

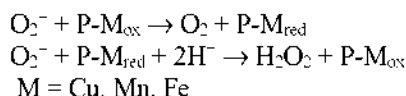
Synthesis and Characterization of Ferric Complex of Biomimetic Tripodal Ligand, Bis(2-benzimidazolymethyl)ethanolamine

Byunghoon Kwak, Hakjune Rhee, and Myoung Soo Lah*

Department of Chemistry, College of Science, Hanyang University, 1271 Sa-1-dong, Ansan, Kyunggi-do 425-170, Korea

Received July 15, 1999

Model systems that mimic the active sites of the metalloproteins are very important tools for understanding the reaction mechanism of the metalloproteins and for the development of the new low molecular weight biomimetic molecules. Superoxide dismutases (SODs) are metalloenzymes that disproportionate superoxide radical, a toxic byproduct of cellular respiration, to molecular oxygen and hydrogen peroxide through a cyclic oxidation-reduction mechanism as shown below.¹



Many low molecular weight biomimetic molecules have been proposed as Mn- and Fe-SOD mimics.^{2,3} However, these structures are quite different from the active site structure of Mn- and Fe-SODs.⁴ The active site geometry of Fe-SOD is the distorted trigonal bipyramid with nitrogen/oxygen mixed donor atoms. Recently, we reported a mononuclear iron complex containing tripodal tetradentate ligand, tris(2-benzimidazolymethyl)amine (ntb) that had four nitrogen donor atoms. However, the SOD activity of the complex is an order of magnitude smaller than that of the best known.⁵ In this study, we synthesized and characterized a mononuclear high spin Fe(III) complex with a biomimetic tripodal ligand, bis(2-benzimidazolymethyl)ethanolamine (Hbbee) which had three nitrogen atoms and one oxygen atom.

Experimental Section

Materials. The following chemicals were used as received with no further purification: iron(III) chloride hexahydrate and DMSO-*d*₆ from Aldrich Inc.; methanol from Carlo Erba. Hbbee was prepared according to literature procedure.⁶

Instrumentation. C, H, N and Fe determinations were performed by the Elemental Analysis Laboratory of the Korea Institute of Basic Science. Infrared spectra were recorded as KBr pellets in the range 4000-600 cm⁻¹ on a Bio-Rad FT-IR spectrometer. Absorption spectra were obtained using a Perkin Elmer Lambda spectrometer. NMR spectra were obtained using a Varian-300 spectrometer. Positive-ion FAB mass spectra were obtained using a JEOL

HX110A/HX110A tandem mass spectrometer in glycerol matrix. Room-temperature magnetic susceptibilities of well-ground solid samples were measured by using an Evans balance. The measurements were calibrated against a Hg-[Co(SCN)₄] standard.⁷

Synthesis. [Fe^{III}(Hbbee)Cl₂]Cl. **1.** A 0.65 g (2.0 mmol) amount of Hbbee was dissolved in 30 mL of methanol. When a 0.54 g (2.0 mmol) amount of iron(III) chloride hexahydrate was added to the solution. After an hour of stirring the solution was filtered. The red powder was obtained (0.83 g, 96% yield). Slow evaporation of the filtrate solution for 4 days gave red crystals. The IR spectrum of the crystal was identical to that of the red powder sample. Anal. Calcd. for [Fe^{III}(Hbbee)Cl₂]Cl (FeC₁₈H₁₉N₃OCl₃) (F.W. = 483.59): C, 44.71; H, 3.96; N, 14.48; Fe, 11.55%. Found: C, 44.48; H, 4.00; N, 14.48; Fe, 11.52%. ¹H NMR (DMSO-*d*₆): δ 27: 39: 60. FAB mass spectrum: m/z of [Fe(Hbbee)Cl₂ - HCl]⁺, 412. UV-vis (MeOH) [λ_{max} (ε)]: 236.5 nm (16100 M⁻¹cm⁻¹), 270 nm (18900 M⁻¹cm⁻¹), 277 nm (18600 M⁻¹cm⁻¹), 321 nm (4000 M⁻¹cm⁻¹). μ_{eff}: 5.70 μ_B.

X-ray crystallography. A single crystal suitable for X-ray analysis was attached to a glass fiber. Preliminary examination and data collection were performed with Mo Kα radiation (= 0.71069 Å) on an Enraf-Nonius CAD4 computer-controlled κ-axis diffractometer equipped with a graphite crystal, incident-beam monochromator. Cell constants and orientation matrix for data collection were obtained from least-squares refinement, using the setting angles of 25 reflections. Data were collected at room temperature using the ω scan technique. Three standard reflections were monitored every 1 h, but no intensity variations

Table 1. Crystal Data and Structure Refinement for **1**

Empirical formula	FeC ₁₈ H ₁₉ N ₃ OCl ₃
Formula weight	483.58
Temperature	293(2) K
Crystal system, space group	monoclinic, P2 ₁ /n
Unit cell dimensions	a = 7.5874(8) Å b = 18.804(1) Å β = 98.730(9)° c = 14.630(2) Å
Volume	2063.1(4) Å ³
Z, Calculated density	4, 1.557 mg/m ³
Absorption coefficient	1.139 mm ⁻¹
Reflections collected / unique	2923 / 2692 [R(int) = 0.0479]
Final R indices [I > 2σ(I)]	R1 = 0.0477, wR2 = 0.1137
R indices (all data)	R1 = 0.0592, wR2 = 0.1203

*To whom correspondence should be addressed. Phone: +82-345-400-5496, Fax: +82-345-407-3863, E-mail: mslah@email.hanyang.ac.kr

were monitored. Lorentz and polarization corrections were applied to the data; however, no correction was made for absorption. The structure was solved by direct methods using SHELXS-86⁸ and refined by full-matrix least-squares calculation with SHELXL-97.⁹ Three non-coordinating methanol sites were identified, and one of them was disordered. All non-hydrogen atoms were refined anisotropically; all hydrogen atoms were allowed to ride on geometrically ideal positions with isotropic temperature factors 1.2 times those of the attached non-hydrogen atoms. Crystal and intensity data are given in Table 1.

Results and Discussion

Preparation and Characterization of Complex 1.

[Fe(Hbba)Cl₂]Cl. **1** can be synthesized using ferric chloride as a metal source and Hbba as a neutral tripodal tetradentate ligand. The magnetic moment of complex **1** at room temperature, 5.70 μ_B , is comparable to the spin-only value of high spin d^5 Fe^{III}, 5.92 μ_B . The DMF solution of complex **1** in a glycerol matrix gave a peak at m/z 498 in the FAB mass spectrum. This peak corresponds to the five-coordinate metal complex ion, [Fe(Hbba)Cl-H]⁺. Paramagnetically shifted ¹H NMR spectrum of complex **1** in DMSO-*d*₆ gave three broad bands at 27, 39, 60 ppm which are tentatively assigned as the benzimidazole protons of the ligand. Similar downfield bands were observed and assigned to the benzimidazole protons of the ligand in the complex, [Fe(ntb)Cl₂]-ClO₄.⁵

Molecular Structure of Complex 1. An ORTEP drawing of complex **1** is shown in Figure 1. Complex **1** is a cis-dichloro distorted octahedral complex. Two nitrogen atoms of benzimidazole groups and an oxygen atom of alcohol group in the Hbba, and a chloride anion formed the base of the octahedral geometry. One of two axial positions was occupied by apical nitrogen of Hbba and the other site was occupied by another chloride anion. Two chloride anions in complex **1** are in a cis geometry. The geometry of the complex **1** is very similar to that of the iron(III) complex of ntb ([Fe(ntb)Cl₂]ClO₄). An oxygen atom of the alcohol group replaced one of the basal nitrogen atoms of the benzimidazole group.

The average bond distance between the iron(III) ion and the two basal nitrogen atoms of the benzimidazole groups is

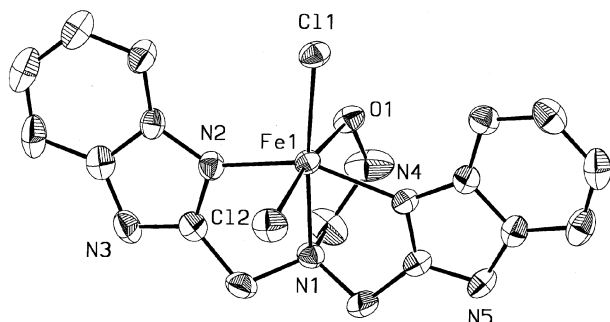


Figure 1. ORTEP drawing of the cation of complex **1**, [Fe(Hbba)Cl₂]⁺.

Table 2. Selected Bond Lengths (Å) and Angles (°) for **1**

Fe(1)-N(1)	2.296(4)	Fe(1)-O(1)	2.131(4)
Fe(1)-N(2)	2.086(4)	Fe(1)-Cl(1)	2.240(1)
Fe(1)-N(4)	2.070(4)	Fe(1)-Cl(2)	2.285(2)
N(2)-Fe(1)-N(1)	74.8(2)	Cl(2)-Fe(1)-N(2)	91.25(12)
N(4)-Fe(1)-N(1)	75.98(15)	O(1)-Fe(1)-N(4)	83.0(2)
O(1)-Fe(1)-N(1)	76.65(15)	Cl(1)-Fe(1)-N(4)	103.82(12)
Cl(1)-Fe(1)-N(1)	162.85(11)	Cl(2)-Fe(1)-N(4)	91.00(12)
Cl(2)-Fe(1)-N(1)	94.58(11)	Cl(1)-Fe(1)-O(1)	86.27(12)
N(4)-Fe(1)-N(2)	150.7(2)	Cl(2)-Fe(1)-O(1)	170.36(12)
O(1)-Fe(1)-N(2)	90.3(2)	Cl(2)-Fe(1)-Cl(1)	102.57(6)
Cl(1)-Fe(1)-N(2)	104.13(12)		

2.078 Å (2.086, 2.070 Å). The bond distance between the iron(III) ion and the oxygen atom of the alcohol group is 2.131 Å, which corresponds to the distance between the iron(III) ion and the alcoholic oxygen atom, not alkoxy oxygen atom. The bond distance between the iron(III) ion and the basal chloride is 2.285 Å while the distance between the iron(III) ion and the chloride anion at trans position of the apical nitrogen is 2.214 Å. The bond distance between the iron(III) ion and the basal chloride is about 0.06 Å shorter than that in [Fe(ntb)Cl₂]ClO₄.⁵ The bond distance between the iron(III) ion and the apical nitrogen atom (N1) of 2.296 Å is about 0.22 Å longer than those between the iron(III) ion and the basal nitrogen atoms of the benzimidazole groups (Table 2). Similar elongations are also observed in the other iron¹⁰ complexes of tripodal tetradentate ligands with benzimidazolylmethyl group.

In conclusions, we synthesized and characterized a mononuclear high spin iron(III) complex with a biomimetic tripodal ligand, Hbba that had three nitrogen atoms and an oxygen atom. Currently, we are investigating the reactivity of the complex **1** with O₂⁻ radical and bases, and SOD activity of the complex **1**.

Supplementary Material. The following are available on request from the correspondence author: Tables giving the structure determination summary, atomic coordinates, temperature factors, bond lengths, bond angles, and anisotropic thermal parameters for non-hydrogen atoms and atomic coordinates for hydrogen atoms, *F*_o/*F*_c tables, ORTEP drawings with complete atomic numbering for **1**, and ¹H NMR spectrum of complex **1** in DMSO-*d*₆.

Acknowledgment. We thank the Korean Institute of Basic Science for elemental analyses and mass spectrum, and the National Institute of Technology and Quality for use of an X-ray diffractometer. The authors wish to acknowledge the financial support of the Korea Research Foundation (98-015-D00142).

References

- (a) Fridovich, I. *Annu. Rev. Biochem.* **1995**, *64*, 97-112.
(b) Fridovich, I. *J. Biol. Chem.* **1989**, *264*, 7761-7764.
- (a) Riley, D. P.; Lennon, P. J.; Neumann, W. L.; Weiss, R.

11. *J. Am. Chem. Soc.* **1997**, *119*, 6522-6528. (b) Riley, D. P.; Henke, S. L.; Lennon, P. J.; Weiss, R. H.; Neumann, W. L.; Rivers, W. L.; Aston, K. W.; Sample, K. R.; Rahman, H.; Ling, C.-S.; Shieh, J.-J.; Busch, D. H.; Szulbinski, W. *Inorg. Chem.* **1996**, *35*, 5213-5231. (c) Rajan, R.; Rajaram, R.; Nair, B. U.; Ramasami, T.; Mandal, S. K. *J. Chem. Soc., Dalton Trans.* **1996**, 2019-2021. (d) Deroche, A.; Morgenstern-Badarau, I.; Cesario, M.; Guilhem, J.; Keita, B.; Nadjo, I.; Houce-Levin, C. *J. Am. Chem. Soc.* **1996**, *118*, 4567-4573. (e) Riley, D. P.; Weiss, R. H. *J. Am. Chem. Soc.* **1994**, *116*, 387-388. (f) Kitajima, N.; Osawa, M.; Tamura, N.; Moro-oka, Y.; Hirano, T.; Hirobe, M.; Nagano, T. *Inorg. Chem.* **1993**, *32*, 1879-1880. (g) Weiss, R. H.; Flickinger, A. G.; Rivers, W. J.; Hardy, M. M.; Aston, K. W.; Ryan, U. S.; Riley, D. S. *J. Biol. Chem.* **1993**, *268*, 23049-23054. (h) Nishida, Y.; Watanabe, I.; Unoura, K. *Chem. Lett.* **1991**, 1517-1520. (i) Bielski, B. H. J.; Chan, P. C. *J. Am. Chem. Soc.* **1978**, *100*, 1920-1921. (j) Valentine, J. S.; Quinn, A. F. *Inorg. Chem.* **1976**, *15*, 1997-1999.
3. (a) Zhang, D.; Busch, D. H.; Lennon, P. J.; Weiss, R. H.; Neumann, W. L.; Riley, D. P. *Inorg. Chem.* **1998**, *37*, 956-963. (b) Rodriguez, M.; Morgenstern-Badarau, I.; Cesario, M.; Guilhem, J.; Keita, B.; Nadjo, I. *Inorg. Chem.* **1996**, *35*, 7804-7810. (c) Szulbinski, W. S.; Warburton, P. R.; Busch, D. H. *Inorg. Chem.* **1993**, *32*, 5368-5376. (d) Iuliano, L.; Pedersen, J. Z.; Ghiselli, A.; Pratico, D.; Rotilio, G.; Violi, F. *Arch. Biochem. Biophys.* **1992**, *293*, 153-157. (e) Nagano, T.; Hirano, T.; Hirobe, M. *Free Radical Res. Commun.* **1991**, *12*, 221-227. (f) Faraggi, M.; Peretz, P.; Weinraub, D. *Int. J. Radiat. Biol.* **1986**, *49*, 951-968. (g) Bull, C.; McClune, G. J.; Fec, J. A. *J. Am. Chem. Soc.* **1983**, *105*, 5290-5300.
4. Lah, M. S.; Dixon, M. M.; Patridge, K. A.; Stallings, W. C.; Fec, J. A.; Ludwig, M. L. *Biochemistry* **1995**, *34*, 1546-1660.
5. Kwak, B.; Cho, K. W.; Pyo, M.; Lah, M. S. *Inorg. Chim. Acta* **1999**, *290*(1), 21-27.
6. (a) Oki, A. R.; Bommarreddy, P. R.; Zhang, H. *Inorg. Chem. Acta* **1995**, *231*, 109-114. (b) Takahashi, K.; Ogawa, E.; Oishi, N.; Nishida, Y.; Kida, S. *Inorg. Chem. Acta* **1982**, *66*, 97-103.
7. Evans, D. F. *J. Chem. Soc.* **1958**, 2003-2005.
8. Sheldrick, G. M. *Acta Crystallogr.* **1990**, *A46*, 467-473.
9. Sheldrick, G. M. SHELXL97: University of Göttingen: Göttingen, Germany, 1997.
10. (a) Buchanan, R. M.; O'Brien, R. J.; Richardson, J. F.; Latour, J.-M. *Inorg. Chim. Acta* **1993**, *214*, 33-40. (b) Wang, S.; Luo, Q.; Wang, X.; Wang, L.; Yu, K. *J. Chem. Soc., Dalton Trans.* **1995**, 2045-2055.
-