THE CATALYTIC OXIDATION OF THIOLS TO DISULFIDES BY THE CLUSTER $[Fe_4S_4(SR)_4]^{2-}$ AND ASSOCIATED LIGAND EFFECTS

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The cluster $(nBu_4N)_2[Fe_4S_4(SR)_4]$, the analogue of the active site of nonheme iron-sulfur proteins, catalyzed the oxidation of thiols to disulfides extremely and the ligand effects for the catalytic oxidation were investigated.

The Fe-S clusters $[Fe_4S_4(SR)_4]^{2-}$ have been synthesized by R. H. Holm et al. and their electronic properties were characterized thoroughly by measurements of proton magnetic resonance, Mössbauer photoelectron and electronic spectra.[1] The structural and collective electronic features of the cluster revealed it to be the first well defined synthetic analogue of the active site of nonheme iron-sulfur proteins such as the oxidized Fe ferredoxin from Peptococcus aerogenes or the reduced Fe protein from Chromatium. Holm's studies have thus made great contributions to molecular level investigations on the functions of such proteins.

In this paper we wish to report the catalytic function of the above cluster for the oxidation of thiol to disulfide by oxygen.[2] It is well known that

$$4 R'SH + O_2 \xrightarrow{\;[Fe_4S_4(SR)_4]^{2-}\;} 2 R'SSR' + 2 H_2O$$
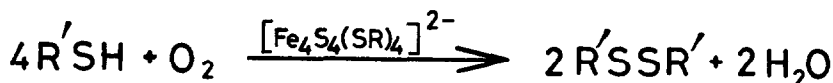
thiols are oxidized to disulfides by oxygen in the presence of catalysts, e. g., alkali, metal, light etc,[3] but we have now found that the Fe-S cluster markedly catalyzes the above reaction relative to simple metals. Further the catalytic effect of the cluster $[Fe_4S_4(SR)_4]^{2-}$ depends upon the ligand R (R· C_6H_5, p-$C_6H_4CH_3$, p-C_6H_4Cl, p-$C_6H_4NO_2$). The oxidation mechanism, which seems to be the same as that of the autooxidation of thiol by oxygen, includes the electron transfer from thiol to oxygen with the cluster as a mediator. Therefore this reaction provides significant information regarding electron transfer functions of iron-sulfur proteins.

The cluster $(n\text{-}Bu_4N)_2[Fe_4S_4(SC_6H_5)_4]$[4] (0.07mmol) in CH_3CN (10ml) was added to thiol R'SH (R' C_6H_5, $C_6H_5CH_2$, C_2H_5) (2.5mmol) in CH_3CN (1ml) and was stirred at 0°C under an oxygen atmosphere. Disulfide was formed quantitatively and other products were not detected. Fig.1 shows the timecourse of the quantity
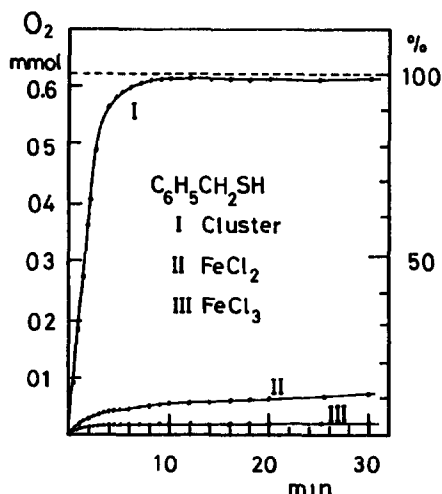
Fig.1. The timecourse of the quantity of oxygen uptake in the oxidation of $C_6H_5CH_2SH$ (2.5mmol) in the presence of the cluster $[Fe_4S_4(SC_6H_5)_4]^{2-}$ (0.07mmol)(I), $FeCl_2$(0.09mmol)(II) or $FeCl_3$(0.12mmol)(III).
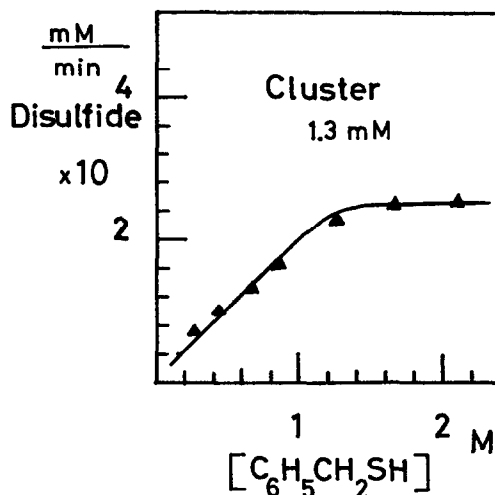
Fig.2. The initial rate of disulfide production in oxidation of $C_6H_5CH_2SH$ (0.25M-2.14M) with a constant cluster concentration (1.3mM).

of oxygen uptake in the oxidation of $C_6H_5CH_2SH$ catalyzed by the cluster $(n-Bu_4N)_2[Fe_4S_4(SC_6H_5)_4]$.[5] The reaction was completed within ten minutes and afterwards oxygen uptake was not observed. The quantity of oxygen uptake was exactly 1/4 equimolar with thiol. In the case of $FeCl_2$ or $FeCl_3$[5] as catalyst[6] oxygen uptake was only slightly observed. In the absence of $C_6H_5CH_2SH$ no oxygen uptake was observed. The results have stimulated us to investigate the turnover (molecular activity) of the cluster in the oxidation of thiols. The initial rate of disulfide formation due to oxygen consumption in the oxidation of $C_6H_5CH_2SH$ (0.25-2.14M) was estimated when the cluster concentration was held constant (1.3mM) as shown in Fig.2. Fig.2. indicates that the initial rate

Table 1. V_{max} (the maximum rate) and K_o (the molecular activity) in the oxidation of thiols in the presence of the cluster $(n-Bu_4N)_2[Fe_4S_4(SC_6H_5)_4]$

Thiols	V_{max}(mM/min)	K_o(1/min)
C_6H_5SH	2.48x10	19.1
$C_6H_5CH_2SH$	2.52x10	19.4
C_2H_5SH	2.86x10	22.0
$t-C_4H_9SH$	0.20x10	1.5

obeys first-order kinetics at low thiol concentrations (0-1.2M) and zero-order kinetics at higher thiol concentrations (> 1.2M). Also for other thiols C_6H_5SH, C_2H_5SH and t-BuSH similar measurements were performed. On the basis of these data V_{max} (the maximum rate of disulfide formation) and K_0[7] (the molecular activity) values were determined.(Table 1) The K_0 values demonstrate that the cluster is an excellent catalyst for the oxidation of thiols independent of the thiols acidity. The relatively low K_0 values in the case of t-BuSH would be due to the steric hindrance associated with the tertiary alkyl group.

The ligand effects for the catalytic oxidation by the clusters $[Fe_4S_4(SR)_4]^{2-}$ (R: C_6H_5, p-C_6H_4Cl, p-$C_6H_4NO_2$)[8] were also investigated. It became apparent that the catalytic effects of the clusters for the oxidation of thiol $C_6H_5CH_2SH$ decreased in the following order: R, $C_6H_5(K_0=19.1)$ > $C_6H_4Cl(K_0=13.5)$ > $C_6H_4NO_2$ ($K_0=4.7$).(Table 2) Namely the electron withdrawing groups on the cluster decreased the activity for catalytic oxidation.

Further their redox potentials ($E_{1/2}$(V)2-/3- vs S.C.E.) were measured in DMF and CH_3CN solution respectively.(Table 2) The redox potentials in DMF solution were in fair agreement with those reported by R. H. Holm.[9] The potentials become more positive with increase of the electron attracting tendency of the ligand and an approximately linear relationship exists between the halfwave potentials ($E_{1/2}$) and the K_0 values.[10] This fact suggests that the catalytic effects of the clusters increase as their potentials become more negative.

For the oxidation mechanism it is considered that an electron transfer from thiol to oxygen is accelerated by the cluster. Namely RS· and the superoxide ($O_2^{\overline{\cdot}}$) are generated respectively from thiol and oxygen.[11] The correlation between the K_0 values and the redox potentials shows that the electron transfer

Table 2. Cathodic polarography[a] of $[Fe_4S_4(SR)_4]^{2)}$ and the molecular activity values of $[Fe_4S_4(SR)_4]^{2-}$ as catalyst in the oxidation of $C_6H_5CH_2SH$ to $C_6H_5CH_2SSCH_2C_6H_5$.

| $(nBu_4N)_2[Fe_4S_4(SR)_4]$ | 2-/3-$E_{1/2}$(V) | | K_0 |
R	in DMF	in CH_3CN	(1/min)
C_6H_5	-1.04(-1.039)[b]	-0.94	19.1
p-C_6H_4Cl	-0.95(———)	-0.85	13.5
p-$C_6H_4NO_2$	-0.72(-0.695)	-0.69	4.7
p-$C_6H_4CH_3$	-1.09(-1.086)	——[c]	——[c]

a). Measured at 25.0°C

b). The data in parentheses are reported by R. H. Holm et al.[9]

c). This cluster (R = p-$C_6H_4CH_3$) is slightly soluble in CH_3CN.

from the cluster to oxygen is the rate-determining step. The evidence for the formation of O_2^- in this reaction was shown by the fact that the nitro blue tetrazolium ion was reduced to monoformazan and further to diformazan[12] in the above cluster-O_2 system in the same way as by the KO_2-crown ether system.

Further studies on the mechanism of electron transfer of the cluster are in progress.

References and Notes

1) As summaries of this research,
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4) a) B. A. Averill, T. Herskovitz, R. H. Holm and James A. Ibers, J. Am. Chem. Soc., 95, 3523 (1973); b) R. H. Holm, W. D. Philips, B. A. Averill, J. J. Mayerle and T. Herskovitz, J. Am. Chem. Soc., 96, 2109 (1974).

5) These reaction systems are homogeneous over the timecourses of Fig.1 and 2.

6) a) W. G. Prescott, S. Smiles, J. Chem. Soc., 99, 640 (1911); b) T. L. Wallace, A. Schriesheim, H. B. Jonassen, Chem. Ind., 1963, 743, c) J. Barnett, J. Chem. Soc., 1944, 5.

7) K_o values (1/min)(the molecular activity) represent the quantities (moles) of the disulfide produced by 1 mole of the cluster per minute.

8) The clusters were prepared according to Ref. (4)-a).

9) B. V. Depamphilis, B. A. Averill, T. Herskovitz, L. Que, Jr., and R. H. Holm, J. Am. Chem. Soc., 96, 4159 (1974).

10) Half-wave potentials of $[Fe_4S_4(SR)_4]^{2-}$ are known to be linearly correlated with the σ^* and σ_p substituent constants, respectively. See Rf. (9) p.4164.

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