Complexation-induced Catalysis in Zinc Insertion into Cationic Porphyrin

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Insertion of zinc to a cationic porphyrin in water was accelerated by the addition of catechols and related compounds **2**–**5**, while decelerated by the addition of pyridine derivatives **6**–**7**. Complexes between zinc and **2**–**7** with different stoichiometric ratios showed different activity toward the zinc insertion reaction. The reaction becomes slower as the ionic strength is higher in the presence of tiron, indicating that electrostatic force plays an important role in the catalysis.

Insertion of ferrous ion into protoporphyrin IX is catalyzed by ferrochelatase. Catalysis of metallation of porphyrins[1–5] by a designed model compound is thus of interest in the field of bioinorganic chemistry. Several factors are suggested for the acceleration of metallation reactions of synthetic porphyrins: (1) a base assists the reaction by accommodating the hydrogen from the N-H group of porphyrin, (2) porphyrin plane deformation facilitates the metal–nitrogen bond formation. In the present paper we studied the metallation kinetics of a cationic porphyrin in the presence of several guest molecules (G). The catalytic effects were attributed to the different reactivity of guest-zinc complexes of different stoichiometry $G_n{\bullet}Zn^{2+}$. Electrostatic interaction was found to be one of important factors controlling the metallation reaction.

A water-soluble cationic porphyrin bearing four quaternary ammonium ions **1** was synthesized by a condensation reaction of (3,3'-bis(carbomethoxyethyl)-4,4'-dimethyl-2,2'-dipyrryl)-methane with 2-hydroxy-1-naphthaldehyde, followed by the conversion of the carbomethoxy groups to hydroxyl groups and then to ammonium groups. Two naphthyl groups at 5 and 15-positions inhibit the aggregation of the porphyrin in water. The trans atropisomer of **1** was used. The rate of zinc insertion was determined by monitoring the absorbance increase at 422 nm after the addition of zinc in Tris buffer solutions at 25°C, pH 7. Under the conditions that [**1**] = 6 μM, [Zn^{2+}] = 0.1 mM, [guest] = 0–0.5 mM, the metallation rate was first order in [**1**] and the pseudo-first order rate constant (k_{obs}) was determined by fitting the absorbance change to the rate equation: $-d[\mathbf{1}]/dt = k_{obs}[\mathbf{1}]$.

Figure 1 shows the plot of the rate constants (k_{obs}) against the guest concentrations. Compounds **2**-**5** accelerate the zinc insertion reaction, whereas compound **7** decelerates the reaction in the concentration range of 0—3 × 10^{-4} M. Compounds **8**–**11**

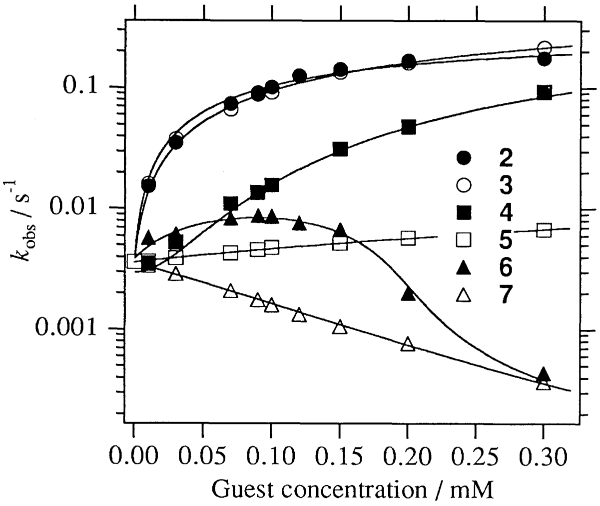
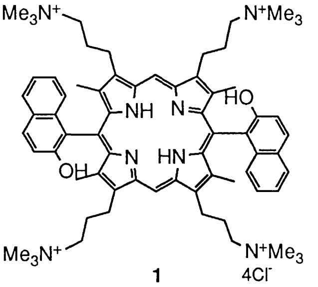
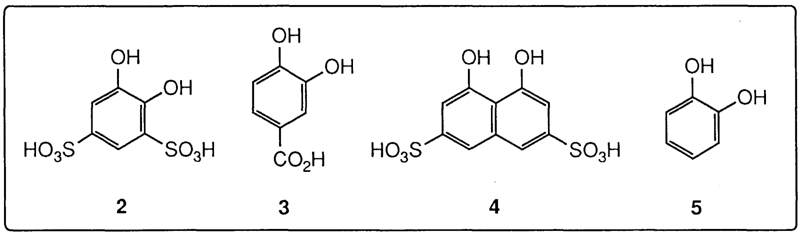


Figure 1. Plot of pseudo-first order rate constants against guest concentrations at 25 °C, pH 7, in 50 mM Tris buffer, [$ZnCl_2$] = 0.1 mM, and [**1**] = 6 × 10^{-6}M.

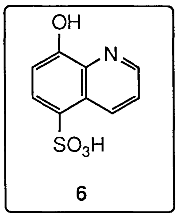


1

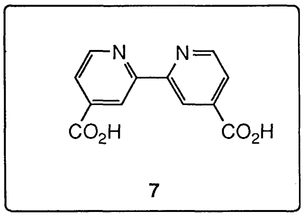
Acceleration



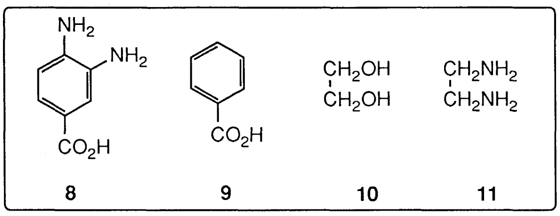
Acceleration at low conc.
Retardation at high conc.



Retardation



No catalysis



showed little effect on the reaction kinetics. Compound **6** accelerates the reaction in the low concentration range (0—1.8 × 10^{-4} M) and then decelerates in the higher concentration (1.8 × 10^{-4}—3 × 10^{-4} M). The rate follows first order kinetics in porphyrin, zinc and guest concentration at a low concentration and shows saturation at a higher concentration of guest, suggesting that a ternary complex among these species is involved in the reaction. The dependence of the rate constants on the concentration of **2**–**7** was fitted to the following equations:

$$k_{obs} = k_{Zn}[Zn^{2+}] + k_{ZnG}\,[Zn^{2+}G] \quad (1)$$

$$k_{obs} = k_{Zn}[Zn^{2+}] + k_{ZnG}\,[Zn^{2+}G] + k_{ZnG2}\,[Zn^{2+}G_2] + k_{ZnG3}\,[Zn^{2+}G_3] \quad (2)$$

where the rate constant k_{Zn} is an uncatalyzed rate constant, k_{ZnG} is a catalyzed rate constant by a Zn^{2+}—guest (1:1) complex, k_{ZnG2} is a catalyzed rate constant by a Zn^{2+}—guest (1:2) complex, and so on. The rates for **2** and **3** were fitted reasonably well to equation 1 with an association constant K = 11800 M^{-1}, a rate constant k_{ZnG} = 2500 $s^{-1}\cdot M^{-1}$ and K = 2280 M^{-1}, k_{ZnG} = 5670 $s^{-1}\cdot M^{-1}$, respectively, where $K = [Zn^{2+}\cdot G]/[Zn^{2+}][G]$. Fitting of the rates for **4**, **6**–**7** was not so good even if equation 2 was used and contributions from up to a 1:3 complex were considered. However the dependence of k_{obs} on the guest concentration clearly indicates that 1:2 or 1:3 complexes show very little reactivity toward the metal insertion reaction, that is inhibitory effects.

The effects of ionic strength on the reaction rate were examined for metallation in the presence of **2** at 25°C, pH 7 in 50 mM Tris. In the absence of guest, the reaction becomes slightly faster as the ionic strength is higher: k_{obs}, s^{-1} (NaCl, mM) 0.0034 (0), 0.0035 (2), 0.0038 (10), and 0.0049 (50), whereas the reaction becomes slower as the ionic strength is higher in the presence of 0.1 mM of guest **2**: k_{obs}, s^{-1} (NaCl, mM) 0.094 (0), 0.085 (2), 0.077 (10), and 0.051 (50). Because both of porphyrin and zinc are cationic, the electrostatic force impedes the approach of these species. This can account for the slight increase in the rate as the ionic strength is higher in the absence of guest. The inhibitory effect of the ionic strength for the catalyzed reaction in the presence of **2** suggests that anionic **2** seizes two reactants, porphyrin and zinc, through an electrostatic force. Diminished catalytic effects of neutral guest **5** compared to **2**-**3** also support this mechanism. A schematic representation of the ternary complex is shown in Figure 2.

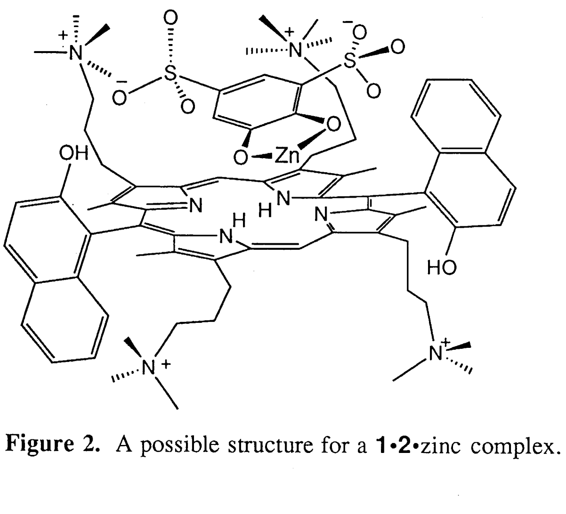


Figure 2. A possible structure for a **1**•**2**•zinc complex.

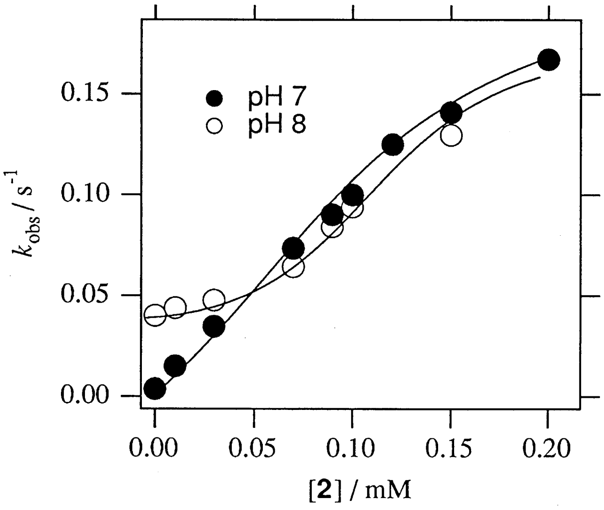


Figure 3. Plot of pseudo-first order rate constants against the concentration of **2** at 25 °C, pH 7 and pH 8, in 50 mM Tris buffer, $[ZnCl_2]$ = 0.1 mM and [**1**] = 6 × 10^{-6} M.

The rate constants at pH 7 and pH 8 are plotted against the guest concentrations in Figure 3. The rate is faster at pH 8 in the low concentration of **2**. However at a high concentration of **2**, the rate at pH 7 becomes similar to that at pH 8. This observation suggests that the active species or the rate determining step changes as the guest is added. In the presence of the guest, the active zinc species or the rate determining step becomes the same between pH 7 and pH 8. Compounds **6** and **7** also show a similar behavior: at a low concentration, the rate is faster at pH 8 than at pH 7, while the rate becomes similar as the concentration of compounds **6** and **7** becomes higher.

The present study demonstrates that the metal insertion reaction can be controlled by the addition of guest molecules. Electrostatic forces play an important role in the zinc insertion reaction to cationic porphyrin **1**.

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References and Notes

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