COMMUNICATIONS TO THE EDITOR

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

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[Fe(SPh)₄]⁻ (1ox) and [Fe(S-p-tol)₄]⁻ (2ox), new oxidized
rubredoxin model compounds, were synthesized in solution by the
ligand-substitution of [Fe(S₂-o-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-substitu-
tion; tetrakis(benzethiolato)ferrate(III); tetrakis(4-methyl-
benzenethiolato)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-Cys)₄]²⁻, and the other is the ferredoxin type,
[Fe₂S₃(S-Cys)₄]²⁻/³⁻ and [Fe₄S₄(S-Cys)₄]¹⁻ (n = 1, 2, 3). Recently a new type of
ferredoxin, [Fe₃S₅], has been reported.²) The chemical properties of the
ferredoxin models, [Fe₄S₄(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⁻
(red)⁵⁻) and [Fe(S-p-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 thiocyanates 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 (Et₄N)[Fe(S₂-o-xyl)₂] (3ox)⁷⁻ and (Et₄N)[Fe(SC₆H₄₃)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 3ox has not been
successfully prepared in this way.⁹) It is thought that Fe(III)-S₄ 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 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, CH₃CN glass). This is similar to oxidized rubredoxin and 4ox, 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 CH₃CN 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

![Graph showing absorbance changes over time and wavelength](https://example.com/graph.png)

**Fig. 1. Ligand-Substitution with Disulfide**

Visible spectra of the solution resulting from the reaction of 0.10 mM (Et₄N)[Fe(S₂-o-xy1)₂] (at 0 min reaction time) with 2.0 mM PhSSPh in the presence of 0.40 mM o-xylene-α,α'-dithiol in CH₃CN at 25°C under Ar. The spectrum recorded at 200 min reaction time is that of an equilibrium solution containing [Fe(SPh)₄]⁻.
viologen, red oxidation was accompanied by stoichiometrical dye reduction. These observations show that \( \text{ox} \) and \( \text{ox} \) are prepared in the ligand-substitution reaction of \( \text{ox} \) with disulfides in quantitative yield.

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

\[
\begin{align*}
[\text{Fe}(S_2\text{-o-xyl})_2]^+ & \quad \text{p-CH}_3\text{C}_6\text{H}_4\text{SH} \quad [\text{Fe}(\text{S-p-tol})_4]^2- \\
\text{ox} & \quad \text{2red}
\end{align*}
\]

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-\( \text{a}, \text{a}'-\text{dithiol} \), showing that the reaction starts between \( \text{ox} \) and thiol. (2) The S-S bond can be cleaved by the thiolate anion. (3) PhSSPh can not oxidize \( \text{ox} \) or \( \text{ox} \) (unpublished data). So the charge of iron can not possibly be changed in the course of the reaction. (4) The reaction of \( \text{ox} \) with p-toluenethiol gave \( \text{ox} \) on the way. These observations suggest that the intermediate thiolate anion resulting from the reaction between \( \text{ox} \) and o-xylene-\( \text{a}, \text{a}'-\text{dithiol} \) 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\( ^{3+}/ \text{Fe}^{2+} \) redox potentials of \( 1 (-0.53 \text{ V vs. SCE}), 2 (-0.62), 3 (-1.03), 4 (-0.85) \) 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.

REFERENCES AND NOTES

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b) D.G. Holah and D. Coucouvanis, J. Am. Chem. Soc., 97, 6917 (1975);
9) The visible spectra in acetonitrile at 25°C, \( \lambda_{\text{max}} \) nm (\( \epsilon \)): 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.
11) The ligand-substitution reaction of \( 2^\text{red} \) with thiol can be examined with NMR spectroscopy. Because \( 1^\text{red} \) and \( 2^\text{red} \) are paramagnetic, their spectra are distinguished distinctively from that of free thiol by isotropic interaction. \(^{5c}\) When 10 eq benzenethiol was added to about 80 mM \( 2^\text{red} \) in \( \text{CD}_3\text{CN} \), the \( \text{p-Me} \) peak of \( 2^\text{red} \) (\( \delta \) 33.8 ppm) disappeared after 10 minutes and the \( \text{p-H} \) peak of \( 1^\text{red} \) (\( \delta \) -24.6 ppm) and the \( \text{p-Me} \) peak (\( \delta \) 2.2) of free \( \text{p-toluene thiol} \) appeared. This shows that the ligand-substitution of the Fe(II) tetra-thiolate complex containing simple thiolate ligand can occur.

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