Effects of Organization of Zinc Porphyrin Hosts on Binding Enhancements and Recognition of Axial Ligands

Hiroyasu Imai* and Yoshio Uemori
Faculty of Pharmaceutical Sciences, Hokuriku University, 3 Ho Kanagawa-machi, Kanazawa 920-11, Japan

Two zinc porphyrin hosts, **2** and **3**, containing an insufficiently preorganized binding pocket above each porphyrin plane have been synthesized and characterized. The binding behaviour of these hosts with various amine ligands as guests were examined spectrophotometrically in $CHCl_3$ and were compared with that of a 'bis-roof' porphyrin zinc(II) complex, **1**, which has a similar but fully preorganized binding pocket. The binding enhancements and shape selectivity revealed by **1** for saturated amines were almost diminished in **2** and **3**. Proton NMR data showed that an induced fit of **2** for amine guests was incomplete probably owing to a weak driving force by non-polar host–guest interactions. Therefore, preorganization of the porphyrin hosts is indispensable to show recognition ability for amines in non-polar environments. The binding enhancements that provide the recognition phenomenon for amine guests are attributed to the dispersion force between the porphyrin hosts and the amine guests.

Effective host–guest complexation can be achieved both in cases where preorganization of host molecules has been provided prior to the host–guest association and where guest molecules structurally or electrostatically fit the binding site of a host molecule.[1] These two factors may essentially be independent of each other, because the former factor concerns the potential activity or instability of host molecules before complexation, whereas the latter factor, that is complementarity between host and guest, depends on the stability of the host–guest complex. The preorganization of the host strengthens binding of any guests,[1] and the complementarity dominates molecular recognition that is critical to enzyme functions, where various polar, non-polar and steric interactions apparently act as driving forces for such complexation.[1–4]

The relevance of metalloporphyrin hosts to haem-containing enzymes has led to the design and synthesis of a variety of superstructured porphyrins.[4,5] The binding behaviour of the metalloporphyrin hosts with organic guests as an axial ligand has provided useful information on multiple recognition in which the coordination bond acts as a recognition site.[6–14] In earlier work, Imai and co-workers[14] reported that a zinc 'bis-roof' porphyrin, Zn(BRP) (**1** in Fig. 1), apparently recognizes N-donor axial ligands in non-polar organic solvents on the basis of non-polar attractive interactions of the superstructure with the axial ligands. Although the superstructure constructing the binding pocket of host **1** seems sufficiently preorganized in the absence of a guest, whether the preorganization actually participates in the ability of molecular recognition remained obscure. In this work, we focused our attention on the relationship between the organization of host structures and selectivity for guests by the hosts, and we have synthesized porphyrin hosts **2** and **3**, which are less preorganized compared with **1**. Comparisons of the binding behaviour of these porphyrin hosts with axial ligands provide an opportunity to explore non-polar attractive interactions and also to gain a fundamental understanding of host–guest complexation in hydrophobic environments.

Experimental

Measurements.—Proton NMR spectra were recorded on a JEOL JMN-EX-90A, a JEOL JMN-FX-100, or a JEOL GSX-400 spectrometer. Visible absorption spectra were obtained with a Hitachi 340 or a Hitachi U-3000 spectrophotometer. The equilibrium data for N-donor axial ligands were determined by spectrophotometric titrations of porphyrin complexes with ligand solutions as previously described.[8b]

Materials.—Amine ligands, except for az,† prl and iqu, were purified by distillation from KOH. Azetidine (Aldrich) and prl (Aldrich) were dried over molecular sieves (4 Å). Isoquinoline was purified by vacuum distillation. Chloroform for spectral measurements was ethanol-free (HPLC grade, Merck) and was dried over molecular sieves (4 Å). Dichloromethane, dimethylformamide (DMF) and tetrahydrofuran (THF) were of reagent grade quality and were dried over molecular sieves (4 Å). 2,6-Lutidine was distilled from KOH. The silica gel for chromatography was Wakogel C-200 (200 mesh). Zn(BRP) (**1**)[14] and Zn(T-*p*-CH_3PP)[15] were prepared according to the literature.

Ethyl 3-hydroxy-5-methoxybenzoate **5**. To a mixture of 7.0 g (38 mmol) of ethyl 3,5-dihydroxybenzoate **4** in 120 cm^3 of acetone and 11 g of K_2CO_3 was added a solution of 2.4 cm^3 (38 mmol) of methyl iodide in 40 cm^3 of acetone. The mixture was stirred for 3 h at 55 °C under N_2. After filtration, the reactant solution was reduced in volume on an evaporator. The residual oily mixture was chromatographed on a silical gel column (4 × 35 cm, benzene) and eluted with benzene. After the 3,5-dimethoxy derivative as a by-product had passed through the column, elution with benzene–diethyl ether (20:1) eluted the desired benzoate. Removal of the solvent resulted in white crystals (2.2 g, 30%); m.p. 68–69 °C; δ_H($CDCl_3$) 1.38 (3 H, t), 3.81 (3 H, s), 4.37 (2 H, q), 6.29 (1 H, br s), 6.64 (1 H, t) and 7.1–7.2 (2 H, m).

Diethyl 5,5'-dimethoxy-3,3'-(pentane-1,5-diyldioxy)dibenzoate **6a**. To a mixture of 3.0 g (15 mmol) of **5** in 100 cm^3 of acetone and 6 g of K_2CO_3 was added a solution of 1.0 cm^3 (7.4 mmol) of 1,5-dibromopentane in 30 cm^3 of acetone. The mixture was refluxed for 60 h under N_2. After filtration, the

† Abbreviations: az, azetidine; dea, diethylamine; pip, piperidine; py, pyridine; iqu, isoquinoline; ba, butylamine; T-*p*-CH_3PP, dianion of *meso*-tetrakis(*p*-methylphenyl)porphyrin; BRP, dianion of 'bis-roof' porphyrin; MPBHP, dianion of methoxyphenyl 'basket-handle' porphyrin; TMBPP, dianion of α,β,α,β-*meso*-tetrakis[*o*-(3,5-dimethoxybenzoylamino)phenyl]porphyrin; TamPP, dianion of *meso*-tetrakis(*o*-aminophenyl)porphyrin.

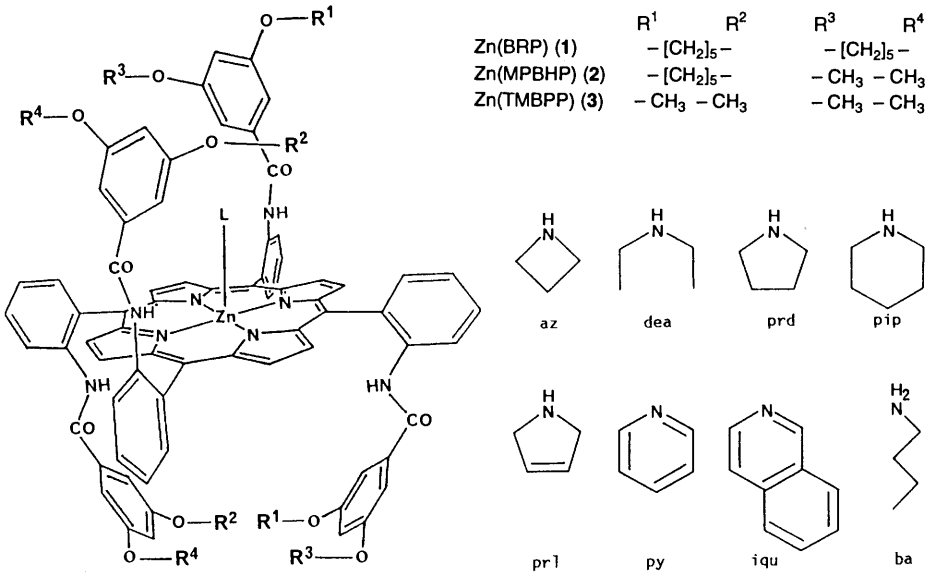


Fig. 1 Zinc porphyrin hosts and amine ligands L

reactant solution was evaporated to dryness. The residual solid was chromatographed on a silica gel column (4 × 35 cm, benzene) and eluted with benzene–diethyl ether (40:1), yielding the desired dibenzoate (2.3 g, 65%); m.p. 105–106 °C; $\delta_H(CDCl_3)$ 1.39 (6 H, t), 1.6–2.0 (6 H, m), 3.83 (6 H, s), 4.02 (4 H, t), 4.37 (4 H, q), 6.64 (2 H, t) and 7.18 (4 H, d).

5,5′-Dimethoxy-3,3′-(pentane-1,5-diyldioxy)di(benzoic acid) **6b**. The precursor diester **6a** (1.3 g, 2.8 mmol) was suspended in 150 cm^3 of acetone. A solution of 5.0 g of NaOH in 50 cm^3 of H_2O was added to the mixture. The mixture was then stirred for 4 h at 40 °C, and the suspended solid was dissolved by this treatment. To the solution was added 2 mol dm^{-3} HCl until the pH of the mixture was lowered to about 2. Removal of acetone from the mixture by evaporation yielded a white solid. The solid was filtered off, washed well with H_2O, and dried at 80 °C under vacuum (1.1 g, 96%); m.p. 153–154 °C; $\delta_H(D_2O–K_2CO_3)$ 1.5–1.9 (6 H, m), 3.76 (6 H, s), 4.00 (4 H, t), 6.54 (2 H, s) and 7.06 (4 H, s).

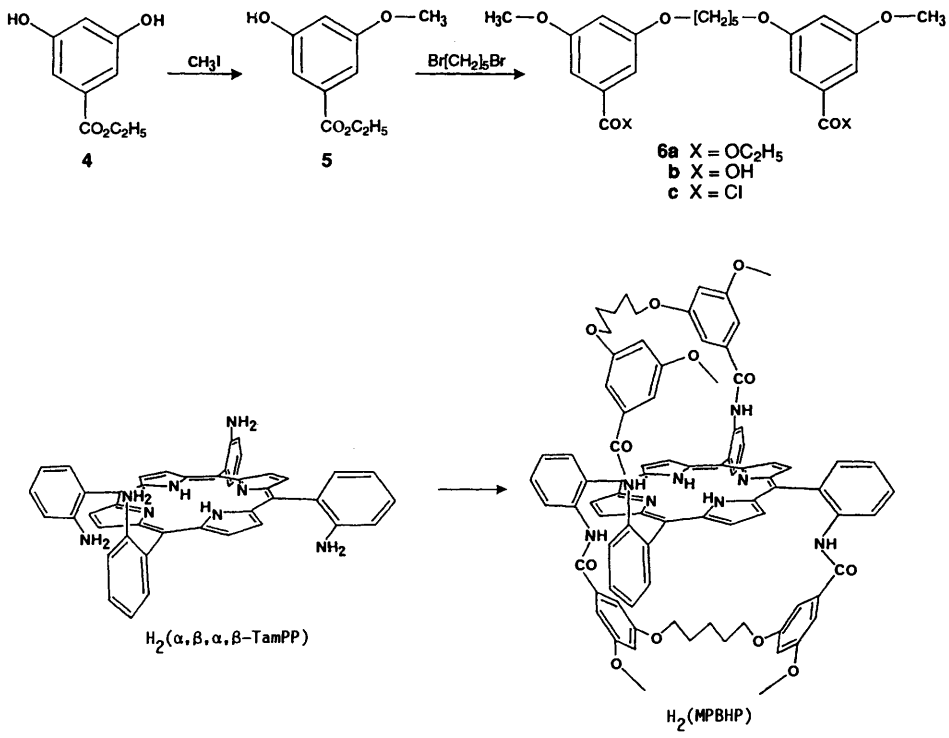
5,5′-Dimethoxy-3,3′-(pentane-1,5-diyldioxy)di(benzoyl chloride) **6c**. The precursor diacid **6b** (1.0 g, 2.5 mmol) was heated at reflux for 3 h in 20 cm^3 of $SOCl_2$ containing a drop of DMF. Removal of excess of $SOCl_2$ from the mixture under vacuum gave a pale-yellow solid (0.95 g, 87%); m.p. 87–90 °C; $\delta_H(CDCl_3)$ 1.7–2.0 (6 H, m), 3.84 (6 H, s), 4.02 (4 H, t), 6.74 (2 H, t) and 7.23 (4 H, d).

Methoxyphenyl Basket Handle Porphyrin, H_2 (MPBHP).— To a solution of 0.40 g (0.59 mmol) of α,β,α,β-*meso*-tetra(*o*-aminophenyl)porphyrin in 600 cm^3 of dry CH_2Cl_2 containing 1 cm^3 of *N*-methylmorpholine in an ice bath was added a solution of 0.73 g (1.7 mmol) of the diacid chloride, **6c**, in 350 cm^3 of dry CH_2Cl_2. The solution was allowed to stand for 40 h in a refrigerator. After the volume of the reactant was reduced to 200 cm^3 on an evaporator, the organic solution was washed with aqueous ammonia, then twice with H_2O, and was dried over anhydrous Na_2SO_4. After filtration, the solution was evaporated to dryness. The residue was purified by silica gel column chromatography (3 × 40 cm, benzene) and eluted with benzene–acetone (30:1). The resulting porphyrin was recrystallized from $CHCl_3$–hexane (0.45 g, 54%); $\delta_H(CDCl_3)$ −2.59 (2 H, s), 0.35 (4 H, m), 0.59 (8 H, m), 2.84 (8 H, t), 3.54 (12 H, s), 5.36 (4 H, s), 6.00 (4 H, s), 6.76 (4 H, s), 7.45 (4 H, t), 7.62 (4 H, d), 7.88 (4 H, t), 7.95 (4 H, s), 8.89 (8 H, s) and 8.93 (4 H, d); $\lambda_{max}(CHCl_3)$/nm 403sh, 424.2 Soret, 482sh, 517.2, 551.2, 590.4 and 646.4; *m/z* (FAB MS) 1413 $[(M + 1)^+]$ (Found: C, 71.7; H, 5.3; N, 7.6. $C_{86}H_{74}N_8O_{12}\cdot\frac{1}{4}CHCl_3$ requires C, 71.87; H, 5.19; N, 7.77%).

H_2(TMBPP). To a solution of 0.30 g (0.44 mmol) of α,β,α,β-*meso*-tetra(*o*-aminophenyl)porphyrin in 100 cm^3 of dry CH_2Cl_2 containing 1 cm^3 of *N*-methylmorpholine in an ice bath was added 1.3 g (6.5 mmol) of 3,5-dimethoxybenzoyl chloride. After the mixture was stirred for 4 h at that temperature, the solution was washed with aqueous ammonia, then twice with H_2O. The organic solution was dried over anhydrous Na_2SO_4 and then evaporated to dryness. The residue was purified by silica gel column chromatography, (3 × 30 cm, $CHCl_3$) and eluted with $CHCl_3$–diethyl ether (10:1) yielding the desired porphyrin (0.48 g, 82%); $\delta_H(CDCl_3)$ −2.60 (2 H, s), 2.48 (24 H, s), 5.50 (8 H, d), 5.72 (4 H, t), 7.45 (4 H, s), 7.56 (4 H, t), 7.8–8.1 (8 H, m), 8.83 (4 H, d) and 8.93 (8 H, s); $\lambda_{max}(CHCl_3)$/nm 403sh, 423.4 Soret, 482sh, 516.0, 549.8, 589.8 and 649.0 (Found: C, 70.8; H, 4.9; N, 8.15. $C_{80}H_{66}N_8O_{12}\cdot\frac{1}{4}CHCl_3$ requires C, 70.81; H, 4.91; N, 8.23%).

Zn(MPBHP), **2**. A zinc ion was inserted into H_2(MPBHP) by a method similar to one described elsewhere.[8b] To a solution of 0.30 g (0.21 mmol) of H_2(MPBHP) in 50 cm^3 of THF were added 0.50 g of $ZnCl_2$ and 0.2 cm^3 of 2,6-lutidine. After being stirred for 3 h at 60 °C, the reaction mixture was evaporated and the residue was dissolved in 200 cm^3 of $CHCl_3$. The organic layer was washed twice with 200 cm^3 of H_2O and dried over anhydrous Na_2SO_4. After removal of the solvent, the solid was purified on a silica gel column (3 × 30 cm, $CHCl_3$), eluting with $CHCl_3$–diethyl ether (15:1) (0.27 g, 86%); $\delta_H(CDCl_3)$ 0.44 (4 H, m), 0.71 (8 H, m), 2.91 (8 H, t), 3.39 (12 H, s), 5.34 (4 H, s), 5.89 (4 H, s), 6.52 (4 H, s), 7.40 (4 H, t), 7.66 (4 H, d), 7.81 (4 H, t), 7.96 (4 H, s), 8.87 (4 H, d) and 8.94 (8 H, s); $\lambda_{max}(CHCl_3)$/nm 403sh, 424.2 Soret, 511sh, 549.8 and 588sh; *m/z* (FAB MS) 1475 (M^+) (Found: C, 68.9; H, 5.1; N, 7.1. $C_{86}H_{72}N_8O_{12}Zn\cdot\frac{1}{4}CHCl_3$ requires C, 68.84; H, 4.84; N, 7.45%).

Zn(TMBPP), **3**. This compound was obtained from H_2(TMBPP) by a method similar to that for **2**, except for the zinc-insertion temperature. The metallation reaction was carried out at 50 °C for 2 h so as not to allow thermal isomerization to other atropisomers; $\delta_H(CDCl_3)$ 2.58 (24 H), 5.28 (8 H, d), 5.66 (4 H, t), 7.46 (4 H, s), 7.54 (4 H, t), 7.87 (4 H, t), 8.10 (4 H, d), 8.84 (4 H, d) and 8.93 (8 H, s); $\lambda_{max}(CHCl_3)$/nm 403sh, 428.0 Soret, 518sh, 556.2, 595.4 and 625.2; *m/z* (FAB MS) 1395 (M^+) (Found: C, 67.7; H, 4.5; N, 7.8. $C_{80}H_{64}N_8O_{12}Zn\cdot\frac{1}{4}CHCl_3$ requires C, 67.66; H, 4.55; N, 7.87%).



Scheme 1

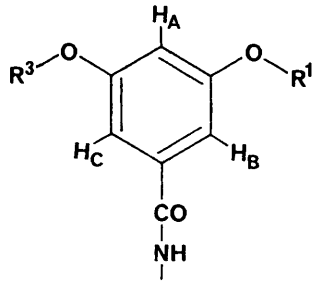
Results and Discussion

Synthesis and Characterization.—Each of the zinc porphyrins used in the present work has the same superstructure above each porphyrin plane. This prevents the occurrence of two regioisomers of five-coordinated complexes by addition of an axial ligand. For the preorganized porphyrin complex, Zn(BRP) **1**, we tried to break successively the two linking chains between the two phenyl spacers (3,5-disubstituted-benzoylamino groups in Fig. 1). Scheme 1 outlines the procedure used to prepare the insufficiently preorganized porphyrin, H_2(MPBHP). Coupling of **4** and CH_3I in an equimolar ratio gave the mono-methoxy derivative, **5**. Bridging of two molecules of **5** by dibromopentane afforded **6a** in fair yield. Upon treatment with basic aqueous acetone, the diester **6a** was hydrolysed to the diacid **6b**, which was then easily converted into the diacid chloride **6c** with thionyl chloride. The final high-dilution coupling between the diacid chloride and H_2(α,β,α,β-TamPP) gave the desired porphyrin, H_2(MPBHP), in a satisfactory yield of greater than 50%, which may result from the complementary geometries of the diacid chloride and the amino groups of H_2(TamPP). The zinc ion was inserted into H_2(MPBHP) by a published method.[8b]

The visible absorption spectra of metal-free porphyrins used in the present work are substantially similar, indicating the resemblances in the electronic nature of these porphyrins. By contrast, such similarities in spectra are not observed for their zinc complexes. The absorption maxima of Zn(TMBPP) (**3**) are obviously red-shifted by several nanometers from those of Zn(MPBHP) (**2**) (see the Experimental section) and **1**.[14] This result suggests that a water molecule ligates tightly to **3** as well as in the cases for a few zinc superstructured porphyrin complexes.[8b,14]

The ^{1}H NMR spectrum for **2** is essentially similar to that of **1** or **3**, except for the phenyl proton signals of the spacers forming the binding pocket and for the methyl and methylene proton signals. Table 1 lists the chemical shifts of the phenyl protons of the spacers. The H_B and H_C signals for **1** and its amine adducts appear in the same magnetic fields because of the symmetrical face-to-face geometry of the spacers. In contrast, the corresponding H_B and H_C protons for **2** give rise to largely different chemical shifts by 1.18 ppm. This suggests that the two phenyl spacers are probably in an edge-to-edge geometry as shown schematically on the left in Fig. 2.

Table 1 Chemical shifts of phenyl spacers[a]



	H_A	H_B	H_C
2	5.89	5.34	6.52
2-(az)	5.93	5.38	6.57
2-(pip)	5.96	5.46	6.64
2-(dea)	5.96	5.51	6.60
1	5.81	5.87	
1-(az)	5.82	5.89	
1-(dea)	5.84	5.93	

[a] δ, in $CDCl_3$.

Binding Behaviour.—It is generally accepted that zinc porphyrins (ZnP) show a well-defined equilibrium between four- and five-coordination, eqn. (1), where L is an axial ligand.

$$ZnP + L \overset{K}{\rightleftharpoons} ZnPL \quad (1)$$

From a comparison of the equilibrium data of two axial ligands (L_1 and L_2) with two porphyrin complexes (ZnP_1 and ZnP_2), the recognition parameter for L_1 by ZnP_1 can be expressed as

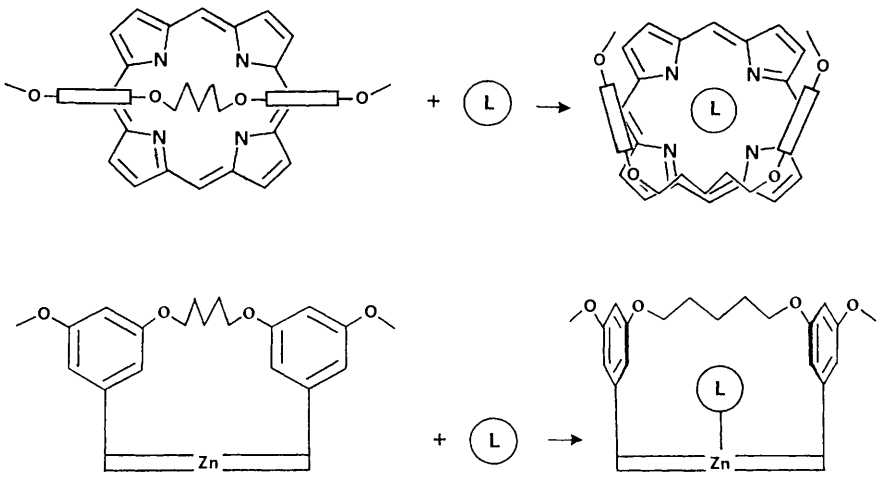


Fig. 2 Schematic representation for possible reorganization of **2** upon guest binding

Table 2 Binding constants[a] of zinc porphyrins with amines

	az	dea	prd	pip	prl	py	iqu	ba
1	1.4×10^{7}[b]	5.8×10^{4}	2.7×10^{6}[b]	2.2×10^{5}[b]	1.8×10^{6}	1.4×10^{4}	6.1×10^{2}	7.7×10^{4}[b]
	(18)[c]	(8.7)	(4.4)	(0.70)	(10)	(0.78)	(0.030)	(1)
2	1.8×10^{6}	1.2×10^{4}	1.3×10^{6}	6.5×10^{5}	4.3×10^{5}	9.0×10^{4}	1.1×10^{5}	7.6×10^{4}
	(2.3)	(1.9)	(2.2)	(2.1)	(2.4)	(5.2)	(5.5)	(1)
3	7.5×10^{5}	4.2×10^{3}	6.9×10^{5}	2.5×10^{5}	2.2×10^{5}	3.7×10^{4}	7.7×10^{4}	4.9×10^{4}
	(1.5)	(1.0)	(1.8)	(1.5)	(1.9)	(3.3)	(6.0)	(1)
Zn(T-*p*-CH_3PP)	1.1×10^{5}[b]	9.6×10^{2}	8.7×10^{4}[b]	4.5×10^{5}[b]	2.6×10^{4}	2.5×10^{3}	2.9×10^{3}	1.1×10^{4}[b]

[a] At 25 °C in $CHCl_3$ cm^3 mol^{-1}. [b] Ref. 14. [c] K_{recog} values are in parentheses.

shown in eqn. (2) where the differences in Zn–L bond strength

$$K_{recog} = [K(ZnP_1\text{–}L_1)/K(ZnP_1\text{–}L_2)]/[K(ZnP_2\text{–}L_1)/K(ZnP_2\text{–}L_2)] \quad (2)$$

that depend on the pK_a of L are cancelled by each other, and further, solvation of the binding sites or ligation of H_2O prior to L binding cannot affect the K_{recog} values. If ZnP_1 prefers L_1 in terms of attractive interligand interactions, the K_{recog} values become larger than unity. In accordance with a previous report,[14] we chose Zn(T-*p*-CH_3PP) and ba as ZnP_2 and L_2, respectively, for comparison. These two compounds, ZnP_2 and L_2, interact less with L_1 and ZnP_1, respectively, even if L_1 is large or ZnP_1 is an encumbered porphyrin.

Table 2 summarizes the binding data obtained by photometric titration of a complex solution with amine ligands. In agreement with a previous report,[14] **1** which has a fully preorganized structure shows shape-selective recognition for amine ligands. Moderately bulky amines, az and dea, bind more strongly to **1** than a less hindered amine, ba. These binding enhancements are also explained in terms of increased van der Waals contacts with the binding pocket.[14] However, binding of the larger amine, iqu, is drastically weakened due to greater steric repulsions from the binding pocket. The observation that the K_{recog} values for pip and py are about unity may result from the balance of attractions against repulsions between these amines and the binding pocket of **1**.

In the case of a partially preorganized porphyrin, **2**, the K_{recog} values are consistently different from those of **1**. The binding enhancements observed for az and dea with **1** are drastically decreased in **2** to about 2 for K_{recog}. Interestingly, K_{recog} for pip binding increases to 2.1 in **2**. This is due to the lack of steric repulsions from the binding pocket that occur in the preorganized porphyrin, **1**. Thus, the recognition phenomenon observed for saturated amines by **1** is considerably diminished by partially releasing the preorganization. This fact suggests that the reorganization of the binding pocket cannot successfully occur in **2** as shown in Fig. 2. The incompleteness of the induced fit of **2** for amines is supported well by the ^1H NMR data in Table 1. Upon amine binding, the proton signals of the phenyl spacers of **2** shift to a greater extent, compared with the shift changes of **1**. However, the chemical shifts of amine adducts of **2** are very far apart from those of **1** in which the organization of the superstructure may be best for the bound amines.*

Further information on the relationship between preorganization and binding enhancements is given by the equilibrium data for **3** of which the binding pocket is more flexible in terms of having no bridging chain between the two phenyl spacers. The K_{recog} values of **3** equal about unity for az, pip, and dea, indicating that no stabilization of the binding has occurred. Thus, in this system, two bridging chains linking the two spacers are almost indispensable for showing shape-selective binding behaviour for saturated amines on the basis of non-polar attractive interactions. Therefore, preorganization of the binding pocket of the porphyrin hosts definitively dominates both recognition and binding enhancements of saturated amines. In non-polar organic solvents, such non-polar inter-

* The chemical shifts for the amine adducts of these porphyrins are averaged values of binding and non-binding sites on the porphyrin plane, due to a rapid ligand exchange in the NMR timescale. Even if this fact is taken into account, the chemical shifts show clearly that **2** cannot fully reorganize upon amine binding.

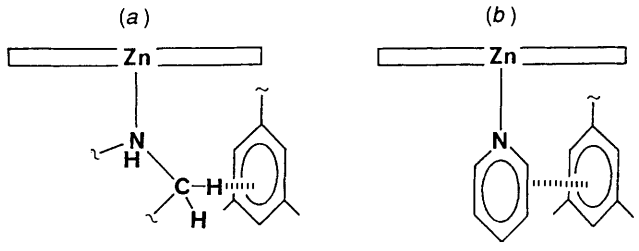


Fig. 3 Two possible interacting modes of phenyl spacers of hosts with saturated and aromatic amine ligands: (*a*) CH–π interaction; (*b*) π–π interaction

actions would be too weak to accompany reorganization that causes an induced fit for the amine guests.

These situations presented for saturated amines are also partially observed for aromatic amines. The K_{recog} values of smaller than unity for py and iqu with **1** obviously increase as the steric repulsions from the binding pocket are released in **2*** and **3**. An interesting feature of the binding data is that the K_{recog} values for aromatic amines with **2** and **3** are substantially larger than those for saturated amines.† One plausible explanation for this result is that, as shown in Fig. 3, the non-polar attractive interactions between amine ligands and the aromatic spacers of the hosts are CH–π[8b,16] and π–π[17] interactions for saturated and aromatic amines, respectively. In this case, however, the distinction of these interactions does not seem significant because of the following reason; introduction of the π system to amine ligands would not provide binding enhancements to the porphyrin hosts, since the K_{recog} values of prd are comparable to those of prl for both **2** and **3**.‡ Rather, the binding enhancements can reasonably be related to the number of van der Waals contacts, irrespective of the presence of the π system in amine guests. Consequently, the non-polar interactions between the porphyrin hosts and the amine guests would mainly be ascribed to the dispersion force in terms of the van der Waals contacts. The improved steric complementarity of iqu rather than py with **3** also reflects the difference in their K_{recog} values.

The non-polar interactions presented here must be weak in one van der Waals contact but are a potentially strong recognition factor in optimizing host–guest steric complementarity. In a suitably designed host, shape selectivity and binding enhancements of guests by the host on the basis of the non-polar interactions can be realized even in non-polar organic solvents. However, this requires rigidity and/or preorganization of the host since an induced fit of the host for guests would be insufficient in such non-polar environments.

* The comparable K_{recog} values for iqu binding to **2** and **3** suggest that slight steric repulsions from the binding pocket may still remain in the iqu adduct of **2**, thereby, the expected binding enhancement would just be cancelled.

† It may be worthwhile to note that the difference in solvation of unligated amines L_1 and L_2 in eqn. (2) affects the K_{recog} value since these amines must be desolvated upon incorporation into a binding pocket of the hosts. Therefore, attention should be paid to the use of ba for comparing the K_{recog} values of aromatic amine binding. In this case, however, the effect of solvation on K_{recog} values is substantially small and may be negligible, since the K_{recog} value for Zn(BRP)–py binding on the basis of ba binding is 1.5 in toluene (ref. 14) and 0.78 in chloroform (Table 2). This difference is also similar to those observed for the binding of saturated amines to Zn(BRP) (ref. 14).

‡ The observed difference of the corresponding values for **1** can be ascribed to the larger steric repulsions of prd than prl from the rigid binding pocket of **1**.

Acknowledgements

This work was partially supported by Grants for Scientific Research from the Ministry of Education (No. 03640530 and No. 05640636, H. I.). Y. U. acknowledges the Kisshoukai Foundation for financial support.

References

1 D. J. Cram, *Angew. Chem., Int. Ed. Engl.*, 1986, **25**, 1039; *Angew. Chem., Int. Ed. Engl.*, 1988, **27**, 1009; *J. Inclusion Phenom.*, 1988, **6**, 397.
2 J.-M. Lehn, *Angew Chem., Int. Ed. Engl.*, 1988, **27**, 89; *J. Inclusion Phenom.*, 1988, **6**, 351.
3 C. Seel and F. Vögtle, *Angew. Chem., Int. Ed. Engl.*, 1992, **31**, 528.
4 T. J. Meade and D. H. Busch, *Prog. Inorg. Chem.*, 1985, **33**, 59; D. H. Busch, *Chem. Rev.*, 1993, **93**, 847.
5 R. M. Izatt, J. S. Bradshaw, K. Pawlak, R. L. Bruening and B. J. Tarbet, *Chem. Rev.*, 1992, **92**, 1261.
6 P. E. Ellis, Jr., J. E. Linard, T. Szymanski, R. D. Jones, J. R. Budge and F. Basolo, *J. Am. Chem. Soc.*, 1980, **102**, 1889; J. E. Linard, P. E. Ellis, Jr., J. R. Budge, R. D. Jones and F. Basolo, *J. Am. Chem. Soc.*, 1980, **102**, 1896.
7 J. P. Collman, J. I. Brauman, J. P. Fitzgerald, P. D. Hampton, Y. Naruta, J. W. Sparapany and J. I. Ibers, *J. Am. Chem. Soc.*, 1988, **110**, 3477; J. P. Collman, J. I. Brauman, J. P. Fitzgerald, J. W. Sparapany and J. I. Ibers, *J. Am. Chem. Soc.*, 1988, **110**, 3486.
8 (*a*) H. Imai and E. Kyuno, *Inorg. Chim. Acta*, 1988, **153**, 175; (*b*) H. Imai and E. Kyuno, *Inorg. Chem.*, 1990, **29**, 2416.
9 Y. Uemori, H. Munakata, K. Shimizu, A. Nakatsubo, H. Imai, S. Nakagawa and E. Kyuno, *Inorg. Chim. Acta*, 1986, **113**, 31; Y. Uemori, A. Nakatsubo, H. Imai, S. Nakagawa and E. Kyuno, *Inorg. Chim. Acta*, 1986, **124**, 153; Y. Uemori, H. Miyakawa and E. Kyuno, *Inorg. Chem.*, 1988, **27**, 377.
10 Y. Aoyama, M. Asakawa, A. Yamagishi, H. Toi and H. Ogoshi, *J. Am. Chem. Soc.*, 1990, **112**, 3145; Y. Aoyama, M. Asakawa, Y. Matsui and H. Ogoshi, *J. Am. Chem. Soc.*, 1991, **113**, 6233; Y. Kuroda, Y. Kato, T. Higashioji and H. Ogoshi, *Angew. Chem., Int. Ed. Engl.*, 1993, **32**, 723.
11 C. A. Hunter, M. N. Meah and J. K. M. Sanders, *J. Am. Chem. Soc.*, 1990, **112**, 5773; H. L. Anderson, C. A. Hunter, M. N. Meah and J. K. M. Sanders, *J. Am. Chem. Soc.*, 1990, **112**, 5780; R. P. Bonar-Law and J. K. M. Sanders, *J. Chem. Soc., Chem. Commun.*, 1991, 574; S. Anderson, H. L. Anderson and J. K. M. Sanders, *Angew. Chem., Int. Ed. Engl.*, 1992, **31**, 907; R. P. Bonar-Law, L. G. Mackay and J. K. M. Sanders, *J. Chem. Soc., Chem. Commun.*, 1993, 456.
12 D. R. Benson, R. Valentekovich, C. B. Knobler and F. Diederich, *Tetrahedron*, 1991, **47**, 2401.
13 I. P. Danks, I. O. Sutherland and C. H. Yap, *J. Chem. Soc., Perkin Trans. 1*, 1990, 421; I. P. Danks, T. G. Lane, I. O. Sutherland and M. Yap, *Tetrahedron*, 1992, **48**, 7679.
14 H. Imai, S. Nakagawa and E. Kyuno, *J. Am. Chem. Soc.*, 1992, **114**, 6719.
15 A. D. Adler, F. R. Longo, J. D. Finarelli, J. Goldmacher, J. Assour and L. Korsakoff, *J. Org. Chem.*, 1967, **32**, 476.
16 M. Nishio and M. Hirota, *Tetrahedron*, 1989, **45**, 7201.
17 W. L. Jorgensen and D. L. Severance, *J. Am. Chem. Soc.*, 1990, **112**, 4768; C. A. Hunter and J. K. M. Sanders, *J. Am. Chem. Soc.*, 1990, **112**, 5525.

Paper 4/01681E
Received 21*st March* 1994
Accepted 21*st April* 1994