Kinetics and Mechanism for the Formation and Dissociation Reactions of 21-(4-Nitrobenzyl)-5,10,15,20-tetrakis(4-sulfonatophenyl)-23*H*-porphyrinatozinc(II) and -cadmium(II)

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(Received December 9, 1996)

The incorporation reaction of zinc(II) and cadmium(II) into 21-(4-nitrobenzyl)-5,10,15,20-tetrakis(4-sulfonatophenyl)-23*H*-porphyrin ($NO_2Bz(Htpps)^{4-}$; HP^{4-}) and the dissociation reaction of the metalloporphyrins ($[MP]^{3-}$) have been studied spectrophotometrically at $I=0.1$ mol dm^{-3} ($NaNO_3$). The formation rate of the metalloporphyrins is expressed by the following equation: $d[MP^{3-}]/dt = k^f_M[M^{2+}][HP^{4-}] + k^f_{MOH}[MOH^+][HP^{4-}] - k^d_{MP}[MP^{3-}][H^+]$. The rate constants and the activation parameters of the reaction were found to be $k^f_{Zn} = (4.86\pm0.06)\times10^2$ mol^{-1} dm^3 s^{-1} (25 °C), $\Delta H^\ddagger = 62.1\pm1.6$ kJ mol^{-1}, and $\Delta S^\ddagger = 14.8\pm5.3$ J mol^{-1} K^{-1}; $k^f_{ZnOH} = (6.39\pm0.14)\times10^3$ mol^{-1} dm^3 s^{-1} (25 °C), $\Delta H^\ddagger = 22.8\pm0.9$ kJ mol^{-1}, and $\Delta S^\ddagger = -90.2\pm3.1$ J mol^{-1} K^{-1}; $k^d_{ZnP} = 122.3\pm2.3$ mol^{-1} dm^3 s^{-1} (25 °C), $\Delta H^\ddagger = 19.8\pm2.2$ kJ mol^{-1}, and $\Delta S^\ddagger = -139\pm18$ J mol^{-1} K^{-1} for zinc(II) and $k^f_{Cd} = (1.17\pm0.02)\times10^5$ mol^{-1} dm^3 s^{-1} (25 °C), $\Delta H^\ddagger = 42.5\pm1.3$ kJ mol^{-1}, and $\Delta S^\ddagger = -5.3\pm4.2$ J mol^{-1} K^{-1}; $k^d_{CdP} = (2.51\pm0.04)\times10^7$ mol^{-1} dm^3 s^{-1} (25 °C), $\Delta H^\ddagger = 14.6\pm0.5$ kJ mol^{-1}, and $\Delta S^\ddagger = -54.3\pm1.7$ J mol^{-1} K^{-1} for cadmium(II).

Nitrobenzyl group lowers the basicity of porphyrin. The effect of the lowered basicity appeared strongly in the following order for the formation rate and equilibrium constants of the metalloporphyrins: $Cd^{2+} < Zn^{2+} < [ZnOH]^+$. A hydrogen-bond formation between $[ZnOH]^+$ and the pyrrole proton in $NO_2Bz(Htpps)^{4-}$ is proposed for the reaction based on the larger rate constant than the water-exchange rate constant enhanced by the hydroxide ion bound to zinc(II), the small activation enthalpy, the negative activation entropy, and the dependence of porphyrin basicity.

N-substituted porphyrins show some characteristic behavior compared to non-*N*-substituted porphyrins:[1] (1) the rate of metalation of *N*-substituted porphyrins is 10^3—10^5 times faster than that of non-*N*-substituted porphyrins due to the deformed structure in which the pyrrole rings in *N*-substituted porphyrins incline up- and downwards from a mean porphyrin plane; (2) the C–N bond in *N*-alkylporphyrins is cleaved by metalation and heating[2] and the nitrobenzyl groups is more easily released by the metalation of copper(II), even at room temperature;[3,4] (3) *N*-substituted porphyrins are more basic compared to non-*N*-substituted porphyrins;[5] and (4) *N*-substituted porphyrins inhibit the role of ferrocheratase, which is an enzyme that accelerates the heme synthesis.[6] Thus, *N*-substituted porphyrins are versatile compounds.

The mechanism of metalation of *N*-substituted porphyrins has been intensively studied in nonaqueous media by the Hambright,[7] Lavallee,[8] and Tanaka[9,10] groups, and a dissociative interchange mechanism has been proposed.[11] The observed rate constant (k) is given by

$$k = K_{os}K_D k_{ex}, \quad (1)$$

where K_{os} and K_D refer to the equilibrium constants of the outer-sphere association of porphyrins with metal ions and the deformation of porphyrins, respectively; k_{ex} is the solvent-exchange rate of metal ions. The rate of formation of metalloporphyrin is slower by several orders of magnitudes than that of complex formation with open-chain ligands.[10,12] The extremely slow rate of metalloporphyrin formation is due to a difficulty for a change in the structure of porphyrin in the reaction process (i.e. small K_D value). The ratio of k to k_{ex} is about 10^{-3} for Cu(II), Zn(II), Co(II), and Ni(II) for 21-methyl-5,10,15,20-tetraphenyl-23*H*-porphyrin in *N*,*N*-dimethylformamide.[11] Since these studies were carried out in nonaqueous solvents, the effect of the basicity of *N*-substituted porphyrins and of hydrolyzed metal ions on the metalation process has not been clarified in aqueous solution. In order to do this, we synthesized 21-(4-nitrobenzyl)-5,10,15,20-tetrakis(4-sulfonatophenyl)-23*H*-porphyrin ($NO_2Bz(Htpps)^{4-}$), which is a suitable porphyrin for determining the effect of a low basicity of porphyrins on the metalation rate of porphyrins due to electron-withdrawing of the nitrobenzyl group; we also studied the kinetics and mechanism of the incorporation reaction of zinc(II) and cadmium(II) into $NO_2Bz(Htpps)^{4-}$ and the dissociation reaction of the zinc(II) and cadmium(II) porphyrins in aqueous solution. The present paper focuses on the effect of the basicity of porphyrins on the metalation of *N*-substituted porphyrins and the reactivity of $[ZnOH]^+$.

Experimental

Reagents. 21-(4-Nitrobenzyl)-5,10,15,20-tetrakis(4-sulfonatophenyl)-23*H*-porphyrin was synthesized by modifying Lavallee et al.'s method,[3] and purified with Sephadex LH-20 resin. The purity

was checked by ^{1}H NMR and absorption spectra. The yield was 27.8%. ^{1}H NMR data (δ/ppm in DMF from TMS): 4.56 (2H, d, 2,6-benzyl), 7.34 (2H, d, 3,5-benzyl), −3.93 (2H, s, methylene of benzyl), 8.2—8.5 (16H, overlapped for 2,3,5,6-phenyl), 7.93 (2H, s, 2,3-pyrrole), 8.79 (2H, d, 7,8-pyrrole), 8.60 (s, 2H, 12, 13-pyrrole), 8.84 (d, 2H, 17,18-pyrrole). Sodium nitrate was purified by recrystallization of analytical-grade sodium nitrates, and used for adjusting the ionic strength. Zinc(II) and cadmium(II) nitrates were of analytical grade and used without further purification. The concentrations of Zn^{2+} and Cd^{2+} in stock solutions were determined by titration with H_4edta. Buffer solutions were prepared by the addition of nitric acid or sodium hydroxide to solutions of sodium acetate for pH 4 to 6, MES (2-morpholinoethanesulfonic acid) and PIPES (piperazine-1,4-bis(ethanesulfonic acid)) for pH 6—7.5. These buffers have negligible complexing abilities and the equilibrium constants and rate constants were not altered by the buffers ($(1.00—5.00)\times10^{-3}$ mol dm^{-3}). Most of the experiments were carried out at a concentration of 1.00×10^{-3} mol dm^{-3} buffer. All of the solutions were prepared in ultrapure water treated by a Mili-Q SP TOC (Nippon Millipore Ltd., Japan).

Apparatus. The absorption spectra were recorded on a Shimadzu UV-2100 spectrophotometer. The temperature was controlled by a Neslab RTE-100 thermostat and the temperature of the sample solution in a cuvette was directly measured using a needle-type thermometer. The pH values were determined by a Radiometer Ion 85 Analyzer with a combined electrode (GK2401 C). A 1.000×10^{-2} mol dm^{-3} nitric acid solution (I=0.1 (HNO_3–$NaNO_3$) was employed as a standard hydrogen-ion concentration ($-\log[H^+]$)=2.000). From the pH-meter reading in various hydrogen-ion concentrations, a pH-meter and electrode system was calibrated in terms of $-\log[H^+]$ at an ionic strength of 0.1 mol dm^{-3} (HNO_3–$NaNO_3$).[13,14]

Kinetic studies were carried out by mixing two solutions for a metalloporphyrin-formation reaction, i.e., one containing NO_2Bz-(Htpps)$^{4-}$, sodium nitrate, and buffer, and the other containing zinc(II) or cadmium(II) nitrate, sodium nitrate, and buffer. For the dissociation reaction of zinc(II) porphyrin, a $[Zn(NO_2Bztpps)]^{3-}$ solution containing an excess of zinc(II) was mixed with a nitric acid solution. The change in the absorbance was monitored as a function of time at 434 nm (λ_{max} of $[Zn(NO_2Bztpps)]^{3-}$) and 444 nm (λ_{max} of $[Cd(NO_2Bztpps)]^{3-}$) by an Otsuka Denshi RA415 stopped-flow apparatus.

Results

Equilibrium of $[Cd(NO_2Bztpps)]^{3-}$. The formation constants of [Zn- and $Cd(NO_2Bztpps)]^{3-}$ are essential for determining the chemical species involved in the reaction and elucidating the reaction mechanism. Since we reported the formation constant of $[Zn(NO_2Bztpps)]^{3-}$ previously,[15] we determined, here, the formation constant of $[Cd(NO_2Bztpps)]^{3-}$ at 15,20,25, and 30 °C in I=0.1 $NaNO_3$ mol dm^{-3} under the following conditions: $C_{Cd}=(1\times10^{-5}$ to $2.0\times10^{-3})$ mol dm^{-3}, pH=6.98 ([PIPES]$=1.00\times10^{-3}$ mol dm^{-3}), $[NO_2Bz(Htpps)^{4-}]=1.19\times10^{-6}$ mol dm^{-3}.

The formation constant of the cadmium(II) porphyrin is defined as $K_{CdP}=[CdP^{3-}][H^+][Cd^{2+}]^{-1}[HP^{4-}]^{-1}$,[16] where HP^{4-} and $[CdP]^{3-}$ denote the free base porphyrin anion $NO_2Bz(Htpps)^{4-}$ and the corresponding cadmium(II) complex anion, $[Cd(NO_2Bztpps)]^{3-}$, respectively. Since the 21-(4-nitrobenzyl)-15,10,15,20-tetrakis(4-sulfonatophenyl)-23*H*-porphyrin anion exists in the free base form, NO_2Bz-(Htpps)$^{4-}$ (abbr. HP^{4-}) and 22,24-protonated form, NO_2Bz-(H_2tpps)$^{3-}$ (abbr. H_2P^{3-}) in neutral pH,[4,17] the apparent molar absorptivity (ε) at 444 nm, the absorbance divided by the total concentration of porphyrin, is given by following equations for the formation of $[Cd(NO_2Bztpps)]^{3-}$:

$$\varepsilon=\frac{\text{Abs.}}{C_{H_2P}}=\frac{\varepsilon_1[HP^{4-}]+\varepsilon_2[H_2P^{3-}]+\varepsilon_{CdP}[CdP^{3-}]}{[HP^{4-}]+[H_2P^{3-}]+[CdP^{4-}]} \quad (1)$$

$$=\frac{\varepsilon_1+\varepsilon_2K_2[H^+]+\varepsilon_{CdP}K_{CdP}[Cd^{2+}][H^+]^{-1}}{1+K_2[H^+]+K_{CdP}[Cd^{2+}][H^+]^{-1}}, \quad (2)$$

where, ε_1, ε_2, and ε_{CdP} are the molar absorptivities of HP^{4-}, H_2P^{3-}, and $[CdP]^{3-}$, respectively. The K_2 is protonation constant of the free-base form of $NO_2Bz(Htpps)^{4-}$, defined as $K_2=[H_2P^{3-}][HP^{4-}]^{-1}[H^+]^{-1}$, and the equilibrium constant and the thermodynamic parameters are as follows: $\log K_2=7.75\pm0.02$ mol^{-1} dm^3 (25 °C); $\Delta H°=-21.2\pm0.5$ kJ mol^{-1}; $\Delta S°=77\pm1$ J mol^{-1} K^{-1}.[15] The observed absorbance is plotted against the concentration of cadmium(II) in Fig. 1 at 15, 20, 25, and 30 °C. The value of K_{CdP} was determined by a nonlinear least-squares minimization program of Eq. 2, and was found to be $\log K_{CdP}=-2.19\pm0.05$ (25 °C); $\Delta H°=21.1\pm0.7$ kJ mol^{-1}; $\Delta S°=29.1\pm2.5$ J mol^{-1} K^{-1}. The solid lines in Fig. 1 were drawn by using the determined value of $[Cd(NO_2Bztpps)]^{3-}$. The value are summarized in Table 1 with the value of $[Zn(NO_2Bztpps)]^{4-}$; the species

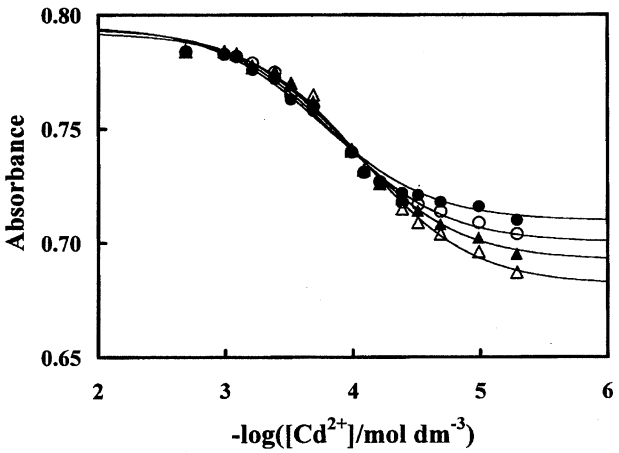

Fig. 1. Change in absorbance at various concentrations of cadmium(II) and temperatures of 15 (●), 20 (○), 25 (▲), and 30 (△) °C in I=0.1 mol dm^{-3} ($NaNO_3$). pH=6.98; $[NO_2Bz(Htpps)^{4-}]=2.72\times10^{-6}$ mol dm^{-3}.

Table 1. Equilibrium Constants and Thermodynamic Parameters of Protonation and Metalation of NO_2Bz-(Htpps)$^{4-}$ with Zinc(II) and Cadmium(II)[a]

	$\log K_2$[b,c]	$\log K_{ZnP}$[c]	$\log K_{CdP}$
25 °C	7.75±0.02	0.63±0.02	−2.19±0.05
$\Delta H°$/kJ mol^{-1}	−21.2±0.05	31.8±0.8	21.0±0.7
$\Delta S°$/J mol^{-1} K^{-1}	77±1	116±3	29.1±2.5

a) I=0.1 mol dm^{-3} ($NaNO_3$). b) Unit in mol^{-1} dm^3. c) Ref. 15.

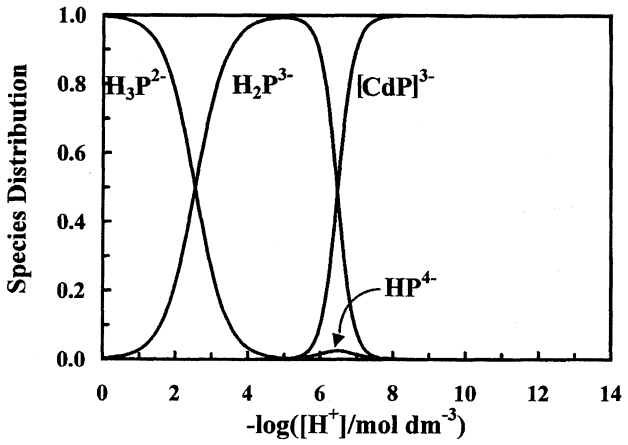

Fig. 2. Species distribution of $NO_2Bz(Htpps)^{4-}$ and $[Cd(NO_2Bztpps)]^{3-}$ at $[Cd^{2+}]=10^{-3}$ mol dm^{-3} and $[NO_2Bz(Htpps)^{4-}]=1.00\times10^{-6}$ mol dm^{-3} in various pHs.

distribution of $[Cd(NO_2Bztpps)]^{3-}$ is shown in Fig. 2.

Kinetics of Incorporation of Zinc(II) and Cadmium(II) into $NO_2Bz(Htpps)^{4-}$. (a) Reaction of Zinc(II) with $NO_2Bz(Htpps)^{4-}$. The rate of incorporation of zinc(II) into $NO_2Bz(Htpps)^{4-}$ was studied in a large excess of zinc(II) in order to ensure the pseudo-first-order conditions. The observed first-order rate constant (k_0), determined from the change in the absorbance at 434 nm, is plotted against the concentration of zinc(II) at pH 6.85 ([PIPES]$=1.00\times10^{-3}$ mol dm^{-3}) and at 15, 25, and 35 °C in Fig. 3. The rate constant is proportional to the concentration of zinc(II), and the reverse reaction is negligible. Figure 4 shows the pH dependence of the observed first-order rate constant at 15, 20, 25, 30, and 35 °C. The rate constants gradually increase with pH. The large rate constants at higher pH are ascribed to the hydrolysis of zinc(II) and the deprotonation of H_2P^{3-}. The hydrolysis constant of aquazinc(II) is $K^h_{Zn}=[ZnOH^+][H^+][Zn^{2+}]^{-1}$, 6.76×10^{-10} mol dm^{-3} (25 °C); $\Delta H°=56$ kJ mol^{-1}; $\Delta S°=12$ J mol^{-1} K^{-1}.[18] The acidic form of the

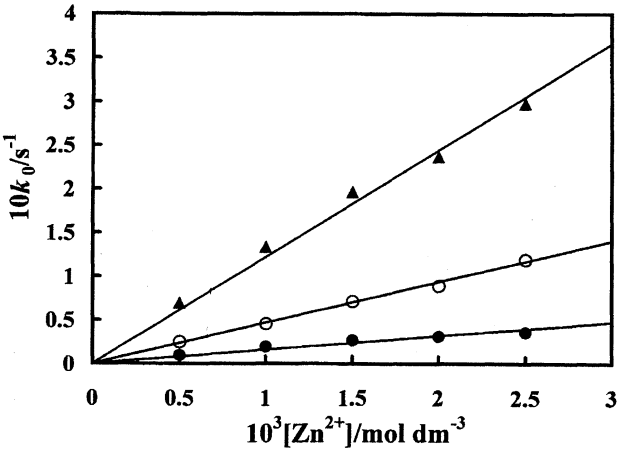

Fig. 3. Plot of the observed rate constant, k_0, for the reaction of $NO_2Bz(Htpps)^{4-}$ with zinc(II) at 15 (●), 25 (○), and 35 (▲) °C in $I=0.1$ mol dm^{-3} ($NaNO_3$). pH=6.85; $[NO_2Bz(Htpps)^{4-}]=1.14\times10^{-6}$ mol dm^{-3}.

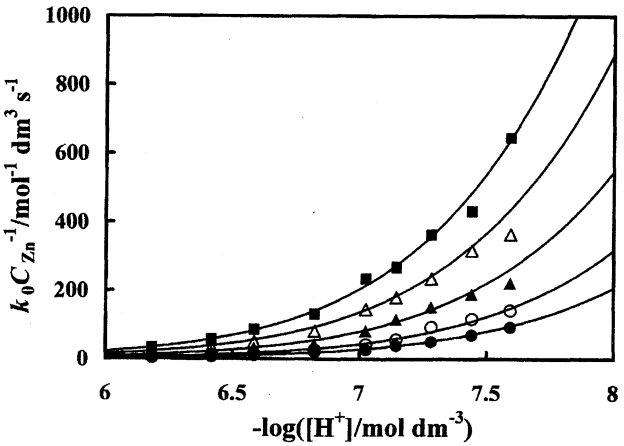

Fig. 4. Dependence of the rate constant, $k_0C_{Zn}^{-1}$, on pH for the reaction of zinc(II) with $NO_2Bz(Htpps)^{4-}$ at 15 (●), 20 (○), 25 (▲), 30 (△), and 35 (■) °C in $I=0.1$ mol dm^{-3} ($NaNO_3$). $C_{Zn}=1.01\times10^{-3}$ mol dm^{-3}; $[NO_2Bz(Htpps)^{4-}]=1.14\times10^{-6}$ mol dm^{-3}.

porphyrin, H_2P^{3-}, is an unreactive species, and the free-base form, HP^{4-}, reacts with metal ions. Thus, the rate of incorporation of zinc(II) into $NO_2Bz(Htpps)^{4-}$ is expressed by the following equations:

$$H_2P^{3-} \overset{K_2^{-1}}{\rightleftharpoons} HP^{4-} + H^+ \quad (3)$$

$$Zn^{2+} \overset{K_h}{\rightleftharpoons} [ZnOH]^+ + H^+ \quad (4)$$

$$Zn^{2+} + HP^{4-} \xrightarrow{k^f_{Zn}} [ZnP]^{3-} + H^+ \quad (5)$$

$$[ZnOH]^+ + HP^{4-} \xrightarrow{k^f_{ZnOH}} [ZnP]^{3-} + H_2O \quad (6)$$

The conditional first-order rate constant (k_0) is correlated with the above equilibrium and rate constants as follows:

$$k_0 = \frac{(k^f_{Zn} + k^f_{ZnOH}K^h_{Zn}[H^+]^{-1})C_{Zn}}{(1+K_2[H^+])(1+K^h_{Zn}[H^+]^{-1})}, \quad (7)$$

where $C_{Zn}=[Zn^{2+}]+[ZnOH^+]$. The rate constants, k^f_{Zn} and k^f_{ZnOH}, were determined by a nonlinear least-squares minimization program of Eq. 7, and are summarized in Table 2 along with the activation enthalpies and entropies. The solid curves in Fig. 4 are lines calculated from the determined value.

(b) Reaction of Cadmium(II) with $NO_2Bz(Hpps)^{4-}$. The rate constants for the reaction of cadmium(II) with $NO_2Bz(Htpps)^{4-}$ (1.19×10^{-6} mol dm^{-3}) were determined at pH 6—7.5 in the presence of a large excess of cadmium(II) from the change in absorbance at 444 nm. The observed rate constant is plotted against the concentration of cadmium(II) at pH 6.1, 6.6, and 7.1 (Fig. 5). Although the rate constant increases linearly with the concentration of cadmium(II), the straight lines give interceptions at pH 6.1 and 6.6, $[Cd(NO_2Bztpps)]^{3-}$ is not formed completely at low pH, and a reverse reaction occurs; this is also supported by an equilibrium study (see Fig. 2). The rate constants measured at different pHs and temperatures (15, 20,

Table 2. Kinetic and Activation Parameters for the Formation and Dissociation of [Zn- and $Cd(NO_2Bztpps)]^{3-}$ a)

	$k^f/mol^{-1}\,dm^3\,s^{-1}$			$k^d/mol^{-1}\,dm^3\,s^{-1}$	
	Zn^{2+}	$[ZnOH]^+$	Cd^{2+}	$[ZnP]^{3-}$	$[CdP]^{3-}$
25 °C	$(4.86\pm0.069)\times10^2$	$(6.39\pm0.14)\times10^3$	$(1.17\pm0.02)\times10^5$	122.3±2.3	$(2.51\pm0.04)\times10^7$
$\Delta H^{\ddagger}$ / kJ mol^{-1}	62.1±1.6	22.8±0.9	42.5±1.3	19.8±2.2	14.6±0.5
$\Delta S^{\ddagger}$ / J mol^{-1} K^{-1}	14.8±5.3	−90.2±3.1	−5.3±4.2	−139±18	−54.3±1.7

a) I=0.1 mol dm^{-3} ($NaNO_3$).

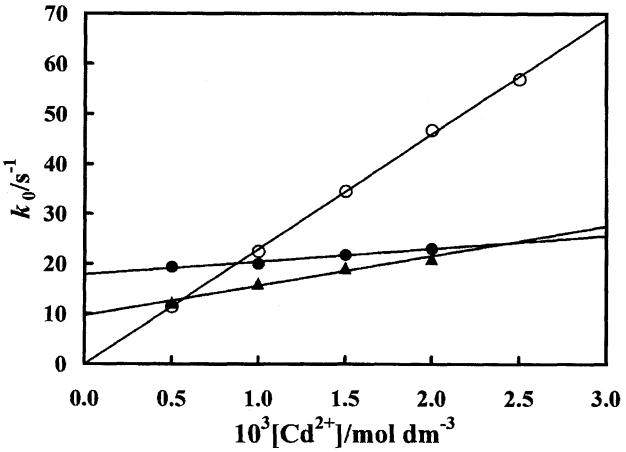

Fig. 5. Dependence of the observed rate constant, k_0, on the concentration of cadmium(II) at pH 6.1 (●), 6.6 (▲), and 7.1 (○), and at 25 °C in I=0.1 mol dm^{-3} ($NaNO_3$). $[NO_2Bz(Htpps)^{4-}]=1.19\times10^{-6}$ mol dm^{-3}.

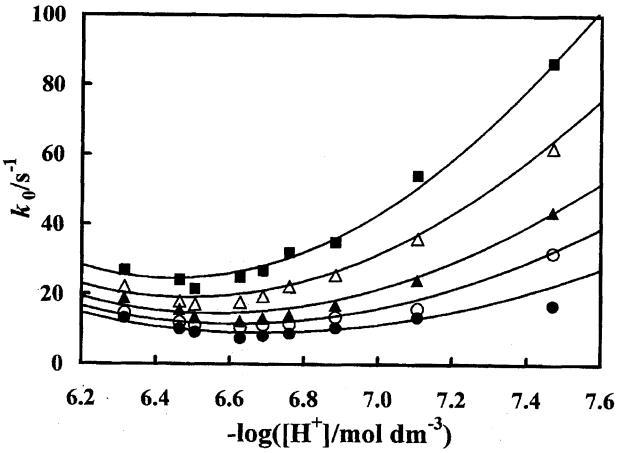

Fig. 6. Dependence of the observed rate constant, k_0, on pH at 15 (●), 20 (○), 25 (▲), 30 (△), and 35 (■) °C in 0.1 mol dm^{-3} ($NaNO_3$). $C_{Cd}=1.03\times10^{-3}$ mol dm^{-3}; $[NO_2Bz(Htpps)^{4-}]=1.14\times10^{-6}$ mol dm^{-3}.

25, 30, and 35 °C) are given in Fig. 6. Free-base porphyrin reacts with aquacadmium(II), and the hydrolysis of the cadmium(II) ion is neglected at pH 6 to 7.5 because of its small hydrolysis constant ($K^h_{Cd}=[CdOH^+][H^+][Cd^{2+}]^{-1}=4.72\times10^{-11}$ mol dm^{-3}).[18] Thus, the reaction of cadmium(II) with $NO_2Bz(Htpps)^{4-}$ is expressed

$$Cd^{2+} + HP^{4-} \underset{k^d_{CdP}}{\overset{k^f_{Cd}}{\rightleftharpoons}} [CdP]^{3-} + H^+. \quad (8)$$

Taking the protonation of $NO_2Bz(Htpps)^{4-}$ (Eq. 3) into account, we have

$$k_0 = \frac{k^f_{Cd}[Cd^{2+}]}{1+K_2[H^+]} + k^d_{CdP}[H^+]. \quad (9)$$

The rate constants of k^f_{Cd} and k^d_{CdP} were calculated by a least-squares minimization program of Eq. 9; the results are summarized in Table 2. The calculated lines are given in Fig. 6 as the solid lines. Since the hydrolysis constant of cadmium(II) is low and cadmium(II) hydroxide precipitated at higher pH than 8, we were not able to observe a reaction path of $[CdOH^+]$ under the present experimental conditions.

Dissociation Reaction of $[Zn(BzNO_2tpps)]^{3-}$ and $[Cd(NO_2Bztpps)]^{3-}$. The zinc(II) porphyrin forms quantitatively at pH 6—7, but dissociates at pH<3. Thus, the proton-assisted dissociation rate constant of $[Zn(NO_2Bztpps)]^{3-}$ was determined by the addition of nitric acid to a $[Zn(NO_2Bztpps)]^{4-}$ solution at 15, 20, 25, and 30 °C. The rate constant is proportional to the concentration of the hydrogen ion (Fig. 7) and independent of the concentration of zinc(II). A self-dissociation process of $[Zn(NO_2Bztpps)]^{4-}$ that is independent of the hydrogen ion is negligible. The

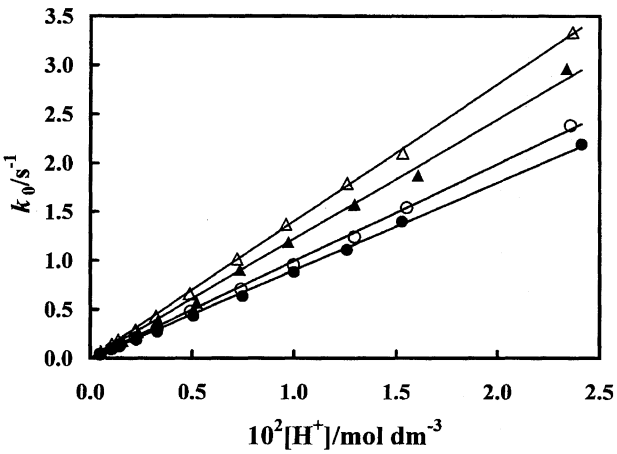

Fig. 7. Dependence of the dissociation rate constant, k_0, of $[Zn(NO_2Bztpps)]^{3-}$ at various hydrogen ion concentration at 15 (●), 20 (○), 25 (▲), and 30 (△) °C in I=0.1 mol dm^{-3} ($NaNO_3$). $C_{Zn}=1.00\times10^{-5}$ mol dm^{-3}; $[NO_2Bz(Htpps)^{4-}]=1.92\times10^{-6}$ mol dm^{-3}.

value of k^{d}_{ZnP} was determined from the slope shown in Fig. 7.

Since the formation constant of $[Cd(NO_2BzBztpps)]^{3-}$ is small compared to that of $[Zn(NO_2Bztpps)]^{3-}$, $[Cd(NO_2Bztpps)]^{3-}$ partly dissociates in pH 6—7 (Fig. 2). Thus, the proton-assisted dissociation rate constant of $[Cd(NO_2Bztpps)]^{3-}$ was determined together with the formation rate constant, k^{f}_{Cd} (Eq. 9). The rate constants and activation parameters for the dissociation reactions of Zn(II)- and $[Cd(NO_2Bztpps)]^{3-}$ are summarized in Table 2.

Discussion

Equilibrium Constants of [Zn- and Cd(NO_2Bztpps)]$^{3-}$. The equilibrium constants of metalloporphyrins depend on the structure of the porphyrins and the ionic radii of the metal ions: Planar nondeformed porphyrins are suitable for medium-sized metal ions to accommodate well into the porphyrin core. For example, the equilibrium constant of zinc(II) with 5,10,15,20-tetrakis(4-sulfonatophenyl)-21*H*, 23*H*-porphyrin, which is a non-*N*-substituted porphyrin, is larger than 10^9-times compared to that of the cadmium(II) porphyrin, since the ionic radius of cadmium(II) (92 pm) is too large for the radius of the porphyrin core.[19] The equilibrium constant of zinc(II) with $NO_2Bz(Htpps)^{4-}$, however, is only 660-times larger than that of the cadmium(II) porphyrin. Similarly, the equilibrium constants of zinc(II) with 21-methyl-5,10,15,20-tetrakis(4-sulfonatophenyl)-23*H*-porphyrin ($Me(Htpps)^{4-}$) is 2.1×10^3-times larger than that of cadmium(II).[20] These *N*-substituted porphyrins, especially $NO_2Bz(Htpps)^{4-}$, decrease the difference in the equilibrium constants between zinc(II) and cadmium(II) porphyrins compared to nondeformed porphyrins, due to the deformation of *N*-substituted porphyrins. Furthermore, the nitrobenzyl group in $NO_2Bz(Htpps)^{4-}$ lowers the basicity of porphyrin by 13.3-times compared to that of $Me(Htpps)^{4-}$. However, the equilibrium constants of the metalloporphyrins of zinc(II) and cadmium(II) with $NO_2Bz(Htpps)^{4-}$ decrease 6.2- and 1.8-times for Zn(II) and Cd(II), respectively. The effect of the electron-withdrawing of the nitrobenzyl group in $NO_2Bz(Htpps)^{4-}$ appears strongly in the order $Cd^{2+}<Zn^{2+}<H^+$. Since cadmium(II) can not fit well in porphyrin core, the equilibrium constants of cadmium(II) with *N*-substituted porphyrins are small, and are not seriously affected by a change in the porphyrin basicity.

Reaction of $NO_2Bz(Htpps)^{4-}$ with Zn^{2+} and Cd^{2+}. Because of the deformed structure of *N*-substituted porphyrins, the metalation reaction of *N*-substituted porphyrins proceeds more rapidly than do non-*N*-substituted porphyrins. $NO_2Bz(Htpps)^{4-}$ is 430- and 221-times more reactive than H_2tpps^{4-} for the metalation reaction of zinc(II) and cadmium(II), respectively. Similarly, the ratios of the metalation of $Me(Htpps)^{4-}$ to H_2tpps^{4-} are 1.85×10^3 and 4.84×10^2 for zinc(II) and cadmium(II), respectively. Thus, the incorporation rate of zinc(II) and cadmium(II) into *N*-substituted porphyrins is faster by a few hundred to thousand times than non-*N*-substituted porphyrins; however, the enhancement of metalation is small for cadmium(II). Furthermore, the ratio of the rate constants of $Me(Htpps)^{4-}$ to $NO_2Bz(Htpps)^{4-}$ is only 2.2 for the incorporation of cadmium(II). Cadmium(II) does not require a very large change in the conformation of the porphyrin core before incorporating cadmium(II), due to its large ionic radius. Thus, the effect of a change in the structure of porphyrins is small for the incorporation rate of cadmium(II).

For non-*N*-substituted porphyrins, the basicity of porphyrin is an important factor governing the rate of metalloporphyrin formation, which has been linearly correlated to protonation constant of free-base porphyrin. The slopes of the straight lines are 0.7 and 0.42 for copper(II)[21] and cadmium(II)[22] in aqueous solution, respectively. However, the effect of the basicity of *N*-substituted porphyrins has not been studied in detail, because of the difficulty to synthesize porphyrins having a lower basicity, such as $NO_2Bz(tpps)^{4-}$. The nitrobenzyl group in $NO_2Bz(Htpps)^{4-}$ withdraws an electron and decreases the basicity of porphyrin. The first protonation constants ($\log K_2$/mol^{-1} dm^3 at 25 °C) of the free-base *N*-substituted porphyrins are 7.76 for $NO_2Bz(Htpps)^{4-}$, 8.82 for $Me(Htpps)^{4-}$, 9.93 for 21-phenyl-5,10,15,20-tetrakis(4-sulfonatophenyl)-23*H*-porphyrin ($Ph(Htpps)^{4-}$), and 9.94 for 15,21-diphenyl-5,10,20-tris(sulfonatophenyl)-23*H*-porphyrin ($Ph(Htpps_3)^{3-}$.[15,20,23] The rate constants for the incorporation of zinc(II) into *N*-substituted porphyrins are 4.86×10^2 for $NO_2Bz(Htpps)^{4-}$, 2.1×10^3 for $Me(Htpps)^{4-}$, 5.3×10^3 for $Ph(Htpps)^{4-}$, and 2.8×10^3 mol^{-1} dm^3 s^{-1} for $Ph(Htpps_3)^{3-}$.[20,23] The rate constants are plotted against the first protonation constants of the *N*-substituted porphyrins together with the rate constants of $[ZnOH]^+$ in Fig. 8. The rate constant increases with the basicity of the *N*-substituted porphyrin; the slopes are 0.4 and 1.1 for Zn^{2+} and $[ZnOH]^+$, respectively. The basicity of *N*-substituted prophyrins affects the metalation rate as well as non-*N*-substituted porphyrins.[24] Consequently, the formation of an intermediate of a sitting-atop complex (SAT complex) in which Zn^{2+} or $[ZrOH]^+$ interacts with *N*-substituted porphyrins is implied before the final incorporation of

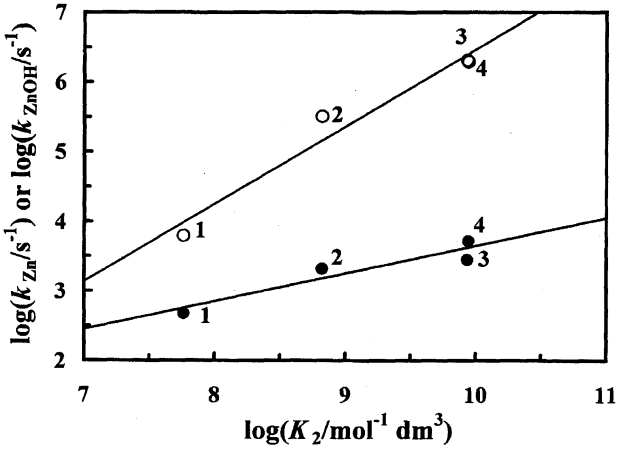

Fig. 8. A correlation between the rate constant for the reaction of Zn^{2+} (●) or $[ZnOH]^+$ (○) with *N*-substituted porphyrins and their first protonation constant ($\log K_2$) for (1), $NO_2Bz(Htpps)^{4-}$; (2), $Me(Htpps)^{4-}$; (3), $Ph(Htpps_3)^{3-}$; (4), $Ph(Htpps)^{4-}$.

the metal ions into the porphyrin core.

Reaction of $[ZnOH]^+$ with $NO_2Bz(Htpps)^{4-}$. The reaction of $[ZnOH]^+$ with $NO_2Bz(Htpps)^{4-}$ is faster than Zn^{2+}, and the rate constant of $[ZnOH]^+$, as shown in Fig. 8, depends greately on the porphyrin basicity. The ratios of the rate constants, k^f_{ZnOH}/k^f_{Zn}, are 13 for $NO_2Bz(Htpps)^{4-}$, 157 for $Me(Htpps)^{4-}$, and 377 for $Ph(Htpps)^{4-}$. Such a rate enhancement is also reflected in the decreasing activation enthalpy of $[ZnOH]^+$: $\Delta H^{\ddagger}$(ZnOH)/kJ mol^{-1} are 22.8 for $NO_2Bz(Htpps)^{4-}$, 18 for $Me(Htpps)^{4-}$, and 34 for $Ph(Htpps)^{4-}$. These activation enthalpies of $[ZnOH]^+$ are less than half of Zn^{2+}. The increased rate constants of $[ZnOH]^+$ were also observed for other non-*N*-substituted porphyrins by Thompson and Krishnamurthy[25] and Hambaight et al.[26,27] They have ascribed the enhanced rate constants to a more rapid water-exchange rate and differing geometry of the hydrolyzed zinc species. However, the increased rate constants of $[ZnOH]^+$ for the metalation of porphyrins are too large for the water-exchange rate enhanced by the bonding of hydroxo ligand, as described bellow.

Tanaka and Yamada extensively studied the labilizing effect of a bound ligand, A, on the water-exchange reaction at a metal M and have proposed the equation $\log k_{MA}^{-H_2O} = \log k_M^{-H_2O} + \gamma E(A)$, where $k_{MA}^{-H_2O}$ and $\log k_M^{-H_2O}$ denote the water-exchange rate of MA and M, respectively, and γ is a value which depends on metal M, and E(A) is the electron-donor ability of ligand A.[28,29] They determined the γ value of Zn^{2+} (γ=0.3) from a kinetic study of the reaction of Zn^{2+} with 1,10-phenanthroline. When A=OH^-, the value of E(A) is 1.65. Thus, the water-exchange rate of $[ZnOH]^+$ increases 3-times compared to that of Zn^{2+}. However, $[ZnOH]^+$ reacts with *N*-substituted porphyrins 13—377 times faster than does Zn^{2+}.

The large enhancement by a hydroxide ion bound to zinc(II) suggests another reaction mechanism for the metalation of *N*-substituted porphyrin with $[ZnOH]^+$ in addition to the labilization of a water molecule by OH^-. The possible mechanism is a hydrogen bonding of a pyrrole proton in porphyrin with the oxygen atom in $[ZnOH]^+$:

$$[ZnOH]^+ + NO_2Bz(Htpps)^{4-} \overset{K}{\rightleftarrows} [ZnO(H)\cdots H \text{ of pyrrole in } NO_2Bz(Htpps)]^{3-}$$

intermediate

$$\xrightarrow{\text{r.d.s}} [Zn(NO_2Bztpps)]^{3-} + H_2O \qquad (10)$$

Taking the formation of the intermediate into account, the over-all rate constant (k) in Eq. 1 can be rearranged as follows for the reaction of $[ZnOH]^+$ with $NO_2Bz(Htpps)^{4-}$:

$$k = KK_{os}K_Dk_{ex}. \qquad (11)$$

The k value increases with the equilibrium constant K.

N-substituted porphyrins are deformed, and the pyrrole rings are tilted toward up and down from the mean porphyrin plane. Thus, the formation of hydrogen bonding becomes easy for *N*-substituted porphyrins. The hydrogen-bonding mechanism can also be supported by large negative activation entropies (J mol^{-1} K^{-1}), such as -90.2 for $NO_2Bz(Htpps)^{4-}$, -11.8 for $Ph(Htpps)^{4-}$, and -80 for $Me(Htpps)^{4-}$. The large slope for $[ZnOH]^+$ compared to that of Zn^{2+}, as shown in Fig. 8, indicates the stabilization of an intermediate of Eq. 10 with the basicity of *N*-substituted porphyrins by hydrogen bonding.

The zinc(II) hydroxide ion reacts with *N*-substituted porphyrin more associatively than does aquazinc(II). Since the such enhancement by a hydroxide ion has not been observed for the reaction of open-chain ligands, such as 1,10-phenanthroline with $[ZnOH]^+$, the deprotonation process of pyrrole is an important factor in the metalation of porphyrins.

Dissociation Reaction of [Zn(II)- and Cd(II)-$(NO_2Bztpps)]^{3-}$. The rate constant of the dissociation reaction (k^d_{MP}) was determined for [Zn- and Cd-$(NO_2Bztpps)]^{3-}$. Since the ionic radius of cadmium(II) is larger (r=92 pm) than that of zinc(II) (r=74 pm), cadmium(II) can be easily replaced with a proton. The ratio of the rate of the proton-assisted dissociation reaction of Cd^{2+} to Zn^{2+} is 2.05×10^5 for $NO_2Bz(Htpps)^{4-}$. We previously reported on the proton-assisted dissociation reaction of zinc(II) and cadmium(II) complexes of non-*N*-substituted porphyrins.[17] The reaction rate constants were 5.49×10^{12} and 9.37 mol^{-2} dm^6 s^{-1} for [Cd- and Zn(tpps)]$^{4-}$, respectively; the ratio of the rate constants of cadmium(II) and zinc(II) is 5.8×10^{11}. The large difference has been developed to a trace-determination method of zinc(II) in a large excess of cadmium(II).[30] Although *N*-substituted porphyrins diminish the difference in the dissociation rate constants between zinc(II) and cadmium(II) porphyrins, the difference in reactivity of zinc(II) and cadmium(II) porphyrins is still large compared to those of the metal complexes of other open-chain ligands.[12]

Conclusion

The kinetics and equilibrium studies concerning the reaction of zinc(II) and cadmium(II) with $NO_2Bz(Htpps)^{4-}$ have clarified the following interesting points: 1) Although the lower basicity of the *N*-nitrobenzyl-substituted porphyrin decreases the equilibrium constants and the rate constants of zinc(II) and cadmium(II) porphyrins, the effect is smaller for cadmium(II) due to its large ionic radius compared to that of zinc(II). 2) Hydroxozinc(II) shows a higher reactivity for metalation of *N*-substituted porphyrins than do the values observed for 1,10-phenanthroline and those calculated based on the bound-ligand effect on complex formation. 3) The enhanced reactivity of $[ZnOH]^+$ suggests hydrogen-bond formation between the pyrrole proton in the porphyrin and the oxygen atom in $[ZnOH]^+$ as a pre-equilibrium. The hydrogen-bond formation mechanism is also supported by the small activation enthalpy, the negative entropy, and the large dependence on the basicity of porphyrins.

We are grateful for the Grant-in-Aid for Scientific Research

No. 07640812 from the Ministry of Education, Science and Culture.

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