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Effects of Polarity on Dioxygen Binding to Cobalt(II) Porphyrins

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Abstract

Some picket fence porphyrinatocobalt(II) complexes which contain a replaced polar or non-polar group in their fences were newly prepared and characterized, and their oxygen affinities were measured spectrophotometrically. The O_2 affinities of the complexes containing a replaced polar group other than amido linkages are appreciably reduced as compared with those of the complexes with a similar non-polar group, regardless of the charge sign of the polarity in the cavity. On the other hand, solvent polarity affects the O_2 affinity of the complex with a polar group which is accessible to the coordinated dioxygen molecule, while solvation effects of the corresponding complex without such a group are little. On the basis of these results the relationships between O_2 affinity and pocket polarity or solvent polarity are discussed.

Introduction

Many studies have been reported on the nature of dioxygen binding to myoglobin (Mb) and hemoglobin (Hb) [1–3], and several model systems have also been developed in an effort to mimic the effective and reversible oxygenation of native hemoproteins [4–9]. Some of these contain an intramolecular 'cavity' which protects the dioxygen molecule coordinated to the central metal ion. These approaches suggested that the following factors control O_2 affinity of model complexes: (1) electronic nature of porphyrin [10, 11]; (2) axial base ligation as a fifth ligand [12–14]; (3) steric interactions between 'cavity' and coordinated dioxygen molecule [5–7]; (4) electrostatic interactions between 'cavity' and coordinated dioxygen molecule [8, 15]; and (5) solvation [6(b), 9, 16]. While the cavity stabilizes substantially the dioxygen binding to the complex, which factor of (4) or (5) is mainly responsible for the high O_2 affinity has been in question [17], although it is difficult to completely separate the above two factors [9].

In natural systems, studies on mutant hemoproteins demonstrated that the replacement of an amino acid residue forming part of a cavity greatly affects the oxygenation reaction of the central metal ion [1–3]. Probably, this is partly due to the electrostatic interactions. A typical example of the electrostatic interactions may be hydrogen-bonding formation between the distal histidine (E7) and the coordinated dioxygen molecule in Mb and Hb [18]. The hydrogen bond may stabilize the dioxygen binding to Mb and Hb. In model systems, the complexes containing protic groups capable of forming the intramolecular hydrogen bond have relatively higher O_2 affinity than those without such groups [8, 9, 19, 20]. On the contrary we have reported that the incorporations of an additional protic group to a 'picket fence' porphyrinato complex dramatically reduce the O_2 affinity [15]. Therefore, factors other than simple electrostatic interactions might play an important role in that case.

In order to clarify this discrepancy and to understand the electrostatic interactions in detail, we designed and synthesized some picket fence porphyrinatocobalt(II) complexes **1b**–**6b** which contain one replaced polar or non-polar group as part of a cavity. The moderately or weakly polar group used here permits a precise estimation of O_2 affinity, although strong polarity inhibits the estimation by a relatively rapid and irreversible oxidation of the cobalt(II) ion [15]. Other parts of the cavity consist of three neopentyl groups and four amido groups linking the two kinds of substituents to the porphyrin. While pival groups have been conventionally used as a picket fence, neopentyl groups make the complexes more easily soluble to organic solvents and increase the O_2 affinity more than the pival groups [17]. As noted above the amido groups have an important role on the O_2 affinity by the hydrogen bond or the like. In fact, studies on 'basket handle' porphyrins indicated that the amido groups induce a ten-fold increase in the $P_{1/2}$ (half saturation O_2 pressure) value above that of the corresponding ether groups [8]. Since the complexes prepared contain four similar amido groups, comparisons

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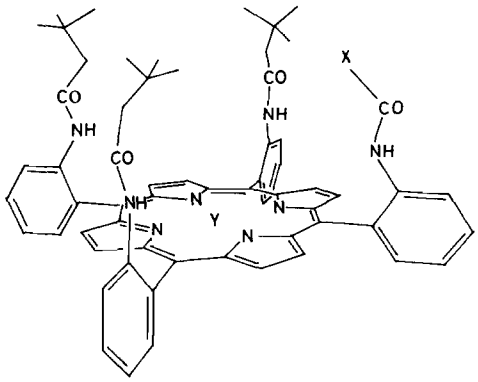


	Y = 2H	Y = Co(II)
X = $-(CH_2)_3CH_3$	H_2tNvalP (**1a**)	Co(tNvalP) (**1b**)
X = $-CF_2CF_2CF_3$	H_2tNFP (**2a**)	Co(tNFP) (**2b**)
X = $-CH_2OCOCH_3$	H_2tNAcmP (**3a**)	Co(tNAcmP) (**3b**)
X = 	H_2tNBP (**4a**)	Co(tNBP) (**4b**)
X = 	H_2tN2,6-mBP (**5a**)	Co(tN2,6-mBP) (**5b**)
X = 	H_2tN3,5-mBP (**6a**)	Co(tN3,5-mBP) (**6b**)
X = $-CH_2C(CH_3)_3$		Co(α^4-TneoPP) (**8**)
X = $-CH_2OH$		Co(tNHP) (**9**)
X = $-CH_2CONH_2$		Co(tNC$_3$AP) (**10**)
X = $-CH_2CH_2CONH_2$		Co(tNC$_4$AP) (**11**)

Fig. 1. Picket fence porphyrins.

can be made on the additional part of the cavity. The difference of the additional part will reflect the O_2 affinity. Here, the relationship between the pocket polarity and O_2 affinity is elucidated by the spectrophotometric determination of the $P_{1/2}$ values of the complexes prepared. Additionally, the effects of the solvent polarity on O_2 affinity are also discussed.

Experimental

General

Proton NMR spectra were measured on a JEOL JNM-MH-100 spectrometer. ESR spectra were obtained from a JEOL JES-FE2GX spectrometer. The magnetic field was calibrated with a JEOL ESFC4 frequency meter and field corrections for samples were made with Mn(II) in MgO. The ESR parameters were estimated according to the literature [21]. Visible spectra were recorded on a HITACHI 340 spectrophotometer thermostated to a constant temperature (±0.1 °C). Axial ligation constants were determined by the published procedure [14, 22], using the visible spectral changes. Error limits of $P_{1/2}$ were ±10% at 25 °C and ±5% at 0 °C.

Materials

All chemicals were purchased commercially and further purified as follows. Pyridine (py) and 1-methylimidazole (1-MeIm) were purified by vacuum distillation from KOH. Chlorobenzene and *o*-dichlorobenzene were distilled under reduced pressure after drying over a molecular sieve (4A). Toluene was stirred with conc. H_2SO_4, then washed with H_2O, 5% NaOH, and H_2O in turn, dried over $CaCl_2$, and distilled. Dichloromethane, 1,2-dimethoxyethane, tetrahydrofurane and *o*-nitrotoluene were dried over a molecular sieve (4A or 5A).

Synthesis

meso-5α,10α,15α-Tris[2-(neopentylcarbonylamino)phenyl], 20α(2-aminophenyl)porphyrin was obtained by the published method [15]. Reactions of the porphyrin with acid chlorides in CH_2Cl_2 containing *N*-methylmorpholine gave porphyrins **1a**–**6a**. Purifications were carried out by silica-gel column chromatography, yield *ca.* 80%.

meso-5α,10α,15α-Tris[2-(neopentylcarbonylamino)phenyl], 20α-(2-valeramidophenyl)porphyrin H_2tNvalP (**1a**). ^{1}H NMR ($CDCl_3$): δ −2.80 (2H), 0.57–1.67 (42H), 6.93 (4H), 7.37–8.89 (24H). *Anal.* Calc. for $C_{67}H_{72}N_8O_4$: C, 76.40; H, 6.89; N, 10.64. Found: C, 75.36; H, 6.64; N, 10.50%.

meso-5α,10α,15α-Tris[2-(neopentylcarbonylamino)phenyl], 20α-[2-(heptafluoropropylcarbonylamino)phenyl]porphyrin H_2tNFP (**2a**). ^{1}H NMR ($CDCl_3$): δ −2.73 (2H), 0.48 (18H), 0.57 (9H), 1.37 (4H), 1.47 (2H), 6.87–6.93 (3H), 7.37–8.87 (25H).

meso-5α,10α,15α-Tris[2-(neopentylcarbonylamino)phenyl, 20α-[2-(acetoxymethylcarbonylamino)phenyl]porphyrin H_2tNAcmP (**3a**). ^{1}H NMR ($CDCl_3$): δ −2.80 (2H), 0.15 (9H), 0.37 (18H), 1.22–1.31 (9H), 3.91 (2H), 6.71–6.84 (4H), 7.12–8.83 (24H). *Anal.* Calc. for $C_{66}H_{68}N_8O_6$: C, 74.13; H, 6.41; N, 10.48. Found: C, 74.87; H, 6.53; N, 10.35%.

meso-5α, 10α, 15α-Tris[2-(neopentylcarbonylamino)phenyl], 20α-(2-benzoylaminophenyl)porphyrin H_2tNBP (**4a**). ^{1}H NMR ($CDCl_3$): δ −2.73 (2H), 0.40 (18H), 0.49 (9H), 1.22 (4H), 1.29 (2H), 6.55–6.95 (10H), 7.33–8.91 (24H). *Anal.* Calc. for $C_{69}H_{68}N_8O_4$: C, 77.21; H, 6.39; N, 10.44. Found: C, 76.54; H, 6.41; N, 10.44%.

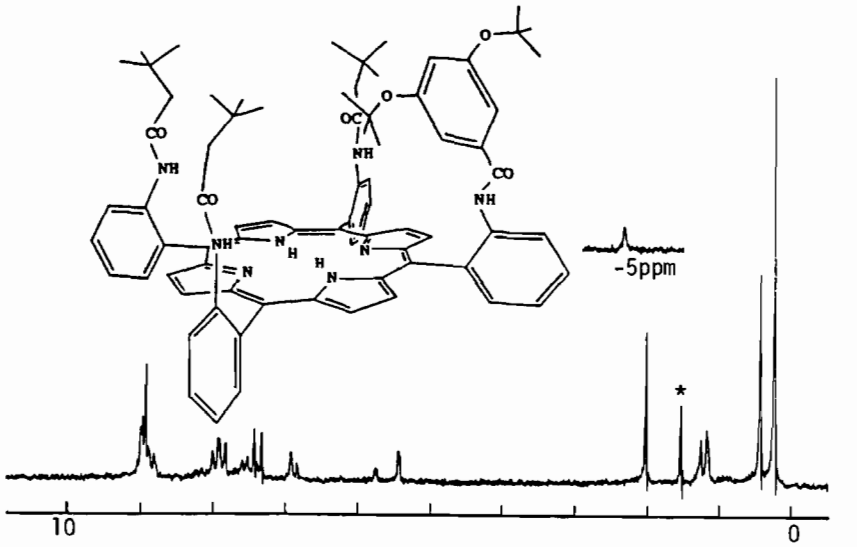
meso-5α, 10α, 15α-Tris[2-(neopentylcarbonylamino)phenyl], 20α-[2-(2,6-dimethoxybenzoylamino)-phenyl]porphyrin H_2tN2,6-mBP (**5a**). ^{1}H NMR ($CDCl_3$): δ −2.80 (2H), 0.50 (27H), 1.20 (4H), 1.28 (2H), 3.30 (6H), 5.88–5.96 (3H), 6.87 (4H), 7.36–8.98 (24H). *Anal.* Calc. for $C_{71}H_{72}N_8O_6$: C, 75.24; H, 6.40; N, 9.89. Found: C, 74.48; H, 5.97; N, 9.66%.

meso-5α, 10α, 15α-Tris[2-(neopentylcarbonylamino)phenyl], 20α-[2-(3,5-dimethoxybenzoylamino)-

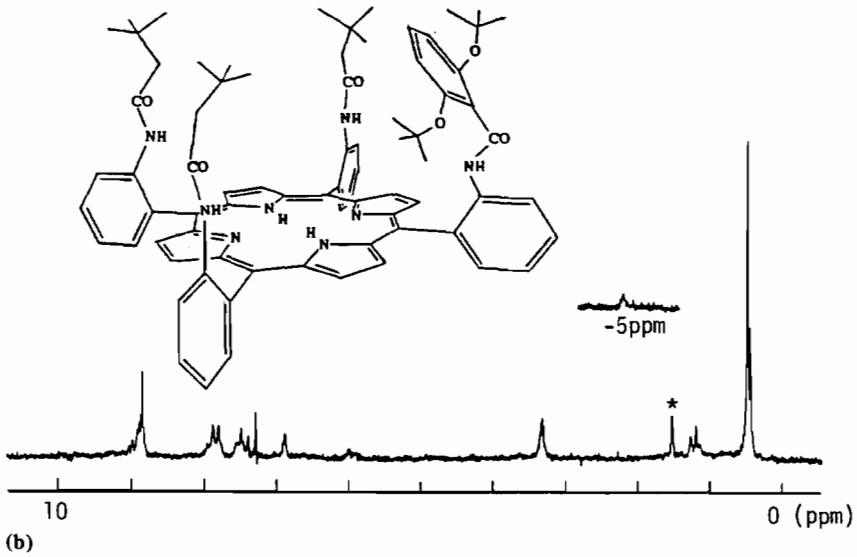
TABLE I. Analytical Data and Visible Absorption Maxima of Porphyrinatocobalt(II) Complexes

Complex	C(%)		H(%)		N(%)		Visible absorption λ_{max} (nm)[a]
	found	calc.	found	calc.	found	calc.	
1b	71.53	72.48	6.19	6.36	10.05	10.09	412, 527, 558(sh)
2b							412, 527, 558(sh)
3b	69.90	70.39	5.55	5.19	10.02	9.95	412, 526, 558(sh)
4b	72.49	73.32	5.92	5.89	9.95	9.91	412, 527, 559(sh)
5b	70.93	71.64	5.88	5.93	9.46	9.41	412, 527, 560(sh)
6b	71.45	71.64	5.40	5.93	9.02	9.41	412, 527, 558(sh)
7	75.29	75.32	4.29	4.21	10.08	9.76	413, 528, 560(sh)

[a]In toluene.



(a)



(b)

Fig. 2. Proton NMR spectra of: (a) H_2tN3,5-mBP, and (b) H_2tN2,6-mBP, in $CDCl_3$. *: Impurity in the solvent.

phenyl]porphyrin H_2tN3,5-mBP (**6a**). ^{1}H NMR ($CDCl_3$): δ −2.76 (2H), 0.22 (18H), 0.40 (9H), 1.13 (4H), 1.23 (2H), 2.02 (6H), 5.40 (2H), 5.69 (1H), 6.80–6.88 (4H), 7.30–8.92 (24H). *Anal.* Calc. for $C_{71}H_{72}N_8O_6$: C, 75.24; H, 6.40; N, 9.89. Found: C, 75.18; H, 6.44; N, 9.78%.

Cobalt(II) Insertion

Free porphyrins **1a**–**6a** were treated with anhydrous $CoCl_2$ according to the literature [23], yielding the corresponding complexes (**1b**–**6b**). *meso*-5α,10α,15α,20α-Tetrakis(2-benzoylaminophenyl)porphyrinatocobalt(II) Co(α^4-TBPP) (**7**) was obtained by the published method [17]. Analytical data and visible absorption maxima are listed in Table I.

Results and Discussion

^{1}H NMR Spectra

The trimethyl signals of H_2tN3,5-mBP are split with a ratio of 2:1 at 0.22 and 0.40 ppm (Fig. 2(a)). Similar phenomenon can also be seen for the methylene protons. These observations can be understood in terms of ring current shifts of the dimethoxyphenyl group; the plane of the phenyl ring is perpendicular to the adjacent two trimethyl groups, and another trimethyl group is nearly coplanar with the phenyl ring. However, since the resonance of methoxy protons (2.02 ppm) is not split, the phenyl ring is not so rigid but rotating as illustrated in Fig. 3. The spectral pattern of H_2tNBP was similar to that of H_2tN3,5-mBP (not shown) so that both porphyrins may have a similar structure.

In the case of H_2tN2,6-mBP (Fig. 2(b)) the spectral pattern is not consistent with that of H_2tN3,5-mBP in this region. The trimethyl signal of H_2tN2,6-mBP is not split, indicating that the trimethyl groups are little affected by the ring current shift. Contrary to this the methylene resonances are observed to be splitting (1.20–1.28 ppm) similar to that of H_2tN3,5-mBP. Furthermore, HGS stereo model indicated that the methoxy groups in H_2tN2,6-mBP restrict the free rotation of the 2,6-dimethoxyphenyl ring by a steric hindrance between the methoxy groups and the porphyrin plane. Judging from these results the plane of the dimethoxyphenyl ring in H_2tN2,6-mBP may be rigidly faced not to the adjacent trimethyl groups but to the center of the porphyrin ring.

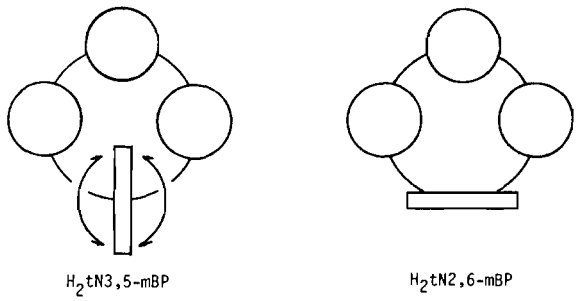


Fig. 3. Schematic representation of cavities shown from above. ○: Trimethyl group, □: dimethoxyphenyl ring.

ESR Spectra

Table II shows ESR parameters of the deoxy and oxy complexes. Although the spectra of the oxy complexes were rhombic, the parameters are listed as axial symmetry ($g_\parallel = g_1$, $g_\perp = 1/2(g_2 + g_3)$, $A_\parallel = A_1$, and $A_\perp = 1/2(A_2 + A_3)$) because of an ambiguity of the parameters in the perpendicular region [21(b), 24]. Among the deoxy complexes little variation is observed for the parameters. Therefore, the electronic nature of cobalt(II) ion is similar for these complexes. With the oxy complexes a slight distinction is found for the hyperfine coupling constant in the parallel region $A_\parallel$. The value of Co(tN3,5-mBP)(1-MeIm)O_2 is larger than the other by 0.8–0.9 G. Drago *et al.* [25] reported that increased polarity of the solvent makes the $A_\parallel$ value larger. Probably, the coordinated dioxygen molecule in Co(tN3,5-mBP) experiences a more polar environment than the other. This interpretation is in agreement with the result obtained from ^{1}H NMR spectra for free porphyrins.

TABLE II. ESR Parameters of Porphyrinatocobalt(II) Complexes[a]

Complex	$g_\parallel$	$g_\perp$	$A_\parallel^{Co}$ (G)	$A_\perp^{Co}$ (G)	$A_\parallel^{N}$ (G)
Co(tNBP)(1-MeIm)	2.038	2.315	78.3		16.5
+ O_2	2.086	2.002	18.2	13.2	
Co(tN2,6-mBP)(1-MeIm)	2.038	2.316	78.3		16.5
+ O_2	2.086	2.001	18.3	13.6	
Co(tN3,5-mBP)(1-MeIm)	2.039	2.315	78.3		16.5
+ O_2	2.086	2.003	19.1	13.2	

[a]At −120 °C in toluene–1-MeIm (10:1).

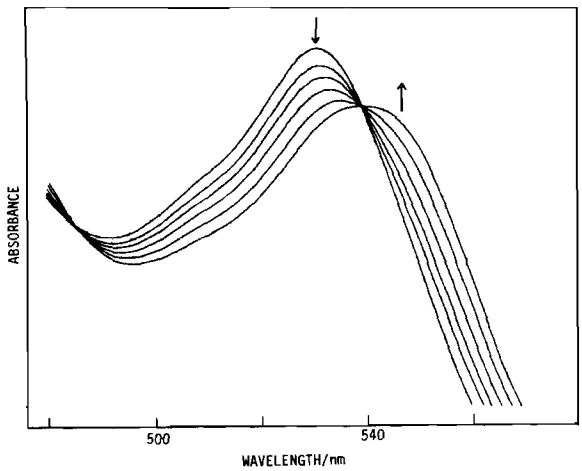


Fig. 4. Visible absorption spectra on oxygenation of Co(tN3,5-mBP)(1-MeIm). At 25 °C in toluene. Complex = 4.6 × 10^{-5} M, 1-methylimidazole = 4.3 × 10^{-3} M. Oxygen pressures are 0, 68, 125, 213, 332, and 498 torr.

TABLE III. Equilibrium Data of Porphyrinatocobalt(II) Complexes[a]

Complex	K_B (M^{-1})	$P_{1/2}$ (torr)
Co(tNvalP) (1b)	2.4 × 10^4	145
Co(tNFP) (2b)	3.3 × 10^4	1100[b]
Co(tNAcmP) (3b)	2.7 × 10^4	600[b]
Co(tNBP) (4b)	4.1 × 10^4	88
Co(tN2,6-mBP) (5b)	4.0 × 10^4	230
Co(tN3,5-mBP) (6b)	3.9 × 10^4	660
Co(α^4-TBPP) (7)	4.5 × 10^4	550
Co(α^4-TneoPP) (8)	2.9 × 10^4	120[c]
Co(α^4-TpivPP) (9)	2.2 × 10^4	170[c]
		140[d]
Co(tNHP) (10)		1300[e]
Co(tNC_3AP) (11)		1600[e]
Co(tNC_4AP) (12)		800[e]

[a]At 25 °C in toluene. Axial base = 1-methylimidazole. [b]Error limits are ± 30% because of relatively rapid oxidation of cobalt(II) ion. [c]Ref. 17. [d]Ref. 22. [e]Ref. 15.

Solution Equilibria

The major reactions among square planar porphyrinatocobalt(II) (CoP), axial base (B), and dioxygen molecule are as follows:

$$CoP + B \rightleftharpoons CoPB \quad (1)$$

$$CoPB + O_2 \rightleftharpoons CoPBO_2 \quad (2)$$

The equilibrium data are listed in Table III. The K_B values are not very varied, indicating that the electronic natures of the porphyrins are essentially similar to one another. If the difference of the electronic nature of the porphyrins affected the O_2 affinity, the K_B values should be substantially varied [10]. Therefore, the variation of the $P_{1/2}$ values is independent of the electronic nature of the porphyrins in this system.

With the oxygenation reaction, appreciable differences are observed for the $P_{1/2}$ values. The complexes with high O_2 affinity (low $P_{1/2}$ value) are Co(α^4-TpivPP), Co(α^4-TneoPP), Co(tNvalP), and Co(tNBP) which have no polar site other than four amido groups. Of these complexes Co(tNBP) has the lowest $P_{1/2}$ value, that is about half of the 'picket fence' complex, *meso*-5α,10α,15α,20α-tetrakis(2-pivalamidophenyl)porphyrinatocobalt(II) Co(α^4-TpivPP). It is interesting to note that the O_2 affinity of Co(α^4-TBPP) is not so high, because this complex has no other polar site than amido groups. Moreover, the cavity of Co(tNBP) is a mixture of those of Co(α^4-TneoPP) and Co(α^4-TBPP) so that the O_2 affinity of Co(tNBP) would be expected to be intermediate with additivity, since the intimately packed geometry of the cavity increases the O_2 affinity [17, 23]. This interaction may be interpreted as a 'side influence' [23], stabilizing the Co–O_2 bond by weakly electrostatic interactions such as van der Waals forces. Probably, in Co(α^4-TBPP) the steric interactions among four bulky phenyl groups forming the cavity would give some distortion to the structure of the complex.

In the case of Co(tNFP) the O_2 affinity is the lowest among the complexes prepared. A plausible explanation might be the electrostatic repulsion between the fluorocarbon substituent and the negatively charged dioxygen molecule coordinated to the central metal ion, although free dioxygen molecule will prefer the substituent, and the concentration of free dioxygen might be locally high around the cavity. A similar account could also be expected for Co(tNAcmP) with relatively low O_2 affinity. From this standpoint Co(tN3,5-mBP) should have high O_2 affinity, since the methoxy group would be more positively charged than the alkyl methyl one or the unsubstituted proton. However, the reverse is found for the complex, as in the case of complexes **10–12** which incorporate an additional protic group capable of forming an intramolecular hydrogen bond. The isomer Co(tN2,6-mBP) which contains similar methoxy groups has a larger $P_{1/2}$ value than that of Co(tNBP), but smaller than that of Co(tN3,5-mBP). Judging from the ESR parameters and ^{1}H NMR spectra, the methoxy groups in Co(tN2,6-mBP) may not be present near the coordinated dioxygen molecule so that the effect of the polar groups would be weaker than in the case of Co(tN3,5-mBP). These results indicate that incorporation of an additional polar group into the cavity of the picket fence complex reduces the O_2 affinity regardless of the charge sign of the polarity. Therefore, other factors will affect the O_2 affinity in this system.

Steric interactions between the cavity and the coordinated dioxygen molecule might be present

TABLE IV. $P_{1/2}$ Values of Porphyrinatocobalt(II) Complexes in Several Solvents[a]

Complex	Solvent	$P_{1/2}$ (torr)
Co(tNBP)(py)	toluene (2.38)	128
	chlorobenzene (5.67)	125
	chlorobenzene:*o*-nitrotoluene = 10:1 (7.84)	120
	o-dichlorobenzene (9.93)	130
Co(tN2,6-mBP)(py)	toluene	315
	chlorobenzene	300
	chlorobenzene:*o*-nitrotoluene = 10:1	290
	o-dichlorobenzene	320
Co(tN3,5-mBP)(py)	toluene	1200
	chlorobenzene	880
	chlorobenzene:*o*-nitrotoluene = 10:1	590
	o-dichlorobenzene	800
Co(tN3,5-mBP)(1-MeIm)	toluene	122
	chlorobenzene	90
	chlorobenzene: *o*-nitrotoluene = 10:1	81
	o-dichlorobenzene	86

[a]At 0 °C. Dielectric constants from ref. 26 are in parentheses.

for Co(tN3,5-mBP). These interactions have been studied on a few model systems, 'cyclophane heme' [5], 'capped' [6] and 'pocket' [7]. The cavities of these systems have a rigid conformation causing steric hindrance to the sixth ligand, reducing their O_2 affinities by the hindrance. In Co(tN3,5-mBP) the methoxy groups would not interact sterically as much with the coordinated dioxygen molecule as in those model systems, because the dimethoxyphenyl ring can rotate freely. Furthermore, complexes **9**–**11** will never give such hindrance. Consequently, we may propose 'solvation effects' as an alternate and tenable factor affecting the O_2 affinities of this system.

Solvation

In order to examine solvation effects on oxygenation, we used complexes **4b**–**6b** because of their similarity in structure. To obtain a more precise determination of $P_{1/2}$ values, the measurements of $P_{1/2}$ were performed at 0 °C, and pyridine was used as an axial base instead of 1-methylimidazole so as to keep a similar thermodynamic balance (O_2 affinity) at 25 °C*. Nonetheless, we did not succeed in obtaining precise $P_{1/2}$ values in a strongly polar solvent such as dimethylformamido or *o*-nitrotoluene, because of considerably rapid oxidation from Co(II) to Co(III).

Solvation effects on reaction (2) may be defined in terms of a difference of solvation free energy between five and six coordinate complexes. Since the difference depends on electrostatic solvent–solute interactions, more polar species are stabilized with increasing solvent polarity, consequently shifting the equilibrium to the polar species. A few reports [9, 16] may support this description; the $P_{1/2}$ values are smaller in more polar solvent, stabilizing the charge separation of $M(II)^{\delta+}$–$O_2^{\delta-}$ bond. While the porphyrins of those systems have no polar site such as amido groups in the cavity or have no cavity, the complexes prepared have four amido groups in the cavity. The amido groups will stabilize the polar linkage of $Co(II)^{\delta+}$–$O_2^{\delta-}$ by a hydrogen bond or the like, even in non-polar solvent, so that the solvation effects on these complexes should be weakened. In fact, little variation of the $P_{1/2}$ values of Co(tNBP) strongly supports this explanation (Table IV). A similar phenomenon has also been observed for the 'capped' Fe(II) complex [6(b)], although the polar sites of the complex are ether and ester linkages. Thus, the pocket polarity would reduce the solvation effects on oxygenation.

In contrast to Co(tNBP) the $P_{1/2}$ values of Co(tN3,5-mBP) varies with solvent polarity, although both complexes might have a similar structure. This result indicates that in Co(tN3,5-mBP), the two methoxy groups in addition to Co(tNBP) would be responsible for this variation. While Co(tN2,6-mBP) has the same number of methoxy groups, the variation of $P_{1/2}$ is small as in the case of Co(tNBP). This may be a reasonable observation because the methoxy groups in the complex could not be accessible to the coordinated dioxygen molecule (*vide supra*). It should be emphasized that solvation effects would again appear on oxygenation reaction when an additional polar group is incorporated into the

*Precise $P_{1/2}$ values were obtained in a range between 50 and 1000 Torr in this work.

cavity in picket fence complexes, as with 'flat-open' and 'bis pocket' porphyrin complexes. Further, the solvation effects would be responsible for the decrease of O_2 affinity for the complexes containing a replaced polar substituent in the cavity. The amido groups linking the four substituents to the porphyrins are also strongly polar. Nonetheless, these groups may be rigidly placed in space at the bottom of the cavity and the solvent molecule could not access to the –NH– sites, so that the 'protected' –NH– groups themselves would not be affected by solvation. Similar reasoning may be also expected for the 'capped' porphyrin complex. Consequently, protected polar sites in the cavity may weaken the solvation effects on oxygenation, but unprotected polar groups accessible to coordinated dioxygen molecule would again bring about the effects.

The $P_{1/2}$ values of Co(tN3,5-mBP) in the mixed solvent chlorobenzene–*o*-nitrotoluene (10:1) are the lowest among those for other solvents. A similar tendency is also observed for Co(tN2,6-mBP) and Co(tNBP). The empirical polarity scale is used here as dielectric constants, and the value of the mixed solvent is a weighted mean of those of *o*-nitrotoluene and chlorobenzene. This value may be different from the true value, but would not deviate so much [26(a)]. However, considering the solvent–solute interactions in a mixed solvent system, the use of this value as a measure of polarity may be less firm, because solvation of the solute molecule by one of the two solvents would occur preferentially [27]. Accordingly, the local polarity may be at least one of the dominant factors for the highest O_2 affinity in the mixed solvent system; probably oxy complexes would be solvated preferentially by *o*-nitrotoluene. A similar tendency is also observed when changing the base concentrations (Table V). In determining the $P_{1/2}$ values, excess base concentration was required to keep the predominant species as a five coordinate complex (99%) in the absence of oxygen. Recognizing that the solvent is a mixture of toluene and free base, these results would also be reasonable.

TABLE V. Influence of Base Concentration on $P_{1/2}$ Values[a]

Complex	Base concentration (M)	$P_{1/2}$ (torr)
Co(tNBP)(py)	1.3×10^{-2}	128
	1.3×10^{-1}	117
Co(tN2,6-mBP)(py)	1.3×10^{-2}	315
	1.3×10^{-1}	260
Co(tN3,5-mBP)(py)	1.3×10^{-2}	1200
	1.3×10^{-1}	600
Co(tN3,5-mBP)(1-MeIm)	4.1×10^{-3}	122
	4.1×10^{-2}	83

[a]At 0 °C in toluene.

In natural systems, the solvent molecule (H_2O) may not present near the active sites both in the oxy and deoxy states so that these solvation effects would not need to be considered. However, in discussing the intramolecular electrostatic interactions by O_2 affinity in model systems, it may be necessary to take into account the solvation effects. Even if the solvation free energy of the oxy state in the complexes containing an unprotected polar site was similar to that of the complexes with a protected polar site, the solvation free energy of the deoxy state might differ in the two kinds of the complexes.

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