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Metal Ion Interactions with Porphyrins. I. Exchange and Substitution Reactions

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Due to the insolubility of both metal ions and porphyrins in many common solvents, the available data on substitution reactions of one metal ion for another coordinated in the porphyrin macrocycle have been mainly limited to studies using pyridine as the reaction medium.[1,2] Such results are difficult to interpret owing to the lack of knowledge of metal ion species present in hot pyridine. No exchange reactions between zinc and zinc porphyrins, which could elucidate the features of such substitution processes, have been published.[3]

The synthetic derivative tetrakis(*N*-methyltetrapyridyl)porphine (TMTPyP), however, is soluble from below pH 0 to above pH 14 and is monomeric in aqueous solution.[4,5] These favorable properties have led to widespread interest in the coordination, kinetic, and equilibrium behavior of this ligand and its metal complexes.[6]

We report kinetics of the substitution of Cu^{2+} for zinc in ZnTMTPyP (in aqueous solution) and in other zinc porphyrins (in pyridine). Results of studies of the exchange reaction of zinc with zinc porphyrins in aqueous and nonaqueous media are also described.

Experimental Section

General Procedures. TMTPyP and its metal complexes were synthesized by literature methods.[4,5] $ZnTMTPyP(tosylate)_4$ could be made by refluxing zinc tetrapyridylporphine (Mad River Chemical Co., Yellow Springs, Ohio) in DMF with methyl *p*-toluenesulfonate for 3 hr and filtering off the purple precipitate after cooling. The adduct was washed with benzene and vacuum dried. The absorption spectra of the complexes of TMTPyP were similar to those reported for tetrapyridylporphine.[6]

Exchange Reactions. The exchange reaction Zn-Zn*TMTPyP was followed using ^{65}Zn incorporated into the porphyrin. Samples of the reaction mixture at 52° were rapidly brought to room temperature and divided into portions labeled "before" and "after." $NaClO_4$ (3.0 *M*) containing 10^{-2} *M* $Zn(NO_3)_2$ at pH 6 was added to the "after" samples to precipitate $ZnTMTPyP(ClO_4)_4$. This was allowed to settle, spun down, and reprecipitated twice again. The "after" and "before" samples were made 3.0 *M* in H_2SO_4 and counted, and the absorption spectra were determined. Due to loss of porphyrin in the extraction process, the "after" samples had a lower optical density at 639 nm than the "before" samples. This ratio was used to correct the "after" counts for loss of total porphyrin, which amounted to 7-10%. The absorption spectra and counts per minute of blank determinations of samples heated to 55° did not change within 3 days. When treated with 0.1 *M* HCl, 99% of Zn* was removed from Zn*TMTPyP by the extraction procedure.

For the exchange reactions of zinc with zinc tetraphenylporphine (Zn*TPP), studied in pyridine at 114°, samples were cooled rapidly to room temperature. Aliquots were evaporated to remove pyridine, taken up in trichloroethylene, extracted with water containing 10^{-2} *M* $Zn(NO_3)_2$, dried over Na_2SO_4, and counted.

Substitution Reactions in Pyridine. The kinetics of the substitution of $Cu(OAc)_2$ into zinc porphyrins were run in refluxing pyridine (114°). Samples were withdrawn, evaporated, dissolved in trichloroethylene, extracted with water, filtered over Na_2SO_4, and made 3.0 *M* in pyridine. Knowledge of the extinction coefficients of the zinc and copper porphyrins at two wavelengths allowed a calculation of the fraction of zinc replaced by copper as a function of time.

Table I. Kinetic Data for the Replacement of Zn^{2+} in ZnTMTPyP by Cu^{2+} in Aqueous Solution ($\mu = 2.0$ ($NaNO_3$))

10^3k_{obsd},[a] min^{-1}	$10^2[Cu^{2+}]$, *M*	$10^2[Zn^{2+}]$, *M*	pH[b]	$10^2k_{obsd}/[Cu^{2+}]$, min^{-1} M^{-1}	Temp, °C
22.5	15.2		3.55	14.8	48.9
14.6	10.0		3.85	14.6	
11.3	8.00		3.85	14.1	
6.09	4.00		4.13	15.2	
3.18	2.00		4.40	15.7	
14.6	10.0	10.0	3.92	14.6	
14.3	10.0	1.00	3.87	14.3	
8.45	6.00		3.00	14.1	
9.87	6.00		4.08	16.4	
4.57	3.20		4.33	14.3	
4.80	3.20		4.31	15.0	
32.3	15.2		3.85	21.2	53.8
21.9	10.0		3.72	21.9	53.8
41.5	10.0		3.84	41.9	58.6

[a] [ZnTMTPyP] = 2.5×10^{-5} *F* for all entries except no 10, which was 6.25×10^{-5} *F*. [b] pH measured at 23°.

Results

Cu-ZnTMTPyP Reactions. The kinetics of the electrophilic substitution of Cu^{2+} for Zn^{2+} in ZnTMTPyP was studied from 45 to 55° in aqueous solution from pH 3.0 to 4.4 at an ionic strength of 2.0 ($NaNO_3$).

$$Cu^{2+} + ZnTMTPyP \rightarrow CuTMTPyP + Zn^{2+} \qquad (1)$$

As shown in Table I the rate was first order in total porphyrin over a threefold range and first order in total copper over a sevenfold dilution. The observed rate was independent of added zinc in concentrations equal to or tenfold less than the copper concentration. The rate was pH independent from pH 3.0 to 4.4, with a second-order rate constant of $(14.8 \pm 0.4) \times 10^{-2}$ F^{-1} min^{-1} at 48.9°. The activation parameters for reaction 1 were $\Delta H^{\ddagger} = 15.2 \pm 0.8$ kcal/mol and $\Delta S^{\ddagger} = 25 \pm 4$ eu.

The absorption spectra of ZnTMTPyP at 55° did not change by more than 1% after 20 hr of observations, indicating no solvolysis to the free base form. With 0.1 *F* Zn^{2+} and CuTMTPyP at 55°, $\mu = 2.0$ ($NaNO_3$), no reaction was found after 20 hr. Both Ni^{2+} (1.8 *F*, $\mu = 4.0$) and Co^{2+} (0.4 *F*, $\mu = 2.0$) were heated for 15 hr with ZnTMTPyP. No reaction was noted in either case.

Several experiments were run to determine whether, during the course of the reaction of H^+ with ZnTMTPyP, a protonated zinc-containing intermediate formed that would react with Cu^{2+} to produce CuTMTPyP. The rates and pH dependence of the following reactions are known:[7] Zn-TMTPyP, Cu-TMTPyP, and H^+-ZnTMTPyP.[8] Also, Cu^{2+} does not react with the mono- or dication forms of TMTPyP. At pH 0 and 1, the results were consistent with CuTMTPyP being produced only by way of the free base TMTPyP.

Copper-Zinc Porphyrin Reactions. To determine the effect of porphyrin basicity on the substitution of copper for zinc in zinc porphyrins, studies were run with various zinc porphyrins and $Cu(OAc)_2$ in refluxing pyridine (114°).

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Table II. Relative Rates for the Substitution of $Cu(OAc)_2$ for Zn^{2+} in Zinc Porphyrins in Refluxing Pyridine

Zinc porphyrin[a]	Time, hr	% Cu substituted[b]
Etioporphyrin	68	17
Mesoporphyrin DME	63	13
Protoporphyrin DME	67	30
Dibromodeuteroporphyrin DME	68	49
ms-Tetraphenylporphine	36	56
ms-Tetrapyridylporphine	2	47

[a] DME is dimethyl ester. [b] $[Cu(OAc)_2] = 5 \times 10^{-2}$ *F*.

While the dimethyl esters decomposed to various extents during the reaction, etioporphyrin and the meso-substituted complexes were quite stable. As shown in Table II, the results qualitatively indicate that as porphyrin basicity increases, the electrophilic substitution rate decreases.

Zinc-Zinc Porphyrin Exchange. By using ^{65}Zn incorporated into zinc porphyrins, it should be possible to follow the exchange reaction

$$Zn^{2+} + Zn^{*}P = Zn^{*2+} + ZnP \tag{2}$$

With ZnTPP (6×10^{-6} *F*) and $Cu(OAc)_2$ (6×10^{-2} *F*) in refluxing pyridine (114°) and dimethylformamide (153°), 12 samples were taken over a 3-day period and worked up as described in the Experimental Section. The observed counts per minute (*ca.* 40,000 per sample for pyridine and 12,000 for DMF) decreased by about 5% over 3 days, which was approximately the same amount as shown by a blank sample without added $Zn(OAc)_2$. The conclusion is that little exchange occurs in this time period.

The exchange reaction of Zn^{2+} with Zn*TMTPyP was studied in aqueous solution at 52° with *ca.* 10^{-5} *F* Zn*-TMTPyP, 0.2 *F* $Zn(NO_3)_2$, and $\mu = 2.0$ ($NaNO_3$). No evidence for exchange was found for up to 44 hr.

Discussion

Replacement and Exchange Reactions. The kinetics of the substitution of Cu^{2+} for Zn^{2+} in ZnTMTPyP at constant ionic strength show a first-order dependence on Cu^{2+} and ZnTMTPyP. The reaction was not retarded by Zn^{2+}, and no evidence for intermediates was observed. The stability toward solvolysis of ZnTMTPyP and the lack of exchange of Zn with Zn*TMTPyP during the time scale of the Cu-Zn-TMTPyP reaction argue for an activated complex having both copper and zinc bonded to the porphyrin entity. Such bimetalated complexes with metal ions on opposite sides of the ring are presumed for ionic porphyrins (Na_2P) and have been definitely demonstrated for more inert systems[9] (*e.g.*, μ-[mesoporphyrin IX dimethyl esterato]-bis[tricarbonylrhenium(I)]). Spectral[10] and kinetic[11] evidence has also been advanced for porphyrins containing two metal entities.

When compared with Cu^{2+}, Zn^{2+}, Co^{2+}, and Ni^{2+} show no substitution into ZnTMTPyP under the reaction conditions. This could be due to kinetic or thermodynamic reasons. Toward the similarly charged free base of TMTPyP, the insertion rates of these metal ions[7] are in the ratio 1:70:1800:5000. This could imply a kinetic control of the reaction products.

The kinetics of the substitution of Cu for Zn in a water-soluble ethylenediamine-substituted protoporphyrin show first-order behavior in porphyrins, a lack of appreciable Zn^{2+} inhibition, and a rate decreasing with increasing pH.[12] The rate tends toward a limiting value dependent on pH with an increase in Cu^{2+} concentration. While the author favors the rate-limiting dissociation $ZnPH^{+} = Zn^{2+} + HP^{-}$ followed by Cu^{2+} incorporation into HP^{-} rather than the direct displacement mechanism postulated above, no strong evidence is advanced that both mechanisms do not in fact operate simultaneously.

The reactions Zn-CdTPP and Zn-HgTPP studied in pyridine have simple bimolecular rate laws with the cadmium reaction about 30 times slower than that of mercury.[2] Coupled with the observations that the Cu-ZnP rates increase with a decrease in porphyrin basicity, this leads to the conclusion that bond breaking is more important than bond making in such substitution reactions. In the Cu-ZnTPP reaction in pyridine, a small rate inhibition[2] was found with added Zn^{2+}. While we feel that this small inhibition (less than a factor of 2 for a tenfold increase in zinc) is a medium effect, the extremely high activities of ^{65}Zn required to test this hypothesis precluded any definitive test.

In general mechanistic terms, both acid-catalyzed solvolysis reactions of zinc porphyrins and metal ion substitution reactions can be viewed in the same manner. One of the four zinc to porphyrin bonds breaks which facilitates attack by a proton or metal atom at this central nitrogen atom's lone pair. A gradual breaking of the other three zinc to porphyrin bonds occurs with the simultaneous attachment to the porphyrin of additional protons or more coordination sites on the entering metal ion. For the substitution reactions it appears that bond breaking overrides bond making whereas the reverse is true for solvolysis reactions. The roles of porphyrin deformation and chelate stability in this process have been discussed before.[13]

Acid Solvolysis Reactions. With the exception of Mn^{3+}, the ions listed below were removed from their TMTPyP complexes at room temperature by concentrated H_2SO_4 to form the diacid porphyrins.[14] Using lower acid concentrations, the relative order of solvolysis was found to be $Zn^{2+} \gg Cu^{2+} > Fe^{2+} > VO^{2+} > Ni^{2+} \gg Mn^{3+}$.

This general trend has been noted by many workers.[3] It has been shown that the one-electron oxidation and reduction potentials of the porphyrin ring depend on the metal ion,[15] with ionic, easily solvolyzed ions leaving the ring with a higher negative charge than covalent, difficultly solvolyzed ions. In this context, the covalent charge transfer makes the ring and central nitrogen atoms more positive and the metal atom more negative and could explain why the nucleophilic substitution reactions[16,17] of cobalt(III) and chromium(III) porphyrins are rapid compared to most usual metal complexes. The covalency changes the electron configurations which are formally low-spin d^6 and d^3 toward the more labile d^7 and d^4 arrangements. The recent demonstration that the lability of the axial position of iron(III) porphyrins increases with porphyrin basicity is in line with this reasoning.[18] The extreme covalency of Mn^{3+} postulated here is in

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(9) D. Ostfeld, M. Tsutsui, C. P. Hrung, and D. C. Conway, *J. Amer. Chem. Soc.*, 93, 2548 (1971).

(10) D. Ostfeld, M. Tsutsui, C. P. Hrung, and D. C. Conway, *J. Coord. Chem.*, 2, 101 (1972).

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

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

(14) Co^{3+} turned green in concentrated H_2SO_4 but exhibited a spectrum different from the diacid.

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(18) G. N. La Mar and F. A. Walker, *J. Amer. Chem. Soc.*, 94, 8607 (1972).

accord with speculations concerning the strong mixing of metal and porphyrin orbitals and the low stabilities of its axial ligand complexes.[19,20]

Registry No. ZnTMTPyP, 40603-58-5; Zn(etioporphyrin), 40148-68-3; Zn(mesoporphyrin DME), 15376-02-0; Zn(protoporphyrin DME), 15304-09-3; Zn(dibromodeuteroporphyrin DME), 40603-60-9; Zn(*ms*-tetraphenylporphine), 14074-80-7; Zn(*ms*-tetrapyridylporphine), 31183-11-6; zinc, 7440-66-6; copper, 7440-50-8.

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(20) Note Added in Proof. We find that the Cu-ZnTPyP reaction is strongly catalyzed by NO_3^-, possibly indicating an activated complex containing all three species. This is reasonable since both metal ion incorporation[6] and acid-catalyzed solvolysis reactions[8] of zinc-TMTPyP involve a nitrate term.

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Cobalt-59 Nuclear Magnetic Resonance Shifts and the Acidity of Amine Protons in Tris(ethylenediamine)cobalt(III)

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The acidity of NH protons in metal-amine complexes is relevant to several proposed mechanisms for substitution reactions of these complexes, as, for example, in the SN1 conjugate base mechanism for substitution of cobalt(III) amines.[2] Since such NH protons are only very weakly acidic, nmr techniques are useful in supplementing other measures of the extent of neutralization in strongly basic solutions.[3,4] We report here a ^{59}Co nmr determination of K_n, the pseudothermodynamic constant for the neutralization reaction HA + $OH^- = H_2O + A^-$, where HA represents tris(ethylenediamine)cobalt(III)–$Co(en)_3{}^{3+}$–and A^- its conjugate base. In our work, the ratio of maximum observed shift to line width was about 20, which corresponds to a greater effective resolution than that reported in proton nmr determinations of the neutralization constant for $Co(en)_3{}^{3+}$ [3] and for platinum-amine complexes.[4]

Experimental Section

Cobalt-59 nmr measurements were taken as free induction decay spectra at 1.41 T (14.1 kG) and 30° on a Bruker BKR 321s variable-frequency pulsed spectrometer which had been modified for external lock, field-frequency control. Frequency shift measurements (taken with respect to the ^{59}Co resonant frequency of $Co(en)_3{}^{3+}$ in aqueous neutral solutions) were reproducible, for a given sample, to ±10 Hz over a 24-hr period. The relatively short relaxation times–3-10 msec–were the principal source of error in frequency measurements. Samples were run immediately on preparation (in tightly stoppered tubes to prevent CO_2 absorption) as 0.5 *M* aqueous solutions of $Co(en)_3Cl_3$ to which known volumes of *ca.* 19 *M* NaOH solutions were added. These NaOH solutions were standardized just before use by titration against primary standard KHP.

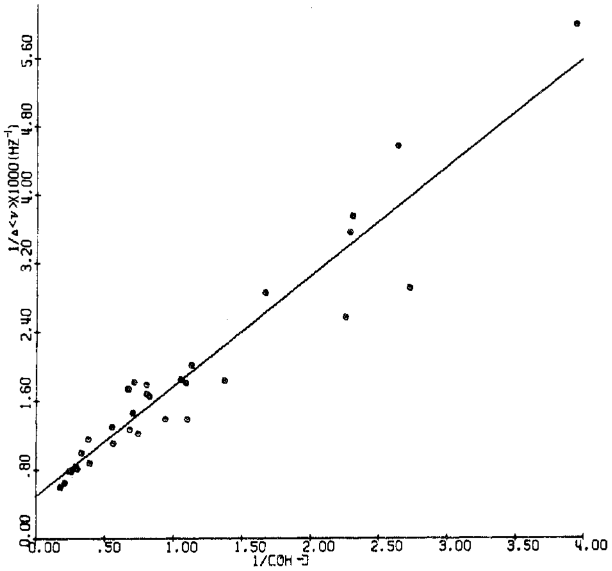

Figure 1. Least-squares fit to eq 1 of the inverse observed frequency shift as a function of inverse molar hydroxide ion concentration, corrected for the amount consumed by neutralization.

Results and Discussion

The variation of ^{59}Co frequency with OH^- concentration is most conveniently analyzed by the double-reciprocal plot[5] shown in Figure 1. This linear plot follows from eq 1, which

$$(\Delta\langle\nu\rangle)^{-1} = (\Delta\nu_0)^{-1} + (K_n\Delta\nu_0(OH^-))^{-1} \qquad (1)$$

is valid for fast exchange between $Co(en)_3{}^{3+}$ and its conjugate base and for ideal solution behavior. In eq 1, $\Delta\langle\nu\rangle$ and $\Delta\nu_0$ are, respectively, the observed frequency shift and the frequency shift of the conjugate base, both taken with respect to the frequency of $Co(en)_3{}^{3+}$ in neutral solution; K_n is the neutralization constant defined above. An iterative least-squares procedure, which corrected the nominal OH^- concentration for the amount consumed by the neutralization, was used to fit the data points to eq 1. This least-squares treatment gave $K_n = 0.39 \pm 0.05\ M^{-1}$ and $\Delta\nu_0 = -(2.0 \pm 0.3) \times 10^3$ Hz.[6] The value for K_n is in agreement with that determined by Navon, *et al.*,[3] from proton nmr and optical measurements.

Two other explanations for the large ^{59}Co nmr shifts produced by increased OH^- concentration could, in principle, be offered: (1) base-catalyzed substitution of a coordinated nitrogen by OH^- or by H_2O; (2) ion-pair formation between OH^- and $Co(en)_3{}^{3+}$. The first explanation is precluded on the following grounds. The ^{59}Co frequencies changed immediately to their equilibrium values on addition of appropriate amounts of strong acid; however, it is known that the hydrolysis of $Co(en)_3{}^{3+}$ is slow ($k_2 = 7 \times 10^{-4}\ M^{-1}$ at 70°).[7] Ion-pair formation as a source of the ^{59}Co frequency shifts is unlikely, since the frequencies of $Co(en)_3{}^{3+}$ in 1.7 *M* NaCl solution and in neutral solution without added salt differed by less than 10 Hz.

The value of $\Delta\nu_0$, the frequency shift for the $Co(en)_3{}^{3+}$

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(4) L. E. Erickson, *J. Amer. Chem. Soc.*, 91, 6284 (1969).

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(6) This negative shift corresponds to the frequency for the conjugate base being less than that for $Co(en)_3{}^{3+}$ or to an *upfield* shift for the conjugate base.

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