

to an oxygen donor. Indeed the isotropic shifts of the macrocyclic polyether protons in the samarium and europium compounds were insignificant; these two metals were among those found by Horrocks and Sipe<sup>15</sup> to shift the H-2 protons in 4-vinylpyridine by less than 4 ppm. On the other hand, the isotropic shifts of the water protons in the thulium and ytterbium compounds were too large to be observed on the available spectrometer; these two metals were among those found by Horrocks and Sipe<sup>15</sup> to shift the H-2 proton in 4-vinylpyridine by more than 10 ppm.

**(D) Lanthanide Separation Experiments.** The close similarities in the ionic radii of the different lanthanides make their chemistry very similar and hence their separation relatively difficult. The significant and systematic differences in the coordinating properties of the macrocyclic polyethers with the different lanthanides suggested that differential complexing behavior with a rigid macrocyclic polyether could be used as a basis for lanthanide separation. In order to test this possibility we chromatographed a mixture of praseodymium and erbium nitrates on a column of dibenzo-18-crown-6 (II) and analyzed the eluates by visible spectroscopy. Dibenzo-18-crown-6 (II) rather than benzo-15-crown-5 (I) was selected as a column material for this experiment for the following reasons: (1) it is more readily available than benzo-15-crown-5; (2) it is essentially insoluble in acetone whereas benzo-15-crown-5 is highly soluble in acetone; (3) it forms less stable complexes

with the lanthanides which should make the lanthanides more readily eluted from a column of dibenzo-18-crown-6 than from one of benzo-15-crown-5. We were able to find conditions in such a chromatography experiment where praseodymium was adsorbed sufficiently more strongly than erbium on a dibenzo-18-crown-6 column that not only qualitative separation between the two metals could be detected spectroscopically but also praseodymium spectroscopically free from erbium could be obtained from the latest lanthanide-containing eluates of such a chromatogram. The demonstrated weaker retention of erbium relative to praseodymium on a dibenzo-18-crown-6 column is a further indication of the previously discussed decreasing stability of lanthanide macrocyclic polyether complexes upon increasing atomic number of the lanthanide. Whether this effect can be exploited to improve the ease, efficiency, and practicality of lanthanide separation can only be determined after considerably more extensive experimentation with macrocyclic polyethers under conditions more closely approximating those currently used for lanthanide separation by ion exchange and related methods.

**Acknowledgment.** We are indebted to the Air Force Office of Scientific Research for partial support of this work under Grant AF-AFOSR-71-2000. One of us (R. B. K.) also acknowledges helpful discussions with Dr. W. C. Zipperer in 1970 which led to initiation of this research project.

### Metal-Porphyrin Interactions. III. A Dissociative-Interchange Mechanism for Metal Ion Incorporation into Porphyrin Molecules<sup>1</sup>

Peter Hambright\* and P. B. Chock

*Contribution from the Department of Chemistry, Howard University, Washington, D. C. 20001, and Laboratory of Biochemistry, National Heart and Lung Institute, National Institutes of Health, Bethesda, Maryland. Received October 31, 1973*

**Abstract:** The kinetics of divalent metal ion incorporation into the monomeric tetrakis(4-*N*-methylpyridyl)porphine (TMTPyP), tetrasulfonated tetraphenylporphine (TPPS<sub>4</sub>), and uroporphyrin I (Uro) were studied in acidic and basic solutions. The TMTPyP reactions were nitrate catalyzed if the formal charge in the activated complex was 6+ and either catalyzed or uncatalyzed pathways operate for lower charges. No anion catalysis was found in the TPPS<sub>4</sub> or Uro reactions. The majority of observations on the incorporation of metal ions into porphyrins can be explained with a dissociative-interchange mechanism, by taking into account porphyrin deformation.

Over the past 10 years, a number of studies<sup>2</sup> have been addressed to the question of how metal ions are incorporated into porphyrin molecules to form metalloporphyrins. While there are many elegant ways to synthesize metalloporphyrins,<sup>3,4</sup> the mechanisms of

such reactions are by no means clear. The earliest kinetic studies used derivatives of protoporphyrin IX which, in combination with Fe(II), is the prosthetic group of hemoglobin.<sup>5</sup> However, their free-base forms are insoluble in acids, and they appear to show extensive association in basic solution.<sup>6</sup> In the presence of detergents such porphyrins and their esters are

(1) Part II: H. Baker, P. Hambright, and L. Wagner, *J. Amer. Chem. Soc.*, **95**, 5942 (1973).

(2) P. Hambright, *Coord. Chem. Rev.*, **6**, 247 (1971).

(3) J. W. Buchler, G. Eikelmann, L. Puppe, K. Rohbock, H. H. Schneehage, and D. Weck, *Justus Liebigs Ann. Chem.*, **745**, 135 (1971).

(4) M. Tsutsui, R. A. Velapoldi, K. Suzuki, F. Vohwinkel, M. Ichikawa, and T. Koyano, *J. Amer. Chem. Soc.*, **91**, 6262 (1969).

(5) J. E. Falk, "Porphyrins and Metalloporphyrins," Elsevier, Amsterdam, 1963, p 62.

(6) W. B. Elliot and W. A. Gallagher, *Ann. N. Y. Acad. Sci.*, **206**, 463 (1973).

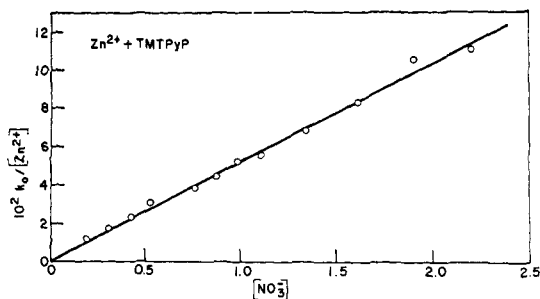


Figure 1. Nitrate dependence of the specific rate of the  $Zn^{2+}$ -TMTPyP reaction, 22°. See eq 1.

soluble and presumably monomerized,<sup>7,8</sup> but the detergents themselves influence strongly the properties under consideration. Nonaqueous media such as acetic acid,<sup>9,10</sup> pyridine,<sup>11</sup> dimethylformamide,<sup>12,13</sup> and methanol<sup>14</sup> have been used to circumvent the solubility problems of natural porphyrins, but in most cases the unclear nature of the metal ion species present prevents clear-cut interpretation.

The recent trend has been to abandon the "biologically active" porphyrins in favor of synthetic compounds having more well-defined behavior, especially the para-substituted derivatives similar to *ms*-tetraphenylporphyrine (TPP). For example *ms*-tetrapyrrolylporphyrine (TPyP),<sup>15</sup> tetra-<sup>16</sup> and trisulfonated<sup>17</sup> TPP (TPPS<sub>4</sub> and TPPS<sub>3</sub>), tetracarboxy TPP,<sup>18</sup> and tetrakis(4-*N*-methylpyridyl)porphyrine (TMTPyP)<sup>19</sup> have been synthesized. Along with sulfonated-<sup>20</sup> and ethylenediamine-substituted<sup>21</sup> deuteroporphyrins and the octacarboxylic acid<sup>22</sup> containing uroporphyrin I (Uro), such derivatives are water soluble and potentially capable of kinetic analysis.

The study of metal ion incorporation is simplified if the porphyrin ligand is monomeric and stable in aqueous solution. Only TPyP and TMTPyP have been shown by kinetic relaxation studies<sup>17</sup> to be monomeric. Uro and TPPS<sub>4</sub> follow Beers law over extreme dilutions and are considered monomeric.<sup>16,22</sup> The other water soluble porphyrins mentioned above show definite evidence for aggregation equilibria being present.<sup>17,23</sup> TPyP is soluble only below pH 4, while TPPS<sub>4</sub> polymerizes<sup>16,17</sup> and Uro is insoluble below this pH. TMTPyP slowly decomposes above pH 11. With these

limitations in mind, we present a study of the kinetics of incorporation of various complexes of the zinc ion into TMTPyP (in the acid region) and into Uro and TPPS<sub>4</sub> under basic conditions. Zinc was chosen because (1) it is amphoteric, (2) the stability constants with many simple ligands are well established,<sup>24</sup> (3) it reacts fairly rapidly with porphyrins, and (4) metal ion exchange<sup>25</sup> and acid solvolysis reactions involving zinc porphyrins<sup>26,27</sup> have been studied. We have suggested<sup>1</sup> that the nature of the peripheral substituents on porphyrins not only influences the rate of metal ion incorporation but also the observed mechanisms of such reactions. TMTPyP, Uro, and TPPS<sub>4</sub> having peripheral charges of (4+), (8-), and (4-), respectively, allow a test of this hypothesis. Our results clearly show certain basic reactivity patterns that allow further elucidation of the incorporation process. It is suggested that a dissociative interchange incorporation process occurs in many cases.

### Experimental Section

The perchlorate salt<sup>19</sup> of TMTPyP and the sodium salt of TPPS<sub>4</sub> were synthesized by literature methods.<sup>16</sup> Uroporphyrin I octamethyl ester (from Sigma Chemical Co.) was hydrolyzed with 6 *M* HCl as described previously.<sup>22</sup> PIPES buffer (piperazine-*N,N'*-bis(2-ethanesulfonic acid monosodium monohydrate) was obtained from Calbiochem. PIPES has a negligible complexing ability for the zinc ion.<sup>28</sup> 2,6-Lutidine was distilled before use. All other chemicals were reagent grade and standardized following conventional methods. The slow kinetics were followed on either a Beckman Acta III or a Cary 17 recording spectrophotometer which had thermostated cell compartments. Faster reactions were observed using a Durrum-Gibson stopped-flow system. The reactions were run at constant wavelength under pseudo-first-order conditions using a greater than twentyfold excess of total metal ion to total porphyrin. All of the reactions were found to be first order in porphyrin. The observed rate constant,  $k_0$ , was calculated as described before.<sup>16</sup>  $k_0$  was found to be independent of whether the disappearance of the free-base porphyrin band or the appearance of the metalloporphyrin peak in the visible or Soret regions was monitored. When studied in detail, isobestic points were found in the visible region as the porphyrin was transformed into the metalloporphyrin. This indicates that the porphyrin and metalloporphyrin are the major absorbing species present. Nitrate salts were used for the kinetic studies, as low concentrations of perchlorate precipitated TMTPyP.

### Results

**$Zn^{2+}$ -TMTPyP, pH 1-4.** The kinetics of  $Zn^{2+}$  incorporation into TMTPyP in unbuffered solutions was studied from pH 1 to 4 at 22°. The rate law was of the form

$$k_0 = \frac{k_1[Zn^{2+}][NO_3^-]}{(1 + (H^+)/K_3 + (H^+)^2/K_3K_4)} \quad (1)$$

At a constant pH and zinc concentration, Figure 1 shows the reaction to be first order in total nitrate from 0.19 to 2.4 *M*  $NO_3^-$ . This is not considered an ionic strength effect on the rate, since the observed rate goes to zero as the nitrate concentration decreases to zero. In addition, no evidence exists<sup>24</sup> for complexes such as  $(Zn(NO_3)_4^+)$  at low nitrate concentrations. Table I

- (7) M. B. Lowe and J. N. Phillips, *Nature (London)*, **190**, 262 (1961).
- (8) M. B. Lowe and J. N. Phillips, *Nature (London)*, **194**, 1058 (1962).
- (9) D. J. Kingman and D. A. Brisbin, *Inorg. Chem.*, **9**, 2034 (1970).
- (10) J. James and P. Hambright, *Inorg. Chem.*, **12**, 474 (1973).
- (11) P. Hambright, *Ann. N. Y. Acad. Sci.*, **206**, 443 (1973).
- (12) F. Longo, E. Brown, and D. Quimby, *Ann. N. Y. Acad. Sci.*, **206**, 420 (1973).
- (13) B. Shah, B. Shears, and P. Hambright, *Inorg. Chem.*, **10**, 1828 (1971).
- (14) S. J. Baum and R. A. Plane, *J. Amer. Chem. Soc.*, **88**, 910 (1966).
- (15) E. B. Fleischer, E. I. Choi, P. Hambright, and A. Stone, *Inorg. Chem.*, **3**, 1284 (1964).
- (16) E. B. Fleischer, J. M. Palmer, T. S. Srivastava, and A. Chatterjee, *J. Amer. Chem. Soc.*, **93**, 3162 (1971).
- (17) R. F. Pasternack, P. R. Huber, P. Boyd, G. Engasser, L. Francesconi, E. Gibbs, P. Fasella, G. Cerio Venturo, and L. De C. Hinds, *J. Amer. Chem. Soc.*, **94**, 4511 (1972).
- (18) F. R. Longo, M. G. Finarelli, and J. B. Kim, *J. Heterocycl. Chem.*, **6**, 927 (1969).
- (19) P. Hambright and E. B. Fleischer, *Inorg. Chem.*, **9**, 1757 (1970).
- (20) J. Weaver and P. Hambright, *Inorg. Chem.*, **9**, 1757 (1970).
- (21) T. P. Stein and R. A. Plane, *J. Amer. Chem. Soc.*, **91**, 607 (1969).
- (22) D. Mauzerall, *J. Amer. Chem. Soc.*, **82**, 2601 (1960).
- (23) R. R. Das, R. F. Pasternack, and R. A. Plane, *J. Amer. Chem. Soc.*, **92**, 3312 (1970).
- (24) L. G. Sillen and A. E. Martell, *Chem. Soc., Spec. Publ.*, No. 17 (1964), and Supplement No. 1, *ibid.*, No. 25 (1971).
- (25) H. Baker, P. Hambright, L. Wagner, and L. Ross, *Inorg. Chem.*, **12**, 2200 (1973).
- (26) B. Shah and P. Hambright, *J. Inorg. Nucl. Chem.*, **32**, 3420 (1970).
- (27) B. Shears, B. Shah, and P. Hambright, *J. Amer. Chem. Soc.*, **93**, 776 (1971).
- (28) N. E. Good, G. D. Winget, W. Winter, T. N. Connolly, S. Izawa, and R. M. M. Singh, *Biochemistry*, **5**, 467 (1966).

**Table I.** Rate Data for the Zn-TMTPyP Reaction at 22°, pH 25

$k_0,^a \text{ sec}^{-1}$	$[\text{Zn}], M$	$[\text{NO}_3^-], M$	$10^2 k_0 / [\text{Zn}][\text{NO}_3^-], M^{-2} \text{ sec}^{-1}$
$3.47 \times 10^{-3}$	$1.41 \times 10^{-1}$	0.68	3.61
$2.17 \times 10^{-3}$	$1.01 \times 10^{-1}$	0.60	3.58
$1.63 \times 10^{-3}$	$8.06 \times 10^{-2}$	0.56	3.61
$7.61 \times 10^{-4}$	$4.03 \times 10^{-2}$	0.48	3.93
$3.77 \times 10^{-4}$	$2.02 \times 10^{-2}$	0.44	4.25
$1.59 \times 10^{-3}$	$8.06 \times 10^{-2}$	0.56	3.51
$1.51 \times 10^{-3}$	$8.06 \times 10^{-2}$	0.56	3.34
$1.61 \times 10^{-3}$	$8.06 \times 10^{-2}$	0.56	3.55
Av $3.67 \pm 0.15$			

<sup>a</sup>  $[\text{TMTPyP}] = 4.2 \times 10^{-5} M$  for the first five reactions and  $1.65 \times 10^{-5}, 8.27 \times 10^{-5}$ , and  $3.32 \times 10^{-6} M$  for the last three, respectively.

shows that, at pH 2.51, the reaction is first order in porphyrin and first order in total zinc over a sevenfold dilution and that the observed rate is independent of total porphyrin over a 12-fold range.

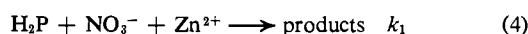
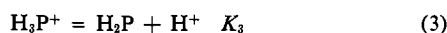
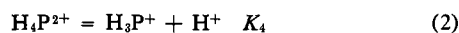
The reaction was studied from pH 4.03 to 1.01 at a nitrate concentration of 0.7 M, and the results are shown in Table II. (At lower pH values the acid-

**Table II.** pH Dependence of the Zn-TMTPyP Reaction, 22°

pH	$(k_0 / [\text{Zn}][\text{NO}_3^-])_{\text{obsd},^a}$ $M^{-2} \text{ sec}^{-1}$	$10^2 k_1,^d$ $M^{-2} \text{ sec}^{-1}$	$(k_0 / [\text{Zn}][\text{NO}_3^-])_{\text{calcd},^e}$ $M^{-2} \text{ sec}^{-1}$
4.03	$4.81 \times 10^{-2}$	4.87	$4.91 \times 10^{-2}$
3.56	$4.68 \times 10^{-2}$	4.84	$4.81 \times 10^{-2}$
3.03	$4.17 \times 10^{-2}$	4.62	$4.47 \times 10^{-2}$
2.54	$3.60 \times 10^{-2}$	4.83	$3.67 \times 10^{-2}$
2.03	$2.31 \times 10^{-2}$	4.97	$2.30 \times 10^{-2}$
1.51	$1.04 \times 10^{-2}$	5.45	$9.43 \times 10^{-3}$
1.01	$2.52 \times 10^{-3}$	4.82	$2.61 \times 10^{-3}$
Av $4.9 \pm 0.2) \times 10^{-2}$			

<sup>a</sup>  $[\text{TMTPyP}] = 4.6 \times 10^{-5} M$ . <sup>b</sup>  $[\text{Zn}] = 1.51 \times 10^{-1} M$ . <sup>c</sup>  $[\text{NO}_3^-] = 0.7 M$ . <sup>d</sup> Calculated from eq 1 with  $pK_3 = (2.07 \pm 0.05)$  and  $pK_4 = (0.8 \pm 0.1)$ . <sup>e</sup> Calculated from eq 1 with the observed parameters.

catalyzed dissociation<sup>19,26</sup> of zinc from ZnTMTPyP would complicate the incorporation kinetics.) Assuming that the porphyrin can exist as the dication ( $\text{H}_4\text{P}^{2+}$ ), monocation ( $\text{H}_3\text{P}^+$ ), and free-base ( $\text{H}_2\text{P}$ ) forms in this pH range and that only the free base can incorporate  $\text{Zn}^{2+}$ , the following mechanism can be written



$K_3$  and  $K_4$  are rapid preequilibria. The total porphyrin concentration ( $P_T$ ), is expressed as

$$P_T = (\text{H}_3\text{P}^+) + (\text{H}_4\text{P}^{2+}) + (\text{H}_2\text{P}) + (\text{ZnP}) \quad (5)$$

Equation 1 can be derived from reactions 2-5. The reciprocal of the denominator in eq 1 is the fraction of porphyrin in the free-base form ( $(\text{H}_2\text{P}) / (P_T - \text{ZnP})$ ). The term  $(\text{H}^+)^2 / K_3 K_4$  in eq 1 is small between pH 2 and 4. Thus a plot of  $([\text{NO}_3^-][\text{Zn}^{2+}] / k_0)$  vs.  $(\text{H}^+)$  was used to find  $1/k_1$  (the intercept) and  $(1/k_1 K_3)$ , the slope.  $K_4$  was chosen to fit the observed data using the derived  $k_1$  and  $K_3$  values. With  $pK_3 = 2.06 \pm 0.5$ ,  $pK_4 = 0.8 \pm 0.1$ , and  $k_1 = (3.7 \pm 0.2) \times 10^{-2} M^{-1} \text{ sec}^{-1}$ ,

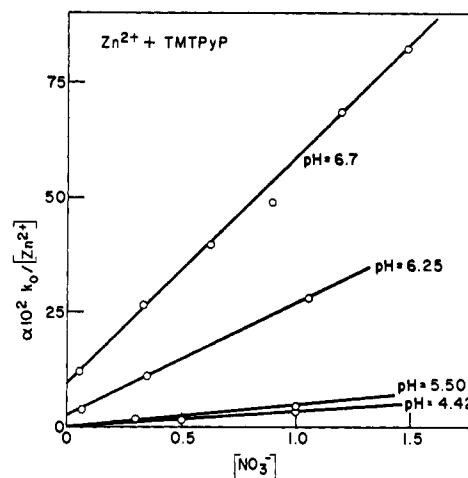
**Figure 2.** Nitrate dependence of the  $\text{Zn}^{2+}$ -TMTPyP reaction as a function of pH. See eq 6.

Table II shows the agreement between the calculated and observed values of  $(k_0 / [\text{Zn}^{2+}][\text{NO}_3^-])$ . The  $K_4$  value is not well known because, as noted above, satisfactory data could not be obtained below pH 1 where  $K_4$  has most effect on the reaction rate.

**$\text{Zn}^{2+}$ -TMTPyP, pH 4-7.** Figure 2 shows plots of  $(k_0 / [\text{Zn}^{2+}])$  vs.  $[\text{NO}_3^-]$  for  $\text{Zn}^{2+}$  incorporation into TMTPyP above pH 4. The pH 4.42 and 5.50 data are in unbuffered solutions and are approximately the same. The 6.25 and 6.7 data are run in 2,6-lutidine- $\text{HNO}_3$  buffers. At pH 6.7 with 1 M  $\text{NaNO}_3$  and 0.05 M buffer, the rate was first order in total zinc from  $1.53 \times 10^{-3}$  to  $15.3 \times 10^{-3} M$ , with a specific rate constant of  $(52 \pm 2) \times 10^{-2} M^{-1} \text{ sec}^{-1}$ . The observed rate depended strongly on total buffer concentration. The absorption spectra of the porphyrin was unaffected by  $10^{-2} M$  buffer. At constant zinc, plots of  $k_0$  vs.  $[\text{NO}_3^-]$  at various buffer concentrations were straight lines, whose slopes and intercepts increased with a decrease in total buffer. It is concluded that although steric hinderance is present, 2,6-lutidine does form reactive complexes with zinc species. The data in Figure 2 suggest that a rate law of the form

$$k_0 = k'(\text{ZnOH}^+) + [k''(\text{Zn}^{2+}) + k'''(\text{ZnOH}^+)][\text{NO}_3^-] \quad (6)$$

might be operative, with  $k'$ ,  $k''$ , and  $k'''$  functions of 2,6-lutidine concentration. Since other available buffers are either strongly complexing or have zwitterion forms that would probably catalyze the reaction, no definite conclusions can be drawn in this pH range with TMTPyP.

**$\text{Zn}^{2+}$ -TPPS<sub>4</sub>, pH 6-7.** TPPS<sub>4</sub> has  $(pK_3 + pK_4)^{29} = 4.6$  and is thus in the free-base form above pH 6. Table III shows the kinetic results found for  $\text{Zn}^{2+}$  incorporation at 25°. The reaction was first order in porphyrin and first order in total zinc over a fivefold range at constant pH and PIPES concentration. The observed rate was independent of PIPES and showed little dependence on nitrate from 0.02 to 0.6 M. The absorption spectra of TPPS<sub>4</sub> was not altered by PIPES ( $10^{-2} M$  buffer, pH 7). The rate increased with an increase in pH between 6.3 and 7.1. At higher pH values

(29) N. Johnson, R. Khosropour, and P. Hambricht, *J. Inorg. Nucl. Chem. Lett.*, **8**, 1067 (1972).

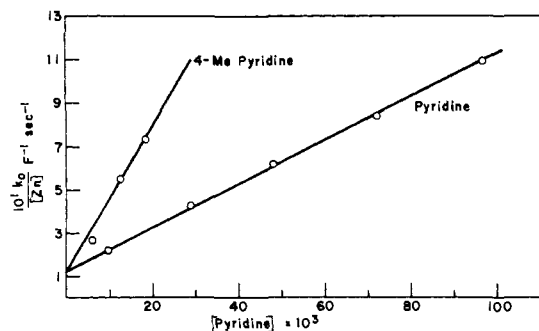


Figure 3. Pyridine catalysis of the  $Zn^{2+}$ -TMTPyP reaction. See eq 9.

Table III. Rate Data for Zn-TPPS<sub>4</sub> Reactions, 25°

$10^3 k_0$ , $sec^{-1}$ <sup>a,b</sup>	$10^3 [Zn^{2+}]$ , $M$	$10 k_0 / [Zn^{2+}]$ , $M^{-1} sec^{-1}$	pH	$10 [NO_3^-]$ , <sup>c</sup> $M$
12.1	10.0	12.1	6.51	0.21
11.0	10.0	11.0	6.52	1.00
9.30	10.0	9.30	6.52	2.20
10.2	10.0	10.2	6.51	4.20
9.82	10.0	9.82	6.52	6.20
1.92	2.00	9.60	6.51	0.20
3.96	4.00	9.90	6.52	2.00
3.62	4.00	9.10	6.50	2.00
12.6	8.00	15.7	7.08	2.00
10.3	8.00	12.9	6.87	2.00
8.32	8.00	10.4	6.67	2.00
7.98	8.00	9.99	6.49	2.00
6.79	8.00	8.49	6.29	2.00

<sup>a</sup> [PIPES] =  $1.41 \times 10^{-2} M$  except entry 8, which is  $5.60 \times 10^{-3} M$ . <sup>b</sup> [TPPS<sub>4</sub>] =  $1.3 \times 10^{-7} M$ . <sup>c</sup> Nitrate from  $Zn(NO_3)_2$  and  $NaNO_3$ .

zinc precipitates from  $10^{-3} M$  solutions. The rate law is of the form

$$k_0 = k_2(Zn^{2+}) + k_3(ZnOH^+) \quad (7)$$

This can be transformed into

$$\frac{(1 + K'(OH^-))k_0}{[Zn]} = k_2 + k_3 K'(OH^-) \quad (8)$$

$K'$  is the ratio of the hydrolysis constant ( $10^{-8.79}$  at 27°)<sup>24</sup> of  $Zn^{2+}$ -( $ZnOH^+$ ) to the ion product of water ( $K_w$ ) and is equal to  $1.62 \times 10^5$ . Using data from Table III, a plot of the left-hand side of eq 7 vs.  $K'(OH^-)$  gave  $k_2 = (7.6 \pm 0.1) \times 10^{-1}$  and  $k_3 = (41 \pm 4) M^{-1} sec^{-1}$ .

**Pyridine Catalysis of the Zn-TMTPyP Reaction.** The reaction of zinc with TMTPyP was initially studied at pH 5.2 in a 2,6-lutidine- $HNO_3$  buffer, in the presence of pyridine or 4-methylpyridine. The rate was first order in porphyrin and independent of total porphyrin over a twofold ( $11$ – $5.1 \times 10^{-6} M$ ) range. With a constant total lutidine (ca.  $0.04 M$ ) and nitrate ( $0.1 M$ ) concentration, Figure 3 shows the linear relationship between ( $k_0/[Zn]$ ) vs. [pyridine], of the form

$$(k_0/[Zn]) = k_A + k_B[\text{pyridine}] \quad (9)$$

$k_A = 11.3 \times 10^{-2} M^{-1} sec^{-1}$  while  $k_B(\text{pyridine}) = 10 \times 10^{-2}$  and  $k_B(4\text{-methylpyridine}) = 34 \times 10^{-2} M^{-2} sec^{-1}$ , at 27°. Equation 7 is purely empirical and is a rough representation of the data for one zinc concentration. Since the 2,6-lutidine buffer was shown to affect the reaction rate, more extensive data were taken at pH 5.3 (27°) using pyridine- $HNO_3$  as the buffer system.

Table IV. Effect of  $NO_3^-$  on the Zn-TMTPyP Reaction with Pyridine, 27°

$k_0$ , <sup>a-c</sup> $sec^{-1}$	$[NO_3^-]$ , $M$	$10 k_0 / [Zn][NO_3^-]$ , $M^{-2} sec^{-1}$
$1.80 \times 10^{-3}$	$9.50 \times 10^{-2}$	4.71
$4.51 \times 10^{-3}$	$2.42 \times 10^{-1}$	4.64
$6.93 \times 10^{-3}$	$3.88 \times 10^{-1}$	4.49
$1.31 \times 10^{-2}$	$6.81 \times 10^{-1}$	4.79
$1.81 \times 10^{-2}$	$9.74 \times 10^{-1}$	4.62
$2.34 \times 10^{-2}$	$12.7 \times 10^{-1}$	4.57

<sup>a</sup>  $[Zn] = 4.02 \times 10^{-2} M$ . <sup>b</sup> (py) =  $4.31 \times 10^{-3} M$ . <sup>c</sup> pH 5.30.

Table V. Rate Data for Zn-TMTPyP with Pyridine,<sup>a,b</sup> 27°

$[NO_3^-]$ , $M$	$10^2 [Zn]$ , $M$	$10^3 (\text{py})$ , $M$	Obsd	Calcd
$1.68 \times 10^{-1}$	8.05	1.68	20.1	19.6
$1.76 \times 10^{-1}$	8.05	2.86	32.1	32.0
$1.83 \times 10^{-1}$	8.05	3.96	44.6	44.5
$1.64 \times 10^{-1}$	8.05	5.16	58.5	60.3
$1.97 \times 10^{-1}$	8.05	6.03	73.3	73.0
$2.05 \times 10^{-1}$	8.05	6.95	88.5	88.3
$2.12 \times 10^{-1}$	8.05	7.86	104.2	104.8
$4.2 \times 10^{-2}$	2.11	6.93	88.1	86.9
$1.41 \times 10^{-1}$	6.33	3.32	35.9	36.9
$2.68 \times 10^{-1}$	12.7	1.89	23.8	22.6

<sup>a</sup> pH 5.30. <sup>b</sup> [TMTPyP] =  $3.2 \times 10^{-5} M$ .

The results listed in Tables IV and V are analyzed in terms of the four-term rate law

$$k_0 = [k_1(Zn^{2+}) + k_4(Zn(\text{py})^{2+}) + k_5(Zn(\text{py})_2^{2+}) + k_6(Zn(\text{py})_3^{2+})][NO_3^-] \quad (10)$$

This can be transformed into

$$\left[ \frac{\alpha k_0}{[Zn][NO_3^-]} - k_1 - k_4 \beta_1 (\text{py}) \right] (\text{py})^{-2} = k_5 \beta_2 + k_6 \beta_3 (\text{py}) \quad (11)$$

$\beta_1$ ,  $\beta_2$ , and  $\beta_3$  are the formation constants for the zinc-pyridine species and were taken<sup>24</sup> as ( $1.2 \times 10^2$ ), ( $5.89 \times 10^3$ ), and ( $6.3 \times 10^4$ ), respectively. ( $1/\alpha$ ) is the fraction  $(Zn^{2+})/[Zn]$ , and the  $pK$  of pyridine used was 5.11. The free pyridine concentrations were determined by solution of the cubic equation in pyridine derived from the mass balances present in this system.

Table IV shows that at constant pyridine and zinc concentration, the reaction is first order in total nitrate over a 12-fold range.  $k_1$  was determined by a method similar to eq 9. At low pyridine concentrations, the  $k_5$  and  $k_6$  terms are negligible, and a plot of ( $\alpha k_0/[Zn][NO_3^-] - k_1$ ) vs. (pyridine) gave as a slope  $k_4 \beta_1$ .  $k_5$  and  $k_6$  were then determined from a plot of the left-hand side of eq 9 vs. pyridine, which is shown in Figure 4. The resulting  $k$  values are listed in Table VIII. Using these, Table V shows (1) the excellent agreement between the calculated and observed values of ( $k_0/[Zn][NO_3^-]$ ) and (2) the fact that the reaction is first order in total zinc.

**Acetate Catalysis of the Zn-TMTPyP Reaction.** The kinetics of the Zn-TMTPyP reaction in acetic acid buffers (22°) could be fitted to a rate law of the form

$$k_0 = k_7(Zn(OAc)^+) + k_8((Zn(OAc)_2) + [k_1(Zn^{2+}) + k_9(Zn(OAc)^+)] [NO_3^-] \quad (12)$$

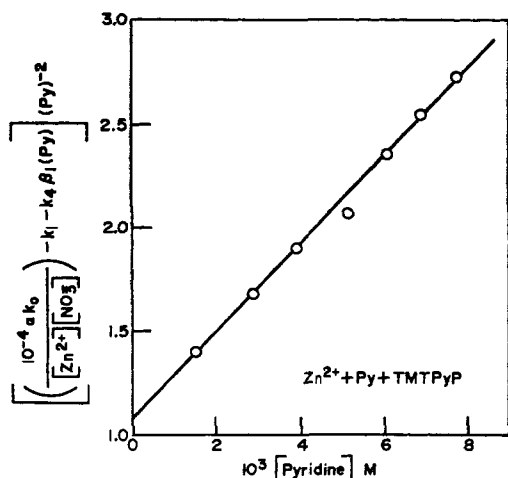


Figure 4. Graph of eq 11, for  $Zn^{2+}$ -TMTPyP with pyridine.

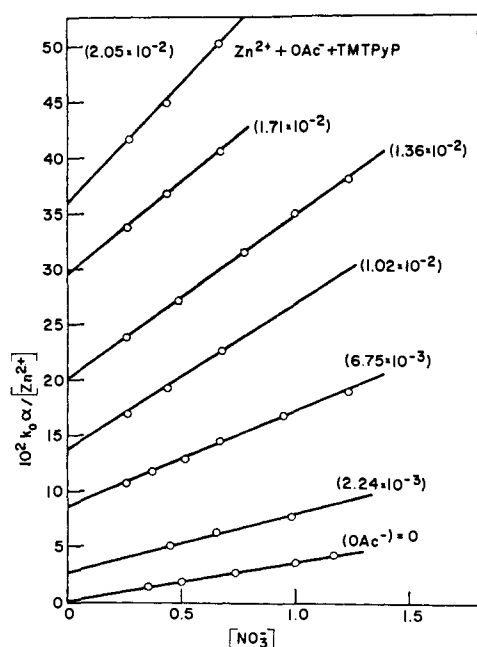


Figure 5. Graph of  $(\alpha k_0/[Zn])$  vs.  $NO_3^-$  for the Zn-TMTPyP reaction at various  $(OAc^-)$  concentrations,  $22^\circ$ . See eq 12.

This can be transformed into

$$\frac{k_0}{[Zn]} = k_7\beta_1'(OAc^-) + k_8\beta_2'(OAc^-)^2 + \frac{[k_1 + k_9\beta_1(OAc^-)][NO_3^-]}{[Zn^{2+}]} \quad (13)$$

$\beta_1'$  and  $\beta_2'$  are the cumulative formation constants<sup>24</sup> for  $Zn(OAc)^+$  and  $Zn(OAc)_2$ , taken as 19.05 and 123, respectively. The reaction was studied at pH 3.70, with the pK of acetic acid equal to 4.55. The free acetate concentrations were determined by solution of the cubic equation in acetate derived from the mass balances present. Figure 5 shows a plot of  $\alpha k_0/[Zn]$  vs.  $[NO_3^-]$  at different acetate concentrations. Both the slopes and intercepts depend on acetate. Figure 6 is a plot of  $[\text{intercept}/(OAc^-)]$  vs.  $(OAc^-)$  used to determine  $k_7$  and  $k_8$ . Figure 7 shows a plot of the slopes of Figure 5 vs.  $(OAc^-)$  used to determine  $k_1$  and  $k_9$ . The results are listed in Table VIII.

Kinetics of Cu, Co, Mn, and Ni with TMTPyP.

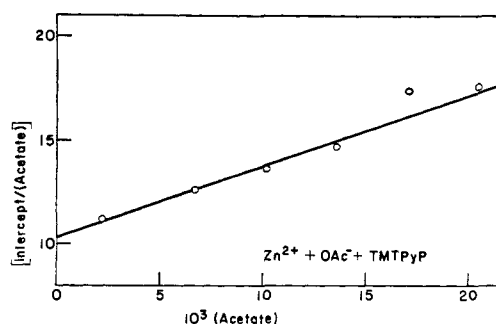


Figure 6. Graph of the  $(\text{intercept}/OAc^-)$  vs.  $(OAc^-)$  from Figure 5. See eq 12.

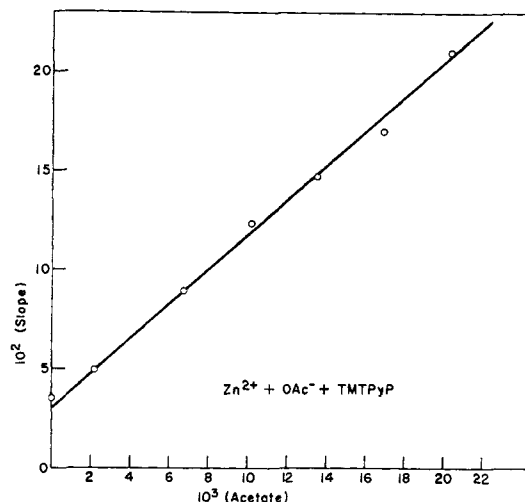


Figure 7. Graph of the  $(\text{slopes})$  vs.  $(OAc^-)$  from Figure 5, for the acetate catalysis of  $Zn^{2+}$ -TMTPyP. See eq 12.

Table VI. Rate Data for the  $M^{2+}$  TMTPyP Reactions,  $22^\circ$

Metal	$k_0, a, b \text{ min}^{-1}$	$[M^{2+}], M$	$[NO_3^-], M$	$\frac{k_0}{[M^{2+}][NO_3^-]}, M^{-2} \text{ min}^{-1}$
Copper	53.4	$5.01 \times 10^{-1}$	2	53.3
	41.6	$4.00 \times 10^{-1}$	2	51.9
	20.9	$2.01 \times 10^{-1}$	2	52.1
	$10.2 \times 10^{-2}$	$9.66 \times 10^{-4}$	2	52.5
			Av	$52.5 \pm 0.5$
Manganese	$1.39 \times 10^{-2}$	$1.45 \times 10^{-1}$	0.68	$14.4 \times 10^{-2}$
	$9.57 \times 10^{-3}$	$1.01 \times 10^{-1}$	0.60	$15.8 \times 10^{-2}$
	$4.76 \times 10^{-3}$	$6.06 \times 10^{-2}$	0.52	$15.1 \times 10^{-2}$
	$2.84 \times 10^{-3}$	$4.04 \times 10^{-2}$	0.48	$15.0 \times 10^{-2}$
			Av	$(15.1 \pm 0.4) \times 10^{-2}$
Cobalt	$8.25 \times 10^{-3}$	$1.44 \times 10^{-1}$	0.49	$11.7 \times 10^{-2}$
	$5.58 \times 10^{-3}$	$1.03 \times 10^{-1}$	0.41	$13.2 \times 10^{-2}$
	$2.73 \times 10^{-3}$	$6.18 \times 10^{-2}$	0.32	$13.8 \times 10^{-2}$
	$1.69 \times 10^{-3}$	$4.12 \times 10^{-2}$	0.28	$14.6 \times 10^{-2}$
			Av	$(13.3 \pm 0.8) \times 10^{-2}$
Nickel	$2.15 \times 10^{-3}$	$6.40 \times 10^{-1}$	1.28	$2.6 \times 10^{-3}$
	$1.17 \times 10^{-3}$	$4.61 \times 10^{-1}$	0.92	$3.2 \times 10^{-3}$
				Av

<sup>a</sup> [TMTPyP] from  $1.0$  to  $6.2 \times 10^{-5} M$ . <sup>b</sup> Copper data at pH 2.1, the rest at pH 4.0.

Table VI contains the kinetic results found for Co, Ni, and Mn reacting with the free-base form of TMTPyP at pH 4 and  $Cu^{2+}$  at pH 2.1. After correcting the data

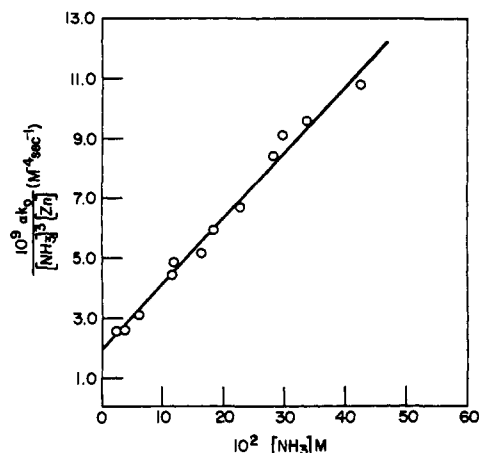


Figure 8. Graph of eq 15 for the  $Zn^{2+}$ -TPPS<sub>4</sub> reaction in ammonia buffers, 25°.

for the nitrate ion dependence, the reactions were all first order in total metal ion. It is noted that the copper data were taken over the widest metal ion range possible. No deviation from first-order behavior was observed.

**Zn<sup>2+</sup>-TPPS<sub>4</sub> and Uro in NH<sub>3</sub> Buffers.** The procedure used for the Zn-TPPS<sub>4</sub> reaction in ammonia buffers will be described. The logarithms of the stability constants for the Zn<sup>2+</sup>-NH<sub>3</sub> complexes<sup>24</sup> are  $\beta_1 = 2.32$ ,  $\beta_2 = 4.61$ ,  $\beta_3 = 6.79$ , and  $\beta_4 = 9.36$ , at 30°,  $\mu = 2.0$ . The NH<sub>4</sub><sup>+</sup>-NH<sub>3</sub> pK was taken as 9.31. The reactions were run at 28° at  $\mu = 1.0$  (NaNO<sub>3</sub>) from pH 8.72 to 9.85, with the free ammonia concentrations varying from  $2.51 \times 10^{-2}$  to  $32.9 \times 10^{-2}$  M. In this range, the predominant species are Zn(NH<sub>3</sub>)<sub>3</sub><sup>2+</sup> and Zn(NH<sub>3</sub>)<sub>4</sub><sup>2+</sup>. At a constant pH and total ammonia concentration, the reactions were first order in porphyrin and first order in total zinc from  $8.96 \times 10^{-5}$  to  $35.8 \times 10^{-5}$  M. The rate law was assumed to be of the form

$$k_0 = k_{10}(Zn(NH_3)_3^{2+}) + k_{11}(Zn(NH_3)_4^{2+}) \quad (14)$$

This can be transformed into

$$\frac{k_0}{[Zn^{2+}]} = \frac{[k_{10}\beta_3(NH_3)^3 + k_{11}\beta_4(NH_3)^4]}{[1 + \beta_1(NH_3) + \beta_2(NH_3)^2 + \beta_3(NH_3)^3 + \beta_4(NH_3)^4]} \quad (15)$$

Calling the denominator of the right-hand side of eq 15  $\alpha$ , a graph of  $\alpha k_0/([Zn^{2+}](NH_3)^3)$  vs.  $(NH_3)$  gives  $k_{10}\beta_3$  as the intercept and  $k_{11}\beta_4$  as the slope, as shown in Figure 8. The data were least squared giving  $k_{10}\beta_3 = (1.81 \pm 0.33) \times 10^9$  and  $k_{11}\beta_4 = (2.44 \pm 0.12) \times 10^{10}$ . Thus  $k_{10} = (194 \pm 24) M^{-1} sec^{-1}$  and  $k_{11} = (11 \pm 1) M^{-1} sec^{-1}$ . The same procedure was used to find  $k_{10}$  and  $k_{11}$  for Uro, and the results are shown in Table VIII. By varying the nitrate concentration from 0.3 to 1.2 M, less than 5% rate increase was found. Thus the TPPS<sub>4</sub> and Uro reactions are not nitrate catalyzed.

The Zn<sup>2+</sup>-TMTPyP reactions in ammonia buffers showed a different reactivity pattern. At constant pH and ammonia concentration, the reactions were first order in porphyrin and total zinc and showed little

NO<sub>3</sub><sup>-</sup> dependence. At constant pH, the rates were first order in Zn(NH<sub>3</sub>)<sub>3</sub><sup>2+</sup>, with Zn(NH<sub>3</sub>)<sub>4</sub><sup>2+</sup> apparently unreactive. In contrast to the TPPS<sub>4</sub> and Uro reactions which were pH independent, the TMTPyP reaction rates increased with pH. We were unable to fit a rate law to the complex pH dependence. It appeared as if both the monoanion (HP<sup>-</sup>) and dianion (P<sup>2-</sup>) forms were reacting with only Zn(NH<sub>3</sub>)<sub>3</sub><sup>2+</sup> with very large specific rate constants ( $>10^5 M^{-1} sec^{-1}$ ). While TMTPyP has been shown<sup>19</sup> to have a free-base monoanion pK<sub>2</sub> of 12.9, we were unable to rationalize the results with this parameter. It was found that the intensity of the absorption bands of TMTPyP decreased with time in the absence of light above pH 11.

**Uro, Zn(OH)<sub>3</sub><sup>-</sup>-Zn(OH)<sub>4</sub><sup>2-</sup>.** The reaction of the free base form or Uro with zinc species in the pH range 9.6-11 was studied at 28° in unbuffered solutions,  $\mu = 0.2$  (NaNO<sub>3</sub>). The reaction was first order in total zinc ( $(1.2$  to  $7.7) \times 10^{-5}$  M), independent of NO<sub>3</sub><sup>-</sup> from 0.1 to 0.5 M, and first order in porphyrin (*ca.*  $10^{-7}$  M). The pK<sub>b</sub> of Zn(OH)<sub>3</sub><sup>-</sup>-Zn(OH)<sub>4</sub><sup>2-</sup> was taken<sup>24</sup> as 5.11 (25°). The observed rate law was of the form

$$k_0 = k_{12}(Zn(OH)_3^{2-}) + k_{13}(Zn(OH)_4^{2-}) \quad (16)$$

This can be rewritten as

$$k_0 = \frac{(k_{12} + k_{13}K_b^{-1}(OH^-))[Zn^{2+}]}{[1 + K_b^{-1}(OH^-)]} \quad (17)$$

A plot of  $k_0([Zn^{2+}]^{-1}(1 + K_b^{-1}(OH^-)))$  vs.  $K_b^{-1}(OH^-)$  was linear, and a least-squares analysis gave  $k_{12} = (5.9 \pm 1.5) M^{-1} sec^{-1}$  and  $k_{13} = (76 \pm 2) M^{-1} sec^{-1}$ .

## Discussion

**Comparisons with Similar Reactions.** The form of the rate law for the Zn<sup>2+</sup>-TMTPyP reaction (eq 1) is the same as that found<sup>1</sup> for Cu<sup>2+</sup>-TMTPyP. This is not a trivial observation since different rate laws have been reported for copper and zinc incorporation into an ethylenediamine-substituted protoporphyrin.<sup>30</sup> In the Cu<sup>2+</sup>-TMTPyP reaction, pK<sub>3</sub> and pK<sub>4</sub> increase with an increase in ionic strength. At the same ionic strength (0.7 M NaNO<sub>3</sub>), the copper reaction gives (2.0, 0.7) for these parameters, which is essentially the same as found for Zn<sup>2+</sup>-TMTPyP (2.1, 0.8) even though the zinc reaction is 46 times slower than that of copper. The fact that these pK values can be independently arrived at from H<sup>+</sup>-TMTPyP titrations,<sup>1</sup> and the observations that the Mn and Co reactions are also nitrate catalyzed, lends support to the proposed reaction mechanism. The order (Table VII) of divalent metal ion reactivities

Table VII. Rate Data for Divalent Aquo Ion Incorporation into TMTPyP Compared to the Corresponding Water Dissociation Rate Constants

Ion	TMTPyP <sup>a</sup> 10 <sup>2</sup> k <sub>1</sub> , M <sup>-2</sup> min <sup>-1</sup>	k <sub>d</sub> , <sup>b</sup> min <sup>-1</sup>	10 <sup>9</sup> k <sub>1</sub> /k <sub>d</sub> , M <sup>-2</sup>
Cu <sup>2+</sup>	13,800 ± 1800	3 × 10 <sup>10</sup>	4.6
Zn <sup>2+</sup>	300 ± 20	1.8 × 10 <sup>9</sup>	1.7
Mn <sup>2+</sup>	15 ± 1	3.6 × 10 <sup>8</sup>	0.42 <sup>c</sup>
Co <sup>2+</sup>	13 ± 1	2.4 × 10 <sup>7</sup>	5.4
Ni <sup>2+</sup>	0.3	1.8 × 10 <sup>6</sup>	1.7

<sup>a</sup> Data from Table VI and ref 1, 22°. <sup>b</sup> Data from ref 38 and ref 49. <sup>c</sup> The observed product is Mn<sup>III</sup>P.

(30) R. R. Das, *J. Inorg. Nucl. Chem.*, **34**, 1263 (1972).

Cu  $\gg$  Zn > Mn  $\sim$  Co > Ni has been shown qualitatively by other workers.<sup>21</sup>

The Zn<sup>2+</sup>-TPPS<sub>4</sub> reaction was previously<sup>31</sup> found to have a specific rate constant of  $4.76 \times 10^{-1} M^{-1} \text{sec}^{-1}$  (30°) at pH 7.0,  $\mu = 1.0$  (NaClO<sub>4</sub>), and 0.05 M Tris. This is in fair agreement with our value of  $15.7 \times 10^{-1} M^{-1} \text{sec}^{-1}$  at 25°. It is concluded from our work that the former rate<sup>31</sup> is a composite of that for Zn<sup>2+</sup> and ZnOH<sup>+</sup>, where ZnOH<sup>+</sup> is about 50 times more reactive than Zn<sup>2+</sup>. The specific rate of  $29.1 M^{-1} \text{sec}^{-1}$  reported in acetic acid buffers<sup>29</sup> for Zn-TPPS<sub>4</sub> is also a composite rate since we find the Zn<sup>2+</sup>-TMTPyP reaction to be strongly acetate catalyzed.

The incorporation of zinc into a water soluble ethylenediamine-substituted protoporphyrin was catalyzed by substituted pyridines<sup>21</sup> in the same manner (eq 9) as Zn<sup>2+</sup>-TMTPyP. This catalysis can now be explained by the reaction proceeding through Zn<sup>2+</sup>, Zn(Py)<sup>2+</sup>, Zn(Py)<sub>2</sub><sup>2+</sup>, and Zn(Py)<sub>3</sub><sup>2+</sup>, which react at different rates. The imidazole catalysis found with the substituted protoporphyrin<sup>21</sup> presumably can be interpreted in a similar fashion.

The reactions of ferrous ion in pyridine solutions with porphyrins<sup>32</sup> showed rates which increased with the number of negative peripheral substituents on the porphyrin. This was due to an activation entropy effect. The same trend is noted in the zinc-ammine reactions with Uro and TPPS<sub>4</sub> having peripheral charges of 8- and 4-, respectively. The rate ratio Zn(NH<sub>3</sub>)<sub>8</sub><sup>2+</sup>-Zn(NH<sub>3</sub>)<sub>4</sub><sup>2+</sup> is 31 for Uro and 17 for TPPS<sub>4</sub>, possibly indicating a small discrimination factor between the reactants and the two porphyrins. Qualitative work showed that TMTPyP (4+) incorporated anionic forms of copper in basic solution orders of magnitude faster than<sup>33</sup> hematoporphyrin (2-). The periphery effect here could be aided by the increased reactivity of the mono- and dianion forms, compared to the free base of TMTPyP. As expected,<sup>20</sup> the mono- and dication porphyrins do not incorporate metal ions.

**Anion Catalyzed and Uncatalyzed Incorporation Mechanisms.** The TMTPyP results clearly show that an activated complex having a formal 6+ charge, which could consist of a divalent metal ion and the free-base form of TMTPyP (4+ by virtue of the four  $\gg$ NCH<sub>3</sub><sup>+</sup> groups) does not lead to metal ion incorporation.<sup>34</sup> Transition states (5+) which have TMTPyP and (1) divalent ions [M<sup>2+</sup>, Zn(Py)<sub>2</sub><sup>2+</sup> (x = 1, 2, 3)] and a nitrate anion or (2) monovalent ions [Zn(OAc)<sup>+</sup> and

probably Zn(OH)<sup>+</sup>] will incorporate metals. Similarly 4+ activated complexes with TMTPyP and either Zn(OAc)<sub>2</sub> or (NO<sub>3</sub><sup>-</sup>, Zn(OAc)<sup>+</sup>) are reactive. It is noted that in metal ion exchange reactions<sup>25</sup> (Zn-TMTPyP, NO<sub>3</sub><sup>-</sup>, Cu<sup>2+</sup>) and acid-catalyzed solvolysis reactions<sup>26</sup> (ZnTMTPyP, 2H<sup>+</sup>, NO<sub>3</sub><sup>-</sup>), the composition of the activated complexes as defined by the rate law always have formal charge less than 6+.

In contrast, the incorporation of divalent ions into Uro (8-) and TPPS<sub>4</sub> (4-) is not anion catalyzed. The metal ion exchange<sup>31</sup> (Cu<sup>2+</sup>, ZnTPPS<sub>4</sub>) and acid-catalyzed solvolysis<sup>31</sup> (ZnTPPS<sub>4</sub>, 2H<sup>+</sup>) reactions of TPPS<sub>4</sub> also show little anion catalysis. This is presumably because the activated complexes in such reactions always have formal charges less than 6+.

It must be concluded that the charge on the porphyrin periphery can influence the form of the rate law for metal ion incorporation, metal ion exchange, and acid-catalyzed solvolysis processes. Similar conclusions have been reached in ligand substitution reactions of iron porphyrins. Porphyrins having positive substituents favor reaction with imidazole,<sup>35</sup> while negatively substituted iron porphyrins react with the imidazolium ion.<sup>36</sup>

**Reactivity Patterns.** Factors which favor the loss of ligands coordinated to the metal in the activated complex should promote the metal ion incorporation process. Thus the relative incorporation order of the divalent metal ions, Cu > Zn > Mn  $\sim$  Co > Ni, parallels their rates<sup>37</sup> of water exchange (Table VII). Similarly an increase in the number of nitrogen donor ligands around a metal ion has a labilizing effect on coordinated water molecules, and this is clearly shown in the incorporation order Zn(Py)<sub>3</sub><sup>2+</sup> > Zn(Py)<sub>2</sub><sup>2+</sup> > Zn(Py)<sup>2+</sup> > Zn<sup>2+</sup>, and Zn(NH<sub>3</sub>)<sub>3</sub><sup>2+</sup> > Zn(NH<sub>3</sub>)<sub>4</sub><sup>2+</sup> > Zn<sup>2+</sup>. The tetrahedral nature of these complexes *vs.* the presumed octahedral character of Zn<sub>aq</sub><sup>2+</sup> could also favor incorporation.

The substitution rate patterns for zinc complexes parallel those of nickel systems.<sup>38</sup> For nickel, the charge of the complex does not in general influence the ligand dissociation rate. It has been shown<sup>39</sup> that the lability of water in monosubstituted [(H<sub>2</sub>O)<sub>5</sub>NiX] complexes increases with the electron donor power of X. Our incorporation rates show the same trend. Using Edwards' E<sub>A</sub> as a measure of donor ability<sup>40</sup> (and assuming the Zn<sup>2+</sup>-Zn(OH)<sup>+</sup> rate ratio is the same for TPPS<sub>4</sub> and TMTPyP), the order of the nitrate catalyzed zinc insertion (Table VIII) into TMTPyP with [ZnX] complexes is OH<sup>-</sup> (1.65 = E<sub>A</sub>) > pyridine (1.20) > acetate (0.95) > H<sub>2</sub>O (0.00).

**Mechanisms of Metal Ion Incorporation.** An important observation is that the rate law in the zinc-ammine reaction is first order in Zn(NH<sub>3</sub>)<sub>4</sub><sup>2+</sup> and first order in free base porphyrin. This demonstrates that metal ions with intact coordination shells can exist with the porphyrin in the activated complex. The subsequent rearrangement of the metal ions' coordination

(31) S. F. Cheung, F. L. Dixon, E. B. Fleischer, D. Y. Jeter, and M. Krishnamurthy, *Bioinorg. Chem.*, **2**, 281 (1973).

(32) R. J. Kassner and J. H. Wang, *J. Amer. Chem. Soc.*, **88**, 5170 (1966).

(33) D. K. Cabiness and D. W. Margerum, *J. Amer. Chem. Soc.*, **92**, 2151 (1970).

(34) The protonated tetrapositive TPyP behaves in the same manner<sup>1</sup> as TMTPyP. The electron transfer reaction between Cr<sup>2+</sup> and Fe<sup>3+</sup>-TPyP studied at  $\mu = 1.0$  (HClO<sub>4</sub>-NaClO<sub>4</sub>) has a rate law of the form rate =  $[k_c + k_x[X^-]][Cr^{2+}][FeTPyP]$ : P. Hambricht and E. B. Fleischer, *Inorg. Chem.*, **4**, 912 (1965). The interpretation was that  $k_c$  is the uncatalyzed pathway and  $k_x$  the electron transfer route mediated by anions (Cl<sup>-</sup>, Br<sup>-</sup>, I<sup>-</sup>, SCN<sup>-</sup>). In the present context, one could assume that 7+ activated complexes are unreactive and thus  $k_c = k_c^-(ClO_4^-)$ . The  $k_x$  term may be simply a reflection of the necessity for an anion in the transition state to reduce total charge, and hence  $k_x$  would give no definite information on the mediating properties of anions. The observation (A. Forman and N. Sutin, *J. Amer. Chem. Soc.*, **93**, 5274 (1971)) of a dependence of SCN<sup>-</sup> in the oxidation of Cr<sup>2+</sup> by metal-free TPyP could arise from the same causes. Preliminary results show other iron porphyrin reductions by Cr<sup>2+</sup> to be very slightly halide catalyzed.

(35) G. B. Kolski and R. A. Plane, *J. Amer. Chem. Soc.*, **94**, 3740 (1972).

(36) B. B. Hasinoff, H. B. Dunford, and D. G. Horne, *Can. J. Chem.*, **47**, 3225 (1969).

(37) A. McAuley and J. Hill, *Quart. Rev., Chem. Soc.*, **23**, 18 (1969).

(38) D. J. Hewkin and R. H. Prince, *Coord. Chem. Rev.*, **5**, 75 (1970).

(39) S. Funahashi and M. Tanaka, *Inorg. Chem.*, **8**, 2159 (1969).

(40) J. O. Edwards, *J. Amer. Chem. Soc.*, **76**, 1540 (1954).

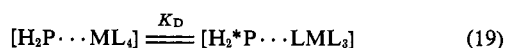
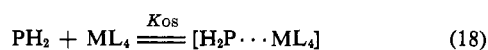
Table VIII. Summary of the Rate Constants for Zinc Species Reacting with Different Porphyrins in Aqueous Solution

Zinc type		TMPyP (4+) <sup>a</sup>	TPPS <sub>4</sub> (4-) <sup>a</sup>	Uro (8-) <sup>a</sup>
Zn <sup>2+</sup> -NO <sub>3</sub> <sup>-</sup>	(k <sub>1</sub> ) <sup>a,b</sup>	(4.9 ± 0.2) × 10 <sup>-2</sup>		
Zn <sup>2+</sup>	(k <sub>2</sub> ) <sup>c,d</sup>		(7.6 ± 0.1) × 10 <sup>-1</sup>	ca. 18
Zn(OH) <sup>+</sup>	(k <sub>3</sub> ) <sup>c,d</sup>		41 ± 4	ca. 1260
Zn(Py) <sup>2+</sup> -NO <sub>3</sub> <sup>-</sup>	(k <sub>4</sub> ) <sup>a,e,f</sup>	(68 ± 7) × 10 <sup>-2</sup>		
Zn(Py) <sub>2</sub> <sup>2+</sup> -NO <sub>3</sub> <sup>-</sup>	(k <sub>5</sub> ) <sup>a,e</sup>	(183 ± 20) × 10 <sup>-2</sup>		
Zn(Py) <sub>3</sub> <sup>2+</sup> -NO <sub>3</sub> <sup>-</sup>	(k <sub>6</sub> ) <sup>a,e</sup>	(3360 ± 400) × 10 <sup>-2</sup>		
Zn(OAc) <sup>+</sup>	(k <sub>7</sub> ) <sup>b,d</sup>	(54 ± 6) × 10 <sup>-2</sup>		
Zn(OAc) <sub>2</sub>	(k <sub>8</sub> ) <sup>b,d</sup>	(289 ± 40) × 10 <sup>-2</sup>		
Zn(OAc) <sup>+</sup> -NO <sub>3</sub> <sup>-</sup>	(k <sub>9</sub> ) <sup>a,b</sup>	(49 ± 7) × 10 <sup>-2</sup>		
Zn(NH <sub>3</sub> ) <sub>3</sub> <sup>2+</sup>	(k <sub>10</sub> ) <sup>c,d</sup>		194 ± 24	11,600 ± 600
Zn(NH <sub>3</sub> ) <sub>4</sub> <sup>2+</sup>	(k <sub>11</sub> ) <sup>c,d</sup>		11 ± 1	372 ± 11
Zn(OH) <sub>3</sub> <sup>-</sup>	(k <sub>12</sub> ) <sup>c,d</sup>			5.9 ± 1.5
Zn(OH) <sub>4</sub> <sup>2-</sup>	(k <sub>13</sub> ) <sup>c,d</sup>			76 ± 2

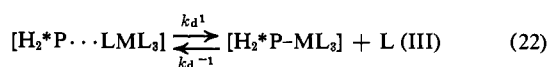
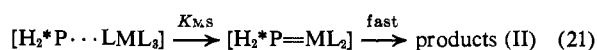
<sup>a</sup> Units M<sup>-2</sup> sec<sup>-1</sup>. <sup>b</sup> T = 22°. <sup>c</sup> T = 25°. <sup>d</sup> Units M<sup>-1</sup> sec<sup>-1</sup>. <sup>e</sup> T = 27°. <sup>f</sup> k<sub>1</sub> = (8 ± 1) × 10<sup>-2</sup> M<sup>-2</sup> sec<sup>-1</sup> at 27°. <sup>g</sup> Total formal charge on the porphyrin periphery.

shell with the loss of coordinated ligands must occur during or after the rate determining step.

The following schemes represent possible pathways for the presumed four-coordinate zinc species (ML<sub>4</sub>) to incorporate into porphyrins and can be generalized into six-coordinate (ML<sub>6</sub>) forms:



then either



In common to all mechanisms, the porphyrins form an outer sphere (K<sub>OS</sub>) complex with the metal species and then the porphyrin nucleus deforms (K<sub>D</sub>) to provide a suitable configuration to complex with the metal ion. There is ample evidence that the porphyrin nucleus is flexible.<sup>2</sup> This conformer might have its opposite pyrrole planes and the central nitrogen sp<sup>2</sup> hybrids pointing upwards, and the other two downwards, with respect to the mean porphyrin plane. This conformation both enhances the coordinating ability of the lone pairs by directing them away from the central porphyrin cavity and increases the apparent acidity of the central protons by destroying the N-H tautomerism.<sup>41</sup>

Following the rapid K<sub>OS</sub> and K<sub>D</sub> preequilibria, the rate determining transition state can form in various ways. In the k<sub>EX</sub> pathway (I), the coordination shell of zinc can expand by one or two positions without ligand loss, to accommodate bonding with the porphyrin. This pathway would probably be unavailable for metal ions which are initially six-coordinate, and it does not account for our observations that factors which favor zinc-ligand bond breaking are featured in the reactivity patterns. Nevertheless pathway I may not be rate determining and thus cannot be ruled out for four-coordinate metals.

Several workers<sup>32,33</sup> have suggested that the slow

(41) C. B. Storm, Y. Teklu, and E. A. Sokoloski, *Ann. N. Y. Acad. Sci.*, 206, 631 (1973).

metal-porphyrin incorporation rates (compared to those of simpler ligands) arise from the necessity of using a multiple desolvation pathway, k<sub>D</sub>, II, for such rigid macrocycles. The small probability of the simultaneous removal of two ligands from the metal accounts for the slow porphyrin reaction rates. Our feeling is that the slow rates are better accounted for in part by an unfavorable porphyrin deformation preequilibria (K<sub>D</sub> ≪ 1), rather than by a multiple desolvation of the metal ion. The k<sub>MD</sub> pathway might form a chelated transition state that could be further along toward the products and of a lower energy than would a more probable single ligand dissociation route. This is because many *relatively stable* intermediates are known where the porphyrin is bonded in two positions to the metal ion. For example, hematoporphyrin containing two free-base protons and inert PtCl<sub>2</sub>, which could bond to two opposite pyrrole nitrogen atoms has been synthesized.<sup>42</sup> In the acid catalyzed solvolysis of zinc porphyrins,<sup>27</sup> the addition of two protons which could form a chelate-type intermediate are not sufficient to cause zinc solvolysis. A third proton, which makes the zinc one-coordinate with respect to the porphyrin leads to rapid zinc removal. Also with *N*-methyl porphyrins which may be bonded by three nitrogen atoms to zinc, two protons (not simply one) are necessary for solvolysis.<sup>27</sup>

We believe that much of our incorporation data can be explained by pathway III, a dissociative exchange mechanism, with the rate limiting step (k<sub>d</sub>), the dissociation of a single ligand from the metal species. The observed incorporation rate k<sub>I</sub> for III is related to k<sub>d</sub>, K<sub>OS</sub>, and K<sub>D</sub> by the expression

$$k_{\text{I}} = k_{\text{d}}K_{\text{OS}}K_{\text{D}} \quad (24)$$

Pathway III is consistent with the following observations. (1) With porphyrins having the same peripheral charges (K<sub>OS</sub> ≈ constant), the rate of zinc<sup>10</sup> or copper<sup>12</sup> incorporation is relatively independent of porphyrin basicity (toward protons) and porphyrin structure. (2) Deuterium isotope effects<sup>29,31</sup> of 1.37 and 2.22, found under different conditions for Zn<sup>2+</sup>-TPPS<sub>4</sub> are in accord with porphyrin deformation. (3) There is ample evidence that factors which facilitate ligand loss from a metal enhance the reaction rate. Such evidence is presented in the present study for aqueous solutions.

(42) J. T. MacQuet and T. Theophanides, *Can. J. Chem.*, 51, 219 (1973).



The same trend is found from the observations that metal carbonyls in nonaqueous media<sup>4</sup> and metal ions in phenol and imidazole melts<sup>3</sup> and reactions run<sup>43</sup> in DMF have been used to successfully incorporate metals that do not readily insert from aqueous solution. Such high temperatures and weak M-CO bonding in low oxidation states would favor ligand dissociation. (4) From eq 24, the ratio ( $k_I/k_d$ ) should be fairly independent of the metal ion for cations and porphyrins of the same charge. This ratio for first-row transition metal ions and TMTPyP (Table VII) is  $\text{Cu}^{2+}$  ( $4.6 \times 10^{-9}$ ),  $\text{Zn}^{2+}$  ( $1.7 \times 10^{-9}$ ),  $\text{Co}^{2+}$  ( $5.4 \times 10^{-9}$ ),  $\text{Mn}^{2+}$  ( $0.42 \times 10^{-9}$ ), and  $\text{Ni}^{2+}$  (*ca.*  $1.7 \times 10^{-9} M^{-2}$ ). The  $\text{Fe}^{2+}$  ratio<sup>15</sup> is of a similar order of magnitude. Since the observed product of the  $\text{Mn}^{2+}$  reaction is  $\text{Mn}^{\text{III}}\text{P}$ , its anomalous ratio is understandable. The  $k_I$  values span a 6900-fold range from  $\text{Cu}^{2+}$  to  $\text{Ni}^{2+}$ , while the ratios vary by less than a factor of five. (5) Metal ions incorporate into the predeformed *N*-methyl porphyrins 10<sup>5</sup> times faster than with the corresponding non-*N*-alkylated porphyrin.<sup>13</sup> This is evidence for the confirmational preequilibrium,  $K_D$ . (6) The increase in the rate of cation incorporation as the number of negative porphyrin substituents increase<sup>32</sup> could reside in an increase in the outer sphere preequilibrium constant,  $K_{OS}$ , as has been shown for simpler metal complexes.

It is not suggested that all metal ions insert by a "normal" dissociative-interchange process. For example small divalent<sup>44</sup> transition metal ions ( $\text{Mg}^{2+}$ ) and trivalent ions ( $\text{Fe}^{3+}$ ) react with porphyrins much more slowly than expected with III. Here mechanism IV might be applicable for such small ions having high effective charges. Pathway IV is that found for sterically controlled substitution (SCS),<sup>45</sup> where the rate of the second ligand dissociation ( $k_d^2$ ) is slower than the rate of re-formation of the M-L bond, due to an unfavorable porphyrin conformation. For such cases,

(43) A. D. Adler, F. R. Longo, F. Kampas, and J. Kim, *J. Inorg. Nucl. Chem.*, **32**, 2443 (1970).

(44) S. J. Baum and R. A. Plane, *J. Amer. Chem. Soc.*, **88**, 910 (1966).

(45) D. B. Rorabacher, T. S. Turan, J. A. Defever, and W. G. Nickels, *Inorg. Chem.*, **8**, 1498 (1969).

$k_I$  would be less than ( $k_d K_{OS} K_D$ ), as observed. In general,<sup>46</sup> it is difficult to distinguish between mechanisms of type III and IV.

Several special cases might arise depending on the type of metal reactant and porphyrin. Thus  $\text{Zn}(\text{OH})_4^{2-}$  might attack the distorted porphyrin intermediate on the pyrrole proton side, with hydrogen ion transfer and subsequent zinc incorporation. For the *N*-methyl porphyrins<sup>13</sup> the  $sp^3$  character of the alkylated nitrogen atom<sup>46</sup> makes such derivatives strongly basic ( $pK_3 \approx 11$ ), and an internal conjugate base (ICB)<sup>47</sup> mechanism could account in part for their enormously enhanced metal incorporation kinetic behavior. The alkyl nitrogen could hydrogen bond with water or DMF molecules in the first-coordination shell of the metal, facilitating coordination at another nitrogen position, thus increasing the magnitudes of  $K_{OS}$  and/or  $k_d$ , over and above that expected for the deformation ( $K_D$ ) effect.

In conclusion, the mechanisms of metal ion incorporation into porphyrins do not appear to be vastly different from similar processes observed with simpler mono- or bidentate ligands.<sup>48,49</sup> The necessity for the extreme porphyrin deformation needed to place the lone pairs in a reasonable coordination position both for incoming metal ions in the incorporation reaction and for protons or other metals in the metalloporphyrin solvolysis or exchange processes, dominates the coordination chemistry of porphyrins. Metalloporphyrins are slow to form and difficult to dissociate, which is apparently a general consequence in macrocycles where deformation rather than dissociation is the major theme.

**Acknowledgments.** We gratefully acknowledge the USAEC, Contract No. AT(40-1)-4047, and the Gulf Educational Foundation for partial financial support. National Institutes of Health is thanked for a special fellowship to P. H. during the course of this work.

(46) A. H. Jackson and G. R. Dearden, *Ann. N. Y. Acad. Sci.*, **206**, 151 (1973).

(47) D. B. Rorabacher, *Inorg. Chem.*, **5**, 1890 (1966).

(48) K. Kustin and J. Swinehart, *Progr. Inorg. Chem.*, **13**, 107 (1970).

(49) M. Eigen and R. G. Wilkins, *Advan. Chem. Series*, No. 43, 55 (1965).