Kinetics of Electrophilic Substitution Reactions Involving Metal Ions in Metalloporphyrins

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Abstract: The kinetics of electrophilic substitution reactions involving the replacement of one metal ion for another coordinated in tetraphenylporphin (TPP) complexes have been investigated in pyridine solutions. The reactions studied were Zn(II)–CdTPP, Zn(II)–PbTPP, Zn(II)–HgTPP, and Cu(II)–ZnTPP. These reactions were all first order in metalloporphyrin. The Hg(II) and Cd(II)TPP reactions were first order in Zn(II), while the PbTPP system was second order in Zn(II). With ZnTPP, the kinetics were first order in Cu(II) and inhibited by Zn(II). Hg(II) was found to catalyze the Zn(II)–PbTPP reaction. The replacement reactions can be faster or slower than the corresponding insertion of the metal ion into the free-base porphin, and no evidence for a free-base intermediate was observed.

The kinetics of metal ions (M(II)) inserting into free base prophyrins (H_2P) to form metalloporphyrins

$$M(II) + H_2P \longrightarrow M\text{–}P + 2H \qquad (1)$$

(M–P) have been extensively studied,[2–6] while only qualitative information is available on the mechanisms of substitution of one metal ion for another coordinated in a metalloporphyrin complex.

$$M^*(II) + M\text{–}P \longrightarrow M^*\text{–}P + M(II) \qquad (2)$$

In exchange reactions where M*(II) and M(II) are identical, most metalloporphyrins are inert. Thus, little exchange has been found under various conditions with Mg(II) chlorophyll a and b,[7] Fe(III) protoporphyrin and tetraphenylporphin (TPP),[8] Cu(II) pheophytin,[8] Zn(II) phthallocyanine,[9] and Co(II) mesoporphyrin.[10] Sodium ions, however, do exchange readily with Na_2(I)TPP.[11]

For substitution reactions where M*(II) and M(II) are different, Barnes and Dorough[11] found that small divalent ions could replace larger divalent ions, both of which would replace alkali metal ions from their TPP complexes in pyridine solutions. Caughey and Corwin[12] showed that the rates of these substitution reactions also depended on the nature of the porphyrin. Under conditions in which the Cu(II)–ZnTPP reaction occurred, no exchange between Cu(II) and Zn etioporphyrin could be detected. Falk and Nyholm's[13] observations on protoporphyrin chelates were similar to the TPP results.[11]

These substitution reactions have been previously studied by noting if a reaction occurred, and the approximate time to go to completion. To gain further insight into these systems, we report the kinetics in pyridine of the following reactions: Zn(II)–CdTPP, Zn(II)–PbTPP, Zn(II)–HgTPP, and Cu(II)–ZnTPP and the Hg(II) catalysis of the Zn(II)–PbTPP reaction.

Experimental Section

Tetraphenylporphin was prepared and purified by reported methods.[14] The copper, lead, zinc, cadmium, and mercury complexes were made by standard techniques[15–17] and their spectra and extinction coefficients agreed with those of other workers.[17]

The reactions were run in pyridine distilled from BaO, since reactants and products were fairly soluble in this solvent. Zinc acetate dihydrate and cupric acetate monohydrate were used as the replacing ions. The kinetics were followed on a Cary Model 14 recording spectrophotometer by observing the decrease with time of a particular absorption band of the metalloporphyrin, which was well separated from the peaks of the newly formed metal complex. The wavelengths (in mμ) followed were: ZnTPP, 610; CdTPP, 630; HgTPP, 630; and PbTPP, 670. The Cu(II)–ZnTPP reaction was followed by taking samples as a function of time from the refluxing solution of Cu(II) and ZnTPP. The reaction was quenched to room temperature with cold water and benzene, and extracted with water to separate the Cu(II) and Zn(II) from the porphyrins. The resulting pyridine–benzene solution was put through anhydrous sodium sulfate, and diluted with more pyridine to form the corresponding metalloporphyrin pyridinates, whose spectra could then be recorded. The Zn(II)–PbTPP reaction, run at 44° in pyridine, was followed by removing samples and quenching to 25° with benzene. The Zn(II)–CdTPP and HgTPP reactions were run at 25°. All of the reactions were followed under pseudo-first-order conditions, with at least a hundredfold excess of metal ion to porphyrin, which was always approximately 10^{-5} *M*. The rate constant, k_{obsd}, was obtained from the slope of log ($OD_\infty - OD_t$) *vs.* time plots. These plots were linear over three half-lives. OD_∞ is the optical density at the end of the reaction while OD_t is that observed at a particular time. The spectra from 450 to 700 mμ were scanned at the completion and during the reaction to note the species formed, since each porphyrin species has a rather definitive set of peaks in this range.

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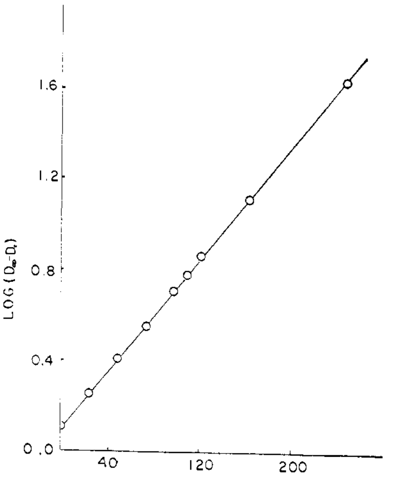

Figure 1. A typical rate plot for the Cu(II)–ZnTPP reaction, in the presence of added Zn(II): [Cu(II)] 3.22 × 10^{-2} *F*, [Zn(II)] 1.50 × 10^{-2} *F*, [ZnTPP] 1.71 × 10^{-5} *F* at 115°.

Results

The Cu(II)–ZnTPP Reaction. This system was studied at 115° in refluxing pyridine. Figure 1 shows the linearity of a typical log ($OD_\infty - OD_t$) *vs.* time plot observed with an excess of Cu(II), indicating that the reaction is first order in ZnTPP. Although the reaction times were rather long and the extraction procedure rather delicate, the data were extremely reproducible, as shown in Table I. For example, at a constant [Cu(II)] of 3.22 × 10^{-2} *F*, three separate experiments gave half-lives of 52.9, 54.0, and 52.6 hr. k_{obsd} increased with total [Cu(II)] while the ratio [Cu(II)]/k_{obsd} remained constant (2.6 ± 0.1) over a sevenfold range in copper, indicating the reaction to be first order in Cu(II). The addition of Zn(II) to the reaction mixture decreased k_{obsd}, and Figure 2 shows the linearity of [Cu(II)]/k_{obsd} *vs.* [Zn(II)]. To ensure that this decrease was not due to the added acetate, three experiments were run with [Cu(II)] = 3.22 × 10^{-2} *F*, [Zn(II)] = 5.0 × 10^{-2} *F*, and sodium acetate at 0, 1.0, and 5.0 × 10^{-2} *F*. The added acetate had no effect on the observed rate.

Table I. Rate Data for the Cu(II)–ZnTPP Reaction at 115°

[Cu(II)] × 10^2 *F*	[Zn(II)] × 10^2 *F*	10^3k_{obsd}, hr^{-1}	[Cu(II)]/k_{obsd}, *F* hr Obsd	Calcd[a]
0.83		3.16	2.63	2.53
1.66		6.21	2.67	2.53
3.22		13.1	2.47	2.53
3.22		12.2	2.51	2.53
3.22		13.1	2.46	2.53
4.83		19.1	2.51	2.53
6.45		25.1	2.58	2.53
3.22	1.50	11.5	2.81	2.92
3.22	3.00	9.82	3.28	3.34
3.22	5.55	8.45	3.88	3.93
3.22	6.00	7.60	4.24	4.18
3.22	9.00	6.31	5.10	5.02
3.22	12.0	5.53	5.81	6.16

[a] Calculated from the parameters derived from eq 6.

ZnTPP and CuTPP did not change concentration after refluxing in pyridine for a week. This indicates that pyridine itself did not demetalate the complex. The presence of 0.12 *F* zinc acetate in refluxing pyridine with CuTPP formed less than 5% ZnTPP in 2 weeks. No spectral evidence was found for species other than the zinc and copper porphyrins, during the reaction. The solubility of the zinc and copper salts in pyridine limited the collection of data over a wide range of concentrations. It was shown that Cu(II) and Zn(II) insert into the free base prophyrin within 5 min under the reaction conditions.

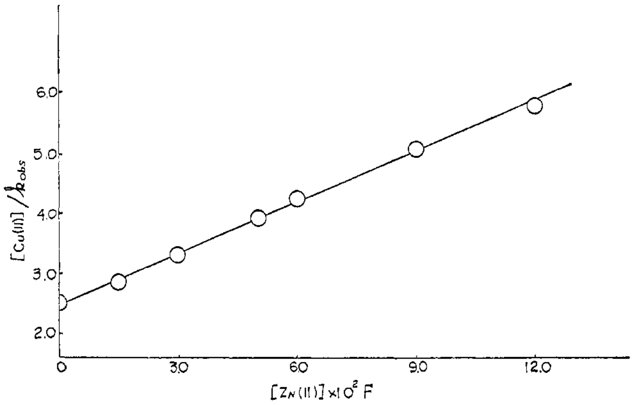

Figure 2. Effect of added Zn(II) on the rate of the Cu(II)–ZnTPP reaction. See eq 6.

We suggest the following mechanism to be in agreement with the kinetic data.

$$\mathrm{Cu(II)} + \mathrm{ZnTPP} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} [\mathrm{Cu^*TPP}] + \mathrm{Zn(II)} \qquad (3)$$

$$[\mathrm{Cu^*TPP}] \xrightarrow{k_2} \mathrm{CuTPP} \qquad (4)$$

Formally a copper species reacts with the zinc porphyrin to form a copper porphyrin adduct which is transformed in the rate-determing step into the normal CuTPP product. A steady-state approximation on [Cu*TPP] gives

$$k_{obsd} = k_1k_2[\mathrm{Cu(II)}]/(k_2 + k_{-1}[\mathrm{Zn(II)}]) \qquad (5)$$

which rearranges to

$$[\mathrm{Cu(II)}]/k_{obsd} = 1/k_1 + (k_{-1}/k_1k_2)[\mathrm{Zn(II)}] \qquad (6)$$

From a least-squares analysis of the data in Table I, $1/k_1 = (2.5 \pm 0.1)$ *F* hr and $k_{-1}/k_1k_2 = (2.8 \pm 0.2) \times 10^1$ hr. When no zinc other than that formed from ZnTPP is present in the system, the maximum concentration of Zn(II) in eq 6 can be no more than [ZnTPP], about 10^{-5} *F*, making [Cu(II)]/k_{obsd} = $1/k_1$. The value of $1/k_1$ obtained from the intercept in Figure 2 (2.5 ± 0.1) is in excellent agreement (2.6 ± 0.1) with that observed by varying Cu(II) without adding Zn(II).

The Zn(II)–CdTPP and Zn(II)–HgTPP Systems. These reactions were followed at 25° and were shown to be first order in porphyrin. Table II shows both reactions to be first order in the replacing metal ion. Thus

$$\text{rate} = k_3[\mathrm{M\text{-}TPP}][\mathrm{Zn(II)}] \qquad (7)$$

For M as Cd(II), $k_3 = (1.9 \pm 0.1) \times 10^{-2}$ F^{-1} sec^{-1} and for M as Hg(II), $k_3 = (27 \pm 1) \times 10^{-2}$ F^{-1} sec^{-1}. The addition of 2.0 × 10^{-2} *F* Hg(II) to 1.82 × 10^{-2} *F* Zn(II) decreased the rate of the Zn(II)–HgTPP reaction by 15%. The turbidity of higher mercuric acetate concen-

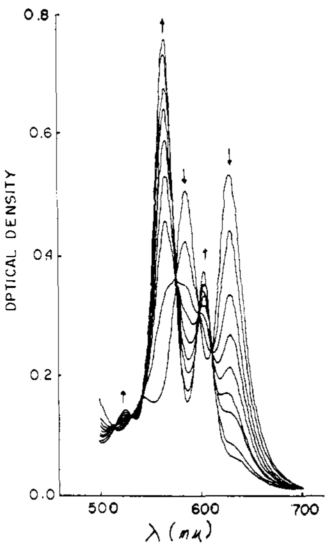

Figure 3. Optical density *vs.* wavelength figure showing the seven isosbestic points found during the Zn(II)-HgTPP reaction at 25°.

trations prevented further study. Cadmium acetate was too insoluble to attempt a rate inhibition study.

The spectra of ZnTPP and HgTPP intersect at seven wavelengths between 700 and 450 mμ. Figure 3 shows the seven isosbestic points obtained during a Zn(II)-HgTPP reaction. This indicates that the free base TPP, with bands at 649, 592, 520, and 517 mμ, is not an intermediate in this reaction. The reaction of Zn(II) at 1.0 × 10^{-2} *F* with the free base TPP was very slow (hours) compared to the Zn(II)-HgTPP rate at 25°. Small amounts of added water of the order of magnitude of the concentrations of the reacting ions did not change the rate of the reaction. The rate increased markedly in an 8 *M* water-pyridine solution, but the only product formed was the ZnTPP. Both the zinc and mercury porphyrins were stable with respect to hydrolysis in the water-pyridine mixture.

Table II. Rate Data for the Zn(II)-CdTPP and Zn(II)-HgTPP Reactions at 25°

Reaction	[Zn(II)], *F*	10^3k_{obsd}, sec^{-1}	$10^2(k_{obsd}/[Zn(II)])$, F^{-1} sec^{-1}
Zn(II)-CdTPP	4.68 × 10^{-2}	0.867	1.85
	14.4	2.76	1.95
	18.7	3.89	2.08
	23.2	4.45	1.92
Zn(II)-HgTPP	1.82 × 10^{-3}	0.500	28.0
	4.55	1.35	29.7
	9.10	2.33	25.7
	13.6	3.60	26.5
	18.2	4.64	25.5
	22.7	5.80	25.6

The Zn(II)-PbTPP Reaction and Hg(II) Catalysis. This reaction was very slow at room temperature and rather fast in refluxing pyridine, but could be conveniently followed at 44°. The kinetics were found to be first order in the lead porphyrin, and Figure 4 shows the second-order rate behavior in Zn(II). Thus

$$\text{rate} = k_4[\text{PbTPP}][\text{Zn(II)}]^2 \tag{8}$$

k_4 is equal to (4.0 ± 0.2) × 10^{-4} F^{-2} sec^{-1}.

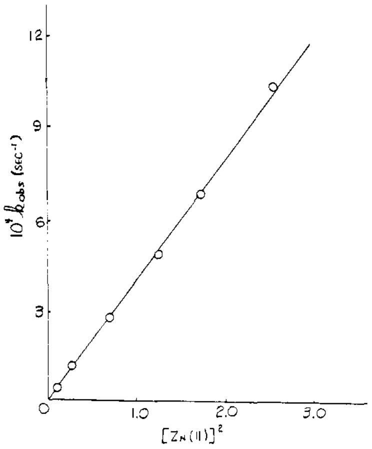

Figure 4. The second-order dependence on Zn(II) in the Zn(II)-PbTPP reaction at 44°.

Lead acetate was too insoluble in pyridine to test product ion inhibition. For a similar reason, the Hg(II)-PbTPP system could not be rectified. The mercuric acetate was somewhat soluble but weakly colloidal. First-order rate plots could be obtained from 10^{-2} to 10^{-3} *F* Hg(II), but the kinetics were of an indefinite order in Hg(II). In these concentration limits, the half-lives were from 35 to 615 sec. Since the reaction went cleanly to HgTPP, the possibility of catalyzing the Zn(II)-PbTPP reaction was investigated. With 4.7 × 10^{-2} *F* Zn(II) and 1.0 × 10^{-2} *F* Hg(II), the complete formation of ZnTPP occurred in 17 min, at 25°. Less than 1% ZnTPP formed in this time without the addition of Hg(II). The observed buildup and disappearance of HgTPP as ZnTPP formed and PbTPP was consumed make the following sequence a reasonable explanation of the catalysis.

$$\text{Hg(II)} + \text{PbTPP} \longrightarrow \text{HgTPP} + \text{Pb(II)} \tag{9}$$

$$\text{Zn(II)} + \text{HgTPP} \longrightarrow \text{ZnTPP} + \text{Hg(II)} \tag{10}$$

Discussion

The data obtained are in general agreement with the qualitative results of Barnes and Dorough's study[11] of the relative stabilities of metal ions in metalloporphyrins. While it could not be explicity shown in the Cu(II)-ZnTPP system, the Zn(II)-HgTPP results (isosbestic points and slow free base reaction) indicate that the free base porphyrin (H_2P) is not always a reaction intermediate in metalloporphyrin systems. This is not obvious from studies in aqueous solutions, where the free base is usually present in the rate law.[2-6]

The monoanion and dianion porphyrins in aqueous solution are such strong bases with respect to hydroxide that the only form observed under normal conditions is the free base. It might be expected that, if these anions did have appreciable existence during the Zn(II)-HgTPP reaction, they would prefer to abstract protons to form the free base, rather than combine with Zn(II) to produce ZnTPP. The fact that no free base was found under these conditions might argue for more SE2 than SE1 character in the detailed mechanism.

Metalloporphyrin substitution reactions with the fairly rigid coordination requirements of porphyrins appear to be somewhat different in detail from the M*(II)-M-EDTA type systems. These reactions have been explained in terms of the use of multiple coordination sites on the same flexible ligand.[18] Examples of catalysis, however, have been demonstrated in both systems.

If the Zn(II)–ZnTPP exchange is slow (in view of the Zn phthallocyanine data[9]), then the rates of the Zn(II)–MTPP reactions are in the order Hg(II) > Cd(II) > Zn(II). This has been interpreted as due to the fact that since the ionic radii of cadmium and mercury are large, they cannot fit as well into the plane of the four central porphyrin nitrogen atoms as can the smaller ion zinc, and hence the bonding is weaker.[11] It was also noted that on the basis of rates, PbTPP only fits into this sequence if Hg(II) and not Zn(II) was the replacing ion. Our observation of a different rate law in the lead porphyrin reaction could indicate different substitution mechanisms operate for lead on one hand, and cadmium and mercury, on the other.

Another possibility is that all of the porphyrin substitution reactions, of one metal ion by another, and of one metal ion for the two central protons, occur by a similar mechanism with different observed rate-determining steps. For example, when M′ is a coordinated metal ion or two protons, these reactions could be formally

$$M_1 + M'P \leftrightarrows (M_1 \cdot\cdot P \cdot\cdot\cdot M') \qquad (11)$$

$$(M_1 \cdot\cdot P \cdot\cdot\cdot M') \leftrightarrows (M_1{*}P) + M' \qquad (12)$$

$$(M_1{*}P) \leftrightarrows (M_1{*}{*}P) \qquad (13)$$

$$(M_1{*}{*}P) + M_2 \leftrightarrows M_2P + M_1 \qquad (14)$$

With the zinc, cadmium, and mercury porphyrins step 13 could be rate determining while step 14 would apply in the Zn(II)–PbTPP reaction. Most free base porphyrins would use step 12, while 14 would be applicable to the insertion of divalent ions into tetrapyridylporphin, in which Fleischer and coworkers[5] found a second-order dependence on metal ion.

In this scheme, the [Cu*TPP], postulated from the kinetic results (eq 4), might resemble a sitting-atop complex[19] lacking its two central protons. It is conceivable that the copper ion in this intermediate is not the copper ion that ends up in the final complex. For example, the kinetics of the insertion of copper and zinc into tetrapyridylporphin in the presence of an excess of metal ions that can form sitting-atop complexes, but not metalloporphyrins (Li^+, Na^+, Ca^{2+}), have been briefly studied.[20] The kinetics are first order in the inserting and the stiting-atop, nonentering ion. This indicates that in cases where the sitting-atop ion is also capable of inserting, another ion that does not sit atop is the one that enters the porphyrin.

Our exchange studies in pyridine give no information on the active role that pyridine plays in such reactions. Plane and coworkers[4,21,22] have demonstrated the importance of pyridine in catalyzing the metal ion insertions and demetalations of porphyrins.

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