Reaction of Copper(II) with a Metalloporphyrin. A Type of Supramolecular-driven Porphyrin Metallation

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The reaction of the transfer of copper(II) from a chelating environment to a porphyrin core, accelerated by cadmium(II) previously inserted into the porphyrin, shows an unusual kinetic profile which is interpreted as being the result of supramolecular assembly formation.

The kinetics of porphyrin metallation continues as an active research area, not only for the mechanistic implications of such studies but for a number of practical applications as well.[1,2] The general emphasis of reports related to this area has been on the influence of bound ligands on the rate of metallation.[3-9] In one such study[9] we showed that for $[Cu(en)_2]^{2+}$ (en = ethylenediamine) the first-order rate constant *vs.* concentration profiles are anomalous. Under most conditions the rate of metallation is very slow but an apparent discontinuity occurs at some critical concentration of $[Cu(en)_2]^{2+}$ at which point the rate constant jumps by about two orders of magnitude. With increasing $[Cu(en)_2]^{2+}$ concentration, the observed rate constant decreases (albeit more gradually) until it again approaches zero. Based upon these kinetic results, as well as light scattering and conductance measurements, we concluded that a supramolecular assembly of reactants forms over a narrow range of conditions in which the metallation reaction rate is enhanced.

In a quite different set of investigations, several workers have shown that the presence of Cd^{2+}, Pb^{2+} or Hg^{2+} greatly increases the rate of formation of cobalt(II), manganese(II), copper(II) or zinc(II) porphyrins.[10-14] Intermediates have been proposed in which one of the three first mentioned ions is bound to two or three of the central nitrogens, deforming the porphyrin core and thereby making one or two nitrogens accessible for metal-ion attack, *i.e.*, the activated complex contains both entering and departing metal ions.[10] We now report on the formation of 5,10,15,20-tetrakis(*N*-methyl-4-pyridinio)porphyrinatocopper(II), [Cu(tmpp)], from $[Cu(en)_2]^{2+}$ and [Cd(tmpp)]. Our aims were to determine whether the copper(II) insertion reaction is accelerated by cadmium ion and whether the anomalous rate constant *vs.* concentration profile observed for the free base porphyrin persists.

The reaction under study involves the transfer of copper(II) from a bis(ethylenediamine) environment to a porphyrin core, as influenced by cadmium ion. The design and interpretation of experiments for this ternary system require prior knowledge of the reactions of H_2tmpp with $[Cu(en)_2]^{2+}$ or Cd^{2+} alone. We have therefore considered reactions under conditions convenient for studies involving all three species (10 mmol dm^{-3} collidine, 0.25 mol dm^{-3} $NaNO_3$, pH 7.0, 25 °C). For the reaction shown in equation (1) conducted under pseudo first-

$$Cd^{2+} + H_2tmpp \longrightarrow [Cd(tmpp)] + 2H^+ \qquad (1)$$

order conditions (Cd^{2+} in a large excess), a linear dependence of k_{obs} on $[Cd^{2+}]$ is obtained with a slope of 14.8 $dm^3\ mol^{-1}\ s^{-1}$. This value is similar to that obtained at pH 4–6 (39.6 $dm^3\ mol^{-1}\ s^{-1}$) using a 2-morpholinoethanesulfonic acid buffer.[10] The equilibrium constant for reaction (1) has been determined[10] as $K_{Cd} = 2 \times 10^{-8}$ mol dm^{-3}. Therefore, at pH 7, the pH dependent equilibrium constant $K'_{Cd} = [Cd(tmpp)]/([Cd^{2+}][H_2tmpp]) = 2 \times 10^6\ dm^3\ mol^{-1}$.

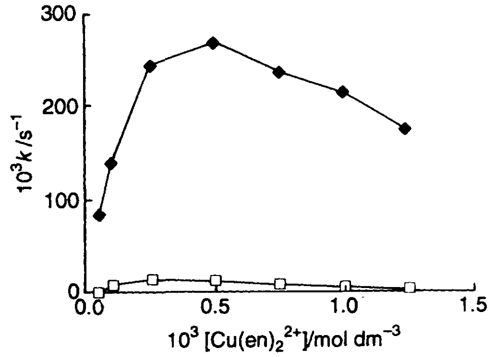

Fig. 1 Experimental rate constant dependence on the concentration of $[Cu(en)_2]^{2+}$ in the presence (◆) and absence (◇) of Cd^{2+}. For the Cd^{2+} reactions, 35 μmol dm^{-3} H_2tmpp was preincubated with 35 μmol dm^{-3} Cd^{2+} overnight. All reactions were run at 25 °C, pH 7.0 (10 mmol dm^{-3} collidine) in the presence of 0.25 mol dm^{-3} $NaNO_3$

The reaction of $[Cu(en)_2]^{2+}$ with H_2tmpp was studied under the same conditions maintaining $[en]/[Cu^{2+}] = 3.0$) [equation (2)] and gave the same results as those obtained

$$[Cu(en)_2]^{2+} + H_2tmpp \longrightarrow [Cu(tmpp)] + 2Hen^+ \qquad (2)$$

previously.[9] The copper(II) concentration at the maximum rate constant ($k_{max} = 12.7 \times 10^{-3}\ s^{-1}$), $[M]_C$, was determined to be 2.5×10^{-4} mol dm^{-3}, consistent with previous results obtained over a range of ionic strengths.[9]

The influence of Cd^{2+} on the metallation of H_2tmpp by $[Cu(en)_2]^{2+}$ was studied by first preincubating the porphyrin with Cd^{2+} to allow the formation of [Cd(tmpp)]($[Cd^{2+}] = [H_2tmpp] = 35$ μmol dm^{-3}). Then $[Cu(en)_2]^{2+}$ was added ($[en]/[Cu^{2+}] = 3.0$) and the reaction monitored at 548 {λ_{max} for [Cu(tmpp)]} or 575 nm {λ_{max} for [Cd(tmpp)]} using the stopped-flow technique. Fig. 1 shows the first-order rate constant obtained as a function of $[Cu(en)_2]^{2+}$ concentration and includes the results obtained under the same solvent conditions in the absence of Cd^{2+} for comparison. As can be seen the rate constant *vs.* concentration profile is characteristic of the reaction of $[Cu(en)_2]^{2+}$ with the free base porphyrin.

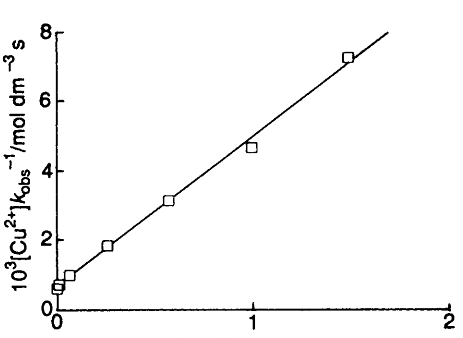

Fig. 2 Plot of $[Cu^{2+}]/k_{obs}$ *vs.* $[Cu^{2+}]^2$ for the reaction of $[Cu(en)_2]^{2+}$ with [Cd(tmpp)]; $I = 0.25$ mol dm^{-3} ($NaNO_3$), 25 °C and pH = 7.0 ($k_1K_1 = 0.687 \times 10^{-3}$ dm^3 mol^{-1} s^{-1}, $K_2/k_1 = 4.289$ dm^3 mol^{-1} s)

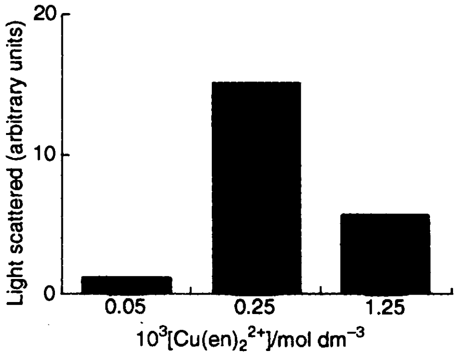

Fig. 3 Results of light scattering experiments in the presence of Cd^{2+}. The initial conditions in each case at 25 °C were 35 µmol dm^{-3} [Cd(tmpp)], 10 mmol dm^{-3} collidine (pH 7), 0.25 mol dm^{-3} $NaNO_3$, and the concentration of $[Cu(en)_2]^{2+}$ shown ($[en]/[Cu^{2+}] = 3.0$)

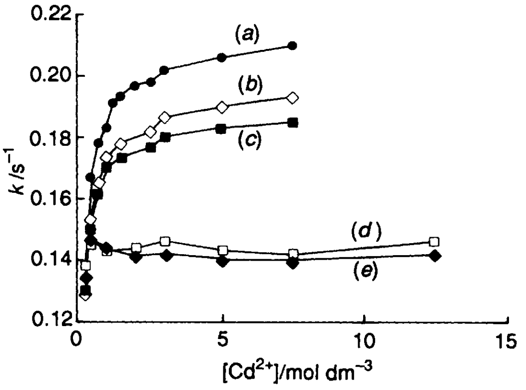

Fig. 4 Dependence of experimental rate constant on $[Cd^{2+}]$ at various concentrations of $[Cu(en)_2]^{2+}$ ($[en]/[Cu^{2+}] = 3.0$): (*a*) 0.25, (*b*) 0.75, (*c*) 1.00, (*d*) 1.50 and (*e*) 2.00 mmol dm^{-3}. In all experiments $[H_2tmpp] = 35$ µmol dm^{-3}, [collidine] = 10 mmol dm^{-3}, $[NaNO_3] =$ 0.25 mol dm^{-3}, pH 7 and 25 °C

While there may be some shifting of $[M]_C$ to higher concentration in the accelerated pathway, the most dramatic effect of added cadmium(II) is a 30-fold increase in k_{max}.

These results may be explained by equations (3) and (4),

$$P + Cu^{2+} \overset{K_1}{\rightleftharpoons} P/Cu \qquad (3)$$

$$P/Cu + Cu^{2+} \overset{K_2}{\rightleftharpoons} P/Cu_2 \qquad (4)$$

where P is the cadmium porphyrin species and P/Cu or P/Cu_2 the corresponding reaction intermediates or precursor species. Additionally, the two pathways shown by equations (5) and (6)

$$P/Cu \xrightarrow{k_1} PCu \qquad (5)$$

$$P/Cu_2 \xrightarrow{k_2} PCu_2 \qquad (6)$$

might be considered for the formation of the copper porphyrin. The observed pseudo-first-order rate constant takes the form of equation (7), where $[Cu^{2+}]$ represents $[Cu(en)_2{}^{2+}]$.

$$k_{obs} = \frac{k_1K_1[Cu^{2+}] + k_2K_1K_2[Cu^{2+}]^2}{1 + K_1[Cu^{2+}] + K_1K_2[Cu^{2+}]^2} \qquad (7)$$

If $K_2[Cu^{2+}] \gg K_1$ and k_2 is slow, then equation (8) applies.

$$k_{obs} = \frac{k_1K_1[Cu^{2+}]}{1 + K_1K_2[Cu^{2+}]^2} \qquad (8)$$

Thus, $[Cu^{2+}]/k_{obs} = 1/k_1K_1 + K_2[Cu^{2+}]^2/k_1$. Fig. 2 gives a plot of $[Cu^{2+}]/k_{obs}$ *vs.* $[Cu^{2+}]^2$. The linear relationship demonstrates the agreement of the experimental data and the proposed rate law.

Light scattering measurements were performed for the cadmium-containing system at three different $[Cu(en)_2]^{2+}$ concentrations, one of which corresponds to $[M]_C$. Fig. 3 shows the results all of which were conducted at an initial concentration of [Cd(tmpp)] equal to 3.5×10^{-5} mol dm^{-3}, with 10 mmol dm^{-3} collidine and 0.25 mol dm^{-3} $NaNO_3$. When $[Cu^{2+}] = [M]_C$, the light scattering is considerably greater than at other concentrations at which the kinetics of metal replacement are slower, indicating that the presence of Cd^{2+} does not interfere with the assembly function. Therefore, we conclude that the same (or similar) supramolecular assemblies form in the metal replacement reaction of [Cd(tmpp)] as in the metallation of the free base porphyrin[9] and that the presence of Cd^{2+} markedly enhances the reaction rate presumably *via* a porphyrin deformation pathway.

The kinetic dependence on cadmium ion concentration was investigated at a constant concentration of porphyrin of 3.5×10^{-5} mol dm^{-3}. A series of runs were performed at a fixed $[Cu(en)_2]^{2+}$ concentration and various $[Cd^{2+}]$. The process was repeated several times at different fixed $[Cu(en)_2]^{2+}$ concentrations and the results are shown in Fig. 4. The influence of cadmium(II) appears to be two-fold. The more significant effect is the result of the conversion of H_2tmpp to [Cd(tmpp)]; an excess of Cd^{2+} is needed to drive the equilibrium of equation (1) in the direction of the metalloporphyrin intermediate. When both $[Cd^{2+}]$ and $[H_2tmpp]$ are 3.5×10^{-5} mol dm^{-3}, for example, more than 10% of the porphyrin exists in the metal-free form at equilibrium at pH 7. However, when $[Cd^{2+}] = 8.5 \times 10^{-5}$ mol dm^{-3}, the porphyrin exists as 99% [Cd(tmpp)]. Yet even above this value, the rate constant rises by as much as 15% with increasing $[Cd^{2+}]$. As shown previously[9] there are specific electrolyte effects in the assembly-based metallation, depending primarily on the cation. This may account for the fact that curves (*a*), (*b*) and (*c*) of Fig. 4 do not level off even at the high concentrations considered.

These results suggest that, at least as they pertain to the Cd^{2+} ion process, similar mechanistic pathways apply for assembly-driven kinetics as for the previously studied, more typical monodispersed systems. The Cd^{2+} serves to significantly distort the porphyrin nucleus (as is evidenced by the green colour of the complex) which in turn facilitates the metal replacement reaction, presumably through an intermediate in which both Cd^{II} and Cu^{II} are simultaneously bound to the porphyrin.[10,15] In conclusion, it seems apparent that certain structural requirements must be met for the assemblies to form and, as these are elucidated, the detailed nature of the arrangement of the species and their interaction will become more apparent.

Experimental

5,10,15,20-Tetrakis(*N*-methyl-4-pyridinio)porphyrin (H_2tmpp) was obtained in the chloride form from Midcentury Chemical Company and used without further purification. Ethylenediamine and collidine (2,4,6-trimethylpyridine) were obtained from Sigma while the other reagents including $Cd(NO_3)_2 \cdot 4H_2O$ were Fisher Scientific products. Kinetic studies and light scattering experiments were conducted as previously reported.[9] The metal-substitution reactions were followed either at 548 for [Cu(tmpp)] or 575 nm for [Cd(tmpp)]. Blank experiments showed that ethylenediamine alone did not remove Cd^{2+} from [Cd(tmpp)] under the experimental conditions used.

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