Oxo-molybdenum(V) complexes with sulfide and hydrogensulfide ligands: models for the molybdenum(V) centers of xanthine oxidase and xanthine dehydrogenase

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variable-temperature pattern for **1** differs from that obtained for **2** and $ReH_5(PEtPh_2)_3$. The reasons for this are not clear and may be either electronic or steric in origin.

The T_1 data obtained for the complex $ReH_7(PPh_3)_2$ are given in Table I. This complex exhibits a triplet in the hydride region, for the seven magnetically equivalent hydrogen atoms, which is still clearly defined down to −90 °C. However, as reported previously, the T_1 values at the low temperatures do indicate a fluxional process with involvement of nonclassical hydrogen atoms accounting for the low T_1 values.[3a]

Finally, we have made the first T_1 observations on a complex of the type $Re_2H_8(PR_3)_4$, namely, the one where $PR_3 = PPh_3$ (**4**).[11] We find for **4** that $T_1(min) = 65$ ms in CD_2Cl_2 at −40 °C and 200 MHz. The related complex with $PR_3 = PEtPh_2$ (**4'**) is known[12] to have four μ_2-H^- and four terminal H^- ligands. Thus, it is uncertain whether a low T_1 value is necessarily diagonistic of the ligand H_2. If it is, the structure of **4** in solution must differ from that of **4'**.

In summary, the above results (a) require reclassification of **1** as nonclassical, probably as $Re(H_2)H_3(PPh_3)_3$, (b) show that even a slight change in auxiliary ligands (from PPh_3 to $PMePh_2$) can alter the behavior of the H atoms, and (c) raise a question as to the rigor of always ascribing low T_1 values to the presence of H_2 as a ligand.

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Note Added in Proof. More resolved low-temperature spectra for **1**, which are also consistent with our assignment of a nonclassical formulation for this complex, were recently obtained in CD_2Cl_2.

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Oxomolybdenum(V) Complexes with Sulfide and Hydrogensulfide Ligands: Models for the Molybdenum(V) Centers of Xanthine Oxidase and Xanthine Dehydrogenase

Sir:

Recent evidence from EXAFS and EPR studies of xanthine oxidase (XO) and xanthine dehydrogenase indicates their molybdenum(VI) centers have both terminal oxo and terminal sulfide ligands.[1] Upon reduction by substrate to the molybdenum(IV) state, the sulfide group is apparently protonated to SH;[1b-d] one-electron reoxidation to the molybdenum(V) state generates the Very Rapid[1e] and Rapid[1b,c] EPR signals, which are thought to arise from Mo^VOS and $Mo^VO(SH)$ centers, respectively. No model oxomolybdenum(V) complexes with these ligands have been isolated, although their presence in solution has been convincingly demonstrated.[2,3]

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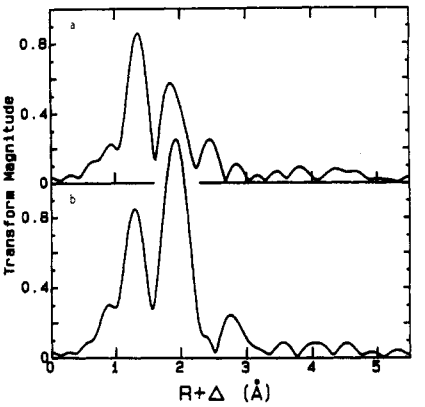


Figure 1. K-edge EXAFS transforms (transform k range 4-15 $Å^{-1}$): (a) $[Ph_4P][MoOSL]$ (**1**); (b) *trans*-MoO(SH)L (**2**).

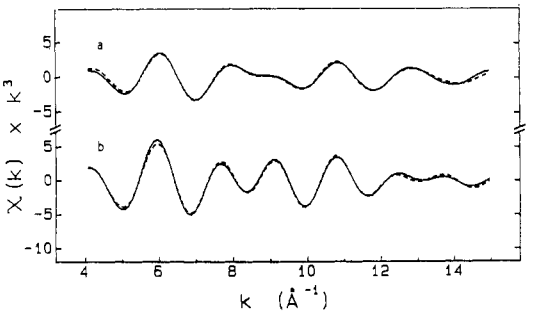


Figure 2. EXAFS curve fits: (a) $[Ph_4P][MoOSL]$ (**1**); (b) *trans*-MoO(SH)L (**2**).

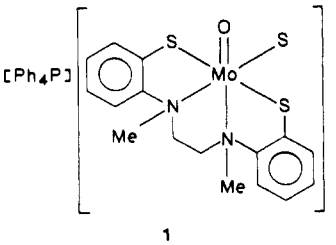
Table I. EXAFS Curve-Fitting Results

	Mo=O		Mo—S		Mo—N/O[a]	
complex	bond length, Å[b]	N[c]	bond length, Å[b]	N[c]	bond length, Å[b]	N[c]
$[Ph_4P][MoOSL]$ (**1**)	1.68	1	2.36	2-3	2.02	~1
trans-MoO(SH)L (**2**)	1.66	1	2.39	3-4	2.02	~1

[a] Mo—N/O: Mo—N or Mo—O bonds, not distinguished by EXAFS. [b] Uncertainty ±0.03 Å. [c] Number of bonds.

The synthesis and characterization of $Mo^{VI}O_2L$ (L = *N,N'*-dimethyl-*N,N'*-bis(2-mercaptophenyl)ethylenediamine) has recently been reported from this laboratory.[2] One-electron electrochemical reduction of MoO_2L in MeCN, followed by addition of $[n\text{-}Bu_4N]SH$, generates $[MoOSL]^-$ in solution. Protonation of $[MoOSL]^-$ at low temperature (<−40 °C) gives *cis*-MoO(SH)L, which appears to rearrange to *trans*-MoO(SH)L at room temperature. The latter species is also obtained in solution by treatment of *trans*-MoOClL with $[n\text{-}Bu_4N]SH$ at room temperature.[2]

We report here the synthesis and characterization of complexes formulated as $[Ph_4P][MoOSL]$ (**1**) and *trans*-MoO(SH)L (**2**), apparently the first oxomolybdenum(V) complexes with sulfide and hydrogensulfide ligands to be isolated.



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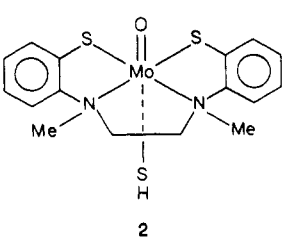

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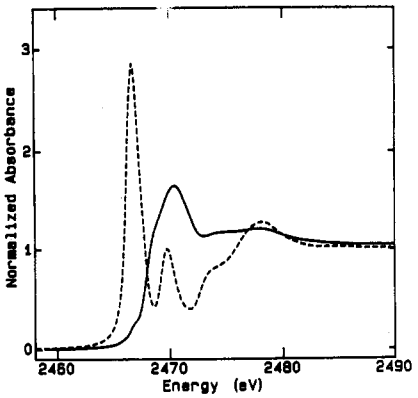

Figure 3. Sulfur K-edge X-ray absorption spectra: (—) $[Ph_4P][MoOSL]$ (**1**); (---) $MoSCl_2(HB(Me_2C_3N_2H)_3)$.[11]

Reduction of MoO_2L with excess $[n\text{-}Bu_4N]SH$ in the presence of $[Ph_4P]Cl$ gives **1**.[4] Reduction of MoO_2L with excess $[n\text{-}Bu_4N]SH$ followed by protonation with CF_3COOH at room temperature gives **2**.[4] The complexes have been characterized by elemental analysis, electrochemistry, and IR, electronic, EPR, and sulfur and molybdenum X-ray absorption K-edge spectroscopy.[4] Attempts to grow suitable crystals for X-ray crystallography have been unsuccessful for either complex.

The EPR and electronic spectra of **1** in solution are identical with those reported for $[MoOSL]^-$ generated by reduction of MoO_2L in solution.[2] A strong, broad EPR signal is observed for **1** in the solid state, as expected for a mononuclear compound.

The solid-state Mo K-edge EXAFS transform of **1** indicates the presence of 1 Mo=O bond, 2–3 Mo—S bonds and ~1 Mo—N(O) bond (Figures 1 and 2, Table I). The Mo—S bond length is somewhat shorter (2.36 Å) than that normally observed for a thiolate S (~2.40 Å),[2] and the large Debye–Waller factor (0.008 $Å^{-2}$) for the interaction implies that some heterogeneity of bond lengths is present. Most interestingly, no evidence for a short Mo=S bond (~2.15 Å) was found. The S K-edge X-ray absorption spectrum also provides no evidence of a Mo=S bond. In the few Mo complexes with this bond that have been examined, a strong K-edge resonance is observed at lower energy than that of thiolate (Mo—S) sulfur (the S K-edge X-ray absorption spectra of $MoSCl_2(HB(Me_2C_3N_2H)_3)$ and **1** are shown for comparison in Figure 3);[5] the S K-edge spectrum of **1** is typical of thiolate

Table II. Electrochemical and EPR Parameters

complex	E_{pc}	E_{pa}	$E_{1/2}$
$[Ph_4P][MoOSL]$ (**1**)[a]	−0.70	−0.54	−0.62
trans-MoO(SH)L (**2**)[a]	−0.91	−0.54	−0.73

complex	g_1	g_2	g_3	A_1	A_2	A_3
trans-MoO(SH)L[b]	2.0204	1.9625	1.9537	55.0	23.0	22.0
XO Very Rapid[c] signal	2.0252	1.9550	1.9494	44.3	18.2	19.1
$[Ph_4P][MoOSL]$[d]	2.0165	1.9330	1.8885	47.0	23.9	38.8
$[Ph_4P][MoOSL]$[e]	2.0165	1.9330	1.8885	52.7	23.7	23.7

[a] Volts vs SCE, in DMF with 0.10 M $[n\text{-}Bu_4N][BF_4]$, Pt electrode, scan rate 0.100 V s^{-1}. E_{pc} = cathodic peak; E_{pa} = anodic peak. [b] g values refined from those reported in ref 2. $A(^{95,97}Mo)$ values in $cm^{-1} \times 10^4$. Both g and A values obtained by computer simulation; noncoincidence angle of g and A tensors $\alpha_{1,3}$ = 16° (DMF, 77 K). [c] Reference 9. [d] Reference 2. [e] Reference 9; $\alpha_{1,3}$ = 35°.

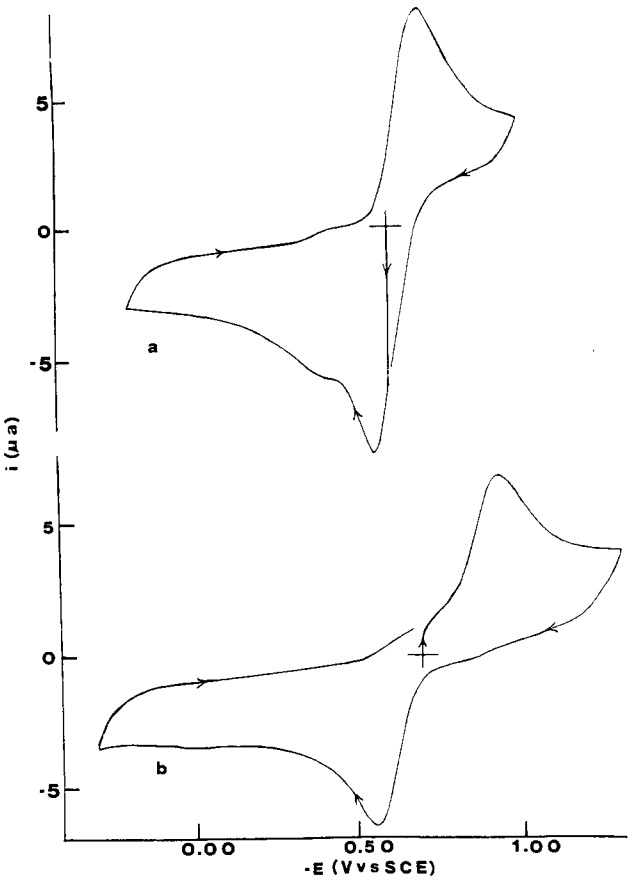

Figure 4. Cyclic voltammograms (in DMF with 0.10 M $[n\text{-}Bu_4N][BF_4]$, Pt electrode, scan rate 0.100 V s^{-1}): (a) $[Ph_4P][MoOSL]$ (**1**); (b) *trans*-MoO(SH)L (**2**).

Mo—S bonds. While a strong peak is observed in the IR spectrum of **1** at 526 cm^{-1}, the region expected for Mo=S,[6] $[Ph_4P]^+$ also absorbs strongly at 527 cm^{-1}. Several weak to medium peaks are seen for **1** in the region from 500 to 360 cm^{-1}, possibly arising from Mo—S bonds;[7] MoO_2L, *trans*-MoO(SH)L, and $[Ph_4P]^+$, however, also absorb in this region, precluding an unequivocal assignment. While the electronic structure of **1** is unknown, the unpaired electron is likely to be in a π^* antibonding orbital de-

(4) The preparation of $[Ph_4P][MoOSL]$ (**1**) was as follows. A solution of MoO_2L (0.30 mmol in 20 mL of anhydrous THF) was added to a solution of $[n\text{-}Bu_4N]SH$ (2.60 mmol in 20 mL of THF containing a few drops of MeCN). After the mixture was stirred for 3 h, the volume was reduced to 10 mL, a solution of $[Ph_4P]Cl$ (1.50 mmol in 10 mL of MeOH) was added, and stirring was continued for 3 h. The volume was reduced to 10 mL, and 10 mL of H_2O was added. The dark brown precipitate was collected by filtration, washed with EtOH, and recrystallized from THF/hexane. Anal. Calcd for $C_{40}H_{38}MoN_2OPS_3$: C, 61.14; H, 4.87; N, 3.56; P, 3.94; S, 12.24. Found: C, 60.96; H, 5.16; N, 3.53; P, 4.12; S, 12.19. IR: 926 cm^{-1} (Mo=O); strong absorption is observed at 526 cm^{-1}, the region expected for Mo=S; $[Ph_4P]^+$ also absorbs strongly in this region, however, precluding an unambiguous assignment. Electronic spectrum (λ, nm (log ε ($L\ mol^{-1}$) cm^{-1}))): 554 (3.52), 410 (3.79). The preparation of *trans*-MoO(SH)L (**2**) was as follows. A solution of MoO_2L (10 mmol in 10 mL of THF) was added to a solution of $[n\text{-}Bu_4N]SH$ (100 mmol in 5 mL of THF with a few drops of MeCN). After the mixture was stirred for 4 h, 500 mmol of CF_3COOH in 2 mL of THF was added and stirring was continued for 16 h. A 1-mL aliquot of the CF_3COOH solution was added and stirring continued for 20 h. The solvent was removed under vacuum. The viscous residue was dissolved in 80 mL of CH_2Cl_2; the solution was washed with 2 × 15 mL of H_2O and dried over Na_2SO_4. The solvent was removed under vacuum, 50 mL of Et_2O was added, and the volume was reduced to 25 mL. Standing overnight at −20 °C gave dark purple microcrystals, which were collected by filtration, washed with Et_2O, and dried under vacuum. Anal. Calcd for $C_{16}H_{19}MoN_2OS_3$: C, 42.95; H, 4.28; N, 6.26; S, 21.50. Found: C, 43.08; H, 4.39; N, 6.28; S, 21.55. IR: 931 cm^{-1} (Mo=O). Electronic spectrum (λ, nm (log ε ($L\ mol^{-1}$ cm^{-1}))): 552 (3.49), 404 (3.66). All solvents were anhydrous, and operations were carried out in Schlenk apparatus or a glovebox under N_2 or Ar.

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localized to some extent on S (the *g* values are significantly larger and the *A* values smaller for **1** than for $[MoO_2L]^-$); this would increase the Mo—S bond length beyond that found for Mo(VI) complexes having the oxo–sulfido core. The heterogeneity in Mo—S bond lengths implied by the large EXAFS Debye–Waller factor is compatible, for example, with the presence of two Mo—S thiolate bonds of ~2.40 Å and one shorter Mo—S bond. The EPR data for **1** in solution indicate MoO(SH)L, rather than MoS(OH)L, is obtained upon protonation,[2] a result expected if a weakly π-bonded S (as compared to the strongly π-bonded oxo) is present. It should also be noted that recent EXAFS results from rapid-freeze experiments on XO provide no evidence for a Mo=S bond in the reduced state of the enzyme[1d] and the Rapid type 1 EPR signal of the enzyme is believed to arise from a MoO(SH) center.[1b-d,g] These considerations suggest the terminal Mo—S bond in **1** in the solid is significantly longer than the terminal Mo=S bond of the few reported Mo(VI) and Mo(IV) complexes.[6]

Both the EPR and electronic spectra of **2** in solution are identical with those reported for *trans*-MoO(SH)L obtained from *trans*-MoOClL or by protonation of $[MoOSL]^-$ at room temperature.[2] The EPR spectrum exhibits no ^1H superhyperfine coupling to Mo(V) (in contrast to the EPR spectrum of *cis*-MoO(SH)L obtained by protonation of $[MoOSL]^-$ at low temperature).[2] Lowering the temperature of the solution of *trans*-MoO(SH)L below −40 °C does not change the EPR spectrum, indicating *cis*-MoO(SH)L, generated in solution at −40 °C, is kinetically, rather than thermodynamically, stabilized at low temperature.[2] Treatment of **2** with 1 equiv of $[n\text{-}Bu_4N]OH$ gives a solution having an EPR spectrum identical with that of $[MoOSL]^-$.

The K-edge EXAFS transform of **2** (Figures 1 and 2, Table I) indicates the presence of 1 Mo=O bond, 3–4 long Mo—S bonds, and 1 Mo—N(O) bond, consistent with its formulation as MoO(SH)L.

The cyclic voltammogram (CV) for **1** shows a quasi-reversible one-electron-oxidation process centered at −0.62 V vs SCE (Figure 4, Table II). The oxidation is most likely to $Mo^{VI}OSL$. The CV of **2** shows an electrochemically irreversible reduction process centered at −0.73 V vs SCE; no oxidation process in the voltage range −0.40 to +0.50 V vs SCE was observed (Figure 4, Table II).

The electrochemical and EPR results for **1** and **2** are summarized in Scheme I. Since the oxo and sulfide ligands of **1** are almost certainly cis, while the oxo and SH ligands of **2** appear to be trans, a rearrangement must accompany the $[MoOSL]^-$/MoO(SH)L transformation. In fact, upon protonation of $[MoOSL]^-$ in solution at room temperature, a transient blue color, characteristic of *cis*-MoO(SH)L,[2] is observed, indicating the cis isomer is first formed and then rearranges.

Scheme I

$$Mo^{VI}OSL \underset{-e^-}{\overset{+e^-}{\rightleftharpoons}} [Mo^{V}OSL]^- \underset{OH^-}{\overset{H^+}{\rightleftharpoons}} \textit{trans}\text{-}Mo^{V}O(SH)L \underset{-e^-}{\overset{e^-}{\rightleftharpoons}} [Mo^{IV}O(SH)L]^-$$

Coupled electron/proton transfer has been proposed for the Mo center in xanthine oxidase.[1,8] The results reported here support this proposal. We have previously suggested $[MoOSL]^-$ as a model for the Very Rapid EPR signal (which exhibits no ^1H coupling) observed with this enzyme.[2] Recently reported values of the anisotropic $^{95,97}Mo$ coupling constants for the Very Rapid signal by George and Bray,[9] taking into account noncoincidence of the **g** and **A** tensors (Euler angle), indicates a pattern different from that observed for $[MoOSL]^-$. These authors report an equally good simulation of the EPR spectrum of $[MoOSL]^-$ is obtained, however, using a noncoincidence angle of 35° and a set of $^{95,97}Mo$ *A* values having a pattern quite similar to that of the Very Rapid signal. This has been confirmed by simulation in this laboratory (Table II). Because of the great rhombicity of this signal, measurement at low frequencies using ^{95}Mo-enriched samples will be necessary to obtain correct values. It is interesting that the *g* values for the Mo(V) EPR signal of *trans*-MoO(SH)L (Table I) are remarkably close to those of the Very Rapid signal and the *A* values display a similar pattern.[9,10] The measurement of ^{33}S coupling constants for **1** and **2** should provide additional structural data for interpreting the enzyme signals. The results, however, clearly support the presence of both sulfide and hydrogensulfide ligands at the Mo center of xanthine oxidase and confirm the solution results for MoO_2L previously reported.[2] Work to obtain ^{95}Mo-, ^{17}O-, and ^{33}S-substituted complexes as well as $Mo^{VI}OSL$ and *cis*-$Mo^{V}O(SH)L$ is under way and will be reported later.

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Note Added in Proof. The EPR parameters for **1** with a 35° noncoincidence angle between **g** and **A** tensors have been confirmed at 3.600 and 2.333 GHz.[12]

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