Communications to the Editor

Reactions of $Mo_2O_4^{2+}$ with Mercaptans and Implications for Molybdoenzymes

Sir:

There is evidence to suggest that the molybdenum-containing site(s) in molybdoenzymes interacts with the substrate and is also monomeric in nature. However, all such enzymes which have been reasonably characterized contain two molybdenum atoms per mole. Similarly, many molybdenum complexes used as enzyme models exist as dimers but are believed to cleave to produce catalytically active monomers.[1-3] We have investigated the reactions of the $Mo_2O_4^{2+}$ unit in di-μ-oxo-bis[oxo-*N*,*N*-diethyldithiocarbamatomolybdenum(V)], $[MoOL]_2O_2$ (ref 4), as probes for elucidating the pathways by which these bridged systems may be modified or cleaved (see Figure 1). Three distinct reaction types occur: (a) substitution of bridging and/or terminal oxo groups, with the structure remaining intact; (b) bridge modification reactions; and (c) bridge cleavage to produce monomers. The last reaction may remove either bridging oxo groups to produce pentacoordinate oxomolybdenum(V) monomers or all oxo groups to produce hexacoordinate molybdenum(V) monomers.[5] Such bridge cleavage reactions may be important in both the natural and model catalytic systems. A critical feature of all these new reactions is the requirement for sulfur on the incoming reagent.

Reactions of type (a) occur with H_2S and P_4S_{10}. One μ-oxo group only is replaced by μ-sulfido on reaction with H_2S (1 mol) at ambient temperature in chloroform solution[6] (reaction i in Figure 1), while excess H_2S produces mixtures of μ-OS and μ-S_2 complexes. However, in boiling chloroform, only $[MoOL]_2OS$ is produced even with excess H_2S (reaction ii). In H_2S-saturated, 1,2-dichloroethane solution at 80° in a bomb (reaction iii), complete substitution of μ-oxo or di-μ-oxo groups occurs. With P_4S_{10} in boiling xylene, both terminal and bridging (when present) oxo groups are replaced giving $[MoSL]_2S_2$ (reaction iv).[8] Extraction with CH_2Cl_2 and crystallization gives $[MoSL]_2S_2$ (32% yield) in an improved procedure over that originally reported.[9]

Two bridge modification reactions (type b) occur, both resulting in the loss of one μ-oxo group. Reaction v with QH (Q = R_2NCS_2,[1] R_2PS_2) in 1:1 $CHCl_3$-CH_3OH at 25° gives $[MoOLQ]_2O$, while thiols (RSH; R = Me, Et, Ph) in dichloromethane give[10] $[MoOL]_2O(SR)_2$ (see reaction x in Figure 1). A bridging environment for the mercaptide groups is postulated based on spectroscopic observations.[11] Similar "three-atom-bridged" products are also formed with excess 2-mercaptoethanol and *o*-mercaptobenzoic acid and with *N*-methylaminobenzenethiol (1 mol) and *o*-mercaptophenol (1 mol), where each acts as a μ^2 [either μ^2-OS or μ^2-SN(CH_3)] system (reaction viii). No reaction occurs with phenol, *o*-phenylenediamine, dimethylglyoxime, *o*-aminophenol, or with succinic, maleic, and *o*-hydroxybenzoic acids. Support for this "three-atom-bridged" system comes from a recent x-ray crystallographic study of a very closely related quinolin-8-olato complex.[13]

Complete cleavage of the di-μ-oxo bridge (type c) occurs with *o*-mercaptophenol (2 mol) in CH_2Cl_2 at 25° to give ~20% yield[14] of pentacoordinate MoOL(*o*-C_6H_4OS) with ν(Mo═O) at 930 cm^{-1}, in addition to some $[MoOL]_2O$(*o*-C_6H_4OS) (reaction vii). An excess of some other ortho-substituted benzenethiols (reaction vi) in CH_2Cl_2 at 25 °C gives a second type of monomeric species MoL(*o*-C_6H_4XS)$_2$ (X = S, NH, N(CH_3)[15]). Similar complexes have been postulated to exist in solution (from EPR studies[16]) but have not previously been isolated and characterized. The amino proton was found to be labile, exchanging rapidly with MeOD in CH_2Cl_2.[17] Chemical and EPR studies on these products are reported separately.[18]

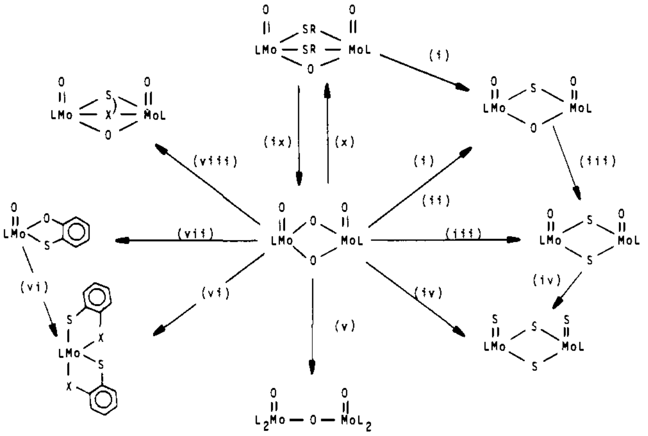

Figure 1. Reactions of $Mo_2O_4L_2$ and interrelationships of products: (i) H_2S (1 mol) in CH_2Cl_2 at 25°; (ii) excess H_2S in boiling $CHCl_3$; (iii) excess H_2S in 1,2-$C_2H_4Cl_2$ at 80 °C in bomb; (iv) P_4S_{10} in boiling xylene; (v) NaL or R_2PS_2H in 1:1 $CHCl_3$/MeOH at 25°; (vi) excess ortho-substituted benzenethiol [*o*-C_6H_4(XH)SH; X = S, NH, N(CH_3)] in CH_2Cl_2 at 25°; (vii) *o*-mercaptophenol (2 mol) in CH_2Cl_2 at 25°; (viii) *o*-C_6H_4(XH)SH [X = O, N(CH_3)] (1 mol), excess *o*-C_6H_4(SH)CO_2H or excess 1,2-C_2H_4(SH)OH in CH_2Cl_2 at 25 °C; (ix) C_5H_5N/H_2O in $CHCl_3$ at 25 °C; (x) excess RSH (R = Me, Et, Ph) in CH_2Cl_2 at 25 °C.

Various interconversions are possible and those for $[MoYL]_2X_2$ (Y = O, X_2 = O_2, S_2, OS; and Y = X = S) are shown in Figure 1. Successive substitution of oxo by sulfido occurs until $[MoSL]_2S_2$ is produced. This last species is inert to O_2 and H_2O and, as yet, the bridging and/or terminal sulfido groups have not been removed from such compounds without causing extensive decomposition. MoOL(*o*-C_6H_4OS) reacts with excess *o*-dimercaptobenzene or *o*-aminobenzenethiol in CH_2Cl_2 at 25 °C to give MoL(*o*-C_6H_4XS)$_2$ (X = S or NH) (reaction vi). However, $[MoOL]_2O$(*o*-C_6H_4OS) does not give MoOL(*o*-C_6H_4OS) with excess *o*-mercaptophenol; i.e., cleavage to monomers surprisingly does not occur, suggesting that the triply-bridged complex is not an intermediate in the cleavage pathway. H_2S (1 mol) does not react with MoL(*o*-$C_6H_4S_2$)$_2$ or with $[MoOL]_2OX$ (X = 1,2-C_2H_4OS, *o*-C_6H_4OS) under argon in CH_2Cl_2 within 20 h at 25 °C, but the similar reaction with $[MoOL]_2O(SR)_2$ produces $[MoOL]_2OS$ and RSH (2 mol) (reaction i). Analogous reactivity toward hydrolysis is also found, with only $[MoOL]_2O(SR)_2$ hydrolyzing (slowly) in wet chloroform at 25 °C to produce $[MoOL]_2O_2$. The hydrolysis occurs rapidly if a few drops of pyridine are added (reaction ix).

The remarkable outcome from these experiments is the ease with which oxo groups are removed from molybdenum. Oxo groups have been removed by atom transfer from *cis*-dioxomolybdenum(VI) by reaction with tertiary phosphines[19] and from molybdenum(IV) and -(VI) by protonation with strong acids.[20-22] The reactions reported herein show that acidity per se is not a necessary prerequisite because, e.g., RSH (R = Me, Et, Ph; pK_a = 6.5–10.6)[23] removes a μ-oxo group from $Mo_2O_4^{2+}$, while phenol (pK_a = 10.0)[23] does not. Of comparable importance, then, is the nucleophilicity of sulfur and the subsequent binding of additional ligands. Further, mercaptans easily remove terminal oxo groups, producing non-oxo molybdenum(V) monomers from $Mo_2O_4^{2+}$, i.e., stripping the molybdenum completely of both bridging and terminal oxo groups. All the successful reactions described above involve -SH groups; if such groups are omitted, the molybdenum complex is recovered unchanged. The aqueous chemistry of molybdenum, particularly in its higher oxidation states, is dominated by oxo-containing species produced from water, but its nonaqueous chemistry may well be equally dominated by the mercaptan, with the formation of sulfur-coordinated species and the occurrence of molybdenum-catalyzed reactions of mercaptans with various substrates.[24] As the Mo-containing sites of enzymes may be hydrophobic in nature, these studies reveal a host of interesting possibilities for their modes of reaction.

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References and Notes

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(2) G. N. Schrauzer, *J. Less-Common Met.*, **36**, 475 (1974); *Angew. Chem., Int. Ed. Engl.*, **14**, 514 (1975).

(3) P. W. Schneider, D. C. Bravard, J. W. McDonald, and W. E. Newton, *J. Am. Chem. Soc.*, **94**, 8640 (1972).

(4) Throughout this paper, the repeating unit in the dimeric compounds is enclosed in square brackets with the bridging atoms or groups following.

(5) All compounds synthesized in this work have satisfactory elemental analysis and are produced in 70–100% yields (except where otherwise stated). Ir, NMR, and/or EPR also support the formulations shown. All reactions go to completion within 5 h.

(6) $[MoOL']_2OS$ has also been prepared from the reaction of $MoO_2L'_2$ (L' = S_2CN-*n*-Pr_2) with P_4S_{10}, but not with H_2S in the presence of air.[7] In contrast, we isolate only $OMo(S_2)L''_2$ from $MoO_2L''_2$(L'' = S_2CNMe_2) and P_4S_{10} anaerobically in benzene while Weiss et al. produce $OMo(S_2)L'_2$ from $MoO_2L'_2$ and H_2S in acetone under air.[7]

(7) J. Dirand, L. Ricard, and R. Weiss, *Inorg. Nucl. Chem. Lett.*, **11**, 661 (1975); *Inorg. Chim. Acta*, **18**, L21 (1976).

(8) Those compounds containing terminal molybdenum–oxygen bonds have the two typical[1] infrared absorptions at ~965 cm^{-1}, which are replaced in $[MoSL]_2S_2$ by a similar doublet at ~540 cm^{-1}. ν(MoOMo) occurs at ~730 cm^{-1} in the μ-O_2 complex[1] and at ~710 cm^{-1} in the μ-OS complex. No absorption occurs in this region in the μ-S_2 analogue.

(9) T. Sakurai, H. Okabe, and H. Isoyama, *Bull. Jpn. Pet. Inst.*, **13**, 243 (1971); B. Spivak, Z. Dori, and E. I. Stiefel, *Inorg. Nucl. Chem. Lett.*, **11**, 501 (1975).

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(11) If only the oxo group were bridging, then a linear MoOMo system (as in $[MoOL_2]_2O$) is most likely, which should absorb at ~510 nm. These compounds are yellow-orange and do not absorb between 450 and 700 nm. Further, their ir Mo═O absorptions are typical of nonlinearly bridged molybdenum(V) dimers,[1,12] e.g., $[MoOL]_2O_2$, but are lowered by ~40 cm^{-1} to ~940 cm^{-1}. The weak ir band at ~750 cm^{-1} is reminiscent of a single μ-oxo group. These data suggest a bent MoOMo system, probably imposed by other bridging groups. The mercaptides occupy inequivalent positions (two NMR signals are observed at 35 °C in $CDCl_3$), which also supports a bridging function. The μ^2-OS and μ^2-$SN(CH_3)$ products exhibit similar ir properties.

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(14) Yields of ~70% are obtained in this reaction for L = $S_2P(i\text{-}C_3H_7)_2$.

(15) $MoL[o\text{-}C_6H_4SN(CH_3)]_2$ is obtained in 50% yield from the filtrate after removal of precipitated $[MoOL]_2O[o\text{-}C_6H_4SN(CH_3)]$.

(16) I. F. Gainulin, N. S. Garif'yanov, and V. V. Trachevskii, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 2176 (1969).

(17) The complexes $MoL(o\text{-}C_6H_4XS)_2$ are too insoluble for molecular weight determinations, but their formulation is supported by their EPR spectra.[18] They show no ir absorption assignable to ν(Mo═O) between 900 and 1000 cm^{-1}. With X = NH, ν(NH) is observed at 3290 cm^{-1}, which shifts to 2410 cm^{-1} on deuteration.

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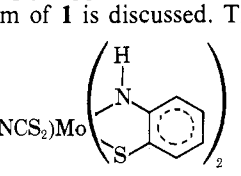
Monomeric Molybdenum(V) Complexes Showing Hydrogen-1, Hydrogen-2, and Nitrogen-14 Superhyperfine Splitting in Their Electron Paramagnetic Resonance Spectra. Implications for Molybdenum Enzymes

Sir:

An electron paramagnetic resonance (EPR) signal characteristic of molybdenum(V) has been found in all molybdoenzymes which catalyze substrate oxidation.[1,2] Under certain conditions, near isotropic superhyperfine splitting from a single proton is clearly resolved. These results are particularly significant because the hydrogen responsible for this splitting in xanthine oxidase has been shown to originate in the substrate.[3] Evidence indicates that this proton is transferred from substrate to enzyme in conjunction with the flow of two electrons in the same direction.[4,5] Mechanistic schemes based on these results have been suggested for xanthine oxidase[4-6] and other molybdoenzymes.[5-7] Alternate suggestions favor either the location of the exchangeable proton on an N atom ligated to Mo[6,7] or the formation of a molybdenum hydride.[4] Evaluation of the feasibility of these suggestions requires EPR analysis of simple Mo(V) complexes wherein the magnitude of proton and nitrogen superhyperfine couplings can be assessed. Although proton couplings have previously been reported for Mo complexes,[8-10] these have been for species in solution[8,9] or for ill-defined reaction products[10] and no isolated and stoichiometrically distinct compounds which display this property have been studied. This communication describes our results in which both proton and nitrogen superhyperfine splittings have been resolved for isolated Mo(V) compounds. The magnitude of the coupling constants and the observed proton exchangeability are consistent with previous proposals made for Mo enzymes.[5-7] In addition, significant temperature effects on the spectral shape are reported.

The monomeric Mo(V) complexes presented here are prepared by the general procedure of Newton et al.[11] Their EPR spectra (Table I) strongly support the formulas shown. As an example, the spectrum of **1** is discussed. The spectrum, as displayed in Figure 1A, shows hyperfine splitting from the $I = \frac{5}{2}$, ^{95}Mo and ^{97}Mo nuclei (as satellite spectra) although only the central pattern from even Mo isotopes (I = 0) is shown. Superhyperfine splitting is clearly resolved for two equivalent N and two equivalent H atoms confirming both the state of ligation of the complex and the state of protonation of the li-



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