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Note

Effect of aromatic–aromatic interaction on ligand binding to zinc porphyrins

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Abstract

Two zinc porphyrins with a superstructure around the ligand binding sites have been prepared and characterized by ^1H NMR spectroscopy. The binding properties of amine ligands to the zinc porphyrins were analyzed by UV–Vis and ^1H NMR spectroscopy. The thermodynamic parameters for ligand binding to the zinc porphyrins were estimated and compared to those of zinc porphyrins with and without the superstructure. The binding of aromatic amines to the superstructured zinc porphyrins bearing phenyl groups was found to be strong compared to the binding of butylamine to the zinc porphyrins. The enhanced binding of aromatic ligands to the zinc porphyrins was discussed in terms of the relation between ligand geometries and the superstructure.

Keywords: Zinc complexes; Porphyrin complexes; Ligand binding; Aromatic interaction; NMR spectroscopy

1. Introduction

Zinc porphyrins (ZnP) are known to bind an axial ligand (L) such as pyridines to form five-coordinated complexes (ZnP·L) as shown in Eq. (1)

$$ZnP + L \overset{K}{\rightleftharpoons} ZnP \cdot L \qquad (1)$$

where K is the formation constant of ZnP·L. There have been many studies on the factors affecting the K values of ZnP·L:ligand basicities [1–3], porphyrin basicities [4,5] and solvents [6,7]. We have studied the effects of non-bonding interaction between ligands and zinc porphyrins on K values using zinc porphyrins with a superstructure constructed near the ligand binding sites [8,9]. Non-bonding interactions such as hydrogen bonding and aromatic–aromatic interactions play important roles for the binding of substrates to enzymes or for the stabilization of the conformation of proteins [10,11].

In this paper, we report the synthesis of superstructured porphyrins and their zinc complexes and the formation constants for aromatic amines or butylamine adducts of the zinc prophyrins, and the effects of aromatic–aromatic interaction between the ligands and the superstructures on the formation of the ligand adducts are also discussed.

2. Experimental

2.1. Measurements

The formation constants for the ligand adducts to the zinc porphyrins in $CHCl_3$ were determined by spectrophotometric titration as described previously [8]. Proton NMR spectra were recorded on a JEOL GSX-400 spectrometer. The chemical shift values for the porphyrin moieties in ZnP·L were obtained from a sample solution containing ZnP ($\sim$2 mM) and L ($>$10 mM) and those for the bound ligand (L) were obtained from a sample solution containing ZnP ($\sim$2 mM) and L ($\sim$1.4 mM) in $CDCl_3$.

To discuss the binding properties of amine ligands to the superstructured zinc porphyrins (ZnP1) toward a ligand (L1), we define K_{recog} as Eq. (2) [12].

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$$K_{recog} = [K(ZnP1\text{–}L1)/K(ZnP1\text{–}ba)]/[K(Zn\text{-}\mathbf{1}\text{–}L1)/K(Zn\text{-}\mathbf{1}\text{–}ba)] \quad (2)$$

According to Eq. (2), the differences in Zn–L bond strength that depend on the pK_a of L are cancelled by each other. If ZnP1 prefers L1 in terms of attractive interligand interactions, the K_{recog} value becomes larger than unity.

2.2. Materials

Pyridine (py), 4-methylpyridine (4-mepy), isoquinoline (iqu) and butylamine (ba) were vacuum distilled from KOH. 4-Phenylpyridine (4-phpy) was recrystallized from benzene/hexane. Zn-**1** and Zn-**2** were prepared by the method reported previously [13,8].

H_2-3b. A CH_2Cl_2 solution (200 ml) containing 200 mg (0.24 mmol) of 5β,15β-bis(2-aminophenyl)-10α,20α-(nonanediamidodi-*o*-phenylene)porphyrin, H_2-Azamββ [14], was treated with pyridine (0.8 ml) and $C_6H_5CH_2COCl$ (0.64 ml, 4.84 mmol) in an ice bath. The mixture was stirred for 0.5 h, then 10% aqueous ammonia (200 ml) was added and the mixture was stirred for 0.5 h. The organic layer was separated and stripped to dryness. The resultant solid was dissolved in CH_2Cl_2 and chromatographed on a silica-gel column (CH_2Cl_2, 3×25 cm). The column was eluted with 5:1 CH_2Cl_2/ether. The product was recrystallized from CH_2Cl_2/hexane, yielding 180 mg (69%). *Anal.* Calc. for $C_{69}H_{58}N_8O_4 \cdot H_2O$: C, 76.65; H, 5.59; N, 10.36. Found. C, 76.75; H, 5.46; N, 10.28%.

H_2-3c. This porphyrin was prepared from H_2-Azamββ (200 mg, 0.24 mmol) and $C_6H_5(CH_2)_2COCl$ (0.72 ml, 4.85 mmol) in a similar manner as described above for H_2-**3b**, yielding 120 mg (44%). *Anal.* Calc. for $C_{71}H_{62}N_8O_4 \cdot H_2O$: C, 76.87; H, 5.82; N, 10.10. Found. C, 76.78; H, 5.64; N, 10.01%.

Zinc porphyrins. A solution of acetic acid (100 ml) containing CH_3COONa (1 g), porphyrin (0.1 mmol) and $Zn(CH_3COO)_2 \cdot 2H_2O$ (0.6 mmol) was heated at 50 °C for 15 min. The solution was stripped to dryness and the residue was dissolved in CH_2Cl_2. The solution was washed three times with 10% aqueous ammonia, then with water. The organic layer was separated and dried over Na_2SO_4. The solution was stripped to dryness. The resultant solid was dissolved in CH_2Cl_2 and chromatographed on a silica-gel column (CH_2Cl_2, 2.5×20 cm). The column was eluted with 4:1 CH_2Cl_2/ether. The product was recrystallized from CH_2Cl_2/hexane. The yield was quantitative.

Zn-3b. Anal. Calc. for $ZnC_{69}H_{56}N_8O_4 \cdot H_2O$: C, 72.40; H, 5.11; N, 9.79. Found. C, 71.88; H, 4.92; N, 9.55%. UV–Vis ($\lambda_{max}(CHCl_3)$): 400(sh), 422, 510, 547, 580 nm.

Zn-3c. Anal. Calc. for $ZnC_{71}H_{60}N_8O_4 \cdot H_2O$: C, 72.72; H, 5.33; N, 9.56. Found. C, 72.62; H, 5.07; N. 9.44%. UV–Vis ($\lambda_{max}(CHCl_3)$): 400(sh), 421, 511, 547, 580 nm.

3. Results and discussion

Because the binding of ligands to zinc porphyrins occurs at both sides of the prophyrins, a heptamethylene chain was strapped over one side of the porphyrin to prevent the binding of ligands to that side [8]. Fig. 1 shows the complexes used in this study and illustrates the structure of the fence – the superstructure around the ligand binding site. The UV–Vis data for Zn-**3b** and Zn-**3c** indicate that these are four-coordinated complexes [15]. The chemical shift values and the ring current shift values for the phenyl protons in the fence are given in Table 1. The ring current shift values for H_2-**3b** are more negative than those for both H_2-**3a**

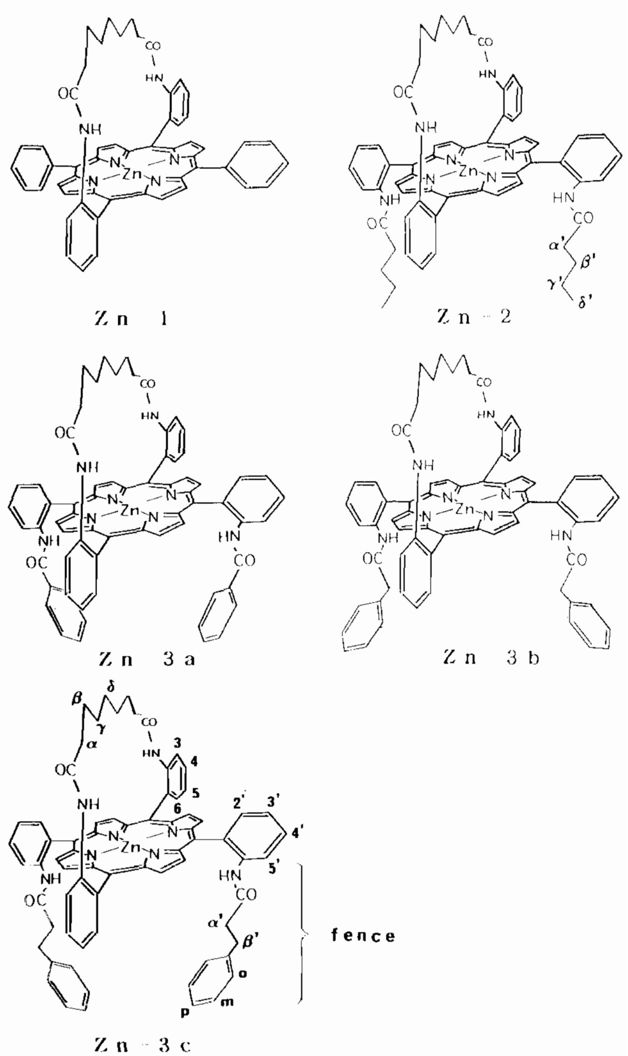


Fig. 1. Zinc porphyrins and labeling scheme.

Table 1
^{1}H NMR data for the phenyl protons in the fence of the prophyrins and their zinc prophyrins in $CDCl_3$ at 24 °C[a]

	o-proton	*m*-proton	*p*-proton	Reference
H_2-**3a**	6.57 (−1.30)	6.50 (−0.86)	6.83 (−0.60)	[9]
Zn-**3a**	6.40 (−1.47)	6.40 (−0.96)	6.74 (−0.69)	[9]
H_2-**3b**	5.63 (−2.24)	5.13 (−2.23)	5.00 (−2.43)	this work
Zn-**3b**	5.69 (−2.18)	5.10 (−2.26)	4.57 (−2.86)	this work
H_2-**3c**	6.30 (−1.57)	6.59 (−0.77)	6.68 (−0.75)	this work
Zn-**3c**	6.15 (−1.72)	6.36 (−1.00)	6.52 (−0.91)	this work

[a]For the labelling system, see Fig. 1. In parentheses are the ring current shifts: δ(proton in the porphyrins or Zn prophyrins) − δ(proton in benzamide). The δ values for the *o*-, *m*- and *p*-protons in benzamide are 7.87, 7.36 and 7.43, respectively.

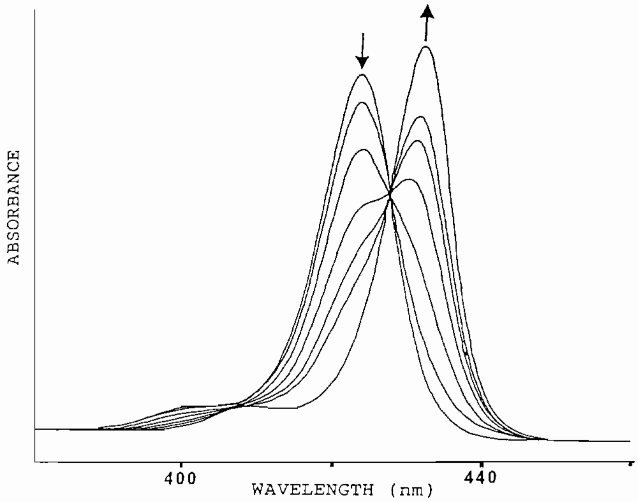
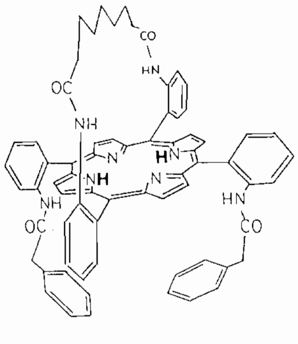


Fig. 2. Visible spectra of Zn-**3b** in $CHCl_3$ as aliquots of 4-phenylpyridine are added.



Scheme 1.

and H_2-**3c**. This implies that the phenyl groups in H_2-**3b** are closer to the porphyrin plane than those in H_2-**3a** and H_2-**3c** [16,17]. Furthermore the ring current shift value for the *p*-proton is more negative than those for the *o*- and *m*-protons. We, therefore, speculate the conformation of the fence structure in H_2-**3b** as shown in Scheme 1. Because the listed values for both the porphyrins and the corresponding zinc prophyrins are similar to each other, it is confirmed that the conformation of the fence structure is not affected by zinc insertion [8].

The *K* value for Zn-**3a**(ba) (butylamine adduct of Zn-**3a**) is similar to that for Zn-**1**(ba) as listed in Table 2. Thus, it is clear that the fence in Zn-**3a**, C_6H_5–CONH–, does not affect the binding of ba to the zinc porphyrins. The K_{recog} value for py binding to Zn-**3a** is larger than unity which implies the presence of attractive interaction between the fence and the bound py. To obtain details of the interaction, the *K* values for 4-substituted pyridines and isoquinoline (iqu) were measured. The K_{recog} values for 4-phpy and 4-mepy binding to Zn-**3a** are virtually unchanged from the values for py binding. The K_{recog} values for the ligand adducts of Zn-**3b** show a similar trend (Fig. 2). Thus, it is clear that substituents at the 4-position of pyridine do not affect the K_{recog} values for ligand binding to Zn-**3a** and Zn-**3b**. The K_{recog} values for iqu binding to Zn-**3a** and Zn-**3b** are 1.5 and 1.2-fold greater, respectively, than the values for py binding. Because CPK model experiments showed that the phenyl moiety of the bound iqu is closer in space to the phenyl group in the fence of Zn-**3a** than that of Zn-**3b**, we therefore suggest that the increase in K_{recog} for iqu binding is due to the attractive interaction between the fence and the phenyl ring in iqu in addition to the interaction between the fence and the pyridine ring in iqu. The *K* values for both Zn-**3b**(L) and Zn-**3c**(L) are small compared to that for Zn-**3a**(L). These

Table 2
Formation constants (*K*, M^{-1}) for ligand adducts of zinc porphyrins[a]

	py	4-phpy	4-mepy	iqu	ba
Zn-**1**	8.9×10^3 [b]	1.7×10^4	2.0×10^4	1.0×10^4	5.1×10^4
Zn-**3a**	3.8×10^4 (4.3)[c]	7.8×10^4 (4.6)	1.0×10^5 (5.0)	6.4×10^4 (6.4)	5.1×10^4
Zn-**3b**	1.5×10^3 (7.8)	2.9×10^3 (7.9)	3.4×10^3 (7.9)	2.0×10^4 (9.3)	1.1×10^3
Zn-**3c**	2.6×10^4 (11)	2.4×10^4 (5.1)	4.1×10^4 (7.5)	2.2×10^4 (8.0)	1.4×10^4

[a]At 25 °C in $CHCl_3$. Error limits $<10\%$. K_{recog} values are in parentheses.
[b]Ref. [8].
[c]Ref. [9].

Table 3
Thermodynamic values for ligand binding to zinc porphyrins in $CHCl_3$[a]

	Pyridine		4-Methylpyridine		4-Phenylpyridine	
	$\Delta H°$ (kJ/mol)	$\Delta S°$ (J/mol/K)	$\Delta H°$ (kJ/mol)	$\Delta S°$ (J/mol/K)	$\Delta H°$ (kJ/mol)	$\Delta S°$ (J/mol/K)
Zn-**1**	−43±2	−69±4	−46±1	−71±2	−45±1	−70±2
Zn-**3a**	−43±1	−55±2	−55±2	−88±6	−41±3	−44±8
Zn-**3b**	−37±2	−64±5	−37±1	−57±3	−34±1	−48±3
Zn-**3c**	−37±2	−40±5	−46±1	−66±3	−38±1	−44±2

Table 4
Chemical shift values of fence protons in the ligand adducts of zinc porphyrins[a]

	Zn-**3a**(py)	Zn-**3b**(py)	Zn-**3c**(py)
o	6.34 (−0.06)	5.78 (0.09)	6.40 (0.25)
m	6.24 (−0.16)	6.74 (1.64)	6.91 (0.55)
p	6.65 (−0.09)	7.00 (2.43)	6.96 (0.44)
	Zn-**3a**(4-phpy)	Zn-**3b**(4-phpy)	Zn-**3c**(4-phpy)
o	6.32 (−0.08)	5.74 (0.05)	6.20 (0.05)
m	6.04 (−0.36)	6.68 (1.58)	6.78 (0.42)
p	6.31 (−0.43)	6.93 (2.36)	6.89 (0.37)
	Zn-**3a**(iqu)	Zn-**3b**(iqu)	Zn-**3c**(iqu)
o	5.87 (−0.53)	5.56 (−0.10)	6.15 (0.00)
m	5.63 (−0.77)	6.55 (1.45)	6.90 (0.54)
p	5.95 (−0.79)	6.81 (2.24)	6.97 (0.45)

[a]At 24 °C in $CDCl_3$. For the labelling system, see Fig. 1. Chemical shift changes ($\Delta\delta$) of fence protons upon ligand binding to zinc porphyrins are in parentheses; $\Delta\delta = \delta$(proton in ZnP·L) − δ(proton in ZnP).

Table 5
Chemical shift changes[a] ($\Delta\delta$) of pyridine protons upon binding to zinc porphyrins

	Zn-**2**(py)	Zn-**3a**(py)	Zn-**3b**(py)	Zn-**3c**(py)
α	−5.41	−5.98	−6.0	−5.83
β	−1.47	−2.52	−2.0	−2.24
γ	−1.05	−2.06	−1.4	−2.17
	Zn-**2**(4-phpy)	Zn-**3a**(4-phpy)	Zn-**3b**(4-phpy)	Zn-**3c**(4-phpy)
α	−5.60	−6.15	[b]	[b]
β	−1.66	−2.73	−3.8	−2.04
o'	−0.77	−1.29	−1.1	−1.03
m'	−0.35	−0.46	−0.5	−0.38
p'	−0.25	−0.31	−0.3	−0.25

[a]At 24 °C in $CDCl_3$. $\Delta\delta = \delta$(proton in ZnP·L) − δ(proton in py or 4-phpy). The symbols o', m' and p' represent *o*, *m* and *p* protons of 4-phpy, respectively.
[b]Signals could not be calculated.

small values are due to less negative $\Delta H°$ values (Table 3).

As given in Table 4, the chemical shift values for the *o*- and *m*-phenyl protons of the fence are similar to each other in the ligand adducts of Zn-**3b** and Zn-**3c**. Thus, it is clear that the change in conformation of the fence in Zn-**3b** occurs to accommodate a ligand. On the other hand, the protons of the bound pyridines in the ligand adducts of Zn-**3a**, and Zn-**3b** and Zn-**3c** resonate at upfield compared with those in Zn-**2** (Table 5). These upfield shifts are due to the ring current of phenyl in the fence [9]. Furthermore, the phenyl protons in the bound 4-phpy resonate at virtually identical magnetic field in all the zinc porphyrins. This is consistent with the ligand behaviour described above and supports our suggestion that the attractive interaction between the bound ligands and the fence occurs mainly between the phenyl ring of the fence and the pyridine moiety of the ligands.

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