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Catalytic Activity of *m*-Phenylene- and 2,6-Pyridinediyl-linked Manganese Porphyrin Dimers. Role of Nitrogen Bases on the Development of Catalase Activity

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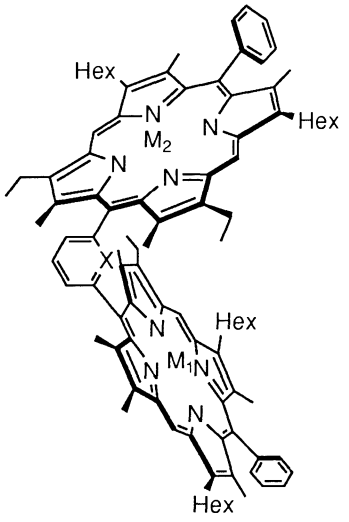
Catalase activity of *m*-phenylene-linked manganese porphyrin dimer was measured in the presence of various nitrogen bases. The catalase activity was dependent upon the the basicity as well as the concentration of the additive nitrogen bases where formation of the corresponding five-coordinated manganese species was less favorable. Deprotonation of hydrogen peroxide is the key step in the development of catalase activity.

Manganese ion in metalloenzymes has shown versatile roles through its oxygenated species.[1] Especially, on account of the strong affinity of manganese ion to oxygen atom coupled with its redox process, manganese-containing enzymes function disproportionation of superoxide anion and hydrogen peroxide.[2,3] Manganese catalases are also interested in their functional resembrance to oxygen evolving complex in photosynthetic reaction center of green plants.[4] Recently, we have reported their model compound containing two manganese(III) ions fixed in rigidly-linked porphyrin dimers exhibited high catalase activity in comparison with the corresponding monomers.[5] We also found the importance of a nitrogen base in the reaction system.

$$2H_2O_2 \xrightarrow[\text{N-Base}]{\text{Mn catalyst}} O_2 + 2H_2O$$

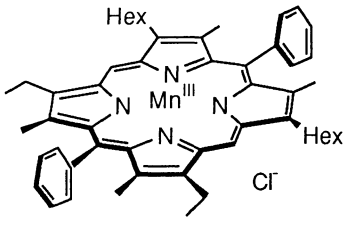


X = CH

$M_1 = M_2 = H_2$	**$(H)_2$PhD**
$M_1 = H_2$, $M_2 = Mn^{III}Cl$	**Mn(H)PhDCl**
$M_1 = M_2 = Mn^{III}Cl$	**Mn_2PhDCl_2**

X = N

$M_1 = M_2 = H_2$	**$(H)_2$PyD**
$M_1 = M_2 = Mn^{III}Cl$	**Mn_2PyDCl_2**



MnPCl

Problems arising in our study are (1) the role of the added nitrogen base, which will work as an axial ligand stabilizing high valent state of manganese ion and/or as a base assisting deprotonation of hydrogen peroxide resulting in the reactive hydroperoxide anion, and (2) the electronic structure of intermediate high-valent manganese ions, which have two options, Mn^{IV}-O-O-Mn^{IV}·2(X^-) or 2Mn^{IV}(=O). To clarify these problems, we have synthesized *m*-phenylene- (**Mn_2PhDCl_2**) or 2,6-pyridinediyl-linked manganse porphyrin dimers (**Mn_2PyDCl_2**),[6,7] both of which have sufficiently large separation (≈10Å)[8] between their two manganese ions not to make a μ-peroxo bond between them. Furthermore, the latter dimer contains a basic pyridyl group at the very proximal position between two manganese ions. The lone pair of the pyridyl nitrogen atom convergently directs the reaction site. It will be a good probe for clarification of the role of a nitrogen base in our modeling reaction of manganese catalases.

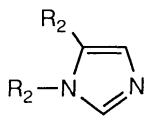
Catalase activity was measured about four manganese porphyrins, **MnPCl**, **Mn(H)PhDCl**, **Mn_2PhDCl_2**, and **Mn_2PyDCl_2** in the presence of various nitrogen bases according to the method shown in Table 1. Since the metal-metal separation is large enough to be coordinated by a less bulky imidazole such as 1-methylimidazole (1MeIm) to form each di(imidazole) complex, we synthesized imidazole derivatives, PIm and tBuIm, with bulky substituents on the ring.[9] These bulky imidazole is expected not to form the corresponding tetra(imidazole) complexes with the Mn porphyrin dimers, because their bulkiness would prevent the simultaneous coordination of the two imidazole inside the cavity and leave at least one vacant coordination site for hydrogen peroxide [10,11] The catalase activity, however, was not dependent upon the bulkiness of the base. The less bulky 1MeIm, which selectively forms the corresponding tetra(imidazole) complex with the Mn porphyrin dimers at the examined concentration, showed higher activity than the tBuIm. Furthermore, 4-(dimethylamino)pyridine enhanced the catalytic activity of the Mn porphyrin dimers in several times and gave the highest turnover rate (302 min^{-1}) in this catalytic system. This activity was comparable to our previous data recorded with the anthracene-linked manganese porphyrin dimers in the presence of 1MeIm.[5] Since the order of the base strength is estimated to be DMAP>>1MeIm>tBuIm≥PIm,[12] the catalase activity accords with the order of their basicity. The effect of the added nitrogen bases on the catalase activity was most typically observed in the reaction of Mn monomers. Their highest catalytic turnover numbers were comparable to those of **Mn_2PhDCl_2**.[13] On the other hand, the **Mn_2PyDCl_2** exhibited much lower activity in spite of our initial expectation. Since the basicity of the linker pyridyl nitrogen is estimated to be ≈3.8,[12] the pyridyl group will work as a kind of weak base buffer fixed vely closely to the reaction center.[14]

From the kinetic study of Mn_2PDCl_2-catalyzed reaction, the O_2 evolution rate is proportional to the first order for both [H_2O_2] and Mn_2PDCl_2]. Quantitative analysis of the evolved O_2 in the reaction with the 1:1 mixture of $H_2{}^{16}O_2$ and $H_2{}^{18}O_2$ indicated no isotope scrambling. Spectroscopic study of the reaction did not exhibit formation of the resultant high-valent Mn porphyrin dimer, which would be rapidly reduced to the Mn(III) complex by the second H_2O_2 molecule. These results confirmed that the rate determining step was in the initial reaction of H_2O_2 to the catalyst. The added nitrogen bases would increase the concentration of the reaction of reactive HOO^-, which is proportional to both the base strength and its concentration. The obseved activity was comparable to our previous data.[5] This is very striking because of the longer Mn-Mn separation (≈10 Å) in the present dimers than that (≈5.4 Å) of the anthracene-linked ones. This means that Mn^{IV}-O-O-Mn^{IV} is not necessarily essential as the active intermediate of the catalase reaction but the 2Mn^{IV}(=O) could be the most probable candidate that formed in the present case in consideration of their Mn-Mn saparation.

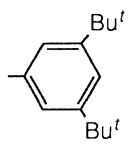
Table 1. Catalase Activity of Manganese Porphyrins[a)]

Run	Mn porphyrin	Nitrogen base		O_2 Evolution initial	Turnover
		(pK_a[b)])	concentration/mol dm^{-3}	rate/mol min^{-1}	number/min^{-1}
1	MnPCl	PIm	7.09×10^{-3}	6.77×10^{-8}	0.34
2		(≈5.9)	1.24×10^{-1}	3.10×10^{-7}	1.55
3		1MeIm	7.15×10^{-3}	3.27×10^{-7}	1.6
4		(7.33)	1.25×10^{-1}	5.86×10^{-7}	2.93
5		DMAP	7.06×10^{-3}	3.45×10^{-5}	172
6		(9.70)	1.24×10^{-5}	2.30×10-5	115
7	Mn(H)PhDCl	PIm	7.14×10^{-3}	5.64×10^{-8}	0.28
8		DMAP	7.06×10^{-3}	5.11×10^{-5}	255
9			7.09×10^{-2}	3.49×10^{-5}	175
10	Mn_2PhDCl_2	PIm	7.09×10^{-3}	5.64×10^{-8}	0.28
11			1.24×10^{-1}	3.92×10^{-6}	19.6
12		tBuIm	7.08×10^{-3}	1.10×10^{-7}	0.55
13		(≈6.0)	1.24×10^{-1}	1.14×10^{-5}	57.2
14		1MeIm	7.15×10^{-3}	1.84×10^{-6}	9.2
15			7.15×10^{-2}	9.56×10^{-6}	47.8
16			1.25×10^{-1}	1.61×10^{-5}	80.4
17		DMAP	1.24×10^{-1}	6.03×10^{-5}	302
18	Mn_2PyDCl_2	PIm	7.09×10^{-3}	3.60×10^{-3}	0.18
19			1.24×10^{-1}	3.29×10^{-7}	1.65
20		tBuIm	7.08×10^{-3}	9.31×10^{-8}	0.47
21			7.08×10^{-2}	6.69×10^{-7}	3.35
22		1MeIm	7.15×10^{-3}	1.43×10^{-6}	7.16
23			7.15×10^{-2}	2.94×10^{-6}	14.7
24			1.25×10^{-1}	1.66×10^{-6}	8.31

a) Catalase activities of manganese porphyrins were measured according to the following procedure: An acetonitrile-benzonitrile solution (1:0.03-1:0.27 v/v, total 1.5 ml) of the manganese porphyrin (0.26×10^{-3} mol dm^{-3}, normalized to the concentration of manganese ion) and a nitrogen base were added to the thermostated reaction vessel fitted with an micro oxygen-electrode at 10.0±0.2 °C, and the solution was purged with high purity argon. To the solution, a deaerated acetonitrile solution of hydrogen peroxide (1.0 mol dm^{-3}, 100 μl) was added and the evolution of O_2 was monitored. b) pK_a values in an aqueous solution, taken from Ref. 12.

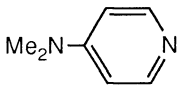


$R_1 = R_2 = Ph$ **PIm**



$R_1 = R_2 =$ **tBIm**

$R_1 = Me, R_2 = H$ **1MeIm**



DMAP

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5) Y. Naruta and K. Maruyama, *J. Am. Chem. Soc.*, **113**, 3595 (1991).

6) Preparation of the free base porphyrin dimers, **$(H)_2$PhD** and **$(H)_2$PyD**, was performed by the similar method as reported. The yields of the porphyrins at the final coupling stage were 9 and 7%, respectively. *cf.* J. L. sessler, J. Hugdahl, and M. R. Johnson, *J. Org. Chem.*, **51**, 2838 (1986).

7) Spectroscopic data of typical compounds, **$(H)_2$PhD**; ^{1}H NMR ($CDCl_3$) δ 10.14 (s, 4H), 8.89 (dd, 2H), 8.29 (t, 1H), 8.05–7.93 (m, 5H), 7.75–7.68 (m, 6H), 4.00 (q, 8H), 3.91 (t, 8H), 3.10(s, 12H), 2.41 (s, 12H), 2.1 (m, 8H), 1.75 (t, 12H), 1.70-1.62 (m, 18H), 1.46–1.39 (m, 8H), 1.35–1.25 (m, 8H), 0.85 (t, 12H), -2.12 (s, 4H); FAB MS m/z=1409 ($M+H^+$); UV-vis (CH_2Cl_2) λ_{max} 578, 543, 510, 416 nm. **Mn_2PhDCl_2**: FAB MS m/z= 1514 (M^+); UV-vis (CH_2Cl_2) λ_{max} 572, 480, and 369 nm. **$(H)_2$PyD:** ^{1}H NMR ($CDCl_3$) δ 10.14 (s, 4H), 8.86 (d, 2H), 8.56 (t, 1H), 8.01 (m, 4H), 7.75–7.69 (m, 6H), 3.97–3.88 (m, 16H), 3.05 (s, 12H), 2.41 (s, 12H), 2.13–2.09 (m, 8H), 1.35–1.26 (m, 8H), 0.85 (t, 12H), -2.01–-2.08 (m, 4H); FAB MS m/z=1410 ($M+H^+$); UV-vis (CH_2Cl_2) λ_{max} 577, 544, 511, 417 nm. **Mn_2PyDCl_2**: FAB MS m/z= 1515 (M^+); UV-vis (CH_2Cl_2) λ_{max} 561, 468, and 374 nm.

8) Estimated by CPK model.

9) These imidazole derivatives were chosen so that they did not subject to intensive electronic perturbation by the substituent. tBuIm was prepared according to the similar method as that of PIm. *cf.* A. M. van Leusen, J. Wilderman, and O. H. Oldenziel, *J. Org. Chem.*, **42**, 1153 (1977).

10) Generally, water molecule is a weak axial ligand in Mn porphyrins, but it is easily substituted by other anions or bases.

11) Formation constants of PIm and tBuIm to the Mn porphyrin dimers applied in this study were determined by means of photometric titration. It revealed that the formation of tetraimidazole complex with these Mn porphyrin dimers was negligible.

12) *p*Ka values of PIm, tBuIm, and 2,6-diarylpyridine were estimated from those of the analogous nitrogen bases. *cf.* A. Albert, "Physical Methods in Heterocyclic Chemistry," ed by A. R. Katritzky, Academic, New York (1963),Vol. 1, Chap. 1; A. Albert, *ibid.*, (1971), Vol.3,Chap.1.

13) For the catalase reaction with the Mn porphyrin monomers as the catalyst, different mechanism with those of the Mn dimer can be proposed.

14) Similar low catalase activity (1.59 turnover min^{-1}) was observed in the catalytic reaction with the anthracene-linked Mn porphyrin dimers in the presence of methyl 4-pyridinecarboxylate (pKa = 3.49) as the added base.

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