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# Clusters $[Fe_4S_4(SR)_4]^{2-}$ as Novel Catalysts in Organic Reductions

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The cluster $[Fe_4S_4(SR)_4]^{2-}$ catalyzed the reductions of nitro compounds, quinones and *N*-oxide compounds to amines, hydroquinones, and deoxygenated compounds, respectively, in the presence of thiols in $CH_3CN$ solution. The reaction mechanism was also investigated by electron spin resonance spectroscopy, and it was concluded that these reactions proceed *via* one-electron transfer from the cluster to the substrates.

**Keywords**——ferredoxin; cluster; electron transfer; iron–sulfur protein; reduction; super-oxidized cluster

Nonheme iron–sulfur proteins are implicated as electron carriers in diverse processes of cell metabolism,1) and ferredoxins and rubredoxin form an important and comprehensive class of such proteins.2) The abilities of these proteins to act as electron carriers are related to their iron–sulfur active sites, which have several different oxidation levels interrelated by one-electron transfer reactions. Tetranuclear complexes $[Fe_4S_4(SR)_4]^{2-}$ synthesized by Holm2-4) *et al.* are close structural and electronic analogs of the active sites of oxidized 4-Fe5) and 8-Fe ferredoxin6) proteins and the reduced "high potential" *Chromatium* proteins.7,8) These tetranuclear complexes can be formed in the absence of the cysteinyl-containing polypeptides found in the above proteins,3,4,9) and the complexes can be regarded as fully delocalized rather than trapped valence species [2Fe(II)+2Fe(III)]. The complexes undergo electron transfer reactions which afford the redox species $[Fe_4S_4(SR)_4]^z$ with $z=4-, 3-, 2-$ and $1-$.10)

We have been attempting to develop novel and selective reductants for use in organic chemistry. The iron–sulfur complexes may be expected to be useful catalysts in organic reductions, because the abilities of the complexes as reductants are related to their redox potentials, which depend on the ligands (SR), and the reactivities of the complexes should thus be easily controllable by replacement of the ligands. In the previous paper, we reported that the complex cluster $[Fe_4S_4(SR)_4]^{2-}$ catalyzes the oxidation of thiol to disulfide.11) In the reaction, thiol and oxygen act as the electron donor and the electron acceptor, respectively, to form disulfide and superoxide.

Thus, we have examined whether organic compounds instead of oxygen can be reduced by thiol in the presence of the cluster under $O_2$-free conditions (Ar atmosphere). In this paper, we report that aromatic nitro compounds, quinones and *N*-oxide compounds are reduced to amines, hydroquinones and deoxygenated compounds, respectively.

## Experimental

**Materials**——The clusters were prepared according to the method of Holm *et al.*2-4) Nitro compounds and quinones were purchased from Tokyo Kasei Co., Ltd. and used after recrystallization. Pyridine *N*-oxide and 3-acetylpyridine *N*-oxide were obtained by the treatment of pyridine and 3-acetylpyridine, respectively, with *m*-chloroperbenzoic acid.

**Reductions of Substrates**——In the general procedure, the cluster (0.1 mmol) was added to a $CH_3CN$ (20 ml) or $CH_3CN$ (10 ml)/$CH_3OH$ (10 ml) solution containing 1 mmol of substrate and 10 mmol of thiol and stirred for 20 h at 20 °C under an Ar atmosphere. Then, the mixture was filtered to remove the iron complex and the solvent was evaporated off. The resulting residue was chromatographed on silica gel to isolate the product, which was identified by comparison with an authentic sample. Reduction yields were determined by gas-liquid chromatography (GLC) (Shimadzu 6AM).

**Redox Potentials**——Redox potentials were measured *vs.* saturated calomel electrode (SCE) using a Yanaco voltammetric analyzer, model P-1000. Samples ($10^{-3}$ M) were dissolved in $CH_3CN$ containing 0.1 M $n$-$Bu_4NClO_4$ with bubbling of $N_2$ gas for 20 min to remove dioxygen dissolved in the solution. All measurements were done in triplicate.

**Electron Spin Resonance (ESR) Spectra**——The cluster (0.02 mmol) and a substrate (2 mmol) were stirred in $CH_3CN$ (2 ml) for 5 min under an Ar atmosphere, and the ESR spectrum of the solution was measured using a JEOL-FE instrument (the diameter of the glass tube used for measurement of ESR spectra was 4 mm at 20 K or 1 mm at 297 K).

## Results and Discussion

### Reduction of Nitro Compounds

In a typical experiment, the cluster $(n\mathrm{Bu}_4\mathrm{N})_2[\mathrm{Fe}_4\mathrm{S}_4(\mathrm{SR})_4]$[3,4] was added to *p*-nitroacetophenone and thiophenol in $CH_3CN$ with stirring at 20 °C under an Ar atmosphere (Chart 1, R = *p*-$COCH_3$). The keto group was inert in the reaction. The yields of amines in Table I show that nitrobenzene (−1.10 V *vs.* SCE), which has a halfwave potential more negative than that of the cluster (−1.04 V 2−/3− $E_{1/2}$ *vs.* SCE $[\mathrm{Fe}_4\mathrm{S}_4(\mathrm{SC}_6\mathrm{H}_5)_4]^z$), was not reduced to aniline (Table I, entry 4). Thus, the results indicate that the more positive the potentials of nitro compounds are, the better the yields of amines are.

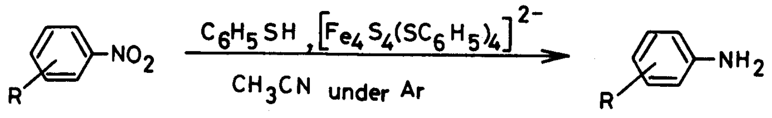

Chart 1

Table I. Yields in the Reduction of Aromatic Nitro Compounds to Amines by $C_6H_5SH$ in the Presence of Cluster $(n\mathrm{Bu}_4\mathrm{N})_2[\mathrm{Fe}_4\mathrm{S}_4(\mathrm{SC}_6\mathrm{H}_5)_4]$

| Entry | Substrate $C_6H_4(NO_2)R$ | | Amine $C_6H_4(NH_2)R$ |
|---|---|---|---|
| | R | ($E_{1/2}$ *vs.* SCE) | Yield (%) |
| 1 | *m*-$NO_2$ | (−0.94 V) | 85 |
| 2 | *p*-$CH_3CO$ | (−0.98 V) | 56 |
| 3 | *p*-Br | (−1.02 V) | 25 |
| 4 | H | (−1.10 V) | 0 |

Substrate, 1.0 mmol; $(n\mathrm{Bu}_4\mathrm{N})_2[\mathrm{Fe}_4\mathrm{S}_4(\mathrm{SC}_6\mathrm{H}_5)_4]$ (−1.04 V 2−/3− $E_{1/2}$ *vs.* SCE), 0.1 mmol; $C_6H_5SH$, 10 mmol; reaction time, 20 h; reaction temp., 20 °C; solvent, $CH_3CN$ (20 ml).

The ligand effects on the catalytic reduction by the cluster were also investigated using *m*-dinitrobenzene as the substrate. The correlation between the yields of *m*-nitroaniline and the halfwave potentials of the clusters is shown in Table II. It was found that the clusters having more negative halfwave potentials than that of the nitro compound were excellent catalysts of the reduction (Table II, entries 1 and 2). When $FeCl_2$ or $FeCl_3$ was used as the catalyst instead of the cluster in the presence of thiol, only small amounts of amine were obtained (1% or 4% yield, respectively).[12] The results indicate that the clusters are good catalysts of the reduction of nitro compounds and that the reaction yields depend on the ligands of the clusters, which

TABLE II. Yields in the Reduction of *m*-Dinitrobenzene to *m*-Nitroaniline by Thiol in the Presence of Clusters and Halfwave Potentials of the Clusters $(n\mathrm{Bu_4N})_2[\mathrm{Fe_4S_4(SR)_4}]$

| Entry | $(n\mathrm{Bu_4N})_2[\mathrm{Fe_4S_4(SR)_4}]$ | | Thiol | *m*-Nitroaniline Yield (%) |
|---|---|---|---|---|
| | R | $(2-/3-E_{1/2}$ *vs.* SCE) | | |
| 1 | $\mathrm{CH_2C_6H_5}$ | (−1.25 V) | $\mathrm{C_6H_5CH_2SH}$ | Quant. |
| 2 | $\mathrm{C_6H_5}$ | (−1.04 V) | $\mathrm{C_6H_5SH}$ | 85 |
| 3 | *p*-$\mathrm{C_6H_4Cl}$ | (−0.94 V) | *p*-$\mathrm{ClC_6H_4SH}$ | 10 |
| 4 | *p*-$\mathrm{C_6H_4NO_2}$ | (−0.70 V) | *p*-$\mathrm{NO_2C_6H_4SH}$ | 21 |

$(n\mathrm{Bu_4N})_2[\mathrm{Fe_4S_4(SR)_4}]$, 0.1 mmol; thiol, 10 mmol; reaction time, 20 h; reaction temp., 20 °C; solvent, $\mathrm{CH_3CN}$ (20 ml).

control the redox potentials.

## Reductions of Quinones and *N*-Oxide Compounds

Quinones and *N*-oxides instead of nitro compounds were used as substrates in the reaction. Quinones and *N*-oxide compounds could be reduced to the corresponding hydroquinones and deoxygenated compounds in good yields (Table III). The reaction

TABLE III. Reductions of Quinones and *N*-Oxide Compounds by $\mathrm{C_6H_5SH}$ in the Presence of Cluster

| Entry | Substrate | Product | Yield (%) |
|---|---|---|---|
| 1 | *p*-Quinone | *p*-Hydroquinone | 90 |
| 2 | 2-Methyl-1,4-naphthoquinone | 2-Methyl-1,4-naphthohydroquinone | Quant. |
| 3 | Duroquinone | Durohydroquinone | Quant. |
| 4 | Pyridine *N*-oxide | Pyridine | 55 |
| 5 | 3-Acetylpyridine *N*-oxide | 3-Acetylpyridine | 86 |

Substrate, 1 mmol; $\mathrm{C_6H_5SH}$, 10 mmol; $(n\mathrm{Bu_4N})_2[\mathrm{Fe_4S_4(SC_6H_5)_4}]$, 0.1 mmol; solvent, $\mathrm{CH_3CN}$ (10 ml) + $\mathrm{CH_3OH}$ (10 ml); reaction time, 20 h; reaction temp., 20 °C; under an Ar atmosphere.

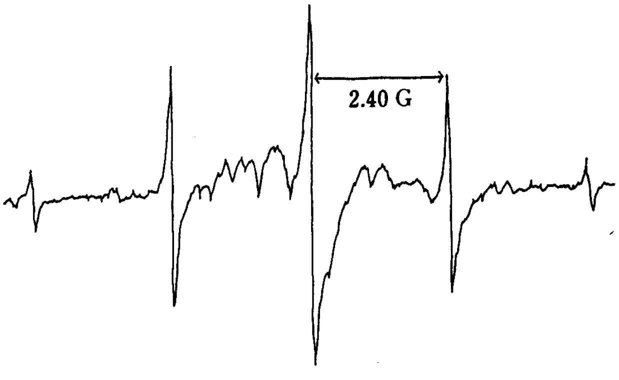

Fig. 1. ESR Spectrum of the Reaction Mixture of *p*-Benzoquinone and $(n\mathrm{Bu_4N})_2$-$[\mathrm{Fe_4S_4(SC_6H_5)_4}]$ in $\mathrm{CH_3CN}$ Solution at 297 K

Microwave power, 5 mW; modulation amplitude, $1.25\times10^{-2}$ G; field, 3337±25 G.

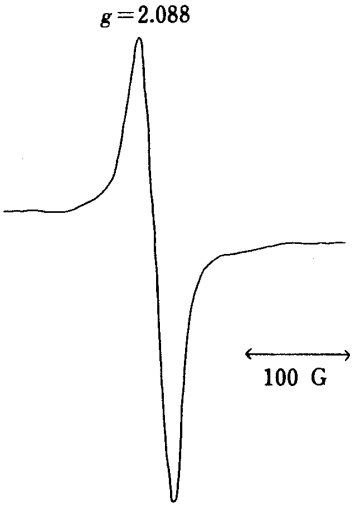

Fig. 2. ESR Spectrum of the Reaction Mixture of *p*-Benzoquinone and $(n\mathrm{Bu_4N})_2$-$[\mathrm{Fe_4S_4(SC_6H_5)_4}]$ in $\mathrm{CH_3CN}$ Solution at 20 K

Microwave power, 5 mW; modulation amplitude, 5 G; field, 3250±500 G.

mechanisms were examined by using ESR spectroscopy. Figure 1 shows the ESR spectrum of the semiquinone anion radical (at 297 K in $CH_3CN$) which could be the intermediate in the reaction of *p*-benzoquinone with the cluster. Quinone can be reduced by one electron to give the semiquinone anion radical, while on the other hand the complex $[Fe_4S_4(SR)_4]^z$ ($z=2-$) should be oxidized to the species ($z=1-$). When the reaction mixture of *p*-benzoquinone and the cluster in $CH_3CN$ was cooled to 20 K, a new ESR signal was observed (Fig. 2). The cluster ($z=3-$) has a less sharp ESR spectrum ($g_{\text{values}}=1.93, 2.06$ $g_{\text{av}}=1.97$ in $CH_3CN$ at 4.2—104 K) than that shown in Fig. 2,[10,13] while the species ($z=2-$) is inert to ESR. Thus, the novel signal could be assigned to the species ($z=1-$). When *p*-dinitrobenzene or $O_2$ was used instead of quinone, *p*-dinitrobenzene anion radical or superoxide anion radical was formed similarly. These results indicate that the cluster can donate one electron to the substrate. That is, the cluster in the oxidized state ($z=2-$) can transfer one electron to the substrate and the super-oxidized cluster ($z=1-$) should accept one electron from thiol to produce the oxidized cluster ($z=2-$) and disulfide, though it is not clear why the reduction of nitro compounds to amines depends upon the redox potential ($2-/3-$ $E_{1/2}$ *vs.* SCE) of the cluster $[Fe_4S_4(SR)_4]^z$.[14]

In summary, the clusters $[Fe_4S_4(SR)_4]^{2-}$ are available as catalysts in organic reductions. In biological systems, only high potential iron–sulfur proteins (HiPIP) are known to have the super-oxidized form[15]; the ESR spectra have been measured at low temperature. On the other hand, in 1985 Millar and O'Sullivan[16] crystallized the cluster ($n$Bu$_4$N) $[Fe_4S_4(SC_{15}H_{23})_4]$ ($z=1-$) and confirmed the formation by an X-ray crystallographic study. Holm *et al.* have reported the polarographic data of the $Fe_4S_4$ complex, suggesting the existence of the super-oxidized cluster.[17] Thus, it is of interest to examine the reactivities and ESR spectra of the super-oxidized cluster in model complexes of iron–sulfur proteins. This paper should contribute not only to the development of novel catalysts for use in organic reductions, but also to the elucidation of the enzymatic mechanism of high potential iron–sulfur proteins.

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clusters and the catalytic activities of clusters in the reduction of nitro compounds was examined.
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