# Kinetics and mechanism of the acid–base reaction of the diacid salts of porphyrin with pyridine in chloroform

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**The acid–base reaction of the diacid salts of 5,10,15,20-tetraphenylporphyrin [$(H_4tpp)^{2+}(X^-)_2$; $X^- = Cl^-$ and $Br^-$] with pyridine is so slow in chloroform that the reaction has been followed using a conventional stopped-flow apparatus. The reaction rate is first-order with respect to the concentrations of porphyrin and pyridine. The reaction rate is enhanced by water and suppressed by 1,4-dioxane. The rate equation is given by the following equation:**

$$-d[(H_4tpp)^{2+}(X^-)_2]/dt = k_1'[(H_4tpp)^{2+}(X^-)_2][H_2O][py] + k_2'[(H_4tpp)^{2+}(X^-)_2][H_2O]^2[py] = k_1[(H_4tpp)^{2+}(X^-)_2(H_2O)][py] + k_2[(H_4tpp)^{2+}(X^-)_2(H_2O)_2][py]$$

**The values of $k_1'$ and $k_2'$ are $(4.5 \pm 0.2) \times 10^4$ dm$^6$ mol$^{-2}$ s$^{-1}$ and $(4.3 \pm 0.3) \times 10^5$ dm$^9$ mol$^{-3}$ s$^{-1}$ for $Br^-$, and $(1.95 \pm 0.07) \times 10^4$ dm$^6$ mol$^{-2}$ s$^{-1}$ and $(1.11 \pm 0.14) \times 10^5$ dm$^9$ mol$^{-3}$ s$^{-1}$ for $Cl^-$ at 25 °C, respectively. The reaction mechanism is discussed from the viewpoint of hydration of the diacid porphyrin, pyridine and 1,4-dioxane.**

## Introduction

Porphyrins and metalloporphyrins are particularly interesting compounds for many researchers due to their widespread occurrence and important role in nature.[1] Thus, the equilibrium and kinetics of metalloporphyrin formation have been studied extensively to elucidate the mechanism of metalation of porphyrins.[1,2] In general, the reactivity of diprotonated (or diacidic) porphyrins is very low toward metalation compared with that of free base porphyrins. The free base porphyrins react with metal ions after 'rapid' deprotonation of the diprotonated porphyrins.[1,2]

The acid dissociation process of diprotonated porphyrins occurs stepwise and the difference between the deprotonation constants is very small for planar porphyrins [$pK_{a1} = 4.76$, $pK_{a2} = 4.99$ for 5,10,15,20-tetrakis(4-sulfonatophenyl)porphyrin ($H_2tpps^{4-}$) in aqueous solution],[3] while the difference is very large for deformed porphyrins substituted in the peripheral position [$pK_{a1} = 2.51$, $pK_{a2} = 7.70$ for *N*-nitrobenzyl-5,10,15,20-tetrakis(4-sulfonatophenyl)porphyrin (*p*-$NO_2tpps^{4-}$)].[4] Karaman and Bruice reported an unusual acid–base equilibrium between protonated 5,10,15,20-tetraphenylporphyrin [$(H_4tpp)^{2+}$] and Brønsted base solvents like dimethyl sulfoxide (DMSO) and *N*,*N*-dimethylformamide (DMF).[5] The diprotonated porphyrin released protons in chloroform in the presence of DMSO and DMF, but the pyridinium ion did not, though the $pK_a$ values of diprotonated porphyrin (*e.g.* $pK_{a1} = 4.8$ for $H_4tpps^{2-}$) are comparable to that of protonated pyridine ($pK_a = 5.18$).[6] The different acid–base behavior of the porphyrin and pyridine towards Brønsted bases has not been clarified yet, but it may be ascribed to the difference in the degree of solvation strength of Brønsted bases toward protonated porphyrins and the pyridinium ion in chloroform.

We found that the proton dissociation process of the diprotonated porphyrin was so slow in chloroform that the reaction could be followed using a conventional stopped-flow apparatus. We describe in this paper the kinetics of the acid–base reaction between the diacid salts of 5,10,15,20-tetraphenylporphyrin [$(H_4tpp)^{2+}(X^-)_2$; $X^- = Cl^-$, $Br^-$, $ClO_4^-$)] and pyridine in chloroform to clarify the unusual reactivity of the protonated porphyrin. Furthermore, we will discuss the effect of water and 1,4-dioxane on this reaction rate.

## Experimental

### Reagents and solvents

5,10,15,20-Tetraphenylporphyrin ($H_2tpp$, chlorin-free) was obtained from Tokyo Chemical Industry Co., Ltd. (Tokyo, Japan). Chloroform was purchased from Wako Pure Chemical Industries, Ltd. (Kyoto, Japan) and was washed five times with water to remove ethanol. Chloroform solution was stored in a bottle protected from light and used within half a day of the purification. Pyridine (Wako Pure Chemical Industries, Ltd.) was dehydrated with 4 Å molecular sieves and distilled. 1,4-Dioxane (Wako Pure Chemical Industries, Ltd.) was distilled in the presence of metallic sodium. [$^2$H]Chloroform and [$^2H_5$]-pyridine were purchased from Aldrich Chemical Company, Inc. and used as received. All other reagents were of analytical reagent grade (Wako Pure Chemical Industries, Ltd.) and used without further purification. Aqueous solutions were prepared with water distilled and deionized through a Milli-Q system (Millipore, Milli-Q.SP.TOC.).

### Procedures

Chloroform solutions of $(H_4tpp)^{2+}(X^-)_2$ ($X^- = Cl^-$, $Br^-$ or $ClO_4^-$) were prepared by solvent extraction of $(H_4tpp)^{2+}(X^-)_2$ from aqueous solutions containing 1 mol dm$^{-3}$ sulfuric acid and various concentrations of sodium chloride, sodium bromide or sodium perchlorate into chloroform. Solvent extraction was carried out by shaking organic and aqueous solutions for at least 1 h at 25 ± 1 °C in order for them to be completely equilibrated. The absorption spectra were recorded on a JASCO UVIDEC-610C Double Beam Spectrophotometer.

The acid–base reaction of $(H_4tpp)^{2+}(X^-)_2$ with pyridine was studied under the following conditions: $(3–20) \times 10^{-3}$ mol dm$^{-3}$ pyridine, $(3–50) \times 10^{-7}$ mol dm$^{-3}$ $(H_4tpp)^{2+}(X^-)_2$, $(2–7) \times 10^{-2}$ mol dm$^{-3}$ water and (0–1.5) mol dm$^{-3}$ 1,4-dioxane. The water contents were varied by mixing wet and dried chloroform solutions, the latter treated with 4 Å molecular sieves, and were measured by Karl Fisher titration on a Karl Fisher moisture titrator (MKL-200, Kyoto Electronics, Japan). The change in absorbance was monitored as a function of time at 445 nm [$\lambda_{max}$ of $(H_4tpp)^{2+}(Cl^-)_2$], 449 nm [$\lambda_{max}$ of $(H_4tpp)^{2+}(Br^-)_2$] or 440 nm [$\lambda_{max}$ of $(H_4tpp)^{2+}(ClO_4^-)_2$] using a Unisoku stopped-flow apparatus. An Otsuka Denshi RA415 rapid-scan spectro-

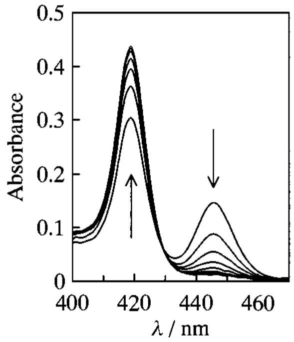

**Fig. 1** Typical change in rapid-scan spectra, recorded at an interval of 40 ms, for the reaction of $(H_4tpp)^{2+}(Cl^-)_2$ with pyridine in chloroform at $C_{water} = 4.4 \times 10^{-2}$ mol dm$^{-3}$, $C_{pyridine} = 4.9 \times 10^{-3}$ mol dm$^{-3}$ and 25 °C

photometer was used to measure the spectral change during the reaction. Association constants of water with pyridine or 1,4-dioxane were determined by a $^1H$ NMR method using a JEOL GX-270 spectrophotometer (270 MHz). All experiments except extraction were carried out at 25 ± 0.1 °C.

## Results and discussion

### Chemical composition of the protonated porphyrins in chloroform

By mixing aqueous solutions containing sulfuric acid (1.074 mol dm$^{-3}$) and sodium chloride, bromide or perchlorate with a chloroform solution containing $H_2tpp$, $H_2tpp$ in chloroform completely changed to $(H_4tpp)^{2+}(X^-)_2$. Neither the protonated porphyrin $[(H_4tpp)^{2+}(X^-)_2]$ nor the free base porphyrin ($H_2tpp$) was observed in aqueous sulfuric acid solution containing sodium halide or sodium perchlorate. On the other hand, without NaCl, NaBr or $NaClO_4$ in aqueous solution, the absorption spectrum of $H_2tpp$ ($\lambda_{max} = 418$ nm) in chloroform did not change on mixing the chloroform solution with an aqueous sulfuric acid solution (1.074 mol dm$^{-3}$); $(H_4tpp)^{2+}(SO_4^{2-})$ was not extracted into chloroform.

The chemical species of the protonated porphyrins were determined by a solvent extraction method at various concentrations of NaCl, NaBr or $NaClO_4$ using a constant concentration of sulfuric acid. The equilibrium of the solvent extraction is expressed by eqn. (1) and $K_{ex} = [(H_4tpp)^{2+}(X^-)_2]_o[H_2tpp]_o^{-1} \times [H^+]_a^{-2}[X^-]_a^{-2}$, where the subscripts o and a denote the chemical species in organic and aqueous phases, respectively. The value of log $([(H_4tpp)^{2+}(X^-)^2]_o/[H_2tpp]_o)$, which was determined from the change in absorption spectra for different values of $[X^-]_a$, was linearly correlated to $[X^-]$ with a slope of 2. Under the present experimental conditions, formation of the monoprotonated species, $(H_3tpp)^+(X^-)$, was not observed. The hydrogen ion concentration in a 1.074 mol dm$^{-3}$ $H_2SO_4$ solution was calculated to be $[H^+] = 1.15$ mol dm$^{-3}$ from the acid dissociation constant of $HSO_4^-$.[7,8] Therefore, the extraction constants of $(H_4tpp)^{2+}(X^-)_2$, $K_{ex}$, were determined to be $(2.4 \pm 0.2) \times 10^4$ for $ClO_4^-$, $(5.3 \pm 0.5) \times 10^4$ for $Br^-$ and $(9.1 \pm 0.8) \times 10^3$ for $Cl^-$.

$$[H_2tpp]_o + 2[H^+]_a + 2[X^-]_a \overset{K_{ex}}{\rightleftharpoons} [(H_4tpp)^{2+}(X^-)_2]_o \quad (1)$$

### Kinetics of acid–base reaction between the protonated porphyrins and pyridine

The reaction of $(H_4tpp)^{2+}(X^-)_2$ with pyridine was studied in the presence of large excesses of pyridine to confirm pseudo-first-order rate conditions. The reaction was so slow that it could be followed by a conventional stopped-flow method. A typical spectral change which was recorded at an interval of 40 ms is given in Fig. 1. Completion of the reaction took more than 300 ms. A clear isosbestic point (429.5 nm) was observed during the reaction. The observed rate constants determined from the change in absorbance were independent of $[(H_4tpp)^{2+}(X^-)_2]$ when the concentration of water and pyridine were constant. Hence, the kinetic equation for the reaction is given by eqn. (2), where $k_0$ is a pseudo-first-order rate constant.

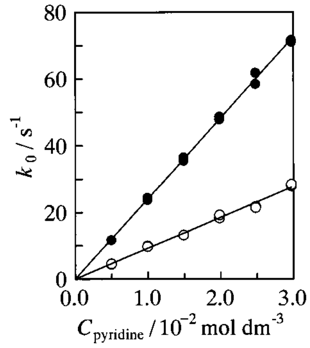

**Fig. 2** Plots of the conditional first-order rate constant $k_0$ against pyridine concentration in chloroform at $C_{water} = 4.3 \times 10^{-2}$ mol dm$^{-3}$ and 25 °C for $(H_4tpp)^{2+}(Br^-)_2$ (●) and $(H_4tpp)^{2+}(Cl^-)_2$ (○)

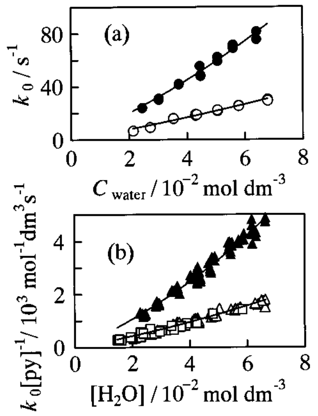

**Fig. 3** (a) Plots of the conditional first-order rate constant $k_0$ against water concentration in chloroform at $C_{pyridine} = 1.98 \times 10^{-2}$ mol dm$^{-3}$ and 25 °C for $(H_4tpp)^{2+}(Br^-)_2$ (●) and $(H_4tpp)^{2+}(Cl^-)_2$ (○). (b) Value of $k_0$/[pyridine] against monomeric water concentration in chloroform at 25 °C for $(H_4tpp)^{2+}(Br^-)_2$ (▲) and $(H_4tpp)^{2+}(Cl^-)_2$ (△) in the absence of 1,4-dioxane, and $(H_4tpp)^{2+}(Cl^-)_2$ (□) in the presence of 1,4-dioxane.

$$-d[(H_4tpp)^{2+}(X^-)_2]/dt = d[H_2tpp]/dt = k_0[(H_4tpp)^{2+}(X^-)_2] \quad (2)$$

The dependence of $k_0$ on pyridine concentration at $C_{water} = 4.3 \times 10^{-2}$ mol dm$^{-3}$ is shown in Fig. 2 for chloride and bromide salts of the protonated porphyrin. The $k_0$ value for perchlorate was too large to be determined by a stopped-flow method. Both $k_0$ for chloride and bromide increased linearly with the concentration of pyridine through a zero intercept. In order to confirm whether pre-dissociation of $(H_4tpp)^{2+}(X^-)_2$ to $(H_4tpp)^{2+}$ and $2X^-$ occurs in chloroform, we measured the conductivity of $(H_4tpp)^{2+}(X^-)_2$ in chloroform, the spectral change during the reaction using a rapid-scan spectrophotometer and the rate constants in the presence of tetrabutylammonium salts. The conductivity of $(H_4tpp)^{2+}(X^-)_2$ solution was the same as that of chloroform solution without $(H_4tpp)^{2+}(X^-)_2$. Isosbestic points and absorption peaks were not observed in the reaction except for $(H_4tpp)^{2+}(X^-)_2$ or $H_2tpp$, as shown in Fig. 1. The rate constants were independent of the concentrations of tetrabutylammonium salts at $[Bu_4NX]_t = (0–1) \times 10^{-3}$ mol dm$^{-3}$. Thus, pre-dissociation of $(H_4tpp)^{2+}(X^-)_2$ did not occur during the reaction.

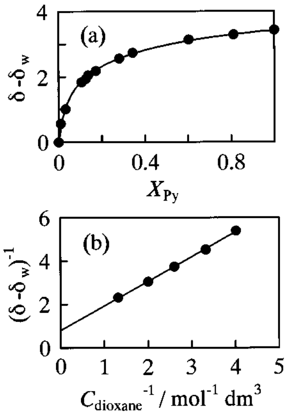

**Fig. 4** Determination of association constants of pyridine (a) or 1,4-dioxane (b) with water by a $^1$H NMR method

### Effect of water

The dependence of $k_0$ on the water concentration at $C_{pyridine} = 1.86 \times 10^{-2}$ mol dm$^{-3}$ is shown in Fig. 3(a). The observed rate constants increased with the concentration of water, but the rate constants were not first-order with respect to $H_2O$. In order to clarify the role of the water molecule in this reaction, the association constants of water and pyridine were determined by a $^1$H NMR method.[9] The following equation can be derived for the relationship between the chemical shifts of the proton in the water molecule and the mole fraction of water–pyridine complexes [eqn. (3)], where $\delta_w$ is the chemical shift of monomeric

$$\delta(X_w + X_{wpy} + X_{wpy2}) = \delta_w X_w + \delta_{wpy} X_{wpy} + \delta_{wpy2} X_{wpy2} \quad (3)$$

water in chloroform, and $\delta_{wpy}$ and $\delta_{wpy2}$ are the chemical shifts of the 1:1 water–pyridine and 1:2 water–pyridine complexes, respectively. $X_w$ is the mole fraction of monomeric water, and $X_{wpy}$ and $X_{wpy2}$ are the mole fractions of the 1:1 water–pyridine and 1:2 water–pyridine complexes, respectively. Eqn. (3) is related to the equilibrium constants of the chemical species involved in this reaction [eqn. (4)], where $X_{py}$ is the mole fraction of pyridine, $K_1 = X_{wpy}X_w^{-1}X_{py}^{-1}$ and $K_2 = X_{wpy2}X_{wpy}^{-1}X_{py}^{-1}$.

$$\delta = \delta_w + (\delta_{wpy2} - \delta_{wpy})\,(0.5K_1X_{py} + K_1K_2X_{py}^2) \times (1 + K_1X_{py} + K_1K_2X_{py}^2)^{-1} \quad (4)$$

The values of $(\delta - \delta_w)$ are plotted against the mole fraction of pyridine [Fig. 4(a)]. The values of $K_1$ and $K_2$ (expressed in mole fraction units) were determined by a least-squares minimization program and were found to be 25.2 ± 2.2 and 1.6 ± 0.6, respectively. The $K_1$ value expressed in mole fraction units can be converted to the $K_{wpy}$ value expressed in concentration units: $K_{wpy} = 2.0$ dm$^3$ mol$^{-1}$ in chloroform. The $K_{wpy}$ values determined by IR spectrophotometry were reported to be 2.4[10] and 2.6[11] in tetrachloromethane. Since the chloroform interacts with pyridine, the interaction between water and pyridine in chloroform is weaker than in tetrachloromethane.

The distributions of monomeric water, monomeric pyridine and the 1:1 water–pyridine complex under the experimental conditions for kinetic measurements are shown in Fig. 5. Although an equilibrium between monomeric water and trimeric water has been reported in chloroform, the existence of trimeric water can be ignored under the present experimental conditions due to a small equilibrium constant ($1.6 \times 10^{-3}$ dm$^6$ mol$^{-2}$).[12] Furthermore, water exists mainly as a monomer in chloroform, as reported in an NMR study.[13] With increasing concentration of water or pyridine, the concentration of monomeric water or monomeric pyridine increases linearly as shown in Fig. 5. The change in the concentrations of monomeric pyridine and the 1:1 water–pyridine complex, however, is small compared with the increase of monomeric water concentration at different concentrations of water [Fig. 5(a)]. Similarly, the change in the concentrations of monomeric water and the 1:1 water–pyridine complex is negligible for the variation of pyridine concentration [Fig. 5(b)]. From these results, the chemical species of water and pyridine which are reactive toward the protonated porphyrins are monomeric water and monomeric pyridine.

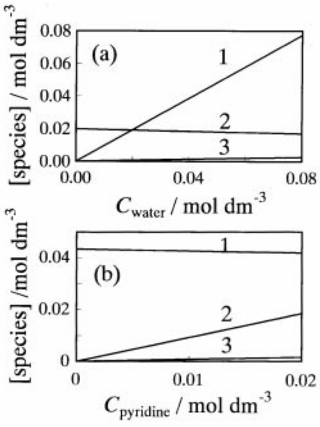

**Fig. 5** Species distribution of monomeric water (1), monomeric pyridine (2) and the 1:1 water–pyridine complex (3) at $C_{pyridine} = 1.98 \times 10^{-2}$ mol dm$^{-3}$ in various concentrations of water (a) and of pyridine (b) at $C_{water} = 4.3 \times 10^{-2}$ mol dm$^{-3}$

**Table 1** Observed rate constants for the reaction of $H_4tppX_2$ with pyridine in chloroform at 25 °C

| | $k_1'/10^4$ dm$^6$ mol$^{-2}$ s$^{-1}$ | $k_2'/10^5$ dm$^9$ mol$^{-3}$ s$^{-1}$ |
|---|---|---|
| $Br^-$ | (4.5 ± 0.2) | (4.3 ± 0.3) |
| $Cl^-$ | (1.95 ± 0.07) | (1.1 ± 0.1) |
| $Cl^{-\,a}$ | (1.75 ± 0.12) | (1.3 ± 0.3) |
| $ClO_4^-$ | Too fast | Too fast |

[a] Measured in the presence of 1,4-dioxane and determined by using the formation constant of the 1:1 water–dioxane complex.

Taking the equilibrium constants of the 1:1 and 1:2 water–pyridine complexes into consideration, the concentrations of monomeric pyridine and monomeric water were calculated and the observed rate constants divided by the concentration of monomeric pyridine are plotted against the concentration of monomeric water in Fig. 3(b). The rate constants are first- and second-order with respect to the concentration of monomeric water for all observed data at different concentrations of pyridine and water. Consequently, eqn. (2) can be rewritten as eqn. (5), where $\beta_1$ and $\beta_2$ denote the overall formation constants of

$$\begin{aligned}
&-\mathrm{d}[(H_4tpp)^{2+}(X^-)_2]/\mathrm{d}t \\
&= k_1'[(H_4tpp)^{2+}(X^-)_2][H_2O][py] + k_2'[(H_4tpp)^{2+}(X^-)_2][H_2O]^2[py] \\
&= k_1'\beta_1^{-1}[(H_4tpp)^{2+}(X^-)_2(H_2O)][py] + \\
&\qquad k_2'\beta_2^{-1}[(H_4tpp)^{2+}(X^-)_2(H_2O)_2][py] \\
&= k_1[(H_4tpp)^{2+}(X^-)_2(H_2O)][py] + \\
&\qquad k_2[(H_4tpp)^{2+}(X^-)_2(H_2O)_2][py] \quad (5)
\end{aligned}$$

$[(H_4tpp)^{2+}(X^-)_2(H_2O)]$ and $[(H_4tpp)^{2+}(X^-)_2(H_2O)_2]$, respectively. The values of $k_1'$ and $k_2'$ are summarized in Table 1.

### Effect of 1,4-dioxane

The rate of reaction of $(H_4tpp)^{2+}(Cl^-)_2$ with pyridine decreased in the presence of 1,4-dioxane as shown in Fig. 6. In order to clarify the effect of 1,4-dioxane, the association constant of water and 1,4-dioxane was determined by a $^1$H NMR method. Neglecting the formation of $H_2O(dioxane)_2$, eqn. (4) can be rearranged to eqn. (6), where $\delta_{wdio}$ is the chemical shift of

$$1/(\delta - \delta_w) = 1/(\delta_{wdio} - \delta_w) + 1/[(\delta_{wdio} - \delta_w)K_{wdio}C_{dioxane}] \quad (6)$$

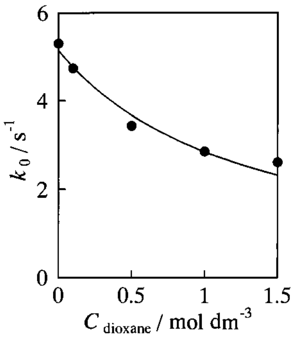

**Fig. 6** Plots of the conditional first-order rate constant $k_0$ against 1,4-dioxane concentration in chloroform at $C_{water} = 4.0 \times 10^{-2}$ mol $dm^{-3}$, $C_{pyridine} = 6.2 \times 10^{-3}$ mol $dm^{-3}$ and 25 °C. (—) was calculated from the values of $K_{wdio}$, $K_{wpy}$, $k_1'$ and $k_2'$.

the 1 : 1 water–dioxane complex and $C_{dioxane}$ is the concentration of 1,4-dioxane. The plot of the left-hand side of eqn. (6) against the concentration of 1,4-dioxane is given in Fig. 4(b). The equilibrium constant $\{K_{wdio} = [H_2O(dioxane)][H_2O]^{-1}[dioxane]^{-1}$ in concentration units$\}$ of the 1 : 1 water–dioxane complex was found to be 0.71 ± 0.04 $dm^3$ $mol^{-1}$ from the slope and intercept of Fig. 4(b). IR spectroscopic experiments also supported the formation of the 1 : 1 water–dioxane complex, which shows absorption peaks at 3489 and 3680 $cm^{-1}$. The 1 : 2 water–dioxane complex began to form at a concentration of 1,4-dioxane higher than 0.3 mole fraction, as shown by peaks at around 3520 and 3580 $cm^{-1}$. Thus, the concentration of the 1 : 2 water–dioxane complex is negligible at a concentration of 1,4-dioxane less than 2 mol $dm^{-3}$, at which the present kinetic studies were carried out.

The reaction rate of $(H_4tpp)^{2+}(Cl^-)_2$ with pyridine decreased with increasing concentration of 1,4-dioxane as shown in Fig. 6. 1,4-Dioxane associates with monomeric water, leading to a decrease in the concentration of $(H_4tpp)^{2+}(Cl^-)_2(H_2O)_{1 \text{ or } 2}$. The values of $k_1'$ and $k_2'$ were calculated by using $K_{wpy}$ and $K_{wdio}$, and are shown in Table 1. These values agree adequately with the values determined in the absence of 1,4-dioxane.

## Reaction mechanism

From the above results, the reaction of $(H_4tpp)^{2+}(X^-)_2$ with pyridine can be summarized as follows: (1) the rate constant is first-order with respect to both the protonated porphyrin and pyridine; (2) the rate constant increases with water content and is first- and second-order, respectively, with respect to water; (3) water is monomeric in chloroform and associates with pyridine and 1,4-dioxane in chloroform; (4) the rate constant decreases with the concentration of 1,4-dioxane due to the decreasing concentration of monomeric water; (5) the rate constants decrease in the order $ClO_4^- \gg Br^- > Cl^-$; (6) the reactive chemical species are the solvated porphyrins, $(H_4tpp)^{2+}(X^-)_2(H_2O)$ and $(H_4tpp)^{2+}(X^-)_2(H_2O)_2$, and monomeric pyridine. Hence, a possible reaction mechanism is given in Scheme 1.

$$H_2O + py \rightleftharpoons H_2O(py), \qquad K_{wpy} \quad (7)$$

$$H_2O + dioxane \rightleftharpoons H_2O(dioxane), \qquad K_{wdio} \quad (8)$$

$$(H_4tpp)^{2+}(X^-)_2 + H_2O \rightleftharpoons (H_4tpp)^{2+}(X^-)_2(H_2O), \qquad \beta_1 \quad (9)$$

$$(H_4tpp)^{2+}(X^-)_2 + 2H_2O \rightleftharpoons (H_4tpp)^{2+}(X^-)_2(H_2O)_2, \qquad \beta_2 \quad (10)$$

$$(H_4tpp)^{2+}(X^-)_2(H_2O) + py \longrightarrow (H_3tpp)^+(X^-)(H_2O) + HpyX, \qquad k_1 \quad (11)$$

$$(H_4tpp)^{2+}(X^-)_2(H_2O)_2 + py \longrightarrow (H_3tpp)^+(X^-)(H_2O) + HpyX(H_2O), \qquad k_2 \quad (12)$$

$$(H_3tpp)^+(X^-)(H_2O) + py \longrightarrow H_2tpp + HpyX(H_2O), \qquad \text{very fast} \quad (13)$$

**Scheme 1** Reaction mechanism for the reaction of the protonated porphyrin with pyridine in the presence of water or 1,4-dioxane

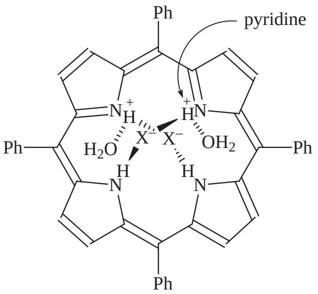

**Fig. 7** Proposed reactive intermediate for reaction of $(H_4tpp)^{2+}(X^-)_2$ with pyridine in chloroform containing water

The rate of the acid–base reaction of the protonated porphyrin with pyridine in chloroform is much slower than the rate of the reaction in aqueous solution. The reason for the slow reaction is the stabilization of the ion-pair complex, $(H_4tpp^{2+})(X^-)_2$, in chloroform. In the crystal of $(H_4tpp^{2+})(X^-)_2$, chloride is bound to the proton of $NH^+$ in the porphyrin by electrostatic interaction.[14] Hydrogen bond formation was also confirmed by IR, visible and NMR spectroscopy for the triiodide salt of diprotonated octaethylporphyrin in chloroform.[15] The stronger the interaction between $NH^+$ and the anions is, the lower the density of positive charge on the hydrogen ion of $H_4tpp^{2+}$ becomes. This leads to the slower reaction rate. The dependence of anions on the rate constants reflects the strength of ionic interaction in the ion-pair complexes in chloroform. The rate constants decreased in the order $ClO_4^- \gg Br^- > Cl^-$. Water molecules solvate the $NH^+$ and $X^-$ in $(H_4tpp^{2+})(X^-)_2$ to form $(H_4tpp^{2+})(H_2O)(X^-)_2$ or $(H_4tpp^{2+})(H_2O)_2(X^-)_2$ and weaken both the electrostatic interaction and the hydrogen bonding between $NH^+$ and $X^-$. Thus, the rate constant increases with the solvation of the protonated porphyrins. The existence of 1,4-dioxane decreases the monomeric water concentration by its association and decreases the observed rate constants. The rate determining step is the reaction of monomeric pyridine with the solvated $(H_4tpp^{2+})(H_2O)(X^-)_2$ or $(H_4tpp^{2+})(H_2O)_2(X^-)_2$ and the proposed intermediate is shown in Fig. 7.

It is interesting to compare the effect of anions on the extraction constants of $(H_4tpp^{2+})(X^-)_2$ into chloroform with the kinetic effect of the anions. The extraction constants increased in the order $Cl^- < ClO_4^- < Br^-$, but the rate constants of the protonated porphyrins, $(H_4tpp^{2+})(H_2O)(X^-)_2$ or $(H_4tpp^{2+})(H_2O)_2(X^-)_2$, increased in the order $ClO_4^- \gg Br^- > Cl^-$. The extraction constants depend on both the solvation energies of the anions in aqueous solution and the electrostatic interaction of the ion-pair complexes in chloroform. The extraction constant cannot give direct information about the interaction of the ion-pair complexes in chloroform. The kinetic data, however, directly show the stability of the ion-pair complex in chloroform and indicate the reactivity of the ion-pair complexes in chloroform. The rate constants increased in the order $Cl^- < Br^- < ClO_4^-$ as expected from the electrostatic interaction of the ion-pair complexes in chloroform.

The present paper clarifies the reactivity of the protonated porphyrin in chloroform and demonstrates the extremely slow acid–base reaction in chloroform compared to that in aqueous solutions and the importance of aquation of the ion-pair complexes for the acid–base reaction in inert organic solvents.

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