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Water Sensitivity of a $[Fe_4S_4(SR)_4]^{1-}$ Cluster and Its Stabilization

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The electrochemical studies of 4Fe-4S high potential iron-sulfur protein model complexes revealed the high sensitivity of $[Fe_4S_4(SR)_4]^{1-}$ cluster to water. Such sensitivity was lowered by hydrophobic groups of thiolate ligands in close proximity to a cluster.

Biologically relevant $Fe_4S_4(SR)_4$ clusters have the function of electron transfer.[1)] The three Fe_4S_4 core oxidation levels are shown together with the oxidation states of ferredoxins (Fd) and high potential iron-sulfur proteins (HP).

$$\begin{array}{ccccc} [Fe_4S_4(SR)_4]^{1-} & \rightleftharpoons & [Fe_4S_4(SR)_4]^{2-} & \rightleftharpoons & [Fe_4S_4(SR)_4]^{3-} \\ [Fe_4S_4]^{3+} & & [Fe_4S_4]^{2+} & & [Fe_4S_4]^{1+} \\ [HP_{ox}] & & [HP_{red}, Fd_{ox}] & & [Fd_{red}] \end{array}$$

The studies of numerous model complexes of $Fe_4S_4(SR)_4$ clusters have revealed the instability of the highest core oxidation level ($[Fe_4S_4]^{3+}$), while the oxidized HP has a stable $[Fe_4S_4]^{3+}$ core. Clusters with $[Fe_4S_4]^{2+}$ and $[Fe_4S_4]^{1+}$ cores were readily synthesized or isolated.[1-3)] However, clusters with a $[Fe_4S_4]^{3+}$ core were detected only by electrochemical oxidation in a few instances, viz., $[Fe_4S_4(S\text{-}\underline{t}\text{-}Bu)_4]^{2-}$,[4,5)] $[Fe_4S_4(Z\text{-cys-Ile-Ala-OMe})_4]^{2-}$,[6)] $[Fe_4S_4(2,4,6\text{-triisopropylbenzenethiolato})_4]^{2-}$,[6,7)] and $[Fe_4S_4\{cyclo\text{-}[XN(CH_2)_8]_4\}]^{2-}$($X=\underline{p}\text{-}SC_6H_5CO$ etc.).[8)] The causes of both the instability of model complexes with $[Fe_4S_4]^{3+}$ cores and the stability of the oxidized HP have not been clarified. In this paper, we report the stabilizing influences of thiolate ligands on $[Fe_4S_4]^{3+}$ cores and report further water sensitivity of $[Fe_4S_4]^{3+}$ cores.

$[Et_4N]_2[Fe_4S_4(SR)_4]$ clusters with R= Ph (**1**), i-Pr (**2**) and other alkyl groups were prepared by the method reported by Christou et al.[2] $[Et_4N]_2[Fe_4S_4$(2,4,6-triisopropylbenzenethiolato)$_4]$ (**3**) was prepared by the method reported by Averill et al.[9] Cyclic voltammograms (CV) were measured with a three-electrode system under an argon atmosphere. A working electrode was a glassy carbon. A saturated calomel electrode was used as a reference for potential measurements. Solutions were 2 mM in samples and 100 mM in n-Bu_4NClO_4 as a supporting electrolyte. DMF, isobutyronitrile (IBN) and CH_2Cl_2 were distilled, dried over activated Linde 4A molecular sieves, degassed, and stored under an argon atmosphere. Water contents of these solvents were less than 0.01 wt.%. The reversibility of a 2-/1- redox couple was evaluated by the i_{pc}/i_{pa} ratio of CV. The diffusion peak current was corrected for the baseline drift due to the solvent.

Preliminary to studies involving the stabilizing influences of thiolate ligands on $[Fe_4S_4]^{3+}$ cores, conditions to stabilize $[Fe_4S_4]^{3+}$ cores were investigated. Figure 1 shows solvent effect on the oxidation of **1**. DePamphilis et al.[4] reported that no discrete anodic wave was observed in the electrochemical oxidation of **1** in DMF. Actually, in DMF **1** exhibited multi-electron oxidation reaction at potentials more positive than 0 V (vs. SCE) as shown in Fig. 1. On the other hand, discrete one-electron oxidation processes of **1** were observed at 0.15 V (vs. SCE) in non-polar solvents, such as CH_2Cl_2 and IBN. Especially, a well-defined cathodic peak appeared in CH_2Cl_2. Thus CH_2Cl_2 was found to be an appropriate solvent to stabilize a $[Fe_4S_4]^{3+}$ core.

$[Fe_4S_4(SR)_4]^{2-}$ clusters with several kinds of thiolate ligands were similarly oxidized in CH_2Cl_2 (Table 1). While **2** having sec-alkanethiolate ligands gave the i_{pc}/i_{pa} ratio comparable to that of **1**, other clusters with prim-alkanethiolate ligands exhibited no

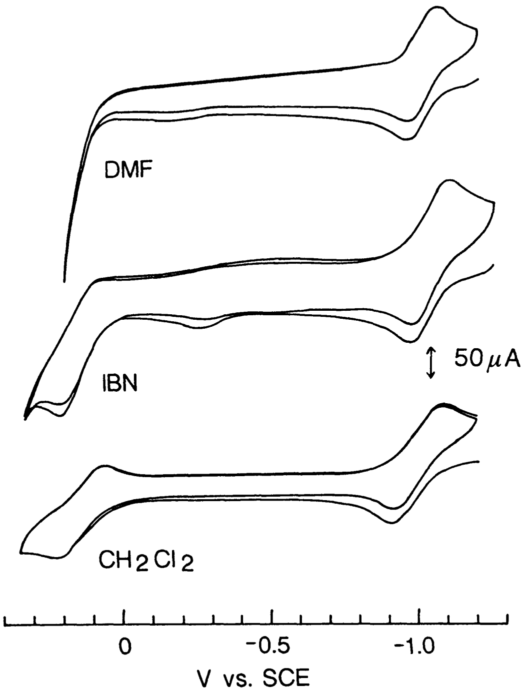

Fig. 1. Solvent effect on the oxidation of $[Et_4N]_2[Fe_4S_4(SPh)_4]$, scan rate 100 mV/s
IBN; isobutyronitrile

Table 1. Electrochemical oxidation data for $[Et_4N]_2[Fe_4S_4(SR)_4]$ in CH_2Cl_2, scan rate 100 mV/s

R	E_{pa}	E_{pc}	$E_{1/2}$	i_{pc}/i_{pa}
	(V vs. SCE)			
Ph	0.22	0.08	0.15	0.41
CH_2Ph	0.06	a)	a)	a)
Et	-0.01	a)	a)	a)
i-Pr	-0.05	-0.21	-0.13	0.36
i-Bu	-0.01	a)	a)	a)

a) Ill-defined process.

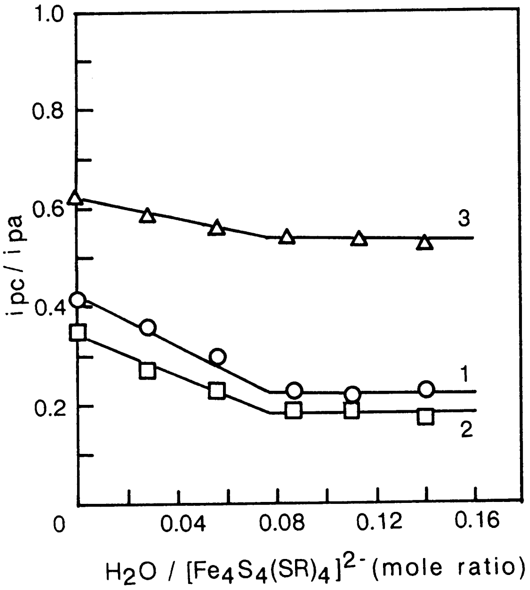

Fig. 2. Effect of water addition on the 2-/1- redox couples of $[Et_4N]_2[Fe_4S_4(SR)_4]$ in CH_2Cl_2, scan rate 100 mV/s
1; R= Ph, 2; R= *i*-Pr,
3; R= 2,4,6-triisopropylbenzene

cathodic peak current in spite of the obseration of the anodic one. From this result one may conclude that branched alkyl groups of thiolate ligands in close proximity to a cluster exert a marked influence on the stability of a $[Fe_4S_4]^{3+}$ core. This is supported by electrochemical quasi-reversibility of the 2-/1- redox couples of $[Fe_4S_4(S\text{-}\underline{t}\text{-}Bu)_4]^{2-}$ and **3**.$^{4-7)}$

In order to confirm the sensitivity of a $[Fe_4S_4]^{3+}$ core to water, effect of water addition on the 2-/1- redox couples of **1** to **3** was examined (Fig. 2). The i_{pc}/i_{pa} ratios of the 2-/1- redox of these three complexes decreased in proportion to the amounts of added water until saturation. Obviously, $[Fe_4S_4]^{3+}$ cores are highly sensitive to water, though $[Fe_4S_4]^{2+}$ cores were reported to be relatively stable in water.$^{10)}$ From this result it is concluded that high sensitivity to water is at least one of causes associated with the instability of a $[Fe_4S_4]^{3+}$ core. Furthermore, the results make the foregoing solvent effect on the oxidation of **1** clear: the decomposition rate of a $[Fe_4S_4]^{3+}$ core in the presence of water depends on the polarity of solvents.

The oxidized **3** was less sensitive to water than the oxidized **1** and **2**. This fairly good stability of the oxidized **3** is most reasonably attributed to the hydrophobic isopropyl groups near a cluster, which prevent the access of water molecules to the cluster. Furthermore, the observed dependence of the stability of a $[Fe_4S_4]^{3+}$ core on the structure of a thiolate ligand is reasonably explained by the protection of a core against water molecules.

Our present result suggests that the stability of oxidized HP can be attributed mainly to hydrophobic amino acid side chains around the core.$^{11)}$ Further study is requirred to elucidate details of the reaction between $[Fe_4S_4(SR)_4]^{1-}$ and water. Bulky thiolate ligands probably suppress the thiolate dissociation and also associative reactions with water. The conformational effect of the bulky thiolate ligands upon the nature of Fe-S bonds which was considered in the previous paper may be responsible for the observed trend.$^{12)}$

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