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# Reduction of Tris(benzene-1,2-dithiolate)molybdenum(VI) by Water. A Functional Mo–Hydroxylase Analogue System

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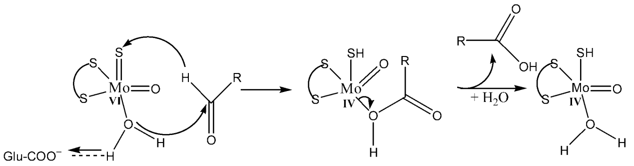
$Mo^{VI}(S_2C_6H_4)_3$ reacts cleanly and completely with $H_2O$ in THF to afford $[H_3O]^+[Mo^V(S_2C_6H_4)_3]^-$. Kinetic data were fit by the rate equation $-d[Mo^{VI}(S_2C_6H_4)_3]/dt = k[Mo^{VI}(S_2C_6H_4)_3]/[H_3O^+]$, which is consistent with a coupled electron–proton transfer mechanism involving a coordinated $H_2O$ molecule. The $Mo^{VI}(S_2C_6H_4)_3$ reduction is accelerated by the presence of $PPh_3$ and affords $OPPh_3$. $^{18}O$ isotope tracing shows that $H_2O$ is the source of oxygen transferred to $PPh_3$.

Molybdenum and tungsten enzymes are referred to as *oxotransferases* when the substrate is transformed by primary oxygen atom transfer and as *hydroxylases* when bound or unbound water or hydroxide is directly involved in the substrate transformation reaction.[1] Although there has been progress in the generation of synthetic and functional analogue systems relevant to *oxotransferases* containing $Mo^{VI}O_2$ (sulfite oxidase) and $Mo^{VI}O$ (DMSO reductase) centers,[1] the dearth of oxo-thio species, $Mo^{VI}OS$, especially any with reactive aqua or hydroxo co-ligands, has provided little opportunity for the development of good chemical models for some characteristic reactions of hydroxylases.[2] The proposed structure-based mechanism for the xanthine oxidase-related aldehyde oxidoreductase indicates that a water ligand is deprotonated by a nearby glutamate basic residue and thus primed to attack the carbonyl carbon atom of the substrate.[3] This would trigger hydroxylation of the carbon center, causing an electron drift into the vacant $Mo^{VI}$ d orbital and reduction to $Mo^{IV}$ (Scheme 1).

We have been studying the reduction of tris-dithiolene complexes of Mo(VI) and W(VI) with tetrabutylammonium hydroxide to develop a mechanistic understanding.[4] Their kinetics are first-order in the concentrations of both complex and $Bu_4NOH$, the rate-limiting step being the coordination of $OH^-$ ion to the metal atom. Mo complexes are more difficult to reduce than their corresponding W complexes, which presumably reflects a better interaction of $OH^-$ with W (bond energy order W−OH > Mo−OH). Presented here is the first systematic investigation of the reduction of a transition-metal dithiolene complex of any type using water as the sole reductant. Enzymatically relevant mechanistic insights follow the kinetic analysis.

**Scheme 1**



When $Mo^{VI}(S_2C_6H_4)_3$ is placed into a THF/water solution, under strict anaerobic conditions, a rapid conversion to $Mo^V(S_2C_6H_4)_3^-$ occurs. Figure 1 shows that $Mo^{VI}(S_2C_6H_4)_3$ is completely consumed and $Mo^V(S_2C_6H_4)_3^-$ is progressively generated in equimolar amounts. The same spectrophotometric change was observed in 1-propanol/water or chlorobenzene/methanol/water, where both complexes have a good solubility. Equation 1 represents this redox interaction,[5] which was found to be accompanied by a drop in pH.

$$2Mo^{VI}(S_2C_6H_4)_3 + H_2O \rightarrow 2[Mo^V(S_2C_6H_4)_3]^- + 2H^+ + {}^1/_2O_2 \quad (1)$$

The evolution of $O_2$ according to eq 1 was measured by GC analysis of the headspace above the reaction mixture. Experiments were carried out using 5−15 mg of complex in 25 mL of argon-purged chlorobenzene/methanol (9:1 v/v) and adding an aqueous solution of phosphoric/phosphate buffer at pH 6.0. Minute amounts of air were detected after the 2-h reaction period. Because all of the $N_2$ observed was from air, we calculated the amount of $O_2$ from air and

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(5) $Mo^{VI}(S_2C_6H_4)_3$ voltammograms in neat THF exhibit two one-electron reversible reductions centered at +610 and −40 mV vs NHE, supporting the three-member $Mo(S_2C_6H_4)_3^{0/1-/2-}$series. Thus, eq 1 is uphill by 0.2 V at pH 7 [$E°(O_2/H_2O) = +0.8$ V in water]. The expected dependence of $E°(O_2/H_2O)$ on solvent nature (THF/water) and oxygen concentration must be more than sufficient to overcome such a low unfavorable energy.

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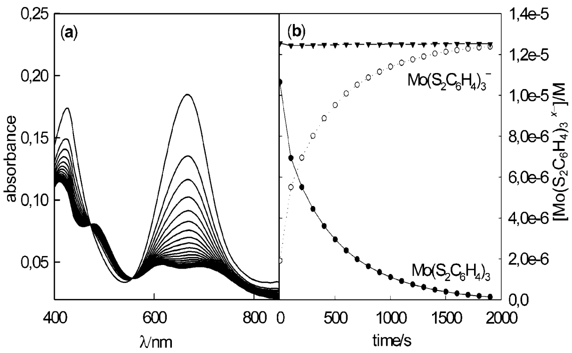


**Figure 1.** (a) Spectral changes during the reaction of $Mo(S_2C_6H_4)_3$ ($1.25 \times 10^{-5}$ M) with $H_2O$ (4.38 M) in THF at 22.5 °C. (b) Concentration vs time curves for the $Mo^{VI}(S_2C_6H_4)_3$ and $Mo^{V}(S_2C_6H_4)_3^-$ complexes obtained from the deconvolution of the spectra shown in part a. The sum of the two curves is always the initial concentration of $Mo^{VI}(S_2C_6H_4)_3$.

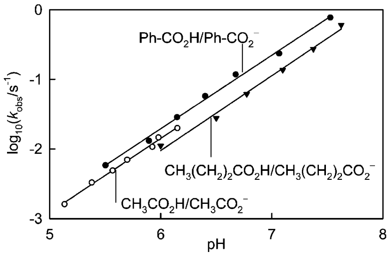


**Figure 2.** Observed logarithmic rate [log ($k_{obs}$)] variation with pH at fixed concentration of water (27.8 M, $pK_w = 15.13$[6]) in buffered media. Sets of kinetic run were performed at 22.0 °C in the three buffers noted.

subtracted this amount from the observed $O_2$ signal. A 60−75% yield was obtained based on eq 1. This might be indicative of some reoxidation of the Mo(V) complex product by the $O_2$ formed (see below). In more reactive THF/$H_2O$ media, there is no $O_2$ evolution.

Reaction rates were measured over a wide range of complex concentrations. Substantial rate retardation and gradual deviation from first order was observed as the initial concentration of $Mo^{VI}(S_2C_6H_4)_3$ was increased. This appears to be a general proton effect because the $H^+$ concentration increases as the reaction progresses (eq 1). The participation of $H^+$ as a moderator becomes evident by analyzing the role of pH with buffered solutions. An excellent fit to first-order kinetics in the $Mo^{VI}(S_2C_6H_4)_3$ concentration was obtained at all pHs for completed reactions. Plots of log $k_{obs}$ vs pH were all linear with the slope of 1 (Figure 2).

The empirical rate law in eq 2

$$r = k\frac{[Mo^{VI}(S_2C_6H_4)_3]}{[H_3O^+]} = k\frac{[Mo^{VI}(S_2C_6H_4)_3]}{[Mo^{V}(S_2C_6H_4)_3^{-}]} \qquad (2)$$

is then deduced in the *absence of buffer* ($[H_3O^+] = [[Mo^V(S_2C_6H_4)_3^-]]$), and there will exist a linear dependence between $r = d[Mo^{VI}(S_2C_6H_4)_3]/dt$ and the $Mo^{VI}(S_2C_6H_4)_3/[Mo^V(S_2C_6H_4)_3^-]$ concentration quotient. The calculation of $r$ values from absorbance ($\lambda$, $t$) surfaces in Figure 1 is available as Supporting Information. The system displays the linear behavior required by eq 2 in all studied THF/water media, as shown in Figure 3.

The kinetic results can be satisfactorily modeled by invoking the coordination and acid−base equilibria in Scheme 2, which are closely related to those in Scheme 1. The $pK_a$ for bound water decreases by 2 units,[7] and water coordination must be followed by deprotonation. There is precedent for such an expansion of coordination number in the chemistry of a $W^{VI}S_6$ tris-chelate.[8]

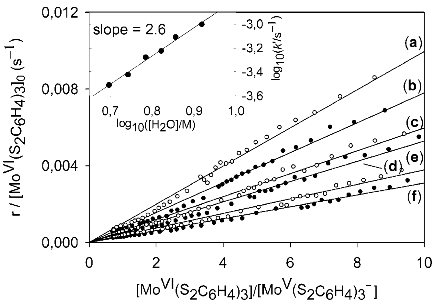
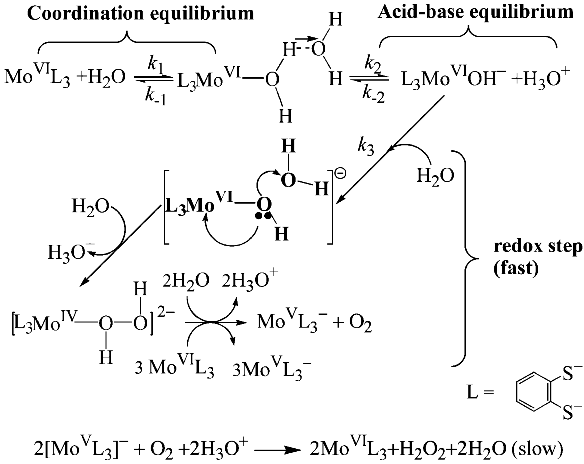


**Figure 3.** $Mo(S_2C_6H_4)_3$ reduction by water in different THF/water media. $[H_2O]$/M: (a) 8.6, (b) 7.2, (c) 6.6, (d) 6.1, (e) 5.5, and (f) 4.9. $T = 22.5$ °C. These plots of $r$ vs $[Mo^{VI}(S_2C_6H_4)_3]/[H_3O^+]$ display the linear behavior required by eq 2.

**Scheme 2**



The pH dependence of the rate constants in Figure 2 clearly indicates that protonation of the coordinated $OH^-$ limits the overall reaction rate. Thus, the redox steps would then involve nucleophilic attack at a solvent water molecule by the metal-bound hydroxide, generating a $H_2O_2$ molecule coordinated to a Mo(IV) center. Such an interaction is apparently too fast to allow kinetic data analysis of the fate of this Mo(IV) species. However, the stable products are $Mo^V(S_2C_6H_4)_3^-$ and $O_2$, which implies that this Mo(IV) intermediate breaks down by one-electron oxidation interacting with unreacted $Mo^{VI}(S_2C_6H_4)_3$. Alternative mechanisms that exclude the formation of Mo(IV) intermediates can also be devised.

A further reaction is also necessary to account for the observation that the decay of the $Mo^{VI}(S_2C_6H_4)_3$ concentration in air-saturated solutions followed no first-order kinetics and was much slower. This result suggests that a mechanism exists for re-forming $Mo^{VI}(S_2C_6H_4)_3$, thus making its decay slower. One possible reaction is oxidation of $[Mo^V(S_2C_6H_4)_3]^-$

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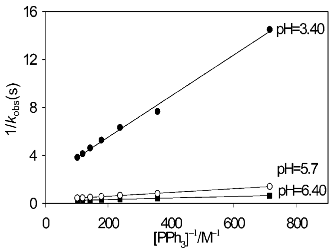

**Figure 4.** Plot of $1/k_{obs}$ vs $1/[PPh_3]$ for the reduction of $Mo^{VI}(S_2C_6H_4)_3$ by $PPh_3$ in buffered $THF-H_2O$ (15.3 M) solutions at 23 °C

by $O_2$, which initially gives $O_2^-$ and subsequently $H_2O_2$[9] (last equation in Scheme 2). It must be noted that $[Mo^V(S_2C_6H_4)_3]^-$ itself can be oxidized by air to $Mo^{VI}(S_2C_6H_4)_3$, but this takes place much more slowly than $[Mo^V(S_2C_6H_4)_3]^-$ formation from water and $Mo^{VI}(S_2C_6H_4)_3$ (see Supporting Information).

Equation 3 is the rate law obtained by applying the steady-state approximation to all intermediates in Scheme 2.

$$r = \frac{k_1k_2k_3[H_2O]^3[Mo^{VI}(S_2C_6H_4)_3]}{k_{-1}k_{-2}[H_3O^+] + k_3(k_{-1} + k_2[H_2O])[H_2O]} \qquad (3)$$

The magnitude of the pH-dependent component in the denominator of eq 3 must be dominant because experimental data indicate that the reaction rate is proportional to the $Mo^{VI}(S_2C_6H_4)_3/[Mo^V(S_2C_6H_4)_3^-]$ concentration quotient, which is equal to $[Mo^{VI}(S_2C_6H_4)_3]/[H_3O^+]$. Thus, eq 3 reduces to $r \approx k_3K_1K_2[H_2O]^3[Mo^{VI}(S_2C_6H_4)_3]/[H_3O^+]$. This rate expression leads us to expect that the value of $k$ in eq 2 increases with the third power of the water concentration. We have examined this dependence and found that a straight line of slope ~3 is obtained when log $k$ values are plotted vs $\log[H_2O]_0$ (see inset in Figure 3).

Finally, we have used triphenylphosphine as a far stronger oxygen acceptor than free water. $PPh_3$ is a common substrate that is proposed to attack Mo═O groups in nonbiological oxygen atom transfer reactions.[1] We wished to examine the kinetics and compare the results with the $2Mo^{VI}O_2^{2+} \rightarrow (OMo^V)_2O^{4+}$ reduction by $PPh_3$.

$Mo^{VI}(S_2C_6H_4)_3$ is unaffected by $PPh_3$ in anhydrous THF. However, if water is present at reactant rather than solvent concentrations, the $Mo^{VI}(S_2C_6H_4)_3$ reduction proceeds faster than the reduction by water observed in the absence of $PPh_3$. This behavior is consistent with the oxygen transfer mechanism shown in eq 4.

$$(S_2C_6H_4)_3Mo^{VI}\ddot{\underset{\cdot\cdot}{O}}H^- + PPh_3 \xrightarrow{k'_3} [Mo^{IV}(S_2C_6H_4)_3]^{2-} + H^+ + OPPh_3 \quad (4)$$

Complementary information from HPLC and GC/MS confirms that $OPPh_3$ is formed in stoichiometric yield under anaerobic conditions. Moreover, under aerated conditions, $PPh_3$ was completely converted to the oxide even when its initial concentration was 10 times the initial concentration of complex. Such an observation confirms the occurrence of $[Mo^V(S_2C_6H_4)_3]^-$ reoxidation by $O_2$ above. Importantly, mass spectral results showed that, in $THF/H_2{}^{18}O$ solutions and in the presence of $^{16}O_2$, all of the $OPPh_3$ produced was $^{18}O$-labeled.

As observed in the absence of $PPh_3$, complicated kinetics were found if the pH was not maintained. However, the reaction is first-order in Mo(VI) complex in buffered solutions at all pHs in excess of $PPh_3$. This is an expected result if the reaction proceeds via phosphine attack on the hydroxo ligand (eq 4). The rate law derived from this mechanism is of the same form as that from Scheme 2 (eq 3), but now $k_{obs}$ is given by (see Supporting Information)

$$k_{obs} = \frac{k_1k_2k'_3K_{HB}[H_2O][PPh_3]}{k_{-1}k_{-2}[H_3O^+] + k'_3K_{HB}(k_{-1}/[B^-] + k_2)[PPh_3]} \qquad (5)$$

Therefore, a plot of $1/k_{obs}$ vs $1/[PPh_3]_0$ should give a straight line with $[H_3O^+]/(k'_3K_1K_2K_{HB}[H_2O])$ as the slope. This double-reciprocal plot is shown in Figure 4 at several pHs. The slopes confirm the expected dependence of the $1/k_{obs}$ values on the hydronium concentration.

$PPh_2Me$, a more basic phosphine, was also employed under the same conditions as $PPh_3$. The reaction was quite a bit faster, as expected from the postulated nucleophilic attack on the hydroxo group by phosphine (eq 4).

The reaction of $MoO_2(S_2CNEt_2)_2$ and $PPh_3$ in 1,2-dichloroethane is the fastest for which kinetic data are available ($k = 7.1 \times 10^{-2}$ $M^{-1}$ $s^{-1}$; $T = 25$ °C).[10] Comparison with the current system indicates that this reaction rate is, depending on the pH and the water concentration, *3 or 4 orders* of magnitude lower.

On the basis of this work, it appears that reduction of $Mo^{VI}$ centers in enzymes can be greatly facilitated through hydration, followed by coupled electron−proton transfer reactions, rather than direct oxygen atom transfer from a $Mo^{VI}$═O group.

As a final point of interest, the chemical reactivity of $W^{VI}(S_2C_6H_4)_3$ with water was examined. Kinetic data indicate that this reaction is analogous to the above reduction of $Mo^{VI}(S_2C_6H_4)_3$ by water, although the reaction is faster with tungsten. A similar difference has been previously found in their reductions by $Bu_4NOH$.[4]

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**Supporting Information Available:** Kinetic measurements, dioxygen analysis apparatus and procedure, calculation of concentration vs time curves and reaction rates, derivation of rate law for reaction of $Mo^{VI}(S_2C_6H_4)_3$ with water, reaction of $Mo^V(S_2C_6H_4)_3^-$ with dioxygen. This material is available free of charge via the Internet at http://pubs.acs.org.

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