Synthesis and Axial-Ligand Binding of Zinc Complexes of Amphiphilic Porphyrins Containing a Hydrophobic Binding Pocket

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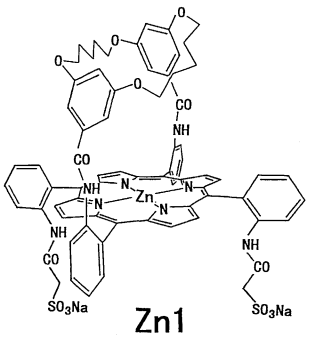
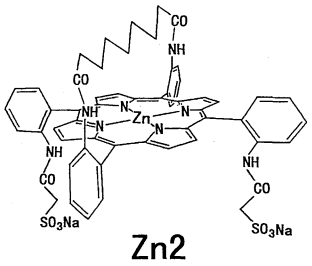
Amphiphilic zinc porphyrins containing two sulfonate groups and a hydrophobic binding pocket were synthesized efficiently and characterized. Binding of pyridine, butylamine, and pyrrolidine to the zinc complexes was examined spectrophotometrically in water and in chloroform. The binding behavior was discussed on the basis of the binding constants.

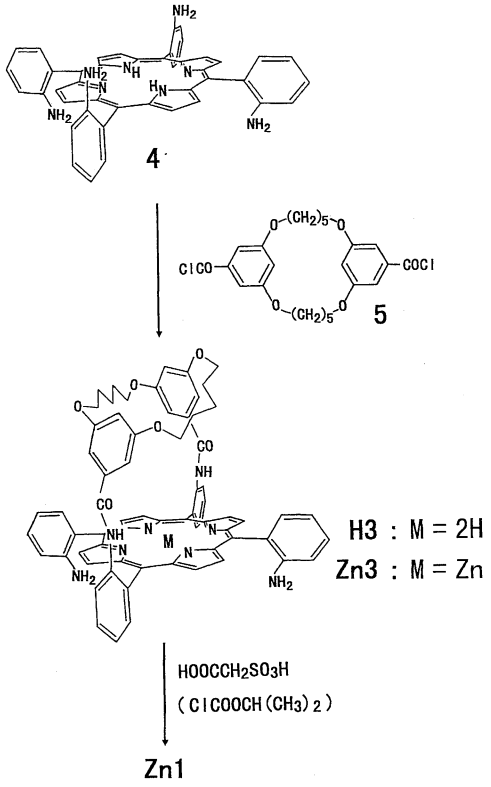
To understand structure-function relationships of metalloproteins, a variety of artificial porphyrins have been synthesized and studied.[1] Most of these porphyrins are, however, not soluble in water, hence their experimental conditions are substantially different from physiological conditions. Only limited reports[2-6] dealt with superstructured porphyrins in aqueous solutions but the synthetic methods sometimes require complicated and/or hard conditions. In order to realize a similar environment to that of biomolecules by use of artificial and low molecular weight compounds, we designed and synthesized water-soluble porphyrins and their zinc(II) derivatives (**Zn1** and **Zn2**) that contain an intramolecular hydrophobic cavity. Binding of amines to such zinc porphyrins can also be related to host-guest association phenomena.[7] Since these zinc porphyrins are amphiphilic, binding reaction of amines could be measured similarly even in quite different solvent systems.





The synthetic route is outlined in Scheme 1. High-dilution coupling of $\alpha,\beta,\alpha,\beta$-*meso*-tetrakis(*o*-aminophenyl)porphyrin **4** (570 mg, 0.84 mmol) and equimolar 3,3',5,5'-bis(1,5-pentanediyldioxy)dibenzoyl chloride **5**[7] (420 mg) in 900 cm^3 of CH_2Cl_2 containing 1 cm^3 of triethylamine gave **H3** (270 mg, 28%). Treatment of **H3** (150 mg, 0.14 mmol) with $ZnCl_2$ (450 mg, 3.3mmol) in tetrahydrofuran (40 cm^3) containing 2,6-lutidine (1 cm^3) afforded **Zn3** almost quantitatively (150 mg, 95%). To a solution of 85 mg (0.074 mmol) of **Zn3** in CH_2Cl_2 (150 cm^3) was added a solution of 400 mg (2.85 mmol) of sulfoacetic acid, 0.32 cm^3 of isobutyl chloroformate, and 0.6 cm^3 of triethylamine in CH_2Cl_2 (60 cm^3). The mixture was stirred for 10 h at room temperature, then was reduced in volume on an evaporator. The residual oily mixture was dissolved in 200 cm^3 of $CHCl_3$, and the solution was washed twice with dilute NaOH solution

Scheme 1.



(0.1 mol dm^{-3}), then twice with NaCl solution (3 mol dm^{-3}). The organic layer was dried over anhydrous Na_2SO_4, filtered, and evaporated to dryness. The solid was purified by recrystallization from $CHCl_3$/diethylether/heptane (1/5/5), yield 72 mg (68%). This porphyrin **Zn1** showed similar spectroscopic properties in both aqueous and $CHCl_3$ solutions.[8] Complex **Zn2** for comparison was prepared similarly by using 1,7-pentanedicarbonyl chloride instead of **5**. All of these reactions were carried out at room temperature where no atropisomerization of the porphyrins took place. The absence of other isomers in the porphyrins was confirmed by their ^1H NMR spectra. The synthetic procedure of the amphiphilic superstructured porphyrins presented here provides a general route to make water-soluble of porphyrins containing amino groups in mild conditions and in good yields.

It is generally accepted that zinc porphyrins form four or five coordination in solution.[7,9] Binding of amines (pyridine, butylamine, and pyrrolidine) to **Zn1** and **Zn2** was examined spectrophotometrically in water[10] and in chloroform (ethanol free)[11] as described previously.[7] In those experimental conditions, the visible spectra of these porphyrins showed that, in the absence of amines, the central zinc ion binds H_2O to form five

Table 1. Binding constants of amines to zinc porphyrins[a]

complex	solvent	amine		
		pyridine	butylamine	pyrrolidine
Zn1	$CHCl_3$	30	88	540
	H_2O	180	250	1000
Zn2	H_2O	27	28	76

[a] K/dm^3 mol^{-1}; at 25 °C. Errors in K values were smaller than 30%.

coordination in both solvents.[12] Then, the binding of amines (L) to the zinc porphyrins (ZnP) can be explained as follows:

$$ZnP \cdot OH_2 + L \rightleftharpoons ZnP \cdot L + H_2O$$

Thus, the binding constants (K = [ZnP·L]/[ZnP·OH_2][L]) of these zinc porphyrins must be decreased in terms of releasing the coordinated H_2O, compared to those for true formation of the five coordinated complex.

Table 1 lists the binding constants obtained. In aqueous solution, amines bind to **Zn1** several times more strongly than to **Zn2**. For the amine adducts of these zinc porphyrins, two regioisomers are possible because of the asymmetry on the porphyrin plane, suggesting that the observed K values are the sum of the two different equilibrium constants. In earlier studies, Uemori et al[13] have shown that a heptamethylene strap of metalloporphyrins such as **Zn2** substantially weakens the coordination of amine ligands by steric blocking. In contrast, the hydrophobic pocket of **Zn1** is suitable in size for accommodating the amine ligands.[7] Further, the binding site surrounded by the two sulfonate groups is common for **Zn1** and **Zn2**. Therefore, the large K values of **Zn1** suggest that most of the binding of the amines to this complex occurs on the hydrophobic cavity side.

In addition to the Zn-N bond, the driving forces for the amine binding to **Zn1** in aqueous solution are thought to be a hydrophobic effect and amine-porphyrin attractions which were shown for similar zinc porphyrins.[7,9] Differences in binding constants in the two solvent systems may provide information about the two factors.[14] However, further discussion on this issue will require more detailed binding data.

References and Notes

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8 Selected data: **Zn1**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.00 (m, 4H), 1.25 (m, 8H), 3.17 (s, 4H), 3.34 (br s, 8H), 5.80 (s, 2H), 5.88 (s, 4H), 6.94 (s, 2H), 7.53 (t, J = 7.5 Hz, 4H), 7.82 (m, 4H),8.08 (d, J = 7.6 Hz, 2H), 8.15 (d, J = 7.7 Hz, 2H), 8.48 (d, J = 8.4 Hz, 2H), 8.74 (d, J = 8.4 Hz, 2H), 8.79 (dd, J = 10.3 and 4.8 Hz, 8H), 8.89 (s, 2H); vis ($CHCl_3$) λ_{max} 426.0, 558.5, 596.5, (H_2O/K_2CO_3) 426.4, 560.6, 599.0 nm; Anal. Found: C, 55.20; H, 4.07; N, 6.86%; M^+, 1433. Calcd for $C_{72}H_{58}N_8O_{14}S_2Na_2Zn \cdot 2H_2O \cdot CHCl_3$: C, 55.14; H, 4.00; N, 7.05%; M, 1433. **Zn2**: ^{1}H NMR (400 MHz, CD_3OD) δ -2.41 (m, 2H), -1.29 (m, 4H), -0.74 (m, 4H), 1.11 (m, 4H), 2.95 (s, 4H), 7.58 (m, 2H), 7.73 (m, 2H), 7.84 (m, 6H), 8.02(m, 2H), 8.47 (m, 4H), 8.74 (s, 8H); vis (H_2O/K_2CO_3) λ_{max} 423.8, 556.2, 593.8 nm; Anal. Found: C, 50.36; H, 3.44; N, 8.24%; M^+, 1177. Calcd for $C_{57}H_{46}N_8O_{10}S_2Na_2Zn \cdot 2H_2O \cdot 1.5CHCl_3$: C, 50.36; H, 3.86; N, 8.03%; M, 1177. **Zn3**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.84 (m, 4H), 1.12 (m, 8H), 3.20 (br s, 8H), 5.66 (t, J = 2.2 Hz, 2H), 5.71 (d, J = 2.4 Hz, 4H), 6.67 (s, 2H), 7.03 (t, J = 7.3 Hz, 2H), 7.22 (m, 2H), 7.45 (d, J = 6.8 Hz, 2H), 7.61 (t, J = 7.6 Hz, 2H), 7.86 (t, J = 8.1 Hz, 2H), 8.07 (d, J = 7.8 Hz, 2H), 8.39 (br s, 4H), 8.40 (d, J = 8.3 Hz, 2H), 8.64 (d, J = 4.4 Hz, 4H) ; vis ($CHCl_3$) λ_{max} 422.0, 507(sh) 548.5 nm.

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10 The aqueous solutions were basic (10^{-2} mol dm^{-3} K_2CO_3; pH 11.5), and this prevents pH changes upon amine titration.

11 Complex **Zn2** is soluble in water, alcohols, and acetone, but not in chloroform to allow spectral measurements.

12 Even in such basic conditions, ligation of OH^- was not observed. The visible spectra of the zinc complexes in aqueous solution at pH 11.5 were almost the same to those at pH 6.2. Upon ligation of OH^-, the visible spectral peaks should show substantial red shifts; M. Nappa and J. S. Valentine, *J. Am. Chem. Soc.*, **100**, 5075 (1978).

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14 In general, polar binding such as coordination is stronger in non-polar solvents than in aqueous solution. However, this is not the case for **Zn1**, probably due to the hydrophobic interaction in aqueous solution.