
PAR	12.66; 12.31[b]	13.95; 13.60[b]
PAN	—	12.30[c]
SAP	—	10.48
PMA	—	11.10
SAT	—	9.10

a) K_a^c=[A][H]/[HA], μ=0.1 (KNO_3) for the azo derivatives and μ=0.01 (KNO_3) for the azomethines.
b) At 25 °C and μ=0.1 ($NaClO_4$). See Ref. 15.
c) At 25 °C and μ=0.1($NaClO_4$). See Ref. 21.

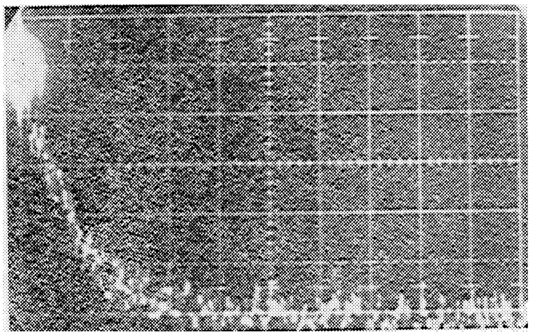


Fig. 3. A stopped-flow-temperature-jump signal for the proton-transfer reaction between *N*-salicylidene-2-amino-thiazole and OH^- ion in 50% (v/v) dioxane-water. $\bar{C}_{OH}$ (after mixing) = 7.78×10^{-6} M (pH* = 10.52), $\bar{C}_{SAT}$ = 1.05×10^{-5} M, at 25±1 °C and μ= 0.01 (KNO_3). Abscissa: 50 μs/div., ordinate: 0.1 V/div.

Table 2. Rate constants for $HA + OH^- \underset{k_r}{\overset{k_f}{\rightleftharpoons}} A^- + H_2O$ in aqueous solution at 25 °C

Brønsted acid	k_f/M^{-1} s^{-1}	k_r/s^{-1}	K_b^c (=k_f/k_r)/M^{-1}	pK_a^c (= −log K_a^c)[a]
TPO	6.9×10^5	1.6×10^4	4.5×10	12.4
PAR	6.4×10^5	6.2×10^3	1.0×10^2	12.0[b]

a) K_a^c=$K_b^c \cdot K_w^c$ at μ=0.1(KNO_3). b) At 25 °C and μ=0.1 ($NaClO_4$). See Ref. 23.

Table 3. Rate constants for $HA+OH^- \underset{k_r}{\overset{k_f}{\rightleftharpoons}} A^-+H_2O$ in 50% (v/v) dioxane-water solution at 25 °C

Brønsted acid	k_f/M^{-1} s^{-1}	k_r/s^{-1}	K_b^c (=k_f/k_r)/M^{-1}	pK_a^c (= −log K_a^c)[a]
TPO	3.2×10^5	5.8×10^3	5.5×10	14.2
PAR	4.4×10^4	1.4×10^3	2.9×10	14.5
PAN	9.7×10^5	2.4×10^3	4.0×10^2	13.3
PMA	2.8×10^8	6.2×10^4	4.5×10^3	12.0
SAP	4.4×10^7	1.3×10^4	3.2×10^3	12.2
SAT	6.1×10^8	3.6×10^3	1.7×10^5	10.5

a) K_a^c = $K_b^c \cdot K_w^c$, μ=0.1(KNO_3) for the azo compounds and μ=0.01 (KNO_3) for the azomethines.

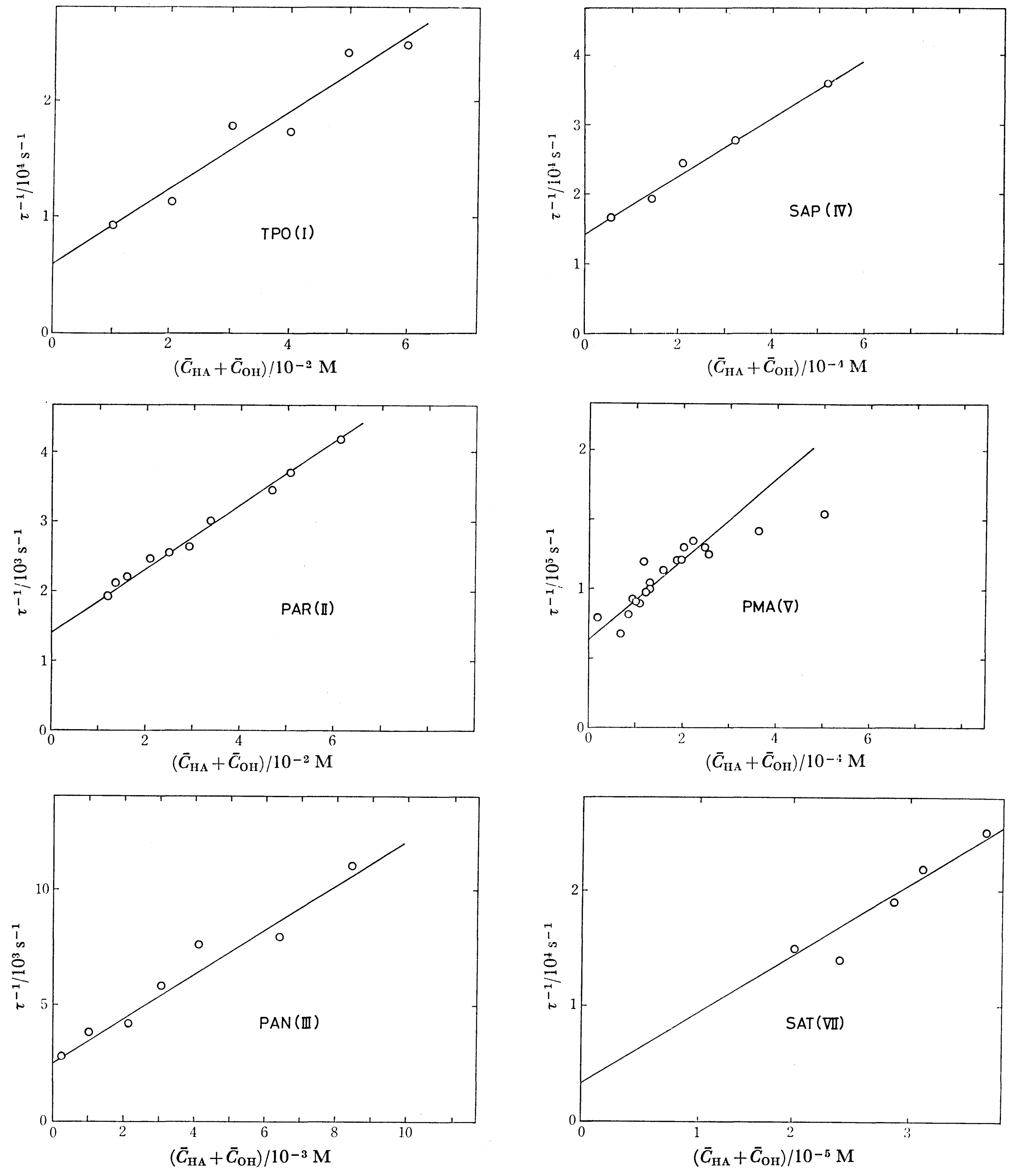


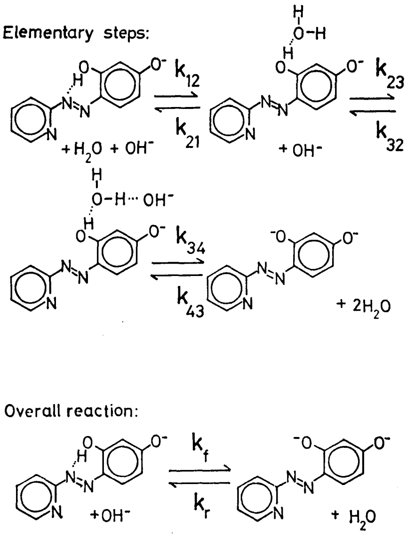
Fig. 4. Dependence of τ^{-1} on $(\bar{C}_{HA}+\bar{C}_{OH})$ for the proton-transfer reaction in 50%(v/v) dioxane-water. At 25 °C. $\mu=0.01$ (KNO_3) for azomethines (IV, V, VII) and $\mu=0.1$ (KNO_3) for azo derivatives (I—III).

ments of the rate of the proton-transfer reactions for TAN, TAR, and NAP were tried, but the observed signal-amplitude was too small.

The rate constants given in Tables 2 and 3 were calculated from the slope and the intercept of the straight lines in Fig. 4. The equilibrium constants K_a^c evaluated as $K_a^c=K_b^c \cdot K_w^c$ from the kinetic data are compared with those from the equilibrium data given in Table 1. The values are in good agreement with each other for the aqueous media, whereas in 50%(v/v) dioxane-water, the values of K_a^c derived from the *kinetic* data are always 1—2 orders of magnitude smaller than the corresponding spectrophotometric *equilibrium* constants K_a^c. As for the water-soluble Brønsted acid such as TPO these differences are quite small. The reason will be discussed in detail elsewhere.

Discussion

The overall reaction of the proton transfer is shown in Scheme 1. Equation 7 indicates that the observed increase in pK_a^c derived from the kinetic data is due to both the kinetic term $k_f/k_r = K_a^c$ and to the calculated ionic product K_w^c of water in the bulk mixed solvent. On the basis of the suggestion by Eigen *et al.*[3] concerning the proton-transfer reactions in aqueous solution, we propose the following reaction mechanism also in the mixed solvent for the recombination with OH^- ion of the Brønsted acid having an intramolecular hydrogen-bond.[24]



In the step of the intramolecular rearrangement $HA \rightleftharpoons HA^*$ the hydrogen-bonded proton sets free from the azo-nitrogen atom and interacts with a solvent *water* molecule. The second step $HA^* + OH^- \rightleftharpoons HA^* \cdots OH^-$ involves the formation and the dissociation of an encounter complex between OH^- ion and an activated Brønsted acid HA^* caused by thermal motion. The third step $HA^* \cdots OH^- \rightleftharpoons A^- + H_2O$ is the net chemical transformation involving the proton-transfer through the intervening *water* molecule and the charge-neutralization or the charge-separation.

A rate equation for such a reaction is derived as follows. In general, the stationary-state approximation is applied for HA^* and the encounter complex:

$$dC_{HA^*}/dt = 0 \tag{6}$$

$$C_{HA^*} = (k_{12}C_{HA} + k_{32}C_{enc})/(k_{21} + k_{23}C_{OH}), \tag{7}$$

and

$$dC_{enc}/dt = 0 \tag{8}$$

$$C_{enc} = (k_{12}C_{HA^*}C_{OH} + k_{43}C_A)/(k_{32} + k_{34}). \tag{9}$$

The rate equation is expressed as:

$$-dC_{HA}/dt = k_{12}C_{HA} - k_{21}C_{HA^*}. \tag{10}$$

For the small perturbation ΔC_{HA} near the equilibrium, it can be approximated as:

$$-dC_{HA}/dt = -d\Delta C_{HA}/dt \tag{11}$$

$$= \Delta C_{HA} \cdot \frac{k_{12}k_{23}k_{34}(\bar{C}_{OH} + \bar{C}_{HA}) + k_{21}k_{32}k_{43}}{k_{32}k_{21} + k_{34}k_{21} + k_{34}k_{23}\bar{C}_{OH}} \tag{12}$$

with the reciprocal relaxation time:

$$\tau^{-1} = \frac{k_{12}k_{34}k_{23}(\bar{C}_{OH} + \bar{C}_{HA}) + k_{21}k_{32}k_{43}}{k_{32}k_{21} + k_{34}(k_{21} + k_{23}\bar{C}_{OH})} \tag{13}$$

Assuming the second step is the rate-determining for the bimolecular reaction:

$$k_{21} \gg k_{23},\ k_{34} \gg k_{32}, \tag{14}$$

and considering the larger value for $k_{21} > 10^{10}\ s^{-1}$ ($k_{23} = 10^{10}\ M^{-1}\ s^{-1}$ and $\bar{C}_{OH} = 10^{-4} - 10^{-2}$ M):

$$k_{23}\bar{C}_{OH} \ll k_{21}, \tag{15}$$

the reciprocal relaxation time is reduced to

$$\tau^{-1} = K_{12}k_{23}(\bar{C}_{OH} + \bar{C}_{HA}) + k_{32}/K_{34}, \tag{16}$$

where K_{12} and K_{34} represent k_{12}/k_{21} and k_{34}/k_{43} respectively. Equations 5 and 16 lead to the most important relation:

$$k_f = K_{12}k_{23} \tag{17}$$

and

$$k_r = k_{32}/K_{34}. \tag{18}$$

The values of k_f and k_r for the proton transfer in the dioxane–water media are found to be smaller than those in aqueous media. This effect is especially remarkable in the case of PAR. If as a first approximation the k_{23} in the mixed solvent also be equal to that of $k_{23} = 10^9$—$10^{10}\ M^{-1}\ s^{-1}$ in aqueous system, this decrease in the overall rate constant k_f in the mixed solvent may primarily be attributed to the decrease in the value of the equilibrium constant K_{12}. Similarly the decrease in the k_r value is attributed to the increase in the value of equilibrium constant K_{34} assuming the change in the value of k_{32} is also small. With respect to these assumptions direct evidence is needed, which will be reported in the near future.

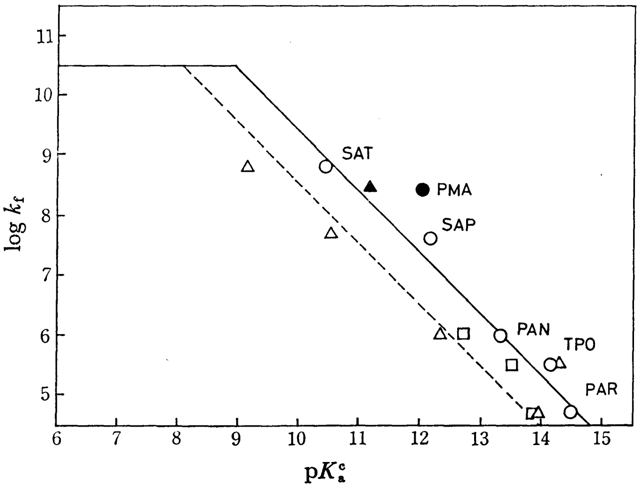


Fig. 5. Dependence of the recombination rate constants log k_f on the acid dissociation constants pK_a^c in 50%-(v/v) dioxane-water.

A full line shows the curve based on the value of $pK_w^c = 15.68$ ($\mu = 0.01$) and $pK_w^c = 15.37$ ($\mu = 0.1$). A broken line is the curve reproduced on the basis of the value measured for the azo compounds in aqueous solution. △ is the plot of log k_f *vs.* spectrophotometric pK_a^c. ○ is the plot of log k_f *vs.* kinetic pK_a^c using $pK_w^c = 15.68$ ($\mu = 0.01$). □ is the plot of log k_f *vs.* kinetic pK_a^c using $pK_w^c = 15.37$ ($\mu = 0.1$).

Figure 5 gives the Brønsted-plots with the slope $-\mathrm{d}\log k_f/\mathrm{d}\,\mathrm{p}K_a^c=1$. If the reaction approaches the diffusion-controlled limit, the rate constants k_f do not reflect the thermodynamical stability of the hydrogen-bond. For the higher pK_a^c than 9.0, the recombination rate constants k_f show the linear dependence on the basicity of the Brønsted acid. This implies that the linear-free-energy relationship holds in this system. The intramolecular hydrogen-bonds in the azomethines are weaker than those in the corresponding azo compounds even for the same type of the intramolecular hydrogen-bonds O–H···N. Therefore the value of k_f for the azomethines is by 2—3 orders of magnitude larger than that for the azo compounds. The plot for PMA having an O–H···π-type intramolecular hydrogen-bond deviates from the straight line in Fig. 5.

Since the solvation on the given Brønsted acids with dioxane is involved, in particular, on the encounter-complex species in the transition state of the proton-transfer reaction, at present we allow for a possibility for a branched path involving a more or less preferential solvation of the reaction site with dioxane molecule to inhibit the formation of the hydrogen-bridged encounter complex available as a precursor of the proton-jump step. Further studies using the mixed solvent of various dioxane contents would give valuable informations on the liquid structure of the mixed solvent which may affect the protolytic behavior of the Brønsted acids.

Finally, it would be noteworthy from the biochemical standpoints[25] that the hitherto unknown data on the rate constants k_f and k_r for the proton-transfer reactions of the Schiff base were obtained in the present work.

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Note Added in Proof:

Recently Liphard and Jost reported the mechanism of the proton-transfer reaction of Brønsted acid Alizarin Yellow GG, which has an intramolecular hydrogen bond -COO$^-$···HO-, with hydroxide ion OH$^-$ in aqueous solution. From the activation volumes of the overall reaction determined by the temperature-jump study under pressure they directly proved the existence of the first step $HA \rightleftarrows HA^*$ and pointed out the significant role of *this* step in the proton-transfer reaction $HA+OH^- \rightleftarrows A^- + H_2O$. [K. Q. Liphard and A. Jost, *Ber. Bunsenges. Physik. Chem.*, **80** (2), 125 (1976)].

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