Kinetics and Mechanism of Acceleration of Copper(II) Incorporation into a Porphyrin by Reducing Agents

Masaaki Tabata* and Mie Babasaki

Department of Chemistry, Faculty of Science and Engineering, Saga University,
Honjo-machi, Saga, 840 Japan

The catalytic effect of the reducing agents hydroxylamine and metallic copper on the rate of the copper(II) incorporation into tetrakis(1-methylpyridinium-4-yl)porphyrin (H_2tmpyp^{4+}) was studied at pH 2–4, 25 °C, and $I = 0.1$ (NaNO$_3$). Copper(I), formed from reduction of the copper(II) by the reducing agents, reacts with H_2tmpyp^{4+} to form Cu^I-(tmpyp)$^{3+}$. Because of its large ionic radius (96 pm), copper(I) cannot incorporate well into the porphyrin core and just sits on the porphyrin plane. Copper(I) deforms the porphyrin plane favorably for attack of copper(II) from the back side. The kinetic studies suggest the formation of an intermediate of the heterovalence metalloporphyrin [Cu^I(tmpyp)Cu^{II}]$^{5+}$, from which the final incorporation of copper(II) into the porphyrin core is the rate–determining step. Copper(I) concentrations as low as 5×10^{-7} mol dm^{-3} also accelerated the reaction of H_2tmpyp^{4+} with manganese(II) in the presence of hydroxylamine at pH 6.0.

Introduction

Because of their widespread occurrence and important role in biological systems, metalloporphyrins have attracted many researchers. In the biosynthesis of heme, the protoporphyrin IX ring is synthesized and iron(II) is subsequently incorporated. The general mechanism for the metalation of porphyrins was first proposed by Hambright and Chock[1] and further supported and reviewed by the groups of Hambright,[2] Lavallee,[3] Schneider,[4] and Tanaka.[5] However, the overall mechanism is relatively complex, since the rate of metalloporphyrin formation is several orders of magnitude slower than that of the complex formation of open-chain ligands. In order to accelerate the metalation, several methods have been proposed, especially from the analytical points of view:[6] (1) the use of substitution reactions of cadmium-(II) or mercury(II) porphyrin,[7,8] (2) the use of porphyrins with substituents at the pyrrole nitrogen,[9,10] (3) the addition of aromatic heterocyclic bases such as pyridine and imidazole,[11,12] (4) the introduction of functional groups to bind metal ions in the vicinity of the porphyrin nucleus (e.g. tetracarboxylic acid "pocket-fence" porphyrins),[13] and (5) the use of reducing agents such as hydroxylamine and ascorbic acid.[14,15]

One of the above mentioned enhanced reactions emphasizes the reactivity of different oxidation states of the metal ions. The rate of metalloporphyrin formation is sensitive to the dissociation rate of the solvents coordinated to metal ion, and the latter rate generally depends on the oxidation state of metal ions. Rapid metalation is favored by lower oxidation state metals such as iron(II) and cobalt(II) compared with iron(III) and cobalt(III).

Schneider has reported that, in a mixed solvent of water-acetonitrile, copper(I) is more reactive than copper(II) due to more rapid dissociation of the solvent molecule compared with copper(II).[4] However, the dissociation rate of the water molecule from the aquacopper(II) ion is ca. 10^9 s^{-1}, which is close to the diffusion-controlled rate.[16] Therefore, it is expected that copper-(I) could be more reactive by a factor of 10 if the dissociation of the water molecule bound to copper(I) is the rate-determining step in the metalloporphyrin formation. We have noted much faster metalloporphyrin formation involving copper(II) in the presence of reducing agents, such as hydroxylamine, ascorbic acid, and metallic copper, than that expected from the water-dissociation rate of the aquacopper(I) ion.

The present paper describes the catalytic effect of reducing agents such as hydroxylamine and metallic copper on the copper-(II) incorporation into 5,10,15,20-tetrakis(1-methylpyridinium-4-yl)porphyrin (H_2tmpyp^{4+}) and focuses on the deformation of the porphyrin core caused by the binding of copper(I) formed by reduction of copper(II). The ionic radius of Cu$^+$ (96 pm) is significantly larger than that of the Cu^{2+} (72 pm) and deforms the porphyrin core by a mechanism similar to that found earlier for large metal ions such as cadmium(II), mercury(II), and lead-(II).[5,7,8]

Experimental Section

Reagents. 5,10,15,20-Tetrakis(1-methylpyridinium-4-yl)porphyrin (H_2tmpyp^{4+}) was purchased from Dojindo Chemical Institute, Kumamoto, Japan, as a tosylate. The concentration of the porphyrin was determined spectrophotometrically using copper(II). A copper(II) solution was prepared by dissolving copper(II) nitrate in water, and its concentration was determined by ethylenediaminetetraacetate titration using 4-(2-thiazolylazo)resorcinol as an indicator. Sodium nitrate and hydroxyl-ammonium sulfate were recrystallized from distilled water. Metallic copper particles (2-mm diameter) were washed with nitric acid and rinsed with water just before use. Buffer solutions were prepared with chloroacetic acid and sodium hydroxide (pH 2–4). All solutions were prepared under nitrogen atmosphere, and then nitrogen was bubbled into the solutions to deaerate them.

Kinetic Measurements. All experiments were carried out under anaerobic conditions and in a room thermostated at 25 ± 1 °C. The ionic strength was maintained at 0.1 mol dm^{-3} with sodium nitrate. Absorption spectra were recorded on a Shimazu UV-2100 spectrophotometer. The spectral changes in the course of the reaction were the disappearance of

(1) Hambright, P.; Chock, P. B. *J. Am. Chem. Soc.* **1974**, *96*, 3123.
(2) Hambright, P. In *Porphyrins and Metalloporphyrins*; Smith, K. M., Ed.; Elsevier: Amsterdam, 1975; pp 232–278.
(3) Lavallee, D. K. *Coord. Chem. Rev.* **1985**, *61*, 55.
(4) Schneider, W. *Struct. Bonding (Berlin)* **1975**, *23*, 123.
(5) Tanaka, M. *Pure Appl. Chem.* **1983**, *55*, 151.
(6) Tabata, M.; Tanaka, M. *Trends Anal. Chem.* **1991**, *10*, 126.
(7) Shamim, A.; Hambright, P. *J. Inorg. Nucl. Chem.* **1980**, *42*, 1645.
(8) Tabata, M.; Tanaka, M. *J. Chem. Soc., Dalton Trans.* **1983**, 1955.
(9) Funahashi, S.; Ito, Y.; Kakito, H.; Inamo, M.; Hamada, Y.; Tanaka, M. *Mikrochim. Acta* **1986**, *No. 1*, 33.
(10) Lavallee, D. K. *The Chemistry and Biochemistry of N-Substituted Porphyrins*; VCH Publishers: New York, 1987.
(11) Kawamura, K.; Igarashi, S.; Yotsuyanagi, T. *Anal. Sci.* **1988**, *4*, 175.
(12) Tabata, M.; Tanaka, M. *Inorg. Chem.* **1988**, *27*, 203.
(13) Buckingham, D. A.; Clark, C. R.; Webley, W. S. *J. Chem. Soc., Chem. Commun.* **1981**, 192.
(14) Ishii, H.; Koh, H. *Bunsekikagaku* **1979**, *28*, 473.
(15) Makino, T.; Itoh, J. *Clin. Chim. Acta* **1981**, *111*, 1.
(16) Margerum, D. W.; Cayley, G. R. *Coordination Chemistry*; Martell, A. E., Ed.; American Chemical Society: Washington, DC, 1978; pp 1–194.
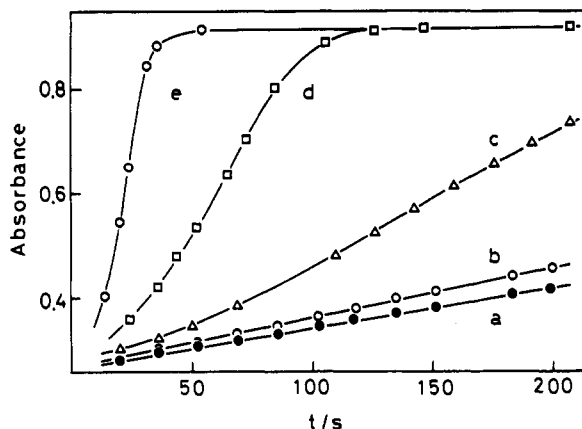
Figure 1. Absorbance at 550 nm as a function of time during the reaction of copper(II) with H_2tmpyp^{4+} in the presence of the hydroxylammonium ion (mol dm^{-3}): (a) 0; (b) 1.000×10^{-5}; (c) 1.000×10^{-4}; (d) 1.000×10^{-3}; (e) 1.000×10^{-2}. $[H_2tmpyp^{4+}]_0 = 2.00 \times 10^{-5}$ mol dm^{-3}, $[Cu^{2+}]_0 = 2.07 \times 10^{-3}$ mol dm^{-3}, pH = 2.85, $I = 0.1$, and $T = 25$ °C.

the characteristic absorption bands of H_2tmpyp^{4+} (Q-bands at 520, 558, and 647 nm) and the growth of the characteristic band of $C^{II}(tmpyp)^{4+}$ (Q-band at 550 nm). The isosbestic points were observed at 490, 534, and 577 nm. The absorbance change at 550 nm was monitored with a thermostated 10-mm cell. The temperature of the reaction solutions was controlled at 25 ± 0.1 °C by a Neslab small refrigerated thermostat, Type RTE-100. The reaction was started by mixing two deaerated solutions, i.e. one containing copper(II) nitrate, sodium nitrate, and buffer and the other containing H_2tmpyp^{4+}, reducing agent (hydroxylammonium sulfate or metallic copper), buffer, and sodium nitrate. The mixing of the two solutions was carried out with a sample-mixing device (Type MX7, Ohtuka Denshi) under nitrogen atmosphere. The pH was varied by addition of chloroacetate buffer and determined by a Radiometer 85 ion analyzer with a combined electrode (GK2401C). A 1.000×10^{-2} mol dm^{-3} nitric acid solution containing 0.09 mol dm^{-3} sodium nitrate was employed for the standard hydrogen ion concentration (−log [H$^+$] = 2.000; $I = 0.1$). From the pH meter readings in various hydrogen ion concentrations at an ionic strength of 0.1 mol dm^{-3} (HNO$_3$–NaNO$_3$), the pH meter and electrode system were calibrated in terms of −log [H$^+$].

Results

Determination of the Protonation Constant of H_2tmpyp^{4+}. In order to clarify the effect of pH on the reaction, it was necessary to know the protonation constant of H_2tmpyp^{4+}. The protonation constant as shown in eq 1 was determined from the spectral

$$H_2tmpyp^{4+} + H^+ \rightleftharpoons H_3tmpyp^{5+} \quad K_{H_3P} \quad (1)$$
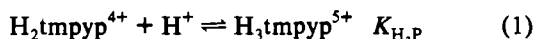
changes at 423 and 443 nm of the Soret band in a pH range of 1–2.5. The log K_{H_3P} value was found to be 1.34 ± 0.07, which is in good agreement with previous work.[17] Hence the porphyrin exists in the free-base and the protonated forms, H_2tmpyp^{4+} and H_3tmpyp^{5+}, under the present experimental conditions (pH 2–4).

Copper Incorporation into H_2tmpyp^{4+}. The reaction of H_2tmpyp^{4+} with copper(II) was studied in the presence of large excesses of copper(II) and the reducing agent, hydroxylammonium sulfate (10^{-4}–10^{-2} mol dm^{-3}) or metallic copper, compared with H_2tmpyp^{4+} ($[H_2tmpyp^{4+}]_0 = (0.4–2) \times 10^{-5}$ mol dm^{-3}) at pH 2–4. The formation of $Cu^{II}tmpyp^{4+}$ was dramatically accelerated by the presence of hydroxylammonium ions or metallic copper. The typical change in absorbance during the reaction is shown in Figure 1. The reaction had an induced-reaction period due to the attainment of a steady-state condition. The reaction also
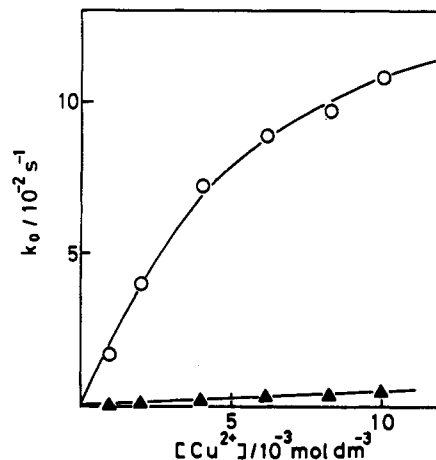
Figure 2. Dependence of the formation rate constant (k_0) of $Cu^{II}(tmpyp)^{4+}$ on the concentration of copper(II) in the presence (O) and absence (▲) of the hydroxylammonium ion (5.00×10^{-4} mol dm^{-3}) at $[H_2tmpyp^{4+}]_0 = 2.00 \times 10^{-5}$ mol dm^{-3} and pH = 2.84.

showed a straight line in the first-order kinetic plot after the induction period. In order to check whether the porphyrin is a monomer or a dimer under the present experimental conditions,[17] the rate constants were measured at different values of $[H_2tmpyp^{4+}]_0$ ($(2.00–9.98) \times 10^{-5}$ mol dm^{-3}) and were found to be independent of $[H_2tmpyp^{4+}]_0$. This result shows that the porphyrin is in a monomeric form under the present experimental conditions. If the porphyrin were a dimer, the rate constant would decrease with the concentrations of the porphyrin. Hence, the kinetic equation for the reaction is described by eq 2, where k_0

$$-d[H_2tmpyp']/dt = d[Cu^{II}(tmpyp)^{4+}]/dt = k_0[H_2tmpyp'] \quad (2)$$
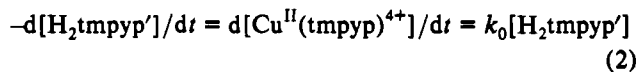
is the conditional rate constant involving concentrations of hydrogen ion, reducing agent (hydroxylammonium sulfate or metallic copper), and copper(II) and $[H_2tmpyp']$ denotes the total concentration of the porphyrin unbound to Cu(II): $[H_2tmpyp'] = [H_3tmpyp^{5+}] + [H_2tmpyp^{4+}]$. The protonated porphyrin, H_3tmpyp^{5+}, did not show reactivity toward copper(II), because of the decreased reaction rate of the porphyrin in acidic medium.

Effect of Hydroxylamine. The reaction of copper(II) with H_2tmpyp^{4+} was carried out in the presence of hydroxylammonium sulfate at pH 2–4. In Figure 2, k_0 is plotted against the concentration of copper(II). The rate of the formation of $Cu^{II}(tmpyp)^{4+}$ increases significantly with the concentration of copper(II) in the presence of the hydroxylammonium ion. The rate constant also increases with the concentration of the hydroxylammonium ion. Figure 3 shows the effect of the hydrogen ion on the rate of the formation of $Cu^{II}(tmpyp)^{4+}$ in the presence and absence of hydroxylammonium ion. As is clear from these results, the formation of $Cu^{II}(tmpyp)^{4+}$ is accelerated more than 10^4 times by the hydroxylammonium ion (Figures 2 and 3).

The rate of the formation of $Cu^{II}(tmpyp)^{4+}$ increases with pH. The increased rate constant, in the absence of the hydroxylammonium ion, can be explained by taking the formation of $Cu(ClCH_2COO)^+$ into account. Considering the formation constant of $Cu(ClCH_2OO)^+$ (log $K_{ML} = 1.07$)[19] and the protonation constants of H_2tmpyp^{4+} and chloroacetate (log $K_{ML} = 2.60$),[19] eq 2 can be written as eq 3, where $[ClH_2COO']$ denotes the total concentration of $ClCH_2COO^-$ unbound to copper(II). Plots of $k_0(1 + K_{H_3P}[H^+])[Cu^{2+}]^{-1}$ vs $[ClCH_2COO']\cdot(1 + K_{HL}[H^+])^{-1}$ give a straight line with an intercept. The values of k_1 and k_2 were determined from the intercept and

(17) Hay, S. E.; Hambright, P. *Inorg. Chem.* **1984**, *23*, 4777.

(18) Kano, K.; Miyake, T.; Uomoto, K.; Sato, T.; Ogawa, T. *Chem. Lett.* **1983**, 1867. Pasternack, R. F.; Gibbs, E. J.; Gaudmer, A.; Antebi, A.; Bassner, S.; Poy, L. De.; Turner, D. H.; Williams, A.; Laplace, F.; Lansard, M. H.; Merienne, C.; Perre-Fauvet, M. *J. Am. Chem. Soc.* **1985**, *107*, 8179. Brookfield, R. L.; Ellul, H.; Harriman, A. *J. Photochem.* **1985**, *31*, 97.

(19) Martell, A. E.; Smith, R. M. *Critical Stability Constants*; Plenum Press: New York, 1977; Vol. 1.
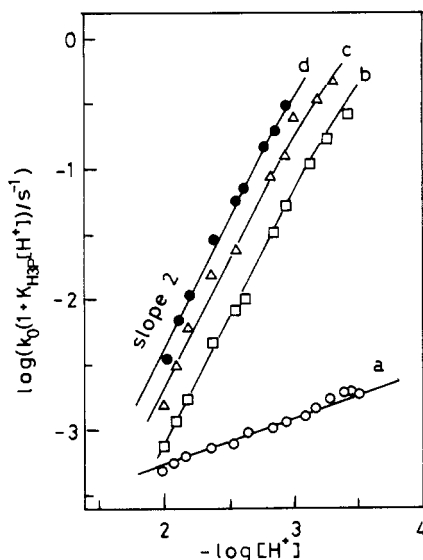
Figure 3. Dependence of the formation rate constant of $Cu^{II}(tmpyp)^{4+}$ on pH in the presence and absence of the hydroxylammonium ion (mol dm^{-3}): (a) 0; (b) 1.000×10^{-3}; (c) 5.00×10^{-3}; (d) 1.000×10^{-2}. $[Cu^{2+}]_0$ = 2.07×10^{-3} mol dm^{-3} and $[H_2tmpyp^{4+}]_0$ = 2.00×10^{-5} mol dm^{-3}.

$$k_0[H_2tmpyp'] = (k_1[Cu^{2+}] +$$

$$k_2[Cu(ClCH_2COO)^+])[H_2tmpyp^{4+}] \quad (3)$$

$$= (k_1 + k_2K_{ML}[ClCH_2COO'](1 + K_{HL}[H^+])^{-1})(1 +$$

$$K_{H_3P}[H^+])^{-1}[Cu^{2+}][H_2tmpyp']$$

the slope: $k_1 = 0.13 \pm 0.02$ mol^{-1} dm^3 s^{-1} and $k_2 = 5.3 \pm 0.2$ mol^{-1} dm^3 s^{-1}. The higher value of k_2 in comparison with k_1 is due to the enhanced lability of the water molecule in Cu-$(ClCH_2COO)(H_2O)_n^+$ and the increased outer-sphere association of $[Cu(ClCH_2COO)^+][H_2tmpyp^{4+}]$.

Effect of Metallic Copper. In order to confirm that the catalytic effect of the hydroxylammonium ion on the formation of $Cu^{II}tmpyp^{4+}$ results from the formation of reactive species, Cu(I), in the presence of the hydroxylammonium ion, we investigated the effect of metallic copper on the formation of $Cu^{II}(tmpyp)^{4+}$. Metallic copper reacts with the copper(II) ion to produce copper(I) as shown in the following reaction:

$$Cu^{2+} + Cu(0) \rightleftharpoons 2Cu^+ \quad K_{Cu} \quad (4)$$
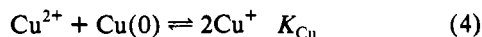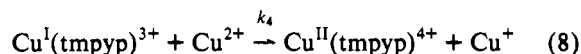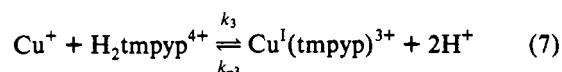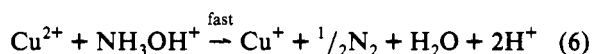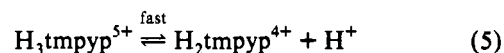
The copper(II) solution equilibrated with metallic copper was mixed with an H_2tmpyp^{4+} solution. The formation rate of $Cu^{II}(tmpyp)^{4+}$ was monitored under nitrogen atmosphere. As shown in Figure 4, the rate constant increases with the total concentration of copper(II) and the slope reaches $^3/_2$ at the concentration of 10^{-2} mol dm^{-3} copper(II). The equilibrium constant $(K_{Cu})^{20}$ of eq 4 is $\sim 10^{-6}$ mol dm^{-3}, and our typical concentration of 2×10^{-3} mol dm^{-3} Cu(II) gives an equilibrium concentration of 4.4×10^{-5} mol dm^{-3} Cu$^+$. A small amount of Cu$^+$ enhances the $Cu^{II}(tmpyp)^{4+}$ formation rate.

Overall Mechanism. The above observation leads to the suggestion that copper(II) incorporation into the porphyrin is enhanced by Cu(I) formed in the presence of the hydroxylammonium ion or metallic copper. Since the rate of reduction of the copper(II) ion to the copper(I) ion is faster than the rate of copper(II) incorporation into the porphyrin core, the catalytic behavior observed for the copper(II)–porphyrin formation can be described by the following reaction scheme:

(20) Sillen, L. G.; Martell, A. E. *Stability Constants of Metal-Ion Complexes*; Special Publication No. 17; The Chemical Society: London, 1964.
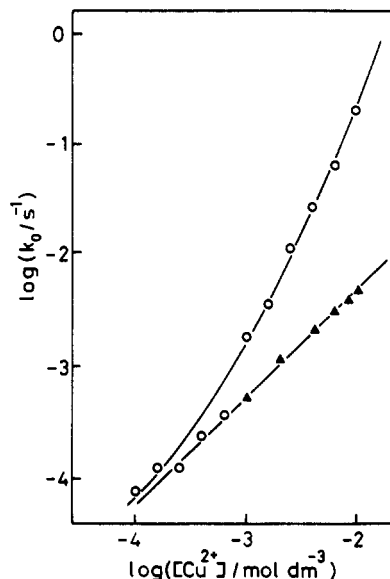
Figure 4. Dependence of the formation rate constant of $Cu^{II}(tmpyp)^{4+}$ on the concentration of copper(II) in the presence (O) and absence (▲) of metallic copper at $[H_2tmpyp^{4+}]_0$ = 2.00×10^{-5} mol dm^{-3} and pH = 3.50.

$$H_3tmpyp^{5+} \overset{fast}{\rightleftharpoons} H_2tmpyp^{4+} + H^+ \quad (5)$$

$$Cu^{2+} + NH_3OH^+ \overset{fast}{\rightharpoonup} Cu^+ + {}^1/_2N_2 + H_2O + 2H^+ \quad (6)$$

$$Cu^+ + H_2tmpyp^{4+} \underset{k_{-3}}{\overset{k_3}{\rightleftharpoons}} Cu^I(tmpyp)^{3+} + 2H^+ \quad (7)$$

$$Cu^I(tmpyp)^{3+} + Cu^{2+} \overset{k_4}{\rightharpoonup} Cu^{II}(tmpyp)^{4+} + Cu^+ \quad (8)$$

The ionic radius of Cu$^+$ (96 pm) is significantly larger than that of Cu^{2+} (72 pm). The copper(I) ion cannot incorporate well into the porphyrin core and just sits on the top of the porphyrin. Copper(I) deforms the porphyrin core favorably for attack of copper(II) from underneath. The mechanism is similar to the effect of large metal ions such as cadmium(II) and lead(II) published earlier.[8] Applying the steady-state approximation for $Cu^I(tmpyp)^{5+}$, we have

$$k_0 = \frac{k_3k_4[Cu^+][Cu^{2+}]}{(k_{-3}[H^+]^2 + k_4[Cu^{2+}])(1 + K_{H_3P}[H^+])} \quad (9)$$

At lower pH, $k_{-3}[H^+]^2 \gg k_4[Cu^{2+}]$, eq 9 is reduced to

$$k_0(1 + K_{H_3P}[H^+]) = \frac{k_3k_4[Cu^+][Cu^{2+}]}{k_{-3}[H^+]^2} \quad (10)$$

The plots of log $(k_0(1 + K_{H_3P}[H^+])$ vs $-$log $[H^+]$ result in straight lines with slopes of 2 at lower pH, as shown in Figure 3, where the solid lines are calculated ones from eq 10. Under the conditions, the rate-determining step is the incorporation of copper(II) into the porphyrin core. A small deviation from the straight line at higher pH is due to the fact that the term $k_4[Cu^{2+}]$ is not negligible compared with $k_{-3}[H^+]^2$. The formation rate of $Cu^{II}(tmpyp)^{4+}$ is also proportional to $[Cu^{2+}]^{3/2}$ in the presence of the catalytic effect of metallic copper, as expected from $[Cu^+]$ = $K_{Cu}[Cu^{2+}]^{1/2}$ and eq 10 (Figure 4). From eq 9, it can be deduced that the catalytic effect of Cu$^+$ becomes independent of $[Cu^{2+}]$ at high concentration of copper(II) $(k_{-3}[H^+]^2 \ll [Cu^{2+}])$ (Figure 2). Thus eq 9 is reduced to $k_0 = k_3[Cu^+]$ under this condition. Since the plot of the observed rate constant vs the concentration

Scheme I. Catalytic Effect of Cu(I) on the Formation of $Cu^{II}(tmpyp)^{4+}$ [a]
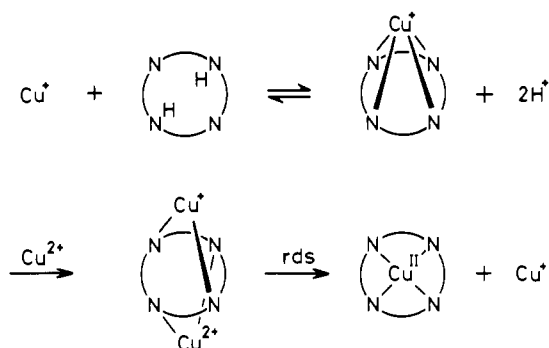
[a] H_2tmpyp^{4+} is depicted by the circle. Copper(I) forms a mixed-valence dinuclear metalloporphyrin, $[Cu^{I}(tmpyp)Cu^{II}]^{5+}$, as an intermediate.
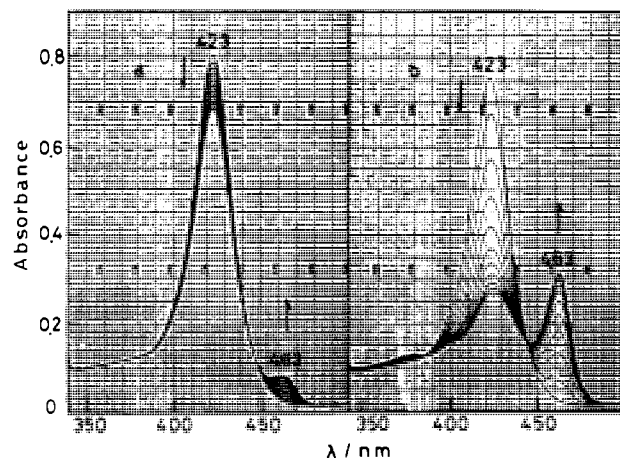
of the hydroxylammonium ion gave a straight line, the concentration of Cu^+ is linearly dependent on the concentration of the hydroxylammonium ion.

A possible reaction mechanism is shown in Scheme I. It is important to note that Cu^+ deforms the porphyrin core and enhances the attack of Cu^{2+} from the back side. The copper(I) porphyrin is very reactive and may give a mixed-valence intermediate, $[Cu^{I}(tmpyp)Cu^{II}]^{5+}$. We have recently detected a heterodinuclear metalloporphyrin intermediate, containing mercury(II) and zinc(II), during the formation of a zinc(II) porphyrin in the presence of mercury(II).[21] Later, Hambright[22] proposed the same type of intermediate.

Catalytic Effect of Cu^+ on the Formation of $Mn^{III}(tmpyp)^{5+}$

From the above experimental results, it is expected that copper(I) can also catalyze the incorporation of other medium-sized metal ions, such as manganese(II), in place of copper(II). In order to confirm this, we studied the catalytic effect of copper(I) on the formation of a manganese(III) porphyrin complex. Figure 5 shows the spectral changes for the formation of $Mn^{III}(tmpyp)^{5+}$ in the presence of copper(I) at a concentration as low as 5×10^{-7} mol dm^{-3}. A small amount of copper(I) enhances the incorporation of manganese(II). The result, furthermore, has been extended to the catalytic determination of copper(I) and some reducing agents, e.g. L-ascorbic acid. The details will be reported elsewhere.

Some authors[14,15] have attributed the catalytic effect of the hydroxylammonium ion and ascorbic acid to the lability of the aquacopper(I) ion compared with the aquacopper(II) ion in their preliminary experiments, especially in spectrophotometric determinations of copper(II) using porphyrins. Most of the formation rates (k) of metalloporphyrins, involving copper(II), have been given by eq 11,[1-3,17] where k_{H_2O} is the water dissociation rate of metal ions and K is a constant related to the equilibrium

(21) Tabata, M.; Miyata, W. *Chem. Lett.* **1991**, 785.
(22) Robinson, L. R.; Hambright, P. *Inorg. Chem.* **1992**, *31*, 652.
(23) Tabata, M.; Ozutumi, K. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 1438.

Figure 5. Catalytic effect of 5.0×10^{-7} mol dm^{-3} copper(I) on the formation of $Mn^{III}(tmpyp)^{5+}$ at $[H_2tmpyp^{4+}]_0 = 3.99 \times 10^{-6}$ mol dm^{-3}, $[Mn(II)]_0 = 1.91 \times 10^{-4}$ mol dm^{-3}, and pH = 5.94. The absorption spectra were measured at an interval of 30 min. Parts a and b show the spectral changes in the absence and presence of Cu(I), respectively.

$$k = Kk_{H_2O} \tag{11}$$

of outer-sphere complexes between metal ions and porphyrins and the deformation of porphyrins. Although copper(II) has two types of water molecules (axial and equatorial), the formation rate constants of copper(II) porphyrins have been correlated to the dissociation rate of the axial water molecule[1-3] ($k \sim 10^9$ s^{-1}), which is close to the diffusion-controlled rate.[16] Therefore, the 10^4 times enhanced reactivity of copper(I) cannot be explained by the lability of the water molecule bound to copper(I), because the water molecule bound to copper(I) may dissociate rapidly by a factor of 10 compared with copper(II). Since the ionic radius of copper(I) is as large as that of cadmium(II), copper(I) may deform the porphyrin core. This makes the incorporation of other metal ions into the porphyrin core easier, as the cases found for mercury(II), cadmium(II), and lead(II).[5,6,8] We have previously reported that cadmium(II) enhances the incorporation of manganese(II) by a factor of 10^4.

A mixed-valence copper porphyrin, where copper(I) and copper(II) are bound simultaneously to the porphyrin, may be formed as an intermediate of this reaction, as detected for $Zn(tpps)Hg^{2-}$,[23] where tpps^{6-} denotes the fully deprotonated anion of tetrakis(4-sulfonatophenyl)porphyrin. An extended X-ray absorption of fine structure (EXAFS) study of $Hg_2(tpps)^{2-}$ has revealed that the porphyrin ring is deformed in a manner where the four pyrrole nitrogens of the porphyrins are oriented alternately in up- and downward directions.[23] The deformed conformation is expected for the $[Cu^{I}(tmpyp)Cu^{II}]^{5+}$ complex, and the deformed structure alters the reaction rate of the formation of the metalloporphyrin dramatically.