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# INTERACTION BETWEEN COFACIALLY ORIENTED METALLOPORPHYRINS IN AQUEOUS MEDIA. UNUSUAL ACIDOLYTIC PROPERTIES OF AN AMPHIPHILIC IRON PORPHYRIN μ-OXO DIMER CARRYING POLY(OXYETHYLENE) SIDE CHAINS.

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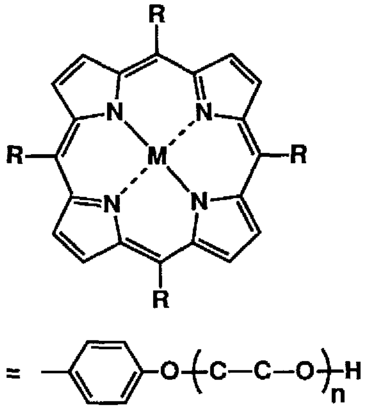
**Summary:** The acid titration of the amphiphilic iron porphyrin μ-oxo dimer carrying poly(oxyethylene) side chains demonstrates the pronounced dependence of the acidolytic property of the internal μ-oxo bridge on the length of the water-soluble polyether side chains.

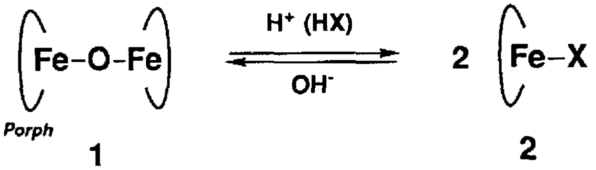
The interaction between cofacially oriented metalloporphyrins in aqueous media has received increasing attention in view of the biological importance of metalloporphyrin aggregates.[1, 2] In the present communication, we wish to report the novel amphiphilic iron porphyrin μ-oxo dimer carrying water-soluble polyether side chains (**1**), whose acidolytic property is dominated by the interaction between two porphyrin disks upon cofacial orientation.



**1** **μ-Oxo Dimer**
**2** **M = FeX**
**3** **M = $H_2$**

The properties of iron porphyrin in aqueous media have been studied using some water-soluble iron complexes of positively or negatively charged porphyrins,[1a, 3] which exist in equilibrium with the corresponding μ-oxo dimers depending upon the pH value of the solution. The acidolysis of the μ-oxo dimers of such iron porphyrins usually occurs in the pH range of 5 to 7, and it has been generally concluded that the μ-oxo bridge of iron porphyrin is essentially acid-labile compared with that of aquoiron (III) species.[3b]

We have recently developed the synthetic route to the



novel amphiphilic porphyrin (**3**) carrying four poly(oxyethylene) side chains of uniform, controllable chain length, which spontaneously forms cofacial aggregates in aqueous media depending upon the length of the polyether side chains.[4] The iron porphyrin μ-oxo dimers (**1**, n = 13, 24, 50 and 149) were prepared by the reaction of the corresponding free-base porphyrins (**3**) with $FeCl_2$ in N, N-dimethylformamide, and characterized by u.v.-visible and i.r. spectroscopies,[5] together with size-exclusion chromatography.[6]

The u.v.-visible spectrum of the aqueous NaOH solution of **1** (n = 13) (pH = 10.5, $[\mathbf{1}]_0 = 2.7 \times 10^{-5}$ M) at 17.5 °C showed three characteristic absorption bands at 414, 575.5 and 618 nm.[7] Upon titration of the above solution with hydrochloric acid,[8] these absorption bands were observed to decrease in their intensities, while three new absorption bands assignable to **2** appeared at 410, 536 and 698 nm. This spectral change showed three distinct isosbestic points at 486, 564 and 644 nm. The absorption bands due to the μ-oxo dimer **1** completely disappeared when the pH value of the solution dropped to 1.8. The spectrophotometric titration curve based on the absorbance at 536 nm (Figure 1) provided the critical pH value for the acidolysis of **1** (n = 13) into **2** ($[pH]_c$) being 2.8. The $[pH]_c$ value for **1** (n = 13) in a higher concentration such as $1.8 \times 10^{-4}$ M (2.7) was almost the same as above. The $[pH]_c$ values thus observed are much lower than those for other water-soluble iron porphyrin μ-oxo dimers with peripheral electronic charges such as $O(Fe(TPPS))_2$ ($[pH]_c$ = 6.5, initial conc. of μ-oxo dimer : $0.5 \times 10^{-4}$ M),[3a] $O(Fe(DDS))_2$ (6.7, $2.3 \times 10^{-5}$ M),[3c] $O(Fe(TMPyP))_2$ (5.4, $4.0 \times 10^{-6}$ M),[3d] and $O(Fe(ENP))_2$ (5.3, $0.53 \times 10^{-5}$ M).[3e, 9]

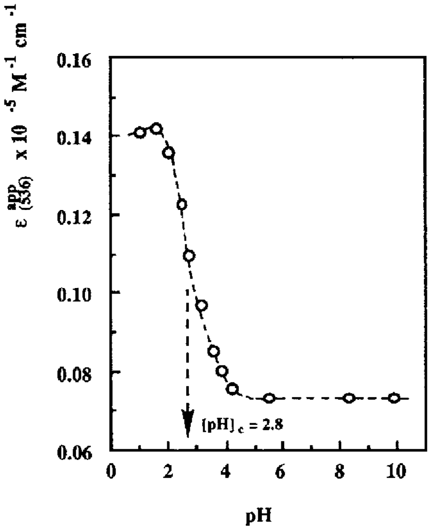


Figure 1. Spectrophotometric titration data for the aqueous solution of **1** at 17.5 °C. $[\mathbf{1}]_0 = 2.7 \times 10^{-5}$ M. $\varepsilon^{app}(536)$ = absorbance at 536 nm/(2 x $[\mathbf{1}]_0$).

The spectral profiles for the μ-oxo dimers **1** with n of 24, 50 and 149 upon acid titration were virtually similar to those for **1** (n = 13). However, it should be noted that the observed $[pH]_c$ values showed a pronounced dependence on the length of the poly(oxyethylene) side chains (Figure 2). As the number of the repeating oxyethylene units (n) was increased from 13 to 149, the $[pH]_c$ value became higher from 2.8 to 4.2. In connection with this observation, the $[pH]_c$ value for **1** (n = 13) remained almost intact upon addition of a 4-fold excess of poly(oxyethylene) (number of repeating oxyethylene unit (Dp) : 193) ($[pH]_c$ = 2.85). On the other hand, the spectrophotometric titration of $O(Fe(TPPS))_2$ under the conditions employed above ($1.9 \times 10^{-5}$ M) gave the $[pH]_c$ value of 7.7, which was found to be little affected by the addition of an 8-fold excess of poly(oxyethylene) ($D_p$ : 13.6) ([pH]$_c$ = 7.9). Thus, the interaction affecting the [pH]$_c$ value for the μ-oxo dimer is absent between iron porphyrin and poly(oxyethylene) molecule unanchored to the porphyrin moiety. Furthermore, although alkali metal ions such as $Na^+$ and $K^+$ are known to dehydrate poly(oxyethylene) molecule in aqueous media to induce coagulation of the polymer chains,[10] the addition of NaCl (0.1 M) to the aqueous solution of **1** (n = 13) (1.8 x 10$^{-5}$ M) did not cause any substantial change in the [pH]$_c$ value (2.9). This observation rules out the possibility of the effect of $Na^+$ ion in the titration media on the [pH]$_c$ value for **1**. Thus, the acidolytic nature of the Fe-O-Fe bond of the amphiphilic iron porphyrin μ-oxo dimer **1** is totally dependent on the net balance of the hydrophobicity and hydrophilicity of the molecule. As the poly(oxyethylene) side chains become shorter and the porphyrin ligand turns more hydrophobic, the μ-oxo bridge of **1** gets greater stabilization toward acidolysis by the interaction between two porphyrin moieties upon cofacial orientation.

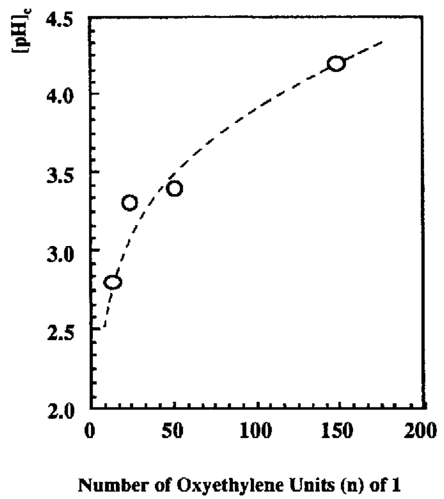


Figure 2. Relationship between the critical pH value for the acidolysis of **1** into **2** ([pH]$_c$) and the number of the repeating oxyethylene units (n) of **1** in aqueous solution at 17.5 °C. [**1** (n = 13)]$_0$ = 2.7 x 10$^{-5}$ M, [**1** (n = 24)]$_0$ = 2.0 x 10$^{-5}$ M, [**1** (n = 50)]$_0$ = 1.8 x 10$^{-5}$ M, [**1** (n = 149)]$_0$ = 2.0 x 10$^{-5}$ M.

Aromatic ring interactions in aqueous media are of general significance in biological processes.[11] The present finding is of interest not only in relation to the biological functions of naturally occurring hemes but also in view of demonstrating the change in the local reactivity of a molecule by non-covalent interaction between proximate aromatic groups.

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5. For **1** (n = 13), u.v.-visible in $C_6H_6$, $\lambda_{max}$ : 416.0 nm [$\varepsilon$ : 105000 $M^{-1}$ $cm^{-1}$], 574.5 [8090], 616.5 [3920] in $C_6H_6$); i.r., 855 $cm^{-1}$ (Fe-O-Fe) (see : ref 3a).

6. The size-exclusion chromatography on a Polystyragel, using tetrahydrofuran as eluent at 38 °C, clearly showed the diffrence in the molecular weights of the μ-oxo dimer **1** and the corresponding monomer **2** derived from the acidolysis of **1** with hydrochloric acid.

7. U.v.-visible for the aqueous solution of **1** (n = 13) at pH 10.5 : 414 nm [$\varepsilon$ : 937000 $M^{-1}$ $cm^{-1}$], 575.5 [105000], and 618 [9700].; for the aqueous solution of **2** (n = 13) at pH 1.8 : 410 nm [$\varepsilon$ : 977000 $M^{-1}$ $cm^{-1}$], 536 [14200], and 698 [2800]. The effect of the concentration of the amphiphilic iron porphyrin on the absorption maxima was very little at pH 10.5 and 1.8 in the concentration range of $10^{-5}$ to $10^{-6}$ M.

8. For the acid titration of **1**, 0.1, 1.0 and 12 N hydrochloric acids were used. The spectral change in the acid titration experiment was instantaneous.

9. TPPS : 5, 10, 15, 20 - tetrakis(*p*-sulfophenyl)porphine, TCPP : 5, 10, 15, 20 - tetrakis(*p*-carboxyphenyl)porphine, DDS : deuteroporphyrin 2, 4 - disulfonic acid, TMPyP : 5, 10, 15, 20 - tetrakis((4-N-methyl)pyridinium)porphine, ENP : ethylenediamine - substituted protoporphyrin IX.

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