Inorganic Chemistry
Communication
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Biomimetic Catalysis of a Porous Iron-Based Metal–Metalloporphyrin Framework

Yao Chen, Tran Hoang, and Shengqian Ma*

Department of Chemistry, University of South Florida, 4202 East Fowler Avenue, Tampa, Florida 33620, United States

Supporting Information

ABSTRACT: A porous metal–metalloporphyrin framework, MMPF-6, based upon an iron(III)-metalated porphyrin ligand and a secondary binding unit of a zirconium oxide cluster was constructed; MMPF-6 demonstrated interesting peroxidase activity comparable to that of the heme protein myoglobin as well as exhibited solvent adaptability of retaining the peroxidase activity in an organic solvent.

As new types of functional materials, porous metal–organic frameworks (MOFs) have experienced rapid development over the past decade.[1] Their amenability to be designed with specific functionality makes them stand out from traditional porous materials[2] and affords them great potential for various applications, such as gas storage/separation,[3] CO_2 capture,[4] sensors,[5] and catalysis.[6] Their tunable pore spaces and functional pore walls[7] also provide a new opportunity for biomimetic catalysis, which, however, has rarely been explored.[8] To develop porous MOFs as platforms for biomimetic catalysis, one can utilize their pore systems to directly immobilize enzymes/proteins[9] or selectively encapsulate the active centers of enzymes into the cavities of MOFs[8] or one can regularly arrange the active centers of enzymes into MOF frameworks using the derivatives of active center molecules as struts.[10] The later strategy is particularly appealing to mimic heme proteins because iron porphyrin that is the active center (iron protoporphyrin IX) of heme proteins can be readily functionalized as struts for the construction of MOFs.[11] In a continuation of our work on the development of porous metal–metalloporphyrin frameworks (MMPFs),[12] herein we report an iron-based MMPF, MMPF-6, which demonstrates interesting peroxidase activity comparable to that of the heme protein myoglobin (Mb).

Dark-red block crystals of MMPF-6 were obtained by reacting iron(III) *meso*-tetrakis(4-carboxyphenyl)porphyrin chloride (Fe-TCPP-Cl; Figure 1a) with zirconyl chloride under solvothermal conditions. Single-crystal X-ray studies revealed that MMPF-6 has the same structure as the recently reported MOF-545-Fe,[13] in which the Fe-TCPP-Cl ligands connect with the in situ generated secondary building units (SBUs) of $Zr_6O_8(CO_2)_8(H_2O)_8$ (Figure 1b) to form a three-dimensional structure consisting of hexagonal and triangular one-dimensional (1D) channels that have diameters of ~36 and ~12 Å (atom-to-atom distance), respectively (Figure 1c). The phase purity of the bulk sample MMPF-6 was confirmed by powder X-ray diffraction (PXRD) studies (Figure S1 in the Supporting Information, SI). The permanent porosity of MMPF-6 was assessed by N_2 sorption at 77 K (Figure 2), which revealed a typical type IV isotherm[14] and a Brunauer–Emmett–Teller surface area of 2100 m^2/g comparable to that

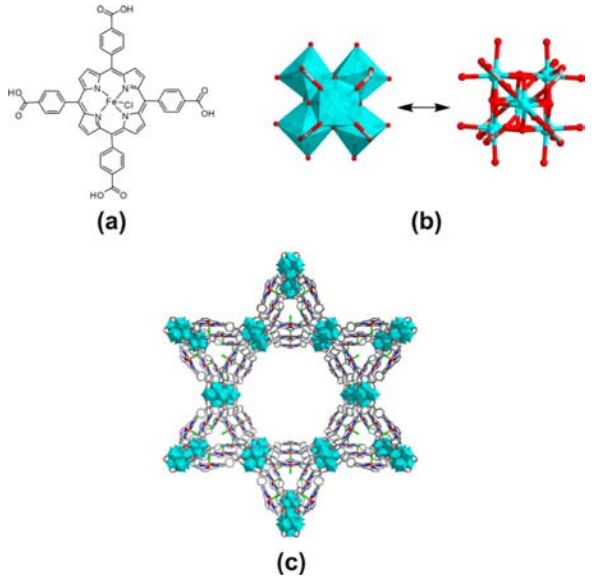


Figure 1. (a) Iron(III) *meso*-tetrakis(4-carboxyphenyl)porphyrin chloride ligand. (b) $Zr_6O_8(CO_2)_8(H_2O)_8$ SBU. (c) Hexagonal and triangular 1D channels of MMPF-6. Color scheme: C, gray; O, red; Cl, green; Zr, turquoise.

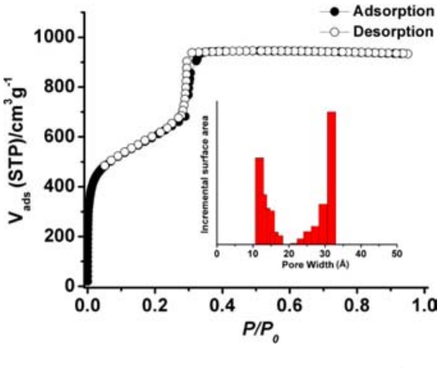


Figure 2. N_2 sorption isotherms of MMPF-6 at 77 K (inset: pore-size distribution based upon the DFT model).

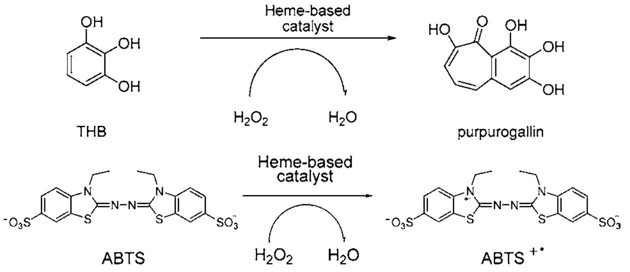
Received: September 3, 2012
Published: November 20, 2012

dx.doi.org/10.1021/ic301923x | *Inorg. Chem.* 2012, 51, 12600–12602

reported in the literature.[13] The pore-size distribution analysis based upon N_2 adsorption data at 77 K by the use of a density functional theory (DFT) model revealed that the pore sizes of MMPF-6 are predominantly around 11 and 33 Å (Figure 2, inset), which are close to the channel sizes observed crystallographically.

It is well-known that heme is the catalytic center for heme proteins, including cytochromes, peroxidases, myoglobins, and hemoglobins, and is capable of performing peroxidation of organic substrates by the use of hydrogen peroxide.[15] The peroxidase activity of heme proteins can be assessed with some standard assays of selected substrates by monitoring the rate of increase in absorbance at feature wavelengths of the oxidation products subsequent to the addition of peroxide, such as oxidation of 1,2,3-trihydroxybenzene (THB) to purpurogallin (420 nm) involving oxygen transfer[16a] and oxidation of 2,2′-azinodi(3-ethylbenzothiazoline)-6-sulfonate (ABTS) to $ABTS^{\bullet+}$ (660 nm) involving electron transfer[16b] (Scheme 1).

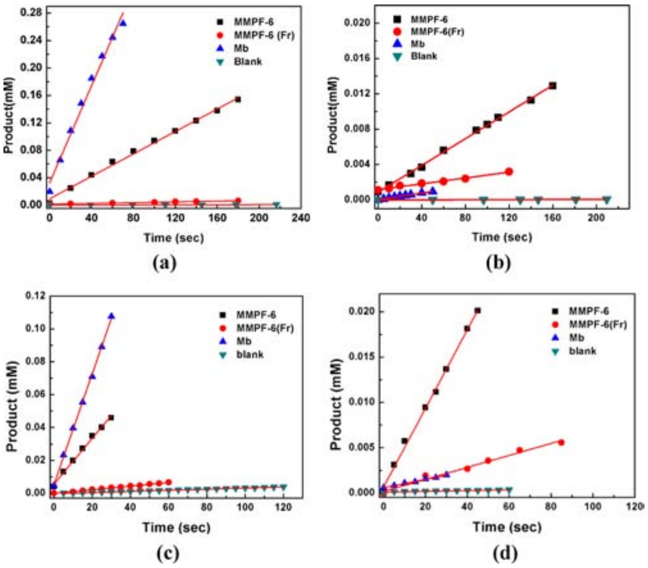
Scheme 1. Reaction Schemes for Oxidation of THB (Top) and ABTS (Bottom) by Hydrogen Peroxide Catalyzed by a Heme-Based Catalyst



The regular arrangement of hemes [iron(III) porphyrin macrocycles] with the five-coordinate iron(III) centers oriented toward the channels in MMPF-6 prompted us to evaluate the potential peroxidase activity of MMPF-6. Catalytic assays were conducted for MMPF-6 and compared with the heme protein Mb. Mb is an oxygen storage protein,[17] and its peroxidase activity has also been widely studied,[18] although the activity is lower than that of native peroxidase.[19]

Before catalytic assays, the content of the heme centers in MMPF-6 was measured to be 6.18×10^{-4} mol/g by inductively coupled plasma mass spectrometry experiments on the activated MMPF-6 sample. The relatively lower measured content of the heme centers compared to that estimated from the single-crystal X-ray crystallography derived formula (7.98×10^{-4} mol/g) should be attributed to the incomplete removal of the high-boiling-point guest *N*,*N*-dimethylformamide molecules during the activation process. Free-base MMPF-6, MMPF-6(Fr), was also synthesized (Figure S1 in the SI) for control experiments.

As shown in Figure 3, without catalyst, the blank reaction is going very slowly with rates of only 3.47×10^{-5} mM/s for THB oxidation and 2.87×10^{-6} mM/s for ABTS oxidation (Table 1) in 4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid (HEPES) buffer. MMPF-6 indicates a very fast initial rate of 1.39×10^{-3} mM/s for purpurogallin formation,[20] which is about one-third as fast as free Mb in HEPES buffer (Figure 3a and Table 1). Notably, MMPF-6 demonstrates impressive activity not only for oxidation involving oxygen transfer but also for oxidation involving electron transfer. In the context of ABTS oxidation, it exhibits a fast initial rate of 8.18×10^{-4} mM/s for $ABTS^{\bullet+}$ formation, which is about one-fourth that for free Mb in HEPES buffer (Figure 3c and Table 1). We reasoned that the slower initial rate for MMPF-6 compared to free Mb should originate from diffusion of the substrates from solution into the channels of MMPF-6. MMPF-6(Fr) demonstrated much lower activities for both reactions compared to MMPF-6 (Figure 3a,c and Table 1), indicating insignificant contributions from the framework and zirconium oxide cluster. MMPF-6 can be reused for four cycles without a significant drop in its peroxidase activity (Table 1) and can also retain its framework integrity, as confirmed by PXRD studies (Figure S1 in the SI), highlighting its heterogeneous feature.



(a) (b)

(c) (d)

Figure 3. Kinetic traces for oxidation of THB in (a) HEPES buffer and (b) an ethanol solution and oxidation ABTS in (c) HEPES buffer and (d) an ethanol solution.

We also assessed the peroxidase activity of MMPF-6 in organic solvents, in which heme proteins are known to easily lose their activities.[17] Catalytic assays performed in ethanol solutions indicated that MMPF-6 demonstrated an initial rate of 4.34×10^{-4} mM/s for purpurogallin formation and 7.56×10^{-5} mM/s for $ABTS^{\bullet+}$ formation (Figure 3b,d), meaning an enhancement of ~107 and ~215 times, respectively, for the reactions without catalyst (Table 1). In comparison, free Mb exhibited a much slower initial rate (Table1 and Figure 3b,d) because of the agglomeration of Mb molecules in ethanol.[17] Slow initial rates were observed for MMPF-6(Fr), furthering supporting the essential role of heme centers in MMPF-6 for the peroxidase activities.

In summary, a porous iron-based MMPF, MMPF-6, was constructed by self-assembly of the iron(III) *meso*-tetrakis(4-carboxyphenyl)porphyrin chloride ligand with the in situ generated $Zr_6O_8(CO_2)_8(H_2O)_8$ SBU under solvothermal conditions. MMPF-6 demonstrated interesting peroxidase activity comparable to that of the heme protein Mb in terms of the initial reaction rates in buffer solutions. MMPF-6 retained the peroxidase activity in an ethanol solution, highlighting its adaptability for organic solvents. This work paves a way to develop MOFs as a new type of biomimetic catalyst and also opens up new perspectives for mimicking heme-based proteins. Ongoing work in our laboratory includes the design and synthesis of new iron-based MMPFs for biomimetic catalysis.

Table 1. Summary of Catalysis Results of Oxidation of THB and ABTS in the Presence of 10 mM H_2O_2

	initial rate for purpurogallin formation in HEPES buffer (mM/s)	initial rate for purpurogallin formation in ethanol (mM/s)	initial rate for $ABTS^{\bullet+}$ formation in HEPES buffer (mM/s)	initial rate for $ABTS^{\bullet+}$ formation in ethanol (mM/s)
blank	3.47×10^{-5}	4.29×10^{-6}	2.87×10^{-6}	3.51×10^{-7}
free Mb[a]	3.37×10^{-3}	4.59×10^{-5}	3.54×10^{-3}	1.87×10^{-5}
MMPF-6	1.39×10^{-3}	4.34×10^{-4}	8.18×10^{-4}	7.56×10^{-5}
MMPF-6(Fr)	9.89×10^{-5}	6.62×10^{-5}	2.82×10^{-5}	1.65×10^{-5}
MMPF-6[b]	9.06×10^{-4}	6.96×10^{-5}	6.26×10^{-4}	6.96×10^{-5}

[a] Diluted to 5 μM. [b] The fourth cycle.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental procedures and PXRD patterns. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: sqma@usf.edu.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

S.M. acknowledges the University of South Florida for financial support of this work.

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