Inorg. Chem. **1992**, *31*, 5089-5093 **5089**

Kinetic and Equilibrium Studies on Porphyrins, Chlorins, and Isobacteriochlorins: Basicities, Zinc Incorporation, and Acid-Catalyzed Solvolysis Reactions in Aqueous and Nonaqueous Solutions

T. P. G. Sutter and P. Hambright*

Department of Chemistry, Howard University, Washington, D.C. 20059

Received June 22, 1992

The water-soluble tetrakis(*N*-methyl-3-pyridiniumyl)chlorin and tetrakis(4-sulfonatophenyl)chlorin were synthesized. These chlorins were stronger Lewis bases and reacted more slowly with Zn^{2+} and at roughly the same rates with $ZnOH^+$ and their zinc complexes were solvolyzed more rapidly by protons as compared with the corresponding porphyrins. In DMF/HCl, tetraphenylisobacteriochlorin (TPiBC) was more basic than tetraphenylchlorin (TPC), and tetraphenylporphyrin (TPP) gave no evidence for a monocation. With pyridine as a solvent, the Zn(II) incorporation kinetics indicated the presence of a ($Zn–H_2$-P) "sitting-atop" intermediate, and the relative reactivities at high Zn(II) levels were H_2-TPiBC > H_2-TPC > H_2-TPP, in the ratios 8:2:1. The zinc-complex acid solvolysis kinetics in DMF/HCl were also in the order H_2-TPiBC > H_2-TPC > H_2-TPP, in the ratios 79:12:1. It is suggested that effective basicity parallels ring saturation.

Introduction

Much of the recent coordination chemistry of porphyrins and metalloporphyrins has been elucidated using the readily available model compounds octaethylporphyrin (H_2-OEP) and especially the many derivatives of tetraphenylporphyrin (H_2-TPP).[1] Properties of the two-electron β-pyrrole reduced chlorins and the four-electron bacteriochlorins (two reduced *trans*-β-pyrrole rings) or isobacteriochlorins (*cis*-β-pyrroles) are of similar interest.[2] The water-insoluble OEP and TPP chlorins and tetrahydroporphyrins have again been the major molecules studied as models for chlorophylls,[3] sirohemes,[4] and the nickel-containing corphin ring[5] in coenzyme F_{430}.

Little is known about the aqueous solution chemistry of reduced porphyrins, and we report the synthesis of the fully water-soluble tetrakis(4-sulfonatophenyl)chlorin (H_2-TSPC) and tetrakis(*N*-methyl-3-pyridiniumyl)chlorin (H_2-TMPyC). The pK_as for protonation, the kinetics of zinc ion incorporation, and the acid-catalyzed removal of zinc from these compounds were studied and compared to the nonreduced tetrakis(4-sulfonatophenyl)porphyrin (H_2-TSPP) and tetrakis(*N*-methyl-3-pyridiniumyl)porphyrin (H_2-TMPyP). It has been reported that the nonaqueous chlorins are weaker Lewis bases[6,7] and their metal ion incorporation rates are either faster or slower[11] than the corresponding porphyrins. We find that the water-soluble chlorins are more basic and react less rapidly with Zn^{2+} and their zinc adducts are solvolyzed by protons faster than the parent porphyrins. Since these aqueous solution results were somewhat different from those reported with water-insoluble reduced compounds, related studies were done in nonaqueous solutions on H_2-TPP, tetraphenylchlorin (H_2-TPC), and tetraphenylisobacteriochlorin (H_2-TPiBC).

Experimental Section

The compounds H_2-TPC,[6] H_2-TPiBC,[6] H_2-TSPPNa$_4$,[12] and H_2-TMPyPCl$_4$[13] were synthesized by literature methods. The pHs were monitored on a Radiometer PHM-64 research pH meter, and the absorption spectra were run on a thermostated Beckman DU-70 recording spectrophotometer. In general, the overall charges of the compounds due to the peripheral groups and the corresponding counterions are omitted for clarity.

Tetrakis(*N*-methyl-3-pyridiniumyl)chlorin. Tetrakis(3-pyridyl)chlorin was produced by diimide reduction of the tetrakis(3-pyridyl)porphyrin by following the procedure of Whitlock and co-workers.[6] The resulting chlorin/bacteriochlorin mixture was treated with *o*-chloranil to oxidize the bacteriochlorin to chlorin and placed on an alumina (Fisher A-540) column to remove the oxidant, and the compound was eluted with 5% MeOH in CH_2Cl_2. The chlorin was made water soluble by methylating the pyridyl groups with excess methyl iodide in chloroform.[13] The iodide salt of TMPyC was converted into the chloride form by passage through an ion-exchange resin. Anal. Calcd for $[H_2\text{-TMPyC}]Cl_4 \cdot H_2O$, $C_{44}N_8H_{42}OCl_4$: C, 62.86; N, 13.33; H, 5.04. Found: C, 62.78, N, 13.36; H, 5.38. UV/vis [pH 7.0, λ_{max}, nm (log ϵ)]: 400.5 s (4.89), 416.0 (5.12), 517.5 (4.07), 548 (3.86), 598.5 (3.79), 651 (4.29).

Tetrakis(4-sulfonatophenyl)chlorin. To 150 mL of refluxing methanol containing 20 mL of H_2O was added 300 mg of H_2-TSPPNa$_4$ (0.24 mmol), 90 mg of (*p*-tolylsulfonyl)hydrazine (0.48 mmol), and 315 mg of K_2CO_3. Approximately 2 g more of reductant was introduced in portions over 48 h,[6] at which time the addition of 5 g of K_2CO_3 caused the chlorin to precipitate. Oven drying for 20 min at 100 °C afforded 125 mg of shiny purple plates. The product was free of unreacted H_2-TSPP since no Zn(II)–TSPP peak at 555 nm was evident upon the addition of zinc nitrate to a solution of H_2-TSPC. This was also the case for H_2-TMPyC. Anal. Calcd for $K_4[H_2\text{-TSPC}] \cdot 14H_2O \cdot 2$ MeOH, $C_{46}N_4S_4O_{12}H_{64}K_4$: C, 39.10; N, 3.97; N, 4.57. Found: C, 39.34; N, 3.99; H, 3.35. UV/vis [pH 7.0, λ_{max}, nm (log ϵ)]: 400 sh (5.08), 414.0 (5.43), 518.5 (4.23), 546.5 (4.02), 591.5 (3.84), 645.5 (4.39).

Results

Monomer–Dimer Equilibria. Deviations from Beer's law are commonly used to assess the monomer–dimer behavior of porphyrins and metalloporphyrins in solution.[14] Spectrophoto-

---

[1] Buchler, J. W. In *The Porphyrins*; Dolphin, D., Ed.; Academic Press: New York, 1978; Vol. 1, Chapter 10.

[2] Scheer, H. In *The Porphyrins*; Dolphin, D., Ed.; Academic Press: New York, 1978; Vol. 2, Chapter 1.

[3] Barkigia, K. M.; Miura, M.; Thompson, M. A.; Fajer, J. *Inorg. Chem.* **1991**, *30*, 2233 and references therein.

[4] Richardson, P. F.; Chang, C. K.; Spaulding, L. D.; Fajer, J. *J. Am. Chem. Soc.* **1979**, *101*, 1737.

[5] Pfaltz, A. In *Bioinorganic Chemistry of Nickel*; Lancaster, J. R., Ed.; VCH Publishers: New York, 1988; Chapter 12.

[6] Whitlock, H. W.; Hanauer, R.; Oester, M. Y.; Bower, B. K. *J. Am. Chem. Soc.* **1969**, *91*, 7485.

[7] Aronoff, S. *J. Am. Chem. Soc.* **1957**, *62*, 428.

[8] Stolzenberg, A. M.; Strauss, S. H.; Holm, R. H. *J. Am. Chem. Soc.* **1981**, *103*, 4763.

[9] Lahiri, G. K.; Summers, J. S.; Stolzenberg, A. M. *Inorg. Chem.* **1991**, *30*, 5049.

[10] Longo, F. R.; Brown, E. M.; Adler, A. D.; Meot-Ner, M. *Ann. N.Y. Acad. Sci.* **1973**, *206*, 420.

[11] Dorough, G. D.; Huennekens, F. M. *J. Am. Chem. Soc.* **1952**, *74*, 3974.

[12] (a) Krishnamurthy, M. *Inorg. Chim. Acta* **1977**, *25*, 215. (b) Fleischer, E. B.; Palmer, J. M.; Srivastava, T. S.; Chatterjee, A. *J. Am. Chem. Soc.* **1971**, *93*, 3162.

[13] (a) Hambright, P.; Gore, T.; Burton, T. *Inorg. Chem.* **1976**, *15*, 2314. (b) Hambright, P.; Fleischer, E. B. *Inorg. Chem.* **1970**, *9*, 1757. (c) Kalyanasundaram, K. *Inorg. Chem.* **1984**, *23*, 2453.

0020-1669/92/1331-5089$03.00/0

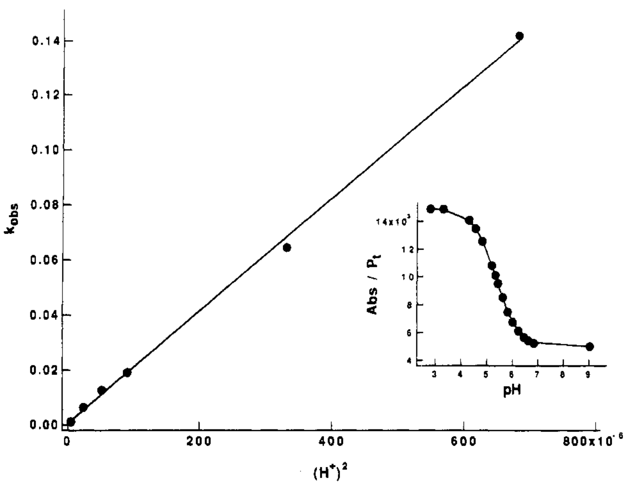

Figure 1. Graph of k_{obs} vs $(H^+)^2$ for the Zn(II)–TSPC/H^+ reaction. Insert: Plot of (A_x/P_T) vs pH for the protonation of H_2-TSPC (eq 3).

metric dilution studies in the Soret region were performed on H_2-TSPC and H_2-TMPyC at 25 °C to determine the dimerization equilibrium constant, K_D, as defined in eq 1. Porphyrin solutions

$$2H_2\text{-P} = (H_2\text{-P})_2 \quad K_D \tag{1}$$

at pH 7 were buffered with 1 mM MES (*N*-morpholineethanesulfonic acid), at 0.10 M ionic strength ($NaNO_3$). Plots of the absorbance vs the total porphyrin concentration from (10^{-4}–10^{-8} M) allowed the calculation[14] of K_D. H_2-TSPC has $K_D = (2.2 \pm 0.1) \times 10^5$ M^{-1}. H_2-TMPyC showed no substantial deviation from Beer's law and is considered monomeric with a $K_D < 10^3$ M^{-1}.

Proton Equilibria. The equilibria for the addition of protons to the water-soluble porphyrins and chlorins were studied spectrophotometrically from pH 1 to 11 at 25 °C with an ionic strength of 0.10 M ($NaNO_3$) at a total porphyrin concentration of $\sim 10^{-7}$ M. The following reactions were considered, where $H_4\text{-P}^{2+}$ is the dication, $H_3\text{-P}^+$ is the monocation, and H_2-P is the porphyrin free base:

$$H_4\text{-P}^{2+} = H_3\text{-P}^+ + H^+ \quad K_4 \tag{2}$$

$$H_3\text{-P}^+ = H_2\text{-P} + H^+ \quad K_3 \tag{3}$$

At a given wavelength, A_x is the absorbance of the porphyrin having a total concentration P_T and ϵ_2, ϵ_3, and ϵ_4 are the extinction coefficients for the free base, monocation, and dication, respectively. Equation 4 With the experimentally determined A_x, pH,

$$\frac{A_x}{P_T} = \frac{(\epsilon_2 K_3 K_4 + \epsilon_3 K_4[H^+] + \epsilon_4[H^+]^2)}{(K_3 K_4 + K_4[H^+] + [H^+]^2)} \tag{4}$$

ϵ_2, and ϵ_4 values, eq 4 was solved for K_3, K_4, and ϵ_3 using a nonlinear least-squares program. Figure 1 (insert) shows a plot of (A_x/P_T) vs pH and the excellent fit of the experimental points for H_2-TSPC with $pK_3 = 5.3_8$, $pK_4 = 4.2_7$, and $\log \epsilon_3 = 4.10$ at $\lambda = 430$ nm. Table I contains the results for the other compounds.

Table I. Kinetic and Protonation Data for the Water-Soluble Compounds

	H_2-P/H^+		Zn–P/H^+	Zn(II)/H_2-P	
porphyrin	pK_3	pK_4	k_2K (M^{-2} s^{-1})	k_1 (M^{-1} s^{-1})	$10^{-1}k_2$ (M^{-1} s^{-1})
TSPP[a]	4.6_7	4.7_7	$(2.2 \pm 0.1) \times 10$	1.2 ± 0.1	3.1 ± 0.3
TSPC	5.3_8	4.2_7	$(2.1 \pm 0.1) \times 10^2$	$(7.8 \pm 0.1) \times 10^{-2}$	3.3 ± 0.2
TMPyP	1.7_9	1.3_4	$(1.4 \pm 0.1) \times 10^{-2}$	$(2.8 \pm 1.4) \times 10^{-2}$	2.5 ± 0.1
TMPyC	2.9_0	$\ll 1$	$(4.5 \pm 0.1) \times 10^{-2}$	$(4.0 \pm 1.2) \times 10^{-3}$	1.5 ± 0.1

[a] Values of $pK_3 = 4.99$ and $pK_4 = 4.76$ have been reported. See: Tabata, M.; Tanaka, M. *J. Chem. Soc., Chem. Commun.* **1985**, *42*.

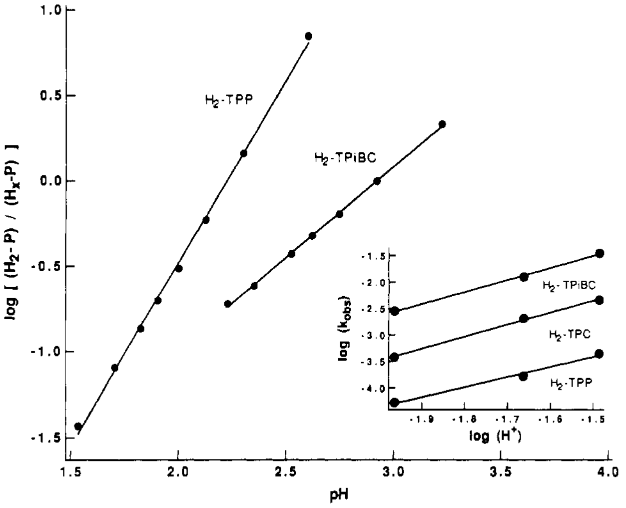

Figure 2. Plot of log $[(H_2\text{-P})/(H_x\text{-P})]$ vs pH for the diprotonation of H_2-TPP ($x = 4$) and monoprotonation of H_2-TPiBC ($x = 3$). Insert: Graph of log (k_{obs}) vs log (H^+) for the zinc acid solvolysis reactions in DMF.

The proton equilibria of the water-insoluble H_2-TPP, H_2-TPC, and H_2-TPiBC were studied at 25 °C in a 95% DMF/5% H_2O solvent system using HCl as the titrant. Excellent isosbestic points[15] were found from 800 to 350 nm for H_2-TPP and H_2-TPiBC, while the "isosbestic points" of H_2-TPC shifted noticeably during the course of the titration. Figure 2 shows a plot of log $[(H_2\text{-P})/(H_x\text{-P})]$ vs pH, where the slope "*n*" is the number of protons added.[16] For H_2-TPP ($x = 4$), $n = 2.1 \pm 0.1$, with a $pK_{3,4} = 4.4_6$ for the two proton process:

$$H_4\text{-TPP}^{2+} = H_2\text{-TPP} + 2H^+ \tag{5}$$

H_2-TPiBC ($x = 3$) had $n = 1.1 \pm 0.1$ and $pK_3 = 3.1_4$. In the case of H_2-TPC, the titration data best fit eq 4, with $pK_3 = 2.4_9$ and $pK_4 = 1.1_4$.

Zn(II) Incorporation Kinetics. The kinetics of Zn(II) incorporation into the water-soluble porphyrins was followed spectrophotometrically at 25 °C, at an ionic strength of 0.050 M ($LiNO_3$). The solutions contained 2.0 mM PIPES (piperazine-*N*,*N'*-bis(2-ethanesulfonic acid) as the buffer, and the total porphyrin concentrations were $\sim 10^{-7}$ M. The reactions were all first order in porphyrin, with an observed pseudo-first-order rate constant, k_{obs}. The dependence of k_{obs} on total Zn(II) was studied at pH 7 over a 5-fold range, and that of k_{obs} on (H^+) from pH 7.2 to 6.2. The postulated reaction mechanism was as follows:

---

(14) (a) Pasternack, R. F.; Huber, P. R.; Boyd, P.; Engasser, G.; Francesconi, L.; Gibbs, E.; Fasella, P.; Cerio Venturo, G.; deC. Hinds, L. *J. Am. Chem. Soc.* **1972**, *94*, 4511. (b) Pasternack, R. F. *Ann. N. Y. Acad. Sci.* **1971**, 615. (c) Turay, J.; Hambright, P.; Datta-Gupta, N. *J. Inorg. Nucl. Chem.* **1978**, *40*, 1687.

(15) Solvent: 95% DMF/5% H_2O. Spectra [λ, nm (relative peak heights)]: H_2-TPP, 417.0 (102), 513.5 (4.28), 547.5 (1.84), 589.5 (1.24), 645.5 (1), $\epsilon_{645.5} = 3.4 \times 10^3$ M^{-1} cm^{-1}; $H_4\text{-TPP}^{2+}$, 358.0 (0.50), 445.0 (7.8), 609.0 (0.18), 662.0 (1), $\epsilon_{662.0} = 3.9 \times 10^4$ M^{-1} cm^{-1}. Isosbestic points (H_2-TPP/$H_4\text{-TPP}^{2+}$, nm): 428, 477, 563, 580, 594, 725. Spectrum for H_2-TPiBC: 390.0 (23.4), 407.0 (18.3), 518.0 (2.8), 553.5 (4.1), 597.0 (5.8), 651.5 (1.0), $\epsilon_{651.5} = 4.8 \times 10^3$. Spectrum for $H_3\text{-TPiBC}^+$: 399.0 (4.27), 416.5 (4.31), 507.0 sh (0.42), 547.5 (0.85), 600.0 (1.0), 645.5 (1.4), $\epsilon_{600.0} = 3.3 \times 10^4$ M^{-1} cm^{-1}. Isosbestic points for (H_2-TPiBC/$H_3\text{-TPiBC}^+$): 356, 384, 496, 508, 521, 760. $H_4\text{-TPiBC}^{2+}$ has bands at 436.0 (7.0), 526.0 sh (0.63), 589.5 sh (1.0), and 625.5 (1.7) in ~5 M HCl/DMF. Spectrum for H_2-TPC: 370.5 (1.0), 408.0 sh (4.3), 418.5 (5.5), 519.0 (0.44), 545.0 (0.30), 597.0 (0.17), 652.5 (1.0), $\epsilon_{652.5} = 4.2 \times 10^4$ M^{-1} cm^{-1}. In ~4 M HCl/DMF, $H_4\text{-TPC}^{2+}$ has bands at 443.0 (14.4), 611.0 (1.0), and 652 (2.7).

(16) For example with eq 5, log $[(H_2\text{-P})/(H_4\text{-P}^{2+})] = \log K_{3,4} + 2\text{pH}$. The porphyrin concentrations were calculated from the initial, final, and intermediate absorbances.

$$Zn^{2+} = ZnOH^+ + H^+ \quad K_h \tag{6}$$

$$H_2\text{-}P + Zn^{2+} \rightarrow Zn\text{-}P + 2H^+ \quad k_1 \tag{7}$$

$$H_2\text{-}P + ZnOH^+ \rightarrow Zn\text{-}P + H^+ \quad k_2 \tag{8}$$

The waters of hydration on Zn^{2+} and $ZnOH^+$ are omitted for clarity. This mechanism leads to the expression

$$\{(k_{obs}Q_{Zn}Q_{H_2P})/[Zn^{2+}]\} = k_1 + (k_2K_h)/(H^+) \tag{9}$$

where $Q_{Zn} = [(H^+ + K_h)/(H^+)]$, $Q_{H_2P} = [\{(H^+)^2 + K_4(H^+) + K_3K_4\}/\{K_3K_4\}]$, and $K_h = 2.92 \times 10^{-9}$ M at an ionic strength[17] of 0.050. Figure 3 is a plot of $\{(k_{obs}Q_{Zn}Q_{H_2P})/[Zn^{2+}]\}$ vs $\{1/(H^+)\}$ for H_2-TMPyC, where $k_1 = (4.0 \pm 1.2) \times 10^{-3}$ M^{-1} s^{-1} and $k_2 = (15 \pm 1)$ M^{-1} s^{-1}. The data for the other compounds are in Table I.

The kinetics of Zn(II) insertion into the water-insoluble ligands were followed in distilled pyridine at 25 °C using $Zn(ClO_4)_2 \cdot 2H_2O$ as the metal ion source. The reactions were found to be first order in porphyrin concentration. Figure 4 (insert) shows that, for H_2-TPiBC, k_{obs} is proportional to Zn(II) at low zinc levels and becomes independent of Zn(II) at higher concentrations. The same behavior was found for H_2-TPP and H_2-TPC. One mechanism consistent with this data[18] involves the formation of a complex $[Zn\text{-}H_2\text{-}P]^{2+}$ between the macrocycle and Zn(II), with a rate-determining decomposition of this species into products:

$$H_2\text{-}P + Zn(II) = [Zn\text{-}H_2\text{-}P]^{2+} \quad K \tag{10}$$

$$[Zn\text{-}H_2\text{-}P]^{2+} \rightarrow \text{products} \quad k_1 \tag{11}$$

The rate law is of the form

$$k_{obs} = (k_1K[Zn(II)])/(1 + K[Zn(II)]) \tag{12}$$

In accord with eq 12, Figure 4 shows a linear plot of $\{[Zn(II)]/k_{obs}\}$ vs [Zn(II)] for H_2-TPiBC, where $k_1 = (1.6 \pm 0.1) \times 10^{-3}$ s^{-1} and $K = (8.5 \pm 3.0) \times 10^2$ M^{-1} s^{-1}. The results for H_2-TPC and H_2-TPP are in Table II.

Zn(II)-P Acid Solvolysis Kinetics. The kinetics of the acid-induced removal of Zn(II) from the water-soluble compounds at $I = 0.50$ (HCl/LiCl) were followed spectrophotometrically at 25 °C. In all cases the reactions were first order in porphyrin and second order in (H^+) concentration. The following mechanism is consistent with the data:

$$Zn(II)\text{-}P + H^+ = [Zn\text{-}P\text{-}H]^+ \quad k_1, k_{-1}, K_{ZnP} \tag{13}$$

$$[Zn\text{-}P\text{-}H]^+ + H^+ \rightarrow \text{products} \quad k_2 \tag{14}$$

With $[Zn\text{-}P\text{-}H]^+$ as a steady-state intermediate

$$k_{obs} = k_1k_2(H^+)^2/[k_{-1} + k_2(H^+)] \tag{15}$$

If $k_{-1} \gg k_2(H^+)$, then $k_{obs} = k_2K_{ZnP}(H^+)^2$. Figure 1 shows the linear dependence of k_{obs} on $(H^+)^2$ for Zn(II)–TSPC, from which $k_2K_{ZnP} = (2.1 \pm 0.1) \times 10^2$ M^{-2} s^{-1}. Results for the other water-soluble derivatives are in Table I.

The kinetics of zinc removal from the water-insoluble species were studied in DMF at three different HCl concentrations. The reactions were first order in porphyrin, and Figure 2 (insert) shows a plot of log k_{obs} vs log (H^+) for the three compounds. The slopes ranged from 1.8 to 2.2, possibly indicating that two protons are required for the demetalation. The relative acid solvolysis rate constant ratios were 79:12:1 for Zn–TPiBC, Zn–TPC, and Zn–TPP, respectively.

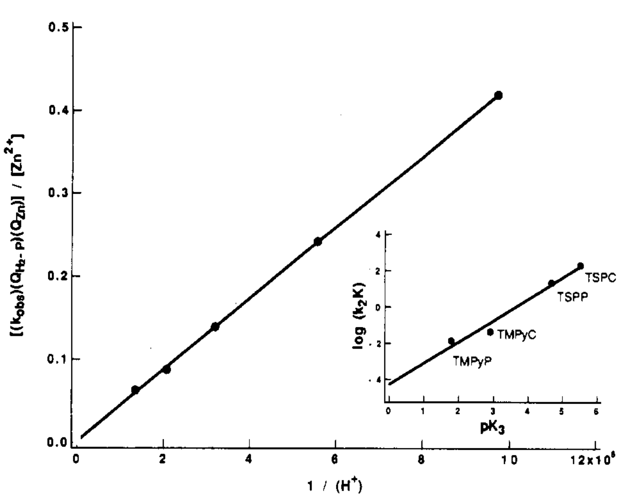

Figure 3. Plot of eq 9 for the kinetics of the Zn(II)/H_2-TMPyC reaction. Insert: Free energy relationship between log (k_2K) and pK_3 for the acid solvolysis reactions of the water-soluble zinc complexes.

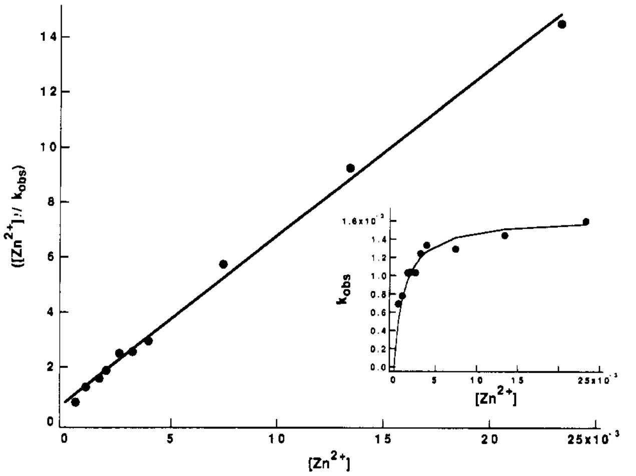

Figure 4. Plot of $[(Zn^{2+})/k_{obs}\}$ vs $[Zn^{2+}]$ for the H_2-TPiBC/Zn^{2+} reaction in pyridine. The insert shows the dependence of k_{obs} on $[Zn^{2+}]$ for the same reaction.

Table II. Basicity and Zinc Incorporation Kinetic Results in Nonaqueous Solutions

	Zn(II)/H_2-P[a]		basicities[b]	
porphyrin	10^4k_1 (s^{-1})	K (M^{-1})	pK_3	pK_4
TPiBC	16.4 ± 0.3	850 ± 300	3.1_4	$\ll 1$
TPC	3.7 ± 0.1	490 ± 130	2.4_9	1.1_4
TPP	2.1 ± 0.1	360 ± 100	4.4_6[c]	

[a] $Zn(ClO_4)_2 \cdot 2H_2O$ in pyridine. [b] 95:5 DMF/H_2O with HCl. [c] $pK_{3,4}$.

Discussion

A considerable amount of information has been collected on the solution kinetic and equilibrium properties of water-soluble and water-insoluble porphyrins.[19-23] Rather less is known concerning the reactivity of chlorins, which contain one reduced

---

(17) Bases, C. F., Mesmer, R. E., Eds. *The Hydrolysis of Cations*, 4th ed.; Wiley-Interscience: New York, 1976.

(18) Wilkins, R. G. *Kinetics and Mechanisms of Reactions of Transition Metal Complexes*, 2nd, ed.; VCH Publishers: New York, 1991; Chapter 1.

(19) Lavallee, D. K. *Coord. Chem. Rev.* **1985**, *61*, 55.

(20) Hambright, P. In *Porphyrins and Metalloporphyrins*; Smith, K. M., Ed.; Elsevier: Amsterdam, 1975; Chapter 6.

(21) Schneider, W. *Struct. Bonding* (Berlin) **1975**, *23*, 123.

(22) Longo, F. R.; Brown, E. M.; Rau, W. G.; Adler, A. D. In *The Porphyrins*; Dolphin, D., Ed.; Academic Press: New York, 1978; Vol. 5, Chapter 10.

(23) Barber, D. C.; Lawrence, D. S.; Whitten, D. G. *J. Phys. Chem.* **1992**, *96*, 1204.

β-pyrrole ring, and the releated bacterio- and isobacteriochlorins, which are formally four equivalents below the porphyrins, in having two of their four pyrrole rings reduced. Crystal structures of a variety of metallochlorins and tetrahydroporphyrins have been solved and compared with porphyrins.[3] Certain of the reduced porphyrin compounds are able to stabilize metal ion oxidation states that are short-lived in their oxidized porphyrin forms. For example, radiolytically produced Ni^{I} and Ni^{III} porphyrins in water have a transient existence: Ni^{I}–P rapidly disproportionates into Ni^{II}–P and ring-reduced $Ni^{II}–P^{2-}$ (either phlorins or chlorins),[24] and Ni^{III}–P also quickly decays into ring-oxidized products.[25] In contrast, Ni^{I} (and Cu^{I})[26] isobacteriochlorins[27] and Ni^{III} β-oxoporphyrins[28] are relatively stable under nonaqueous conditions. As the porphyrin becomes more saturated, the aromaticity decreases, the reduction potentials are more negative, and the ring becomes more flexible and able to accommodate larger ions. In the present work, we explore several solution reactivity trends among porphyrins, chlorins, and isobacterioporphyrins.

Basicities. On the basis of the concentration of acid needed to partition compounds between water and a nonaqueous phase,[6,7] the relative basicities of the compounds of concern are reported to be in the order porphyrin > chlorin, isobacterioporphyrin > bacteriochlorin. Such "acid numbers" depend on proton affinity as well as the relative solubilities of each form in the different solvents. Aronoff[7] titrated various porphyrins dissolved in nitrobenzene with $HClO_4$ and found $pK_3 = 4.85$ and $pK_4 = 3.83$ for H_2-TPP, as compared with 3.85 and 3.38 for H_2-TPC, indicating that the chlorin was less basic than the porphyrin. Our titrations on several porphyrins and chlorins in this solvent system gave good isosbestic points, but pK_as could not be derived from the data. Adler[29] used DMF as a titration medium for porphyrins, and in DMF/HCl, we were able to obtain satisfactory pK_a behavior. H_2-TPiBC showed a single $pK_3 = 3.1_4$ up to 0.33 M HCl, with spectral changes indicating further protonation at much higher acid levels. H_2-TPC has $pK_3 = 2.4_9$ and $pK_4 = 1.1_4$ under the same conditions. Thus, in DMF/HCl, H_2-TPiBC is more basic than H_2-TPC. H_2-TPP, however, gave evidence for an equilibrium between the free base H_2-P and the dication H_4-P^{2+} with a $pK_{3,4}$ of 4.4_6, and there was no spectral or curve analysis indication of the monocation, H_3-P^+. Several chlorophyll chlorins (pheophorbides), purpurin 18, and chlorin e_6 in nitrobenzene[6]/ $HClO_4$ and tetrakis(4-pyridyl)porphyrin in water[30] behave in the same fashion. The difference ($pK_3 - pK_4$) values are ~2 > 1 > ~–2, in the order H_2-TPiBC > H_2-TPC > H_2-TPP.

The one-electron reduction potentials forming the radical anions are –1.70 for H_2-OEiBC, –1.47 for H_2-OEC, and –1.44 V for H_2-OEP.[31] For a variety of porphyrins, linear correlations have been found[32–34] between such $E_{1/2}(1)$ values in DMF and the protonation constants pK_3. The most basic porphyrin is the most difficult to reduce, in rough parallel with the measurements above.

For the water-soluble compounds, the chlorins are more basic than the corresponding porphyrins. Thus, H_2-TSPC has $pK_3 = 5.3_8$ and $pK_4 = 4.2_7$, while values of 4.6_7 and 4.7_7 are found for H_2-TSPP. The chlorin H_2-TMPyC has $pK_3 = 2.9_0$ and $pK_4 \ll 1.0$, while the porphyrin H_2-TMPyP shows 1.7_9 and 1.3_4, respectively. Again, the chlorins show a larger ($pK_3 - pK_4$) difference than do the porphyrins. It should be noted that all of the aqueous solution experiments were done at total porphyrin concentrations of $\sim 10^{-7}$ M with the ionic strength as low as possible in order to minimize the presence of dimers in solution. The dimerization constant K_D of H_2-TSPC at $I = 0.10$ is $\sim 2.2 \times 10^5\ M^{-1}$, which is similar to the $9.6 \times 10^4\ M^{-1}$ value found for H_2-TSPP.[35] The positively charged chlorin H_2-TMPyC showed no evidence of aggregation, and other workers[36] report that H_2-TMPyP is monomeric in solution.

Zinc Incorporation Kinetics. One of the earliest methods to separate H_2-TPP from H_2-TPC involved adding zinc acetate to a hot trichloroethylene solution of the compounds. Zn–TPP formed much faster than Zn–TPC, allowing a talc column separation of the rapidly moving Zn–TPP from the slower H_2-TPC fraction.[11] Longo and co-workers[10] found the kinetics of $CuCl_2$ incorporation in DMF to be first order in ligand and metal at high Cu^{2+} levels, and from the reported activation parameters, H_2-TPC is predicted to react about 10 times faster than H_2-TPP at 25 °C. Stolzenberg gives the order H_2-OEiBC ≫ H_2-OEC > H_2-OEP from qualitative preparative metalation studies.[9] Our Zn(II) incorporation kinetics in pyridine indicates the formation of an adduct (a sitting-atom complex?)[37] between zinc and the porphyrin, and we interpret it as an intermediate rather than as a dead-end species in the metalation process. Such adducts are often found in non-aqueous porphyrin metalation studies. The formation constants are $\sim 5 \times 10^2\ M^{-1}$ for the present compounds in pyridine, $\sim 10^3\ M^{-1}$ for Zn(II)/H_2-TPP in DMF,[38,39] and ~5 M^{-1} for Cu(II)/H_2-TPP in DMSO.[40] These intermediates presumably involve a distorted porphyrin with its two free-base protons on one side and a metal ion coordinated to two nitrogen atoms on the opposite face of the porphyrin. In the present work, both K and k_1 decrease in the order H_2-TPiBC > H_2-TPC > H_2-TPP, and the observed rate constants follow this trend. At low zinc levels, the k_{obs} ratios are ~19:2.5:1, and at high zinc, where k_1 is rate limiting, the ratios are ~8:2:1. In DMF for Zn(II) and Cu(II) incorporation into a variety of substituted tetraphenylporphyrins, the incorporation rate constants increase by roughly a factor of 3 for a 10-fold increase in proton basicity.[22,38]

The kinetics of Zn(II) incorporation into the water-soluble porphyrins and chlorins exhibit a common rate law first order in free base, Zn^{2+}, and $ZnOH^+$, with no leveling behavior apparent.[20,41,42] For the four compounds studied, k_2 for $ZnOH^+$ is typically several orders of magnitude larger than the k_1 term for Zn^{2+}. The higher lability of hydrolyzed species which can have a different structure from the aquo ion might rationalize such results.[20,21] In water, the chlorins react from 7 to 15 times slower with Zn^{2+} than do the corresponding porphyrins, a reversal of the trend found in pyridine and other nonaqueous media, while the porphyrins and chlorins react at very similar rates with $ZnOH^+$. As noted before,[43] electrostatic factors arising from the signs and magnitudes of the charges of the peripheral porphyrin groups result in the observed metalation rate constants in water being strongly influenced by the ionic strength of the medium. While tetrapositive porphyrins similar to H_2-TMPyP are predicted to

---

(24) Nahor, G. S.; Neta, P.; Hambright, P.; Robinson, L. R.; Harriman, A. *J. Phys. Chem.* **1990**, *94*, 6659.

(25) Nahor, G. S.; Neta, P.; Hambright, P.; Robinson, L. R. *J. Phys. Chem.* **1991**, *95*, 4415.

(26) Stolzenberg, A. M.; Schussel, L. J. *Inorg. Chem.* **1991**, *30*, 3205.

(27) (a) Renner, M. W.; Furenlid, L. R.; Barkigia, K. M.; Forman, A.; Shim, H. K.; Simpson, D. J.; Smith, K. M., Fajer, J. *J. Am. Chem. Soc.* **1991**, *113*, 6891. (b) Stolzenberg, A. M.; Stershic, M. T. *J. Am. Chem. Soc.* **1988**, *110*, 5397.

(28) Connick, P. A.; Macor, K. A. *Inorg. Chem.* **1991**, *30*, 4654.

(29) Meot-Ner, M.; Adler, A. D. *J. Am. Chem. Soc.* **1975**, *97*, 5107.

(30) Fleischer, E. B.; Webb, L. E. *J. Phys. Chem.* **1963**, *67*, 1131.

(31) Stolzenberg, A. M.; Spreer, L. O.; Holm, R. H. *J. Am. Chem. Soc.* **1980**, *102*, 364.

(32) Williams, R. F. X.; Hambright, P. *Bioinorg. Chem.* **1978**, *9*, 537.

(33) Worthington, P.; Hambright, P.; Williams, R. F. X.; Reid, J.; Shamim, A.; Burnham, C.; Turay, J.; Bell, D. M.; Little, R. G.; Datta-Gupta, N.; Eisner, U. *J. Inorg. Biochem.* **1980**, *12*, 281.

(34) Worthington, P.; Hambright, P.; Williams, R. F. X.; Feldman, M. F.; Smith, K. M.; Langry, K. *J. Inorg. Nucl. Chem.* **1981**, *43*, 2577.

(35) Sutter, J. R.; Krishnamurthy, M.; Hambright, P. *J. Chem. Soc., Chem. Commun.* **1975**, 13.

(36) Brookfield, R. L.; Ellul, H.; Harriman, A. *J. Photochem.* **1985**, *31*, 97.

(37) Fleischer, E. B.; Wang, J. H. *J. Am. Chem. Soc.* **1960**, *82*, 3498.

(38) Robinson, L. R.; Hambright, P. *Inorg. Chim. Acta* **1991**, *185*, 17.

(39) Funahashi, S.; Yamaguchi, Y.; Tanaka, M. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 204.

(40) Pasternack, R.; Vogel, G.; Skowronek, C.; Harris, R.; Miller, *J. Inorg. Chem.* **1981**, *20*, 3763.

(41) Thompson, A. N.; Krishnamurthy, M. *J. Inorg. Nucl. Chem.* **1979**, *41*, 1251.

(42) Hambright, P.; Chock, P. B. *J. Am. Chem. Soc.* **1974**, *96*, 3123.

(43) Nwaeme, J.; Hambright, P. *Inorg. Chem.* **1984**, *23*, 1990.

react with divalent cations up to 10^6 times slower than the tetranegative H_2-TSPP at zero ionic strength, the observed rate constants approach and cross one another as the ionic strength increases. Thus, studies at any given ionic strength are not terribly informative as to intrinsic relative reactivities.

Zinc Acid Solvolysis Kinetics. In aqueous solutions, the rate law for the acid-catalyzed removal of Zn(II) from the porphyrins and chlorins is first order in complex and second order in (H^+). This rate law in water is followed by other Zn(II),[41,43] Cd(II),[44] and Pb(II)[45] porphyrins, where the addition of H^+ to a (Zn–P–H) intermediate is postulated as the rate-determining step. Classically, the Zn(II) is four-coordinate with respect to the porphyrin. Upon dissociation into a three-coordinate species, a proton can bind to the uncomplexed nitrogen atom, producing the intermediate (Zn–P-H), which begins the solvolysis process. Second proton addition forms the $[Zn{=}PH_2]$ activated complex, involving a chelated N–Zn–N structure. In contrast to the usual insensitivity of the metalloporphyrin formation rates, linear free energy relationships between log (k_2K_{ZnP}) and pK_3 are often found,[44,45] where the dissociation rate constants (k_2K_{ZnP}) increase markedly with an increase in porphyrin basicity. The insert in Figure 3 shows an excellent linear relationship between log (k_2K_{ZnP}) and pK_3 of the form log (k_2K_{ZnP}) = –4.30 + 1.19pK_3, for the water-soluble porphyrins and chlorins. Such acid solvolysis kinetics in DMF appear to follow a similar two-proton rate law, where the relative solvolysis rate constants are 79:12:1 for Zn–TPiBC, Zn–TPC, and Zn–TPP, respectively, a reflection of their relative basicities.

Summary and Conclusions. The chlorins are found to be more basic than the corresponding porphyrins in water, and in DMF, H_2-TPiBC is more basic than H_2-TPC. In both cases, the difference (pK_3 – pK_4) becomes more positive the more saturated the ring, implying that the amount of the monocation H_3-P^+ in solution increases with ring reduction. We speculate that the greater flexibility of the more saturated derivatives allows H_3-P^+ to adopt conformations that do not simultaneously force the lone pair on the remaining nitrogen out of the porphyrin cavity and toward the solution, which would tend to make it more readily protonated. In DMF/HCl, H_3-P^+ is not found for TPP and the addition of the first proton to H_2-TPP greatly facilitates the second protonation producing H_4-TPP^{2+}. This implies that $K_3 \gg K_4$, or p$K_4 \gg$ pK_3. In general, the stability of the monocation depends markedly on the reaction conditions, an indication of how the medium alters porphyrin reactivity. Thus, while all three forms of TSPP are present at pH 5 in water, no H_3-P^+ is detected with this porphyrin in $DMSO/H_2O/HClO_4$ mixtures.[46] Similarly, with uncharged deuteroporphyrin dimethyl esters, three forms are seen in negatively charged detergents, whereas only $K_{3,4}$ behavior is noted in cationic and neutral detergents.[20] Again, $H_3P^+Cl^-$ is not present to a measurable extent in DMF/HCl, whereas H_3-$P^+ClO_4^-$ is produced in nitrobenzene/$HClO_4$.

The kinetics of Zn(II) incorporation into TPP, TPC, and TPiBC in pyridine indicate the formation of a "sitting-atop" reaction intermediate of the composition (Zn–H_2-P) in all three cases. Their formation constants are similar, and the overall incorporation order is H_2-TPiBC > H_2-TPC > H_2-TPP, in the ratios 8:2:1 at high Zn(II) levels. Similar species are found for free-base porphyrins reacting with Cu(II), Zn(II), and Cd(II) in DMF, where the overall metalation rates increase slightly with an increase in porphyrin basicity.[38,39] In water, on the other hand, the porphyrins react with Zn^{2+} from 8 to 15 times faster than do the corresponding chlorins, and both porphyrins and chlorins show equal reactivity toward $ZnOH^+$ at an ionic strength of 0.050. No kinetic evidence for reaction intermediates is noted in aqueous solution. The expectation that an increase in ring deformation with reduction would profoundly alter the relative metalation rates was not realized. Thus, the predeformed and more basic *N*-alkylporphyrins react with metals about 10^3 times more rapidly than do the less basic and more planar porphyrins in both aqueous[47] and nonaqueous solutions,[48,49] and in DMF, the deformed octabromotetramesitylporphyrin incorporates Zn(II) 3.9 × 10^3 times faster than does tetramesitylporphyrin.[38] The nonplanar *β*-octabromo-TSPP derivative[50] in water gives a k_1 value for Zn^{2+} of 3×10^3 M^{-1} s^{-1} and k_2 for $ZnOH^+$ of 1.9×10^5 M^{-1} s^{-1}, as compared to 1.2×10^1 and 3.1×10^1 M^{-1} s^{-1}, respectively, for H_2-TSPP. The reactivity effects shown by the chlorins and isobacteriochlorins are minor compared to the results noted above for certain strongly deformed porphyrins.

For the zinc complex acid solvolysis reactions in DMF/HCl, the rate constant order was Zn–TPiBC > Zn–TPC > Zn–TPP in the ratios 79:12:1, and in water, the solvolysis rate constants paralleled the basicities of the compounds: Zn–TSPC > Zn–TSPP > Zn–TMPyC > Zn–TMPyP. Such reactivity correlations are often found when the metal is bound to the macrocycle,[51] and it appears that the order of effective basicities is isobacteriochlorin > chlorin > porphyrin.

Since second bond breaking is rate determining in the acid solvolysis reactions in water, it is possible that second bond formation is rate determining in metal ion incorporation reactions. This could account in part for the fact that porphyrin metalations, which involve ring deformation, are orders of magnitude slower than shown by most classical ligands, which often feature first bond formation as the rate-limiting step.[18]

---

(44) (a) Shamim, A.; Hambright, P. *Inorg. Chem.* **1980**, *19*, 564. (b) Tabata, M.; Tanaka, M. *J. Chem. Soc., Dalton Trans.* **1983**, 1955.

(45) Haye, S. E.; Hambright, P. *Inorg. Chem.* **1984**, *23*, 4777.

(46) Faus, J.; Jimenez, H. B.; Miguel, J.; Moratal, J. M. *J. Chem. Soc., Chem. Commun.* **1987**, 909.

(47) Funahashi, S.; Ito, Y.; Kakito, H.; Inamo, M.; Hamada, Y.; Tanaka, M. *Mikrochim. Acta* **1986**, *4*, 33.

(48) Lavallee, D. K. *The Chemistry and Biochemistry of N-Substituted Porphyrins*; VCH Publishers: New York, 1987; Chapter 4.

(49) Shah, B.; Shears, B.; Hambright, P. *Inorg. Chem.* **1971**, *10*, 1828.

(50) Sutter, T. P. G. Ph.D. Dissertation, Howard University, 1992.

(51) Shears, B.; Shah, B. Hambright, P. *J. Am. Chem. Soc.* **1971**, *93*, 776.