Thermodynamics for Base Binding to Four Atropisomers of Cobalt(II) Picket Fence Porphyrin. Intramolecular Ligand–Ligand Interactions

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Abstract

Thermodynamic parameters for base binding to four atropisomers of *meso*-tetrakis(*o*-pivalamidophenyl)porphyrinatocobalt(II) were determined by spectrophotometry in toluene. The order of the affinities of the four isomers with 1-methylimidazole and pyridine is $\alpha^4 < \alpha^3 < cis\text{-}\alpha^2 < trans\text{-}\alpha^2$. The higher base affinities of the *trans*-α^2 complex compared with the α^4 complex are due to an increase in the binding energies of the bases, although a substantial decrease of entropy changes also occurs; the differences of thermodynamic values on both complexes are $-\Delta\Delta G = 1.49$ and 1.36 kcal/mol, $-\Delta\Delta H = 3.4$ and 3.1 kcal/mol and $-\Delta\Delta S = 6.4$ and 6.1 eu, with 1-methylimidazole and pyridine, respectively. With saturated bases pyrrolidine and piperidine, the affinities of the *trans*-α^2 complex are comparable to those of the α^4 complex, and those of the *cis*-α^2 complex are the lowest. The increased steric repulsion between the pickets and ligated pyrrolidine or piperidine may cancel out the stabilizing effect on the base binding to the α^2 complexes. Proton NMR study suggests the preferential solvation of the four-coordinate species of the *trans*-α^2 complex to that of the α^4 complex. It could be concluded that the stabilization of the base binding by the pickets is attributed to an intramolecular ligand–ligand interaction between the ligated base and the pickets rather than to the inhibition of the undesirable solvation on the active sites.

Introduction

A number of modified porphyrins have been synthesized to mimic the biological functions of hemoproteins. One of the most extensively investigated models of myoglobin is the picket fence porphyrinatoiron(II) [1] complexes and their cobalt(II) analogs [2]. The picket fence porphyrin compounds have four atropisomers by restricted rotation of the phenyl rings [1]. These isomers are clearly distinguishable by HPLC [3], ^{1}H NMR [4, 5], and RR [6], although the electronic nature of the active sites may be very similar to each other [3]. We [4] have also reported that the affinity with 1-methylimidazole or O_2 differs considerably for each of the isomers of the Co(II) complex.

The affinity and the binding energy of Co(II) porphyrins with a base are affected by many factors [2, 7–10]. In the base adducts of Co(II) picket fence porphyrins, the base plane tends to take the staggered orientation in the *trans*-α^2 complex but eclipsed orientation in the α^4 complex relative to the Np–Co–Np (Np: pyrrole nitrogen) [5, 6, 11]. The staggered orientation due to steric repulsion from the pivalamido groups in the *trans*-α^2 complex should weaken only the π interaction in the Co(II)–base bond [12], when imidazoles or pyridines are used as the base ligand. Also, considerable steric repulsion between the base ligand and the pivalamido group will be expected to occur in the *trans*-α^2 complex, since even a coordinated small molecule such as O_2 suffers from an appreciable steric repulsion [13]. Recently, Lexa *et al.* [9] have reported

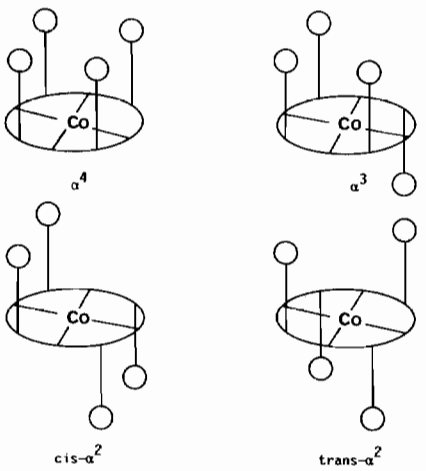

Fig. 1. Schematic representation of four atropisomers of Co(II) picket fence porphyrin.

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that *o*-acetamido groups of phenyl rings of Fe(II) basket handle porphyrin remarkably enhance the base affinity in the opposite site to the porphyrin plane. They attributed this to a 'through space' effect of amide dipoles.

These factors reported so far should weaken the Co(II)–base bond strength and decrease the base affinity of the *trans*-α^2 complex compared with those of the α^4 complex. However, the order of the base affinity with 1-methylimidazole is $\alpha^4 < \alpha^3 <$ *cis*-$\alpha^2 <$ *trans*-α^2; the affinity of the *trans*-α^2 complex was found to be several times higher than that of the α^4 complex [4]. We [11] have suggested that two pivalamido groups in Co(II) 'jelly fish' porphyrin protect the ligated base and act as a cavity similar to that for O_2 binding. The cavity of the *trans*-α^2 complex as a host would stabilize the binding of the base as a guest.

The main purpose of this work is to understand the role of the cavity for base binding. We report the thermodynamic values for base binding to the four atropisomers of Co(II) picket fence porphyrin. The cavity for a base ligand is constructed from one or two pivalamido groups, where weak intramolecular ligand–ligand interactions between the coordinated base ligand and the pickets are expected. One of them is sterically repulsive forces, and these interactions should reduce base affinity. Another is attractive non-covalent interactions. The enthalpic contribution by the effects may be small (smaller than 5 kcal/mol [14]), but in some cases [15] these play an important role in complexation reactions. These mutual interactions may depend on the shape and the size of both the cavity [11] and a base ligand. Such factors will regulate the thermodynamic parameters on base binding to this system.

Experimental

Materials

Each of four atropisomers of *meso*-tetrakis(*o*-pivalamidophenyl)porphyrinatocobalt(II) (Co(TpivPP)*) was prepared in the pure state by the method reported previously [4]. Bases, py, 1-MeIm, 1,2-Me_2Im, pyrro, and pip, were purified by vacuum distillation from KOH. Toluene, chlorobenzene, and *o*-dichlorobenzene were distilled after drying over a molecular sieve (4 Å). Chloroform was purchased as spectroscopic grade and was dried over a molecular sieve (4 Å).

Measurements

Proton NMR spectra were measured on either a Jeol JMN-MH-100 or a Jeol FX-100 spectrometer. ESR spectra at X-band were obtained from a Jeol JES-FE2GX spectrometer, and the magnetic field was calibrated with a Jeol ESFC4 frequency meter. Visible absorption spectra were recorded on a Hitachi 340 spectrophotometer. The equilibrium measurements were carried out by photometric titration of the base solution under N_2 at a constant temperature (±0.1 °C) in the range from −3 to 33 °C. The association constants were determined by the Hill equation [10].

Results and Discussion

Figure 2 shows the visible spectra at various base concentrations. Excellent isosbestic points were obtained in all of the cases investigated. The spectral changes correspond to the equilibrium

$$\mathrm{CoP} + \mathrm{B} \overset{K}{\rightleftharpoons} \mathrm{CoPB} \qquad (1)$$

where CoP represents a four-coordinate cobalt(II) porphyrin, B an axial base, and CoPB a five-coordinate species. As reported previously [2, 4], no amount of bis-base adduct $CoPB_2$ was observed in these experimental conditions. The estimated error limits on K values were less than 12%.

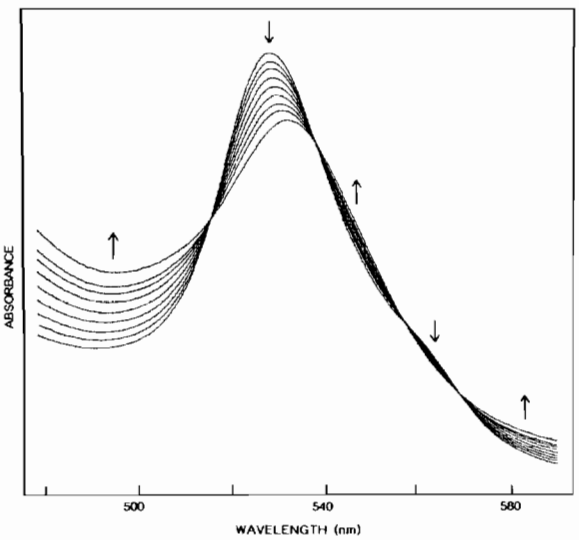
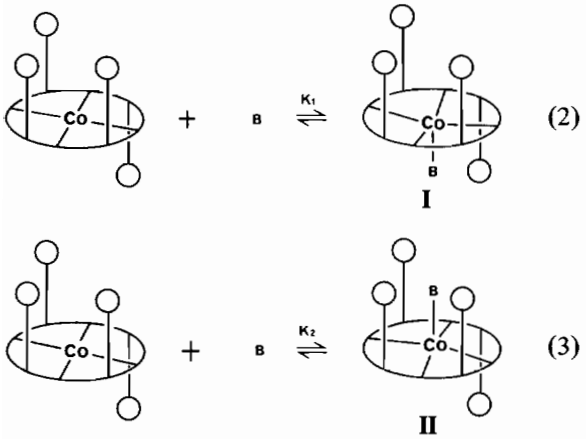


Fig. 2. Spectral changes for the reaction of Co(*trans*-α^2-TpivPP) with pyridine in toluene at 24.4 °C. CoP = 3.77 × 10^{-5} M. Base concentration = 0, 7.69 × 10^{-6}, 1.54 × 10^{-5}, 2.69 × 10^{-5}, 4.23 × 10^{-5}, 6.54 × 10^{-5}, 1.00 × 10^{-4}, 1.58 × 10^{-4}, and 1.7 × 10^{-2} M.

*Abbreviations used are: 1-MeIm, 1-methylimidazole; 1,2-Me_2Im, 1,2-dimethylimidazole; py, pyridine; pyrro, pyrrolidine; pip, piperidine; 1-Mepip, 1-methylpiperidine; TpivPP, dianion of *meso*-tetrakis(*o*-pivalamidophenyl)porphyrin; Tp-OCH_3PP, dianion of *meso*-tetra(*p*-methoxyphenyl)porphyrin; Cap, dianion of capped porphyrin 5,10,15,20-[pyromellytoyl(tetrakis-*o*-oxyethoxyphenyl)]porphyrin.

For the α^4 complex, the base molecule is forced to bind preferentially at the one site on the flat face of the porphyrin plane because of the steric barrier from the four pivalamido groups [2]. On the contrary, the α^2 complexes have two binding sites at both faces, thus effecting K and ΔS by a two-fold and 1.4 eu (R ln 2) increase, respectively, compared with the α^4 complex. The two equilibria are probable for the ligation of a base molecule to the α^3 complex



(2)

(3)

where the apparent equilibrium constant K equals $K_1 + K_2$, since **I** and **II** were not distinguishable. Although no definite evidence was obtained by ^{1}H NMR and ESR, we concluded that $K_1 \gg K_2$ and hence $K \simeq K_1$ for the following reasons. First, the ligated base in **II** will suffer from a considerable steric repulsion by the three pivalamido groups [6, 13]. The steric hindrance substantially decreases the binding energy and the affinity of the complex with the base. Secondly, even one pivalamido group increases the base affinity with 1-MeIm by a factor of 2.3 [11], which is the same as the ratio of the base affinity of the α^3 complex to that of the α^4 complex (*vide infra*). This does not result from an additive contribution by $K_1 + K_2$ but from the interaction between one pivalamido group and the base in **I**.

Comparison of Co(α^4-TpivPP) with Co(Tp-OCH$_3$PP) and Co(Cap)

The thermodynamic values were determined by van't Hoff plots as illustrated in Fig. 3 and are listed in Table I. The affinity and the binding energy of Co(α^4-TpivPP) with 1-MeIm are much larger than those of Co(Tp-OCH$_3$PP) and Co(Cap). This is partially due to the difference of the electron donor effects between amide and methoxy groups. However, the estimated difference of the effect between Co(α^4-TpivPP) and Co(Tp-OCH$_3$PP) may give only a 1.6-fold reduction of the base affinity for the former [17], since the Hammet σ of NHCO is practically zero [9] and that of OCH$_3$ is 0.267

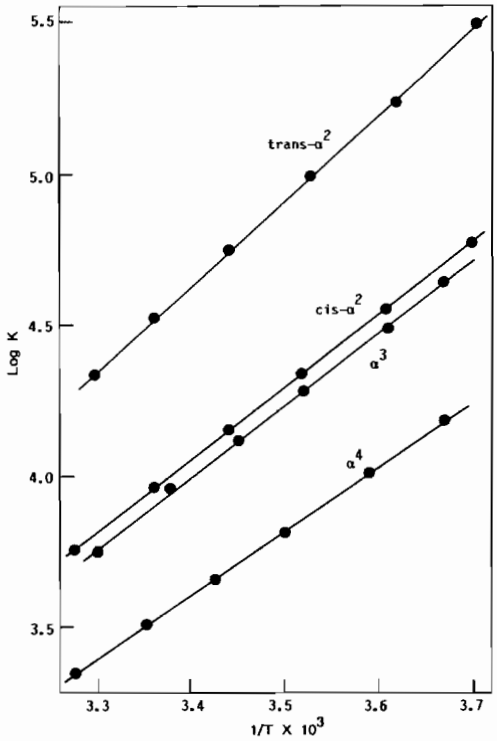


Fig. 3. Plots of log K *vs.* $1/T$ for the determination of enthalpy and entropy changes for pyridine binding to Co(TpivPP).

[17]. The entropic factor arising from the number of binding sites on the porphyrin plane also does not account for the difference between the base affinities of Co(α^4-TpivPP) and Co(Tp-OCH$_3$PP), since this factor should decrease the affinity of the former to a half.

The electronic substituent effect of Co(Cap) will be similar to that of Co(Tp-OCH$_3$PP). The lower base affinity of the former might be due to the greater steric hindrance afforded the base by the rigidity of the *meso*-phenyl groups of the porphyrin [8]. The rigidity imposed by the superstructure of Co(Cap) is also predicted to occur for Co(α^4-TpivPP) so that this effect is unlikely to account for the difference of the base affinities. As reported for the Fe(II) basket handle porphyrin system [9], the *o*-acetamido groups of the phenyl rings remarkably enhance the base affinity of the central metal. Similarly, the dominant factor to explain the higher base affinity of Co(α^4-TpivPP) compared with Co(Tp-OCH$_3$PP) or Co(Cap) might be a 'through space' effect of NHCO dipoles.

Interactions of Base and Porphyrin Plane

There is no interaction between the ligated base and pivalamido groups of Co(α^4-TpivPP); the base affinity and the binding energy are affected by Co(II)–base bond strength (pK_a of base) [4, 7]

TABLE I. Thermodynamic Parameters for Base Binding to Cobalt(II) Porphyrins

Complex[a]	Base	K[b] (l/mol)	ΔH[c] (kcal/mol)	ΔS[c] (eu)
Co(α^4-TpivPP)	1-MeIm (7.06)[d]	1.90×10^4	−10.6 ± 0.3	−16.0 ± 1.1
	py (5.22)[d]	3.21×10^3	−9.8 ± 0.1	−16.7 ± 0.2
	1,2-Me_2Im (7.85)[d]	6.29×10^3	−9.3 ± 0.1	−13.9 ± 0.4
	pyrro (11.3)[e]	4.18×10^4	−11.2 ± 0.6	−16.3 ± 2.1
	pip (11.12)[d]	1.09×10^4	−10.7 ± 0.1	−17.6 ± 0.4
Co(α^3-TpivPP)	1-MeIm	4.33×10^4	−11.2 ± 0.3	−16.2 ± 1.1
	py	7.70×10^3	−10.9 ± 0.2	−18.6 ± 0.5
	1,2-Me_2Im	9.58×10^3	−9.7 ± 0.2	−14.2 ± 0.7
	pyrro	2.61×10^4	−11.1 ± 0.5	−17.0 ± 1.7
	pip	7.18×10^3	−10.6 ± 0.1	−18.1 ± 0.2
Co(*cis*-α^2-TpivPP)	1-MeIm	4.65×10^4	−11.2 ± 0.2	−16.2 ± 0.5
	py	8.81×10^3	−11.0 ± 0.1	−18.7 ± 0.1
	1,2-Me_2Im	9.39×10^3	−10.1 ± 0.1	−15.6 ± 0.4
	pyrro	2.11×10^4	−10.7 ± 0.1	−16.1 ± 0.5
	pip	4.80×10^3	−10.8 ± 0.1	−19.5 ± 0.4
Co(*trans*-α^2-TpivPP)	1-MeIm	2.38×10^5	−14.0 ± 0.5	−22.4 ± 1.8
	py	3.15×10^4	−12.9 ± 0.1	−22.8 ± 0.3
	1,2-Me_2Im	2.73×10^4	−11.3 ± 0.2	−17.6 ± 0.8
	pyrro	4.66×10^4	−12.1 ± 0.4	−19.2 ± 1.4
	pip	1.15×10^4	−11.6 ± 0.1	−20.2 ± 0.2
Co(Tp-OCH_3PP)	1-MeIm	1.5×10^3[f]	−7.6[f]	−11[f]
	py	6.8×10^2[f]	−6.2[f]	−8[f]
	pip	3.0×10^3[f]	−8.6[f]	−13[f]
Co(Cap)	1-MeIm	2.0×10^2[g]	−8.8[g]	−19[g]

[a]In toluene. [b]Calculated at 25 °C from ΔH and ΔS values. [c]Error limits are standard deviations from least-squares method of van't Hoff plots. [d]pK_a values from ref. 7. [e]pK_a value from ref. 16a. [f]Ref. 10. [g]Ref. 8.

and the steric interaction between the base and the porphyrin plane. Both decreases in the base affinity and the binding energy from 1-MeIm to 1,2-Me_2Im are evidently ascribed to the steric repulsion of the 2-methyl group on 1,2-Me_2Im with the porphyrin plane [2, 8], although the displacement of the Co(II) ion from the mean porphyrin plane toward the base will somewhat relax the repulsion [18]. The basicity of pyrro is similar to that of pip, but the substitution of the former to the latter gives a four-fold lowering of the affinity of Co(α^4-TpivPP). This result also suggests that the steric repulsion of the six-membered base pip with the porphyrin plane is larger than that of the five-membered base pyrro. With the more hindered base 1-Mepip, in fact, the affinity of Co(α^4-TpivPP) is very low (K = 22 M^{-1} at 23 °C). Such a steric repulsion with pip is, however, unlikely to occur for Co(Tp-OCH_3PP), because the ratio of the affinity of Co(Tp-OCH_3PP) with 1-MeIm and pip is similar to that of Co(α^4-TpivPP) with 1-MeIm and pyrro. Jameson *et al.* [19] have reported the difference in the structural parameters between Fe(α^4-TpivPP)(2-MeIm) and Fe(TPP)(2-MeIm). The Fe(II)–N(base) bond length of the former is shorter by 0.07 Å than that of the latter. Further, the doming parameter of the former is exceptional and considerably smaller than that of the latter. Such differences probably exist between Co(α^4-TpivPP)(pip) and Co(Tp-OCH_3PP)(pip), consequently leading to the larger steric repulsion on the former.

Interactions of Base and Pivalamido Groups

The electronic nature of the Co(II) ion may be similar to each of the four atropisomers [3]*. Therefore, the base affinities in this system depend mainly on the steric repulsion between the base and pivalamido group(s), on the ability of the pivalamido groups to protect the ligated base (the effectiveness of the cavity), on the Co(II)–base π-bond strength, and on the statistical entropy factor arising from the number of binding sites on the porphyrin

*The porphyrin plane of each isomer may be slightly distorted by the pickets in a different manner, although no structural data is available. This could perturb *the porphyrin orbitals* and somewhat change the feature of electronic spectra. Such a distortion, however, will have little effect on base binding [20], and available data [8, 11] support this situation.

plane*. In the following paragraphs, we discuss simultaneously how each factor is concerned with the base binding in this system.

For imidazoles and pyridine binding, the order of the base affinity is $\alpha^4 < \alpha^3 \simeq cis\text{-}\alpha^2 < trans\text{-}\alpha^2$. (If one corrects the base affinities with the statistical entropy factor, the order will be $\alpha^4 < cis\text{-}\alpha^2 < \alpha^3 < trans\text{-}\alpha^2$.) A similar tendency is also found for the binding energy $-\Delta H$, indicating the enthalpy dependence of the free energy changes in this system. A model building study showed that the steric repulsion between these bases and the pickets is $\alpha^4 \leqslant \alpha^3 \leqslant trans\text{-}\alpha^2 < cis\text{-}\alpha^2$. This factor should reduce the affinity and the binding energy with the bases in this order. The π bond character in the Co(II)–base bond which should increase the base affinity is minimum in the *trans*-α^2 complex [6, 11, 12]. These findings indicate that both increases of the base affinity and of the binding energy of the α^3 and α^2 complexes compared with those of the α^4 complex are undoubtedly attributed to the pivalamido group(s) which protects the ligated base as the cavity [11]. The cavities of this system are useful to enhance the base uptake by strengthening the base binding to the complexes, although some substantial decreases of the entropy changes also occur.

With saturated bases, pyrro and pip, the order of the base affinities is consistently different from that with py and Ims. The base affinities of Co(α^4-TpivPP) are comparable to those of Co(*trans*-α^2-TpivPP), while the binding energies to the former are smaller by 0.9 kcal/mol than those to the latter. And the affinity of Co(*cis*-α^2-TpivPP) with pyrro or pip is the lowest in this system. Both pyrrolidine and piperidine are different from pyridine and imidazoles in terms of bulkiness on molecular dimensions and of the absence of the π system. However, as noted above, the contribution of the π interaction between the Co(II) ion and py or Ims is thought to be negligible in this system. Therefore, the reduced stabilization effect of pivalamido groups on pyrro or pip binding is attributable to the molecular bulkiness of the bases rather than to the absence of the π system. The increased steric repulsions from pivalamido group(s) with pyrro and pip will overcome or cancel out the stabilization effect of the cavities on the base binding to the α^3 and the α^2 complexes. Table II gives the ESR parameters to base adducts of the four atropisomers. Among the 1-MeIm adducts, the values are the same within the experimental errors. However, differences are found in the parameters of the pip adducts. The larger $|A_{Co}|$ and somewhat smaller $|A_N|$ values for the piperidine adducts of the α^2 complexes compared to those for the α^4 complex support the weakness of the Co(II)–N(base) bond by distortion and/or elongation [21] in the α^2 complexes.

The stabilization of base binding by pivalamido groups is evident especially in the *trans*-α^2 complex. The differences of thermodynamic values between the *trans*-α^2 and α^4 complexes are given in Table III where $\Delta\Delta S$ and $\Delta\Delta G$ are corrected with statistical factor and represent the values per one binding site. One may realize that these values are mainly composed of the effectiveness of the cavity and of the repulsive ligand–ligand interactions. These results indicate that the cavity of

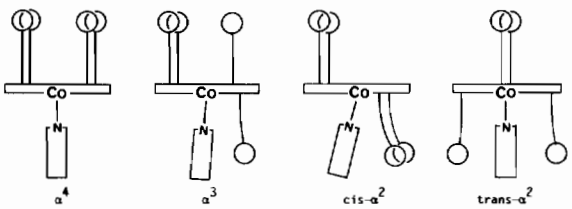


Fig. 4. Steric repulsions between the pickets and ligated base.

*The difference of the distortions of the porphyrin plane will not sterically affect the base binding to each isomer. The affinity with the more hindered base pip compared to pyrro should be more sensitive to the difference since both bases are similar in other factors. However, the ratio of the affinities with these bases is similar in each isomer (see Table I).

TABLE II. ESR Parameters of Base Adducts of Cobalt(II) Porphyrins

Complex[a]	$g_\perp$[b]	$g_\parallel$[b]	$\lvert A_{Co}\rvert$[c] ($\times 10^{-4}$ cm^{-1})	$\lvert A_N\rvert$[d] ($\times 10^{-4}$ cm^{-1})
Co(α^4-TpivPP)(1-MeIm)	2.313	2.031	76.8	16.2
Co(α^3-TpivPP)(1-MeIm)	2.313	2.028	76.9	16.3
Co(*cis*-α^2-TpivPP)(1-MeIm)	2.311	2.029	76.5	16.3
Co(*trans*-α^2-TpivPP)(1-MeIm)	2.314	2.027	76.9	16.1
Co(α^4-TpivPP)(pip)	2.314	2.026	77.0	14.0
Co(α^3-TpivPP)(pip)	2.313	2.027	77.6	13.1
Co(*cis*-α^2-TpivPP)(pip)	2.312	2.023	80.0	13.2
Co(*trans*-α^2-TpivPP)(pip)	2.311	2.025	78.8	13.2

[a]In $CHCl_3$ at 77 K. [b]± 0.003. [c]$\pm 0.8 \times 10^{-4}$ cm^{-1}. [d]$\pm 0.5 \times 10^{-4}$ cm^{-1}.

TABLE III. Differences in Thermodynamic Values between *trans*-α^2 and α^4 Complexes

Base	$-\Delta\Delta G$ (kcal/mol)	$-\Delta\Delta H$ (kcal/mol)	$-\Delta\Delta S$ (eu)
1-MeIm	1.09	3.4	7.8
py	0.94	3.1	7.5
1,2-Me_2Im	0.46	2.0	5.1
pyrro	−0.35	0.9	4.3
pip	−0.38	0.9	4.0

the host *trans*-α^2 complex does not only stabilize the binding of the guest bases but discriminates the bases by their molecular dimensions. With bulkier bases, it is subtle whether the stabilization effect by the cavity or the repulsive force more regulates the base affinity.

Solvation Effects

The effectiveness of the cavity is still ambiguous since it contains both the solvation problem and attractive ligand–ligand interactions. To explore the solvation effects on base binding, thermodynamic parameters were measured in several solvents for the α^4 and *trans*-α^2 complexes and are listed in Table IV. Pyridine was used as the base because the ligated base suffers little the repulsive forces from the pickets or the porphyrin plane in these complexes.

Rillema *et al.* [10] have reported that the enthalpy change for base binding to Co(Tp-OCH_3PP) decreases with an increase in solvent polarity. They also estimated the gas-phase binding energies from extrapolation of linear ΔH *versus* ϵ (dielectric constant) plot to the intercept. However, this is not the case for Co(TpivPP). The enthalpy changes for pyridine binding to Co(TpivPP) are irrespective of the dielectric constants of the solvents, while the free energy changes also depend on the enthalpy changes. Therefore, these data cannot give an estimation of the solvation factor for these complexes.

It is interesting to note that the thermodynamic values of the *trans*-α^2 complex are more sensitive than those of the α^4 complex to solvent polarity and that the stabilization of pyridine binding by the pickets is only 0.8 kcal/mol in chloroform. The thermodynamic parameters of base binding in solution depend on the differences of solvation parameters among free base, four-, and five-coordinate species. The unligated pyridine molecule will be better solvated in chloroform than in toluene, since the mixing heat of py with the former solvent is appreciably more exothermic than that with the latter. On the ligation of py to the *trans*-α^2 complex, the base molecule should release the solvent ($CHCl_3$), while this may not happen in the case of the α^4 complex. Thus, in chloroform solution the thermodynamic values of the *trans*-α^2 complex include positive and relatively larger ΔH and ΔS in terms of the release of the solvent. In contrast to this isomer, the ligated base of the α^4 complex may experience a similar environment to the unligated base. Therefore, in solution where free base is strongly solvated, the stabilization of base binding will be small.

Help towards solving the solvation problem may be given by a study on thermal equilibria among the four atropisomers of picket fence porphyrins [3, 22]. The ratio of the amounts of the *trans*-α^2 isomer to the α^4 isomer in toluene, xylenes, and mesitylene (5:1) was found to deviate considerably from the statistical one (1:1). Recently, Crossley *et al.* [22] have suggested that the deviation may be attributed to the difference of the solvations

TABLE IV. Thermodynamic Parameters for Pyridine Binding to Cobalt(II) Porphyrins in Several Solvents

Complex	Solvent	K[a] (l/mol)	ΔH (kcal/mol)	ΔS (eu)
Co(α^4-TpivPP)	toluene (2.38)[b]	3.21×10^3	−9.8 ± 0.1	−16.7 ± 0.2
	o-dichlorobenzene (9.93)[c]	3.01×10^3	−9.7 ± 0.1	−16.6 ± 0.4
	chlorobenzene (5.67)[b]	2.81×10^3	−9.1 ± 0.1	−14.8 ± 0.4
	chloroform (4.81)[b]	1.88×10^3	−8.2 ± 0.1	−12.4 ± 0.5
Co(*trans*-α^2-TpivPP)	toluene	3.15×10^4	−12.9 ± 0.1	−22.8 ± 0.3
	o-dichlorobenzene	2.17×10^4	−11.7 ± 0.2	−19.2 ± 0.6
	chlorobenzene	1.62×10^4	−10.7 ± 0.1	−16.8 ± 0.4
	chloroform	4.22×10^3	−9.0 ± 0.1	−13.5 ± 0.3
Co(Tp-OCH_3PP)	toluene	6.8×10^2[d]	−6.2[d]	−8[d]
	chlorobenzene	6.6×10^2[d]	−8.3[d]	−15[d]
	chloroform	3.3×10^2[d]	−6.7[d]	−11[d]

[a]Calculated at 25 °C from ΔH and ΔS values. [b]Dielectric constants from ref. 10. [c]Dielectric constant from ref. 16b. [d]Ref. 10.

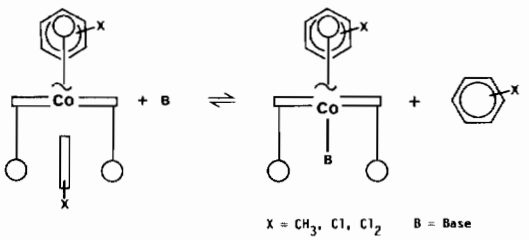
TABLE V. Proton NMR Data of Porphyrins

Compound	Solvent	CH_3 δ (ppm)	NH (pyrrole) δ (ppm)
$H_2(\alpha^4$-TpivPP)	$CDCl_3$	0.07[a]	−2.60
	DMF-d_7	0.08	−2.58
	toluene-d_8 + $CDCl_3$ (7:1)	0.05	−2.54
	chlorobenzene-d_5 + $CDCl_3$ (9:1)	0.11	−2.54
H_2(*trans*-α^2-TpivPP)	$CDCl_3$	0.25[a]	−2.55
	DMF-d_7	0.39	−2.55
	toluene-d_8 + $CDCl_3$ (7:1)	0.05	−2.19
	chlorobenzene-d_5 + $CDCl_3$ (9:1)	0.10	−2.16
Co(α^4-TpivPP)	$CDCl_3$	−6.05[a]	
	toluene-d_8 + $CDCl_3$ (7:1)	−5.76	
Co(*trans*-α^2-TpivPP)	$CDCl_3$	−2.73[a]	
	toluene-d_8 + $CDCl_3$ (7:1)	−3.35	

[a]Ref. 4.

among the isomers, since the ratio approximates to 1:1 in dimethylformamido.

Proton NMR is a useful tool for examining the environments of the active sites in this system. Table V lists the chemical shifts of methyl and pyrrole NH protons of the metal free porphyrins. In toluene and chlorobenzene, the methyl signal for H_2(*trans*-α^2-TpivPP) shifts to higher field but the NH signal shifts to lower field compared to those in non-aromatic solvents, while those for H_2-(α^4-TpivPP) are insensitive to the solvents. Although the α^4 isomer may form a weak 1:1 π complex with aromatic solvents, it will occur only on the porphyrin periphery (pyrrole ring) [23] and hence not affect the chemical shifts of the isomer. Consequently, we assigned these shifts on the *trans*-α^2 isomer to be induced by the π-current shielding of the solvent molecules. This result definitively indicates that the aromatic molecule as the solvent inserts into the cavity of H_2(*trans*-α^2-TpivPP) and also accounts for the preferential solvation of the *trans*-α^2 isomer to the α^4 isomer. Since these solvations may be influenced by the steric factor of pickets rather than the electronic one of the active site*, such a difference of the solvations is also expected for Co(II) complexes. Moreover, the chemical shifts of the methyl protons of the Co(II) complexes may support the difference successfully. The equilibrium for base binding to the α^2 complex is as follows.



(4)

Thus, the four-coordinate Co(II) complex of the *trans*-α^2 isomer is more solvated and stabilized than the α^4 complex in aromatic solvents. Nonetheless, the base adduct of the *trans*-α^2 complex with py or 1-MeIm is stabilized even more than that of the α^4 complex in toluene. Therefore, we concluded that the stabilization of base binding to the *trans*-α^2 complex is dominantly due to non-covalent interactions between the ligated base and the pickets. This interaction may be hydrophobic (and/or the London's dispersion force) in nature, and can be affected by both the shape and the size of the cavity rather than the pocket polarity introduced by amide dipoles, since the affinity with 1-MeIm or py decreases to a half when valeramido groups were used instead of pivalamido groups [11]. The attractive forces between methyl and aromatic groups may be partly similar to those for other systems [15]. Such interactions play an important role in biological

*The ratios of four atropisomers of Cu(II), Ni(II), and Pd(II) complexes are very similar to that of the free porphyrins in thermal equilibria [3b].

systems [14]. The base binding to picket fence porphyrins with a different cavity would also be informative to 'host–guest' associations.

Supplementary Material

Tables of equilibrium constants for base binding (5 pages) are available from the authors on request.

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