nocent role and induces strain in the supercoiled double helix to accelerate phosphate diester hydrolysis. Another factor could be the proximity effect of holding the metal ion near the phosphate diester backbone of DNA, which may accelerate the hydrolysis reaction.

Conclusions

We have presented evidence that the $Ni(tren)^{2+}$-catalyzed hydrolysis of phosphate diesters occurs by an intramolecular mechanism in contrast to that proposed for amino acid hydrolysis. The reaction is first-order in phosphate ester and in $Ni(tren)^{2+}$. Below pH 8.0 little activity is observed. Above pH 8.0 the rate increase is consistent with the generation of $Ni(tren)(OH)(OH_2)^+$ as the active catalyst. Nickel(II) complexes are much better in promoting hydrolysis than either Pd(II) or Pt(II) complexes in the order Ni(II) > Pd(II) > Pt(II). By contrast, $Cu(tren)^{2+}$ and $Zn(tren)^{2+}$ are ineffective as catalysts. The Pt(II) antitumor complexes are ineffective as catalysts. The relative catalytic activities of $Ni(bpy)^{2+}$, $Cu(bpy)^{2+}$, and $Zn(bpy)^{2+}$ parallel the pK_a of a metal-bound water molecule. The $Ni(tren)(OH)(OH_2)^+$ complex exhibits catalytic behavior to 85 turnovers and thereafter decreases in rate. The Pd(II) or Pt(II) complexes show no turnover activity. Rates of hydrolysis of phosphate diesters by the divalent cations examined are not by themselves sufficient to be useful in DNA hydrolysis.

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Supplementary Material Available: Tables and figures of kinetic data for hydrolysis of phosphate diesters by $Ni(tren)^{2+}$, $Pd(bpy)^{2+}$, $Pd(en)^{2+}$, and controls, kinetic schemes containing equations and text, a computer program with data from a simulation, and figures of typical titration curves (20 pages). Ordering information is given on any current masthead page.

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Base Binding to Zinc Picket Fence Porphyrins. Attractive Intramolecular Interactions in Organic Solvents[1]

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Thermodynamic values for the binding of pyridine and isoquinoline to α^4 and trans-α^2 atropisomers of four kinds of zinc(II) picket fence porphyrins, which contain pivalamido, (isopropylcarbonyl)amino, (neopentylcarbonyl)amino, or (butylcarbonyl)amino pickets, were determined in toluene. The binding constants K of the trans-α^2 complexes were remarkably larger than those of the corresponding α^4 complexes, depending on both shape and size of pickets; the stability enhancements by pivalamido pickets were a factor of 20 and 34 in K for pyridine and isoquinoline, respectively, while those by (butylcarbonyl)amino pickets were only a factor of 2.6 and 3.7. These stabilizations of the trans-α^2 complexes were due to increased binding energy ($-\Delta\Delta H$ = 0.8–2.3 kcal/mol), although accompanied by a slight decrease of entropy ($-\Delta\Delta S$ = 0.1–2.2 eu). It was concluded that the stability enhancements of the trans-α^2 complexes can be ascribed as the attractive intramolecular CH–π interactions induced by the London dispersion force in base adducts rather than solvation effects in the weakly polar solvent. Comparisons of the shape of picket fences with both thermodynamic values and ^1H NMR chemical shifts suggested that preorganization of the cavity is essential to the stability enhancements. The variation of binding constants in several noncoordinating solvents also suggested that desolvation processes upon the ligation of free base considerably affect the stability factor $K(\text{trans-}\alpha^2)/K(\alpha^4)$ in this case.

Introduction

Hydrophobic interactions are well-recognized to occur in certain biomolecules and provide the flexibility and specificity required in biochemical processes.[2] Recently, attention has also been directed toward the interactions in artificial systems containing a metal ion in order to understand the fundamental nature of substrates binding to metalloenzymes.[3,4] The contribution of these noncovalent interactions to binding energy (ΔH) may be small but critical to the organic inclusion complex formation[5-7] and also to the stereoselectivity or stability enhancements of metal complexes.[8,9] The nature of hydrophobic interactions are, however, not clear, since such attractive interactions have been observed only in water or polar nonaqueous solvents. This is probably due to the greater solvent liberation driving forces, although the London dispersion force may also play a significant role.[6,7] On the other hand, few works have dealt with porphyrin complexes for the purpose of studying the interactions, despite the importance of those compounds as native metalloenzymes in biological systems. Rather, the chemical behavior of most model porphyrin complexes has been investigated to mimic the biological functions of natural hemoproteins.

Picket fence porphyrin Fe(II) and Co(II) complexes, developed by Collman et al., are an excellent model of natural hemoproteins, and their static and dynamic properties have been studied extensively by using a variety of physicochemical methods.[10-12] These compounds have four atropisomers by the restricted rotation of the phenyl rings,[11] and some interesting points have appeared

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Table I. ASIS[a] Values of Porphyrins in ppm, Internal Me_4Si Reference

	picket fence			pyrrole
	CH	CH_2	CH_3	NH
$H_2(\alpha^4$-TpivPP)			−0.018	−0.122
$H_2(trans$-α^2-TpivPP)			0.215	−0.510
$H_2(\alpha^4$-TisoproPP)	0.720		0.347	−0.368
$H_2(trans$-α^2-TisoproPP)	0.950		0.331	−0.576
$H_2(\alpha^4$-TneoPP)		0.392	0.177	−0.344
$H_2(trans$-α^2-TneoPP)		0.472	0.160	−0.499
$H_2(\alpha^4$-TbutPP)		0.2–0.4	0.209	−0.411
$H_2(trans$-α^2-TbutPP)		0.2–0.7	0.162	−0.515

[a] $\delta(CDCl_3) - \delta$(toluene-d_8).

for the differences in chemical properties among these isomers.[1,13-18] Actually, comparisons of thermodynamic data for base binding among the atropisomers provide an opportunity to explore the interligand interactions between picket(s) and the base, and this approach may offer a simulation of substrates binding to metalloenzymes.

In earlier reports, we have shown that the binding constant for pyridine or 1-methylimidazole with Co(*trans*-α^2-TpivPP) is about 10-fold greater than that with the corresponding α^4 complex in toluene solution.[1,13] The stabilization of the trans-α^2 complex seems to be due to the two pivalamido pickets, which construct a cavity for base binding, because the base molecules may be forced to bind on the flat face of the α^4 complex.[12] We have also suggested that the stability enhancement of the trans-α^2 complex might be due to van der Waals contacts between the pickets and the ligated base, since other factors such as the difference in electronic nature or solvations between the two isomers may be less likely to account for the phenomenon.[1] The picket fence is composed of both amide and alkyl groups, and hence, which part of the pickets affects the base binding is still ambiguous.

In order to solve the question of whether attractive interligand interactions induced by the London force can really occur in weakly polar organic solvents, we introduced a variety of alkyl groups as pickets and determined the thermodynamic parameters for the binding of pyridine and isoquinoline to zinc(II) picket fence porphyrins (Figure 1). On base binding to zinc complexes with flat and modified porphyrins, it is generally accepted that the zinc porphyrins can bind only one N-base axial ligand as well as Co(II) porphyrins. Many works have been reported and have provided valuable information concerning the electronic nature of porphyrin complexes and solvation effects along with thermodynamics in organic solvents.[18-25] For example, peak positions and intensity ratios of α and β bands in visible spectra reflect the electronic nature of zinc porphyrins[23,25] and the effect of solvent on base binding to flat porphyrin complexes in toluene or benzene is estimated to be smaller than 1.8 kcal/mol in ΔH.[24] Comparisons of thermodynamic parameters between the two atropisomers, involving these factors, will be made. Thereby, the elucidation of the interligand interactions that operate molecular recognition mechanisms within the cavities is the main subject of this work.

Table II. Association Constants with Toluene in $CDCl_3$

	K		
compd[a]	CH_2	CH_3	NH, pyrrole
$H_2(trans$-α^2-TpivPP)		0.23 ± 0.06	0.07 ± 0.02
$H_2(\alpha^4$-TisoproPP)		0.12 ± 0.03	0.04 ± 0.01
$H_2(trans$-α^2-TisoproPP)		0.14 ± 0.03	0.08 ± 0.02
$H_2(\alpha^4$-TneoPP)	0.06 ± 0.02	0.11 ± 0.02	0.03 ± 0.01
$H_2(trans$-α^2-TneoPP)	0.12 ± 0.03	0.18 ± 0.05	0.08 ± 0.02
$H_2(\alpha^4$-TbutPP)			0.01 ± 0.01
$H_2(trans$-α^2-TbutPP)			0.05 ± 0.01

[a] Association constants for $H_2(\alpha^4$-TpivPP) were not determined because of the small ASIS value.

Table III. ^1H NMR Shifts of Pyridine and Ligated Pyridines in $CDCl_3$[a]

compd	α_H	β_H	γ_H
Zn(α^4-TpivPP)(py)	2.67	5.70	6.52
Zn(*trans*-α^2-TpivPP)(py)	2.56	5.66	6.47
Zn(α^4-TisoproPP)(py)	2.47	5.63	6.48
Zn(*trans*-α^2-TisoproPP)(py)	2.58	5.65	6.42
Zn(α^4-TneoPP)(py)	2.52	5.65	6.50
Zn(*trans*-α^2-TneoPP)(py)	2.64	5.71	6.5[b]
Zn(α^4-TbutPP)(py)	2.47	5.63	6.47
Zn(*trans*-α^2-TbutPP)(py)	2.67	5.68	6.50
C_5H_5N[c]	8.58	7.21	7.62

[a] δ in ppm. [b] Overlapped with amide signal. [c] Reference 20.

Experimental Section

Materials. Toluene, chlorobenzene, *o*-dichlorobenzene, and dichloromethane were distilled from molecular sieves (4 Å). Pyridine and piperidine were distilled from CaH_2. Isoquinoline was purified by distillation.

Each of the two atropisomers (α^4 and trans-α^2) of picket fence porphyrins was prepared according to the literature.[13] Zinc was incorporated by treating the metal-free porphyrins with $ZnCl_2$ in tetrahydrofuran containing a small amount of 2,6-lutidine at 50 °C for 0.5–3 h. Purification was carried out by silica gel column chromatography. The absence of isomerization during the metal insertion reaction was confirmed by TLC and ^1H NMR spectroscopy.

Measurements. Proton NMR spectra were measured on a JEOL JMN-FX-100 or a JEOL JMN-GSX-400 spectrometer. Association constants of metal-free porphyrins with toluene were obtained according to the literature.[5a] Visible absorption spectra were recorded on a Hitachi 340 spectrophotometer. The binding constants for pyridine, isoquinoline, and piperidine were determined as described elsewhere.[1]

Results

Table I lists the ASIS[26] (aromatic induced chemical shifts) values of metal-free porphyrins. The association constants of porphyrins with toluene obtained at the toluene concentration of 0.5–3 M are listed in Table II. These constants are very small, probably due to the stronger toluene–chloroform interactions, but substantial differences are found between the α^4 and trans-α^2 atropisomers. Figure 2 shows ^1H NMR spectra of Zn(TpivPP)s and their pyridine adducts. In accordance with the results obtained for Zn(TPP),[20] the observed chemical shifts of pyridine protons are a weighted average of the chemical shifts of ligated and unligated pyridines because of rapid ligand exchange on the NMR time scale. Even at −80 °C, only the line broadening of base signals and the picket alkyl proton signal (Zn(*trans*-α^2-TpivPP)(iqu) in toluene-d_8) was observed. At less than a stoichiometric quantity of pyridine, with the high binding constants dealt with here,[18] there is essentially no free pyridine (Figure 2B). Contrary to this, there is no four-coordinate complex at higher concentration of pyridine than zinc (Figure 2C). Thus, the chemical shifts of ligated pyridine and four- and five-coordinate complexes were readily obtained and are listed in Tables III and IV, respectively. It should be noted that the observed chemical shifts of the base adducts of the trans-α^2 complexes are also an

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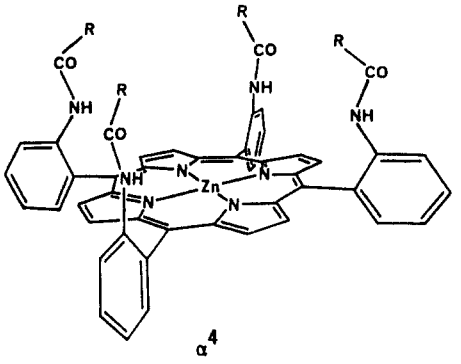
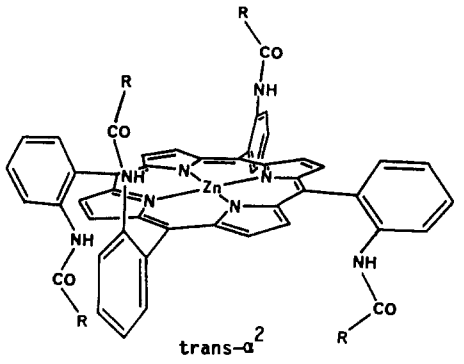




R = $C(CH_3)_3$ Zn(TpivPP)

$CH(CH_3)_2$ Zn(TisoproPP)

$CH_2C(CH_3)_3$ Zn(TneoPP)

$(CH_2)_3CH_3$ Zn(TbutPP)

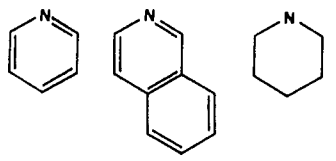


Figure 1. Zinc picket fence porphyrins and bases used.

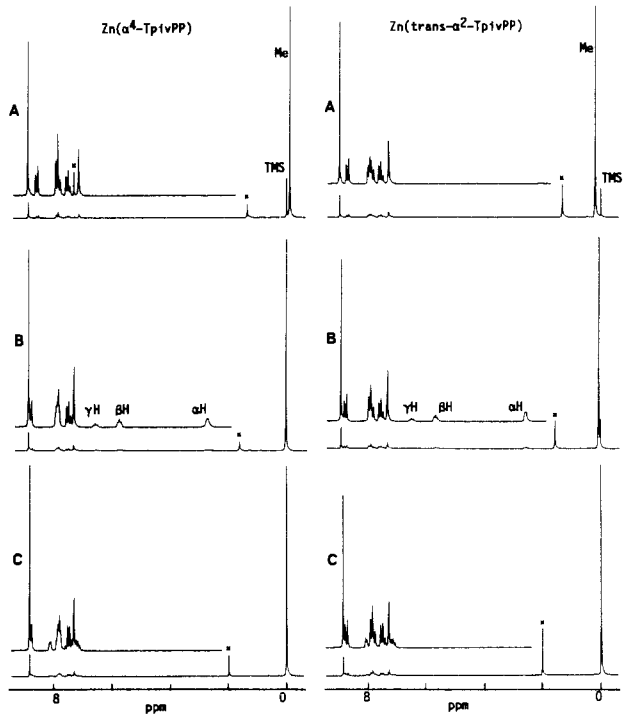


Figure 2. ^1H NMR spectra of Zn(TpivPP)s and their pyridine adducts in $CDCl_3$: A, four-coordinate complex (ZnP); B, ZnP plus py (1/0.7); C, ZnP plus py plus py-d_5 (1/0.7/20).

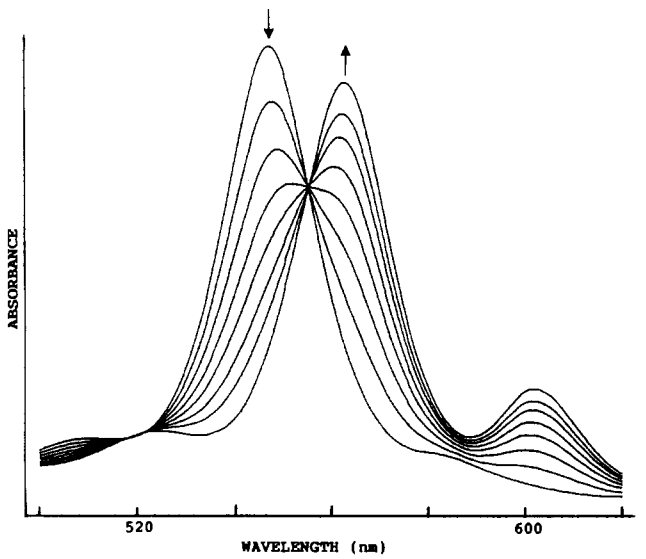


Figure 3. Visible spectra of Zn(*trans*-α^2-TpivPP) in toluene as aliquots of pyridine are added.

average of the chemical shifts of ligated and unligated binding sides on the porphyrin plane. Upon the ligation of aromatic base, the picket proton signals of the α^4 complexes shift to downfield, whereas those of the trans-α^2 complexes show smaller downfield or upfield shifts because of π-current shielding effects by the ligated base.

Figure 3 shows visible spectral changes upon N-base titration to Zn(*trans*-α^2-TpivPP). In all of the titrations examined, good isosbestic points were observed. The peak positions and the intensity ratios of the α and β bands are summarized in Table V. The competition reaction of base against a trace amount of water would affect thermodynamic values for base binding. This factor, however, should be negligible since the absorption ratios of base free porphyrin complex to its base adduct were fairly constant in the temperature range examined. In contrast with the case of Zn(TPP) for which the ligation of a water molecule is not observed even in dilute toluene solution,[23] at low temperature, a water molecule ligates to Zn(*trans*-α^2-TpivPP) as shown in Figure 4. Interestingly, Zn(α^4-TpivPP) did not show such spectral changes under similar experimental conditions, suggesting that the affinity of water for the trans-α^2 complex is considerably higher than that for the α^4 complex.

The thermodynamic values for the binding of pyridine and isoquinoline were obtained from the temperature dependence (14–46 °C) of binding constants and are summarized in Table VI. The binding constants for piperidine are listed in Table VII. Table IX gives the binding constants for pyridine in several noncoordinating solvents.

Discussion

Base Binding to α^4 Complexes. First, a comparison is made on the binding constants among the α^4 complexes. Collman et al. have reported that an N-base axial ligand may be forced to bind preferentially to the flat side of M(α^4-TpivPP) (M = Fe(II), Co(II)) because of steric barriers from the pickets.[10,11] However,

Table IV. ^{1}H NMR Shifts of Zinc Porphyrins in $CDCl_3$

compd	CH (pyrrole)	phenyl H *o*	phenyl H *m*	phenyl H *p*	NH (amide)	CH	CH_2	CH_3
Zn(α^4-TpivPP)	8.84	8.55	7.81	7.74	7.10			0.11
Zn(α^4-TpivPP)(py)	8.80	8.77	7.80	7.42	7.26			0.00
Zn(α^4-TpivPP)(iqu)	8.82	8.77	nd[a]	nd	nd			0.00
Zn(α^4-TpivPP)(pip)	8.81	8.77	7.83	7.47	7.17			−0.04
Zn(*trans*-α^2-TpivPP)	8.93	8.67	7.87	7.52	7.26			0.20
Zn(*trans*-α^2-TpivPP)(py)	8.83	8.73	7.82	7.49	7.27			0.01
Zn(*trans*-α^2-TpivPP)(iqu)	8.86	8.73	nd	nd	nd			−0.17
Zn(*trans*-α^2-TpivPP)(pip)	8.82	8.78	7.75	7.50	7.7			0.40
Zn(α^4-TisoproPP)	8.76	8.41	7.76	7.42	6.91	1.08		0.15
Zn(α^4-TisoproPP)(py)	8.83	8.80	7.79	7.41	7.08	1.25		0.41
Zn(α^4-TisoproPP)(iqu)	8.85	8.80	nd	nd	7.10	1.23		0.38
Zn(α^4-TisoproPP)(pip)	8.85	8.80	7.82	7.45	7.04	nd		0.42
Zn(*trans*-α^2-TisoproPP)	8.87	8.55	7.85	7.51	6.72	1.20		0.22
Zn(*trans*-α^2-TisoproPP)(py)	8.84	8.68	7.87	7.51	6.69	0.96		0.12
Zn(*trans*-α^2-TisoproPP)(iqu)	8.86	8.67	nd	nd	6.59	0.67		−0.09
Zn(*trans*-α^2-TisoproPP)(pip)	8.83	8.76	7.82	7.47	7.13	nd		0.49
Zn(α^4-TneoPP)	8.85	8.63	7.78	7.44	6.85		1.19	0.24
Zn(α^4-TneoPP)(py)	8.82	8.85	7.76	7.38	6.99		1.26	0.42
Zn(α^4-TneoPP)(iqu)	8.83	8.85	nd	nd	7.02		1.25	0.42
Zn(α^4-TneoPP)(pip)	8.83	8.85	7.77	7.42	6.95		1.25	0.42
Zn(*trans*-α^2-TneoPP)	8.84	8.54	7.85	7.51	6.48		0.98	0.10
Zn(*trans*-α^2-TneoPP)(py)	8.81	8.76	7.85	7.49	6.58		0.92	0.18
Zn(*trans*-α^2-TneoPP)(iqu)	8.83	8.77	nd	nd	6.57		0.73	0.00
Zn(*trans*-α^2-TneoPP)(pip)	8.81	8.77	7.82	7.46	7.00		1.25	0.46
Zn(α^4-TbutPP)	8.78	8.40	7.75	7.42	6.76		1.1–0.7	0.15
Zn(α^4-TbutPP)(py)	8.83	8.77	7.81	7.42	6.94		1.3–0.7	0.34
Zn(α^4-TbutPP)(iqu)	8.85	8.81	nd	nd	6.98		1.3–0.7	0.34
Zn(α^4-TbutPP)(pip)	8.85	8.78	7.83	7.46	6.93		nd	0.35
Zn(*trans*-α^2-TbutPP)	8.80	8.40	7.78	7.49	6.53		1.0–0.4	0.05
Zn(*trans*-α^2-TbutPP)(py)	8.82	8.69	7.79	7.48	6.59		1.0–0.6	0.19
Zn(*trans*-α^2-TbutPP)(iqu)	8.85	8.68	nd	nd	6.55		0.8–0.2	0.09
Zn(*trans*-α^2-TbutPP)(pip)	8.82	8.74	7.83	7.47	7.04		nd	0.36

[a] Not determined because of overlapping with other signals.

Table V. Peak Positions (nm) and Intensity Ratios of the α and β bands of Zinc Porphyrins in Toluene

compd	4-coord[a] λ_β	py adduct λ_α	py adduct λ_β	py adduct A_β/A_α	iqu adduct λ_α	iqu adduct λ_β	iqu adduct A_β/A_α	pip adduct λ_α	pip adduct λ_β	pip adduct A_β/A_α
Zn(α^4-TpivPP)	546.5	597.5	559.5	5.93	597.5	560.0	5.90	599.5	561.5	5.11
Zn(*trans*-α^2-TpivPP)	547.0	602.0	562.5	3.85	602.0	562.5	3.82	605.0	565.0	3.37
Zn(α^4-TisoproPP)	548.5	599.0	561.0	5.01	599.0	561.0	4.94	601.0	562.5	4.35
Zn(*trans*-α^2-TisoproPP)	547.5	599.0	560.5	4.39	599.0	561.0	4.37	602.0	562.5	3.79
Zn(α^4-TneoPP)	547.5	598.0	560.5	5.59	598.0	561.0	5.54	600.0	562.0	4.69
Zn(*trans*-α^2-TneoPP)	546.0	597.5	560.0	5.12	597.5	559.5	5.13	600.5	562.0	4.28
Zn(α^4-TbutPP)	549.0	600.0	562.0	4.69	599.5	561.5	4.64	602.0	563.5	4.02
Zn(*trans*-α^2-TbutPP)	547.5	597.5	560.0	5.17	598.0	560.0	5.14	601.0	562.5	4.13

[a] The α band of four-coordinate complexes was observed as a shoulder near 584 nm.

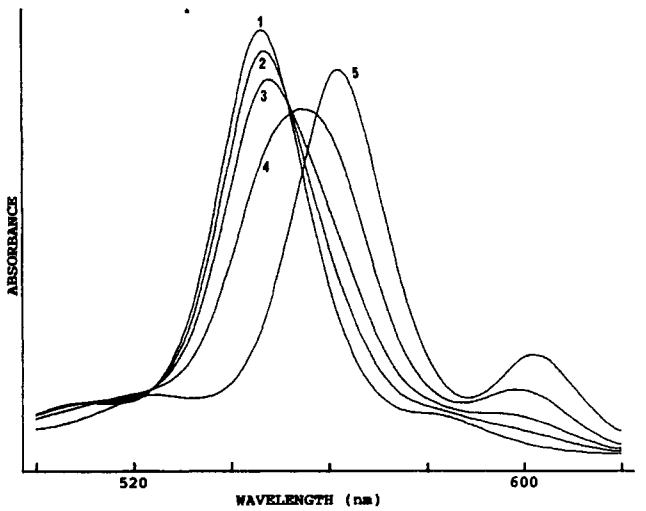
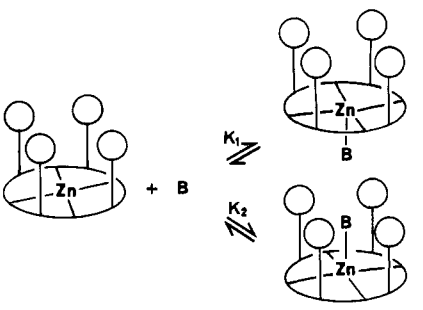


Figure 4. Visible spectra of Zn(*trans*-α^2-TpivPP): 1, compound in dry toluene at 25 °C; 2–4, compound in dilute toluene at 15, 0, and −15 °C, respectively; 5, Zn(*trans*-α^2-TpivPP)(py) adduct.

they have also shown that the base molecule as the sixth ligand can bind to the protected side of the iron complex.[10] In the present case, small differences are observed in the binding constants for both pyridine and isoquinoline among the α^4 complexes, although ΔH and ΔS values are very similar (Table VI). One conceivable explanation for the differences is that the observed binding constant K may reflect a mixture of two different types of equilibrium because of the asymmetrical distribution of the pickets between the two sides of the porphyrin plane



where the apparent K approximates to $K_1 + K_2$.

Table VI. Thermodynamic Values for Base Binding to Zinc Porphyrins in Toluene

	py binding			iqu binding		
compd	K,[a] L/mol	ΔH, kcal/mol	ΔS,[a] cal/(mol K)	K,[a] L/mol	ΔH, kcal/mol	ΔS,[a] cal/(mol K)
Zn(α^4-TpivPP)	2.4×10^4	-10.6 ± 0.2	-15.4 ± 0.6	3.1×10^4	-10.5 ± 0.2	-14.8 ± 0.4
Zn(*trans*-α^2-TpivPP)	4.8×10^5	-12.6 ± 0.4	-16.2 ± 1.2	1.0×10^6	-12.8 ± 0.3	-15.3 ± 0.9
Zn(α^4-TisoproPP)	4.1×10^4	-10.6 ± 0.2	-14.6 ± 0.5	5.4×10^4	-10.4 ± 0.1	-13.3 ± 0.4
Zn(*trans*-α^2-TisoproPP)	1.9×10^5	-11.8 ± 0.2	-15.4 ± 0.5	4.6×10^5	-11.9 ± 0.1	-13.9 ± 0.4
Zn(α^4-TneoPP)	2.7×10^4	-10.5 ± 0.1	-15.1 ± 0.3	3.6×10^4	-10.3 ± 0.3	-13.8 ± 0.9
Zn(*trans*-α^2-TneoPP)	1.1×10^5	-12.0 ± 0.2	-17.2 ± 0.6	2.2×10^5	-12.1 ± 0.2	-16.0 ± 0.6
Zn(α^4-TbutPP)	3.6×10^4	-10.4 ± 0.1	-13.9 ± 0.3	5.0×10^4	-10.3 ± 0.2	-13.1 ± 0.6
Zn(*trans*-α^2-TbutPP)	1.0×10^5	-11.3 ± 0.2	-15.2 ± 0.5	1.9×10^5	-11.1 ± 0.2	-13.2 ± 0.6
Zn(TPP)[b]	3.9×10^3[c] 6.0×10^3[d]	-8.8[c]	-13[c]			

[a] At 25 °C. [b] In benzene. [c] Reference 21. [d] Reference 20.

Table VII. Equilibrium Data for Piperidine Binding to Zinc Porphyrins in Toluene

compd	K(25 °C), L/mol	compd	K(25 °C), L/mol
Zn(α^4-TpivPP)	4.1×10^5	Zn(*trans*-α^2-TneoPP)	2.9×10^5
Zn(*trans*-α^2-TpivPP)	2.9×10^5	Zn(α^4-TbutPP)	5.9×10^5
Zn(α^4-TisoproPP)	6.1×10^5	Zn(*trans*-α^2-TbutPP)	3.7×10^5
Zn(*trans*-α^2-TisoproPP)	5.1×10^5	Zn(TPP)	1.1×10^5[a]
Zn(α^4-TneoPP)	4.1×10^5		

[a] In benzene; ref 20.

To solve the question, we evaluated the binding constants for a bulkier base piperidine (Table VII). Interestingly, the ratios K_{py}/K_{pip} and K_{iqu}/K_{pip} among the α^4 complexes are the same within experimental error. Further, K_{py}/K_{pip} are in fair agreement with that of Zn(TPP). These results have two explanations: first, that steric repulsions between the pickets and the base bound on the protected side do not control K, although K_2 may not be so small, or second, that K_2 is too small to affect K. The first explanation is less likely, since the steric repulsions should decrease substantially the binding of the bulky base piperidine.[1] Consequently, the equilibrium between N-base and zinc ion on the protected side of the porphyrin plane may be, if any, negligible. This suggestion is definitively supported by the fact that the alkyl protons of the α^4 pickets are not influenced by π-current shielding of the aromatic bases (Table IV), since these bases bound on the protected side should give rise to a substantial upfield shift of picket signals.[27] Thus, the equilibrium on the unprotected side of the porphyrin plane reflects the thermodynamic values of the α^4 complexes. Therefore, the small differences in the binding constants among the α^4 complexes are attributed mainly to the electron donor effects from pickets as can be seen in the spectral data in Table V, although the disorder of Zn(α^4-TisoproPP) in a series of Hammet σ^* constants of pickets is not clear at present. The difference of the binding constants between pivalamido and (butylcarbonyl)amino picket fence porphyrins is also in good agreement with the results obtained from α^4-type "jellyfish" porphyrin complexes[15] in which one face of the porphyrin plane is completely protected by both one cross-linked alkyl chain and two pickets.[28]

Solvation of Four-Coordinate Complexes. Before discussing the base-binding aspects between the α^4 and trans-α^2 complexes, it is necessary to explore the solvation effects in toluene and the difference of electronic nature between the two atropisomers, since both factors might regulate the thermodynamic values for the base binding to these complexes. The first suggestion of solvation effects was given by Sternhell and co-workers.[29] On the thermal equilibria among the four atropisomers with ortho-substituted TPPs, the ratio of the concentration of trans-α^2 isomer to that of the α^4 isomer in toluene, xylenes, and mesitylene (5/1) was found to deviate considerably from the statistical abundance (1/1),[30] and the deviation may be attributed to the difference between the solvation of the two isomers, since the ratio is approximately 1/1 in dimethylformamide.[29] This fact suggests that trans-α^2 isomer may be better solvated in aromatic solvents than the corresponding α^4 isomer. In earlier reports, a ^{1}H NMR study showed that an aromatic solvent molecule may insert between two pickets of H_2(*trans*-α^2-TpivPP) and its Co(II) complex;[1] accordingly the O_2 affinity of Co(*trans*-α^2-TpivPP)(1-MeIm) in aromatic solvents decreases relative to that in nonaromatic solvent with similar dielectric constant.[17] Further evidence is provided by the ^{1}H NMR study, as shown in Tables I and II. The trans-α^2 isomers with both faces protected give more negative ASIS values for pyrrole NH than the corresponding α^4 isomers.[31] Judging from this result and the similarity of the chemical shifts of pickets between H_2(*trans*-α^2-TxPP) in toluene and Zn(*trans*-α^2-TxPP)(py) in chloroform, it is best explained, in this case, that the solvent molecule toluene inserts into the cavity and then stands perpendicular to the porphyrin plane of the trans-α^2 isomers. This proposal is not surprising, since similar phenomena occur in a few cases for organic compounds that are capable of forming inclusion complexes.[7,32] Actually, the association constants of the trans-α^2 isomers with toluene are substantially higher than those of the corresponding α^4 isomers, indicating that the trans-α^2 isomer is better solvated in toluene solution than the corresponding α^4 isomer. This finding also provides support for the earlier suggestion on the existent ratio of the atropisomers in thermal equilibria. Thus, in toluene, the solvation factor should reduce, by a few-fold, the binding constants of trans-α^2 complexes compared with the binding constants of the corresponding α^4 complexes.

Electronic Difference between Two Isomers. In visible spectra of zinc porphyrins, the intensities of the α and β bands of Zn(TPPs)(B), as well as their positions, vary with both charge and polarizability of the axial ligand (B)[23] and are correlated well with

(27) ^{1}H NMR data for Zn(*cis*-α^2-TpivPP): methyl chemical shifts of the four-coordinate complex, pyridine adduct, and isoquinoline adduct were 0.10, 0.08, and −0.03 ppm, respectively. This observation suggests that the aromatic base ligand on the protected side of the α^4 complexes should give rise to a similar upfield shift of the alkyl protons, although the methyl signals of the cis-α^2 complex are also an average of the chemical shifts of the coordinating and noncoordinating sides.

(28) (a) The short strap employed has been shown to be effective in preventing coordination on one side, but this is not the case for a longer strap. See refs 15 and 28b. (b) Momenteau, M.; Loock, B.; Tetreau, C.; Lavalette, D.; Croisy, A.; Schaeffer, C.; Huel, C.; Lhoste, J. *J. Chem. Soc., Perkin Trans. 2* **1987**, 249.

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(30) (a) Freitag, R. A.; Mercer-Smith, J. A.; Whitten, D. G. *J. Am. Chem. Soc.* **1981**, *103*, 1226. (b) Freitag, R. A.; Whitten, D. G. *J. Phys. Chem.* **1983**, *87*, 3918.

(31) One possible explanation for this result is that the pyrrole NH signals of the α^4 isomers might appear upfield in toluene solution by π-current shielding of the solvated toluene, which may lie above the porphyrin plane, as had been shown in crystal structures of porphyrins.[31a,b] However, an NMR study[31c,d] has shown that the solvation of TPPs in aromatic solvents is very weak and occurs on the porphyrin periphery (pyrrole ring), and hence, this geometry of the solvent molecule should not affect the pyrrole NH signals. (a) Scheidt, W. R.; Kastner, M. E.; Hatano, K. *Inorg. Chem.* **1978**, *17*, 706. (b) Scheidt, W. R.; Reed, C. A. *Ibid.* **1978**, *17*, 710. (c) Fulton, G. P.; La Mar, G. N. *J. Am. Chem. Soc.* **1976**, *98*, 2119. (d) Fulton, G. P.; La Mar, G. N. *Ibid.* **1976**, *98*, 2124.

(32) Jarri, E. T.; Whitlock, H. W. *J. Am. Chem. Soc.* **1982**, *104*, 7196.

Table VIII. Ratios of Equilibrium Constants

	K(trans-α^2)/K(α^4)		K_{iqu}/K_{py}	
picket	py	iqu	trans-α^2	α^4
piv	20	34	2.14	1.25
isopro	4.7	8.7	2.45	1.32
neo	4.0	6.3	2.08	1.35
but	2.6	3.7	1.88	1.33

the electronic nature of the porphyrins.[25] In this case, there are small differences between the trans-α^2 and α^4 complexes, but no trend can be found for these complexes (Table V). This result indicates that the porphyrin acidities of each isomer are essentially similar, as previously suggested by us[1,14] and others.[16] The observed maximum difference in the spectral data between two isomers may correspond to only less than 2-fold in K, as seen for the difference among the α^4 complexes. The red shifts of peak positions and small A_β/A_α values for base adducts of Zn(*trans*-α^2-TpivPP), which should *decrease* the binding constants for bases,[18,25] are probably caused by the steric interactions between the pickets and the bases.

The chemical shifts of ligated pyridine are regarded as a measure of the magnitude of π-current shielding effect by the porphyrin plane and reflect the distance between the mean porphyrin plane and the pyridine molecule.[20] There was little difference among the complexes examined, suggesting that the ligated pyridine is in a spatially similar environment for each complex, except for the angle of the base plane relative to the N_p–Zn–N_p plane (N_p: pyrrole nitrogen) in which the restricted orientation of the base in the trans-α^2 complexes may rather decrease the binding constant.[15,33] Thus, electronic and structural differences between the two isomers should have little effect on Zn–base bond strength.

Comparison of Picket Fence Porphyrins with Flat Porphyrins. The base affinities of the picket fence porphyrin complexes are obviously higher than those of Zn(TPP). A similar result has also been observed for Co(II) analogues.[1] Since the electron-withdrawing effects of amide groups are not so large,[25] the stability enhancements of the α^4 complexes may come from a "through space" effect of amide dipoles, which enhances the binding of base to the opposite side of the porphyrin plane.[34] This effect, however, should reduce the base affinities of trans-α^2 complexes compared with those of the corresponding α^4 isomers.[1,34]

Intramolecular Interactions. Of particular interest is the comparison of thermodynamic values of the two isomers. In all of the cases examined, the trans-α^2 complexes exhibit considerably higher base affinity for pyridine and isoquinoline than the corresponding α^4 complexes (Table VIII). It may be worthwhile to note that there is a small statistical factor arisen from the blocking of ligation to the one side of the α^4 complexes, which effects K and ΔS by a half and 1.4 eu decrease, respectively, for the α^4 complexes.[1] The stability enhancements of the trans-α^2 complexes are undoubtedly contributable to the increased binding energy ($-\Delta H$), whereas a slight decrease in ΔS accompanies it (Table VI). The increases in both K and $-\Delta H$ values apparently depend on the shape and size of pickets, where the most effective picket examined here is the pivalamido group, of which the acidity of amide NH is the lowest in these complexes. Further, in accordance with our previous suggestion,[14] the amide groups of pivalamido pickets should be the farthest from the central metal, since the NH chemical shifts of Zn(*trans*-α^2-TpivPP) and its base adducts appear to be at lowest field in these complexes, where the chemical shifts of amide proton should be closely correlated with the magnitude of the ring current shielding effects by the porphyrin plane.[35] Thus, it is unlikely to assume that the difference of amide dipoles affects the base binding to the trans-α^2 complexes. Therefore, the stability enhancements may be attributable to the London force (CH–π interactions) between the base and the alkyl groups of pickets. Further evidence is clearly given by comparing the binding constants for pyridine and isoquinoline.

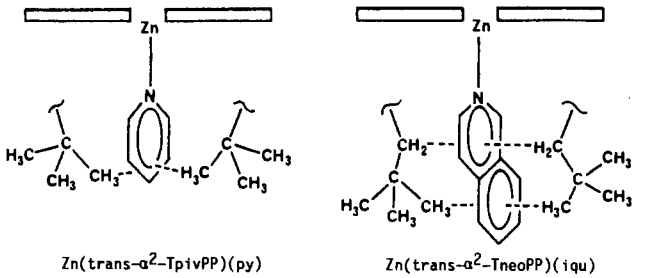


Figure 5. Possible (schematic) representation of the intramolecular CH–π interactions.

Isoquinoline (pK_a = 5.38) is slightly more basic than pyridine (pK_a = 5.22),[36] but the structures of the two bases should not affect differently the porphyrin plane. In fact, spectral data are very similar for both pyridine and isoquinoline adducts. On the basis of the linear relationship between log K vs pK_a value of amine,[22b] the ratio of binding constants K_{iqu}/K_{py} for the α^4 complexes (1.25–1.35) is in good agreement with that estimated from the difference of the amine basicities. In the cases of trans-α^2 complexes, however, K_{iqu}/K_{py} values are in the range 1.88–2.45, indicating that the inconsistency of these values is caused by the increased π system of isoquinoline compared to pyridine and that a more effective *complementarity* between the pickets and isoquinoline has been achieved in the trans-α^2 complexes. As Sigel et al. have shown,[8c] the magnitude of CH–π interactions may be correlated with the upfield shift of alkyl proton signal by π-current shielding effects of aromatic ligands. Accordingly, the picket alkyl protons of Zn(*trans*-α^2-TxPP)(iqu) give rise to remarkable upfield shifts compared to the shifts of the corresponding pyridine adducts, and downfield shifts are observed for the piperidine adducts. These facts definitively support the explanation that CH–π interactions between the ligated base and the pickets enhance the base affinity of the trans-α^2 complexes. Thus, the differences in the thermodynamic values between the two isomers originate mainly from these interactions in which both negative ΔH and ΔS values should be given.

On the details of the thermodynamic values, we expected that neopentyl pickets would better enhance the isoquinoline binding as shown in Figure 5. Similarly, isopropyl groups are capable of interacting with bases in the same manner as pivalamido pickets, and thus, similar ΔH and more negative ΔS values compared with Zn(*trans*-α^2-TpivPP) would also be expected. Proton NMR data show that the methyl proton signals of neopentyl and isopropyl pickets in base adducts give smaller upfield shifts than the signal of pivalamido pickets, suggesting that a weakness of CH–π interactions in Zn(*trans*-α^2-TisoproPP)(B) and Zn(*trans*-α^2-TneoPP)(B) exists. Therefore, it seems reasonable to explain that the rigidity of the cavity is necessary for the stabilization of base binding and that, as Cram et al. have pointed out,[37] *preorganization* of the cavity is also essential to the stability enhancements of these complexes. Since the base binding to the trans-α^2 complexes does not attend the reorganization of pickets and, hence, does not encompass its entropic contribution, the observed ΔS values are similar among these complexes, whereas the binding energy $-\Delta H$ varies with the magnitude of van der Waals contacts.

It is interesting to note that the stabilization of the trans-α^2 complexes is not observed for piperidine binding and that the cavities of these complexes discriminate among base molecules on the basis of their molecular dimensions. This is probably due to steric repulsions between piperidine and the pickets[1] and/or weaker alkyl–alkyl interactions compared to CH–π interactions.[4]

(33) Scheidt, W. R.; Chipman, D. M. *J. Am. Chem. Soc.* **1986**, *108*, 1163.
(34) Lexa, D.; Momenteau, M.; Saveant, J. M.; Xu, F. *J. Am. Chem. Soc.* **1986**, *108*, 6937.
(35) Momenteau, M.; Loock, B.; Huel, C.; Lhoste, J. *J. Chem. Soc., Perkin Trans. 1* **1988**, 283.
(36) *Kagakubinran Kisohen*; 2nd ed.; Maruzen: Tokyo, 1975; p 997.
(37) Cram, D. J.; Kaneda, T.; Helgeson, R. C.; Brown, S. B.; Knobler, C. B.; Maverick, E.; Trueblood, N. *J. Am. Chem. Soc.* **1985**, *107*, 3645.

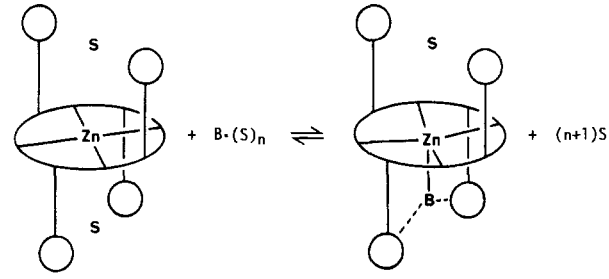
Table IX. Equilibrium Data for Pyridine Binding to Zinc Porphyrins in Several Solvents

compd	K, L/mol			
	$CH_3C_6H_5$	o-$Cl_2C_6H_4$	ClC_6H_5	CH_2Cl_2
Zn(α^4-TpivPP)	2.4×10^4	3.4×10^4 (0.7)[a]	3.1×10^4 (0.8)	5.1×10^4 (0.5)
Zn(*trans*-α^2-TpivPP)	4.8×10^5	2.6×10^5 (1.9)	2.1×10^5 (2.3)	9.3×10^4 (5.2)
Zn(α^4-TneoPP)	2.7×10^4	2.4×10^4 (1.1)	2.5×10^4 (1.1)	5.0×10^4 (0.5)
Zn(*trans*-α^2-TneoPP)	1.1×10^5	6.0×10^4 (1.8)	5.3×10^4 (2.1)	2.5×10^4 (4.4)

[a] K(in toluene)/K values are in parentheses.

Effects of Solvent on Stability Enhancements. Finally, we explored the effects of solvent on the attractive intramolecular interactions (Table IX). A striking feature of our data is that the ratio of binding constants K (in toluene)/K depends on isomeric structure of porphyrin but not on either the shape or size of pickets. The amide groups of these complexes are quite capable of powerful hydrogen-bonding phenomena,[14,28b] and these polar groups may interact with polar solvents or traces of water. This might cause the difference of solvation effects between the two isomers, since only the trans-α^2 complexes could involve such hydrogen-bond formation or cleavage upon base addition. However, our previous work concerning the oxygenation of Co(II) analogues has shown that no specificity resulting from such interactions was observed and that only the solvent polarity affects slightly the O_2 affinities.[17] Hence, the solvation phenomena of the free base, four- and five-coordinate complexes are responsible for the variation of the observed binding constants.

If desolvation from four-coordinate species mainly affected the pyridine binding, K values for both α^4 and trans-α^2 complexes would have similar trends according to solvent, although the magnitude of solvation of four-coordinate complexes is somewhat different for the two isomers as stated earlier. Therefore, this phenomenon can be understood in terms of desolvation processes upon ligation of free base. The base molecule must release solvent molecule(s) on going into the binding pocket of the trans-α^2 complexes and lose $-\Delta H$ and $-\Delta S$ in the desolvation process, while the gained attractive interactions between the pickets and the bases would produce negative ΔH and ΔS as thermodynamic functions. Since the attractive interactions should be independent of solvent, the variation of binding constants of the trans-α^2 complexes with solvent may be reflected mainly according to the magnitude of solvation of unligated base. Thus, in the polar solvent that strongly solvates pyridine molecule, the binding constants of the trans-α^2 complexes will decrease considerably. In fact, the stability enhancement by pivalamido pickets is only less than 2-fold in dichloromethane, and destabilization is found for Zn(*trans*-α^2-TneoPP) in the solvent. Interestingly, this observation is contrary to the previous results that attractive intramolecular interactions become strong with solvent polarity, in which solvent–solute interactions may act as a driving force.[7,8,32] Even in toluene solution, this phenomenon should occur. As seen in Table VI, the ΔH and ΔS values of the trans-α^2 complexes formed from pyridine and isoquinoline binding are very similar. This result can be also understood by the fact that larger isoquinoline molecule is better solvated than pyridine in the solvent. As a whole, the equilibrium between the trans-α^2 complexes and base in toluene is schematically as follows:



Since the base binding to the trans-α^2 complexes encompasses these solvent liberation processes, the observed stability enhancement may be smaller than the net contribution from the attractive intramolecular interactions.

Concluding Remarks. The attractive intramolecular interactions induced by the London force (CH–π interactions here) occur in weakly polar organic solvents, and these interactions can potentially affect thermodynamic properties on base binding. However, the observed stability enhancement by the interactions is subtle, depending on the preorganization of the cavity, along with the shape and size of pickets, and is also sensitive to the solvent nature concerning the solvation of unligated base. In a few cases, similar increments of binding constant have been observed by introducing peripheral substituent(s) to the ortho position of TPP derivatives.[15,24,38] Walker et al. ascribed this phenomenon to solvation effects in toluene.[24] However, our present work definitively shows that intramolecular interactions occur, at least partly, in those cases.

In biological systems, substrates binding to metalloenzymes may proceed in a hydrophobic pocket constructed with amino acid residues. Hence, the attractive intramolecular interactions presented here have also the potential to act as a specific driving force for the recognition of the substrate molecules. This situation would apply to host–guest complexations as artificial enzyme systems that simulate the stereoselectivity of a cavity to substrates. In a study on metal-modified cyclodextrins, Tabushi et al. proposed a "double recognition" mechanism in which a guest molecule is stabilized with additivity by both metal ion and cyclodextrin moieties.[6] In our case, the central metal seems to act to just fix a guest (base) into a host (cavity), and thereby, the incorporation of the guest is *cooperatively* more stabilized than the two additive contributions, since the base binding to trans-α^2 complexes will accompany the release of a solvent molecule from the cavities where both molecular dimensions of the solvent and the base are fairly close.

Acknowledgment. We wish to thank M. Teranishi for recording the 400-MHz NMR spectra at low temperature.

Supplementary Material Available: Tables SI and SII, giving ^1H NMR data of porphyrins in $CDCl_3$ and in toluene-d_8, and SIII and SIV, giving equilibrium data for the binding of pyridine and isoquinoline (4 pages). Ordering information is given on any current masthead page.

(38) Nakamura, M. *Chem. Lett.* **1988**, 453.