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OXIDIZED RUBREDOXIN MODEL. NOVEL SYNTHESIS BY LIGAND-SUBSTITUTION WITH DISULFIDE

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$[Fe(SPh)_4]^-$ (1ox) and $[Fe(S\text{-}p\text{-}tol)_4]^-$ (2ox), new oxidized rubredoxin model compounds, were synthesized in solution by the ligand-substitution of $[Fe(S_2\text{-}o\text{-}xyl)_2]^-$ (3ox) with 10 eq diaryl disulfide in the presence of 2 eq o-xylene-α,α'-dithiol and were characterized by visible and ESR spectra. This method is useful to prepare unstable Fe(III) tetrathiolate complexes containing simple monodentate ligands.

KEYWORDS——rubredoxin; iron-sulfur complex; ligand-substitution; tetrakis(benzenethiolato)ferrate(III); tetrakis(4-methylbenzenethiolato)ferrate(III); bis(o-xylene-α,α'-dithiolato)-ferrate(III)

There are two types of active sites in nonheme iron-sulfur proteins, which are widely dispersed electron carriers in biological systems.1) One is the rubredoxin type, $[Fe(S\text{-}Cys)_4]^{-/2-}$, and the other is the ferredoxin type, $[Fe_2S_2(S\text{-}Cys)_4]^{2-/3-}$ and $[Fe_4S_4(S\text{-}Cys)_4]^{n-}$ (n =1,2,3). Recently a new type of ferredoxin, [3Fe-3S], has been reported.2) The chemical properties of the ferredoxin models, $[Fe_4S_4(SR)_4]^{2-}$,3) have been studied in our laboratory.4) To examine a reduction process by the reduced rubredoxin models, $[Fe(SPh)_4]^{2-}$ (1red)5) and $[Fe(S\text{-}p\text{-}tol)_4]^{2-}$ (2red), we needed the oxidized form, $[Fe(SAr)_4]^-$, for authentic samples. However, Fe(III) tetrathiolate complexes are rare in spite of considerable efforts to prepare them,6) because most Fe(III) compounds are reduced by thiolates to give Fe(II) compounds. Therefore the development of a general synthetic method has been desired.

Controlled air oxidation of the reduced complexes has been useful to prepare only $(Et_4N)[Fe(S_2\text{-}o\text{-}xyl)_2]$ (3ox)7) and $(Et_4N)[Fe(SC_{10}H_{13})_4]$ (4ox),8) where iron(III) is chelated by o-xylene-α,α'-dithiolate or coordinated by sterically hindered 2,3,5,6-tetramethylbenzenethiolate. But 1ox has not been successfully prepared in this way.5a) It is thought that Fe(III)-S_4 species containing a simple monodentate ligand, such as benzenethiol, decompose in oxidation. Here we report a novel synthesis of 1ox and 2ox in solution by the ligand-substitution reaction of 3ox with disulfide, keeping the oxidation state of the Fe(III) complex.

The reaction of 3ox with 10 eq diphenyl or di-p-tolyl disulfide in the presence of 2 eq o-xylene-α,α'-dithiol was monitored by spectrophotometry.

Complex 3ox became 1ox or 2ox smoothly after 200 minutes under anaerobic condition (Fig. 1). No reaction occurred without o-xylene-α,α'-dithiol. The visible spectra[9)] of 1ox and 2ox in acetonitrile resemble the spectrum of 4ox. The ESR spectrum of 1ox showed a sharp resonance at g =4.3 (77 °K, CH_3CN glass). This is similar to oxidized rubredoxin[10)] and 4ox,[8)] but clearly different from 3ox which shows weak resonance at g =4.3 under similar condition.

Methylene blue and methyl viologen oxidized 2red which shows negligibly weak absorption in the visible region. The reaction of colorless 0.108 mM 2red in CH_3CN with 0.74 eq methylene blue at 25 °C gave a visible spectrum similar to that of 2ox. The band of methylene blue (oxidized form) at 650 nm was not observed. The absorbance of 2ox increased stoichiometrically corresponding to additional quantities of methylene blue. Moreover, in the case of methyl

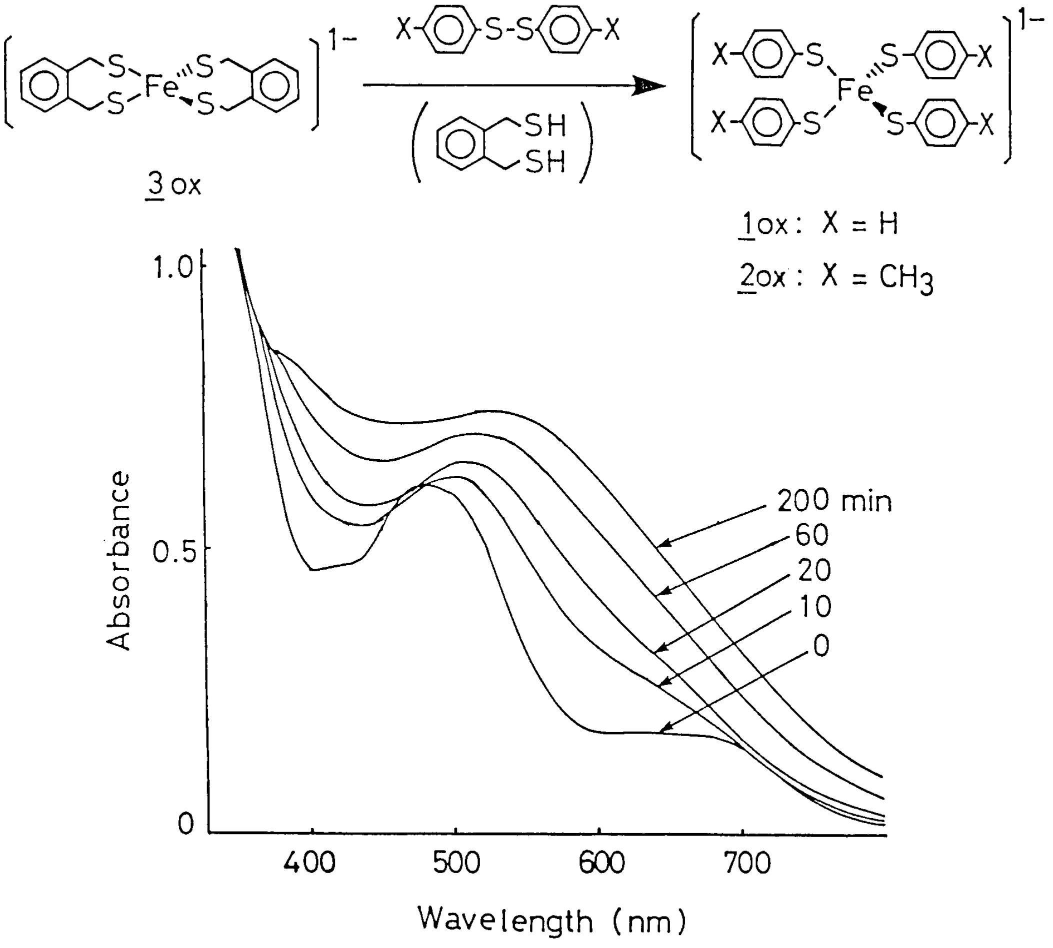

Fig. 1. Ligand-Substitution with Disulfide

Visible spectra of the solution resulting from the reaction of 0.10 mM $(Et_4N)[Fe(S_2\text{-}o\text{-}xyl)_2]$ (at 0 min reaction time) with 2.0 mM PhSSPh in the presence of 0.40 mM o-xylene-α, α'-dithiol in CH_3CN at 25°C under Ar. The spectrum recorded at 200 min reaction time is that of an equilibrium solution containing $[Fe(SPh)_4]^-$.

viologen, 2red oxidation was accompanied by stoichiometrical dye reduction. These observations show that 1ox and 2ox are prepared in the ligand-substitution reaction of 3ox with disulfides in quantitative yield.

The time course of reaction between 3ox and 5 eq p-toluenethiol was followed by spectrophotometry.[11] After the spectrum of 3ox became that of 2ox, the latter decreased. On a preparative scale this reaction afforded 2red in 15% yield after purification (Chart 1). This shows that excess thiol reduces the 2ox resulting from the reaction of 3ox with thiol.

$$\underset{3ox}{[Fe(S_2\text{-}o\text{-}xyl)_2]^-} \xrightarrow{p\text{-}CH_3C_6H_4SH} \underset{2red}{[Fe(S\text{-}p\text{-}tol)_4]^{2-}}$$

Chart 1

The ligand-substitution reaction with disulfide apparently proceeds by an ionic mechanism as these facts indicate: (1) No reaction occurred without o-xylene-α,α'-dithiol, showing that the reaction starts between 3ox and thiol. (2) The S-S bond can be cleaved by the thiolate anion.[12] (3) PhSSPh can not oxidize 1red or 3red (unpublished data). So the charge of iron can not possibly be changed in the course of the reaction. (4) The reaction of 3ox with p-toluenethiol gave 2ox on the way. These observations suggest that the intermediate thiolate anion resulting from the reaction between 3ox and o-xylene-α,α'-dithiol cleaves the disulfide and that the produced ArSH causes the ligand-substitution reaction. We think that in this reaction condition the intermediate,ArSH, can not reduce the Fe(III) complexes.

A comparison of Fe^{3+}/Fe^{2+} redox potentials of 1 (-0.53 V vs. SCE), 2 (-0.62), 3 (-1.03),[7] and 4 (-0.85)[8] shows that the oxidized forms of 3 and 4 are more stable than those of 1 and 2. This indicates that the ligand-substitution reaction with disulfide is useful to prepare even more reducible complexes. It provides a general method to synthesize unstable Fe(III) tetrathiolate complexes containing simple monodentate ligands.

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9) The visible spectra in acetonitrile at 25 °C, 1ox λ_{max} nm (ε): 390sh (8400), 530 (7500); 2ox: 464 (7100), 540sh (6900). The molar extinction coefficient was calculated from the spectrum resulting from the ligand-substitution reaction, proceeding quantitatively at 200 min reaction time.

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11) The ligand-substitution reaction of 2red with thiol can be examined with NMR spectroscopy. Because 1red and 2red are paramagnetic, their spectra are distinguished distinctively from that of free thiols by isotropic interaction.5c) When 10 eq benzenethiol was added to about 80 mM 2red in CD_3CN, the p-Me peak of 2red (δ 33.8 ppm) disappeared after 10 minutes and the p-H peak of 1red (δ -24.6 ppm) and the p-Me peak (δ 2.2) of free p-toluenethiol appeared. This shows that the ligand-substitution of the Fe(II) tetrathiolate complex containing simple thiolate ligand can occur.

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