Preparation and Characterization of a Novel Oxoiron(IV) Chlorin π-Cation Radical Complex. The First Model for Compound I of Chlorin-Containing Heme Enzymes

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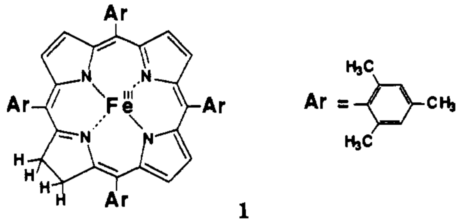
Many proteins and enzymes containing iron chlorin complexes as the prosthetic group play important roles in biological systems.[1] Examples of the iron chlorin-containing enzymes include sulfmyoglobin,[2] HPII catalase,[3] *Neurospora crassa* catalase,[4] and cytochrome *d*[5] and probably myeloperoxidase[6,7] and spleen green heme protein.[8] For some of these enzymes, high-valent oxoiron(IV) chlorin π-cation radicals (compound I) have been postulated to serve as functional intermediates in the catalytic cycles.[6a] However, the structures of these chlorin compound I's have not been elucidated yet. It is therefore very important to prepare and characterize compound I of iron chlorin by using synthetic model complexes.

Theoretical and experimental studies of metallochlorin π-cation radicals[9–15] show that metallochlorin complexes are easily oxidized to yield the corresponding π-cation radicals relative to metalloporphyrin complexes and that the chlorin π-cation radicals have predominantly a_2 radical state. Further, theoretical studies on compound I of *N. crassa* catalase suggested that compound I could occupy the a_2 ground state with a spin distribution and optical spectra analogous to those of zinc(II) and cobalt(III) chlorin π-cation radicals.[15] Along with this line, more *real* model complexes, i.e., oxoferryl chlorin π-cation radicals, have been required to understand the details of compound I of chlorin-containing heme enzymes. We wish to report here the successful preparation of an oxoiron(IV) chlorin π-cation radical by employing sterically hindered iron(III) chlorin, (7,8-dihydro-5,10,15,20-tetrakis(2,4,6-trimethylphenyl)porphinato)iron(III), [TMCFe^{III}] (**1**).



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Oxidation of TMCFe^{III}(*m*-chlorobenzoate),[16] **1**-mCB, was performed with one equimolar amount of *m*-chloroperoxybenzoic acid (mCPBA) in freshly distilled dichloromethane at −80 °C. The oxidation of **1**-mCB caused a decreased intensity of the Soret band, a loss of the characteristic band for chlorin complexes at 592 nm, and the appearance of weak broad bands stretching into the near infrared region to yield a new species, **2** (Figure 1). These spectral features are characteristic of chlorin π-cation radicals.[10–15] To confirm the chlorin π-cation radical formation, ^{2}H-NMR measurements of **2**, derived from deuterated **1**,[17] were carried out in dichloromethane at −80 °C. Three nonequivalent pyrrole deuterium resonances for **2** were observed at 24, −46, and −74 ppm (Figure 2a),[18] largely upfield shifted from those for **1** at 134, 118, and 95 ppm. The specific features of the three pyrrole signals for **2** would be attributed to a chlorin π-cation radical in which substantially different π-spin densities are distributed on the β-carbons of the pyrrole rings,[14,15] rather than to the iron-centered paramagnetic effect. Meta deuterium resonances exhibited a small downfield shift as illustrated in Figure 2b, which implies small spin densities at the meso carbons of the chlorin ring.[19] In Figure 2, pyrrole and meta deuterium resonances of

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(7) The structure of the prosthetic group of myeloperoxidase has not been established unambiguously. Two conflicting proposals for the structure have been reported: an iron chlorin[6b–e] and an iron porphyrin with an electron-withdrawing substituent.[6f,g]

(8) Davis, J. C.; Averill, B. A. *J. Biol. Chem.* **1981**, *256*, 5992–5996.

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(13) The 7,8-deuterium resonances for iron(III) octaethylchlorin π-cation radicals were observed at 640 ppm at 23 °C for the bis(perchlorate) complex and at 480 ppm at −60 °C for the bis(imidazole) complex, respectively; Fujii, H.; Morishima, I. Submitted for publication.

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(16) (a) The chlorin ligand was prepared according to the tetraphenylchlorin synthesis with modification. Cf.: Whitlock, H. W.; Hanauer, R., Jr.; Oester, M. Y.; Bower, B. K. *J. Am. Chem. Soc.* **1969**, *91*, 7485–7489. (b) ^{1}H-NMR ($CDCl_3$, 23 °C), H_2TMC: δ −1.35 (2 H, s, NH), 1.87 (24 H, s, *o*-CH_3), 2.56 (12 H, d, *p*-CH_3), 3.91 (4 H, s, pyrroline), 7.22 (8 H, d, phenyl meta), 8.03, 8.39 (2 H each, d, pyrrole), 8.23 (2 H, s, pyrrole). ^{1}H-NMR ($CDCl_3$, 23 °C), TMCFe^{III}Cl: δ −9.1 (4 H, pyrroline), 3.9, 4.0 (12 H, *p*-CH_3), 13.6, 15.2, 16.0, 17.5 (8 H, phenyl meta), 67.9, 78.1, 86.2 (6 H, pyrrole). (c) TMCFe^{III}(*m*-chlorobenzoate), **1**-mCB, was prepared by adding 10 equiv of *m*-chlorobenzoic acid into a dichloromethane solution of TMCFe^{III}(OH), **1**-OH in situ.

(17) The saturated pyrrole ring-d_2–pyrrole-d_6 TMC derivative was prepared from pyrrole-d_8 TMP. The *m*-TMC-d_8 complex was synthesized from the *m*-TMP-d_8 complex, which was obtained by the condensation of *m*-mesitaldehyde-d_2 and pyrrole.

(18) Upon reduction of **2** by TBAI, the pyrrole deuterium resonances of **1** were recovered. On the other hand, when the temperature was raised, the signals of pyrrole deuterium of **2** were replaced by a pyrrole deuterium resonance for the Fe^{III}TMP complex at 120 ppm.

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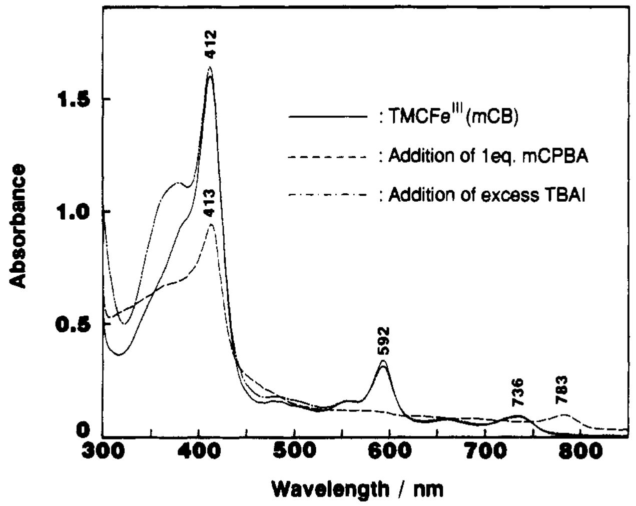


Figure 1. Electronic absorption spectra of 1.8 × 10^{-5} M of TMCFe^{III}(mCB), **1**-mCB (—), its oxidized product by 1 equiv of mCPBA, **2** (– –), and the resultant absorption spectrum of reduction by TBAI (– - –) in dichloromethane at –80 °C.

Fe^{III}TMP[20] complex are contaminated at around 120 and 20 ppm, respectively. This is due to decomposition of **2** at NMR concentrations (~10^{-3} M) even at –80 °C. Unfortunately, attempts to detect the saturated pyrrole ring deuterium (7,8-position) signals, which are expected to be unusually far downfield shifted,[12,13] were unsuccessful at this time possibly due to much broadening of these signals. The absorption spectrum of **1**-mCB was completely recovered by the reduction of **2** with tetra-*n*-butylammonium iodide (TBAI). Careful titration of **2** by TBAI indicated the production of 1 equiv of I_3^-, confirmed by the absorbance at 360 nm (Figure 1).[21] This result shows that **2** is in a two-electron higher oxidation state from the parent complex, **1**. To gain further insight into the formulation of **2**, triphenylphosphine was added to the dichloromethane solution of **2** at –80 °C under Ar atmosphere. That the reaction of **2** with triphenylphosphine afforded 1 equiv of triphenylphosphine oxide, verified by ^{31}P-NMR spectroscopy,[22] shows the presence of the oxoiron ligand in **2**. ESR spectrum of **2** was found to be silent in dichloromethane at 77 K. It is therefore concluded that the formulation of **2** is the TMCFe^{IV}=O π-cation radical.

While **2** was relatively stable at –80 °C under UV concentrations (~10^{-5} M), raising the temperature above –80 °C facilitated the conversion of **2** to the Fe^{III}TMP complex, consistent with the formulation of **2** to be two-electron-oxidized from **1**.[23]

In order to examine the reactivity of **2**, 1000 equiv of norbornene was added to a dichloromethane solution of **2** at –80 °C. Upon addition of norbornene to the π-radical solution, the absorption spectrum of **2** showed no changes within 3 h.[24] On the contrary, the corresponding porphyrin π-cation radical reacted with norbornene even at –80 °C to give norbornene oxide in 3 h.[25] These findings indicate that the chlorin π-cation radical, **2**, has lower reactivity toward olefin than the corresponding porphyrin π-cation radical.

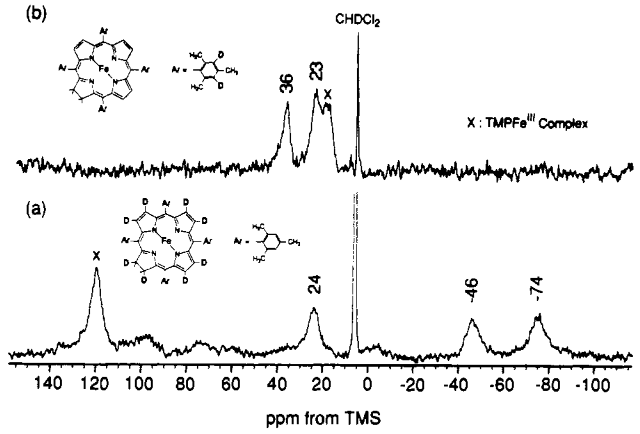
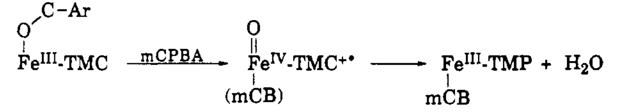


Figure 2. Deuterium NMR spectra of the selectively deuterated oxidation products, **2**, in dichloromethane at –80 °C: (a) saturated pyrrole ring-d_2–pyrrole-d_6 and (b) meta d_8 complexes. The peaks labeled X are due to the Fe^{III}TMP complex.



$$\underset{\textbf{1-mCB}}{\mathrm{Fe^{III}\text{-}TMC}(\mathrm{O{-}C(=O){-}Ar})} \xrightarrow{\mathrm{mCPBA}} \underset{\textbf{2}}{\mathrm{O{=}Fe^{IV}\text{-}TMC^{+\bullet}}(\mathrm{mCB})} \longrightarrow \mathrm{Fe^{III}\text{-}TMP(mCB)} + \mathrm{H_2O}$$

1-mCB **2**

Meso-substituted iron porphyrin π-cation radicals are of the a_{2u} type,[14,26,27] while metallochlorin π-cation radicals have preferentially the a_2 (a_{1u} type) radical state.[10-15] Further, the oxidation potentials of TMCFe^{III}Cl, **1**-Cl are 200–300 mV lower than those for the corresponding porphyrin complex, TMPFe^{III}Cl (the first and second oxidation potentials are +0.89 and +1.17 V (vs SCE) for **1**-Cl and +1.09 and +1.48 V for the porphyrin, respectively).[28] It is therefore likely that the difference in reactivity between **2** and the oxoferryl porphyrin π-cation radical could be rationalized by their radical orbital types and/or oxidation potentials.

In conclusion, the oxoiron(IV) chlorin π-cation radical has been successfully prepared and the chlorin π-cation radical showed lower reactivity than the corresponding porphyrin π-cation radical. The chlorin complex reported here is the first example of a synthetic model of the putative reaction intermediates (compound I) of chlorin-containing heme enzymes. Full characterization and detailed study of reactivities of the chlorin π-cation radical are under investigation.

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(19) Since the NMR spectrum of ferryl chlorin complexes have not been obtained, the detailed spin distribution of **2** is not established yet.

(20) TMP: 5,10,15,20-tetrakis(2,4,6-trimethylphenyl)porphyrin dianion.

(21) The iodide titration was accomplished by the literature procedures. See, for example: Groves, J. T.; Watanabe, Y.; McMurry, T. J. *J. Am. Chem. Soc.* **1983**, *105*, 4489–4490 and ref 25.

(22) The estimation of an amount of OPPh$_3$ has been based on the integration of the resonances for OPPh$_3$ (30 ppm) and triphenyl phosphate as a reference (–18 ppm). When **2** was reacted with triphenylphosphine, TMCFe^{III} complex was recovered.

(23) When the temperature was raised to –60 °C, **2** was completely changed to the porphyrin derivative within 2 h at UV concentrations (~10^{-5} M).

(24) The parent complex, **1**, was reproduced at this time by adding TBAI.

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(27) Fujii, H.; Morishima, I. Submitted for publication.

(28) Both samples for cyclic voltammetric studies were 1.0 mM in dichloromethane containing 0.1 M tetra-*n*-butylammonium perchlorate as supporting electrolyte. Scan rates were 20 mV/s for the TMP complex and 50 mV/s for the TMC complex, respectively.