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Isomerization and Oxygen Atom Transfer Reactivity in Oxo–Mo Complexes of Relevance to Molybdoenzymes

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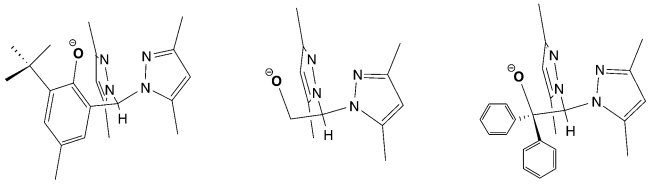
Both dioxo Mo(VI) and mono-oxo Mo(V) complexes of a sterically restrictive N_2O heteroscorpionate ligand are found to exist as *cis* and *trans* isomers. The thermodynamically stable isomer differs for the two oxidation states, but in each case, we have isolated the kinetically labile isomer and followed its isomerization to the thermodynamically stable form. The Mo(VI) complex is more stable in the *cis* geometry and isomerizes more than 6 times faster than the Mo(V) complex, which prefers the *trans* geometry. In OAT reactions with PPh_3, the *trans* isomer of the dioxo–Mo(VI) reacts ~20 times faster than the *cis* isomer. Thus, there are both oxidation state and donor atom dependent differences in isomeric stability and reactivity that could have significant functional implications for molybdoenzymes such as DMSO reductase.

The majority of the mononuclear molybdenum containing enzymes have the general function of catalyzing a net oxygen atom transfer (OAT) to or from a physiological donor/acceptor with the metal cycling between the +6 and +4 oxidation states. They can be conveniently divided into three major groups based on the structure about the metal center, all of which include one or more pterin cofactors.[1] Among the three families, the DMSO reductase family is the most diverse where in addition to the pterin based ligands, the metal center is often coordinated by endogenous ligation from a serine alkoxide oxygen, a cysteinyl thiolate sulfur, or a carboxylate oxygen from aspartate.

Model chemistry has been of particular value in understanding the structure and mechanism of these molybdoproteins. In particular, detailed investigations using the symmetric tris(pyrazolyl)borate Tp^R ligands as a platform have resulted in systems that mimic the majority of the enzymatic processes and the states of the molybdenum centers.[2−6] We have developed a series of polyfunctional, facially coordinating, tridentate ligands containing two pyrazole groups, which also incorporate another biologically relevant donor (e.g., thiolato sulfur as in cysteine, alkoxo oxygen as in serine, carboxylato oxygen as in aspartate, etc.) to produce heteroscorpionate ligands with a similar topology and charge as Tp^R.[7]

Scheme 1. Ligands Refered to in This Study



Recent studies on molybdoenzymes and analogue systems suggest that geometric isomerization at the metal center may contribute to enzymatic function.[8−12] In this regard, the unsymmetrical N_2X ligands provide an excellent opportunity to selectively probe the effect such isomerization may have on fundamental parameters such as stability, redox potential, and atom transfer chemistry. Complexes of the type $[LMoO_xZ_y]$, where L is an N_2X ligand (Scheme 1), can exist

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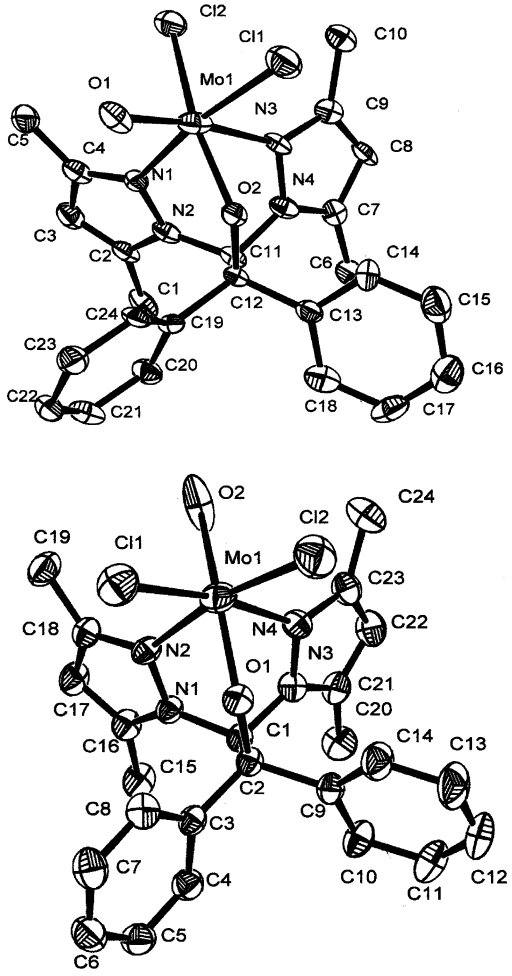

Figure 1. Thermal ellipsoid diagram of [(L10O)$MoOCl_2$], upper (*cis*), and lower (*trans*). The ellipsoids are drawn at the 40% probability level.

in two isomeric forms where the X group is positioned either *cis* or *trans* relative to an oxo group. In this report, we demonstrate for the first time, using a sterically restricted alkoxy funtionalized heteroscorpionate ligand, that both the mono-oxo Mo(V) and dioxo Mo(VI) complexes exist in isolable *cis* and *trans* isomeric forms. The two oxidation states exhibit both different thermodynamic preferences and kinetic ease of *cis/trans* isomerization.

Purification of the as-isolated Mo(V) complex [(L10O)-$MoOCl_2$] by adsorption chromatography on silica gel using dichloromethane as an eluant produces two colored bands, an initial green band of the *cis* isomer followed by a purple band of the *trans*. The stereochemical assignments of the green and purple species have been confirmed by X-ray structural analyses (Figure 1).[13,14] We have already reported

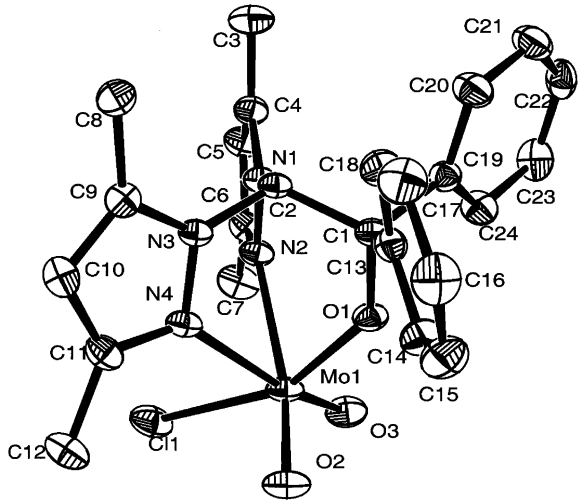

Figure 2. Thermal ellipsoid diagram of *cis*-[(L10O)MoO_2Cl]]. The ellipsoids are drawn at the 40% probability level.

in a related series of complexes that the *cis* isomer spontaneously isomerizes to the *trans*, and this process is associated with distinctive changes in the optical spectra.[9] The current system follows a similar path. Rate constants were determined by monitoring the reaction in DMSO using UV−vis spectrophotometry at 530 and 710 nm. Tight isosbestic points were observed throughout the reaction. The isomerization follows a first-order process, indicating a unimolecular reaction, and the first-order rate constants (Supporting Information), obtained from nonlinear fits to the data, were used to determine the activation parameters. An enthalpy (23 ± 2 kcal/mol) and the entropy (−10 ± 1 cal/mol K) of activation were determined from the Eyring relation.

The *cis* and *trans* isomers of the Mo(VI) complex [(L10O)-MoO_2Cl] were also separated by chromatography on silica gel. The stable *cis*-isomer was eluted first, while the kinetically labile *trans* isomer followed. The two stereoisomers are easily distinguished by NMR since the *cis* isomer is symmetric and shows only a single pyrazole proton resonance at 5.96 ppm while the *trans* isomer is asymmetric and shows two pyrazole peaks in a 1:1 ratio at 6.05 and 5.90 ppm. When a solution of the *trans* isomer is allowed to stand for several days, peaks associated with this complex are lost, with a concomitant increase in the peaks associated with the *cis* isomer. The solid-state molecular structure for the *cis* isomer has been determined (Figure 2).[15] The isomerization of *trans*-[(L10O)MoO_2Cl] to *cis*-[(L10O)MoO_2Cl] was followed by ^{1}H NMR in DMSO-d_6 over the temperature range 35−60 °C. The measured rates give rise to an enthalpy of activation of 19 ± 2 kcal/mol and entropy of activation of −17 ± 1 cal/mol K. These activation parameters are near to those determined for the Mo(V) complex and are suggestive of a similar (twist) reaction mechanism.[11,12] At 60 °C, the rate of isomerization of the Mo(VI) complex (2.9(3) × 10^{-4}

(13) Crystal data for *cis*-[(L10O)$MoOCl_2$]: $C_{24}H_{25}N_4O_2Cl_2Mo$, M = 568.3, monoclinic, a = 19.1477(10) Å, b = 15.6625(8) Å, c = 17.5373(9) Å, α = 90°, β = 116.015(5)°, γ = 90°, V = 4726.6(4) Å^3, T = 100-(2) K, space group $P2_1/c$, Z = 8, μ(Mo Kα) = 0.811 mm^{-1}, 32031 reflections measured, 4961 unique (R_{int}= 0.0663) which were used in all calculations, final R1 = 0.0649, wR2 (on F^2) = 0.1068 (all data).

(14) Crystal data for *trans*-[(L10O)$MoOCl_2$]·2DMF: $C_{30}H_{39}N_6O_4Cl_2Mo$, M = 714.51, triclinic, a = 8.7513(6) Å, b = 13.6366(9) Å, c = 14.8639(10) Å, α = 72.021(1)°, β = 73.220(1)°, γ = 80.756(1)°, V = 1610.4(2) Å^3, T = 213(2) K, space group $P1$, Z = 2, μ(Mo Kα) = 0.618 mm^{-1}, 11908 reflections measured, 7285 unique (R_{int} = 0.0239) which were used in all calculations, final R1 = 0.0852, wR2 (on F^2) = 0.1968 (all data).

(15) Crystal data for *cis*-[(L10O)MoO_2Cl]: $C_{24}H_{25}N_4O_3ClMo$, M = 548.87, monoclinic, a = 9.7589(6) Å, b = 15.5178(10) Å, c = 15.4080(9) Å, α = 90°, β = 94.171(1)°, γ = 90°, V = 2327.2(2) Å^3, T = 213(2) K, space group $P2_1/n$, Z = 4, μ(Mo Kα) = 0.713 mm^{-1}, 16668 reflections measured, 5482 unique (R_{int}= 0.0274) which were used in all calculations, final R1 = 0.0429, wR2 (on F^2) = 0.0955 (all data).

s^{-1}) was over 6.5 times faster than that for the corresponding Mo(V) complex ($4.4(1) \times 10^{-5}$ s^{-1}). Thus, there are both oxidation state and donor atom dependent differences in isomeric stability.

The effect of geometry on the rate of oxygen atom transfer reactions has been probed by reacting both the *cis* and *trans* isomers of [(L10O)MoO_2Cl] with a large excess of PPh_3 at 30 °C in pyridine. The initial products in these reactions are $OPPh_3$ and [(L10O)MoO(py)Cl] as determined by NMR and UV−vis spectrophotometry. Although we have yet to crystallographically characterize the geometry of the Mo(IV) product from this reaction, the complex isolated from an OAT reaction conducted under similar conditions using the related *cis*-[(L1O)MoO_2Cl] has been characterized as the *trans* isomer of [(L1O)MoO(py)Cl]. When the OAT reaction was followed at 700 nm for pure *cis*-[(L10O)MoO_2Cl], a single slow exponential growth was observed giving a k_{obs} of 0.0011(2) min^{-1}. However, the same reaction with a preparation that was greater than 90% *trans* isomer gave a k_{obs} of 0.024(4) min^{-1}. Thus, the rate of OAT for the *trans* isomer is more than 20 times faster than that of the *cis*. It should be noted that at 30 °C the rate of *trans*/*cis* isomerization is much slower than either of the OAT reactions. DFT calculations on the computationally less expensive, but otherwise comparable, L5O ligand (lacking the pendant phenyl rings) predict that in the *trans* isomer one of the Mo═O bonds (the one trans to the alkoxide) will be elongated and therefore presumably weakened by the *trans* influence of the competing alkoxy oxygen. Such an oxo group might be expected to undergo more rapid OAT. Clearly, the nature of the ligand trans to the oxo groups in dioxo−Mo(VI) centers provides an electronic means to select between them.

In conclusion, while we do not propose these complexes as exact structural models for any specific molybdoenzyme, we show that there are oxidation state and donor atom dependent differences in isomeric stability and reactivity and believe that these could have important functional implications for the whole class of such proteins.

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Note Added after Print Publication: The version of this paper published on the Web November 3, 2004 (ASAP), and in the November 29, 2004, print issue incorrectly identified two of the authors' current addresses. The corrected electronic version of this paper was posted on December 14, 2004, and an Addition and Correction appears in the January 10, 2005, issue (Vol. 44, No. 1).

Supporting Information Available: X-ray crystallographic files (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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