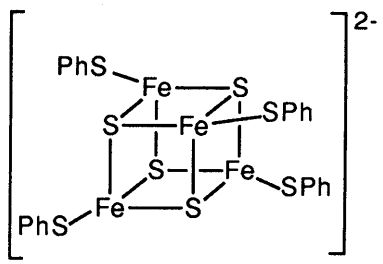
COMPARISON OF THE REACTIVITIES OF $[Fe_4S_4(SPh)_4]^{2-}$ AND $[Fe_2S_2(SPh)_4]^{2-}$

Kazuo YANADA,[1] Tetsuo NAGANO, and Masaaki HIROBE*
Faculty of Pharmaceutical Sciences, University of Tokyo, Hongo, Bunkyo-ku, Tokyo, Japan

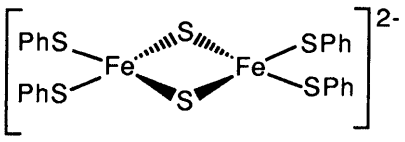
The reactivities of the model complexes, $[Fe_4S_4(SPh)_4]^{2-}$ (**1**) and $[Fe_2S_2(SPh)_4]^{2-}$ (**2**), of nonheme iron-sulfur proteins were compared. Complex **1** catalyzed the oxidation of benzenethiol to diphenyl disulfide with the reduction of dioxygen to H_2O. Complex **2** did not catalyze it, but the reaction proceeded after an induction period during which complex **2** was converted to complex **1**. In addition, complex **1** catalyzed the reduction of 1,4-dinitrobenzene to *N*-(4-nitrophenyl)hydroxylamine (21 %) and 4-nitroaniline (16 %) with the oxidation of benzenethiol to diphenyl disulfide, but complex **2** induced mainly the displacement of nitro group to phenylthio group to give 1-nitro-4-(phenylthio)benzene (92 %). It was revealed that the reactivities of complex **1** and complex **2** are quite different.

KEYWORDS iron-sulfur complex; ferredoxin model; benzenethiol oxidation; diphenyl disulfide; 1,4-dinitrobenzene reduction

Nonheme iron-sulfur proteins act as electron carriers in various processes or cell metabolisms.[2] These proteins are classed by their active sites as rubredoxin ([1Fe]) and ferredoxins ([2Fe-2S], [4Fe-4S], [3Fe-3S], and [3Fe-4S]) types.[3] Many analogues of the active sites of such proteins have been prepared[4] since the successful synthesis of $(Et_4N)_2[Fe_4S_4(SCH_2Ph)_4]$ by Holm and his coworkers.[5] These analogues have contributed to the understanding of the physical properties of the protein active sites.[4] However, there have been no reports of the comparison between the reactivities of such analogues, though it would be interesting for elucidation of the activities of iron-sulfur proteins as electron carriers.



1



2

Chart 1

We reported previously that $(n\text{-}Bu_4N)_2[Fe_4S_4(SPh)_4]$[6] (**1**) catalyzes the oxidation of benzenethiol to diphenyl disulfide with dioxygen[7] and also on the reduction of aromatic nitro compounds to amines with benzenethiol.[8] As part of our research on the catalytic properties of iron-sulfur analogues,[9] the reactivity of $(Et_4N)_2[Fe_2S_2(SPh)_4]$ (**2**)[10] was compared with that of **1** (Chart 1). We report here that the catalytic activities of **1** and **2** were quite different, surprisingly.

The oxidation of benzenethiol with **1** or **2** as a catalyst was followed by monitoring the consumption of dioxygen (Fig. 1).[11] Diphenyl disulfide was formed quantitatively and other products were not detected. The reaction with **1** started immediately and was completed within ten minutes, and afterwards dioxygen uptake was not observed. The quantity of dioxygen uptake was exactly 1/4 equimolar of benzenethiol (Chart 2). In the reaction with **2** as a catalyst, an induction period was observed, and then the reaction proceeded in a manner similar to that with **1**. The induction period became shorter with higher content of **2**. These results and the visible spectral change of **2** during the reaction show that **2** itself does not catalyze the oxidation of benzenethiol with dioxygen but that **2** dimerizes to **1** during the induction period and then **1** induces the reaction.

Holm *et al.* reported that **2** is stable in aprotic solvent such as dimethyl sulfoxide, *N*,*N*-dimethylformamide, and hexamethylphosphoramide under an anaerobic condition.[12] However, Coucouvanis *et al.* reported that **2** is reduced by sodium hydrosulfite and crown ether to form **1**.[13] Complex **2** is probably

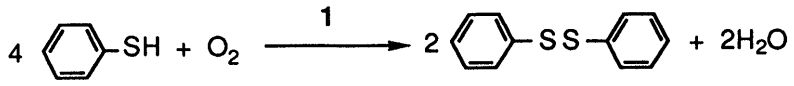


Chart 2

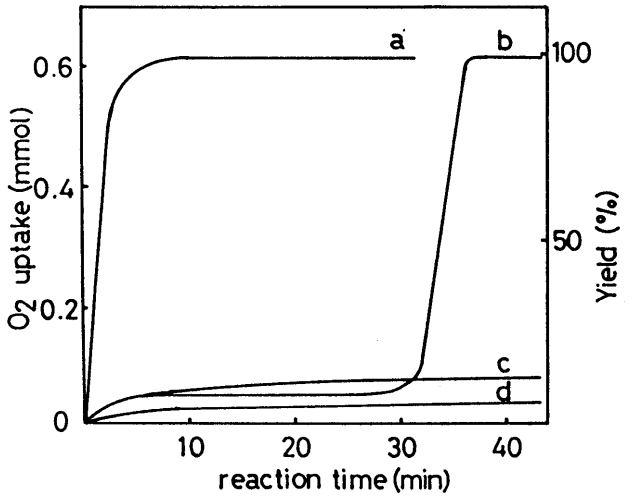


Fig. 1. Catalytic Oxidation of Benzenethiol to Diphenyl Disulfide with Dioxygen in the Presence of **1** or **2**
a) $(n\text{-}Bu_4N)_2[Fe_4S_4(SPh)_4]$ (**1**) (0.07 mmol).
b) $(Et_4N)_2[Fe_2S_2(SPh)_4]$ (**2**) (0.03 mmol).
c) $FeCl_2$ (0.09 mmol). d) $FeCl_3$ (0.12 mmol).

reduced to $[Fe_2S_2(SPh)_4]^{3-}$, also, by benzenethiol and then dimerizes to **1** with formation of thiolate anion (Chart 3).

The reaction of 1,4-dinitrobenzene (**3**) with benzenethiol was used for the comparison of the catalytic activities of **1** and **2** (Table I). The reaction with **1** as a catalyst gave reduction products such as *N*-(4-nitrophenyl)hydroxylamine (**4**, 21 %) and 4-nitroaniline (**5**, 16 %). However, in the case of using **2**, the yield of the reduction product [*N*-(4-nitrophenyl)hydroxylamine] (**4**) was only 7 %, but the catalytic displacement of nitro group by phenylthio group proceeded mainly to give 1-nitro-4-(phenylthio)benzene (**6**, 92 %). The displacement and the reduction proceeded with $FeCl_3$ or $FeCl_3$ and sodium sulfide as a catalyst. As the result, it was shown that the catalytic activity of **1** is quite different from that of **2**. Complex **2** catalyzes the conversion of **3** to **6**. Generally, the nitro group of 1,4-dinitrobenzene causes

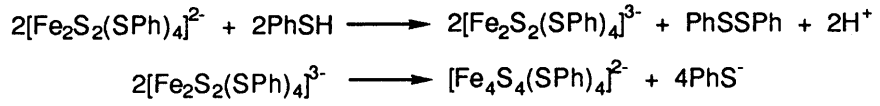
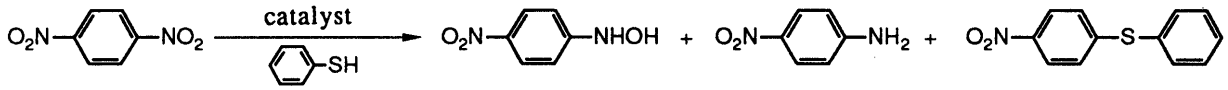


Chart 3

Table I. Catalytic Reaction of 1,4-Dinitrobenzene with Benzenethiol in the Presence of **1** or **2**[a)]



3 **4** **5** **6**

Catalyst	Yield (%)[b)]		
	4	**5**	**6**
$(n\text{-}Bu_4N)_2[Fe_4S_4(SPh)_4]$ (**1**)	21	16	0
$(Et_4N)_2[Fe_2S_2(SPh)_4]$ (**2**)	7	0	92
$FeCl_3 + Na_2S$[c)]	4	4	8
$FeCl_3$	5	0	0
-	4	0	1

a) Reaction conditions: 1,4-Dinitrobenzene (1.0 mmol), catalyst (0.1 mmol), and benzenethiol (10 mmol) in acetonitrile (20 ml) were stirred at 26 °C for 20 h under an argon atmosphere. b) The yield of products was determined by TLC scanner. c) $FeCl_3$ (0.25 mmol) and Na_2S (0.22 mmol).

displacement easily by various nucleophiles.[14]

In conclusion, **1** reduced dioxygen or dinitrobenzene in the presence of benzenethiol. The reduction efficiency of **1** was revealed to be quite different from that of **2**.

This work shows that **1** has high reduction activities, but 2 does not. **2** catalyzes the displacement rather than the reduction. This is the first report about the difference of the reactivities between [4Fe-4S] and [2Fe-2S] iron-sulfur complexes.

REFERENCES AND NOTES

1) Present address: Faculty of Pharmaceutical Sciences, Setsunan University, Nagaotoge-cho, Hirakata, Osaka, 573-01, Japan.
2) L. H. Jensen, "Iron-Sulfur Protein Research," eds. by H. Matsubara, Y. Katsube, and K. Wada, Japan Sci. Soc. Press, Tokyo/Springer-Verlag, Berlin, 1986, pp. 3-21 and references cited therein.
3) R. Cammack, "Iron-Sulfur Protein Research," eds. by H. Matsubara, Y. Katsube, and K. Wada, Japan Sci. Soc. Press, Tokyo/Springer-Verlag, Berlin, 1986, pp. 40-55.
4) J. M. Berg and R. H. Holm, "Iron-Sulfur Proteins," ed. by T. G. Spiro, John Wiley & Sons, New York, 1982, p. 1; R. H. Holm, *Acc. Chem. Res.*, **10**, 427 (1977).
5) T. Herskovitz, B. A. Averill, R. H. Holm, J. A. Ibers, W. D. Phillips, and J. F. Weiher, *Proc. Natl. Acad. Sci. U.S.A.*, **69**, 2437 (1972).
6) B. A. Averill, T. Herskovitz, R. H. Holm, and J. A. Ibers, *J. Am. Chem. Soc.*, **95**, 3523 (1973).
7) T. Nagano, K. Yoshikawa, and M. Hirobe, *Tetrahedron Lett.*, **21**, 297 (1980).
8) T. Itoh, T. Nagano, and M. Hirobe, *Chem. Pharm. Bull.*, **34**, 2013 (1986).
9) T. Itoh, T. Nagano, M. Sato, and M. Hirobe, *Tetrahedron Lett.*, **30**, 6387 (1989); K. Yanada, T. Nagano, and M. Hirobe, *Chem. Pharm. Bull.*, **36**, 535 (1988); M. Hirobe, *Yuki Gosei Kagaku Kyokai Shi*, **45**, 755 (1987) and references cited therein.
10) J. J. Mayerle, S. E. Denmark, B. V. DePamphilis, J. A. Ibers, and R. H. Holm, *J. Am. Chem. Soc.*, **97**, 1032 (1975).
11) Benzenethiol (0.25 ml, 2.5 mmol) and acetonitrile (1 ml) were placed in a two-necked round-bottom flask equipped with a Suba Seal Septa and a three way stopcock which was connected to a dioxygen cylinder and a gas buret. After dioxygen was substituted in the flask, the solution of analogue in acetonitrile (10 ml) was added through Septa with a syringe. The reaction mixture was stirred at 0 °C and dioxygen consumption was followed.
12) a) K. S. Hagen, J. G. Reynolds, and R. H. Holm, *J. Am. Chem. Soc.*, **103**, 4054 (1981); b) J. Cambray, R. W. Lane, A. G. Wedd, R. W. Johnson, and R. H. Holm, *Inorg. Chem.*, **16**, 2565 (1977).
13) D. Coucouvanis, C. N. Murphy, E. Simhon, P. Stremple, and M. Draganjac, *Inorg. Synth.*, **21**, 23 (1982).
14) Nitro groups on benzenoid aromatic systems have been replaced with various nucleophiles, e.g. thiolates, alkoxides, phenoxides, carbanions, cyanide, fluoride, and anilines. P. G. Sammes, D. Thetford, and M. Voyle, *J. Chem. Soc., Chem. Commun.*, **1987**, 1373; G. Iwasaki, S. Saeki, and M. Hamana, *Chem. Lett.*, **1986**, 31; J. H. Gorvin, *J. Chem. Soc., Chem. Commun.*, **1985**, 238; J. H. Clark, and D. K. Smith, *Tetrahedron Lett.*, **26**, 2233 (1985); M. Attina, F. Cacace, and A. P. Wolf, *J. Chem. Soc., Chem. Commun.*, **1983**, 108; P. Cogolli, L. Testaferri, M. Tingoli, and M. Tiecco, *J. Org. Chem.*, **44**, 2636 (1979); J. R. Beck, *Tetrahedron*, **34**, 2057 (1978) and references cited therein; N. Kornblum, L. Cheng, R. C. Kerber, M. M. Kestner, B. N. Newton, H. W. Pinnick, R. G. Smith, and P. A. Wade, *J. Org. Chem.*, **41**, 1560 (1976).

(Received October 12, 1992)