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RUBREDOXIN MODEL COMPLEX $(Et_4N)[Fe(S_2\text{-o-xyl})_2]$ AS A CATALYST IN THE REDUCTION OF AROMATIC NITRO COMPOUNDS TO HYDROXYLAMINES

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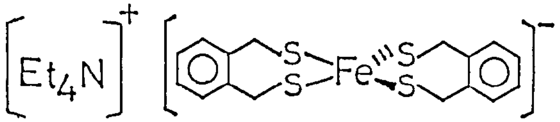
$(Et_4N)[Fe(S_2\text{-o-xyl})_2]$, the analogue of oxidized rubredoxin active sites, can catalyze the reduction of aromatic nitro compounds to N-aryl hydroxylamines by o-xylene-α,α′-dithiol.

Rubredoxin, one of the non-heme iron-sulfur proteins, acts as a one-electron carrier in fatty acid oxidation and hydrocarbon ω-hydroxylation reactions in Pseudomonas oleovorans.[1] It can function in this manner due to its iron-sulfur active sites. The analogous complex $(Et_4N)[Fe(S_2\text{-o-xyl})_2]$(1) prepared by Holm et al. displays close structural and electronic resemblance



complex (1)

Chart 1

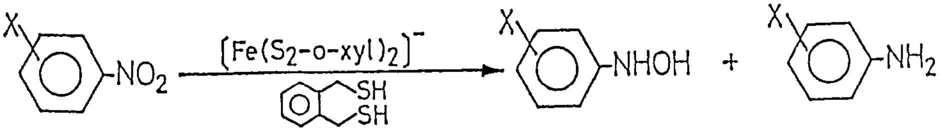


Table 1 Catalytic effects of complex (1) on the reduction of aromatic nitro compounds by o-xylene-α,α′-dithiol.

entry	substrate	$E_{1/2}$ vs SCE[b]	yields (%)	
	$C_6H_4(NO_2)X$	(V)	$C_6H_4(NHOH)X$	$C_6H_4(NH_2)X$
1	X=p-NO_2[a]	-0.75	93	2
2	m-NO_2	-0.94	54	25
3	p-Ac	-0.98	49	n.d.[c]
4	p-CN	n.d.	60	13
5	p-COOMe	-1.00	46	17
6	H	-1.10	0	2

1.0 mmol of Substrate was added to 0.1 mmol of $(Et_4N)[Fe(S_2\text{-o-xyl})_2]$ in the presence of 5.0 mmol of o-xylene-α,α′-dithiol in CH_3CN solution (20 ml) under an Ar atmosphere at 40 °C ([a]26 °C). The mixture was stirred for 6 h ([a]1.5 h). [b]$E_{1/2}$ vs SCE of complex (1) was -1.05 V. [c]n.d.: not determined.

to the active sites of oxidized rubredoxins.[2] The complex (1), which exhibits the Fe(III)/Fe(II) redox cycle, is considered to represent an essentially unconstrained structural model of the oxidized rubredoxin active site. Thus, the complex (1) was expected to be a novel and facile catalyst in organic reductions.[3]

This paper reports our finding that complex (1) catalyzes the reductions of aromatic nitro compounds to N-aryl hydroxylamines by thiol. $[Fe(S_2\text{-}o\text{-}xyl)_2]^{1-}$ has principal absorption spectra at 486 and 640-684 nm, while the reduced form of the complex, $[Fe(S_2\text{-}o\text{-}xyl)_2]^{2-}$, has a much weaker absorption band at ~450nm (sh. ε =390), as reported by Holm et al.[2] As shown in Fig. 1, addition of o-xylene-α,α'-dithiol to the oxidized form caused the absorption spectra at λmax = 486 nm to disappear, indicating that the reduced form was produced. Subsequent exposure of the reduced form to dioxygen increased the absorption spectrum at λ max=486nm. That is, the spectral change shows that complex (1) can catalyze electron transfer from o-xylene-α,α'-dithiol to dioxygen. Some substrates instead of dioxygen were expected to be reduced under O_2-free conditions. When $(Et_4N)[Fe(S_2\text{-}o\text{-}xyl)_2]$ (0.1 mmol), nitro compound(1.0 mmol) and o-xylene-α,α'-dithiol (5.0 mmol) were stirred in 20ml of CH_3CN under an Ar atmosphere, the substrates with electron-withdrawing functional groups were reduced more readily than nitrobenzene which has a more negative redox potential (Chart 1, Table 1).[4] When $FeCl_2$ or $FeCl_3$ was used as the catalyst instead of complex (1), trace amounts of hydroxylamine

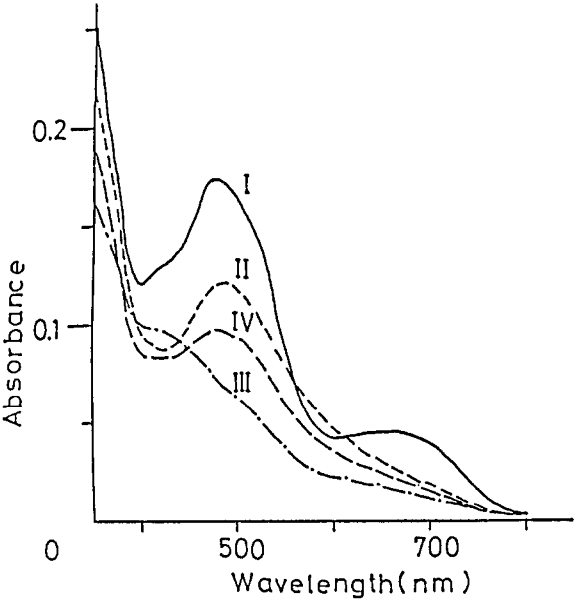


Fig. 1 Spectral Change of Complex $[Fe(S_2\text{-}o\text{-}xyl)_2]^{1-}$
I: complex (1) (0.038 mM) in CH_3CN solution under an Ar atmosphere, II: 1 min after addition of o-xylene-α,α'-dithiol (0.203 M) to complex (0.023 mM) in CH_3CN solution under an Ar atmosphere, III: 75 min after addition, IV: exposure of solution III to dioxygen.

Table 2 Reduction of aromatic nitro compounds to N-aryl hydroxylamines by solution (A)

entry	substrate	yield (%)	
	$C_6H_4(NO_2)X$	$C_6H_4(NHOH)X$	$C_6H_4(NH_2)X$
1	X = p-NO_2[a]	92	8
2	m-NO_2	53	2
3	p-Ac	40	n.d.[b]
4	p-CN	51	4
5	p-COOMe	47	11
6	H	0	7

Solution (A) included $FeCl_2$(0.1 mmol), Et_4NCl(0.2 mmol), o-xylene-α,α′-dithiol(2.6 mmol) and $NaHCO_3$ (1.0 mmol) in CH_3CN solution(10 ml). Solution (A) was added to the substrate(0.5 mmol) in CH_3CN solution under an Ar atmosphere at 40 °C([a] 18 °C). The mixture was stirred for 6 h ([a]1.5 h). [b]n.d.: not determined.

were obtained in 2% or 4% yield, respectively, while addition of Et_4NCl, and sodium hydrogencarbonate to $FeCl_2$ and o-xylene-α,α′-dithiol produced hydroxylamines in high yields (Table 2). Formation of complex (1) was expected in a CH_3CN solution mixture (A) including Et_4NCl, o-xylene-α,α′-dithiol, sodium hydrogencarbonate and $FeCl_2$. Absorption spectral data of the solution (A) have confirmed the formation of complex (1) by comparison of those of complex (1). Table 2 indicates that this solution (A) has the same catalytic effect as complex (1). This offers a very facile and useful reduction method; for example, p-dinitrobenzene could be reduced to p-nitro phenylhydroxylamine by treatment with solution (A) in a higher yield (92 %) than by other reported method (65 %).[5] Table 3 shows that the components of complex (1) are essential to give good yields in the reduction. Nitro

Table 3 Reduction of dinitrobenzene to nitro phenylhydroxylamine and nitroaniline by $FeCl_2$ and o-xylene-α,α′-dithiol in the presence or absence of Et_4NCl and/or $NaHCO_3$.

entry	Components of complex (1)				Product (%)	
	$FeCl_2$ (mmol)	Et_4NCl (mmol)	o-xylene-α,α′-dithiol (mmol)	$NaHCO_3$ (mmol)	$C_6H_4(NHOH)NO_2$	$C_6H_4(NH_2)NO_2$
1	0.1	0.2	2.6	1.0	92	8
2	0.1	—	2.6	1.0	22	2
3	0.1	—	2.6	—	2	0
4	0.1	0.2	2.6	—	4	0

Components of complex (1), dissolved in 10 ml of CH_3CN, was added to dinitrobenzene (0.5 mmol) in CH_3CN solution under an Ar atmosphere at 18.5 °C.

phenylhydroxylamine was in low yields in the absence of Et_4NCl and/or $NaHCO_3$.[6] Thus, our present work demonstrated the potential usefulness of complex (1) or solution (A) for the simple preparation of N-aryl hydroxylamines in good yields.

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3) We have already reported about the catalytic reactions by the model complexes of non-heme iron-sulfur proteins and novel synthesis of oxidized rubredoxin model complexes as shown below: a) The catalytic oxidation of thiols to disulfides by the cluster $[Fe_4S_4(SR)_4]^{2-}$ and associated ligand effects. T. Nagano, K. Yoshikawa and M. Hirobe, Tetrahedron Lett., 21, 297 (1980); b) The $[Fe_4S_4(SR)_4]^{2-}$ catalytic reduction of diphenylacetylene to cis-stilbene in the presence of $NaBH_4$. T. Itoh, T. Nagano and M. Hirobe, Tetrahedron Lett., 21, 1343 (1980); c) Oxidized rubredoxin model, novel synthesis by ligand substitution with disulfide. K. Yanada, T. Nagano and M. Hirobe, Chem. Pharm. Bull., 31, 4589 (1983); d) Reduction of imines by cluster $[Fe_4S_4(SR)_4]^{3-}$. T. Mashino, T. Nagano and M. Hirobe, Tetrahedron Lett., 24, 5113 (1983); e) Clusters $[Fe_4S_4(SR)_4]^{2-}$ as model catalysts in organic reductions. T. Itoh, T. Nagano and M. Hirobe, Chem. Pharm. Bull., 34, 2013 (1986).

4) To stop the reaction, 2N HCl was added to the mixture. The yields of hydroxylamines were determined by Shimadzu CS-920 T.L.C. scanner. The authentic sample p-nitro phenylhydroxylamine was synthesized by reduction of p-dinitrobenzene with ascorbic acid. Other hydroxylamines were prepared by reducing the corresponding nitro compounds with zinc and ammonium chloride.

5) R. Kuhn and F. Weygand, Chem. Ber., 69, 1969 (1936)

6) Excess amounts of $NaHCO_3$ were necessary for the formation of the complex (1). When NaOH was used in place of $NaHCO_3$, p-dinitrobenzene reacted with thiolate anion to form 2-(p-nitrophenylthio)methylbenzylthiol.

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