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# Kinetics and Mechanism of Reactions of Water-Soluble Ferriporphyrins. 1. Monomer–Dimer Interactions

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Concentration jump and concentration/pH jump kinetic studies have been employed to determine the rates of dissociation of a cationic dimeric ferriporphyrin, tetra(4-*N*-methylpyridyl)porphineiron(III), $Fe^{III}P$, and an anionic dimeric ferriporphyrin, tetra(*p*-sulfophenyl)porphineiron(III), $Fe^{III}TPPS$. Rates of monomer formation have been measured over the pH range 4.72–8.26 for $Fe^{III}P$ and 5.90–9.15 for $Fe^{III}TPPS$ ($\mu = 0.10$ (NaCl), 25.0 °C). In both cases the rate expression for monomer formation exhibits saturation of the observed rate constant at low pH, suggesting a rate-limiting step involving monomer formation from a $\mu$-hydroxo dimeric intermediate. Analysis of kinetics data leads to values of $(1.55 \pm 0.16) \times 10^{-1}$ $s^{-1}$ and $2.69 \pm 0.04$ $s^{-1}$ for the rate constants for dissociation of the $Fe^{III}P$ and $Fe^{III}TPPS$ $\mu$-hydroxo dimers, respectively. Acid dissociation constants for the $\mu$-hydroxo bridging groups are $pK_a$ ($Fe^{III}P$) = 5.9 and $pK_a$ ($Fe^{III}TPPS$) = 8.5. Comparisons to other studies on this and related systems are made.

## Introduction

Studies of substitution and electron-transfer reactions of relatively uncomplicated iron porphyrins are becoming increasingly useful probes in the elucidation of the mechanisms of oxygen and electron transport in ferri- and ferroproteins.[1] The availability of water-soluble porphyrin ligands such as $\alpha,\beta,\gamma,\delta$-tetra(4-*N*-methylpyridyl)porphine, the cationic iron(III) complex of which is abbreviated herein as $Fe^{III}P$, has allowed the extension of such studies into aqueous media. An understanding of the extent to which ferriporphyrins such as $Fe^{III}P$ interact to form dimeric and other associated species in solution is crucial to interpretation of kinetics and thermodynamics data obtained in the course of both substitution and oxidation–reduction studies. Recently, Pasternack and co-workers have reported[2] the results of a study of the kinetics of dissociation of dimeric $Fe^{III}P$ in acidic media ($2 \times 10^{-4} \le [H^+] \le 2 \times 10^{-2}$ M) for which they obtained a two-term rate law, $-d[\text{dimer}]/dt = (k_1 + k_2[H^+])[\text{dimer}]$, ascribing the $k_1$ and $k_2$ terms to pathways involving disruption of Fe–O–Fe and Fe–OH–Fe units, respectively. Rate constants $k_1$ and $k_2$ are reported to be 0.42 $s^{-1}$ and 31 $M^{-1}$ $s^{-1}$, respectively. Fleischer and co-workers have obtained the same rate law for dissociation of the anionic porphyrin $Fe^{III}TPPS$,[3] with corresponding $k_1$ and $k_2$ values of 41 $s^{-1}$ and 840 $M^{-1}$ $s^{-1}$. These authors imply that the $k_1$ and $k_2$ pathways correspond to disruption of the $\mu$-oxo dimer and the di-$\mu$-hydroxo or $\mu$-aquo-$\mu$-hydroxo species, respectively. The $Fe^{III}TPPS$ study was also carried out under acidic conditions, $[H^+]$ ranging from $1.1 \times 10^{-3}$ to 0.10 M.

If the two-term rate law obtained in these studies is valid, the values of $k_1$ establish lower limits for $k_{obsd}$, the observed rate constant for monomer formation as $[H^+]$ approaches zero. We have undertaken kinetics studies of the dissociation of dimeric forms of both $Fe^{III}P$ and $Fe^{III}TPPS$ over a wide range in $[H^+]$. The results of these studies demonstrate that the rate law for monomer formation is more complex than reported in the previous studies, and they indicate that the rate law previously obtained for both systems actually corresponds to the dissociation of $\mu$-hydroxo forms of the dimeric porphyrin species.

## Experimental Section

**$\alpha,\beta,\gamma,\delta$-Tetra(4-*N*-methylpyridyl)porphine Hexaperchlorate ($H_4P(ClO_4)_6$).** $\alpha,\beta,\gamma,\delta$-Tetra(4-pyridyl)porphinezinc(II), ZnTPyP, was prepared by the method of Fleischer.[4] N-Methylation was accomplished by the standard method,[5] although reaction time was 10 h rather than 2 (yield ZnP, 88%).

The N-methylated diacid $H_4P(ClO_4)_6$ was prepared by stirring 1.26 g of ZnP in 350 mL of 1.5 M $H_2SO_4$ until the red solid had dissolved to form a deep-green solution. Approximately 100 g of $NaClO_4$ was added, immediately producing a green precipitate. The mixture was refrigerated for several hours, and the product was collected by filtration, washed with absolute ethanol, a small volume of 0.20 M $HClO_4$, and again with ethanol, and dried at 75 °C: yield 1.13 g (88%) of a green powder ($H_4P(ClO_4)_6$).

**$\alpha,\beta,\gamma,\delta$-Tetra(4-*N*-methylpyridyl)porphineiron(III) Pentaperchlorate ($Fe^{III}P$).** $H_4P(ClO_4)_6$ (525 mg, 0.411 mmol) and $Fe(ClO_4)_2 \cdot 6H_2O$ (600 mg, 1.644 mmol) were heated at reflux in water (50 mL) for 3.75 h. At first a precipitate formed, which subsequently dissolved as the solution became intensely red. The solution was cooled and filtered from a trace in insoluble material, and 20 g of $NaClO_4$ was added, producing a dark precipitate. The mixture was chilled for 2 h, and the solid was isolated by filtration and washed with 250 mL of absolute ethanol. Air drying left 447 mg (87%) of a deep red-brown solid ($Fe^{III}P$, $\epsilon = 8.99 \times 10^4$ at 422 nm, pH 7.03). *Caution*! A small amount of this material exploded when scraped with a metal spatula on a glass frit.

**Media.** All experiments were carried out in buffered media (0.010 M phosphate, phthalate, or Tris, adjusted to the desired pH with 0.100 M NaOH or 0.100 M HCl)[6] at $\mu = 0.100$ (NaCl). Deionized (>1 MΩ) or doubly distilled water was used exclusively.

**Experimental Techniques.** $Fe^{III}P$ concentration/pH jump experiments were carried out by rapid syringe delivery of small volumes (0.25, 0.50, or 1.00 mL) of $3.47 \times 10^{-4}$ M $Fe^{III}P$ in pH 8.03 or 9.15 buffers (0.005 M, $\mu = 0.10$ (NaCl)) into 26.0 mL of buffer of desired pH contained in a stirred 10.00-cm spectrometer cell. Absorbance vs. time was monitored at several wavelengths. Formation of $Fe^{III}TPPS$ monomers was monitored at 530 or 610 nm with a stopped-flow spectrophotometer equipped with a Biomation transient recorder and a Wang 2200S minicomputer. Rate constants were determined by direct analysis of the absorbance vs. time curve using the computer program previously described.[7] First-order approach to equilibrium was observed in all cases. Measurements of pH were made before and after mixing, and the final pH was used to calculate $[H^+]$. Determination of pH was accomplished with a Krueger and Eckels 133 digital pH meter equipped with a microelectrode and standardized against Harleco reference buffers. $[H^+]$ was computed from pH using a value of 0.83 ($\mu = 0.10$)[8] for the activity coefficient of $H^+$.

## Results and Discussion

**Dissociation of Dimeric $Fe^{III}P$.** Kinetics experiments were carried out with the aim of determining the rate of dissociation of the dimeric ferriporphyrin. At higher pH values "monomerization" proceeds slowly enough to allow repeat scans of the reaction mixture during the course of reaction. Sample scans, obtained after 52-fold dilution of $3.47 \times 10^{-4}$ M $Fe^{III}P$ in a pH 8.03 (Tris, 25.0 °C) buffer, are shown in Figure 1. Scans were taken after about 1, 5, 11, 17, and 30 min of mixing. The initial absorbance band at 582 nm appears to decrease in intensity with concomitant increases in absorbance at 597.5 (maximum) and 500 nm (shoulder). Isosbestic points are observed at 581.5 and 557 nm. The $[H^+]$ dependence of the rate of monomer formation was examined

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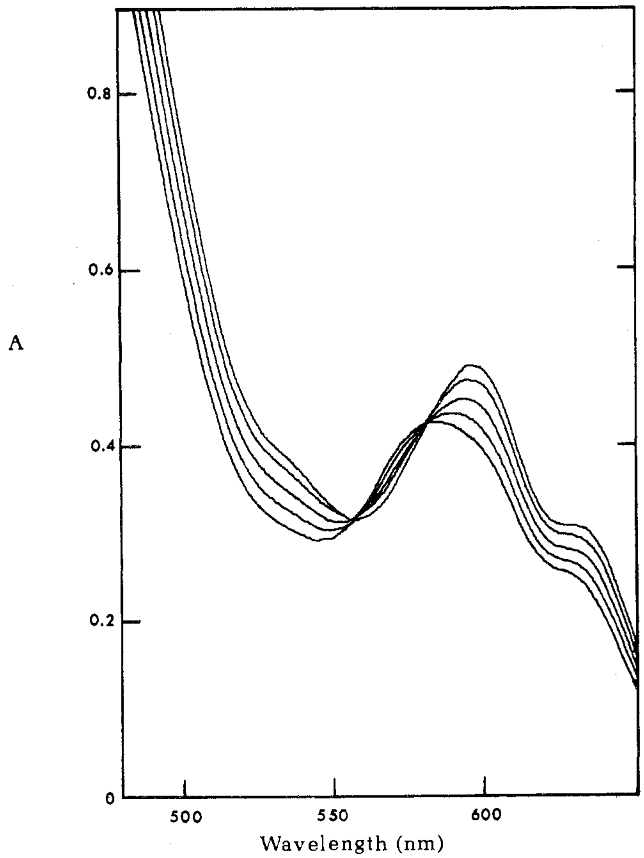

**Figure 1.** Time dependent spectra of $Fe^{III}P$ obtained after 52-fold dilution at constant pH (8.03). Spectra were recorded after 1, 5, 11, 17, and 30 min. Absorbance decreasing with time between isosbestic points, increasing elsewhere. $[Fe^{III}P]_t = 6.67 \times 10^{-6}$ M after mixing, $\mu = 0.10$ (NaCl), 25.0 °C.

**Table I.** Kinetics Data for the Formation of $Fe^{III}P$ Monomer (25.0 °C, $\mu = 0.10$ (NaCl))

| pH[a] | $10^3 k_{obsd}$,[b] $s^{-1}$ | $10^3 k_{calcd}$,[c] $s^{-1}$ |
|---|---|---|
| 4.72 | 132.0 ± 5.3 | 146 |
| 4.94 | 119.9 ± 3.1 | 141 |
| 5.39 | 97.6 ± 2.8 | 121 |
| 5.63 | 86.6 ± 0.9 | 105 |
| 6.04 | 75.9 ± 0.5 | 69.9 |
| 6.16 | 66.0 ± 0.7 | 59.5 |
| 6.32 | 50.0 ± 1.5 | 46.7 |
| 6.55 | 34.5 ± 1.1 | 31.5 |
| 6.76 | 21.5 ± 0.9 | 21.0 |
| 7.00 | 13.2 ± 0.2 | 12.8 |
| 7.23 | 7.74 ± 0.2 | 7.82 |
| 7.38 | 5.73 ± 0.06 | 5.63 |
| 7.56 | 3.71 ± 0.19 | 3.76 |
| 8.03 | 1.29 ± 0.03 | 1.29 |
| 8.26 | 0.758 ± 0.005 | 0.757 |

[a] Final pH, see text. [b] Computer determination of $k_{obsd}$ as $(A_\infty - A_t) = (A_\infty - A_0) \exp(-k_{obsd}t)$, with: $t$, $A_\infty$, $A_0$, and $A_t$ representing time, absorbance at effective infinite time, absorbance at time 0, and absorbance at time $t$, respectively. Error is 1$\sigma$. Most experiments are at 600 nm, but a few are at 500 nm. [c] Calculated by least-squares analysis of $k_{obsd}^{-1}$ vs. $[H^+]^{-1}$.

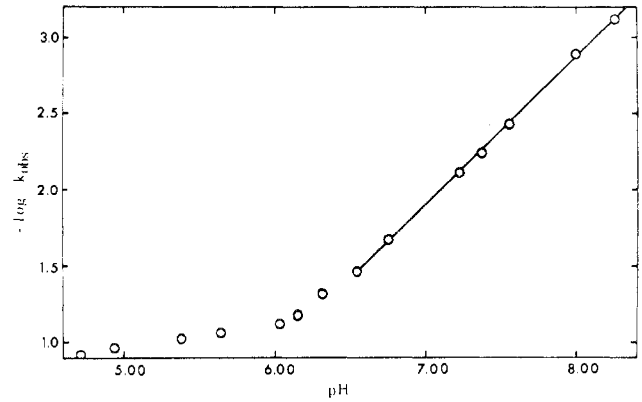

**Figure 2.** Plot of $-\log k_{obsd}$ vs. pH for formation of $Fe^{III}P$ monomer (25.0 °C, $\mu = 0.10$ (NaCl)). Least-squares line.

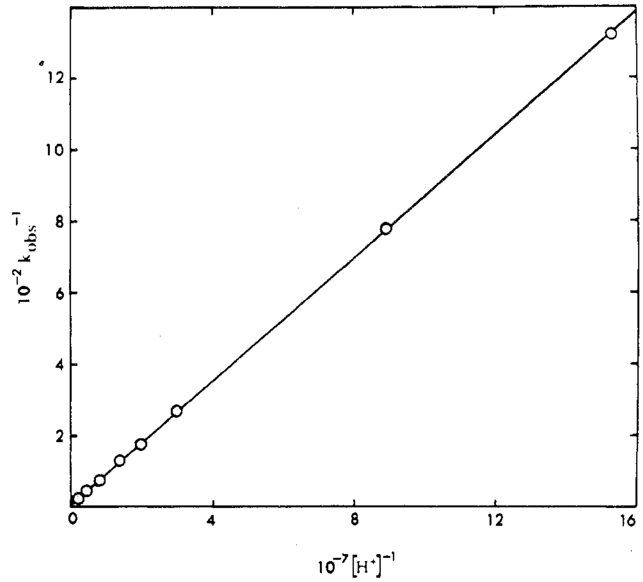

**Figure 3.** Plot of $k_{obsd}^{-1}$ vs. $[H^+]^{-1}$ for formation of $Fe^{III}P$ monomer (25.0 °C, $\mu = 0.10$ (NaCl)). Least-squares line. An additional seven points lie below the first point in the lower left. Although they cannot be shown on such a plot, they were included in the least-squares analysis, Table I.

**Scheme I**

$$\mathrm{PFe{-}O{-}FeP} + H^+ \rightleftharpoons \mathrm{PFe{-}OH{-}FeP} \qquad K_{da} \text{ (rapid)}$$

$$H_2O + \mathrm{PFe{-}OH{-}FeP} \rightarrow \mathrm{PFeOH_2} + \mathrm{PFeOH} \qquad k_m \text{ (rate determining)}$$

$$\mathrm{PFeOH_2} \rightleftharpoons \mathrm{PFeOH} + H^+ \qquad K_{am} \text{ (}10^{-4.7}\text{, ref 2)}$$

by monitoring the rate of increase in absorbance at 500 or 600 nm as a function of $[H^+]$. The results appear in Table I. The observed rate constants for dimer dissociation are seen to increase with decreasing pH, in agreement with the works cited previously. The observed rate constants were found to vary only slightly over the pH range 4.72–6.32, however, decreasing by only a factor of 2.4 for a 40-fold change in $[H^+]$. Above pH 6.32, however, a dramatic decrease in rate constant with increasing pH is seen. A plot of $-\log k_{obsd}$ vs. pH is presented in Figure 2. The plot exhibits linearity above pH 6.32, with least-squares analysis giving a slope of 0.97 ± 0.01. Thus, the rate expression for monomer formation exhibits a first power $[H^+]$ dependence at low $[H^+]$, decreasing to lower order in $[H^+]$ at higher $[H^+]$, corresponding to saturation of the observed rate constant for monomerization at higher acidities. Note that the highest $[H^+]$ used is considerably lower than the lowest $[H^+]$ employed by Pasternack and co-workers.[2]

One mechanism which is consistent with the observed rate expression consists of rapid preequilibrium association of the dimer with $H^+$, followed by rate-limiting decomposition of the protonated dimer. Dimeric $Fe^{III}P$ has been shown to exist in a low-spin, presumably planar, configuration with a $\mu$-oxo-bridging ligand at high pH.[2] Assuming that the $\mu$-oxo ligand is sufficiently basic to associate with $H^+$, Scheme I for monomer formation emerges. For such a mechanism the rate expression for dimer dissociation can be expressed as follows:

**Table II.** Kinetics Data for the Formation of FeTPPS Monomer (25.0 °C, $\mu = 0.10$ (NaCl))

| pH | $k_{\text{obsd}}$, s$^{-1}$ | $k_{\text{calcd}}$, s$^{-1}$ |
|---|---|---|
| 5.90 | 2.78 | 2.68 |
| 6.20 | 2.69 | 2.68 |
| 6.50 | 2.76 | 2.67 |
| 7.37 | 2.40 | 2.53 |
| 8.07 | 2.02 | 2.04 |
| 8.37 | 1.61 | 1.64 |
| 8.74 | 1.08 | 1.08 |
| 9.00 | 0.735 | 0.724 |
| 9.15 | 0.553 | 0.557 |

Let $D_T$, DO, and DOH represent total dimer, μ-oxo dimer, and μ-hydroxo dimer, respectively (see eq 1).

$$[D_T] = [DOH] + [DO] = [DOH](1 + 1/(K_{da}[H^+])) \qquad (1)$$

If the rate-determining process is the decomposition of μ-hydroxo species, we obtain (2), for which the observed rate constant, $k_{\text{obsd}}$, is

$$\text{rate} = -d[D_T]/dt = k_m[DOH] = k_m[D_T](1 + 1/(K_{da}[H^+]))^{-1} \qquad (2)$$

given by (3).

$$k_{\text{obsd}} = k_m(1 + 1/(K_{da}[H^+]))^{-1} \qquad (3)$$

Hence, a plot of $k_{\text{obsd}}^{-1}$ vs. $[H^+]^{-1}$ should be linear, with slope $(k_mK_{da})^{-1}$ and intercept $k_m^{-1}$. Such a plot is indeed linear (Figure 3). Least-squares analysis gives intercept $k_m^{-1} = 6.47 \pm 0.69$ s and slope $(8.61 \pm 0.02) \times 10^{-8}$ M s, leading to values of $K_{da}$ and $k_m$ of $(7.51 \pm 0.85) \times 10^5$ M$^{-1}$ and $(1.55 \pm 0.16) \times 10^{-1}$ s$^{-1}$, respectively. The acid dissociation constant for the μ-hydroxo dimer is properly written as

$$\text{PFe–OH–FeP} \rightleftharpoons \text{PFe–O–FeP} + H^+ \qquad K_{ad}$$

for which $K_{ad} = K_{da}^{-1} = 1.33 \pm 0.15 \times 10^{-6}$ M, corresponding to a value of 5.9 for p$K_a$.

**Dissociation of Dimeric Fe$^{III}$TPPS.** In agreement with the observations of Fleischer and co-workers,[3] we find that the rate of monomer formation for Fe$^{III}$TPPS is considerably greater than in the Fe$^{III}$P system. Consequently, the system was studied by stopped-flow spectrophotometry (results appear in Table II). The observed kinetics behavior is very similar to that found for Fe$^{III}$P. The observed rate constants increase with decreasing pH, attaining saturation at the highest acidities (pH <7). A plot of $k_{\text{obsd}}^{-1}$ vs. $[H^+]^{-1}$ is linear with slope = $(1.22 \pm 0.012) \times 10^{-9}$ M s and intercept = $0.372 \pm 0.006$ s, corresponding to $K_{ad} = (3.27 \pm 0.10) \times 10^{-9}$ and $k_m = 2.69 \pm 0.04$ s$^{-1}$, leading to a value of 8.48 for p$K_a$ of the μ-hydroxo ligand.

Although the rate expressions are identical for the two ferriporphyrin systems, the rate constants for monomer formation and the acid dissociation constants differ considerably. Values of p$K_{ad}$ for Fe$^{III}$P and Fe$^{III}$TPPS are 5.9 and 8.5, respectively. A difference of 2.6 p$K_a$ units is not surprising in light of the vastly different charge types of the respective systems, however. The anionic Fe$^{III}$TPPS dimer should be considerably more basic than the Fe$^{III}$P species.

Rate constants for Fe$^{III}$P and Fe$^{III}$TPPS monomer formation are found to be 0.155 and 2.69 s$^{-1}$, respectively. Thus, the anionic system dissociates about 17 times more rapidly than cationic Fe$^{III}$P. Under conditions of relatively high $[H^+]$, the $[H^+]$-independent rate constant for monomer formation of Fe$^{III}$TPPS is about 100 times greater than the corresponding value for Fe$^{III}$P, whereas the $[H^+]$-dependent path is 27 times greater for Fe$^{III}$TPPS than for Fe$^{III}$P.[2,3,9] Such enhancement of the rate of dissociation of anionic metalloporphyrins has also been observed in cobalt porphyrin systems[10] where negatively charged peripheral substituents increase electron density on the metal center, labilizing axial metal–ligand bonds. The enhanced μ-oxo basicity of the Fe$^{III}$TPPS dimer is also in accord with this premise.

A final question arises. What is the origin of the H$^+$-catalyzed $k_2$ term observed in Pasternack's Fe$^{III}$P and in Fleischer's Fe$^{III}$TPPS studies? They both attribute this term to H$^+$ attack at the μ-oxo group and subsequent rupture of the PFe–OH–FeP moiety, while the results of the present study very strongly suggest that PFe–OH–FeP is the dominant species under the conditions of their experiments. We are inclined to simply attribute the $k_2$ term to H$^+$ catalysis of the rupture of the Fe–OH–Fe link, attack of H$^+$ at the bridging ligand leading to very rapid Fe–O bond breaking. The existence of appreciable concentrations of μ-aquo species is not necessary for such a process and is extremely unlikely in light of the reluctance of $H_2O$ to bridge other metal ions.[11]

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**Registry No.** Fe$^{III}$P(dimer), 64365-02-2; Fe$^{III}$TPPS(dimer), 64365-01-1; $H_4P(ClO_4)_6$, 28323-94-6; Fe$^{III}$P$(ClO_4)_5$, 64365-00-0; H$^+$, 12408-02-5.

## References and Notes

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