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# Synthesis and properties of Zn-porphyrin with bipyridine-terminated side chains: large conformational change induced by metal complexation

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#### ABSTRACT

Zinc porphyrin (1) containing 2,2'-bipyridyl units at the peripheral ends of both conjugated and alkyl side chains was prepared. Upon addition of Fe(II), the three bipyridyl terminals at both ends bind to Fe(II)s to form 1:2 complex 1-2Fe. The formation of 1-2Fe induced a large conformational change in the alkyl side chains and moderately affected the binding between the zinc porphyrin and an imidazole ligand. These results show that this method is useful for the communication between the porphyrin functional site and the remote metal-binding site.

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The molecules that can reversibly change their shape and conformation in response to an external stimulus are attracting broad interest for the construction of intelligent catalysts<sup>1</sup> and receptors<sup>2</sup> as well as molecular-scale machines.<sup>3</sup> One of the challenging tasks for the construction of complex molecular systems is to transfer stimuli-induced structural alteration at a receptor to a remote functional site as a property change. Metalloporphyrins are very popular and valuable functional units for the construction of artificial enzymes where substituents around the porphyrin ring play an essential role in controlling both the catalytic and ligand-binding properties of metalloporphyrins.<sup>4</sup> The function or property change in metalloporphyrins induced by a large geometrical change via an external stimulus at a distant receptor has many potential applications. However, the modulation of the function or property in metalloporphyrins by external stimuli received at the remote receptor has not been achieved. While a natural enzyme employs a complex and precise hydrogen-bonding network to transfer local structural deformation over large distances, a much simpler approach may be possible using the combination of a rigid conjugated chain and flexible non-conjugated chains. Here we propose a relatively simple method for the communication between the porphyrin functional site and the remote stimuli-receiving site. We report the unique design, synthesis, and properties of the metal-switchable system in which the addition of metal ions altered the conformation of substituents around a zinc porphyrin unit. This system is extensively applicable to arosteric regulations of both ligand-binding and catalytic ability of porphyrins.

We designed zinc porphyrin **1** on the basis of previously reported snowflake-shaped architectures.<sup>5</sup> Zinc porphyrin **1** consists of both flexible and rigid chains and a porphyrin core (Fig. 1). Both the flexible and rigid chains are terminated with bipyridine units. The addition of a metal ion  $(M^{n+})$  results in the formation of a couple of  $[M(bpy)_3]$ -type complexes at both the ends of molecule **1**. The rigid chains determine the distance and the relative orientation between the coordinated metal ion and the porphyrin core. As a result, metal complexation induces a large conformational change in the flexible chains and changes the conformation of substituents around the porphyrin core. This may modify several properties of metalloporphyrin units.

In this system, the alkyl chain length is quite important since it affects both the stability of the  $[M(bpy)_3]$ -type complexes and the steric demand of the ligand-binding site in the porphyrin unit. Molecular mechanics (MM) calculations were performed for the model compounds with several alkyl chain lengths that suggested that an undecamethylene chain ( $C_{11}H_{22}$ ) is most suitable for the formation of the stable metal complex (see below).<sup>6</sup>

A metal-ion-responsive unit was prepared according to Schemes 1 and 2. First, the deprotonation of 5-methyl-2,2'-bipyridine (**2**) with LDA and subsequent treatment with excess 1, 10-dibromodecane gave 5-(11-bromoundecyl)-2,2'-bipyridine (**3**) in a 52% yield.<sup>7</sup> Bipyridine-terminated pinacol borate **5** was obtained in a 74% yield by the condensation of bipyridine **3** and pinacol borate **4**. A bipyridine-terminated rigid chain **8** was prepared in

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Figure 1. Chemical structure of porphyrin 1.



Scheme 1. Synthesis of 5.

a 66% yield by the Sonogashira coupling reaction of triazene **6**<sup>8</sup> and 5-ethynyl-2,2'-bipyridine (**7**).<sup>9</sup> The Suzuki–Miyaura coupling reaction of pinacol borate **5** and the rigid chain **8** afforded triazene **9** in a 72% yield. Triazene **9** was heated with iodine in toluene to give arvl iodide **10** in a 71% yield.<sup>10</sup>

The Suzuki–Miyaura coupling reaction of **10** and **11**<sup>11</sup> afforded zinc porphyrin **1** as a purple solid in a 54% yield (Scheme 3). Zinc porphyrin **1** was soluble in various organic solvents such as chloroform and toluene and was unambiguously characterized by means of NMR, MALDI-TOF mass spectroscopy, and elemental analysis.<sup>12</sup>

The complexation of zinc porphyrin 1 and Fe(II) in a toluene–ace-tonitrile (1:1 v/v) solution was monitored by means of UV–vis spectral measurement (Fig. 2). A solution of 1 ( $2 \times 10^{-5}$  M) showed







intense  $\pi - \pi^*$  bands at 290 nm (bipyridine skeletons) and 370 nm (rigid conjugated chains) in addition to the characteristic Soret band absorption (440 nm) and Q-band absorption (550–630 nm) of the zinc porphyrin skeleton. The addition of Fe(II) solution  $(1.20 \times 10^{-3} \text{ M})$  caused a spectral change with clear isosbestic points. The characteristic metal–ligand charge transfer (MLCT) absorption for a [Fe(II)(bpy)<sub>3</sub>]-type complex appeared at around 500 nm.<sup>13</sup> The intensity of the absorption at 500 nm increased linearly up to a plateau value, which was brought at about 2 equiv of Fe(II) (Fig. 2 inset). These results suggest the quantitative formation of [Fe(II)(bpy)<sub>3</sub>]-type complexes at both ends of **1**. The formation of the 1:2 (**1**:Fe(II)) complex is further supported by a series of ion peaks observed at m/z = 3433 ([**1**·2Fe + 3BF<sub>4</sub>]<sup>+</sup>), 1673 ([**1**·2Fe + 2BF<sub>4</sub>]<sup>2+</sup>), 1086 ([**1**·2Fe + 3BF<sub>4</sub>]<sup>3+</sup>), and 793 ([**1**·2Fe]<sup>4+</sup>) in ESI-MS (Fig. 3).

The MM calculations suggest that the alkyl chains in **1** have large conformational freedom since many conformers with similar steric energy are found for  $1.^{6}$  One of the typical structures is



**Figure 2.** UV-vis spectra resulting form the titration of 1 ( $2 \times 10^{-5}$  M) with Fe(BF<sub>4</sub>)<sub>2</sub>·H<sub>2</sub>O in a toluene-acetonitrile (1:1 v/v) solution ( $1.20 \times 10^{-3}$  M). The inset shows the change in the absorbance of MLCT band at 500 nm as a function of Fe(II):1 concentration.

shown in Figure 4(a). In contrast, the formation of 1.2Fe resulted in shifting of the alkyl chains close to the rigid chains as illustrated as a typical structure in Figure 4(b). These results indicate that the formation of 1.2Fe dramatically reduces the conformational freedom of flexible alky chains and changes the steric congestion of the porphyrin core.

The large conformational change of the alkyl chains may affect the steric demand around the ligand-binding site in **1**. This effect can be investigated by the addition of axial ligands with different bulkiness. We selected imidazole and its derivatives **12** and **13** as axial ligands for this purpose and compared the ligand-binding constants for zinc coordination before and after metal complexation.



Figure 3. ESI-MS of 1.2Fe and expanded MS spectra (inset).

Compound **13** is expected to exhibit the largest steric interaction with the alkyl chains, whereas imidazole is expected to show the least effect. First, UV–vis titration was carried out by addition of the solution of **13** to the toluene–acetonitrile (1:1 v/v) solution of **1** ( $2 \times 10^{-5}$  M) (Fig. 5). Upon adding **13**, the porphyrin Q-band of **1** was red-shifted that was attributable to the axial coordination of **13** to a zinc atom in **1**.<sup>4c,14</sup> The selective formation of 1:1 complexes of zinc porphyrins and an imidazole derivatives is well-established.<sup>15</sup> The binding constant  $K_{1.13}$  was determined to be  $(2.5 \pm 0.2) \times 10^4$  M<sup>-1</sup>, from the curve fitting calculations, for the change in the absorbance at 613 nm (Fig. 5(b)). Similar UV–vis titration using the toluene–acetonitrile (1:1 v/v) solution of **1** 



Figure 4. Stable conformers of 1 before (a) and after (b) the addition of Fe(II).



**Figure 5.** (a) UV-vis spectra resulting form the titration of **1** ( $2 \times 10^{-5}$  M) with **13** in a toluene–acetonitrile (1:1 v/v) solution. (b) The change in the absorbance of Q-band at 630 nm as a function of **13:1** concentration. The solid line is a theoretical binding curve obtained by curve fitting calculations.

 $(2 \times 10^{-5} \text{ M})$  containing 2 equiv of Fe(II) gave the binding constant  $K_{(1,2\text{Fe}),13} = (3.1 \pm 0.2) \times 10^4 \text{ M}^{-1}$  (Fig. S2). These results suggest that the formation of the [Fe(II)(bpy)<sub>3</sub>]-type complexes slightly increases the stability of the coordination of the largest ligand 13 to zinc porphyrin **1**. Namely, the structural change at the metal binding site was successively transferred to the distant ligand binding site by bridging alkyl chains. Then, the toluene-acetonitrile (1:1 v/v) solution of  $1 (2 \times 10^{-5} \text{ M})$  was titrated using the solution  $(3.0 \times 10^{-2} \text{ M})$  of imidazole or **12**. The addition of imidazole or **12** resulted in the red-shift of the porphyrin Q-band of 1 to show the formation of 1 imidazole or 1.12, respectively. The Fe(II)-free binding constants were determined to be  $K_{1 \text{-imidazole}} = (1.4 \pm 0.1) \times$  $10^4 \text{ M}^{-1}$  and  $K_{1.12} = (3.6 \pm 0.3) \times 10^4 \text{ M}^{-1}$  from the curve fitting calculations. The similar UV-vis titration using the toluene-acetonitrile (1:1 v/v) solution of 1 ( $2 \times 10^{-5}$  M) containing 2 equiv of Fe(II) gave the binding constant  $K_{(1.2Fe) \text{ imidazole}} = (1.5 \pm 0.1) \times 10^4$  $M^{-1}$  and  $K_{(1.2Fe)\cdot 12} = (4.0 \pm 0.4) \times 10^4 M^{-1}$ .

These results suggest that the formation of the [Fe(II)(bpy)<sub>3</sub>]type complexes shows negligible effect on the axial complexation for imidazole and ligand **12**: the binding constants are almost identical for these complexes within experimental errors. However, there is small but clear difference on the binding constants,  $K_{1.13}$ [ $(2.5 \pm 0.2) \times 10^4 \text{ M}^{-1}$ ] and  $K_{(1.2\text{Fe})\cdot 13}$  [ $(3.1 \pm 0.2) \times 10^4 \text{ M}^{-1}$ ], suggesting a small positive arosteric effect on the axial ligand binding by the [Fe(II)(bpy)<sub>3</sub>]-type coordination.



In conclusion, we designed and synthesized zinc porphyrin that has a couple of metal-ion-responsive units. The formation of [Fe(II) (bpy)<sub>3</sub>]-type complexes induced a large conformational change in alkyl chains. A weak communication between the metal-binding site and the distant ligand-binding site through bridging alkyl chains was observed by using the relatively large axial ligand **13**. Finding tight communications in artificial arosteric system with porphyrins is currently underway.

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### Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2011.11.041.

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- 12. Fluorescence spectra of **1** and **1**·2Fe were measured in degassed solvent (toluene–acetonitrile (1:1 v/v)) (Fig. S8). The excitation of **1** at 575 nm (Q band) gave characteristic fluorescence spectra for the zinc porphyrin unit ( $\lambda_{EM-max} = 617$  and 667 nm). The excitation of **1**·2Fe at 575 nm where both the porphyrin and the [Fe(II)(bpy)<sub>3</sub>]-unit have absorption ( $\varepsilon_{1.2Fe}$ :  $2\varepsilon_{9\cdotFe} = 1:0.4$ ) also showed the characteristic fluorescence spectra for zinc porphyrin but with considerably lower intensity (95% quenching) probably due to the electron transfer from porphyrin to the [Fe(II)(bpy)<sub>3</sub>]-unit.
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