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Kinetics and Mechanism of Copper(II), Zinc(II), and Cadmium(II) Incorporation into 5,10,15,20-Tetraphenylporphine and *N*-Methyl-5,10,15,20-tetraphenylporphine in *N,N*-Dimethylformamide

Shigenobu FUNAHASHI, Yūshi YAMAGUCHI, and Motoharu TANAKA*
Laboratory of Analytical Chemistry, Faculty of Science, Nagoya University, Chikusa-ku, Nagoya 464

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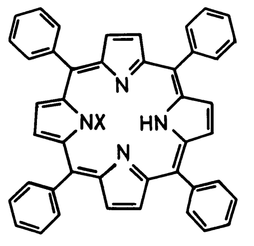
The kinetics of reactions of 5,10,15,20-tetraphenylporphine (H_2(tpp)) and *N*-methyl-5,10,15,20-tetraphenylporphine (H(metpp)) with Cu^{II}, Zn^{II}, and Cd^{II} ions was studied spectrophotometrically in *N,N*-dimethylformamide. The rate of incorporation of metal ions (M^{2+} : Cu^{2+}, Zn^{2+}, Cd^{2+}) into H(metpp) is first order with respect to both H(metpp) and metal ion: $d[M(metpp)^+]/dt=k[H(metpp)][M^{2+}]$ with $k(25\,°C)=11.5\pm0.5\ mol^{-1}\ dm^3\ s^{-1}$ for Zn^{2+} and $(5.8\pm0.8)\times10^2\ mol^{-1}\ dm^3\ s^{-1}$ for Cd^{2+}. The rate of incorporation of copper and zinc into H_2(tpp) is first order in H_2(tpp) and the conditional first-order rate constants are expressed as follows: $k_{0(M)}=K[M^{2+}](1+K[M^{2+}])^{-1}(k_1+k_2[M^{2+}])$ where for Cu^{2+} and Zn^{2+} $K/mol^{-1}\ dm^3$, k_1/s^{-1}, and $k_2/mol^{-1}dm^3\ s^{-1}$ at 25 °C are $(1.6\pm0.2)\times10^4$ and $(7.2\pm1.5)\times10^2$, $(1.2\pm0.1)\times10^{-4}$ and $(3.5\pm0.7)\times10^{-5}$, and $(5.2\pm0.2)\times10^{-2}$ and $(8.6\pm0.2)\times10^{-4}$, respectively. Metal ion incorporation into H_2(tpp) proceeds through the formation of intermediates prior the rate-limiting step. For the H(metpp) system, the methyl group on the pyrrole in H(metpp) prevents the formation of such an intermediate. On the other hand, the rate of cadmium incorporation into H_2(tpp) is first order with respect to Cd^{2+} and H_2(tpp) and its second order rate constant k is $(6.5\pm1.0)\times10^{-3}\ mol^{-1}\ dm^3\ s^{-1}$. The large cadmium(II) ion can not fit into the porphyrin nucleus and its reaction proceeds through a pathway involving a mononuclear activated complex.

The mechanisms of complexation of labile metal ions have attracted a good deal of attention. Now one can make a reasonable accurate assessment of the rate constant for the reaction of a particular metal ion-ligand system.[1,2] More recently attention has been directed to the more unusual ligands such as macrocycles,[3,4] cryptands,[5–7] and porphyrins.[8–12] Their steric restrictions are likely to slow down the "normal" rates and introduce mechanistic novelties.

A number of kinetic studies of metalloporphyrin formation have been published and the work has been reviewed by Schneider,[13] Hambright,[14] and Longo.[15] A classification of kinetics of metalloporphyrin formation has been presented recently.[16] Since the solvents, metal salts, porphyrins, and other conditions are different in these kinetic studies, a quantitative comparison of the available data is difficult. A number of studies have been addressed to the question of how metal ions are incorporated into porphyrin molecules to form metalloporphyrins. A particularly attractive idea was that of "sitting-atop" (SAT) complexes, produced by reaction of metal ions with free base porphyrins prior to metal ion incorporation.[17] Evidence for SAT complexes has been presented in various types of systems.[18–20] On the other hand, there are some papers to show evidence for the nonexistence of SAT complexes.[21,22]

Previously we have investigated the rate of reaction of 5,10,15,20-tetra(4-pyridyl)porphine with cobalt(II) in acetic acid and demonstrated the variation of the reaction order in metal ion with varying metal ion concentration.[8] We have emphasized that it is indispensable to conduct experiments over as wide a concentration range as possible. In order to elucidate the origin of previously reported differences in mechanisms of metalation, reactions of copper(II), zinc(II), and cadmium(II) ions with 5,10,15,20-tetraphenylporphine (H_2(tpp)) and *N*-methyl-5,10,15,20-tetraphenylporphine (H(metpp)) have been studied over a wide range of metal ion concentrations in *N,N*-dimethylformamide (DMF).



X = H, H_2(tpp)
X = CH_3, H(metpp)

Two of the most significant studies which we will refer to are those of Bain-Ackerman and Lavallee,[9] who have provided data for complexation of H(metpp) by Cu^{II}, Zn^{II}, Co^{II}, Mn^{II}, and Ni^{II} and Longo *et al.*,[23] who have provided activation parameters for reactions of H_2(tpp) and its derivatives with metal chloride in DMF.

Experimental

Reagents. In order to prepare sample solutions as dry as possible, extreme care was taken in purification and preparation of all reagents and solutions.

DMF: Reagent grade DMF was dried over calcium hydride and distilled twice under reduced pressure. The water content in DMF was determined to be less than 3×10^{-3} mol dm^{-3} by the Karl-Fisher titration.

Porphyrins: H_2(tpp) (Strem Chemicals) was chromatographed on an alumina column by elution with chloroform. H(metpp) was prepared from methylation of H_2(tpp) by methylfluorosulfonate (Aldrich Chemical Co., "Magic methyl") according to literature procedures.[24] H(metpp) was isolated and purified by a thin-layer chromatograph twice. H(metpp) is characterized by ^{1}H NMR spectrum and electronic spectra. The distinctive NMR spectrum shows a sharp singlet due to *N*-methyl group at 4.1 ppm upfield from

$SiMe_4$ in $CDCl_3$.

Copper(II) Perchlorate DMF Solution: Crystals of hydrated copper(II) perchlorate were obtained by treating copper metal (99.999%) and perchloric acid of special purity (Wakojunyaku) The crystals were dissolved in DMF in the presence of 3A Molecular Sieves and allowed to stand for 1 d under reduced pressure. Then the Molecular Sieves were removed by filtration.

Calcium(II) Perchlorate DMF Solution: Crystals of hydrated calcium(II) perchlorate were obtained from reagent grade calcium(II) carbonate and perchloric acid, and recrystallized twice from distilled water. The crystals were placed in an oven at 110 °C for 1 h and then at 240 °C at least for 24 h. The anhydrous calcium(II) perchlorate was dissolved in DMF.

DMF Solutions of Zinc(II), Cadmium(II), and Calcium(II) Nitrates: Reagent grade zinc(II) nitrate was recrystallized twice from distilled water. Crystals of hydrated zinc(II) nitrate were dissolved in DMF. The water involved was removed by 3A Molecular Sieves under vacuum line. The DMF solutions of cadmium(II) nitrate and calcium(II) nitrate were prepared by the same procedure as above.

The amounts of water involved in the DMF solutions were determined to be less than 5×10^{-3} mol dm^{-3}. The concentrations of copper(II), zinc(II), cadmium(II), and calcium(II) solutions were determined complexometrically by EDTA.

The purification of DMF and the preparation of DMF solutions were carried out just before kinetic measurements.

Measurements. The slow reactions were monitored spectrophotometrically by a Union Giken (Type SM401) spectrophotometer or a Hitachi (Type 124) spectrophotometer with a thermostated cell compartment maintained within ±0.1 °C. The formation of metalloporphyrins was carried out in 1 cm cells by mixing a porphyrin solution and a metal ion solution preequilibrated at the reaction temperature. The absorption spectra change as a function of time with distinct isosbestic points until completion of the reaction. The faster reactions in the H(metpp) system were followed by a Union Giken (Type RA1100) stopped-flow spectrophotometer. Addition of calcium(II) nitrate or perchlorate as an electrolyte did not affect visible spectra and rates.

The kinetics were run under pseudo-first-order conditions at 25 °C with the metal ion concentration at a large excess over the free base porphyrin concentration (10^{-6}—10^{-5} mol dm^{-3}). Pseudo-first-order plots showed good linearity untill three half-lives. Conditional first-order rate constants were obtained from the slope of such plots. The half-life times for the fastest and slowest reaction in the present reaction systems were 1 s and 120 h, respectively.

Results

Kinetics of Metal Ion Incorporation into $H_2(tpp)$. The kinetics of reactions of $H_2(tpp)$ with copper(II) perchlorate and zinc(II) nitrate in DMF at 25 °C was studied. The rate for the formation of metalloporphyrin is first order in porphyrin:

$$\frac{d[M(tpp)]}{dt} = -\frac{d[H_2(tpp)']}{dt} = k_{0(M)}[H_2(tpp)'], \qquad (1)$$

where $k_{0(M)}$ is the conditional first-order rate constant involving the metal concentration and $[H_2(tpp)']$ is the total concentration of porphyrin (C_P) minus the concentration of metalloporphyrin. The values of $k_{0(Cu)}$ are plotted against total concentration of copper C_{Cu} and its square root $C_{Cu}^{1/2}$(Fig. 1). As apparent from Fig. 1 the rate is proportional to neither the concentration of metal ion nor its half power.

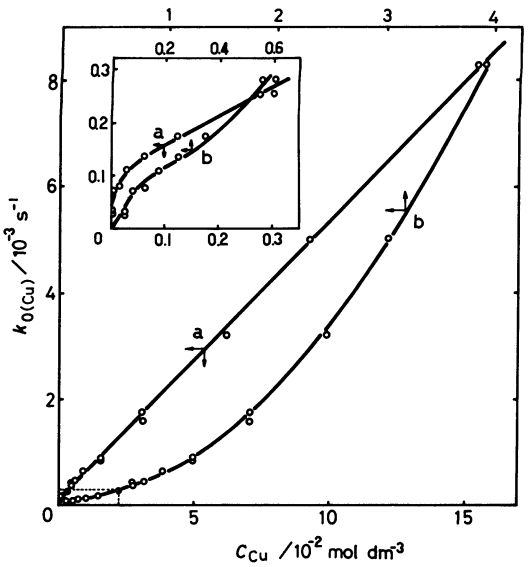


Fig. 1. Relationship between $k_{0(Cu)}$ and copper(II) ion concentration. (a): Plot of $k_{0(Cu)}$ *vs.* C_{Cu}; (b) Plot of $k_{0(Cu)}$ *vs.* $C_{Cu}^{1/2}$. The solid curves are calculated with the rate constants and formation constants obtained. The inset shows the plots in the range of lower concentration.

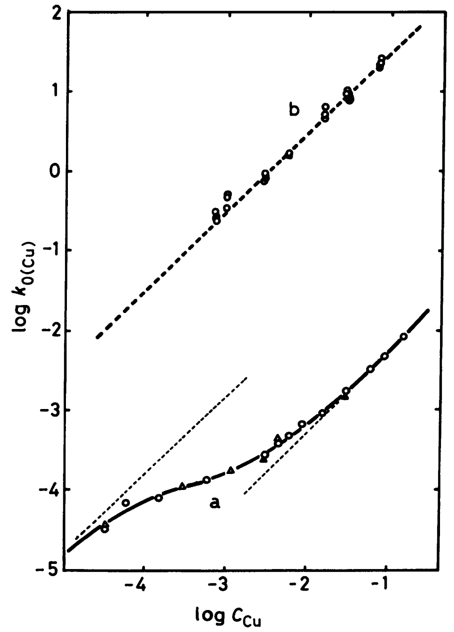


Fig. 2. Plots of log $k_{0(Cu)}$ *vs.* log C_{Cu} for the $H_2(tpp)$ system (a) and the H(metpp) system (b). (a): The data at 25.0 °C in the absence (○) and in the presence (△) of 0.0924 mol dm^{-3} calcium(II) perchlorate; (b): the data given in ref 9.

The logarithmic relationship between rate constants and copper concentrations is shown in Fig. 2a. At lower and higher copper concentration, the reaction tends to be first order in C_{Cu}, while at the intermediate copper concentration $k_{0(Cu)}$ changes with C_{Cu} to a lesser extent. This concentration dependence of the rate constants indicates a mechanism involving a rapid preequilibrium between copper(II) ion and $H_2(tpp)$ prior to metal insertion and proton release:[8]

$$\mathrm{H_2(tpp) + Cu^{2+} \overset{K}{\rightleftharpoons} Cu^{2+}\cdots H_2(tpp)}, \tag{2}$$

$$\mathrm{Cu^{2+}\cdots H_2(tpp) \xrightarrow{k_1} Cu(tpp) + 2H^+}, \tag{3}$$

$$\mathrm{Cu^{2+}\cdots H_2(tpp) + Cu^{2+} \xrightarrow{k_2} Cu(tpp) + Cu^{2+} + 2H^+}, \tag{4}$$

where $Cu^{2+}\cdots H_2(tpp)$ is an intermediate. DMF is sufficiently basic to absorb the low concentration of protons released from the free-base porphyrins as the complexation reaction proceeds. In addition, DMF should strongly solvate metal ions and compete well against trace levels of water for coordination sites on the metal ions. Assuming a rapid preequilibrium step of Eq. 2 and two parallel rate-determining steps of Eqs. 3 and 4, Eq. 5 can be readily derived.

$$k_{0(\mathrm{Cu})} = \frac{K[\mathrm{Cu^{2+}}]}{1+K[\mathrm{Cu^{2+}}]}(k_1+k_2[\mathrm{Cu^{2+}}]) \tag{5}$$

This equation reproduces very nicely the experimental rate data as illustrated in Fig. 2.

The important role of water in the formation of metalloporphyrins has been demonstrated in some systems.[11] We checked the effect of water on the rate in the present systems. An introduction of small amounts of water ($[H_2O]$/mol dm^{-3}=0.0608, 0.151, 0.209, 0.453, 0.867) into the copper(II)–H_2(tpp) system did not appreciably affect the rate constants. Since the water concentration of our systems is at most *ca.* 5×10^{-3} mol dm^{-3}, we believe with confidence that the presence of water, if any, did not affect our results.

Since there are some reports about effects of ionic strength on the rate of metalloporphyrin formation, we studied the effect of added salt on the rate in the present systems. The addition of 0.0924 mol dm^{-3} calcium(II) perchlorate has no effect on the reaction rate (see Fig. 2a). The absence of salt effect on the rate is consistent with the porphyrin reacting as the free-base porphyrin H_2(tpp).

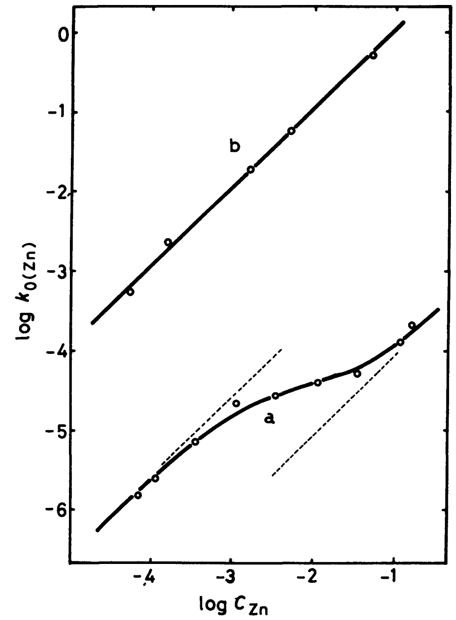


Fig. 3. Plots of log $k_{0(\mathrm{Zn})}$ *vs.* log C_{Zn} for the H_2(tpp) system (a) and the H(metpp) system (b). (a): At 25.0 °C in the presence of 0.30 mol dm^{-3} calcium(II) nitrate; (b): at 25.0 °C in the presence of 0.34 mol dm^{-3} calcium(II) nitrate.

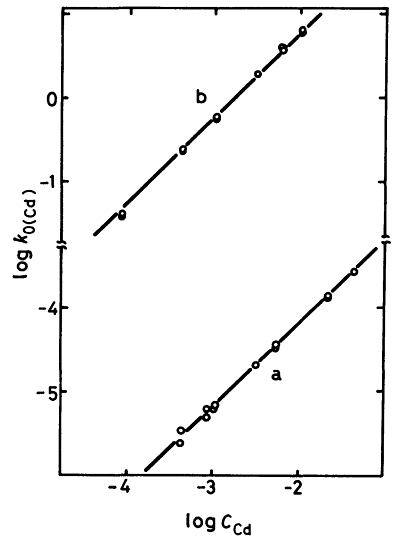


Fig. 4. Plots of log $k_{0(\mathrm{Cd})}$ *vs.* log C_{Cd} for the H_2(tpp) system (a) and the H(metpp) system (b). (a): At 25.0 °C in the presence of 0.42 mol dm^{-3} calcium(II) nitrate; (b): at 25.0 °C in the presence of 0.11 mol dm^{-3} calcium(II) nitrate.

TABLE 1. RATE CONSTANTS (25 °C) FOR METAL(II) ION INCORPORATION INTO H_2(tpp) AND H(metpp) IN DMF

Reaction system	K/mol^{-1} dm^3	k_1/s^{-1}	k_2/mol^{-1} dm^3 s^{-1}	k/mol^{-1} dm^3 s^{-1}	Ref
H_2(tpp) sytem					
Copper(II) perchlorate	$(1.6\pm0.2)\times10^{4}$	$(1.2\pm0.1)\times10^{-4}$	$(5.2\pm0.2)\times10^{-2}$		This work
Copper(II) perchlorate				1.03×10^{-1} a)	25
Copper(II) chloride				8.47×10^{-2}	23
Zinc(II) nitrate	$(7.2\pm1.5)\times10^{2}$	$(3.5\pm0.7)\times10^{-5}$	$(8.6\pm0.2)\times10^{-4}$		This work
Zinc(II) perchlorate				9×10^{-4} b)	11
Zinc(II) perchlorate				1.25×10^{-3} a)	26
Zinc(II) chloride				5.62×10^{-3}	23
Cadmium(II) nitrate				$(6.5\pm1.0)\times10^{-3}$	This work
H(metpp) system					
Copper(II) perchlorate				289	9
Zinc(II) nitrate				11.5 ± 0.5	This work
Zinc(II) perchlorate				10.4	9
Cadmium(II) nitrate				$(5.8\pm0.8)\times10^{2}$	This work

a) At 30 °C. b) For D_2(tpp) the same rate constant was obtained (no kinetic effect).

As shown in Fig. 3a, the dependence of $k_{0(\mathrm{Zn})}$ on zinc(II) concentration is the same as for the Cu(II)-H_2(tpp) system. On the other hand, the cadmium(II)-concentration dependene of $k_{0(\mathrm{Cd})}$ is clearly linear over a wide range of cadmium concentrations, as illustrated in Fig. 4a.

Rate constants were determined by a nonlinear least-squares fitting with weight. The constants obtained are summarized in Table 1.

Kinetics of Metal(II) Ion Incorporation into H(metpp). The kinetics of reaction of H(metpp) with an excess of zinc(II) nitrate was studied in DMF solution containing 0.34 mol $\mathrm{dm^{-3}}$ calcium(II) nitrate. The rate for formation of metalloporphyrin is first order in porphyrin:

$$\frac{\mathrm{d}[\mathrm{Zn(metpp)^+}]}{\mathrm{d}t} = -\frac{\mathrm{d}[\mathrm{H(metpp)}]}{\mathrm{d}t} = k_{0(\mathrm{Zn})}[\mathrm{H(metpp)}]. \tag{6}$$

The values of $k_{0(\mathrm{Zn})}$ determined in the wide range from 10^{-1} mol $\mathrm{dm^{-3}}$ to 10^{-5} mol $\mathrm{dm^{-3}}$ of zinc nitrate are proportional to the total concentration of zinc nitrate C_{Zn} (Fig. 3b).

For the $\mathrm{Cd^{II}}$-H(metpp) system the dependence of $k_{0(\mathrm{Cd})}$ on cadmium nitrate concentration is clearly linear (see Fig. 4b) as in the case of the $\mathrm{Cd^{II}}$-H_2(tpp) system. In Fig. 2b, the values of $k_{0(\mathrm{Cu})}$ obtained by Bain-Ackerman and Lavallee[9] are plotted against C_{Cu}. All the reactions for the H(metpp) system obey a second-order rate law: first order in porphyrin and first order in metal ion. The rate constants obtained are listed in Table 1.

Discussion

Results obtained in the present system are summarized in Table 1 together with data reported previously.[9, 11, 23, 25, 26] In the $\mathrm{Zn^{II}}$-H(metpp) system the rate constant in the perchlorate medium[9] is in good agreement with ours in the nitrate medium. It has been reported that the reaction order of metal ion in the metalation of porphyrins is not always unity.[8] The earlier workers, working over a narrow range of metal ion concentration, may have deduced the first order or half order in metal ion as obvious from Fig. 1. The second-order rate constant k obtained previously in the $\mathrm{Cu^{II}}$- and $\mathrm{Zn^{II}}$-H_2(tpp) systems should be regarded as k_2 in the present work. In fact, as apparent from figures in Table 1, the reported k values are in good agreement with the corresponding k_2 values.

In the $\mathrm{Cu^{II}}$- and $\mathrm{Zn^{II}}$-H_2(tpp) systems, the formation constants (K) of intermediates given by Eq. 2 are considerably large and the K for copper(II) is greater than that for zinc(II). The intermediate may be regarded as a kinetically detected SAT complex. In the k_2 path (Eq. 4), a second metal should be inserted from the opposite side of the metal in the SAT complex with a homodinuclear activated complex. On the other hand, in the k_1 path, the metal ion in the SAT complex just drops into the porphyrin ring. Such a mechanism has been proposed previously for the cobalt incorporation into 5,10,15,20-tetra(4-pyridyl)porphine in acetic acid.[8]

In the H(metpp) systems the rate is first order with respect to metal ion over a wide range of metal ion concentrations. Recent study[27] on the crystal structures of mono-chloro-*N*-methyl metalloporphyrins of Mn, Fe, Co, and Zn shows the out-of-plane displacement of metal ion and deviation of *N*-methylated pyrrole ring from the plane of reminder of the porphyrin core. Judging from these structures, in the metalation of H(metpp) a second metal can not attack from the opposite side due to steric hindrance of the methyl group. Therefore the reaction does not involve a homodinuclear activated complex as observed in the $\mathrm{Cu^{II}}$- and $\mathrm{Zn^{II}}$-H_2(tpp) system: the rate of metal ion incorporation into H(metpp) is invariably first order in metal ion.

The rate of cadmium incorporation into H_2(tpp) is first order in $\mathrm{Cd^{2+}}$ and H_2(tpp). A large metal ion such as $\mathrm{Cd^{2+}}$ ion (its crystal ionic radius is 97 pm[28]) can not fit into the porphyrin nucleus because the N–N distance in H_2(tpp) is 408 pm[29] and its reaction proceeds through a pathway involving a mononuclear activated complex.

In the H(metpp) systems the rate of cadmium incorporation is faster than in the H_2(tpp) systems, whereas the rate is much slower than that for the solvent exchange at this cation.[30] In common to all mechanisms, the porphyrins form an outer-sphere complex with the metal ions (K_{os}) and then the porphyrin nucleus deforms to provide a suitable configuration to complex the metal ion (K_{D}). The rapid K_{os} and K_{D} preequilibria should be followed by the rate-determining step involving a mono-nuclear activated complex.

K_{os} for porphyrins should be smaller than those for small ligands as estimated by the Fuoss theory,[31] because the outer-sphere interaction of solvated metal ions with porphyrins occurs effectively only in the vicinity of the central part of porphyrins.

The *N*-methylated porphyrin is largely deformed in comparison with the non-methylated porphyrin. This deformation enhances both the coordinating ability of the lone pairs by directing them away from the central porphyrin cavity and the acidity of the central protons by destroying the N–H tautomerism.[32] The predeformed *N*-methylated porphyrin incorporates metal ions up to five orders of magnitude faster than the corresponding non-*N*-methylated analogue, pointing to the importance of porphyrin deformation in the metal ion incorporation into porphyrins.

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