

Transition metal thiolates: synthetic, catalytic, and biomimetic aspects

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Abstract - Preparative methods, X-ray structures, and relevant spectroscopic data are summarized for new bis- and tris-complexes of chelating dithiolates of Nb(V) and Ta(V). Similarly, tetrakis(arenethiolato) complexes of divalent transition metals are described. Reactivity of some of these complexes was examined to find novel homogeneous catalysis, e.g. condensation of dithiols. Peptide thiolate complexes of various transition metals are also described as model metalloenzymes. These complexes were investigated by NMR, CD, and electrochemically and their relevance for enzymatic reactions is discussed.

INTRODUCTION

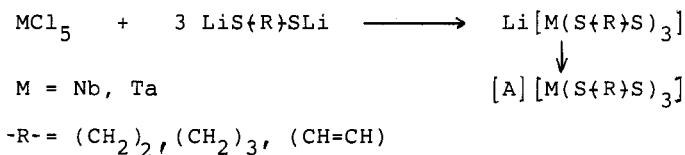
The remarkable propensity of thiolate anions for formation of strong coordinative bonds with many of the transition metals brings about a variegated structures and nature of bonding. The chemistry of thiolates of transition metals still remains largely unexplored due to its extreme complexity in the structures and properties. Recent development of X-ray analysis coupled with high-field NMR technique is now providing effective means for elucidation of structure-property relationship. The inherent difficulty in preparation and subsequent manipulation of thiolates of early-transition metals are now beginning to be overcome by the technique developed in organometallic chemistry. The synthetic achievements are now giving us unique reactivity profiles which are beginning to be utilized as catalysis for chemical transformations or as functional models of metalloproteins and metalloenzymes.

CHELATING DITHIOLATES OF NIOBIUM(V) AND TANTALUM(V)

Homoleptic alkane thiolates of these metals have still been unknown. Only passing reference for their preparative efforts are found. For example, attempts were made for preparation of Nb(s-t-Bu)₄ without success. The inherent sensitivity of the early transition metal-thiolate bonding toward air and water so far prevented characterization of soluble members of these classes of complexes.

When chelating dithiolene dianions were used for these metal ions, fairly stable hexa-coordinate tri(1,2-benzenedithiolato) complexes, [A][M(C₆H₄S₂)₃], were given and were found to have unique trigonal prismatic structures (ref. 1). This novel coordination geometry was then attributed to the distinctive ligand electronic structure. The preparation of the saturated analogs, e.g. [A][M(SCH₂CH₂S)₃], by the reaction of the pentahalides with relevant aliphatic dithiols has since been unavailable.

Utilizing highly dried organic solvents such as anhydrous acetonitrile together with anhydrous lithium salt of the dithiols under argon, we were able to prepare a series of homoleptic alkanedithiolato complexes of Nb(V) and Ta(V) as illustrated below (ref. 2). Similarly, 1,2-ethylenedithiolato complexes were prepared.



The cation exchange from lithium to bulky organic cations, e.g. tetraalkylammonium or tetraarylphosphonium, was found important to obtain relatively stable crystalline products. These tris-chelates were characterized spectroscopically by IR, Raman, and NMR and electrochemically by cyclic voltammetry under argon. Some of the structures in solid were

elucidated by the X-ray analysis (see Fig. 1). A remarkable structural feature is the coordination geometry around the metal. The tris(1,2-ethanedithiolato)complexes of Nb(V), $[\text{Nb}(\text{edt})_3]^-$, was found to have a geometry intermediate between the regular octahedron (Oh) and trigonal prism (TP) (see Fig. 1). The twist angle defined as shown in Fig. 1 were 30.5° for the tris(edt) and 18.5° for the tris(pdt), respectively. The pdt complex is thus approaching a trigonal prismatic limit. This may be due to the presence of 6-rings enabling larger bite angles for chelation.

With more bulky alkanedithiolato ligands the stereochemistry around the metal may be sharply influenced. The tris-complexes of 2,3-exo-norbornanedithiolato ligands were thus prepared for Nb(V) and Ta(V) (see Scheme I). These were found to be a mixture of stereoisomers in solution resulting from the presence of a unique bicyclo[2.2.1] structure of the ligand. An X-ray analysis of the Ta complex with the $[\text{Ph}_4\text{P}]$ cation revealed presence of an anion of C_3 symmetry, designated as synclastic similar to the above edt complex. The Nb analog with less bulky cation, (NEt_4) , was composed of an anion with C_2 symmetry bicapped tetrahedral, bct, designated as anticlastic as shown in Fig. 2. The difference may be thought to be derived from the size of the central metal ion. However, our analysis of the NMR data in solution indicated the presence of an almost statistical mixture of these isomers at ambient temperature. The steric crowding among the three ndt ligands was evaluated by the distance between the nearest C-H bonds to find no effective interaction. The lability of the two geometries in solution was demonstrated by the temperature-dependent ^1H NMR spectroscopy in CD_2Cl_2 ($-80^\circ\sim 40^\circ$). The fluxional process thus was found interpreted by the rapid polytopal rearrangement, synclastic \rightleftharpoons anti-clastic, above 0°C (see Fig. 3).

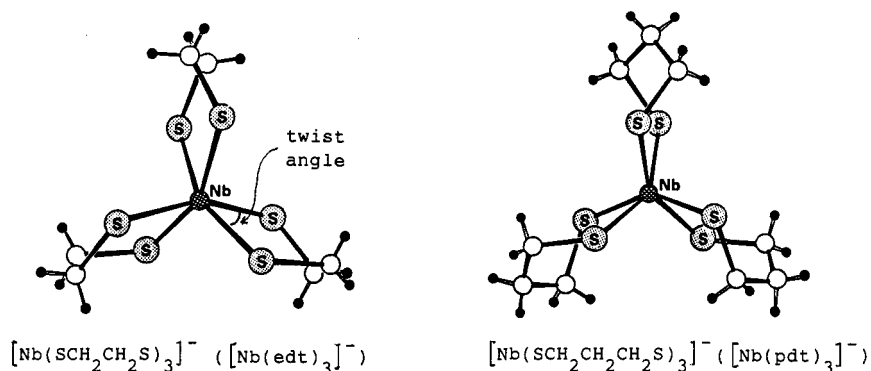
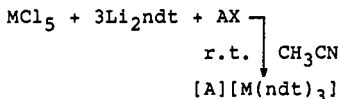


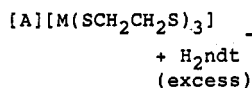
Fig. 1. Structures of the anionic part of alkanedithiolato complexes of Nb(V).

Scheme I

(Method I)



(Method II)



A = Ph_4P ; M = Nb(1a), Ta(2a)
 A = Et_4N ; M = Nb(1b), Ta(2b)
 A = $n\text{-Bu}_4\text{N}$; M = Nb(1c)

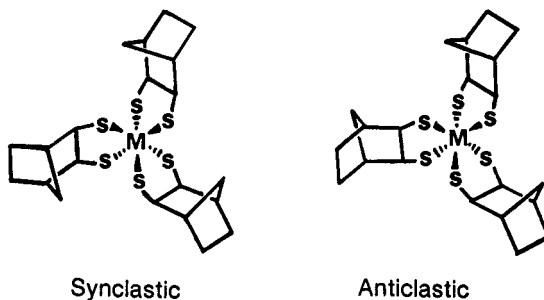


Fig. 2(a). Two isomeric structures found for anions of the tris(ndt) complexes of Nb and Ta.

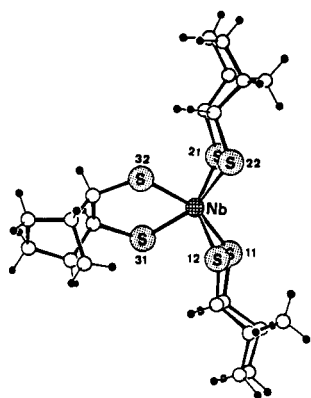


Fig. 2(b). Structure of the anticlastic $[\text{Nb}(\text{ndt})_3]^-$ anion.

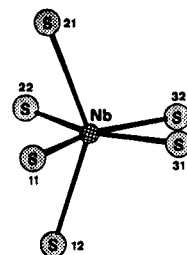


Fig. 2(c). The NbS_6 coordination sphere from the side emphasizing the BCT geometry.

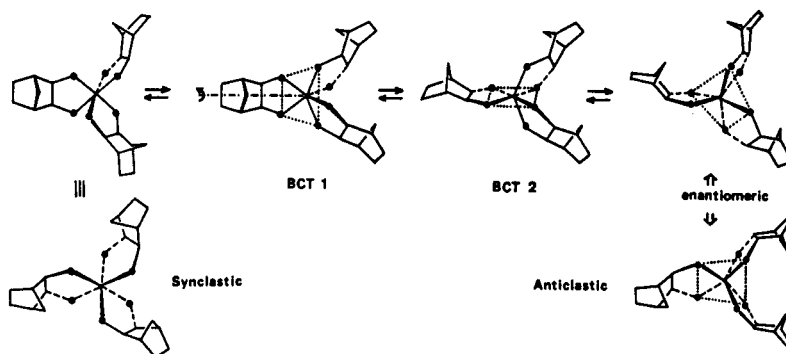


Fig. 3. A fluxional process proposed for the interconversion.

Table 1. Activation Parameters for the Synclastic \rightleftharpoons Anticlastic Interconversion in CD_2Cl_2 .

Complex	E_a kcal/mol	ΔH^\ddagger kcal/mol	ΔS^\ddagger eu
$[\text{Ph}_4\text{P}][\text{Nb}(\text{ndt})_3]$	9.1 ± 0.4	8.6 ± 0.4	-14.4 ± 1.5
$[\text{Et}_4\text{N}][\text{Nb}(\text{ndt})_3]$	9.6 ± 0.5	9.2 ± 0.5	-11.5 ± 1.8
$[\text{Ph}_4\text{P}][\text{Ta}(\text{ndt})_3]$	11.5 ± 0.4	11.1 ± 0.5	-8.8 ± 1.8

All errors are random errors estimated at the 99% confidential level (2.5σ).

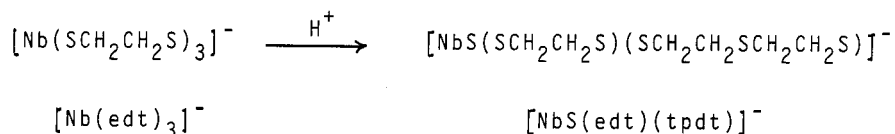
Table 2. Apparent Color and Peak Positions^a of the Electronic Spectra of $[\text{M}(\text{SCH}=\text{CHS})_3]^-$ and $[\text{M}(\text{XCH}_2\text{CH}_2\text{Y})_3]^-$ in Acetonitrile.

M(V)	SCH=CHS	X=Y=S	X=O, Y=S	X=Y=O
Nb	purple 556	deep red 520	yellow 317	colorless < 270
Ta	red orange 493	orange 443	colorless 275	colorless < 270

a) Values in nm.

Identification of the synclastic and anticlastic isomers can be made by the IR spectra in the solid state. The appearance of four IR peaks of about equal intensity at 300-400 cm^{-1} (M-S stretchings;) indicates the synclastic isomer whereas for the corresponding synclastic isomer, the number of peaks increase to six. By careful analysis of the crystal structures, the packing forces among the complex anions and organic cations were found to be a factor for the geometrical preference in solid. In particular, the size of the cation is of utmost importance for this. The more bulky cation, e.g. tetraphenylphosphonium, induces the formation of synclastic (nearly octahedral structure) isomer. The EH-MO analysis of the nature of bonding in these isomers has also been performed to find a modest difference in the metal-thiolate bond strength. Energetically these isomers are similar and the co-existence at ambient temperature in solution is thus validated.

A novel isomerization of the anion, $[\text{Nb}(\text{edt})_3]^-$, was found in solution with small amounts of protic reagents. Thus, a red solution of this anion in DMF turns into orange on standing at 70°C with addition of phenol or water. The complex isolated as crystals was analyzed by X-ray to contain a terminal sulfide and a 3-thiapentane-1,5-dithiolate (tpdt) ligands which were formed by the initial C-S bond cleavage of one of the edt ligands (ref. 3).



This stoichiometric reaction was utilized to realize a novel catalytic condensation between two alkanedithiol molecules to give thioether derivatives by elimination of H_2S . For example, ethanedithiol was heated at 70-100°C in DMF in the presence of $[\text{Ph}_4\text{P}][\text{NbS}(\text{SCH}_2\text{CH}_2\text{S})_2(\text{SCH}_2\text{CH}_2\text{SCH}_2\text{CH}_2\text{S})]$ for 60-80 h to give 3-thiapentane-1,5-dithiol in 30-50% conversion. Since a mixture, $\text{MCl}_n/\text{edtH}_2/\text{Et}_3\text{N}$ (molar ratio, 1:3:6) gives the edt complexes, a catalytic system, $\text{MCl}_n/\text{Et}_3\text{N}$, was examined for the dithiol condensation to find similar catalysis, albeit with low conversion, in DMF at 100°C. Ti(IV), Zr(IV), and W(VI) may be used as the metal in these systems with similar results.

The edt complex also catalyzes ring-opening polymerization of thiranes. For example, 2-methylthiirane (propylene sulfide) in DMF polymerized by catalysis of the Nb-edt complex at 0°C for 3 h to give a viscous mixture from which an off-white sticky amorphous polymer ($M_w 2 \cdot 7 \cdot 10^4$, $M_w/M_n = 1.2-1.7$) may be precipitated by addition of MeOH in 90% yield (ref. 4). The analogous Ta(V) complex also catalyzed the same polymerization in somewhat less efficiency.

The tris(edt) complexes of Nb and Ta were found to be valuable starting material for low temperature preparation of layered sulfides (amorphous or partly crystalline) of these metals. Thus, $[\text{Et}_4\text{N}][\text{Nb}(\text{edt})_3]$ or $[\text{Ph}_4\text{P}][\text{Nb}(\text{edt})_3]$ was heated at 400°C under Ar for 48 h to give NbS_2 as black powder characterized by X-ray (powder) and elemental analysis (ref. 5).

The ligand exchange reaction of the ethanedithiolato complexes was found to give new tris-(ethane-1-oxo-2-thiolato) and tris(ethane-1,2-diolato) complexes. These are obtained as crystalline powder by addition of 2-mercaptoethanol or ethylene glycol to an acetonitrile solution of $[\text{Nb}(\text{edt})_3]^-$ at ambient temperature followed by evaporation of the solvent. The position of absorption maxima and color of these complexes are shown in Table 2. The former could be prepared also from the reaction of pentachlorides with dilithium salt of mercaptoethanol. Two of these complexes with S,O- and O,O-chelates have been analyzed by single crystal X-ray analysis. The complex anions have similar structure to the parent dithiolato complex. The twist angles are 31.1° (S,O) and 34.1° (O,O) indicating some approach to the octahedral value when sulfur atoms are replaced by oxygen atoms.

CYCLOPENTADIENYL TANTALUM COMPLEXES WITH THIOLATO LIGANDS

Introduction of a cyclopentadienyl (Cp) ligand to Ta seems to offer a new possibility for study on Ta-S bondings. Our initial success in synthesis of bis(dithiolato) complexes, $\text{CpTa}(\text{S})_2$ (ref 6), was quite important for further exploitation of related Ta-S complexes. The presence of Cp^* (pentamethylcyclopentadienyl) ligand effectively stabilizes the Ta-SR bonding against external nucleophilic attack and confers enough solubility for purification and characterization. The NMR and mass spectra gave sufficient information about their structure involving the four-legged piano stool geometry of CpTaS_4 skeleton. As already shown for the bis(butadiene) complex, $\text{CpTa}(\text{butadiene})_2$ (ref 7), the ethylenedithiolato complex was found to have two thiolato ligands oriented in an opposite direction, supine and prone as shown in Fig. 4. Weak coordination of the olefinic part to the electron-deficient Ta is evidenced by the low temperature NMR study which shows two peaks for the olefinic

protons at -50°C , but a broad singlet at 36°C . The activation energy was calculated $\Delta G^{\ddagger} = 14.9$ kcal/mol (50°C).

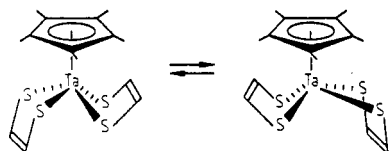


Fig. 4. Fluxional Interconversion of $\text{Cp}^*\text{Ta}(\text{SCH}=\text{CHS})_2$ in CDCl_3 .

An analogous dithiolato complex with sterically demanding ligands, $\text{Cp}^*\text{Ta}(\text{ndt})_2$, (ndt = norbornanedithiolato), was prepared by similar reaction and found to have the two norbornane skeletons asymmetrically oriented around Ta by analysis of the ^1H NMR spectra (NOESY, at 400MHz). This orientation was kept upon heating up to 100°C . The stability and solubility are effectively improved by the bicyclic rings on sulfurs.

In an attempt to displace the dithiolato ligands for two sulfido (S_2^{2-}) ligands, reaction with Li_2S_2 was examined in THF in 1:5 ratio. The yellow product obtained was found to have a composition, $\text{Li}_2[\text{Cp}^*\text{TaS}_3](\text{thf})_2$. X-ray analysis of this complex revealed an interesting hexagonal prismatic $\text{Ta}_2\text{Li}_4\text{S}_6$ cluster as shown in Fig. 5 (ref. 8).

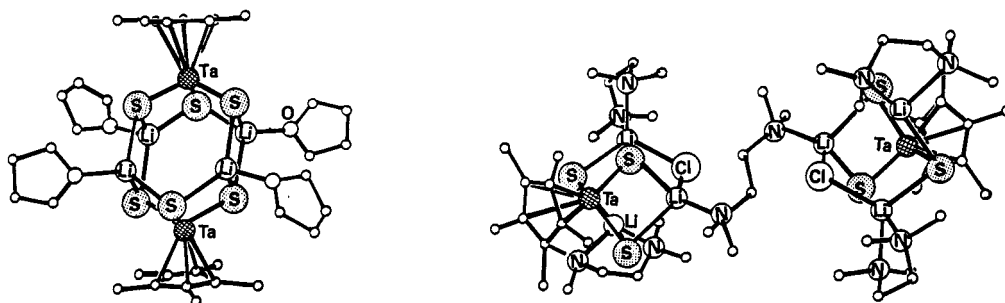


Fig. 5. Structure of new clusters involving Cp^*Ta moieties.

This cluster may be viewed to contain CpTaS_3^{2-} unit which is an analog of the well-known organometallic oxides, CpMO_3 , $M = \text{Re}$ (ref 9). The dianionic moiety, CpTaS_3^{2-} , is associated with two $[\text{Li}(\text{thf})]^+$ parts and dimerized to give the 12-atomic cluster. The two Li ions are important to construct the structure by neutralizing the negative charges at the sulfido ligands. When Cp^*TaCl_4 was treated with Li_2S_2 (4.5 equiv) under the presence of tmeda obtained was $[\text{Cp}^*\text{TaS}_3\text{Li}_4(\text{tmeda})_2\text{LiCl}]_2(\text{tmeda})_2$ with two open-cubane $\text{TaS}_3\text{Li}_3\text{Cl}$ cores (Fig. 5). Utilizing moderate reactivity of the complex, we have performed reactions with a variety of metal chlorides to replace the Li atoms by other metals. Thus, the reaction with $\text{Rh}_2\text{Cl}_2(\text{cod})_2$ in THF gave a trimetallic complex, $\text{Cp}^*\text{TaS}_3(\text{Rh}(\text{cod}))_2$, where the Rh atoms are chelated by the two sulfido ligands (ref 10).

HOMOLEPTIC ARENETHIOLATO AND ARENESELENOLATO COMPLEXES OF TRANSITION METALS

Tetracoordinate arenethiolato metal(II, III) complexes of the type, $(A)_n[\text{M}(\text{SPh})_4]$, are fundamentally important as models of some metalloproteins where thiolato-metal bonding plays crucial roles. In particular, tetrahedral thiolato coordination exists in metallothioneins (Cd, Zn), alcohol dehydrogenase(Zn), and rubredoxin (Fe). Similar selenolato coordination has been proposed in some of hydrogenases and in formate dehydrogenase(Mo). In order to investigate unique properties of these metal coordination sites, we have prepared systematically dianionic tetrahedral complexes of the type, $(A)_2[\text{M}(\text{SPh})_4]$ and $(A)_2[\text{M}(\text{SePh})_4]$, $A = \text{NEt}_4$, PPh_4 , and $M^{II} = \text{Fe, Co, Mn, Zn, Cd}$ (ref. 11).

These are characterized by ir, and Raman spectral measurements. The single crystal Raman data provided important basis for the assignment, especially when combined with the X-ray structural results. Thus, the vibrational data are analyzed by the D_{2d} models utilizing normal coordinate analysis. Typical values of the Raman M-Q vibration (A or A_1) ($Y = \text{S, Se}$) are shown in Table 3.

Typical members of the tetrakis(benzenethiolato)metal(II) dianion family are X-ray analyzed to find the presence of distorted Td geometry (D_{2d}) for $M = \text{Zn, Cd, Mn}$. Although the gross structures are similar, there are some distinctive differences among them as shown metrically

Table 3. Comparison of the M-Q vibration of (A)[M(Q-Ph)₄] in the crystalline state.*

M(II)	Q	
	S	Se
Mn	200	188
Fe	198	185
	(314)**	
Zn	200	135
Cd	180	130

* Frequency of A₁ stretching in cm⁻¹

** R.S. Czernuszewics, J. LeGall, I. Moura, and T.G. Spiro, *Inorg. Chem.*, **25**, 696 (1986).

Table 4. Comparison of the average lengths of M-Q bonds in metal thiolate dianions, [M(Q-Ph)₄] (in Å).

M(II)	Q		
	S	Se	difference
Mn	2.346	2.564	0.25
Fe	2.355 ^a	-	-
Zn	2.357	2.469	0.11
Cd	2.541	2.649	0.11

^a D. Coucouvanis et al., *J. Am. Chem. Soc.*, **103**, 3350 (1981)

Table 5. Comparison of average bond angles and torsion angles of (Q'-M-Q-Ph) (in parenthesis) of M-Q-C in [M(Q-Ph)₄].

M(II)	Q	
	S	Se
Mn	109.4(6.44)	107.3(4.92)
Fe	110.9*	-
Zn	109.3(5.48)	107.0(5.22)
Cd	107.8(5.15)	105.0(13.15)

* D. Coucouvanis, D. Swenson, N.C. Baenziger, C. Murphy, D.G. Holah, N. Sfarnas, A. Simopoulos, and A. Kostikas, *J. Am. Chem. Soc.*, **103**, 3350 (1981).

in Table 4 and 5. In particular, M-S and M-Se bond lengths are compared to find some shortening for the Mn-S bonds due to some degree of enhanced donative π -bonding. The ESR spectra of these Mn(II) complexes indicated a considerable interanionic electronic interaction which is presently analyzed. The M-Q-C bond angles range from 109° for Zn-S to 105° for Cd-Se. Since ionicity of M-S bonds results in the narrow M-S-C bond angle, the value for Cd-Se indicates an increased ionicity of the Cd-Se bonds relative to the Zn-S bonds.

The nature of these bondings may also influence the torsion angles of M-S or M-Se bonds. The average value for Cd-Se deviates from other members to indicate difference in the Cd-Se bonding. The corresponding dihedral torsion angles of native metal thiolate enzymes are generally controlled by the peptide sequence. The consequence of peptide sequence on the nature of metal-thiolate bonding is thus found to be effective to the electronic structure at the metal through the bond angle and torsion angles.

The Mn(II) thiolate and selenolate complexes are active catalysts for air-oxidation of benzaldehyde and benzoin at 20°C in DMF. The presence of binuclear Mn(III) species in the catalysis was inferred from the electronic and ESR spectral measurement during the catalysis (ref. 12).

BULKY THIOLATES

Coordination chemistry of bulky thiolate, e.g. 2,6-dialkylbenzenethiolato ligands, has attracted considerable attention recently and remarkable properties of some of the complexes, e.g. $[\text{Fe}(\text{S}-2,6\text{-diisopropylphenyl})_4]^-$, has been reported (ref. 13). We have prepared homoleptic Mo(IV) complexes, $\text{Mo}(\text{SR})_4$, from sodium salt of 2,4,6-trimethyl- (tmbtH) and 2,4,6-triisopropylbenzenethiol (tibtH) and $\text{MoCl}_4(\text{CH}_3\text{CN})_2$ in dimethoxyethane (DME) as black needles (ref. 14). These are paramagnetic, e.g. $\mu_{\text{eff}}^3 = 2.6$ for $\text{Mo}(\text{tibt})_4$ in CD_3CN . The redox behavior as shown by the cyclovoltammograms in DMF was quite different from those of less bulky thiolates, e.g. $\text{Mo}(\text{S}-t\text{-Bu})_4$. The reactivity of the one-electron reduced Mo(III) species was investigated by cyclic voltammetry to reveal high reactivity toward π -acidic small molecules such as acetylene but inertness to dinitrogen. Similar bulky thiolato complexes of MoO species, $\text{MoO}(\text{tmbt})_4$ and $\text{MoO}(\text{tibt})_4$ have also been prepared as deep blue crystals from $\text{MoOCl}_3(\text{thf})_2$. The electronic spectra of these complexes exhibited a peak at 558 nm in DME which is at lower wavenumber as compared with a less bulky analog, $\text{MoO}(\text{SPh})_4$ (598 nm).

Bulky thiolate complexes of Fe_2S_2 and Fe_4S_4 cores have also been prepared by modification of the literature method (ref. 14). The bulkiness at the thiolate (tibt ligand) in Fe_4S_4 cluster did not cause any appreciable lengthening of bonds within the cluster, but resulted in some lengthening of the Fe-S (thiolato) bonds, average Fe-S length, 2.27 Å, as compared with that of the S-phenyl analog, (2.25 Å). The Fe-S-C bond angles (99.9°) are narrower from the conventional value of 106-110° to indicate absence of conjugation with the phenyl system. In the Fe_2S_2 complex of tibt, $[\text{Fe}_2\text{S}_2(\text{tibt})_4]^-$, the two Fe-thiolate bonds are found to be different by X-ray analysis (ref. 15). One of the Fe-S-C angles (112°) is similar to that of $[\text{Fe}_2\text{S}_2(\text{S-p-tol})_4]^-$ (111°) but the other is narrow (105°).

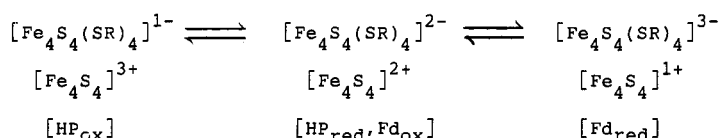
A bulky thiolate ligand with bridging function, 2,4,6-trimethylbenzene-1,3-dithiol, was prepared and macromolecular complexes were prepared utilizing ligand exchange reaction with $(\text{A})_2[\text{Fe}_4\text{S}_4(\text{S}-t\text{-Bu})_4]$ in DMF (ref. 15). The 2:1 reaction in DMF under Ar gave a solution containing agglomerated clusters whose molecular weight was measured by the sedimentation analysis under Ar to find the values, 15,000 (8-10 Fe_4S_4 clusters) for $\text{A} = \text{NMe}_4$, 6,600 for $\text{A} = \text{NEt}_4$, and 9,200 for $\text{A} = \text{PPH}_4$. The solubility in DMF is remarkable although it is highly cross-linked by the dithiolate. Interestingly, the size of the cluster polyanion was found to be controlled by the size of counter cations (A).

The presence of bridging dithiolate was confirmed by the ^1H NMR peaks which were shifted by coordination to two paramagnetic cluster cores. The redox behavior of the macromolecule was investigated by cyclic voltammetry. The redox couple for the 4Fe-core 2+/+ was found at -1.26 V(SCE) with width of 0.11 V in DMF. The redox potentials of similarly cross-linked macromolecules prepared from *m*- and *p*-benzenedithiol were at -1.13 and -0.95 V, respectively. Rapid electron transfers among the cluster cores are thus realized in these macromolecules mimicking the multimetallic enzymes or proteins found in the photosynthetic systems or in various nitrogenases.

PEPTIDE THIOLATE COMPLEXES OF TRANSITION METALS

This class of thiolate complexes is important as higher order models of metalloenzymes and metalloproteins. We have been interested in this area since several years and prepared a number of oligopeptide thiolate complexes of transition metals, e.g. Mn, Fe, Co, Ni, Pd, Ag, Hg etc. We have taken systematic approaches for preparation of peptide thiolate complexes. The use of peptide ligand started from cysteine protected at the N- and/or C-terminals, e.g. N-acetylcysteine, and Z-CysOMe. Then, consideration was made about (a) abundances of specific amino acid residues in native proteins, (b) invariant sequences of some metalloproteins, and (c) ease of peptide preparation without racemization. Thus, the following peptides were prepared by the liquid phase method with protection at the thiolate part by acetoamidomethyl (Acm) group, Z-Cys(Acm)-AlaOMe, Z-Cys(Acm)-GlyOMe etc. The deprotection was performed through the reaction with HgCl_2 in DMF or DMSO to precipitate the chloromercury(II) complex by addition of NaCl-saturated aq. methanol (ref. 16). Similar deprotection may be made by reaction with AgNO_3 or K_2PdCl_4 . The removal of the metal was done by introduction of gaseous H_2 in DMF under Ar. After brief evacuation, the peptide thiol solution is immediately used for complex formation with other metals.

The chelate-philic heavy metal complexes are air-stable and the structure was examined by high-field NMR spectroscopy with selective decoupling or 2D-technique. The complexes of the first-row transition metals are paramagnetic and generally sensitive to air and moisture and crystallization was quite difficult to preclude any single-crystal X-ray analysis. The solution CD spectra are useful to diagnose the mode of coordination. Generally, higher intensity of the extrema was observed for complexes with chelating dithiolates. The invariant peptide sequences found in many metalloproteins are taken into consideration to specify the peptides which are to be used as ligands. For example, a peptide sequence, Cys-Gly-Ala, found in *Peptococcus aerogenes* ferredoxin (an 8Fe-8S ferredoxin) was chosen and the peptide, Z-Cys-Gly-Ala-OMe, was allowed to react with Fe_4S_4 core to give an anion,



$[\text{Fe}_4\text{S}_4(\text{Z-cys-Gly-AlaOMe})_4]^{2-}$. In general, two redox couples exist in 4Fe-4S ferredoxin model complexes as shown below where HP represents high potential iron-sulfur protein and Fd stands for ferredoxin. The redox potential of the peptide complex as measured by cyclic voltammetry in CH_2Cl_2 was found to be remarkably positively shifted at low temperature. Similarly, a tetrapeptide, Z-Cys-Gly-Ala-CysOMe, was used to chelate the core as shown in Fig. 7 to facilitate the formation of NH-S hydrogen bonding. The redox potential of this complex was almost the same to that of the native ferredoxin at room temperature (ref. 17). The invariant peptide sequences of plant-type 2Fe ferredoxins were also utilized to prepare peptide complexes containing a $\text{Fe}_2\text{S}_2^{2+}$ core. Our systematic approach to simulate the chemical environment of the active site of the plant-type ferredoxin was highly successful in mimicking the redox behavior as well as some of the spectroscopic properties, e.g. ESR, NMR etc. The importance of NH-S hydrogen bonding is clearly shown to be an effective factor of the positive shift of the redox potentials of ferredoxins including rubredoxin (1Fe-type) (ref. 18).

The coordinating thiolate part forms a hydrogen bond with NH of the peptide bond at the Ala residue as shown in Fig. 7. The juxtaposition of a Gly residue is important for inducing the folded conformation by its less-bulky CH_2 part. Thus, the observed invariance of the peptide sequence, Cys-Gly, can be understood by its ability to promote the NH-S hydrogen bonding (ref. 19).

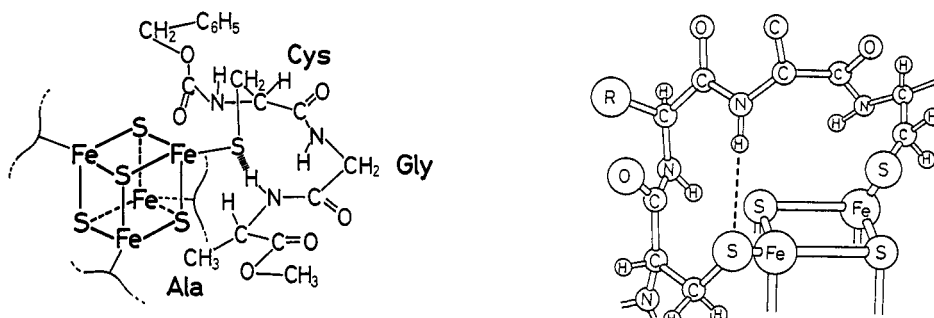


Fig.7. a) Proposed structure of $[\text{Fe}_4\text{S}_4(\text{Z-cys-Gly-Ala-OMe})_4]^{2-}$ in dichloromethane.

b) Schematic illustration of an NH-S hydrogen bond in a tetrapeptide complex with a sequence, cys-A-B-cys.

RUBREDOXIN MODEL COMPLEXES

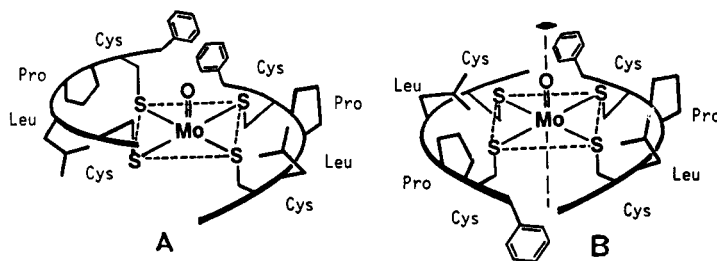
Since rubredoxins have two invariant peptide sequences of the type, Cys-X-Y-Cys, coordinating to iron(II/III) at their active sites, model complexes, $[\text{Fe}(\text{Z-cys-Ala-Ala-cys-OMe})_2]^{2-}$ and the related complexes with Z-Cys-Pro-Leu-Cys-OMe (abbr. CPLC), and Cys-Thr-Val-Cys-OMe etc were prepared and the redox stability was compared. The cyclic voltammetry under Ar in DMF has clearly shown the CPLC complex to be more stable during the one-electron transfer process (Fe(II)/Fe(III)). This stabilization was ascribed to the hydrophobic character of the peptide ligand where Pro and Leu residues cover the iron-sulfur bonds by their alkyl and alkylene side chains. The nature of Fe-S bondings has been investigated by the EH-MO method and an interesting dependence on the S-Fe-S-C dihedral torsion angles was found (ref. 20). Proton NMR investigation (500MHz) on these model Fe(II) complexes in CD_3CN showed many peaks shifted by the paramagnetism in the range of -50 to 270 ppm at 35°C. The assignment of these observed peaks now poses us future problems.

PEPTIDE THIOLATE COMPLEXES OF Mo(IV,V)

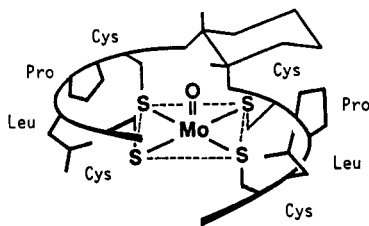
Molybdenum is essential for some important metalloenzymes where cysteine thiolate coordination has been shown and controls the properties at the active sites for promotion of the catalysis. We have been examining the redox properties and catalysis of oligopeptide thiolate complexes of molybdenum. A diamagnetic Mo(IV) complex with two tetrapeptide ligands, Z-Cys-Ala-Ala-Cys-OMe (abbr. CAAC), were prepared by exchange reaction from a labile starting material, $\text{Mo}(\text{S-t-Bu})_4$, in DMSO to give $\text{Mo}(\text{CAAC})_2$ as an air-sensitive brown complex

which was characterized by CD and ^1H NMR spectroscopy (ref. 21). Formation of chelate rings was indicated by the spectroscopic data just as in the case of analogous Pd(II) and Fe(II) complexes (ref. 22). Formation of a MoFe mixed thiolate complex from the Mo(IV) peptide complex and $[\text{Fe}_4\text{S}_4(\text{S-iPr})_4]^{2-}$ was indicated by the CD spectral change occurring upon the mixing the components in 1:1 ratio in DMSO at 25°C. The observed spectral features thus obtained were compared with the CD pattern of nitrogenase from *Az. vinelandii* to find some similarity.

In order to mimic the active site of molybdo-oxidase, a tetrapeptide/Mo(V) complex, $\text{MoO}(\text{Z-cys-Pro-Leu-cysOMe})_2$, was prepared by ligand exchange reaction of $[\text{NMe}_4][\text{MoO}(\text{SPh})_4]$ in acetonitrile. The deep violet square pyramidal complex thus formed was found to be comprised of two stereo-isomers by IR and visible spectra. The ESR spectrum (frozen in acetonitrile



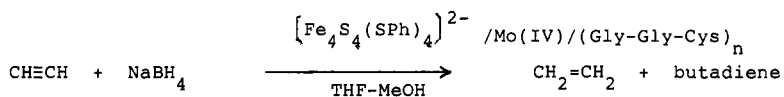
at 80K) showed rhombic signals with $g_{\text{av}} = 1.980$ and 1.990. Two redox couples (Mo(V/VI)) were observed at -0.66 and -0.93 V (SCE) in DMF. The isomer with higher redox potential can be reduced selectively by NET_4BH_4 to give a Mo(IV) complex with the two bidentate peptide thiolate ligands which was characterized by the IR (absence of Mo=O group) and the ^1H NMR spectrum. To assign the structure for these isomers, a tetradentate peptide thiolate ligand was prepared by condensation (DCC/HOBt method) of *cis*-1,2-cyclohexanedicarboxylic acid with two equiv. of Cys(Acm)-Pro-Leu-Cys(Acm)-OMe. This ligand was allowed to coordinate to



oxomolybdenum(V) by the reaction of $[\text{NMe}_4][\text{MoO}(\text{SPh})_4]$ in acetonitrile after deprotection with AgCF_3CO_2 in MeOH. The peptide complex thus obtained showed an ESR signal at $g_{\text{av}} = 1.980$ to indicate the structural type A. The spectroscopic and electrochemical property of the peptide/Mo(V) complex is thus found to be delicately controlled by the peptide conformational effect which is transmitted to the metal through the Mo-S torsion angle.

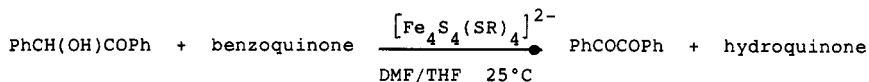
BIOMIMETIC CATALYSIS

Preparation of a series of reactive peptide thiolate complexes of Fe and Mo gives us a unique opportunity of examining the biomimetic catalysis of some of the peptide complexes. For example, nitrogenase active site has been considered to involve mixed metal clusters which may be modeled by mixing the Mo(IV) peptide thiolate complex with 4Fe-4S model complex. Thus, a sequential polypeptide, $(\text{Gly-Gly-Cys})_n$, was prepared and allowed to coordinate to Mo(IV) by ligand exchange reaction and the catalysis in electron transfer reduction was examined as shown in the following equation (ref. 23). The mixed metal catalytic system was



quite effective in reduction of acetylene and nitrile at 30°C.

Biomimetic oxidation of benzoin with p-benzoquinone by the catalysis of peptide thiolato complexes of Fe_4S_4 core as shown below (ref. 24). Here, the oxidative stability of the iron



cluster is very important for the activity of the catalysts. For example, $[\text{Fe}_4\text{S}_4(\text{Z-Cys-Ile-AlaOMe})_4]^{2-}$ was found to be most effective among the similar thiolate complexes of analogous structure.

Electron transfer catalysis of model peptide complexes in a biochemical redox system, NADPH/S. platensis FNR/Fe(II) peptide complex/cytochrome Fe(II), was examined in an aqueous Triton X-100 micelle solution at pH 7.5 (ref 25). The highest efficiency was obtained with the Fe(II) complex with two Z-Cys-Pro-Leu-CysOMe ligands which is the partial invariant sequence of native rubredoxin.

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