Cis-Influence of Hydroporphyrin Macrocycles on Axial Ligation Equilibria and Alkyl Exchange Reactions of Alkylcobalt(III) Porphyrin Complexes

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Stability constants are reported for the coordination of pyridine and substituted pyridines to the alkylcobalt(III) complexes of octaethylporphyrin (OEP), *t*-octaethylchlorin (OEC), and *ttt*-octaethylisobacteriochlorin (OEiBC) in toluene solution. The stability constants correlate with the base strength of the nitrogenous ligand. A cis-influence of the macrocycle saturation level on the stability constants is observed. Stability constants for coordination of a given pyridine ligand to an alkylcobalt(III) complex are roughly 10 times smaller than the stability constants for the corresponding cobalt(II) complex. Analysis of a thermodynamic cycle demonstrates that this leads to decreased stability of the complex with respect to Co−C bond homolysis upon ligand coordination, a "base-on" effect. Alkyl exchange occurs between cobalt complexes of different tetrapyrroles. Equilibrium data establish that the exchange is nonstatistical and that the Co−C bond is stabilized by increasing the saturation of the tetrapyrrole macrocycle.

Introduction

Metal complexes of hydroporphyrins and other non-porphyrin tetrapyrroles play central roles as prosthetic groups in the biochemical pathways of the carbon, nitrogen, and sulfur cycles and in the metabolism of many anaerobes.[1] The absence of enzymes that contain porphyrin prosthetic groups and are competent to catalyze these processes is conspicuous and raises the question of whether non-porphyrin tetrapyrroles 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.

As part of our studies of the chemical differences between porphyrins and hydroporphyrins,[1] we investigated the effects of the macrocycle saturation level on the ligand-binding equilibria of four-coordinate cobalt(II) and zinc(II) porphyrin and hydroporphyrin complexes.[2] The macrocycle saturation level exerted a small but real cis-influence on the equilibria. Stability constants for coordination of a given ligand to OEiBC[3] complexes were typically 4 times greater than those for coordination to OEP complexes and 1.8 times greater than those for coordination to OEC complexes. For most ligands, the stability constant was greater for the zinc complexes than for the cobalt complexes. However, for the weak base 3,5-dichloropyridine, the stability constant was greater for cobalt complexes. This reversal was attributed to a relief of strain due to core expansion that occurs upon ligand coordination to cobalt complexes.

Coordination equilibria are extremely important in the chemistry of vitamin B_{12}, a biologically essential cobalt tetrapyrrole complex. Two such equilibria markedly affect the Co−C bond dissociation energies of coenzyme B_{12} and of B_{12} model complexes. Complexation of adenosylcobalamin by apoenzyme results in a dramatic acceleration of the homolysis of the Co−C bond by a factor of $\geq 10^{10}$ relative to the case of free coenzyme.[4,5] The "base-on" effect, which results from coordination of an axial ligand, accelerates the homolysis of the Co−C bond by a factor of 10^2−10^3.[4−11] Although the manner in which these accelerations occur is not understood, they are thought to involve steric interactions and distortions induced by coordination of the axial ligand or of the coenzyme to the enzyme.

An observation seemingly contradictory to the "base-on" effect, though, is that, for axial bases of similar steric sizes, increasing the strength of the base increases the apparent strength of the Co−C bond in (α-phenethyl)bis(dimethylglyoximato)-cobalt(III) complexes.[12,13] It was suggested that more basic ligands stabilized higher oxidation states and thus favored the six-coordinate alkyl−Co(III)−base complex over the five-coordinate Co(II)−base complex.[12] Our structural studies of $Co(OEP)(CH_3)Py$ cast doubt upon this explanation.[14] The cobalt ion of the six-coordinate complex appeared to be rather electron rich. Moreover, the $Co-N_{ax}$ distances suggested that ligand

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(3) Abbreviations: P, any tetrapyrrole 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-diastereomers unless otherwise noted); Py, pyridine; 3,5-Cl_2Py, 3,5-dichloropyridine; 4-CNPy, 4-cyanopyridine; 4-Pic, 4-picoline; 4-DMAP, 4-(dimethylamino)pyridine.

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binding was substantially stronger in the five-coordinate Co(II) complex than in the six-coordinate Co(III) complex.

We report the stability constants for coordination of a series of pyridine bases to the five-coordinate alkyl−Co(III) complexes of OEP, OEC, and OEiBC in this paper. As in the case of the four-coordinate Co(II) complexes, the macrocycle saturation level exerted a small but real cis-influence on the stability constants. Moreover, the saturation level also influenced the Co−C bond dissociation energy. This was established by the nonstatistical equilibria of the facile alkyl transfer reaction, eq 1, that we discovered during the course of this investigation.

$$\mathrm{Co^{III}(P)R + Co^{II}(P^*) \rightleftharpoons Co^{II}(P) + Co^{III}(P^*)R} \qquad (1)$$

Comparisons of the relative magnitudes of the equilibrium constants for base coordination to four-coordinate Co(II) and five-coordinate alkyl−Co(III) complexes and their dependencies on base strengths provide insights into both the apparent weakening of the Co−C bond upon base coordination ("base-on" effect) and the apparent strengthening of the Co−C bond with increasing base strength.

Experimental Section

Materials. Reactions, recrystallizations, and sample manipulations were carried out on a vacuum line, under a nitrogen atmosphere using standard Schlenk techniques, or in a Vacuum/Atmospheres drybox. Alkylcobalt(III) complexes were handled under subdued lights. All solvents, reagents, and bases were of reagent grade or better. Toluene was distilled from sodium, tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl, and chloroform was distilled from phosphorus pentoxide. Pyridine and 4-picoline were distilled from barium oxide, and 3,5-dichloropyridine was sublimed. 4-(Dimethylamino)pyridine (DMAP) and 4-cyanopyridine were used as received. Alkyl halides were examined for purity and were distilled if necessary.

The free-base compounds H_2(OEP),[15] H_2(OEC),[16] and H_2(OEiBC)[16] and their respective Co(II) complexes[17,18] were prepared by literature methods. The tct- and ttt-stereoisomers of H_2(OEiBC) were separated by chromatography on MgO.[19] The Co(II) complexes of the separated isomers were prepared by the same method as used for the mixture.

Alkylcobalt(III) porphyrin and hydroporphyrin complexes were prepared by reaction of the respective anionic cobalt(I) complex with excess alkyl iodide.[20] Solutions of the cobalt(II) complex in THF were reduced by stirring over 1% sodium amalgam (18 h for Co(OEP) and Co(OEC); 1 h for Co(OEiBC)). After separation from the amalgam by filtration through a fritted glass disk, the solution was frozen and the reaction vessel was evacuated. The alkyl iodide was distilled onto the frozen solution, the vessel was filled with nitrogen, and the solution was allowed to thaw and then was stirred for 1 h at room temperature. The solvent was removed under vacuum. The solid was brought into a drybox and dissolved in a minimal quantity of benzene. The resulting solution was applied to the top of a column of basic alumina that had been deactivated with THF (3 mL/100 g of alumina). The product was eluted with a 4:6 benzene/hexane mixture. The solvent was removed and the residue recrystallized from toluene. Acetylcobalt(III) porphyrin and hydroporphyrin complexes were prepared by an analogous procedure substituting acetyl chloride for the alkyl iodide.

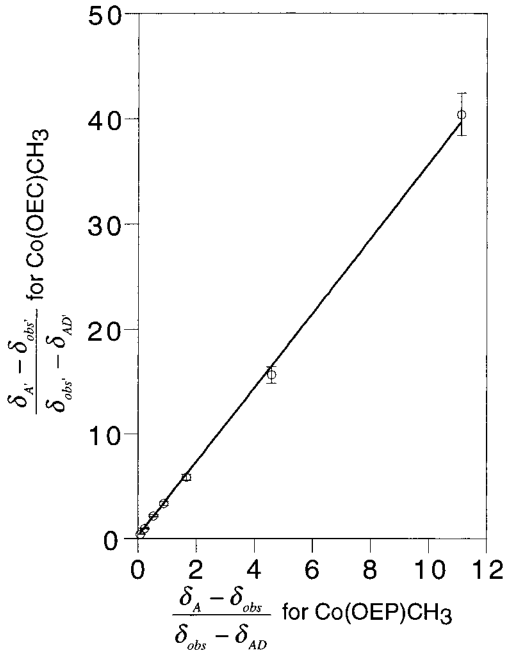

Figure 1. Plot of $(\delta_A - \delta_{obs})/(\delta_{obs} - \delta_{AD})$ for the axial methyl resonance of Co(OEC)CH_3 vs $(\delta_A - \delta_{obs})/(\delta_{obs} - \delta_{AD})$ for the axial methyl resonance of Co(OEP)CH_3 in a competitive titration with DMAP. Error bars indicate the estimated error in the ratio for Co(OEC)CH_3 (y value) for each data point. The estimated error in the ratio for Co(OEP)CH_3 (x value) is not shown but is comparable in magnitude to the y error on a percent basis.

Instrumentation. 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. Proton magnetic resonance spectra were obtained on a JEOL-GSX 270 MHz NMR spectrometer.

Equilibrium Constants for Coordination of Axial Ligands. Stability constants for coordination of substituted pyridines to Co(OEP)CH_3 were determined spectrophotometrically. The procedures employed and the use of the program SQUAD to calculate stability constants and their associated errors were described previously.[2] The stability constants for coordination of substituted pyridines to other alkylcobalt porphyrin and hydroporphyrin complexes were determined by an ^{1}H NMR method. The experiment entailed the titration of a physical mixture of the complex of interest and Co(OEP)CH_3 with the substituted pyridine. If δ_A is defined as the chemical shift of a particular nucleus in the uncomplexed acceptor A, δ_{AD} as the chemical shift of the nucleus in the completely formed complex AD, and δ_{obs} as the observed chemical shift of the nucleus at a specific concentration of donor D and if A and AD are in fast exchange, then a plot of $(\delta_A - \delta_{obs})/(\delta_{obs} - \delta_{AD})$ for the resonances associated with a particular nucleus in one metal complex versus the same function for a resonance associated with the second complex will be linear with slope equal to the ratio of the equilibrium constants, eq 2. A representative plot obtained for

$$\frac{\delta_{A'} - \delta_{obs'}}{\delta_{obs'} - \delta_{AD'}} = \frac{K_{AD'}}{K_{AD}} \frac{\delta_A - \delta_{obs}}{\delta_{obs} - \delta_{AD}} \qquad (2)$$

titration of a mixture of Co(OEC)CH_3 and Co(OEP)CH_3 with DMAP is shown in Figure 1. Note that eq 2 does not require the concentrations of the metal complexes or the donor to be known. Thus, it is not necessary to satisfy the condition $[D]_0 \gg [AD]$ to obtain useful data. The derivation of eq 2 is described in the Supporting Information.

Equilibrium Constants for Alkyl Exchange Reactions. Alkyl exchange reactions were conducted by reacting an alkylcobalt(III) complex of one tetrapyrrole macrocycle with a cobalt(II) complex of a second tetrapyrrole macrocycle. Reactions were conducted anaerobically in toluene-d_8, in which the complexes are five-coordinate and four-coordinate, respectively. Reactions were also conducted in 0.5 M

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pyridine-d_5 in toluene-d_8. Under these conditions, complexation equilibria for coordination of pyridine to alkyl−Co(III) complexes of OEP, OEC, and OEiBC were 97%, 99%, and >99% complete, respectively, and those of cobalt(II) complexes were >99% complete.

The reaction apparatus consisted of a glass tee connected to a 90° Teflon barrel valve on each horizontal arm and a 180° Teflon barrel valve on the vertical arm. One horizontal arm had a tube attached below the valve. The other had a male 14/20 standard taper joint below the valve. An NMR tube blown onto a female 14/20 joint was connected to the male joint. The 180° valve was attached to an O-ring joint, which was used to connect the apparatus to a vacuum line.

The apparatus was assembled in a drybox. A small stir bar and approximately 0.5 mg each of an alkylcobalt(III) complex and a cobalt(II) complex of different tetrapyrrole macrocycles were placed in the tube through the body of the valve. The Teflon barrel was replaced and closed, the apparatus was removed from the drybox, attached to a vacuum line, and evacuated, and 1.0 g of toluene-d_8 was bulb-to-bulb distilled into the tube. Upon thawing, the solids dissolved and the resulting solution was stirred for 30 min at room temperature. The apparatus was then tipped to allow half of the solution to pour through the two 90° valves into the NMR tube. The valves were closed, the solution in the NMR tube was degassed by repeated freeze−pump−thaw cycles, and the NMR tube was sealed off under vacuum. A new NMR tube was connected to the male 14/20 joint, the apparatus was reevacuated, and the remaining solution was poured into the NMR tube and frozen. An aliquot of pyridine-d_5 sufficient to make the solution 0.5 M in pyridine was bulb-to-bulb transferred into the NMR tube. The contents of the NMR tube were subjected to repeated freeze−pump−thaw cycles, and the NMR tube was sealed off under vacuum.

Equilibrium constants for alkyl exchange were calculated from the ratios of the integrations of selected ^{1}H resonances of the two diamagnetic alkylcobalt(III) complexes and the two paramagnetic cobalt(II) complexes, weighted appropriately for the number of protons in these resonances. Assignment of the resonances in the spectra of the mixtures was straightforward, given that the four individual complexes had been independently prepared and spectroscopically characterized. Spectra were monitored for several hours to ensure that equilibrium had been achieved. Reaction solutions involving methyl complexes appeared to be stable indefinitely. In contrast, isopropyl complexes decomposed over several hours to give cobalt(II) complexes and undetermined organic product(s) derived from the alkyl group. Identical equilibrium constants were obtained when equilibrium was approached by reacting the alkylcobalt(III) complex of the second tetrapyrrole and the cobalt(II) complex of the first tetrapyrrole.

Table 1. ^{1}H NMR Data for Axial R Groups of RCo^{III}(P)L Complexes[a]

			δ	
R	P	L	α-CH	β-CH
CH_3	OEP		−4.60	
		Py	−4.73	
	OEC		−3.10	
		Py	−3.30	
	ttt-OEiBC		−1.20	
		Py	−1.38	
	tct-OEiBC	Py	−1.38, −1.56[b]	
C_2H_5	OEP		−3.60 (br m)	−5.14 (t)
	OEC		−2.52 (br q)	−4.43 (t)
	ttt-OEiBC		−0.52 (br q)	−3.03 (t)
	tct-OEiBC		−0.52, −0.73 (br q)	−3.14, −3.19 (t)
i-C_3H_7	OEP		−3.50 (m, 1H)	−5.24 (d, 6H)
	OEC		−2.13 (br m, 1H)	−4.20, −4.22 (d, 3H)
	ttt-OEiBC		−0.25 (br m, 1H)	−2.97, −3.02 (d, 3H)
$CH_3C(O)$	OEP			−2.83
	OEC			−1.81
	ttt-OEiBC			−0.55

[a] In ppm relative to TMS at 21 °C. Solvent is 0.5 M pyridine-d_5 in toluene-d_8 if L = Py and toluene-d_8 if no L is specified. [b] Present in a 41:54 ratio.

Table 2. ^{1}H NMR Data for Meso CH Protons of RCo^{III}(P)L Complexes[a]

R	P	L	δ
CH_3	OEP		10.21
		Py	10.11
	t-OEC		9.65, 9.63, 8.66[b]
		Py	9.67, 9.44, 8.48, 8.38
	ttt-OEiBC		8.98, 7.92, 7.91, ...[c]
		Py	8.91, 7.83, 7.81, ...[c]
$CH_3C(O)$	OEP		9.99
	t-OEC		9.40, 9.34, 8.52, 8.47

[a] In ppm relative to TMS at 21 °C. Solvent is 0.5 M pyridine-d_5 in toluene-d_8 if L = Py and toluene-d_8 if no L is specified. [b] Two nearly coincident singlets. [c] Peak obscured by the solvent residual proton peak.

Results

Synthesis and ^{1}H NMR Spectroscopy of Alkylcobalt(III) Tetrapyrrole Complexes. Alkylcobalt(III) porphyrin complexes have been prepared by two methods: (i) reaction of a Co^{III}(P)X complex (where P = a porphyrin dianion and X = a halide anion) with a Grignard or alkyllithium reagent;[21−23] (ii) alkylation of a Co^{I}(P) complex with an alkyl halide or other electrophile.[20,21,24,25] Application of the first method to hydroporphyrins appeared problematic. Co^{III}(P)X complexes are prepared from Co^{II}(P) complexes by air oxidation in the presence of HX[17,26,27] or in the case of X = I by oxidation with elemental halogen.[28] Hydroporphyrin macrocycles suffer oxidative dehydrogenation under these conditions and are converted to porphyrin.[16] Thus, we pursued the second method.

Reduction of cobalt(II) hydroporphyrin complexes to their cobalt(I) anions and alkylation of the anions with alkyl or acyl halides proceeded readily. The handling characteristics of the hydroporphyrin complexes suggest that the stability and lability of their cobalt−carbon bonds are comparable to those of the corresponding porphyrin complexes. Although no specific instances of photolability were observed, all work was conducted under subdued lighting as a general precaution. Rigorous exclusion of O_2 was a necessity. All complexes react readily with O_2 to afford (alkylperoxo)cobalt(III) complexes.[24,29] Given the susceptibility of hydroporphyrin complexes to oxidative dehydrogenation, they are somewhat less robust than porphyrin complexes. Particular care was exercised in the isolation and purification of the hydroporphyrin complexes.

Reduction of the porphyrin macrocycle has several effects on the ^{1}H NMR spectra of the alkyl- and acylcobalt(III) complexes, Tables 1 and 2. The axial alkyl and acyl proton peaks shift downfield and the meso proton peaks shift upfield with increasing saturation of the macrocycle. The invariant stretching frequency of 1720−1722 cm^{-1} for the axial acetyl

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Table 3. Equilibrium Constants for Coordination of Bases by Methylcobalt(III) Complexes[a]

		log K^b		
base[c]	pK_a[d]	Co(OEP)CH_3	Co(*t*-OEC)CH_3	Co(*ttt*-OEiBC)CH_3
3,5-Cl2Py	0.67	1.531(26)	2.06	2.47
4-CNPy	1.90	1.627(39)		
Py	5.22	1.759(40)	2.33	2.76
4-Pic	6.02	2.063(37)		
4-DMAP	9.71	2.402(25)	2.96	3.42

[a] At 20.0 ± 0.1 °C in toluene. [b] Numbers in parentheses are estimated standard deviations in the least significant digits. [c] See ref 3 for abbreviations. [d] Aqueous for BH^+; see Table 1 of ref 2 for sources.

groups suggests that these shifts reflect the diminished π-systems and smaller ring currents of the hydroporphyrin macrocycles relative to porphyrins rather than differences in electron densities at cobalt. The lower symmetry of the hydroporphyrin macrocycle has two consequences. First, the peaks due to the now inequivalent macrocycle protons become sufficiently great in number and complexity that individual peaks are often difficult to resolve and assign. Typically, alkylcobalt(III) hydroporphyrin pyrroline β-H, CH_2, and CH_3 peaks are found in regions near 4.0, 1.8, and 0.9 ppm and pyrrole CH_2 and CH_3 peaks are found near 3.4−4.0 and 1.5−1.8 ppm, respectively. Second, addition of a proton to a β-carbon of an octaalkylporphyrin creates an asymmetric center and results in stereoisomerism. The method used to reduce octaethylporphyrin specifically affords hydroporphyrins with trans ethyl substituents on the pyrroline (reduced) ring. Both faces of the macrocycle are equivalent in *t*-OEC, which is a racemic mixture. The OEiBC obtained is a mixture of the ttt- and tct-diastereomers, where the middle letter designates the relative stereochemistry of the "inboard" ethyl substitutents (3 and 7) on adjacent pyrroline rings. The ttt-diastereomer is a racemic mixture and has equivalent macrocycle faces. The tct-diasteromer is a meso compound and has inequivalent macrocycle faces. Not unexpectedly, the two equivalent methyls of the isopropyl group are diastereotopic in Co^{III}(OEP)(*i*-Pr) and resolved in Co^{III}(OEC)(*i*-Pr) and Co^{III}(OEiBC)(*i*-Pr). Two or three sets of alkyl peaks were resolved in the spectra of Co^{III}(OEiBC)CH_3 and Co^{III}(OEiBC)Et prepared from the mixture of OEiBC diastereomers. Consequently, all subsequent work was performed with complexes prepared from the separated diastereomers of H_2(OEiBC) in order to simplify the spectra. In addition, equilibrium measurements were made only with *ttt*-Co(OEiBC) complexes to eliminate statistical effects resulting from multiple species.

Equilibrium Constants for Coordination of Substituted Pyridines by Alkylcobalt(III) Tetrapyrrole Complexes. The stability constants for coordination of substituted pyridines by Co(OEP)CH_3 in toluene solution, eq 3 (with P = OEP and R

$$\mathrm{Co(P)R + L \rightleftharpoons Co(P)(R)L} \qquad (3)$$

= CH_3), were determined spectrophotometrically by a nonlinear least-squares fit of absorption data at multiple wavelengths. The data are reported in Table 3.

The spectroscopic method was not as reliable for analogous measurements with cobalt hydroporphyrin complexes. The absorption bands of five- and six-coordinate cobalt(III) hydroporphyrin complexes were sufficiently broad that the presence of significant quantities of unalkylated cobalt(II) complexes, of macrocycle-oxidized alkylcobalt(III) complexes, or of (alkylperoxo) cobalt(III) complexes might not be readily apparent. These impurities contribute to the observed UV/vis spectra and could therefore interfere with an accurate determination of the stability constants. Consequently, an NMR method that involved titration of a mixture of the complex of interest and Co(OEP)CH_3 with the substituted pyridine was used to determine the stability constants for the complex relative to the corresponding stability constant for Co(OEP)CH_3. As shown in Figure 1, a plot of $(\delta_A - \delta_{obs})/(\delta_{obs} - \delta_{AD})$ for the resonances associated with a particular nucleus in one metal complex versus the same function for a resonance associated with a second complex is linear. The slope of the line is equal to the ratio of the equilibrium constants. The method has the advantage that the presence of impurities is readily apparent and does not interfere with the analysis of the data. Moreover, the concentrations of complex and pyridine need not be known to high precision to obtain meaningful results. The significant change in chemical shift of the axial alkyl protons upon pyridine coordination makes them particularly well suited to the method. With the exception of 3,5-Cl_2Py and Co(OEP)CH_3, equilibria could be driven to completion to allow direct determination of δ_{AD}. In this case, the δ_{AD} values were fitted numerically to give the most linear plot. The ratios of stability constants determined by this method are reported in Table 4. Stability constants calculated from the ratios and the spectrophotometrically determined stability constants for Co(OEP)CH_3 are included in Table 3.

Table 4. Ratios of Equilibrium Constants for Coordination of Bases by Alkylcobalt(III) Complexes Relative to Co(OEP)CH_3[a]

	ratio		
base	Co(OEC)CH_3	Co(*ttt*-OEiBC)CH_3	Co(OEP)C_2H_5
3,5-Cl2Py	3.40	8.70	
Py	3.70	10.00	0.21
4-DMAP	3.60	10.30	

[a] Determined by the NMR method in toluene-d_8 at 20 °C. Estimated error = 0.1.

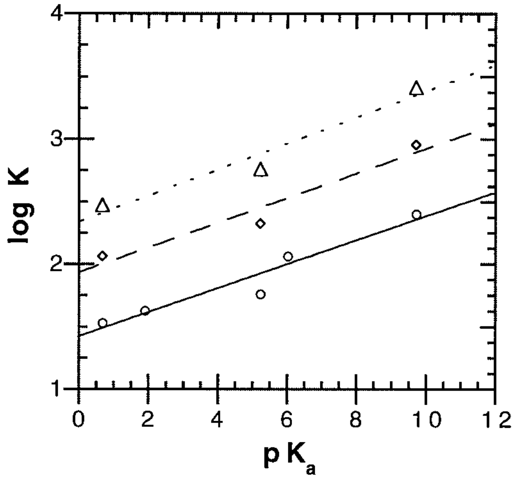

Figure 2. Correlations between log *K* in toluene and ligand basicity (aqueous pK_a of conjugate acid) for CH_3Co(OEP), (circles), CH_3Co(OEC), (diamonds), and CH_3Co(OEiBC) (triangles).

The effect of the variation of the base strength of the axial ligand on the ligand-binding equilibria of Co(P)CH_3 complexes, eq 3, is shown in Figure 2, which is a plot of log *K* vs the aqueous pK_a of the ligand's conjugate acid. The lines representing the response of the OEP, OEC, and OEiBC equilibria to ligand basicity are nearly parallel and are displaced toward larger log *K* values with progressive saturation of the macrocycle. The increase in stability constants represents a $\Delta\Delta G$ relative to OEP complexes of about 0.71−0.77 kcal/mol for *t*-OEC complexes and of 1.26−1.37 kcal/mol for *ttt*-OEiBC complexes. Similar behavior was observed previously for the ligand-binding

Table 5. Equilibrium Constants for Alkyl Exchange Reactions[a]

P	P*	R	*K*	
			Py absent	Py present[b]
OEP	*t*-OEC	CH_3	1.98[c]	4.90[d]
t-OEC	*ttt*-OEiBC	CH_3	1.55[c]	1.10[c]
OEP	*t*-OEC	*i*-C3H7	0.96[c]	

[a] Determined in toluene-d_8 solution at 20 °C. Equilibrium constants for reactions defined in eq 1 and 4. [b] [Pyridine] = 0.5 M. [c] Estimated error = 0.1. [d] Estimated error < 0.5.

equilibria of four-coordinate $Co^{II}(P)$ and $Zn^{II}(P)$ complexes, although the $\Delta\Delta G$ values for *t*-OEC complexes appeared to be somewhat smaller in those cases.[2]

The relative stability constants for coordination of pyridine-d_5 to five-coordinate $Co(OEP)CH_3$ and four-coordinate Co(OEP) were determined by the NMR method in $CDCl_3$. The ratio obtained was the same, within error, as the ratio determined in toluene, either by the NMR method or by the spectrophotometric method. The stability constant for coordination of pyridine to Co(OEP) in toluene solution was determined to be roughly 13 times that in $CHCl_3$.[2] Thus, the stability constant for coordination of pyridine to $Co(OEP)CH_3$ has a similar solvent dependence.

The NMR method also was applied to a mixture of Co(OEP)-CH_3 and $Co(OEP)C_2H_5$ to examine the effect of the bulk of the axial alkyl group on the stability constant for coordination of pyridine. The ratio of stability constants was determined to be 4.8, with the methyl complex having the larger stability constant. Thus, log *K* for coordination of pyridine to $Co(OEP)C_2H_5$ is 1.08.

Equilibrium Constants for Alkyl Ligand Exchange Reactions. One experiment that examined the competition between $Co^{III}(OEP)CH_3$ and a $Co^{III}(OEC)CH_3$ for pyridine coordination was inadvertently performed with a sample of the hydroporphyrin complex that contained a substantial amount of the unmethylated $Co^{II}(OEC)$ complex as an impurity. Within less than 0.5 h of mixing, peaks due to paramagnetic $Co^{II}(OEP)$ appeared in the ^1H NMR spectrum. Concurrently, the peaks due to $Co^{II}(OEC)$ and $Co^{III}(OEP)CH_3$ decreased and those due to $Co^{III}(OEC)CH_3$ increased in intensity. The unexpectedly rapid transfer of the methyl group between cobalt tetrapyrrole complexes led us to investigate alkyl exchange reactions.

The alkyl exchange reactions of alkylcobalt(III) and cobalt(II) tetrapyrrole complexes are of considerable scope. Reactions proceed both in toluene, in which the complexes, respectively, are five-coordinate and four-coordinate, eq 1, and in pyridine in toluene, in which the complexes, respectively, are six-coordinate and five-coordinate, eq 4. Exchange is not limited

$$\mathrm{Co^{III}(P)(R)Py + Co^{II}(P^*)Py \rightleftharpoons Co^{II}(P)Py + Co^{III}(P^*)(R)Py} \tag{4}$$

to methyl groups. Ethyl and isopropyl groups also transfer. Although the kinetics of the reaction were not investigated, our observations suggest that the rate of transfer becomes somewhat slower as the bulk of the alkyl group increases. The exchange reactions proceed to equilibrium. The equilibrium constants, Table 5, are not statistical (i.e., equal to 1.0). Cobalt octaethylhydroporphyrin complexes have a slightly greater affinity for a methyl group than Co(OEP).

Discussion

The data reported in this paper for the ligand-binding equilbria of alkyl−Co(III) porphyrin complexes represent the majority of such data in the literature. One previous report gave the formation constant for conversion of $Co(TPP)C_2H_5$ to Co(TPP)-$(C_2H_5)Py$ in CH_2Cl_2 as $K = 8.9$.[30] This value is in reasonable agreement with the equilibrium constant determined here for $Co(OEP)C_2H_5$ in toluene.

Our results establish that the equilibrium constants for the ligand-binding reactions represented by eq 3 increase with increasing saturation of the tetrapyrrole macrocycle and with increasing base strength (pK_a of the conjugate acid) of the ligand. Equilibrium constants decrease with increasing steric bulk of the trans alkyl group, as expected.[9,31−33] For a given ligand, the equilibrium constants for ligand binding to the methylcobalt(III) tetrapyrrole complexes are about a factor of 10 smaller than those for the corresponding Co(II) tetrapyrrole, which in turn are smaller than those for Zn(II) tetrapyrroles. In addition, equilibrium constants for the $Co(OEP)CH_3$ complexes are about a factor of 10 larger than those for methylcobinamides and are roughly a factor of 100 smaller than those for methylcobaloximes.[34] The increased hydrogen bonding of pyridine bases in water (the solvent used in the measurements with cobinamides and cobaloximes) relative to toluene would be expected to decrease the equilibrium constants for the porphyrin. Thus, cobalt porphyrins are better quantitative models of coenzyme B_{12} axial ligation equilibria than are cobaloximes.

A definitive explanation could not be given for the cis-influence of the macrocycle saturation level on log *K* for coordination of bases to Co(II) and Zn(II) tetrapyrrole complexes.[2] Solvation and π-bonding effects were eliminated as possible sources. Measurements of the pK_a values for deprotonation of the three macrocycles showed that they were similar. However, several lines of evidence suggested that these pK_a's are not good indicators of the σ-donor strengths of the tetrapyrroles. The possibility remains that the cis-influence results from a decreased σ-donor strength upon increasing tetrapyrrole saturation. The origin of the cis-influence on ligand binding in alkylcobalt(III) tetrapyrrole complexes is likely to be similar to that for Co(II) and Zn(II) tetrapyrrole complexes.

In our analysis of the ligand-binding equilibria of Co(II) and Zn(II) tetrapyrroles, we developed the tool of plotting log *K* values for binding of a particular base to a complex vs log *K* values for binding of the base to Zn(OEP), log $K_{Zn(OEP)}$.[2] Zn(OEP) is a more suitable reference acid than $H_{aq}{}^+$. The slope of a line in such plots represented the sensitivity of ΔG for ligand binding to the basicity of the axial ligand. It depended strongly on the identity of the metal but was essentially independent of the identity of the macrocycle. Thus, the slope was identified with the acidity of the metal in the specific environment of the coordination complex. The intercept of a line represented 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 intercept depended strongly on the identities of both the metal and the macrocycle. To the extent that the structural changes occuring upon ligand coordination are independent of the identity of the ligand (a reasonable assumption for para-substituted pyridines), the contribution of the change in strain energy to the energetics

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of the reaction will be independent of the base strength of the ligand. Thus, the change in strain contributes to the intercept, not the slope. The relief of strain due to core expansion that occurs upon ligand coordination to the cobalt complexes was considered responsible both for the larger intercepts of the Co(II) complexes relative to the Zn(II) complexes and for the inverted order $\log K_{\mathrm{Co(II)}} > \log K_{\mathrm{Zn(II)}}$ for the weakest bases.

Analysis of $\log K_{\mathrm{MeCo(P)}}$ vs $\log K_{\mathrm{Zn(OEP)}}$ plots reveals that the slopes for the alkylcobalt(III) complexes are roughly 0.36. This is essentially indistinguishable from the slopes for the Co(II) complexes, within the errors of the determination. The intercepts are respectively 0.7, 1.3, and 1.7 for the OEP, OEC, and OEiBC complexes. These are from 0.3 to 0.6 smaller than the intercepts for the Co(II) complexes and from 0.5 to 1.5 larger than those for the Zn(II) complexes. Less strain appears to be released upon coordination of an axial ligand to the methylcobalt(III) complexes than to the Co(II) complexes. This is consistent with the smaller core expansion and decreased alkyl to porphyrin distance that was observed upon base coordination to $CH_3Co(OEP)$.[14]

Implications for the Base-On Effect. The effect of coordination of an axial ligand on the Co−C bond homolysis can be analyzed by means of a thermodynamic cycle consisting of eqs 3, 5, 6, and 7. The homolysis of the six-coordinate complex, eq 7, is equivalent to the reverse of the process in eq 3 followed by the processes in eqs 5 and 6. Consequently, the $\Delta G°$ values are related by eq 8. Substitution and rearrangement of eq 8 show that $\Delta\Delta G°$ for bond homolysis depends on the log of the ratio of the equilibrium constants, eq 9, where K_3 and K_6 are the respective equilibrium constants for eqs 3 and 6.

$$\mathrm{RCo^{III}(P) + L \rightleftharpoons Co^{II}(P) + R^{\bullet} + L} \tag{5}$$

$$\mathrm{Co^{II}(P) + R^{\bullet} + L \rightleftharpoons Co^{II}(P)L + R^{\bullet}} \tag{6}$$

$$\mathrm{RCo^{III}(P)L \rightleftharpoons Co^{II}(P)\,L + R^{\bullet}} \tag{7}$$

$$\Delta G°_7 = -\Delta G°_3 + \Delta G°_5 + \Delta G°_6 \tag{8}$$

$$\Delta\Delta G°_{\text{6-coord-5-coord}} = -\Delta G°_7 - \Delta G°_5 = 2.303RT\log(K_3/K_6) \tag{9}$$

Our data establish that the equilibrium constant for coordination of an axial ligand to a Co(II) tetrapyrrole is greater than that for coordination to the corresponding alkyl−Co(III) tetrapyrrole. In this situation, eq 9 shows that ΔG for Co−C bond homolysis decreases upon ligand coordination. In other words, the “base-on” effect for cobalt tetrapyrroles simply reflects a greater stabilization by the base of the product of homolysis (Co(II) complex) than of the reactant (alkyl−Co(III) complex). Given that the transition state for homolysis is known to be very product-like,[35] stronger coordination in the Co(II) complex should also stabilize the transition state for homolysis relative to the reactant and thereby increase the rate of homolysis.

Although comparable data are not widely available for other alkylcobalt(III) complexes, there is no compelling reason to expect that the equilibrium constant for coordination to the alkylcobalt(III) complex, $K_{\mathrm{Co(III)}}$, will be larger than that for coordination to the corresponding unalkylated cobalt(II) complex, $K_{\mathrm{Co(II)}}$. In fact, the commonality of certain structural features for five- and six-coordinate alkylcobalt complexes[14] suggests that the relative magnitudes of $K_{\mathrm{Co(III)}}$ and $K_{\mathrm{Co(II)}}$ observed for cobalt tetrapyrroles could be general. Data for other complexes are lacking because it is unusual to find a ligand system that stabilizes both a true four-coordinate Co(II) complex and a true five-coordinate alkyl−Co(III) complex. In most cases, at least one form dimerizes or is strongly associated with a base or solvent. The ligand-binding equilibrium constants measured in these cases are really for displacement of one coordinated base by a second base. Measurements for adenosylcobinamide and cob(II)inamide in the coordinating solvent ethylene glycol show that pyridine and imidazole bases coordinate more strongly to the cobalt(II) form.[36]

The above analysis and our results contradict the rationalization advanced to explain the observation that increasing the strength of the base increases the apparent strength of the Co−C bond in cobaloxime complexes.[12,13] In point of fact, more basic ligands stabilize the Co(II) complex to a greater extent than they stabilize the Co(III) complex. The apparent increase in stability of alkylcobaloxime complexes with increasing base strength could be explained, though, if the sensitivity of $K_{\mathrm{Co(III)}}$ to the pK_a of the base is greater than that of $K_{\mathrm{Co(II)}}$. This is not unreasonable because stronger bases may be better able to compete against the strong trans-effect of the alkyl ligand than weak bases. If so, increasing the pK_a of the base would decrease the $\log(K_{\mathrm{Co(III)}}/K_{\mathrm{Co(II)}})$ term in eq 9, which in turn would decrease the destabilization of the six-coordinate alkyl complex relative to the five-coordinate alkyl complex. If the process in eq 7 was studied by itself, one would conclude that stronger bases stabilize the Co−C bond rather than recognize that they destabilize it less. The slopes of the $\log K_{\mathrm{Co(III)}}$ and $\log K_{\mathrm{Co(II)}}$ vs pK_a plots for OEP complexes are indistinguishable within error. However, this does not rule out a significant difference for cobaloxime complexes, which have much larger $K_{\mathrm{Co(III)}}$ values. Regardless of the explanation, it is not clear that the apparent increase in stability of alkylcobaloxime complexes with increasing base strength is relevant to B_{12} or other alkylcobalt complexes. Increasing base strength does not affect the base-on homolysis rate constant of adenosylcobinamide but increases the heterolysis rate constant.[37]

Alkyl Exchange. Alkyl transfer reactions have been reported previously for the cases of alkylcobalt(III) corrinoids and cobalt(II) corrinoids,[38,39] alkylcobalt(III) macrocycles (including cobaloximes) and cobalt(II) macrocycles,[40−43] and alkyliron(III) porphyrins and iron(II) porphyrins.[44] For corrinoids, exchange has only been demonstrated for methyl groups. A wider range of alkyl groups have been exchanged for cobalt macrocycles. An S_H2 transfer mechanism was suggested for these complexes. In contrast, a free-radical mechanism was proposed for the iron porphyrin complexes. Equilibrium constants for exchange of methyl groups between cobalt complexes containing different equatorial ligands are generally small but are not statistical (i.e., $K = 1$).[44−46]

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The results reported here are the first demonstration of alkyl exchange for cobalt porphyrins and hydroporphyrins. The reaction occurs for both base-on six-coordinate and base-off five-coordinate complexes. The stability of the Co−C bond increased with increasing saturation of the macrocycle for methyl complexes. Exchange also occurred for alkyl groups larger than methyl. Interestingly, exchange was slower for larger alkyl groups. In addition, the exchange reactions of cobalt porphyrins were more rapid than those of iron porphyrins, which are believed to have the weaker metal−carbon bonds. Both of these observations seem inconsistent with a free-radical mechanism for the exchange. An investigation of the mechanisms for alkyl exchange reactions of cobalt porphyrins will be reported in a subsequent paper.[47]

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Supporting Information Available: Text and equations presenting the derivation of eq 2 for analyzing data from the competitive NMR titration method. This material is available free of charge via the Internet at http://pubs.acs.org.

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