Influence of Metallo Core Variation on 1-Methylimidazole Ligation to the Iron(III) in Porphyrin, Porphycene, Corrphycene, and Hemiporphycene

Saburo Neya,* Tyuji Hoshino, Masayuki Hata, and Noriaki Funasaki†
Department of Physical Chemistry, Graduate School of Pharmaceutical Sciences, Chiba University, Inage-Yayoi, Chiba 263-8522
†*Department of Physical Chemistry, Kyoto Pharmaceutical University, Yamashina, Kyoto 607-8414*

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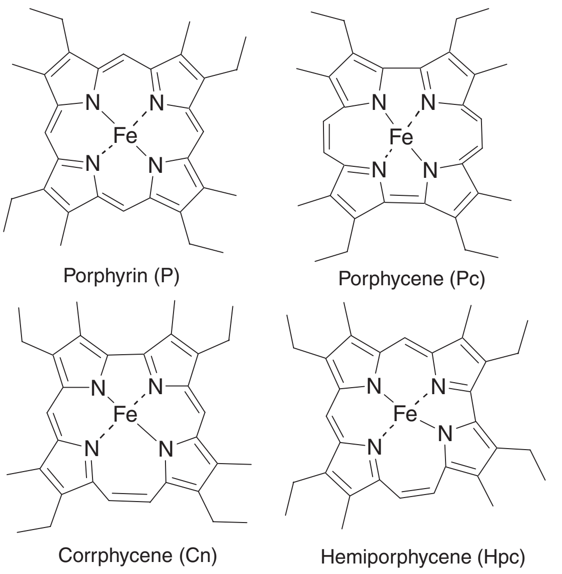
Binding of 1-methylimidazole to five-coordinate iodo-Fe(III) complexes of porphyrin and three porphyrin isomers was spectrophotometrically examined in benzene at 20 °C. The result demonstrates that the geometry of the metallocavity is important to control both iron movement through the aromatic plane and magnitude of the Fe–I interactions.

The iron atom in hemoprotein adopts out-of-plane or in-plane configuration according to the coordination environment. Iron displacement from the porphyrin plane is suggested to be one of critical factors to regulate the function of hemoglobin. Position of heme iron depends on the shape of the metallocavity of porphyrin ring as well as the nature of axial ligand. Modification of the metallo core shape, which is square in porphyrin (P), is now achieved with isomeric porphyrins[1] like porphycene (Pc: rectangular), corrphycene (Cn: trapezoidal), and hemiporphycene (Hpc: distorted quadrilateral). Despite possible importance of the metallocavity geometry to the axial ligation behavior of the central metal, the systematic investigation has been little pursued except for the report by Fowler et al.[2] They examined coordination behavior of pyridine to the Zn, Ni, Mg, and Co complexes of the porphyrin isomers and found a significant dependence on metals.



Porphyrin (P) Porphycene (Pc)

Corrphycene (Cn) Hemiporphycene (Hpc)

Figure 1. Structure of the Fe(III)I complexes of etioporphyrin and the isomers. Coordinating iodide is omitted for clarity.

Iron and imidazole are important because they constitute the coordination structure in most of hemoproteins. We accordingly examined the binding of 1-methylimidazole (1-MeIm) to the Fe(III) complexes P, Pc, Cn, and Hpc (Figure 1) to analyze the geometric stability of the iron in modified metallocavities. We employed the iodo-Fe(III) derivatives because their molecular structures have been well characterized.[3,4] The macrocycles[5–9] and iron complexes[3,4] were prepared as described previously. Optical titration was carried out at 20 °C on Shimadzu MPS-2000 with 8 μM of samples in dry benzene.

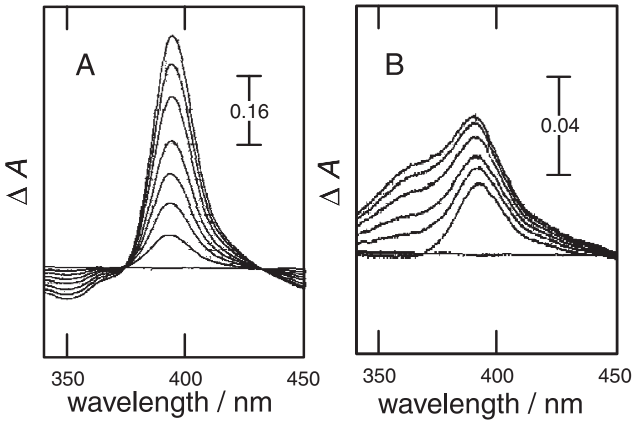


Figure 2. Light absorption changes of PcFe(III)I in benzene at 20 °C. (A) [1-MeIm] = 0–27 μM. (B) [1-MeIm] = 0.05–2.47 mM.

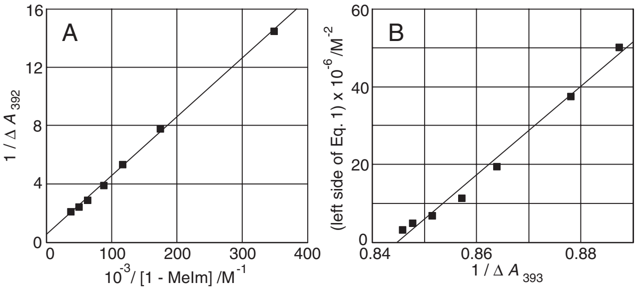


Figure 3. Analysis of the absorption changes in Figure 2. (A) and (B) are from the results in (A) and (B) of Figure 2.

Figure 2 shows the Soret absorption changes of PcFe(III)I with addition of 1-MeIm. Isosbestic points at 374 and 432 nm in Part A indicate formation of the mono-1-MeIm complex. Transition at 392 nm was analyzed with the plots of $1/(A_0 - A)$ vs 1/[1-MeIm] after Benesi and Hildebrand[10] to afforded a linear plot ($r = 0.9997$, Figure 3) and the first binding constant $K_1 = 1.3 \times 10^4\ \mathrm{M}^{-1}$. Higher 1-MeIm concentration caused disappearance of the isosbestic points owing to the mixing of another species, the *bis*-1-MeIm adduct. The overlapping first and second equilibria may be analyzed with Eq 1:[11]

$$\frac{A - A_0}{A[\text{1-MeIm}]^2} + \frac{(A - A_1)K_1}{A[\text{1-MeIm}]} = K_1K_2A_2(1/A) - K_1K_2 \qquad (1)$$

where A_2 denotes the absorbance of the bis-1-MeIm complex. Value of $-K_1K_2$ is determined as the intercept of a linear plot of the left side of Eq 1 against $1/A$. From the analysis of the 390-nm changes in Part B of Figure 2, we obtained a linear plot ($r = 0.9372$, Figure 3) and the second binding constant $K_2 = 5500\,\text{M}^{-1}$. The P, Cn, and Hpc complexes were similarly titrated with 1-MeIm and the resultant binding constants are complied in Table 1.

The overall 1-MeIm affinity $K_1K_2 = 1.7 \times 10^6\,\text{M}^{-2}$ for PFe(III)I is much larger than $6.8 \times 10^3\,\text{M}^{-2}$ reported for octaethylporphyrinatoFe(III)Cl.[12] The observation suggests that the Fe–I bond is weaker than the Fe–Cl bond, consistent with the spectrochemical series of ligands.[13] In five-coordinate iodo-Fe(III) in porphyrinoid, the iron is displaced from heme plane toward the iodide.[3,4] When a small amount of 1-MeIm is added, 1-MeIm preferentially coordinates from the vacant axial site to form the six-coordinate mixed-ligand complex. Since amine is a stronger ligand than iodide,[13] the displaced iron atom moves toward the 1-MeIm through the metallo core. We note a relevant situation of the mixed-ligand heme in aquomet myoglobin.[14] The Fe(III) atom coordinated with a water molecule is displaced from the heme plane by 0.4 Å to the proximal histidine. Thus the first binding constant K_1 is a criterion for the iron mobility through the aromatic plane. The K_1's for Pc, Cn, and Hpc are significantly larger than that of P, suggesting that the N_4 core deviation from square enhances the iron mobility. It is probable that iron d_{x2-y2} orbital less unfavorably interacts with the pyrrole nitrogens and that the Fe–N bonds are destabilized in the deformed N_4 core. Among the Pc, Cn, and Hpc complexes, CnFe(III)I has the largest K_1 (Table 1). The large K_1 is likely to come from the distorted N_4 core because the X-ray crystallography[3,4] revealed that the two N–Fe–N bond angles of 74 and 105° in CnFe(III)I markedly deviate from 90°. Such large angular distortion is not observed in the Pc and Hpc compounds.

Table 1. Binding constants of 1-MeIm to the Fe(III)I complexes of P, Pc, Cn, and Hpc in benzene at 20 °C

Macrocycle	K_1/M^{-1}	K_2/M^{-1}
Porphyrin (P)	1,700 ± 200	1,000 ± 200
Porphycene (Pc)	13,000 ± 2000	5,500 ± 1,000
Corrphycene (Cn)	79,000 ± 9,000	800 ± 200
Hemiporphycene (Hpc)	19,000 ± 4,000	300 ± 100

In the second ligation step, the iron-bound iodide is replaced with 1-MeIm to afford the bis-1-MeIm adduct, and the iron atom falls into aromatic plane. These processes are also subject to the N_4 core variation. It is notable in Table 1 that PcFe(III)I exhibits the largest K_2 despite the narrowest metallo cavity. According to the X-ray analyses, PcFe(III)I has an N_4 cavity of 7.355 Å^2 that is narrower than 8.094–7.882 Å^2 of the P, Cn, and Hpc complexes.[3,4] These results suggest that the second 1-MeIm ligation is dominated by a factor other than the N_4 core size. The Fe–I bond (2.664 Å) in five-coordinate PcFe(III)I is longer than those in the P (2.617 Å), Cn (2.615 Å), and Hpc (2.618 Å) complexes.[3,4] The longer Fe–I bond of Pc is caused by the stronger equatorial ligand-field in a narrower N_4 core.[1,3,4] The strong equatorial field and long Fe–I bond are likely to be retained in six-coordinate 1-MeIm-PcFe(III)I as well. Under these circumstances, the coordinating iodide may be more easily replaced with the second 1-MeIm in Pc than in P, Cn, and Hpc. Thus, the K_2's in Table 1 are interpreted to reflect primarily substitution of 1-MeIm for iodide rather than the in-plane shift of the iron. The K_2's of Cn ($770\,\text{M}^{-1}$) and Hpc ($320\,\text{M}^{-1}$) are slightly smaller than $1030\,\text{M}^{-1}$ of P. It is possible that the iron atom is less favorably accommodated in the constrained metallocore of Cn and Hpc on the second 1-MeIm ligation.

In summary, present analyses reveal a novel aspect of iron configuration that depends on the tetrapyrrole array in the porphyrinoids.

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