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The *Cis*-Influence of Hydroporphyrin Macrocycles on the Axial Ligation Equilibria of Cobalt(II) and Zinc(II) Porphyrin Complexes

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Abstract: Stability constants and thermodynamic data are reported for coordination of piperidine, pyridine, and substituted pyridines to the cobalt(II) and zinc(II) complexes of octaethylporphyrin (OEP), *t*-octaethylchlorin (OEC) and the *tct*- and *ttt*-isomers of octaethylisobacteriochlorin (OEiBC) in toluene, cyclohexane, and chloroform solution at 25.0 °C. Under the conditions of the study, only 1:1 complexes are formed. With the exception of the case of 2-substituted pyridines, the stability constants, log *K*, correlate roughly with the base strength of the nitrogenous ligand but correlate closely with the log *K* for coordination of the base to Zn(OEP). A *cis*-influence of the macrocycle saturation level on the stability constants is observed. Stability constants for coordination of a given ligand to OEiBC complexes are typically 4 times greater than those for coordination to OEP complexes and 1.8 times greater than those for coordination to OEC complexes. The stability constants of both Co- and Zn(OEiBC) complexes were unaffected by the stereochemistry (*tct* vs *ttt*) of the ethyl substituents, unlike the case for nickel. ΔH and ΔS vary between -8 and -12 kcal/mol and -12 and -24 cal K^{-1} mol^{-1}, respectively, and correlate linearly with each other. They do not correlate directly with either log *K* or the saturation level of the macrocycle. For most bases, log *K* is greater for the zinc complexes than for the cobalt complexes. However, for 3,5-dichloropyridine, log *K* is greater for the cobalt complexes. The acid dissociation constants for the free-base compounds H_2(OEP), H_2(OEC), and H_2(OEiBC) were measured in THF/*n*-butanol solution. All three compounds ionize to dianions by simultaneous loss of two protons. OEP and OEiBC have $pK_a = 15.9$. OEC is a weaker acid with $pK_a = 16.6$. The increase in log *K* with macrocycle saturation level does not correlate with the acidity of the respective free bases, but the latter is not necessarily representative of the σ-donor strength of the macrocycle dianion. Solvation and π-effects are not responsible for either the dependence of log *K* on macrocycle saturation level or the reversal for weak bases of the relative Lewis acid strengths of the cobalt and zinc complexes. The latter is attributed to a relief of strain due to core expansion that occurs upon ligand coordination to cobalt complexes. Cobalt complexes are more sensitive than zinc complexes to steric interactions with the ortho-substituents of a pyridine ligand owing to the much smaller out-of-plane displacement of the cobalt atom compared to the zinc atom in five-coordinate complexes.

Metal complexes of hydroporphyrins and other modified porphyrins play central roles as prosthetic groups in the biochemical pathways of the carbon, nitrogen, and sulfur cycles and in the metabolism of many anaerobes. Examples of this type of complex include siroheme, the iron–isobacteriochlorin prosthetic group of assimilatory (biosynthetic) nitrite and sulfite reductases;[1,2] chlorophylls, the magnesium–chlorin and –bacteriochlorin pigments of photosynthesis;[3] heme-d_1, the iron–dioxoporphyrin prosthetic group of dissimilatory (metabolic) nitrite reductases;[4] F430, a nickel–hydrocorphinoid prosthetic group involved in methanogenesis;[5] and coenzyme B_{12}, the cobalt–corrinoid prosthetic group of several methyl-transfer enzymes and the isomerases diol dehydrase, ethanolamine ammonia lyase, and methylmalonyl-CoA mutase.[6] The absence of enzymes that contain porphyrin prosthetic groups and are competent to catalyze these processes is conspicuous. One could wonder whether modified tetrapyrrole prosthetic groups are specifically required. Thus, there is considerable interest in delineating the effects of changes in the structure and saturation level of a tetrapyrrole macrocycle on the chemistry of its complexes and in particular on the chemistry of a coordinated metal ion. Significant differences could suggest properties intrinsic to modified tetrapyrrole complexes that make them better suited to serve as prosthetic groups in specific enzymatic reactions than the corresponding complexes of porphyrins.

Several chemical differences between hydroporphyrins and porphyrins have been noted to date. Hydroporphyrins have intrinsically larger core sizes and exhibit both a greater tendency to adopt nonplanar conformations and greater displacements from planarity than the corresponding porphyrin complexes.[7] Standard reduction potentials of ligand-centered redox processes generally decrease with increasing macrocycle saturation.[8-11] Thus, hy-

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droporphyrin macrocycles are easier to oxidize and more difficult to reduce than porphyrins. This affects metal-centered redox processes too. The resistance of the macrocycle to reduction is one reason that hydroporphyrin ligands can stabilize metal ions in less common, low-valent oxidation states like Ni(I) and Cu(I), which are inaccessible in porphyrins.[9] The shift in macrocycle potentials causes the oxidation of the hydroporphyrin ligand to become competitive with oxidation of the coordinated metal for some systems (see below).

Despite the importance of axial ligation to the function of many metalloproteins, there are few reports that permit comparison of the affinities of porphyrin and hydroporphyrin complexes for axial ligands. The comparisons that can be made suggest that the macrocycle affects the stability constant for coordination of axial ligands, which by necessity occupy coordination sites *cis* to the macrocycle. In other words, the macrocycle exerts a *cis*-influence[12] on these equilibria. Stability constants for binding of amine, pyridine, or imidazole ligands to Mg,[13] Ni,[14,15] and Zn[13,15,16] complexes generally increase with increasing saturation of the macrocycle, i.e. porphyrin < chlorin < isobacteriochlorin. The affinity of Fe(II) complexes for imidazole,[17] CO,[8b,17,18] and THF[19] ligands also increases with saturation of the macrocycle. In contrast, stability constants for coordination of sterically encumbered pyrrolidine or imidazole bases to complexes in the Ni or Zn(TPP)[20] series, respectively, show little dependence on the saturation level of the macrocycle.[21] The largest reported increase in stability constants is by a factor of more than 50 for coordination of THF by Fe(II) complexes, a reaction that is accompanied by a spin-state change from intermediate ($S = 1$) to high ($S = 2$) spin. Stability constants for conversion of low-spin four-coordinate Ni(II) complexes to high-spin six-coordinate complexes also increase substantially (a factor of 30 for piperidine) across the series porphyrin to isobacteriochlorin.[14,15] The increases were attributed to the intrinsically larger core size of the hydroporphyrins, which permits them to better accommodate the longer M–N bond lengths of the high-spin complexes.[19] In general, the increase in stability constants is modest in the absence of a spin-state change or if the change results in a low-spin complex.

The increase in stability constants with tetrapyrrole saturation is large enough to affect chemical reactivity when combined with other effects. The binding of CO stabilizes Fe(II) in $Fe^{II}(iBC)(py)(CO)$[20] sufficiently that oxidation affords $Fe^{II}(iBC^{\bullet+})(py)(CO)$ rather than an $Fe^{III}(iBC)$ complex and free CO.[10c] Indeed, addition of CO, alkyl isocyanides, or PF_3 to $Fe^{III}(iBC)X$ complexes induces an internal electron transfer from the macrocycle to the metal to afford $Fe^{II}(iBC^{\bullet+})(L)X$.[22] Analogous reactions do not occur with ligands like halide anions, pyridine, or imidazole or for porphyrin or chlorin complexes, whose macrocycles are more difficult to oxidize. Co(II) and Fe(II) isobacteriochlorin complexes appear to have higher affinities for NO.[23] In contrast to the case of the corresponding complexes of porphyrins or chlorins, the NO ligand is retained when Co(iBC)NO is reduced or Fe(iBC)NO oxidized. Given that NO is a potential intermediate in nitrite reduction, these observations suggest that the macrocycle could be important in controlling its residence time at the active site of nitrite reductases.[23] Interestingly, the active site of several nitrite and sulfite reductases consists of an Fe_4S_4 cluster axially coordinated to siroheme through a cysteine sulfur or other bridging group.[24] Macrocycle-induced changes in the affinity for coordination of the Fe_4S_4 cluster could affect changes in the properties and reactivity of the active site.

We are currently investigating the ligand-binding equilibria of metallotetrapyrroles in an effort to gain a more detailed and quantitative understanding of the effects of the macrocycle saturation level and the stereochemistry of peripheral substituents on these equilibria. In this paper, we report the stability constants for coordination of piperidine and a series of pyridine bases to the Co(II) and Zn(II) complexes of OEP, *t*-OEC, and *tct*- and *ttt*-OEiBC. Tetrapyrrole complexes of these metals have simple, well-defined equilibria between four- and five-coordinate forms which are not complicated by axial ligand induced oxidation- or spin-state changes. The solvent and temperature dependences of these equilibria are described. We also present the results of a study of the acidity of the free-base macrocycles. The data establish that stability constants increase with progressive saturation of the macrocycle. For most bases, the stability constants are greater for Zn(II) complexes than for Co(II) complexes. However, this order is reversed for 3,5-dichloropyridine. The discussion examines several factors which could be responsible for the positive *cis*-influence of the saturation level on the stability constants and for the reversal of the relative Lewis acid strengths of the cobalt and zinc complexes. These include macrocycle acidity (which is frequencly viewed as a measure of the macrocycle's σ-donor strength), π-interactions, solvation, steric effects, and changes in strain energy that result from core-size changes.

Experimental Section

Materials. The free bases $H_2(OEP)$,[25] $H_2(OEC)$,[8a,26] and $H_2(OEiBC)$[8a,26] and their respective Co(II)[27,28] and Zn(II)[8a,28,29] complexes were prepared by literature methods. The porphyrin compounds were purified by recrystallization from toluene. The metallohydroporphyrin complexes were purified by chromatography on silica gel. Elution was with benzene/hexane mixtures. The *tct*- and *ttt*-stereoisomers of $H_2(OEiBC)$ were separated by chromatography on MgO.[30] The identity and purity of each isomer was established by examining the meso proton peaks in the ^1H NMR spectrum.[30,31] Isomeric purity was typically >95%. The Co(II) complex of each separated isomer and the Zn(II) complex

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[12] We adopt the usage here that differentiates an *influence*, which refers to changes in ground-state properties like structure and thermodynamic stability, from an *effect*, which refers to changes in kinetic phenomena.

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[20] Abbreviations: P, any tetrapyrrole dianion; iBC, any isobacteriochlorin dianion; OEP, 2,3,7,8,12,13,17,18-octaethylporphyrin dianion; OEC, *trans*-2,3-dihydro-2,3,7,8,12,13,17,18-octaethylporphyrin (chlorin) dianion; OEiBC, 2,3,7,8-tetrahydro-2,3,7,8,12,13,17,18-octaethylporphyrin (isobacteriochlorin) dianion (mixture of *tct*- and *ttt*-diasterometers unless otherwise noted); TPP, 5,10,15,20-tetraphenylporphyrin dianion; TPC, 2,3-dihydro-5,10,15,20-tetraphenylporphyrin (chlorin) dianion; TPiBC, 2,3,7,8-tetrahydro-5,10,15,20-tetraphenylporphyrin (isobacteriochlorin) dianion; 4-DMAP, 4-(dimethylamino)pyridine; 2,4-Lut, 2,4-lutidine; 2-Pic, 2-picoline; 4-Pic, 4-picoline; Pip, piperidine; Py, pyridine; 3,5-Cl_2Py, 3,5-dichloropyridine; 4-CNPy, 4-cyanopyridine.

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of the *ttt*-isomer were prepared by the same methods as used for the mixture. The meso proton resonances of *ttt*-Zn(OEiBC) were observed at 8.99 (1 H, C-15), 7.85 (2 H, C-10,20), and 7.00 (1 H, C-5) ppm in toluene-d_8.

All solvents and bases were reagent grade or better. Toluene was distilled from sodium. Chloroform was distilled from phosphorus pentoxide. Cyclohexane was distilled from calcium hydride. Pyridine, 2-picoline, 4-picoline, 2,4-lutidine, and piperidine were distilled from barium oxide. 3,5-Dichloropyridine and potassium *tert*-butoxide were sublimed. 4-(Dimethylamino)pyridine (DMAP) and 4-cyanopyridine were used as received.

Physical Measurements. All solutions were prepared and measurements were carried out anaerobically owing to both the oxygen sensitivity of the majority of the compounds and the elevated temperatures during certain measurements. Solutions in toluene and cyclohexane were prepared using volumetric glassware inside a Vacuum/Atmospheres Co. drybox and were sealed in tightly stoppered quartz cuvettes. Solutions in chloroform were prepared using Schlenk glassware and syringe techniques, in order to prevent the possibility of damage to the drybox catalyst.

Absorption spectra were recorded on a Perkin-Elmer Lambda 6 UV/vis spectrophotometer. The temperature was controlled to ±0.1 °C with a Haake F3-CH circulating bath. The bath water was circulated in series through a water-jacketed single-position cuvette holder in the spectrophotometer cavity and an insulated aluminum block, which was used to store and pre-equilibrate the temperature of cuvettes prior to recording spectra. The sample temperature was measured at the cuvette holder.

Proton magnetic resonance spectra were determined on a JEOL GSX-270 MHz NMR spectrometer. Samples for variable-temperature studies of the spectra of the paramagnetic cobalt porphyrin and hydroporphyrin complexes were prepared on a vacuum line by distillation of the $CDCl_3$ solvent into an NMR tube containing solid complex. Tubes were sealed-off under vacuum. Samples for investigations of the association of paramagnetic Co(OEP) with diamagnetic Ni- or Zn(OEP) were placed in concentric tubes of the type used in Evans' method susceptibility measurements. The outer tube contained a solution of the diamagnetic complex in $CDCl_3$. A sample of Co(OEP) was dissolved in another aliquot of this solution and placed in the inner tube.

Equilibrium Constants for Coordination of Axial Ligands. Stability constants for ligand binding to Co(II) and Zn(II) porphyrin and hydroporphyrin complexes were determined spectrophotometrically. The program SQUAD was used to calculate stability constants and their associated errors.[32] SQUAD calculates the best values of stability constants for a proposed equilibrium model by using a nonlinear least-squares approach to simultaneously fit absorption data at multiple wavelengths for solutions of varying ligand concentration.

Equilibrium measurements in toluene and cyclohexane were conducted with multiple solutions of the metal complex and ligand rather than by titration of a single solution of the metal complex with ligand. This was done to minimize both concentration errors and the possible introduction of oxygen and for greater convenience in variable-temperature experiments. In a typical experiment, a 10^{-4} M solution of the metal complex of interest was prepared in either toluene or cyclohexane. Dilution of 10.00 mL of this solution to 100.0 mL afforded stock solution A, which in a 1-cm cuvette had a maximum absorbance in the visible region of between 0.5 and 1.5. One cuvette was filled with solution A. A second solution, B, was prepared by dissolving a weighed sample of the ligand in 1.00 mL of the 10^{-4} M solution of the metal complex and then diluting to a final volume of 10.00 mL. Solutions of varying ligand concentration but constant metal complex concentration were prepared by serial dilution of solution B with stock solution A and were sealed in cuvettes. Ligand concentrations ranged between 10^{-5} and 1.0 M as needed to saturate the equilibrium. Typically, five ligand-containing solutions were used in variable-temperature experiments and seven were used in room-temperature experiments. Full UV/vis spectra were recorded, and data files were saved on disk for these solutions and for solution A. Overlay of spectra showed isosbestic or near isosbestic behavior. Data from between 10 and 25 wavelengths that spanned the Soret or visible regions were read from the files and formatted as a SQUAD input file by an OBEY program that we wrote. The input file was edited to include complex and ligand concentration values prior to running SQUAD.[33]

Data were fitted to two stoichiometric models, one for binding a single ligand (eq 1) and the other for sequential binding of two ligands (eqs 1 and 2). Consistent with other workers results for porphyrin complexes,

$$M(P) + L = M(P)L \tag{1}$$

$$M(P)L + L = M(P)L_2 \tag{2}$$

our results establish that the first model is appropriate for all the complexes and ligands considered here. Calculations for the second model either failed to converge or gave stability constants for eq 2, K_2, that were small but had large associated errors. The latter shows that the second equilibrium was not sufficiently saturated at the maximum ligand concentration employed for K_2 to be well determined.[34] The values of K_1 calculated with Soret and visible region data agreed within error. Most experiments were repeated several times with independently prepared solutions.

The ΔH and ΔS values associated with coordination of selected ligands were determined by weighted least-squares analysis of plots of log K vs $1/T$. Typically, stability constants were determined at six temperatures between 15 and 65 °C. Concentrations of complex and ligand were corrected for the thermal expansion (density changes) of the toluene solvent.[35] The 25 °C measurement was repeated at the end of the experiment to check for oxidation or decomposition of the complexes. The data were considered unreliable and were discarded if the two calculated values of the stability constant at 25 °C did not agree or if the errors in the stability constant increased substantially with the elapsed time of the individual measurement.

SQUAD permits molar absorptivities to be entered as fixed constants. Because the spectra of the four- and five-coordinate complexes were temperature dependent, density corrections notwithstanding, we found it more convenient to allow the program to calculate absorptivities. This provided an additional check on the spectral fits for each experiment. The calculated molar absorptivities for a given complex agreed within error between different experiments employing the complex.

We investigated the effect of the metal complex concentration on the equilibrium of eq 1 for Co(OEP) and pyridine. Beer's law was obeyed when spectra of solutions of Co(OEP) ranging in concentration from 5 × 10^{-6} to 5 × 10^{-4} M were recorded using optical cells of path lengths ranging from 10.00 to 0.100 cm. Furthermore, at fixed pyridine concentration, the Co(OEP)(py)/Co(OEP) ratio was independent of the total Co(OEP) concentration over the same concentration range.

Chloroform solutions used in measurements of stability constants were prepared using Schlenk glassware and syringe techniques. Owing to the lesser accuracy of this method, competition experiments were used to determine the differences between stability constants. Weighed samples of solid Co(P1) and Co(P2), where P1 and P2 represent different macrocycles, were placed in a two-necked Schlenk flask. One neck was sealed with a septum. Chloroform was distilled into the flask through the second neck, the flask was removed from the distillation apparatus, and a quartz optical cell attached to a standard taper joint was fitted to the flask. The contents of the flask were freeze–thaw-degassed and placed under nitrogen. The flask was inverted to fill the optical cell, and the spectrum was recorded. The solution was titrated by addition of aliquots of pyridine by syringe through the septum.

Acid Strengths of Free-Base Porphyrins and Hydroporphyrins. The equilibrium constants for acid dissociation of free-base porphyrin and hydroporphyrin compounds were determined from the dependence of the UV/vis spectra on the 'pH' of an alcohol/alkoxide-buffered THF solution. Solutions were prepared in a manner analogous to that used for the solutions for ligand-binding studies. Stock solution A was 2 × 10^{-5} M in the free-base macrocycle in a solvent mixture of *n*-butanol in THF (2.00 g of *n*-butanol per 100.0 mL of solution or 0.270 M). Stock solution B was 0.05 M in potassium *tert*-butoxide and 2 × 10^{-5} M in free-base macrocycle in the same mixture of *n*-butanol in THF. Solutions of varying alkoxide/alcohol ratio but constant macrocycle concentration were prepared by serial dilution of solution B with stock solution A.

The stoichiometries of the acid dissociation reactions were determined spectrophotometrically by titration of the free-base macrocycles with potassium *tert*-butoxide in THF. THF was vacuum-transferred into a vessel that contained a weighed sample of the alkoxide, the mixture was

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stirred, and a clear solution was obtained by filtration through a Schlenk frit. The solution was standardized with 0.1000 N HCl. A solution of a weighed sample of the macrocycle was prepared by vacuum transfer of a known quantity of THF into a 250-mL Schlenk vessel equipped with an optical cell side arm and a septum port. Aliquots of alkoxide solution were transferred by syringe to the vessel that contained the macrocycle solution.

Competition experiments were performed to confirm the differences in pK_a's between pairs of free-base macrocycles. The procedure was similar to that of the titration used to determine the stoichiometry of the acid dissociation reactions. A solution of $H_2(P1)$ and $H_2(P2)$ in *n*-butanol/THF was prepared in the 250-mL Schlenk vessel by vacuum transfer of the solvent onto weighed samples of the two free-base macrocycles and was titrated with a standardized solution of potassium *tert*-butoxide in THF. The ratios of protonated to deprotonated species for each of the macrocycles were determined from the UV/vis spectra.

Results

$M(P) + L \rightarrow M(P)L, M = Co(II), Zn(II)$. Addition of pyridine to a solution of Co(OEP) in toluene results in substantial broadening and a roughly 25–35% decrease in the intensities of the α peak (550 nm) and Soret peak (395 nm). The α peak shifts to 545 nm, but the Soret does not shift. Similar changes occur upon ligand coordination to Co(II) protoporphyrin IX dimethyl ester[36] or to Co(II) tetraarylporphyrins,[37,38] although the α bands of the latter red shift. The Soret bands of the hydroporphyrin complexes Co(OEC) and Co(OEiBC) remain roughly the same intensities upon pyridine coordination but red shift by about 5 nm. The α bands decrease in intensity and shift from 613 to 609 nm for Co(OEC) and from 589 to 592 nm for Co(OEiBC). The Soret and visible bands of Zn(OEP), -(OEC), and -(OEiBC) red shift by 5–15 nm upon pyridine coordination. Similar changes were observed for Zn(TPP)[13,39] and Zn(TPC).[13] In all cases investigated here, piperidine or substituted pyridines cause essentially identical spectral changes as pyridine.

The stability constants for coordination of piperidine or substituted pyridines by the cobalt(II) complexes of OEP, OEC, and OEiBC (eq 1) are presented in Table I. Formation of six-coordinate bis-ligated cobalt porphyrin complexes (eq 2) has been reported at high concentrations of strongly coordinating ligands like piperidine (for which K_2 was 0.2 M^{-1} at 25 °C),[36] in EPR samples at −196 °C,[43] and as a consequence of crystallization.[44] We did not observe any evidence of conversion to six-coordinate complexes under the conditions of our investigation, even for the hydroporphyrin complexes Co(OEC) and Co(OEiBC), which coordinate ligands more strongly than Co(OEP). The stability constants for reaction of the same series of bases with the zinc(II) complexes of OEP, OEC, OEiBC, and TPP are reported in Table II.

Table I. Equilibrium Constants for Coordination of Bases by Co(II) Complexes[a]

		log K[b]			
base[c]	pK_a[d]	Co(OEP)	*t*-Co(OEC)	*tct*-Co(OEiBC)[e]	*ttt*-Co(OEiBC)[e]
			Toluene		
3,5-Cl_2Py	0.67[f]	2.457(23)	2.638(19)	2.983(23)	3.037(26)
4-CNPy	1.90[g]	2.734(24)	3.079(46)	3.288(18)	
Py	5.22	2.691(3)	2.998(27)	3.272(35)	3.277(29)
2-Pic	5.97	0.289(26)	0.702(30)	1.049(25)[h]	
4-Pic	6.02	2.870(22)	3.280(24)	3.482(45)	3.461(20)
2,4-Lut	6.63	0.841(24)	1.097(17)	1.409(29)[h]	
4-DMAP	9.71	3.309(13)	3.667(35)	4.132(19)	3.859(28)
Pip	11.12	3.211(37)	3.500(41)	3.773(47)[h]	
			Cyclohexane		
Py	5.22	3.014(62)	3.306(27)	3.694(33)	
			Chloroform[i]		
Py	5.22	1.57	1.91	2.39[h]	

[a] At 25.0 ± 0.1 °C. [b] Numbers in parentheses are estimated standard deviations in the least significant digit. [c] See ref 20 for abbreviations. [d] Aqueous for BH^+. Values from ref 40, unless otherwise noted. [e] Isomeric purity greater than 95%. [f] Reference 41. [g] Reference 42. [h] Result for a mixture of *ttt*- and *tct*-isomers. [i] Solutions prepared by syringe techniques. esd's are probably greater than 0.06, but differences between complexes known to higher precision. See Experimental Section.

Table II. Equilibrium Constants for Coordination of Bases by Zn(II) Complexes[a]

	log K[b]			
base[c]	Zn(TPP)	Zn(OEP)	*t*-Zn(OEC)	*ttt*-Zn(OEiBC)[d]
3,5-Cl_2Py	2.264(35)	2.101(23)	2.399(54)	2.857(54)
4-CNPy	2.918(3)[e]	3.012(3)	3.234(16)	3.554(17)
Py	*f*	3.366(4)	3.748(19)	4.125(12)
2-Pic		1.841(10)		
4-Pic	3.918(4)[g]	3.669(12)	4.039(16)	4.332(48)
2,4-Lut		2.250(25)		
4-DMAP		4.656(10)	4.955(10)	5.85(15)
Pip		4.551(7)		

[a] At 25.0 ± 0.1 °C in toluene solution. [b] Numbers in parentheses are estimated standard deviations in the least significant digit. [c] See ref 20 for abbreviations. [d] Isomeric purity greater than 95%. [e–g] Literature values (at 25 °C in benzene unless otherwise noted): (e) 2.9 ± 0.1, ref 39; 2.8, ref 45. (f) 3.79 ± 0.04 (20.3 °C), ref 13; 3.64, ref 16; 3.78 ± 0.02, ref 39; 3.72 ± 0.02, ref 46. (g) 4.02 ± 0.05, ref 39.

Inspection of the data in Table I shows that the stability constants for coordination of bases to the *tct*- and *ttt*-isomers of Co(OEiBC) are identical within error, with the possible exception of the case of DMAP. This contrasts with the situation for Ni(OEiBC), where the *ttt*-isomer has an affinity for binding pyridine or piperidine that is 4–5 times larger than that of the *tct*-isomer.[47] Equivalent stability constants were measured with the separated *ttt*-isomer of Zn(OEiBC) and with the mixture of isomers. Thus, a complete set of experiments was conducted only with *ttt*-Zn(OEiBC).

We examined whether the cobalt(II) complexes aggregate to any significant extent. The broad line widths of the paramagnetic cobalt(II) complexes precluded studies of the concentration dependence of the ^1H NMR spectra. The chemical shifts and line widths of the spectra of Co(OEP) were not significantly altered by changing the solvent from $CDCl_3$ to C_6D_6 or C_7D_8. We used the diamagnetic Ni- and Zn(OEP) complexes to probe for aggregation with Co(OEP). A solution of the diamagnetic complex was placed in both of the concentric NMR tubes used for Evans' method measurement of magnetic susceptibilities. One tube also contained Co(OEP). Only one peak is observed for the meso protons of the Ni(OEP) in both tubes. In contrast, two peaks are resolved for the meso protons of Zn(OEP). The peaks for Zn(OEP) in the same tube as Co(OEP) are at higher field and are considerably broader than those of Zn(OEP) in the absence of Co(OEP). The frequency shift and line width depend on the concentration of both species. The shift is too large to result merely from the change in the bulk susceptibility of the solvent due to the physical presence of Co(OEP). Thus,

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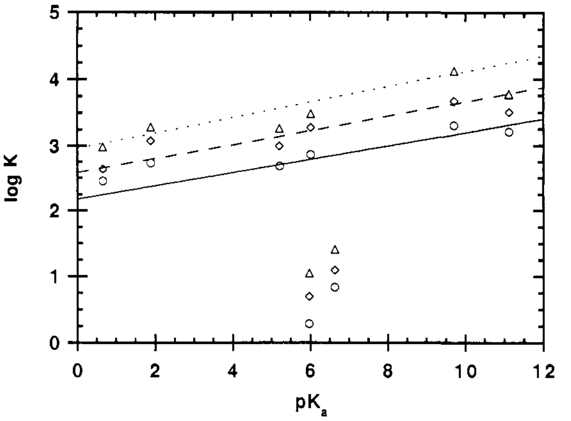

Figure 1. Correlations between log K in toluene and ligand basicity (aqueous pK_a) for Co(OEP), ○; *t*-Co(OEC), ◇; and *tct*-Co(OEiBC), △.

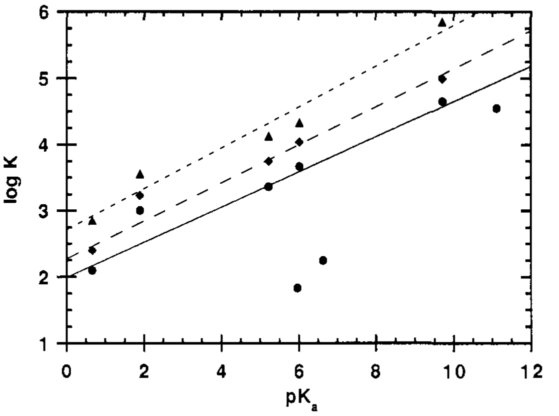

Figure 2. Correlations between log K in toluene and ligand basicity (aqueous pK_a) for Zn(OEP), ●; *t*-Zn(OEC), ◆; and Zn(OEiBC), ▲.

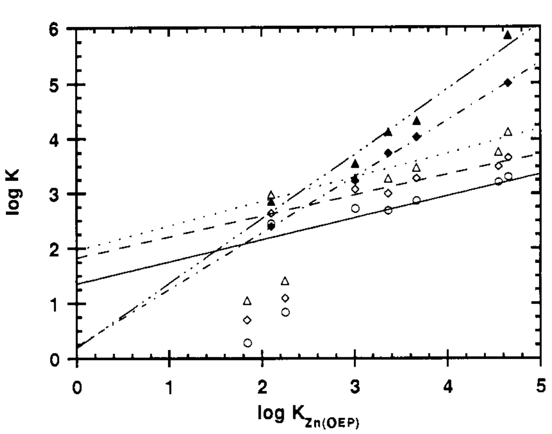

Figure 3. Correlations between log K for coordination of a ligand to a complex and the log $K_{Zn(OEP)}$ for coordination of the ligand to Zn(OEP). Symbols for complexes are defined as in Figures 1 and 2. The line for Zn(OEP), which has slope = 1 and intercept = 0, has been omitted for the sake of clarity.

aggregation between Zn(OEP) and Co(OEP) occurs at the concentration of the NMR experiment. However, the adherence of the spectra of Co(OEP) to Beer's Law at concentrations $\leq 5 \times 10^{-4}$ M and the apparent independence of K_1 from the concentration of Co(OEP) suggest that aggregation is negligible at the concentration of complex used in experiments to measure stability constants (10^{-5} vs 10^{-3} M in NMR experiments).

The effect of the systematic variation of the axial ligand on the equilibrium in eq 1 is commonly examined by means of linear free energy relationships. One such relationship, a plot of log K vs the aqueous pK_a of the ligand's conjugate acid, is presented in Figure 1 for the cobalt complexes and in Figure 2 for the zinc complexes. Figure 3 presents plots of log K for binding a particular base by a metal complex vs the log K for binding the base to Zn(OEP), log $K_{Zn(OEP)}$. Zn(OEP) is expected to be a more suitable reference acid than H^+.

The lines representing the response of the OEP, OEC, and OEiBC equilibria to ligand basicity in Figures 1 and 2 are nearly parallel and are displaced toward larger log K values with progressive saturation of the macrocycle. In other words, the increase in stability constant with saturation of the macrocycle is general for both metals and for a variety of ligands. On a point-by-point basis, the increase in stability constants represents a $\Delta\Delta G$ relative to OEP complexes of 0.25–0.56 kcal/mol for *t*-OEC complexes and of 0.72–1.63 kcal/mol for *tct*-OEiBC complexes. This increase is larger than that observed by others for coordination of pyridine[15] or sterically encumbered imidazoles[20] to the series of complexes Zn(TPP), Zn(TPC), and Zn(TPiBC).

There is appreciable scatter of the experimental data about the lines in Figures 1 and 2. In particular, the log K values for 4-CNPy are greater than expected on the basis of the pK_a of the ligand, and those for the saturated, secondary amine Pip are smaller than expected. The sterically encumbered bases 2-Pic and 2,4-Lut have such small stability constants that they were not included among data used to fit the lines, although their data points are plotted in the figures.

In previous comparisons of log K vs pK_a for coordination of piperidine and substituted pyridines to cobalt and zinc porphyrins, the scatter of data about the line appeared small.[36–39,45] Indeed, in the case of Zn(TPP), the log K values for 4-CNPy and Pip were colinear with those of other non-ortho-substituted pyridines.[39] The disparity between these observations and both our results and reports by others that the stability constant for coordination of 4-CNPy to several metalloporphyrins is anomalously large[38,48,49] led us to reinvestigate ligand binding to Zn(TPP). The stability constants that we determined for 4-CNPy and 4-Pic (Table II) are in good agreement with the values reported by Kirksey et al.[39] However, the stability constant for 3,5-Cl_2Py, which was not measured in prior investigations, is substantially smaller than would have been expected on the basis of the published log K vs pK_a correlation. Thus, the scatter of data for Zn(TPP) is larger than had been appreciated. The same is true for correlations involving Co(TPP)[37] and Co((*p*-CH_3O-)TPP).[38] Appreciable scatter is noted when the data are replotted with the correct pK_a value for 3,5-Cl_2Py. The data point for Pip lies below the line for both cobalt porphyrins.

The scatter of the data in log K vs pK_a plots reflects that H^+ in aqueous solution is a poor reference acid for transition-metal porphyrin complexes in nonaqueous solutions. It also illustrates the fact that a two-parameter model (i.e. one each to measure the strength of the acid and of the base) is insufficient to characterize Lewis acid–base interactions. Pearson's principle of hard and soft acids and bases[50] and the four-parameter (E_A, C_A, E_B, and C_B) model in the Drago-Wayland equation[51] were developed in response to the latter point. In our case, the failure of a two-parameter model also reflects the contribution of factors other than those normally associated with acid–base chemistry to the energetics of the reactions; see below.

Figure 3 differs from Figures 1 and 2 in several important respects. The distinct sets of nearly parallel lines, which are displaced to larger log K with progressive saturation of the macrocycle, are retained for the complexes of each metal. Interestingly, though, the lines for the zinc and cobalt complexes

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Table III. Data for Lines in Figure 3

complex	slope	intercept	correlation coefficient
Co(OEP)	0.400(8)[a]	1.355(29)	0.977
t-Co(OEC)	0.382(12)	1.828(40)	0.986
tct-Co(OEiBC)	0.448(11)	1.962(38)	0.973
t-Zn(OEC)	1.029(36)	0.224(128)	0.998
Zn(OEiBC)	1.176(114)	0.191(393)	0.986

[a] Number in parentheses is error in quantity.

Table IV. Thermodynamic Data for Coordination of Bases by Co(II) Complexes[a]

complex	3,5-Cl$_2$Py	pyridine	DMAP
	$-\Delta H$ (kcal/mol)[b]		
Co(OEP)	7.45 (0.50)	9.66 (0.21)	10.32 (0.09)
t-Co(OEC)	8.16 (0.26)	10.20 (0.23)	12.04 (0.18)
tct-Co(OEiBC)[c]	8.95 (0.35)	8.17 (0.10)	10.40 (0.50)
	$-\Delta S$ (cal K^{-1} mol^{-1})		
Co(OEP)	13.7 (1.6)	20.2 (0.7)	19.4 (0.6)
t-Co(OEC)	15.3 (0.8)	20.5 (0.8)	23.6 (0.6)
tct-Co(OEiBC)[c]	16.1 (1.1)	12.3 (0.6)	17.0 (1.5)

[a] Measured in toluene solution over the range 15–65 °C. [b] Numbers in parentheses are errors of fit. [c] Isomeric purity greater than 95%.

cross at small log $K_{Zn(OEP)}$. The cobalt complexes are stronger Lewis acids than the zinc complexes toward the weakest bases, but the opposite situation is true for the strongest bases! The scatter of data about the five lines in Figure 3 is much less than that in Figures 1 and 2. Strikingly, the data points for 4-CNPy and Pip now lie on or near the lines. This strongly suggests that the deviations noted for these bases in Figures 1 and 2 do not result from any unusual effects in coordination of the base to the metalloporphyrin complexes but rather result from some systematic differences in how these bases interact with H$^+$ and the metal complexes. It should be noted that the data points for 2-substituted pyridines still fall substantially below the lines for the cobalt complexes.

The slope and intercept that characterize each line in Figure 3 are given in Table III. The slope represents the sensitivity of ΔG for ligand binding to the basicity of the axial ligand, which is expressed here with respect to Zn(OEP). For the complexes of interest, the slope depends strongly on the identity of the metal but is essentially independent of the identity of the macrocycle. It can be understood to be the acidity of the metal in the specific environment of the coordination complex. Consistent with the expectation that Zn(II) is a stronger Lewis acid than Co(II), the slopes are substantially greater for the zinc complexes than for the cobalt complexes. The intercepts in Figure 3 represent the ΔG for coordination of a hypothetical ligand which has $\Delta G = 0$ for coordination to Zn(OEP) when all reactants and products are at unit activity. The intercepts depend strongly on the identity of both the metal and the macrocycle and include contributions from the difference in solvation energies of the four- and five-coordinate complexes. Interestingly, it is seen that a substantial portion of the total ΔG for ligand binding to the cobalt complexes results from the macrocycle-dependent intercept term rather than from the acidity (slope) of the complex.

Table IV gives enthalpy and entropy parameters derived from van't Hoff plots of log K vs $1/T$. A plot for the *tct*-Co(OEiBC) plus pyridine equilibrium, which is typical, is shown in Figure 4. The substantial, negative ΔH and ΔS values observed are consistent with the values reported for other cobalt porphyrins.[36,37,52] With the exception of the case of the OEiBC complexes, ΔH and ΔS correlate with the pK_a of the ligand and the saturation level of the macrocycle. ΔH varies linearly with ΔS (or equivalently ΔG varies linearly with ΔH), giving isoequilibrium temperatures of 510 ± 15 K for both OEP and OEC and of 602 ± 30 K for OEiBC.[53]

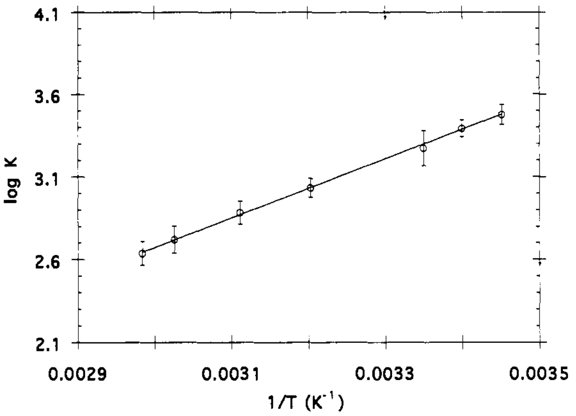

Figure 4. Plot of log K vs T^{-1} for coordination of pyridine to *tct*-Co(OEiBC). Error bars represent 3 standard deviations.

Comparison of the Acid Strengths of Porphyrins and Hydroporphyrins. Porphyrin and hydroporphyrin macrocycles are amphoteric and can exist in the five states of protonation that are related by the equilibria in eqs 3–6 and the respective acid

$$H(P)^- = P^{2-} + H^+ \qquad (3)$$

$$H_2(P) = H(P)^- + H^+ \qquad (4)$$

$$H_3(P)^+ = H_2(P) + H^+ \qquad (5)$$

$$H_4(P)^{2+} = H_3(P)^+ + H^+ \qquad (6)$$

dissociation constants K_{a1} through K_{a4}. The vast majority of studies of porphyrin and hydroporphyrin acid–base properties have been confined to protonation reactions, eqs 5 and 6.[54] The basicity of the macrocycle in these reactions is frequently assumed to be indicative of the σ-donor strength of the macrocycle. Deprotonation reactions, eqs 3 and 4, are obligate steps in the formation of metal complexes from free-base macrocycles. As such, the pK_a's for eqs 3 and 4 might provide a more accurate gauge of the donor ability of the macrocycle toward a coordinated metal ion than the pK_a's for eqs 5 and 6. We decided to measure and compare the pK_a's for eqs 3 and 4 of H$_2$(OEP), H$_2$(OEC), and H$_2$(OEiBC).

Bases that are capable of deprotonating a free-base porphyrin macrocycle are sufficiently strong that they are leveled by water to the weaker base OH$^-$. In order to minimize possible complications from trace quantities of water and other acidic compounds, we examined the UV/vis spectra of the porphyrin and hydroporphyrin macrocycles in a series of THF/alcohol/potassium alkoxide buffer solutions which had different 'pHs', i.e. alcohol/alkoxide ratios. The capacity of the buffer was large compared to the amount of macrocycle added. The spectra of the macrocycles changed isosbestically as the pH of the solution was increased. Separate titration experiments with standardized solutions of alkoxide established that eqs 3 and 4 occurred simultaneously (i.e. pK_{a1} < pK_{a2}) and that K_2(P) is the product of the titrations. The failure to observe H(P)$^-$ monoanions has been reported by others.[55]

Table V presents the p$K_{a1,2}$ values and UV/vis spectroscopic data for the dipotassium complexes of the macrocycles. The UV/vis spectrum of K$_2$(OEP) compares favorably to that of

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Table V. Acid Dissociation Constants and UV/vis Data for Dipotassium Complexes of Free-Base Compounds

$H_2(P)$	p$K_{a1,2}$[a]	λ_{max}[b] (rel absorb.[c]) of $K_2(P)$[d]
$H_2(OEP)$	15.9	330 (1.54), 406 (2.55), 427 (12.99), 562 (1.00), 572 (0.64 sh[e]), 597 (0.42), 621 (0.33)
$H_2(OEC)$	16.6	358 (0.65 sh), 399.5 (1.65 sh), 416 (2.40), 523 (0.12), 551 (0.16 sh), 572.5 (0.19), 590 (0.20), 618.6 (1.00)
$H_2(OEiBC)$[f]	15.9	382 (1.35), 400 (2.52), 411 (2.29), 501 (0.12), 554 (0.27), 597.5 (1.00)

[a] Measured in THF/*n*-butanol solution relative to pK_a = 18 of *n*-butanol; see ref 58. [b] nm. [c] Absorbance relative to main visible peak. [d] In THF/*n*-butanol solution. [e] Shoulder. [f] Mixture of *tct*- and *ttt*-isomers.

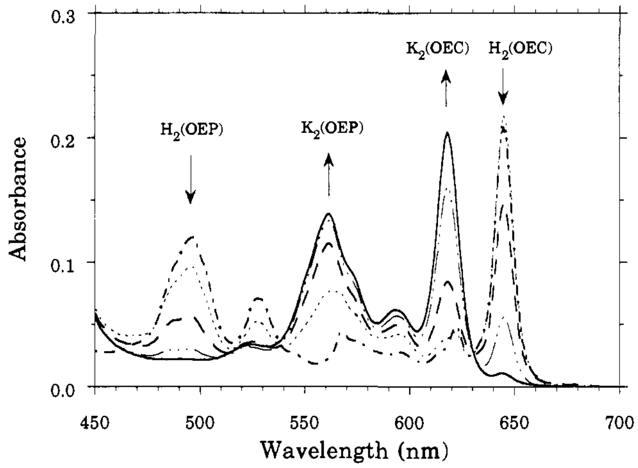

Figure 5. Visible spectral changes during the competitive titration of $H_2(OEP)$ and *t*-$H_2(OEC)$ with potassium *tert*-butoxide in THF/*n*-butanol solution.

$Li_2(OEP)$[56] when allowances are made for the red shift and intensity changes of absorption peaks that occur for other dilithium porphyrins when a heavier alkali metal is substituted.[57] In contrast to the red shift of the main visible bands of OEP and OEiBC upon deprotonation, the corresponding feature of OEC blue shifts. All three compounds have p$K_{a1,2}$ values which are similar to the value of 16 that was reported for etioporphyrin.[58]

Given the similarities of the p$K_{a1,2}$ values of the three macrocycles, we performed competition experiments to confirm their relative differences. Aliquots of alkoxide solution were added to a solution that contained two of the neutral, free-base macrocycles, i.e. P1 and P2. The differences in the p$K_{a1,2}$ values were determined by the ratios of the concentrations of the free-base and dipotassium complexes of each macrocycle (eq 7), which

$$\mathrm{p}K_{a1,2}(2) - \mathrm{p}K_{a1,2}(1) = \log([H_2(P1)][K_2(P2)]/[K_2(P1)][H_2(P2)]) \quad (7)$$

in turn were determined from the UV/vis spectra. Figure 5 shows representative spectra for a competition experiment between $H_2(OEP)$ and $H_2(OEC)$. The greater conversion of $H_2(OEP)$ to $K_2(OEP)$ in the second and third spectra compared to the conversion of $H_2(OEC)$ to $K_2(OEC)$ confirms that $H_2(OEC)$ is a weaker acid than $H_2(OEP)$. A similar experiment established that $H_2(OEP)$ and $H_2(OEiBC)$ have comparable acid strengths.

Discussion

Two major trends were noted in the Results. First, stability constants increase with increasing saturation of the tetrapyrrole macrocycle. Second, the intercepts of the log K vs log $K_{Zn(OEP)}$ plot are substantially larger for the cobalt complexes than for the zinc complexes. An equivalent statement is that weak bases exhibit an unusual, reversed behavior of coordinating more strongly to the cobalt complexes than to the zinc complexes. To explain these trends, we examine the possible influence of such factors as differences in solvation, π-bonding, the σ-donor strength of the macrocycle, and the changes in strain energy of the macrocycle that accompany the structural changes upon coordination of a ligand.

We propose below that changes in the strain energy are responsible for the reversed affinities of weak bases toward zinc and cobalt complexes. The reasons for the increase of stability constants with increasing macrocycle saturation are less clear. Despite their similar pK_a's, the σ-donor strengths of the macrocycles toward a coordinated metal ion might decrease with increasing macrocycle saturation. In addition, changes in the strain energy upon coordination of the ligand could be macrocycle dependent.

Solvation Effects. Solvation energies strongly affect the overall energetics of Lewis acid–base interactions in general and axial ligation equilibria of metallotetrapyrroles in particular. Stability constants for coordination of pyridine to Zn(TPP) vary by almost 2 orders of magnitude in common solvents. The log K drops from 4.40 in cyclohexane[59] to 3.78 in benzene[39] to 2.79 in chloroform.[45] The decrease in this series probably reflects a loss of solute–solvent interactions between the solvent and pyridine base or solvent and 'four-coordinate' metalloporphyrin upon formation of the five-coordinate complex.

Table I includes data for coordination of pyridine by the cobalt complexes of OEP, OEC, and OEiBC in cyclohexane, toluene, and chloroform. The stability constants of each complex follow a similar trend to that observed for Zn(TPP) in the three solvents. Regardless of the complex, the decrease in the log K value is about 0.3 between cyclohexane and toluene and 1.1 between toluene and chloroform. In addition, the differences between the log K values of complexes with different macrocycles do not depend strongly on the solvent. For example, the log K of the OEC complex is roughly 0.3 greater than that of the OEP complex in all solvents. These observations strongly suggest that the net changes in the solvation energies of the porphyrin and hydroporphyrin complexes are quite similar. Thus, the increase in stability constants with macrocycle reduction cannot arise from differences in the solvation of the macrocycles.

Solvation effects are unlikely to be responsible for the suprisingly large ΔG for coordination of weak bases to the cobalt complexes with respect to the zinc complexes (intercepts in Figure 3). The stability constants for pyridine binding to the Zn complexes in toluene (Table II) show the same increases with macrocycle saturation as those for the cobalt complexes. This would be rather fortuitous if there were major differences in the solvation of the zinc and cobalt complexes. There is little reason to expect major differences in solvation, anyway. The four- and five-coordinate zinc complexes are quite similar in size, shape, and charge to the analogous cobalt complexes.

π-Bonding Effects. Backbonding from the filled d-π-orbitals of the metal to the empty π^*-orbitals of an axial ligand has often been invoked to explain deviations of observed stability constants from expected trends. For example, the larger than expected stability constants for coordination of 4-CNPy to cobalt and iron porphyrins were attributed to enhancement of backbonding by the electron-withdrawing 4-cyano group.[38,48a] Additionally, the inability of piperidine to act as a π-acceptor was said to explain the smaller than expected stability constants for coordination of piperidine to cobalt porphyrins.[38] Interactions of the metal d-π-orbitals with the macrocycle LUMO orbitals, which are of the proper symmetry to mix, could serve to modulate the backbonding. This could link the stability constants and macrocycle saturation

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level, because the saturation level of the macrocycle affects the energies of its LUMO.

The data in Tables I and II and its treatment in Figure 3 establish that π-backbonding effects are unimportant here. The log K's of pyridines with electron-withdrawing substituents, pyridines with electron-donating substituents, and piperidine fall on the same line when plotted vs log $K_{\mathrm{Zn(OEP)}}$. In addition, the differences between the log K values of complexes of a particular base with two different macrocycles are essentially the same for cobalt complexes as for zinc complexes. The filled d-π-orbitals of d^{10} zinc(II) porphyrins are at much lower energy than the corresponding orbitals of d^7 cobalt(II) porphyrins.[60] Consequently, the mixing of the metal d-π-orbital and the pyridine LUMO orbital must be quite different for zinc and cobalt. Neither of the above observations would be probable if π-bonding were significant.

Macrocycle σ-Donor Strength. It is generally held that coordination of strong σ-donor ligands to a metal will decrease the affinity of the metal for other σ-donor ligands. If one assumes that the acidity of a macrocycle is controlled by its σ-donor strength, a macrocycle with a larger pK_a for deprotonation (eqs 3 and 4) should have a smaller stability constant for coordination of an axial ligand. The observed dependence of the stability constants on the saturation level of the macrocycle does not conform with these expectations about acidity. The pK_a's of the three free-base compounds are more notable for their similarities than their differences. The stability constants for OEC complexes are larger than those for the corresponding OEP complexes, yet the pK_a of H_2(OEC) is larger than that of H_2(OEP). The stability constants for OEiBC complexes are the largest of the series, yet the pK_a of H_2(OEiBC) is indistinguishable from that of H_2(OEP).

The validity of the assumption that the acidity or basicity of the macrocycle indicates its σ-donor strength toward a coordinated metal ion is suspect. The equilibria in eqs 3 and 4 (and 5 and 6) could be dominated by factors that are irrelevant to the situation where the dianion acts as a σ-donor toward a coordinated transition-metal ion. These factors include specific solvation effects, ion pairing, the ability of the macrocycle to delocalize the buildup of negative charge, and the ability of the macrocycle to accommodate structural changes that minimize charge repulsions or favor interactions with counterions.

Several lines of evidence suggest that interactions of the type mentioned are very important in the protonation and deprotonation reactions of tetrapyrroles. It is remarkable that acid dissociation occurs more readily from the macrocycle monoanion than from the neutral free-base (p$K_{a1} \ll$ pK_{a2}). This situation usually occurs when loss of the first proton induces a major structural or electronic change that decreases the affinity for the second proton. The large variations in the UV/vis spectra of macrocycle dianions with changes in the alkali metal cation show that the dianion has extensive interactions with its counterions.[57] ^{7}Li NMR studies of Li_2(OEP) establish that solvent-separated and contact ion pairs can equilibrate, depending on the nature of the solvent.[56] Solvent effects can be striking. The basicity order H_2(TPP) > H_2(TPC) $\sim$ H_2(TPiBC) > H_2(TPBC) was established, on the basis of the concentration of phosphoric acid required to extract the compounds from benzene.[26] The lesser basicity of H_2(TPC) compared to H_2(TPP) was confirmed by titrations of nitrobenzene solutions of the compounds with $HClO_4$,[61] and titration of DMF solutions with HCl gave the order H_2(TPP) > H_2(TPiBC) > H_2(TPC).[54c] However, for water-soluble compounds derived from tetrakis(*N*-methylpyridiniumyl)porphyrin or tetrakis(4-sulfonatophenyl)porphyrin, the chlorin is more basic than the porphyrin.[54c] Monocations generally are not observed for porphyrins (p$K_{a3} \ll$ pK_{a4}), except in cationic and neutral detergent media, but usually are for hydroporphyrins (p$K_{a3} \gg$ pK_{a4}).[54] The X-ray structures of porphyrin dications show that large deviations from planarity occur to minimize the steric repulsions that would result if the four pyrrolic hydrogen atoms were coplanar and to minimize the electrostatic repulsions of the charged nitrogen atoms.[62]

In summary, the acidity or basicity of a tetrapyrrole is not directly indicative of its σ-donor strength. Thus, the results do not address whether the dependence of the stability constants on the saturation level of the macrocycle originates from differences in σ-donor strength. Evidence for subtle differences in σ-donor strength might be found in the variation of the anisotropy of a paramagnetic metal ion when coordinated to different tetrapyrrole macrocyles.[8b,30,63]

Strain Energy. The structural and conformational changes that occur upon coordination of an axial ligand can result in changes in strain energy. The contribution of the change in strain energy to the energetics of the reaction will be independent of the base strength of the ligand, to the extent that changes in structure do not depend on the identity of the ligand. Thus, strain energy will contribute to the intercepts of the free energy plots (Figures 1–3). We propose that release of strain energy in the tetrapyrrole macrocycle occurs upon coordination of a ligand to the cobalt complexes and is responsible for their larger intercepts compared to the zinc complexes. Changes in strain energy may also contribute to the dependence of the stability constants on the saturation level of the macrocycle.

The gross structural changes that accompany the conversion of four-coordinate M(P) complexes to five-coordinate M(P)L complexes are similar for cobalt and zinc, but the detailed changes differ in several important respects. The cobalt atom in four-coordinate Co(TPP) lies in the plane of the four nitrogen atoms and has average Co–N distances of 1.949(3) Å.[64] In five-coordinate complexes, the average Co–N distance increases to between 1.977 and 2.000 Å and the cobalt atom is displaced 0.14 Å out of the plane of the nitrogens.[65] The Ct–N distance is essentially the same as the Co–N distance, given the small displacement. The zinc atom in four-coordinate complexes lies in the plane of the four nitrogen atoms and has an average Zn–N distance of 2.037 Å.[66] Coordination of pyridine increases the average Zn–N distance (2.067 Å in Zn(OEP)Py, 2.073 Å in Zn(TPyP)Py) but also results in a 0.31–0.33-Å displacement of the zinc out of the plane.[67] The Ct–N distance may increase slightly from 2.036 to 2.045 Å. Thus, ligand binding results in a significant expansion of the porphyrin core for cobalt(II) complexes but essentially no change in the size of the porphyrin core for zinc(II) complexes.

The ideal M–N distance in a porphyrin with minimum strain energy is between 2.01 and 2.03 Å.[68,69] Compression of the macrocycle to achieve the M–N distance in four-coordinate Co(TPP) increases the strain energy of the macrocycle. The expansion of the macrocycle in the five-coordinate form relieves a substantial part of the strain. This represents a favorable contribution to the free energy change for ligand binding. The change in strain energies that occurs upon conversion of four-coordinate to five-coordinate zinc complexes will be significantly smaller.

The ΔG represented by the difference in the intercepts is in suprisingly good agreement with the change in strain energies

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that can be estimated for the cobalt complexes using parameters derived from molecular mechanics calculations.[69] These calculations also suggest that hydroporphyrins have larger ideal core sizes than porphyrins and slightly smaller gradients for core-size changes. Thus, the changes in strain energy will differ somewhat for porphyrin and hydroporphyrin complexes.

Two implicit assumptions here are that solid-state bond distances are indicative of solution distances and that changes in bond distances are similar for porphyrin and hydroporphyrin complexes. Neither assumption is necessarily correct. Indeed, the short Co–N distances in Co(TPP) may reflect the ruffling of the macrocycle, which has been attributed to crystal-packing forces.[64] The cobalt(II) complexes of two different fluorinated TPP compounds, Co(TF$_5$PP) and Co(T(p-Me$_2$N)F$_4$PP), have structures with planar porphyrins and Co–N distances of 1.97 Å.[70] However, both of these complexes might best be considered six-coordinate rather than four-coordinate given the tight interaction of the cobalt with two benzene molecules of solvation. Resonance Raman data reported by Spaulding et al. are consistent with average Co–N distances of 1.96 Å for Co(OEP) in the solid.[71] Preliminary data for the Raman core-size marker bands of Co(OEP) and Co(OEP)Py in CH$_2$Cl$_2$ solution indicate that significant core expansion occurs.[72] In the case of five-coordinate zinc complexes, the structures of the porphyrin and hydroporphyrin complexes resemble each other closely.[73] No structural data are available, though, for cobalt hydroporphyrin or four-coordinate zinc hydroporphyrin complexes.

Steric Effects. The sterically encumbered bases 2-Pic and 2,4-Lut have much smaller stability constants for coordination to the cobalt(II) complexes than would be expected on the basis of their affinities for either aqueous H$^+$ (Figure 1) or Zn(OEP) in toluene (Figure 3). The increased sensitivity of the cobalt complexes to steric effects relative to the zinc complexes can be understood by comparison of the structural parameters of the square-pyramidal coordination groups of both metals. The M–N$_{ax}$ distances for the five-coordinate complexes of the two metals are indistinguishable, ranging between 2.16 and 2.20 Å.[65,67,73,74] The difference is the displacement of the metal atoms from the N$_4$ plane. Zinc is typically 0.33 Å out-of-plane, but cobalt is displaced by only 0.14 Å. The contacts between a pyridine ortho-hydrogen or methyl group and the porphyrin core will be about 0.19 Å shorter in the cobalt complexes than in the corresponding zinc complexes and, therefore, are considerably more severe.

Another noteworthy structural feature of five-coordinate cobalt(II) porphyrin complexes is that the dihedral angle formed by the plane containing the metal and opposite nitrogen atoms and the axial ligand plane, ϕ, is usually small.[7a] The steric interactions in this nearly eclipsed conformation are considerably more extensive than those in the staggered conformation, where ϕ has its maximum value of 45°. Steric interactions in the staggered conformation are often diminished further by ruffling the porphyrin in a manner that moves the meso carbons that lie in the plane of the axial ligand toward the face opposite the axial ligand.[75] Hoard has shown that smaller values of ϕ are associated with and responsible for longer axial Fe–N bonds and that larger values of ϕ are associated with shorter axial Fe–N bonds.[76] Scheidt observed of the situation that the cobalt to axial ligand bond of five-coordinate cobalt porphyrin complexes is "readily extended" and that "the axial bonding is not sufficiently assertive to require the commonly observed ruffling of the core."[75b] Scheidt's statements must also apply to zinc porphyrins, given their observed lesser sensitivity to steric encumberance of the ligand.

Recently, an attempt was made to probe the flexibity of tetrapyrrole macrocycles by comparing the stability constants for coordination of sterically encumbered imidazole bases to the zinc complexes of TPP, TPC, and TPiBC.[21] The authors of the study asserted that a more flexible macrocycle would arrange itself to better minimize steric interactions with the axial ligand. It would then follow that if hydroporphyrins are more flexible than porphyrins, steric hinderance of the axial ligand will have less effect on the stability constant for coordination of the ligand to a metallohydroporphyrin than on that for coordination to a metalloporphyrin. On the basis of the modest differences in stability constants that they observed, the authors concluded that the three macrocycles have comparable rigidity. The discussion in the previous paragraph establishes that, when applied to the zinc complexes, the authors' assertion is incorrect. Thus, the relative flexibilities of the macrocycles cannot be determined from comparisons of the stability constants for coordination of sterically encumbered bases to zinc complexes.

Summary

The principal experimental results of this investigation are as follows. Cobalt(II) and zinc(II) complexes of OEP, *t*-OEC, and the *tct*- and *ttt*-isomers of OEiBC form 1:1 complexes with piperidine and pyridines. The stability constants correlate roughly with the base strength of the ligand but correlate closely with the log K for coordination of the ligand to Zn(OEP). Stability constants increase with increasing saturation of the macrocycle. The stability constants of both Co- and Zn(OEiBC) are unaffected by the stereochemistry (*tct* vs *ttt*) of the ethyl substituents. For a given base, log K is generally larger for zinc complexes than for cobalt complexes. However, for weak bases log K is larger for cobalt complexes. ΔH and ΔS vary between -8 and -12 kcal/mol and between -12 and -24 cal K^{-1} mol^{-1}, respectively. The values do not correlate in any direct fashion with the log K or the identity of the macrocycle. The free-base compounds of the three macrocycles ionize to dianions in THF/n-butanol solution by simultaneous loss of two protons. OEP and OEiBC both have pK_a = 15.9. OEC is a weaker acid and has pK_a = 16.6. Cobalt porphyrin and hydroporphyrin complexes are more sensitive to steric interactions with bulky groups on the ligand than are the corresponding zinc complexes.

Analysis of the data leads us to conclude that the dependence of the stability constants on macrocycle saturation level and the reversal of the relative Lewis acid strengths of the cobalt and zinc complexes do not result from π-bonding effects or solvation effects. No correlation exists between the stability constants and the acidity of the free-base macrocycles. We argue that the affinity of the macrocycle dianion toward aqueous H$^+$ is not indicative of its σ-donor strength toward a metal ion. Thus, whether the dependence of the stability constants on macrocycle saturation level results from differences in the σ-donor strengths of the macrocycle remains an open question. We propose that core expansion upon ligand coordination to the cobalt complexes results in relief of strain energy. This is responsible for the reversal of Lewis acid strengths that occurs for weak bases.

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