pH-Dependent Complexation between Pyridinyl-Azacrown Ether and Amino-Porphyrin

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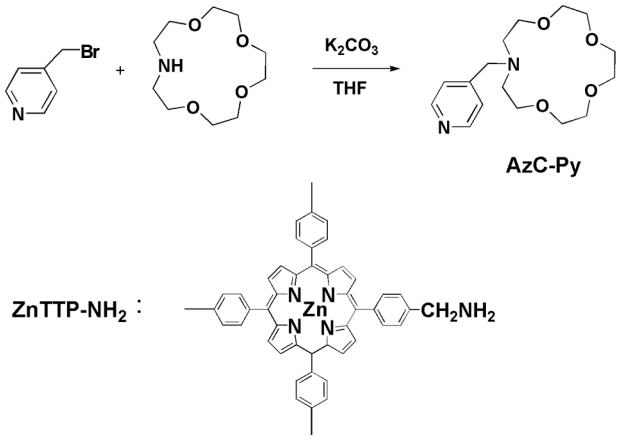
It is very interesting that the presence or absence of hydrogen atoms can remarkably influence operation of molecular systems as well as natural systems. Induction of structural changes of natural receptors through the variations in the pH of the environment is one of the most versatile methods to regulate the activity by enhancing or diminishing the receptor's binding efficacy.[1] Mimicking how natural system uses pH control to regulate the recognition event of binding site and activity, some synthetic molecular systems such as pH-controllable molecular switch have been reported.[2-6] A number of molecular switches have been studied on the basis of the systems whose emission could be modulated by external stimuli such as pH.[7-13]

Porphyrin[14-22] is a well-known luminescent and redox active compound that can accomplish the photoinduced electron transfer upon irradiation and axial coordination on central metal of metalloporphyrin plane. Azacrown ether[23-25] is an ionophore and acts as a substrate binding site that can interact directly with various cations in solution. It has long been known that azacrown ether can form adducts with organic ammonium ions.

To observe dual mode for complexation controlled by pH, we have therefore chosen the axial coordination of pyridine ligand on zinc porphyrin and host-guest complexation between azacrown ether and ammonium cation. According to this respect, amino-functionalized porphyrin ZnTTP-NH_2 and pyridine-appended crown ether AzC-Py were prepared. In normal condition, pyridine moiety of AzC-Py coordinates axially on ZnTTP-NH_2. However, in acidic condition, it is expected that ZnTTP-NH_3^+ is formed by the protonation of ZnTTP-NH_2 and then ammonium ion moiety of ZnTTP-NH_3^+ binds into azacrown ether cavity of AzC-Py, but axial coordination of pyridine-appended crown ether on zinc porphyrin does not take place.



Scheme 1. Compounds in this study

This pH-controllable dual-mode complexation between zinc porphyrin and azacrown ether could be observed by the changes of absorption and fluorescence spectra, depending on pH. The change of mode for the complex formation between amino-functionalized porphyrin ZnTTP-NH_2 and pyridine-appended crown ether AzC-Py in the absence and presence of CF_3COOH were investigated using the absorption and fluorescence spectroscopy.

Experimental Section

Materials. All reagents were purchased from Aldrich and used as received. All solvents were purchased from Duksan Chemical Co. (reagent grade). CH_2Cl_2 was dried over CaH_2 and distilled under nitrogen prior to use. Methyl alcohol was used as received. 5-(4-Aminomethylphenyl)-10,15,20-tris(4-methylphenyl)porphyrin (TTP-NH_2) and zinc 5-(4-aminomethylphenyl)-10,15,20-tris(4-methylphenyl)porphyrin (ZnTTP-NH_2) were prepared as in the literature.[26]

Preparation of pyridine-appended azacrown ether (AzC-Py). Pyridine-appended azacrown ether (AzC-Py) was prepared by the reaction of 4-(bromomethyl)pyridine and 1-aza-15-crown-5 ether (Scheme 1). 4-(Bromomethyl)pyridine hydrobromide (0.7 g, 2.6 mmol) and 1-aza-15-crown-5 ether (0.5 g, 2.0 mmol) were dissolved in acetonitrile (30 mL) and potassium carbonate (0.8 g, 6 mmol) was added. The solution was refluxed for 3 hours. After cooling to room temperature, the reaction mixture was extracted using ethyl acetate and water. Organic layer was evaporated and chromatographed on silica gel column chromatography using methylene chloride/methanol (10/1) as eluent. 1-(Pyridin-4-ylmethyl)-1-aza-15-crown-5 ether (AzC-Py) was obtained as pale yellow oil (yield 45%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (2H, d, J = 5.8 Hz, pyridine), 7.32 (2H, d, J = 5.8 Hz, pyridine), 3.63-3.70 (18H, m, -C$\underline{H}_2$-O- & py-C$\underline{H}_2$-N-), 2.79 (4H, t, J = 5.9 Hz, -N-C$\underline{H}_2$-). MS: m/z 310 (M^+).

Spectroscopic measurements. ^{1}H NMR spectra were measured on a 400 MHz Bruker Avance 400 NMR spectrometer in chloroform-d_1. Mass spectra were measured on Micromass

(UK) platform II GC/LC Mass Spectrometer. Absorption spectra were recorded on a Shimadzu UV-2401PC spectrophotometer. Steady-state fluorescence spectra were recorded on a SLM-Aminco AB2 luminescence spectrophotometer. For fluorescence measurements, the concentrations were controlled to be *ca*. 1×10^{-5} M, where the absorbances of the solutions at the excitation wavelength had usually the value of 0.07-0.08, to avoid inner filter effects.

Results and Discussion

Absorption spectra in normal condition. Complex formation between zinc 5-(4-aminomethylphenyl)-10,15,20-tris-(4-methylphenyl)porphyrin (ZnTTP-NH_2) and AzC-Py was investigated by observing the absorption spectra of ZnTTP-NH_2 (1×10^{-5} M) in dichloromethane with addition of AzC-Py(0, 1, 2, 5, 10, 20×10^{-5} M). In the absence of AzC-Py, the absorption maxima of ZnTTP-NH_2 (1×10^{-5} M) in dichloromethane are shown at 422, 550, and 591 nm.

As shown in Figure 1, upon addition of AzC-Py, absorption bands of ZnTTP-NH_2 in dichloromethane were red-shifted in 8 ~ 15 nm with the appearance of isosbestic points in 426 and 558 nm, indicating the formation of 1:1 complex, probably through the axial coordination of pyridine moiety of AzC-Py on ZnTTP-NH_2. As the concentration of AzC-Py increases, it was observed that the intense Soret band was shifted from 422 to 430 nm and two Q bands at visible region were shifted from 550 and 591 nm to 565 and 606 nm, respectively (Table 1). Table 1 summarized absorption maxima, fluorescence maxima for ZnTTP-NH_2 and its coordinated complex in dichloromethane at room temperature.

The complex formation constant K_f (Table 1) for axial coordination of AzC-Py on ZnTTP-NH_2 was estimated to be 2.1×10^4 M^{-1} from the absorption spectral data by using Benesi-Hildebrand plot[27] and its value showed the formation of a fairly stable complex.

$$1/(A_0-A_x) = 1/(A_0-A) + 1/(A_0-A) \times 1/K_f \times 1/[L]$$

where, A_0 is the absorbance of pure ZnTTP-NH_2 when [AzC-Py]=0, A_x is the absorbance of the solution with arbitrary concentration of AzC-Py, and A is the absorbance of the practically pure coordinated complex between ZnTTP-NH_2 and AzC-Py when the concentration of AzC-Py is very high.

Fluorescence spectra in normal condition. Fluorescence spectrum of ZnTTP-NH_2 (1×10^{-5} M) in dichloromethane (Figure 2) was changed with addition of AzC-Py (0, 1, 2, 5, 10, 20×10^{-5} M), as the complex between ZnTTP-NH_2 and AzC-Py was formed. Upon excitation at 558 nm, ZnTTP-NH_2 itself shows two major fluorescence bands at 601 and 648 nm. The fluorescence emission of ZnTTP-NH_2 was not only red-shifted upto 12 nm but also greatly increased to *ca.* 2.0 fold with addition of AzC-Py as shown in Figure 2. Fluorescence maxima were shifted from 601 and 648 nm to 613 and 649 nm (Table 1). Fluorescence enhancement may be due to the increased electron density of core zinc metal upon the

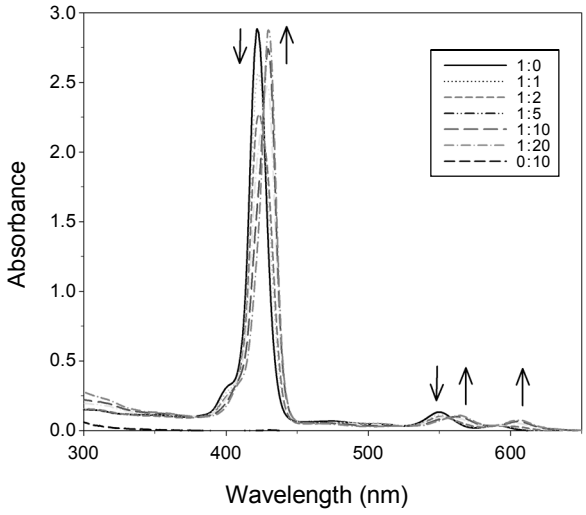


Figure 1. Absorption spectral changes of ZnTTP-NH_2 (1×10^{-5} M) in dichloromethane with addition of Py-AzC (0, 1, 2, 5, 10, 20×10^{-5} M).

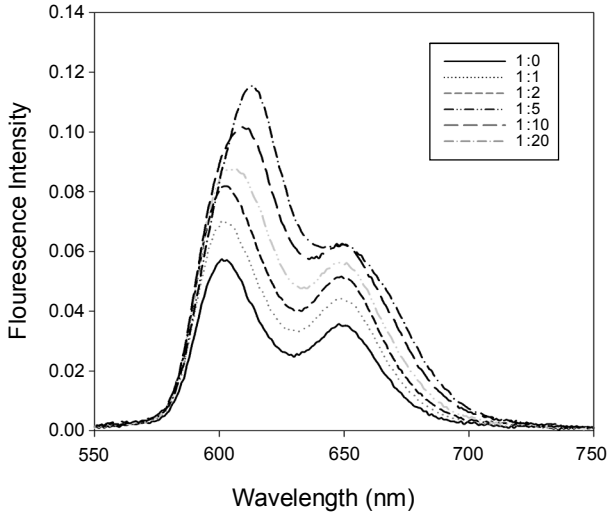


Figure 2. Fluorescence spectral changes of ZnTTP-NH_2 (1×10^{-5} M) in dichloromethane with addition of Py-AzC (0, 1, 2, 5, 10, 20×10^{-5} M).

Table 1. Absorption maxima λ_a, fluorescence maxima λ_f, complex formation constant using absorption spectral change K_f, and complex formation constant using fluorescence spectral change K_f* for ZnTTP-NH_2, ZnTTP-NH_2---AzC-Py, and ZnTTP-NH_3^+---AzC-Py coordination complexes in dichloromethane at room temperature.

compound	λ_a, nm	λ_f, nm	I_f/I_f^0	K_f	K_f*
ZnTTP-NH_2	422, 550, 591	601, 648	1	-	-
ZnTTP-NH_2---AzC-Py complex	430, 565, 606	613, 649	2.0	2.1×10^4	3.2×10^4
ZnTTP-NH_3^+---AzC-Py complex	426, 553, 591	604, 648	1.3	-	-

axial coordination of AzC-Py and the resultant prevention of the electron transfer from amino group to core zinc metal in uncoordinated ZnTTP-NH_2.

The complex formation constant K_f* (Table 1) for axial coordination of AzC-Py on ZnTTP-NH_2 was obtained to be 3.2×10^4 M^{-1} from the fluorescence spectral data by using Benesi-Hildebrand plot[27] in good agreement with the value of 2.1×10^4 M^{-1} from the absorption spectral data and its value showed the formation of a fairly stable complex.

$$1/(I_0-I_x) = 1/(I_0-I) + 1/(I_0-I) \times 1/K_f^* \times 1/[L]$$

where, I_0 is the fluorescence intensity when [AzC-Py] = 0, I_x is the fluorescence intensity of the solution with arbitrary concentration of AzC-Py, and I is the fluorescence intensity when the concentration of AzC-Py is very high, and we have practically only pure coordinated complex.

Absorption spectra in acidic condition. Absorption spectrum of ZnTTP-NH_2 (1×10^{-5} M) in dichloromethane was changed with addition of AzC-Py (0, 1, 2, 5, 10, 20×10^{-5} M) in the presence of CF_3COOH (2×10^{-4} M). In the absence of AzC-Py, the absorption maxima of ZnTTP-NH_2 (1×10^{-5} M) in the presence of CF_3COOH (2×10^{-4} M) are shown at 422, 550, and 591 nm on the exactly same wavelengths as those in the absence of CF_3COOH.

As shown in Figure 3, upon addition of AzC-Py, absorption bands of ZnTTP-NH_2 in acidic condition were only slightly red-shifted in *ca.* 4 nm, while they were greatly red-shifted in the absence of CF_3COOH. As the concentration of AzC-Py increases, it was observed that the intense Soret band was shifted from 422 to 426 nm and two Q bands at visible region were shifted from 550 and 591 nm to 553 and 591 nm, respectively (Table 1).

It is probably because the pyridine moiety of AzC-Py could not be coordinated axially on ZnTTP-NH_2. Benzyl amine(pK_a of conjugate acid = 9.35) moiety is more basic than pyridine(pK_a of conjugate acid = 5.23) moiety. Therefore, on the addition of CF_3COOH, ZnTTP-NH_2 is protonated earlier than AzC-Py. In other words, under the acidic condition, amino group in ZnTTP-NH_2 protonates to form ammonium cation. The formation of ZnTTP-NH_3^+ by the protonation of benzyl amine moiety leads to the complexation of -NH_3^+ moiety into crown ether cavity of AzC-Py. Therefore, complex formation by binding of ammonium ion into azacrown ether cavity is effectively competing with that by axial coordination of pyridine moiety of pyridine-appended azacrown ether on zinc porphyrin and prevents the pyridine moiety of AzC-Py from coordinating axially on ZnTTP-NH_2. Consequently, absorption spectrum of ZnTTP-NH_2 in acidic condition was only slightly changed upon addition of AzC-Py, in comparison with the remarkable red-shift in the absence of acid.

Table 1 summarized absorption maxima, fluorescence maxima for ZnTTP-NH_2 and its coordinated complex in dichloromethane at room temperature in the presence of CF_3COOH (2×10^{-4} M).

Fluorescence spectra in acidic condition. The fluorescence spectrum of ZnTTP-NH_2 (1×10^{-5} M) in dichloromethane was changed with addition of AzC-Py (0, 1, 2, 5, 10, 20×10^{-5} M) and CF_3COOH (2×10^{-4} M).

Upon excitation at 550 nm, ZnTTP-NH_2 in the presence of CF_3COOH shows two major fluorescence bands at 601 and 648 nm, on the exactly same wavelengths as those in the absence of CF_3COOH. The fluorescence intensity of ZnTTP-NH_2 in acidic condition was increased to *ca.* 1.3 fold with addition of AzC-Py as shown in Figure 4, much less increase than *ca.* 2.0 fold increase in the absence of CF_3COOH. Fluorescence maxima were not changed until AzC-Py was added upto 10 fold of ZnTTP-NH_2. Only in high concentration of AzC-Py ([ZnTTP-NH_2] : [AzC-Py] = 1 : 20), fluorescence maxima were slightly shifted from 601 and 648 nm to 604 and 648 nm (Table 1).

Under the acidic condition, the formation of ZnTTP-NH_3^+ by the protonation of benzyl amine moiety leads to the complexation of -NH_3^+ moiety of ZnTTP-NH_3^+ into crown ether cavity of AzC-Py. Therefore, complex formation by binding of ammonium ion into azacrown ether cavity is effectively

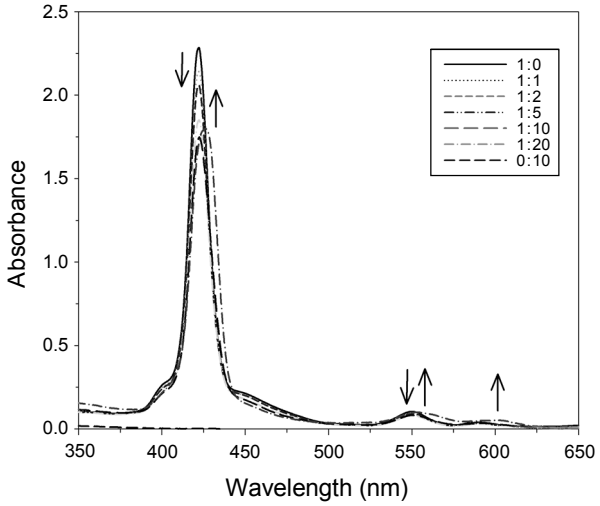


Figure 3. Absorption spectral changes of ZnTTP-NH_2 (1×10^{-5} M) in dichloromethane with addition of Py-AzC (0, 1, 2, 5, 10, 20×10^{-5} M) and CF_3COOH (2×10^{-4} M).

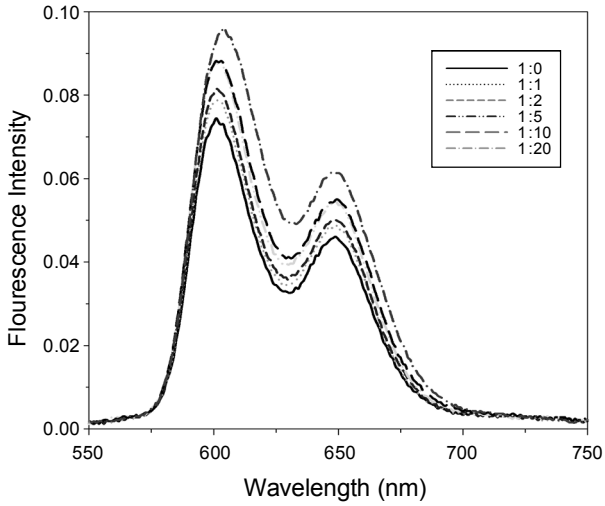
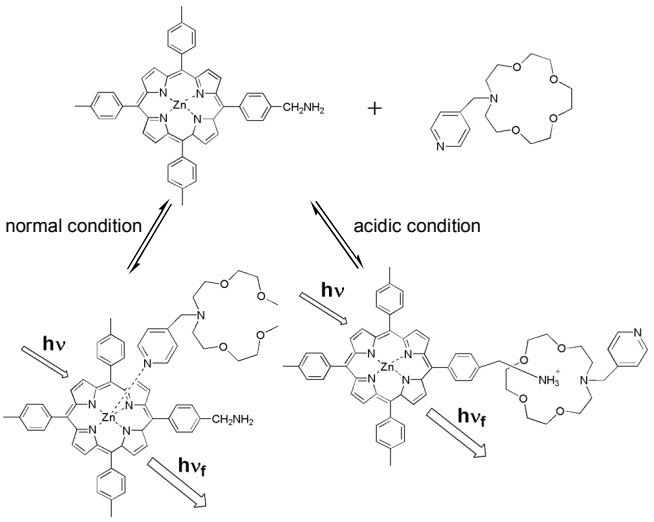


Figure 4. Fluorescence spectral changes of ZnTTP-NH_2 (1×10^{-5} M) in dichloromethane with addition of Py-AzC (0, 1, 2, 5, 10, 20×10^{-5} M) and CF_3COOH (2×10^{-4} M).



Scheme 2. pH-controllable dual-mode complexation between zinc porphyrin and azacrown ether

competing with that by axial coordination of pyridine moiety of pyridine-appended azacrown ether on zinc porphyrin and prevents the pyridine moiety of AzC-Py from coordinating axially on ZnTTP-NH_2. Consequently, absorption and fluorescence spectra of ZnTTP-NH_2 in acidic condition were only slightly changed upon addition of AzC-Py, in comparison with the case in the absence of acid.

In summary, change of mode for the complex formation between amino-functionalized porphyrin ZnTTP-NH_2 and pyridine-appended crown ether AzC-Py in the absence and presence of CF_3COOH were investigated using the absorption and fluorescence spectroscopy. To observe dual mode for complexation, axial coordination of pyridine ligand on zinc porphyrin and host-guest complexation between azacrown ether and ammonium cation were chosen. According to this respect, amino-functionalized porphyrin ZnTTP-NH_2 and pyridine-appended crown ether AzC-Py were prepared. In normal condition, pyridine moiety of AzC-Py coordinates axially on ZnTTP-NH_2. With addition of AzC-Py, absorption and fluorescence spectra of ZnTTP-NH_2 were greatly red-shifted and fluorescence intensity of ZnTTP-NH_2 was remarkably increased. However, in acidic condition, ZnTTP- NH_3^+ was formed by the protonation of ZnTTP-NH_2. Therefore, ammonium ion moiety of ZnTTP-NH_3^+ binds into azacrown ether cavity of AzC-Py, but axial coordination of pyridine-appended crown ether on zinc porphyrin does not take place. In acidic condition, absorption and fluorescence spectra of ZnTTP-NH_2 were only slightly changed with addition of AzC-Py. This shows the pH-controllable dual-mode complexation between zinc porphyrin and azacrown ether (Scheme 2).

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