

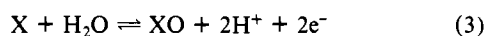
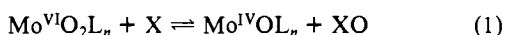
A Model for the Active Sites of Oxo-Transfer Molybdoenzymes: Synthesis, Structure, and Properties

Jeremy M. Berg¹ and R. H. Holm*

Contribution from the Department of Chemistry, Harvard University, Cambridge, Massachusetts 02138. Received August 9, 1984

Abstract: Development of models for the active sites of oxo-transfer molybdoenzymes has been initiated. Suitable models should be capable of oxygen atom transfer to or from the substrate, approach the native coordination unit, and be inert to formation of μ -oxo Mo(V) dimers. Toward this end, the sterically hindered ligands 2,6-bis(2,2-diphenyl-2-hydroxyethyl)pyridine (LN(OH)₂) and 2,6-bis(2,2-diphenyl-2-mercaptoethyl)pyridine (LN(SH)₂) and their Mo(VI) complexes MoO₂(LNO₂)(Me₂SO) (**1**) and MoO₂(LNS₂) (**2**) have been synthesized. Compound **1** crystallizes in the monoclinic space group $P2_1/c$ with $a = 8.738$ (2) Å, $b = 17.799$ (4) Å, $c = 19.927$ (3) Å, $\beta = 93.77$ (1)°, and $Z = 4$. The complex has a distorted octahedral structure with meridional ligand coordination; oxo atoms are cis and cis to trans alkoxide ligands. The very large Mo-O-C angles of 137° and 142° are indicative of strained chelate rings. Compound **2** crystallizes in the orthorhombic space group $P2_12_12_1$ with $a = 8.910$ (2) Å, $b = 16.350$ (4) Å, $c = 19.193$ (5) Å, and $Z = 4$. This complex affords the first example of a five-coordinate dioxo Mo(VI) species, which is a distorted trigonal bipyramid with axial thiolate ligands and the nitrogen and oxo groups in the equatorial plane. In **1** and **2** the *gem*-diphenyl groups are disposed so as to provide an extent of steric shielding near the Mo=O bonds intended to suppress formation of the abiological O=Mo-O-Mo=O bridging group. The different coordination numbers of **1** and **2** are rationalized in terms of chelate ring sizes and conformations. On the basis of prior analysis of Mo EXAFS of enzymes, **2**, with a MoO₂NS₂ coordination unit, is a presently viable structural model of the active sites of several oxo-transfer enzymes. Reaction of **2** with Ph₃P in DMF yields the Mo(IV) complex MoO(LNS₂)(DMF) (**3**, 65%). The preparation of **3** in this way provides one indication that the Mo(IV,VI) complexes of LN(SH)₂ are resistant to dimerization. Absorption spectral and electrochemical properties of **1-3** are presented; **1** is most useful in assessing structural and electronic effects of oxygen vs. sulfur coordination. The Mo(V) complex MoO(LNS₂)Cl was electrochemically detected in a reversible Mo(IV,V) couple. As shown in the following paper in this issue, **2** and **3** satisfy the remaining model property of oxo-transfer reactions involving phosphine and sulfoxide substrates.

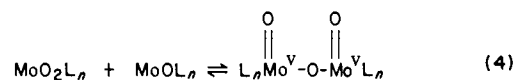
A broad class of molybdoenzymes²⁻⁵ catalyzes reactions that in effect result in addition or removal of an oxygen atom from substrate X or XO. The forward and reverse reactions 1 and 2 are illustrative and lead to the net transformation of reaction 3, which emphasizes the two-electron nature of the reactions catalyzed. Without mechanistic implication, these are referred to



as oxo-transfer reactions and their catalysts as oxo-transfer enzymes. Those enzymes which have been at least partially purified have been shown to contain a prosthetic group (flavin, Fe-S cluster, and heme) capable of mediating electron flow and a dissociable cofactor (Mo-co). Characterization of Mo-co is proceeding⁶⁻¹¹ and thus far has revealed the presence of a pterin nucleus with a sulfur-containing side chain to which a Mo atom is apparently coordinated. Extensive studies of xanthine oxidase/dehydrogenase and sulfite oxidase in particular, by EPR^{2,3,12} and Mo EXAFS¹³⁻¹⁵ spectroscopies, have established that the

catalytic sites are mononuclear. Attainment of functional models of these sites is the initial objective of our investigation of oxo-transfer molybdoenzymes by the synthetic analogue approach.

In the formulation of synthetic representations of catalytic sites, the Mo EXAFS results of Cramer et al.^{14,15} on the oxidized and fully reduced forms of sulfite oxidase, *Chlorella* nitrate reductase, and xanthine dehydrogenase are especially pertinent. These show that the Mo^{VI}O₂ and Mo^{IV}O units are present in the oxidized and reduced forms, respectively, and that in either form the Mo atoms are coordinated to at least two sulfur atoms at distances (2.41-2.47 Å) requiring that these be thiolate rather than thioether ligands. The only exceptions are found with oxidized xanthine dehydrogenase¹⁴ and oxidase,¹³ and in *E. coli* nitrate reductase,¹⁵ where the Mo^{VI}OS unit (containing a sulfido ligand) is present. An acceptable site model must approach the native coordination arrangement, which may also include some N/O ligands.^{2,3,12-15} Inasmuch as the sites are mononuclear, a realistic model system should also suppress reaction 4, which is potentiated in substrate reaction 1 and is pervasive and often irreversible in synthetic Mo



chemistry. If the reaction is irreversible, reactions 1 and 2 cannot be catalytically coupled, and even in a stoichiometric version of reaction 1, one-half of the Mo(IV,VI) reactant is consumed in the μ -oxo dimer formation. If reaction 4 is reversible,¹⁶ stoi-

- (1) National Science Foundation Predoctoral Fellow, 1980-1983.
 (2) Bray, R. C. "The Enzymes"; Boyer, P. C., Ed.; Academic Press: New York, 1975; Vol. XII, Part B, Chapter 6.
 (3) Bray, R. C. *Adv. Enzymol. Relat. Areas Mol. Biol.* **1980**, *51*, 107.
 (4) "Molybdenum and Molybdenum-Containing Enzymes"; Coughlan, M. P., Ed.; Pergamon Press, New York, 1980.
 (5) "Molybdenum Chemistry of Biological Significance"; Newton, W. E., Otsuka, S., Ed.; Plenum Press: New York, 1980.
 (6) Johnson, J. L. In ref 4, Chapter 10.
 (7) Johnson, J. L.; Hainline, B. E.; Rajagopalan, K. V. *J. Biol. Chem.* **1980**, *255*, 1783.
 (8) Johnson, J. L.; Rajagopalan, K. V. *Proc. Natl. Acad. Sci. U.S.A.* **1982**, *79*, 6856.
 (9) Ishizaka, M.; Ushio, K.; Toraya, T.; Fukui, S. *Biochem. Biophys. Res. Commun.* **1983**, *111*, 537.
 (10) Wahl, R. C.; Hageman, R. V.; Rajagopalan, K. V. *Arch. Biochem. Biophys.* **1984**, *230*, 264.
 (11) Johnson, J. L.; Hainline, B. E.; Rajagopalan, K. V.; Arison, B. H. *J. Biol. Chem.* **1984**, *259*, 5414.

- (12) (a) Gutteridge, S.; Bray, R. C. In Ref 4, pp 221-239. (b) Lamy, M. T.; Gutteridge, S.; Bray, R. C. *Biochem. J.* **1980**, *185*, 397. (c) Malthouse, P. G.; George, G. N.; Lowe, D. J.; Bray, R. C. *Ibid.* **1981**, *199*, 629. (d) Wahl, R. C.; Rajagopalan, K. V. *J. Biol. Chem.* **1982**, *257*, 1354. (e) Bray, R. C.; Gutteridge, S. *Biochemistry* **1982**, *21*, 5992. (f) Barber, M. J.; Siegel, L. M. *Ibid.* **1983**, *22*, 618. (g) George, G. N.; Bray, R. C. *Ibid.* **1983**, *22*, 1013. (h) Hille, R.; Stewart, R. C.; Fee, J. A.; Massey, V. *J. Biol. Chem.* **1983**, *258*, 4849.
 (13) Bordas, J.; Bray, R. C.; Garner, C. D.; Gutteridge, S.; Hasnain, S. S. *Biochem. J.* **1980**, *199*, 499.
 (14) Cramer, S. P.; Wahl, R.; Rajagopalan, K. V. *J. Am. Chem. Soc.* **1981**, *103*, 7721.
 (15) Cramer, S. P.; Solomonson, L. P.; Adams, M. W. W.; Mortenson, L. E. *J. Am. Chem. Soc.* **1984**, *106*, 1467.

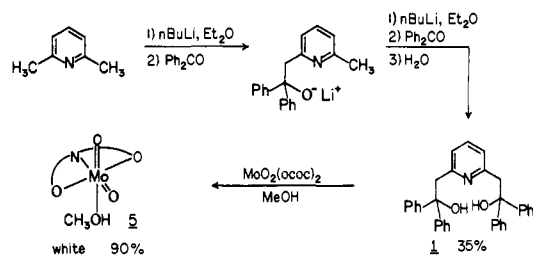


Figure 1. Synthesis of the diol LN(OH)₂ (1) and its Mo(VI) complex MoO₂(LNO₂)(MeOH) (5).

stoichiometric substrate transformations are possible and the rate constants for reaction 1 can be evaluated by our general kinetics analysis.¹⁷ Effective catalytic behavior will depend on a number of factors, including the relative rates of μ -oxo dimer dissociation and the forward and reverse of reaction 1. While catalytic aerial oxidation of tertiary phosphines in the presence of MoO₂(S₂CNR₂)₂^{18a} and MoO₂(S-Cys-OR)₂^{18b,c} has been achieved, reaction 4 is a generally undesirable complication and does not intervene in biological catalysis.

The problem of modeling the catalytic sites of oxo-transfer molybdoenzymes has been discussed by ourselves¹⁹ and others.^{20,21} The majority of research on this problem has been directed toward the synthesis and structural characterization of the complexes MoO₂L_n, possibly related to oxidized sites in the enzymes. In addition, valuable research on the synthesis and properties of Mo(IV, V) complexes has been reported by Spence and co-workers.^{21,22} By the EXAFS criterion,^{14,15} those complexes most pertinent contain in the set L_n two (or more) thiolate ligands.^{18c,20-29} Certain of the crystallographically characterized complexes^{22b-29} are useful structural models. Their reactivities in oxo transfer to substrate, reaction 1, are largely untested. Accordingly, the corresponding Mo^{VO} complexes and the dimerization reaction 4 are uncharacterized. Here we describe our current chemical approach to the enzymatic site problem using Mo(IV, VI) complexes derived from a ligand containing two thiolate binding sites and designed so as to prevent by steric hindrance the formation of a μ -oxo Mo(V) dimer.^{19,30} The synthesis, structure, and certain properties of this complex are presented here. In the following

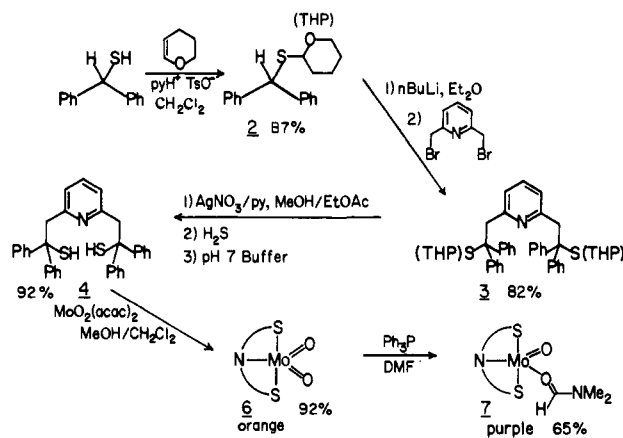


Figure 2. Synthesis of the dithiol LN(SH)₂ (4) and its Mo(VI, IV) complexes MoO₂(LNS₂) (6) and MoO(LNS₂)(DMF) (7).

paper in this issue,³¹ stoichiometric and catalytic oxo-transfer reactions of these complexes are demonstrated. Brief accounts of certain leading aspects of this research have been provided previously.^{19,30}

Experimental Section

Preparation of Compounds. Lithiation reactions and the syntheses of thiols and molybdenum thiolate complexes were carried out under a pure dinitrogen atmosphere; solvents were degassed before use. Synthetic schemes are set out in Figures 1 and 2.

2,6-Bis(2,2-diphenyl-2-hydroxyethyl)pyridine (1, LN(OH)₂). A solution of 5.00 g (47 mmol) of 2,6-lutidine in 50 mL of ether was added to 32 mL of 1.60 M *n*-BuLi in hexane diluted with 100 mL of ether. The mixture was stirred for 90 min. The orange solution was cooled to -78 °C, and a solution of 8.50 g (47 mmol) of benzophenone in 50 mL of ether was added. The mixture was allowed to warm to room temperature over 30 min, and an additional 32 mL of 1.60 M *n*-BuLi in hexane was introduced. After the mixture was cooled to -78 °C, 8.50 g of benzophenone in 50 mL of ether was added. This mixture was warmed to room temperature, stirred for 1 h, and poured into 300 mL of water. The yellow organic layer was separated, and the aqueous phase was extracted with dichloromethane (3 × 50 mL). The combined organic layers were dried over MgSO₄, and the solvent was removed, leaving a yellow oil which solidified on standing. This material was dissolved in 50 mL of dichloromethane and extracted with 25 mL of 0.5 M HCl. The organic layer was quickly separated, and the white solid which precipitated from it was collected. When slurried with 25 mL of saturated K₂CO₃ and 50 mL of dichloromethane, the solid dissolved in the organic phase. The two phases were separated, and the aqueous phase was extracted with 50 mL of dichloromethane. The combined organic layers were dried (MgSO₄), and the solvent was removed to yield a white solid. This was recrystallized from aqueous ethanol, affording 7.85 g (36%) of highly crystalline colorless product: mp 129–131 °C; ¹H NMR (CDCl₃) δ 7.12–7.42 (21 H, m, Ph + 4-H), 6.75 (2 H, d, *J* = 7.5 Hz, 3-H + 5-H), 5.16 (2 H, s, OH), 3.65 (4 H, s, CH₂). The product may also be purified chromatographically (*R*_f = 0.40, silica gel, 20% ethyl acetate/hexane). Anal. Calcd for C₃₃H₂₉NO₂: C, 84.05; H, 6.20; N, 2.97. Found: C, 83.99; H, 6.26; N, 2.77.

2-[(Diphenylmethyl)thio]tetrahydro-2H-pyran (2). Diphenylmethanethiol³² (10.0 g, 0.050 mol) was dissolved in 100 mL of dry dichloromethane. To this solution was added 21.0 g (0.25 mol) of 2,3-dihydropyran and 1.28 g of pyridinium tosylate as a catalyst.³³ The solution was stirred for 50 h, 150 mL of ether was added, and the mixture was washed with 50% NaCl solution (2 × 100 mL). Solvent was removed in vacuo from the separated organic layer to give a colorless liquid, which upon standing began to deposit crystals. The mixture was maintained for 24 h at -20 °C. The crystalline solid was collected by filtration and washed with hexane, giving 10.8 g. Concentration of the filtrate and cooling to -20 °C gave a second crop, for a total of 12.4 g (87%): mp 81–82 °C; ¹H NMR (CDCl₃) δ 7.15–7.55 (10 H, m, Ph), 5.32 (1 H, s, Ph₂CH), 4.52–4.62 (1 H, m, H-1), 4.05–4.14 (1 H, m, 3-H), 3.38–3.58

(31) Berg, J. M.; Holm, R. H. *J. Am. Chem. Soc.*, following paper in this issue.

(32) Klenk, M. M.; Suter, C. M.; Archer, S. J. *Am. Chem. Soc.* **1948**, *70*, 3846.

(33) Miyashita, M.; Yoshikashi, A.; Grieco, P. A. *J. Org. Chem.* **1977**, *42*, 3772.

(16) For well-defined systems exhibiting this reaction, cf.: Chen, G. J.-J.; McDonald, J. W.; Newton, W. E. *Inorg. Chem.* **1976**, *15*, 2612. Matsuda, T.; Tanaka, K.; Tanaka, T. *ibid.* **1979**, *18*, 454. Miyake, S.; Tanaka, K.; Tanaka, T. *J. Chem. Soc., Dalton Trans.* **1981**, 292.

(17) Reynolds, M. S.; Berg, J. M.; Holm, R. H. *Inorg. Chem.* **1984**, *23*, 3057.

(18) (a) Barral, R.; Bocard, C.; S er e de Roch, I.; Sajas, L. *Tetrahedron Lett.* **1972**, 1693; *Kinet. Catal.* **1973**, *14*, 130. (b) Speier, G. *Inorg. Chim. Acta* **1979**, *33*, 139. (c) Ueyama, N.; Yano, M.; Miyashita, H.; Nakamura, A.; Kamachi, M.; Nozakura, S. *J. Chem. Soc., Dalton Trans.* **1984**, 1447.

(19) Holm, R. H.; Berg, J. M. *Pure Appl. Chem.* **1984**, *56*, 1645.

(20) Stiefel, E. I. In ref 4, pp 41–98.

(21) (a) Spence, J. T. *Coord. Chem. Rev.* **1983**, *48*, 59. (b) Subramian, P.; Kaul, B.; Spence, J. T. *J. Mol. Catal.* **1984**, *23*, 163. (c) Subramian, P.; Spence, J. T.; Ortega, R.; Enemark, J. H. *Inorg. Chem.* **1984**, *23*, 2564.

(22) (a) Boyd, I. W.; Spence, J. T. *Inorg. Chem.* **1982**, *21*, 1602. (b) Rajan, O. A.; Spence, J. T.; Leman, C.; Minelli, M.; Sato, M.; Enemark, J. H.; Kroneck, P. H. M.; Sulger, K. *ibid.* **1983**, *22*, 3065.

(23) Yamanouchi, K.; Enemark, J. H. *Inorg. Chem.* **1979**, *18*, 1626.

(24) (a) Berg, J. M.; Hodgson, K. O.; Cramer, S. P.; Corbin, J. L.; Elsberry, A.; Parlyadath, N.; Stiefel, E. I. *J. Am. Chem. Soc.* **1979**, *101*, 2774. (b) Berg, J. M.; Hodgson, K. O.; Bruce, A. E.; Corbin, J. L.; Parlyadath, N.; Stiefel, E. I. *Inorg. Chim. Acta* **1984**, *90*, 25.

(25) (a) Stiefel, E. I.; Miller, K. F.; Bruce, A. E.; Corbin, J. L.; Berg, J. M.; Hodgson, K. O. *J. Am. Chem. Soc.* **1980**, *102*, 3624. (b) Berg, J. M.; Spira, D. J.; Hodgson, K. O.; Bruce, A. E.; Miller, K. F.; Corbin, J. L.; Stiefel, E. I. *Inorg. Chem.* **1984**, *23*, 3412.

(26) Bruce, A. E.; Corbin, J. L.; Dahlstrom, P. L.; Hyde, J. R.; Minelli, M.; Stiefel, E. I.; Spence, J. T.; Zubietta, J. *Inorg. Chem.* **1982**, *21*, 917.

(27) Berg, J. M.; Holm, R. H. *Inorg. Chem.* **1983**, *22*, 1768.

(28) (a) Buchanan, I.; Minelli, M.; Ashby, M. T.; King, T. J.; Enemark, J. H.; Garner, C. D. *Inorg. Chem.* **1984**, *23*, 495. (b) Buchanan, I.; Garner, C. D.; Clegg, W. J. *J. Chem. Soc., Dalton Trans.* **1984**, 1333.

(29) Berg, J. M.; Spira, D.; Wo, K.; McCord, B.; Lye, R.; Co, M. S.; Belmont, J.; Barnes, C.; Kosydar, K.; Raybuck, S.; Hodgson, K. O.; Bruce, A. E.; Corbin, J. L.; Stiefel, E. I. *Inorg. Chim. Acta* **1984**, *90*, 35.

(30) Berg, J. M.; Holm, R. H. *J. Am. Chem. Soc.* **1984**, *106*, 3035.

(1 H, m, 3-H), 1.46–1.93 (6 H, m, 4-H + 5-H + 6-H). Anal. Calcd for $C_{18}H_{20}OS$: C, 76.01; H, 7.09; S, 11.27. Found: C, 76.64; H, 7.16; S, 11.48.

2,6-Bis[2,2-diphenyl-2-[(tetrahydro-2H-pyran-2-yl)thio]ethyl]pyridine (3). A solution of 2.36 g (8.30 mmol) of **2** in 75 mL of ether was cooled to -78°C , and 3.66 mL of 2.11 M *n*-BuLi in hexane was added. The reaction mixture was allowed to warm to 0°C over 1 h and then was cooled again to -78°C . A solution of 1.00 g (3.77 mmol) of 2,6-bis-(bromomethyl)pyridine³⁴ in 50 mL of ether was added, causing a lightening of the orange reaction mixture and formation of a white solid. The mixture was allowed to warm to room temperature and was added to 100 mL of pH 7.0 phosphate buffer. The yellowish organic layer was separated, and the aqueous layer was extracted with ether (3×75 mL). The combined ether layers were dried (MgSO_4), and the solvent was removed to give a yellowish brittle foam. This material was purified by flash chromatography (5% v/v ethyl acetate/hexanes) to afford 2.08 g (82%) of product as a white brittle foam after solvent removal: mp 155–158 $^\circ\text{C}$; $^1\text{H NMR}$ (CDCl_3) δ 7.05–7.61 (20 H, m, Ph), 6.65–6.90 (1 H, t, $J = 8$ Hz, H-3'), 6.20 (2 = H, br d, $J = 8$ Hz, H-2' + H-4'), 3.05–4.30 (6 H, m, H-1 + H-3), 1.25–1.90 (12 H, br m, H-4 + H-5 + H-6) (primes refer to pyridine protons). Anal. Calcd for $C_{43}H_{45}NO_2S_2$: C, 76.86; H, 6.75; N, 2.08; S, 9.54. Found: C, 77.71; H, 7.01; N, 2.04; S, 9.75.

2,6-Bis[2,2-diphenyl-2-mercaptoethyl]pyridine (4, LN(SH)₂). The protected dithiol **3** (1.50 g, 2.23 mmol) was dissolved in 20 mL of ethyl acetate, and 20 mL of methanol was added, causing the formation of some precipitate. To this mixture was added 0.83 g (4.9 mmol) of AgNO_3 and 0.40 g (5.0 mmol) of pyridine in 50 mL of methanol. The solid material dissolved, and the solution became yellow. After 50 min the solvent was removed in vacuo and the residue was washed with ether (2×30 mL), yielding a yellow powder. This material was dissolved in 30 mL of chloroform, and H_2S was bubbled through for 30 min. The copious brown-black precipitate was separated by filtration and washed with dichloromethane (2×50 mL). The combined filtrates were washed with pH 7.0 phosphate buffer, and the aqueous layer was extracted with ether (2×50 mL). The combined organic layers were dried (MgSO_4), and the solvent was removed to yield 1.03 g (92%) of product as a white foam-like solid: $^1\text{H NMR}$ (CDCl_3) δ 7.16–7.42 (20 H, m, Ph), 6.88 (1 H, t, $J = 7.9$ Hz, H-4), 6.13 (2 H, d, $J = 7.9$ Hz, H-3 + H-5), 3.92 (4 H, s, CH_2), 3.72 (2 H, br s, SH). This compound proved somewhat unstable in storage and was not analyzed. Fresh samples were used in the preparation of **6**.

[2,6-Bis(2,2-diphenyl-2-oxyethyl)pyridinato](methanol)dioxomolybdenum(VI) (5, MoO₂(LNO₂)(MeOH)). A solution of 2.00 g (4.24 mmol) of **1** in 50 mL of methanol was added to a solution of 1.39 g (4.26 mmol) of $\text{MoO}_2(\text{acac})_2$ ³⁵ in 50 mL of methanol. A white crystalline precipitate formed quickly. The mixture was stirred for 30 min, and the product was isolated by filtration and washed with methanol to afford 2.40 g (90%): mp 254–257 $^\circ\text{C}$ dec; IR (mull) ν_{MoO} 922, 877 cm^{-1} . Anal. Calcd for $C_{34}H_{31}MoNO_5$: C, 64.87; H, 4.96; Mo, 15.24; N, 2.22. Found: C, 64.18; H, 4.93; Mo, 15.62; N, 2.11.

[2,6-Bis(2,2-diphenyl-2-thioethyl)pyridinato]dioxomolybdenum(VI) (6, MoO₂(LNS₂)). A solution of 1.03 g (2.04 mmol) of **4**, immediately formed by deprotection of **3**, in 5 mL of dichloromethane was added to a solution of 0.67 g (2.1 mmol) of $\text{MoO}_2(\text{acac})_2$ ³⁵ in 25 mL of methanol. The solution quickly turned orange, and an orange precipitate separated. The volume of the solution was reduced to ~ 10 mL, and the mixture was stored at -20°C overnight. The orange solid was collected by filtration to give 1.19 g (92%) of product: mp 205–206 $^\circ\text{C}$ dec; IR (mull) ν_{MoO} 950, 915 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3) δ 7.04–7.23 (21 H, m, Ph + 4-H), 6.41 (2 H, d, H-3 + H-5), 4.04 (4 H, s, CH_2). Anal. Calcd for $C_{33}H_{27}MoNO_2S_2$: C, 62.95; H, 4.32; Mo, 15.24; N, 2.22; S, 10.18. Found: C, 63.12; H, 4.45; Mo, 15.19; N, 2.64; S, 10.53.

[2,6-Bis(2,2-diphenyl-2-thioethyl)pyridinato](*N,N*-Dimethylformamide)oxomolybdenum(IV) (7, MoO(LNS₂)(DMF)). A solution of 0.500 g (0.794 mmol) of $\text{MoO}_2(\text{LNS}_2)$ (**6**) in 25 mL of DMF was treated with a solution of 0.312 g (1.19 mmol) of Ph_3P in 25 mL of DMF, causing an immediate darkening of the mixture. This was stirred for 18 h. Addition of 200 mL of ether caused precipitation of purple microcrystals, which were collected by filtration and washed with ether; 0.353 g (65%) of product was obtained: IR (mull) ν_{MoO} 945 cm^{-1} . Anal. Calcd for $C_{36}H_{34}MoN_2O_2S_2$: C, 62.96; H, 4.99; Mo, 13.97; N, 4.08; S, 9.34. Found: C, 62.84; H, 4.96; Mo, 13.94; N, 4.26; S, 9.30.

X-ray Structural Determinations. Diffraction experiments were performed with a Nicolet R3m diffractometer using graphite-monochromatized $\text{Mo K}\alpha$ radiation. Computer programs were those of the SHELXTL structure determination package (Nicolet XRD Corp., Madison

Table I. Summary of Crystal Data, Intensity Collections, and Structure Refinement Parameters

quantity	MoO ₂ (LNO ₂)- (Me ₂ SO)	MoO ₂ (LNS ₂)
formula	C ₃₄ H ₃₁ MoNO ₅ S	C ₃₃ H ₂₇ MoNO ₂ S ₂
<i>M</i> , amu	675.66	629.65
space group	<i>P</i> 2 ₁ / <i>c</i>	<i>P</i> 2 ₁ 2 ₁ 2 ₁
<i>a</i> , Å	8.738 (2)	8.910 (2)
<i>b</i> , Å	17.799 (4)	16.350 (4)
<i>c</i> , Å	19.927 (3)	19.193 (5)
β , deg	93.77 (1)	
<i>V</i> , Å ³	3122 (1)	2796 (1)
<i>Z</i>	4	4
<i>d</i> _{calcd} (<i>d</i> _{obsd}), ^a g/cm ³	1.437 (1.45)	1.496 (1.49)
temp, $^\circ\text{C}$	23	23
linear abs coeff	5.19	6.31
transmission factors (max/min)	0.576/0.546	0.723/0.649
data collected	<i>h, k, ±l</i> ($30^\circ \leq 2\theta \leq 45^\circ$)	<i>h, k, ±l</i> ($30^\circ \leq 2\theta \leq 45^\circ$)
scan ranges	$K\alpha_1 -0.7$ to $K\alpha_2 +0.7$	$K\alpha_1 -0.8$ to $K\alpha_2 +0.8$
weighting factor, g	0.0005	0.0005
total reflections	3083	2776
unique data	2742	1877
($F_o^2 > 3\sigma(F_o^2)$)		
no. of parameters	346	304
<i>R</i> _{merg}	0.0191	0.0209
<i>R</i> (<i>R</i> _w), %	3.73 (3.69)	3.62 (3.40)
goodness of fit, e ⁻	1.284	1.061

^a Determined by flotation in CCl_4 /hexane.

WI). Crystal data, intensity collection information, and structure refinement parameters are provided in Table I. Neutral atom scattering factors including anomalous dispersion terms were taken from a standard source.³⁶ Diffraction-quality crystals of $\text{MoO}_2(\text{LNO}_2)(\text{Me}_2\text{SO})$ (as small, colorless prisms) and $\text{MoO}_2(\text{LNS}_2)$ (as small, elongated orange plates) were obtained by diffusion of hexanes into solutions of $\text{MoO}_2(\text{LNO}_2)(\text{MeOH})$ in 10:1 v/v ethyl acetate/ Me_2SO and $\text{MoO}_2(\text{LNS}_2)$ in 5:1:1 v/v ethyl acetate/methanol/ Me_2SO .

For each crystal the unit cell dimensions were determined from 25 machine-centered reflections with $15^\circ \leq 2\theta \leq 25^\circ$. Data were collected by using $\theta/2\theta$ scans. During each data collection, three standard reflections monitored every 60 reflections showed no significant fluctuation or decay. Data were corrected for Lorentz and polarization effects and for absorption, using the empirical procedure of the program XEMP. Extinction corrections were deemed unnecessary. For both structures the space group was uniquely determined by the observed systematic absences. The structures were solved by use of the heavy atom method. All non-hydrogen atoms were refined anisotropically by using weighted cascaded blocked-diagonal least squares with weights given by $w = 1/(\sigma^2(F_o) + gF_o^2)$. Hydrogen atoms were included in calculated positions (C–H distance 0.96 Å) with temperature factors set at 1.2 times the equivalent isotropic temperature factor of the bonded carbon atoms. Phenyl rings and methyl groups were refined as rigid groups. Because $\text{MoO}_2(\text{LNS}_2)$ crystallizes in a chiral space group, a polarity factor³⁷ was refined to determine the correctness of the enantiomorph chosen. Its value of 1.1 ± 0.2 revealed that the choice was correct, as was confirmed by inspection of the Friedel pairs collected. Final agreement factors for the two structures are given in Table I, and atomic coordinates are listed in Tables II and III.³⁸

Other Physical Measurements. Absorption spectra were recorded on a Cary Model 219 spectrophotometer. Electrochemical experiments were performed with standard PAR instrumentation using DMF solutions. The working electrode in cyclic voltammetry was a Pt disk; in coulometry a Pt gauze electrode was used. Potentials were measured vs. an aqueous SCE as the reference. Other details are given in the text.

Results and Discussion

Synthesis. We have sought Mo(IV,VI) complexes that contain biologically relevant coordination units and are active in the forward or reverse oxo-transfer reaction 1 without engaging in the μ -oxo dimer formation reaction 4. There being no evident

(36) "International Tables for X-ray Crystallography," Kynoch Press: Birmingham, England, 1974; Vol. IV, pp 99–100, 149.

(37) Flack, H. D. *Acta Crystallogr., Sect. A* **1983**, *A39*, 876.

(38) See paragraph at the end of this article concerning supplementary material.

(34) Baker, W.; Bugge, K. M.; McOmie, J. F. W.; Watkins, D. A. M. *J. Chem. Soc.* **1958**, 3594.

(35) Jones, M. M. *J. Am. Chem. Soc.* **1959**, *81*, 3188.

Table II. Atom Coordinates ($\times 10^4$) for $\text{MoO}_2(\text{LNO}_2)(\text{Me}_2\text{SO})$

atom	x	y	z
Mo (1)	2462 (1) ^a	1639 (1)	1623 (1)
S (1)	6237 (2)	2057 (1)	2052 (1)
O (1)	2730 (4)	2320 (2)	2219 (2)
O (2)	527 (4)	1490 (2)	1543 (2)
O (3)	3040 (4)	814 (2)	2189 (2)
O (4)	2652 (4)	2263 (2)	857 (2)
O (5)	5167 (4)	1662 (2)	1536 (2)
N (1)	2734 (4)	704 (2)	759 (2)
C (1)	3479 (6)	39 (3)	870 (2)
C (2)	3501 (7)	-510 (3)	379 (3)
C (3)	2753 (8)	-383 (3)	-248 (3)
C (4)	2007 (7)	295 (3)	-360 (3)
C (5)	2006 (6)	822 (3)	147 (3)
C (6)	4322 (6)	-98 (3)	1544 (3)
C (7)	3386 (6)	41 (3)	2168 (3)
C (8)	1137 (6)	1546 (3)	28 (3)
C (9)	2107 (6)	2268 (3)	170 (3)
C (10)	5078 (4)	-853 (2)	2894 (2)
C (11)	5876 (4)	-1040 (2)	3501 (2)
C (12)	5952 (4)	-529 (2)	4033 (2)
C (13)	5231 (4)	168 (2)	3959 (2)
C (14)	4433 (4)	354 (2)	3352 (2)
C (15)	4356 (4)	-156 (2)	2820 (2)
C (16)	1737 (4)	-1114 (2)	1861 (2)
C (17)	408 (4)	-1535 (2)	1926 (2)
C (18)	-771 (4)	-1248 (2)	2290 (2)
C (19)	-622 (4)	-541 (2)	2588 (2)
C (20)	706 (4)	-120 (2)	2523 (2)
C (21)	1886 (4)	-406 (2)	2159 (2)
C (22)	393 (4)	3287 (2)	617 (2)
C (23)	-590 (4)	3901 (2)	529 (2)
C (24)	-927 (4)	4195 (2)	-112 (2)
C (25)	-280 (4)	3875 (2)	-666 (2)
C (26)	704 (4)	3261 (2)	-579 (2)
C (27)	1041 (4)	2966 (2)	63 (2)
C (28)	4875 (4)	2607 (2)	47 (1)
C (29)	6124 (4)	2735 (2)	-339 (1)
C (30)	6009 (4)	2577 (2)	-1026 (1)
C (31)	4646 (4)	2291 (2)	-1327 (1)
C (32)	3396 (4)	2163 (2)	-941 (1)
C (33)	3511 (4)	2321 (2)	-254 (1)
C (34)	7520 (7)	2573 (4)	1582 (3)
C (35)	7521 (7)	1346 (4)	2383 (3)

^aEstimated standard deviations in the least significant figure are given in parentheses in this and subsequent tables.

basis for the suppression of this reaction by manipulation of electronic factors, a solution based on steric constraints was pursued. Additional considerations included the presence of a labile coordination site for potential binding of the substrate and the ability to replace thiolate ligands with others, in order that the effects of the former on structure and reactivity could be comparatively assessed. The possibilities offered by 2,6-disubstituted pyridine ligands, as represented in, e.g., the complex $\text{MoO}_2(\text{py}(\text{CO}_2)_2)(\text{HMPA})$,³⁹ appeared attractive. These were initially examined by synthesis of dioxo Mo(VI) complexes of pyridine-2,6-dimethanol and -dimethanethiol (vide infra). The latter complex is sparingly soluble and formed the μ -oxo dimer upon reaction with Ph_3P ,³¹ making evident the requirement of altered ligand design.

The synthetic schemes affording the hindered ditertiary diol **1** and dithiol **4**, based on the 2,6-disubstituted pyridine nucleus, are summarized in Figures 1 and 2, respectively. The diol $\text{LN}(\text{OH})_2$ (**1**) was obtained in 36% yield starting from 2,6-lutidine by two sequences of lithiation and reaction with benzophenone. This method is analogous to the introduction of $\text{CRR}'\text{OH}$ groups by the reactions of 2-(lithiomethyl)pyridines and -quinolines with ketones.⁴⁰ Protection of diphenylmethanethiol with 2,3-di-

Table III. Atom Coordinates ($\times 10^4$) for $\text{MoO}_2(\text{LNS}_2)$

atom	x	y	z
Mo (1)	8581 (1)	7991 (1)	1387 (1)
S (1)	8880 (3)	8629 (1)	263 (1)
S (2)	7260 (2)	7569 (1)	2428 (1)
O (1)	9256 (6)	7087 (4)	1096 (3)
O (2)	9893 (6)	8485 (4)	1870 (3)
N (1)	6272 (8)	8494 (4)	1198 (3)
C (1)	5048 (9)	7988 (5)	1190 (4)
C (2)	3641 (11)	8270 (5)	1016 (4)
C (3)	3474 (12)	9100 (5)	883 (4)
C (4)	4713 (10)	9614 (6)	928 (5)
C (5)	6101 (9)	9294 (5)	1071 (4)
C (6)	7465 (10)	9812 (5)	1073 (4)
C (7)	8386 (9)	9734 (4)	385 (4)
C (8)	5304 (8)	7108 (4)	1372 (4)
C (9)	5657 (8)	6932 (5)	2153 (4)
C (10)	6569 (7)	9525 (3)	-652 (3)
C (11)	5710 (7)	9848 (3)	-1194 (3)
C (12)	5691 (7)	10690 (3)	-1311 (3)
C (13)	6531 (7)	11209 (3)	-886 (3)
C (14)	7390 (7)	10886 (3)	-344 (3)
C (15)	7409 (7)	10044 (3)	-227 (3)
C (16)	10316 (7)	10707 (4)	941 (3)
C (17)	11600 (7)	11191 (4)	886 (3)
C (18)	12447 (7)	11179 (4)	275 (3)
C (19)	12011 (7)	10683 (4)	-281 (3)
C (20)	10728 (7)	10199 (4)	-226 (3)
C (21)	9880 (7)	10211 (4)	385 (3)
C (22)	2846 (6)	7104 (3)	2445 (3)
C (23)	1702 (6)	7222 (3)	2931 (3)
C (24)	2054 (6)	7348 (3)	3632 (3)
C (25)	3550 (6)	7355 (3)	3846 (3)
C (26)	4694 (6)	7237 (3)	3360 (3)
C (27)	4342 (6)	7111 (3)	2660 (3)
C (28)	4846 (6)	5450 (4)	2087 (3)
C (29)	5111 (6)	4611 (4)	2129 (3)
C (30)	6537 (6)	4323 (4)	2303 (3)
C (31)	7697 (6)	4874 (4)	2434 (3)
C (32)	7432 (6)	5714 (4)	2392 (3)
C (33)	6006 (6)	6002 (4)	2219 (3)

hydropyran to give **2** followed by lithiation at the *gem*-diphenyl carbon atom and reaction with 2,6-bis(bromomethyl)pyridine afforded the doubly protected dithiol **3** in 82% yield from **2**. Deprotection of **3** gave the dithiol $\text{LN}(\text{SH})_2$ (**4**) in 92% yield. This compound degrades upon standing and should be stored in the protected form **3**. Treatment of $\text{MoO}_2(\text{acac})_2$ with **1** gave colorless $\text{MoO}_2(\text{LNO}_2)(\text{MeOH})$ (**5**, 90%). Similarly, $\text{MoO}_2(\text{acac})_2$ and **4** (freshly formed from **3**) gave orange $\text{MoO}_2(\text{LNS}_2)$ (**6**, 92%). Reaction of **6** with Ph_3P in DMF solution resulted in smooth conversion to the purple Mo(IV) complex $\text{MoO}(\text{LNS}_2)(\text{DMF})$ (**7**, 65%). When **5** was placed in a $\text{EtOAc}/\text{Me}_2\text{SO}$ mixture and hexanes were added, the adduct $\text{MoO}_2(\text{LNO}_2)(\text{Me}_2\text{SO})$ crystallized. Under similar conditions **6** was recovered in the unsolvated form. These procedures afforded diffraction-quality crystals. Ligands **1** and **4** and their complexes have not been previously reported by others. Other than our recent work,²⁷ studies of pyridine alkanethiols as ligands have been confined to a number of metal(II) derivatives of pyridine-2,6-dimethanethiol⁴¹ and pyridine-2-ethanethiol.⁴² A binuclear Mo(III) complex of the latter ligand has also been described.⁴³ Compound **2** should prove to be a useful synthon for the preparation of other hindered thiol ligands.

Description of Structures. (a) $\text{MoO}_2(\text{LNO}_2)(\text{Me}_2\text{SO})$. Crystals of this compound contain discrete mononuclear species. The structure is displayed in Figure 3, and metric data are collected in Table IV. The coordination sphere is a severely distorted octahedron with *cis* oxo atoms O(1,2), *trans* alkoxide ligands

(41) op den Brouw, P. M.; van der Linden, J. G. M. *Inorg. Nucl. Chem. Lett.* **1977**, *13*, 149.

(42) (a) Wrathall, J. W.; Busch, D. H. *Inorg. Chem.* **1963**, *2*, 1182. (b) Uhlig, E.; Heinrich, G. Z. *Anorg. Allg. Chem.* **1964**, *330*, 40.

(43) Lindoy, L. F.; Livingstone, S. E.; Lockyer, T. N. *Aust. J. Chem.* **1965**, *18*, 1549.

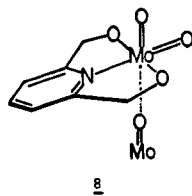
(39) Liebeskind, L. S.; Sharpless, K. B.; Wilson, R. D.; Ibers, J. A. *J. Am. Chem. Soc.* **1978**, *100*, 7061 (HMPA = hexamethylphosphoric triamide).

(40) (a) Büchi, J.; Broger, W.; Schmidt, G. *Helv. Chim. Acta* **1965**, *48*, 275. (b) Kaiser, E. M.; Bartling, G. J.; Thomas, W. R.; Nichols, S. B.; Nash, D. R. *J. Org. Chem.* **1973**, *38*, 71.

Table IV. Selected Interatomic Distances (Å) and Angles (deg) for MoO₂(LNO₂)(Me₂SO)

Mo (1)-O (1)	1.702 (4)	Mo (1)-O (2)	1.708 (4)
Mo (1)-O (3)	1.899 (3)	Mo (1)-O (4)	1.904 (3)
Mo (1)-O (5)	2.382 (3)	Mo (1)-N (1)	2.417 (4)
O (3)-C (7)	1.409 (6)	O (4)-C (9)	1.420 (6)
N (1)-C (1)	1.362 (6)	N (1)-C (5)	1.354 (6)
C (1)-C (2)	1.386 (8)	C (2)-C (3)	1.389 (8)
C (3)-C (4)	1.383 (8)	C (4)-C (5)	1.379 (8)
C (1)-C (6)	1.508 (7)	C (5)-C (8)	1.507 (7)
C (6)-C (7)	1.552 (7)	C (8)-C (9)	1.554 (7)
C (7)-C (15)	1.544 (6)	C (7)-C (21)	1.533 (6)
C (9)-C (27)	1.560 (6)	C (9)-C (33)	1.537 (6)
S (1)-O (5)	1.517 (4)	S (1)-C (34)	1.766 (7)
S (1)-C (35)	1.788 (7)		
O (1)-Mo (1)-O (2)	105.4 (2)	O (1)-Mo (1)-O (3)	96.8 (2)
O (1)-Mo (1)-O (4)	97.3 (2)	O (1)-Mo (1)-O (5)	87.0 (2)
O (1)-Mo (1)-N (1)	166.3 (2)	O (2)-Mo (1)-O (3)	99.1 (2)
O (2)-Mo (1)-O (4)	98.8 (2)	O (2)-Mo (1)-O (5)	167.6 (2)
O (2)-Mo (1)-N (1)	88.3 (2)	O (3)-Mo (1)-O (4)	153.2 (1)
O (3)-Mo (1)-O (5)	80.2 (1)	O (3)-Mo (1)-N (1)	81.7 (1)
O (4)-Mo (1)-O (5)	78.0 (1)	O (4)-Mo (1)-N (1)	79.2 (1)
O (5)-Mo (1)-N (1)	79.4 (1)		
Mo (1)-O (3)-C (7)	141.9 (3)	Mo (1)-O (4)-C (9)	137.3 (3)
Mo (1)-O (5)-S (1)	121.9 (2)	Mo (1)-N (1)-C (1)	123.4 (3)
Mo (1)-N (1)-C (5)	118.2 (3)		
C (1)-N (1)-C (5)	118.2 (4)	N (1)-C (1)-C (2)	121.8 (5)
N (1)-C (5)-C (4)	122.1 (5)	C (1)-C (2)-C (3)	119.6 (5)
C (2)-C (3)-C (4)	118.4 (5)	C (3)-C (4)-C (5)	119.9 (5)
N (1)-C (1)-C (6)	119.1 (4)	C (2)-C (1)-C (6)	119.1 (5)
N (1)-C (5)-C (8)	118.4 (4)	C (4)-C (5)-C (8)	119.4 (5)
C (1)-C (6)-C (7)	115.8 (4)	C (5)-C (8)-C (9)	114.5 (4)
O (3)-C (7)-C (6)	107.7 (4)	O (3)-C (7)-C (15)	107.7 (4)
O (3)-C (7)-C (21)	108.8 (4)	O (4)-C (9)-C (8)	108.4 (4)
O (4)-C (9)-C (27)	107.2 (4)	O (4)-C (9)-C (33)	107.5 (4)
C (6)-C (7)-C (15)	110.4 (4)	C (6)-C (7)-C (21)	113.7 (4)
C (15)-C (7)-C (21)	108.2 (4)	C (8)-C (9)-C (27)	108.7 (4)
C (8)-C (9)-C (33)	113.3 (4)	C (27)-C (9)-C (33)	111.5 (4)
C (7)-C (15)-C (10)	120.7 (2)	C (7)-C (15)-C (14)	119.2 (2)
C (7)-C (21)-C (16)	122.0 (2)	C (7)-C (21)-C (20)	117.7 (2)
C (9)-C (27)-C (22)	119.1 (2)	C (9)-C (27)-C (26)	120.8 (2)
C (9)-C (33)-C (28)	118.4 (2)	C (9)-C (33)-C (32)	121.2 (2)

O(3,4) cis to O(1,2), a pyridine nitrogen atom trans to O(1), and atom O(5) of Me₂SO trans to O(2). The trans alkoxide arrangement arises from the ligand structure, which enforces a meridional donor atom arrangement. However, the structure adheres to the pattern usually found for unconstrained MoO₂X₂Y₂ complexes, where X is an anionic and Y is a neutral ligand. Pertinent examples with alkoxide ligation include MoO₂(OC₂H₄CH₂OH)₂,^{44a} MoO₂(MeCH(O)CH(OH)Me)₂,^{44b} [MoO₂(Hmalate)₂]²⁻,^{44c} and [MoO₂(py(CH₂O)₂)_n]²⁷ (8). As recognized



earlier,^{44b} this configuration places the stronger σ - and π -donor ligands X cis to oxo atoms where they can more effectively compete for available empty d orbitals.

Distances and the angle of the MoO₂ group are conventional, with the latter (105.4 (2)°) near the minimum energy value calculated from MO theory.⁴⁵ Compared to other dioxo Mo(VI)

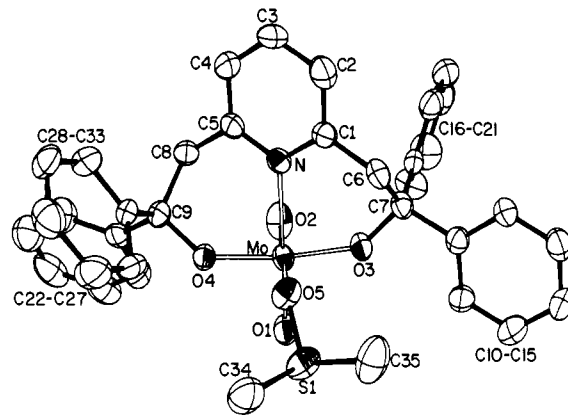


Figure 3. Structure of MoO₂(LNO₂)(Me₂SO) showing atom labeling scheme and 50% probability ellipsoids.

complexes, the mean Mo-O(3,4) distance of 1.902 Å is ~ 0.02–0.08 Å shorter than those involving alkoxide ligands cis to oxo atoms.^{27,44} and the Mo-N distance of 2.417 (4) Å tends to be ~0.02–0.10 Å longer than bonds to nitrogen donors trans to oxo atoms.^{23,24,26,44,46} The latter feature reflects the effects of six-membered chelate rings, inasmuch as the distance in 8 is 2.190 (3) Å.²⁷ The Mo-O(5) distance of 2.382 (3) Å is long for a Y ligand trans to an oxo atom,⁴⁷ implying lability to substitution.

(44) (a) Schröder, F. A.; Scherle, J.; Hazell, R. G. *Acta Crystallogr., Sect. B* **1975**, *B31*, 531. (b) Butcher, R. J.; Penfold, B. R.; Sinn, E. *J. Chem. Soc., Dalton Trans.* **1979**, 668. (c) Knobler, C. B.; Wilson, A. J.; Hider, R. N.; Jensen, I. W.; Penfold, B. R.; Robinson, W. T.; Wilkins, C. J. *Ibid.* **1983**, 1299. (d) Chisholm, M. R.; Foltling, K.; Huffman, J. C.; Kirkpatrick, C. C. *Inorg. Chem.* **1984**, *23*, 1021.

(45) Tatsumi, K.; Hoffmann, R. *Inorg. Chem.* **1980**, *19*, 2656.

(46) (a) Chiesa Villa, A.; Coghi, L.; Manfredotti, A. G.; Guastini, C. *Cryst. Struct. Commun.* **1974**, *3*, 551. (b) Gullotti, M.; Pasini, A.; Zanderighi, G. M.; Ciani, G.; Sironi, A. *J. Chem. Soc., Dalton Trans.* **1981**, 902. (c) Voissat, B.; Rodier, N. *Acta Crystallogr., Sect. B* **1979**, *B35*, 2715.

Table V. Selected Interatomic Distances (Å) and Angles (deg) for MoO₂(LNS₂)

Mo (1)-O (1)	1.691 (6)	Mo (1)-O (2)	1.696 (6)
Mo (1)-S (1)	2.412 (2)	Mo (1)-S (2)	2.419 (2)
Mo (1)-N (1)	2.244 (7)	S (1)-C (7)	1.875 (8)
S (2)-C (9)	1.844 (8)	N (1)-C (1)	1.369 (10)
N (1)-C (5)	1.340 (9)	C (1)-C (2)	1.376 (12)
C (2)-C (3)	1.389 (12)	C (3)-C (4)	1.390 (13)
C (4)-C (5)	1.370 (12)	C (1)-C (8)	1.499 (11)
C (5)-C (6)	1.481 (11)	C (6)-C (7)	1.560 (11)
C (8)-C (9)	1.557 (11)	C (7)-C (15)	1.547 (10)
C (7)-C (21)	1.542 (10)	C (9)-C (27)	1.551 (9)
C (9)-C (33)	1.559 (10)		
O (1)-Mo (1)-O (2)	110.5 (3)	O (1)-Mo (1)-S (1)	92.5 (2)
O (1)-Mo (1)-S (2)	101.3 (2)	O (1)-Mo (1)-N (1)	126.4 (2)
O (2)-Mo (1)-S (1)	101.9 (2)	O (2)-Mo (1)-S (2)	91.2 (2)
O (2)-Mo (1)-N (1)	123.1 (3)	S (1)-Mo (1)-S (2)	156.4 (1)
S (1)-Mo (1)-N (1)	78.4 (2)	S (2)-Mo (1)-N (1)	78.0 (2)
Mo (1)-S (1)-C (7)	106.2 (2)	Mo (1)-S (2)-C (9)	107.5 (2)
Mo (1)-N (1)-C (1)	120.7 (5)	Mo (1)-N (1)-C (5)	119.4 (5)
C (1)-N (1)-C (5)	119.8 (7)	N (1)-C (1)-C (2)	121.7 (8)
N (1)-C (5)-C (4)	120.8 (7)	C (1)-C (2)-C (3)	118.0 (8)
C (2)-C (3)-C (4)	119.6 (9)	C (3)-C (4)-C (5)	119.9 (8)
N (1)-C (1)-C (2)	117.1 (7)	C (2)-C (1)-C (8)	121.1 (7)
N (1)-C (5)-C (6)	117.7 (7)	C (4)-C (5)-C (6)	121.5 (7)
C (1)-C (8)-C (9)	115.6 (6)	C (5)-C (6)-C (7)	112.5 (6)
S (1)-C (7)-C (6)	107.9 (5)	S (1)-C (7)-C (15)	110.7 (5)
S (1)-C (7)-C (21)	106.5 (5)	S (2)-C (9)-C (8)	109.2 (5)
S (2)-C (9)-C (27)	107.4 (5)	S (2)-C (9)-C (33)	111.9 (5)
C (6)-C (7)-C (15)	110.7 (5)	C (6)-C (7)-C (21)	114.3 (6)
C (15)-C (7)-C (21)	108.7 (5)	C (8)-C (9)-C (27)	114.6 (6)
C (8)-C (9)-C (33)	107.3 (6)	C (27)-C (9)-C (33)	106.5 (5)
C (7)-C (15)-C (10)	123.2 (3)	C (7)-C (15)-C (14)	116.9 (3)
C (7)-C (21)-C (16)	122.3 (3)	C (7)-C (21)-C (20)	117.4 (3)
C (9)-C (27)-C (22)	122.3 (3)	C (9)-C (27)-C (26)	117.5 (3)
C (9)-C (33)-C (28)	117.9 (3)	C (9)-C (33)-C (32)	122.1 (3)

The S-O group of Me₂SO is aligned at a O(1)-Mo-O(5)-S(1) torsional angle of 13.1 (3)°. Bond distances and angles within the tridentate ligand are unexceptional. The two chelate rings are somewhat puckered with rather irregular conformations, as seen in atom position deviations (in angstroms) from the following least-squares planes: Mo-N-C(1)-C(6)-C(7)-O(3), 0.17, -0.18, -0.08, 0.41, -0.30, -0.03; Mo-N-C(5)-C(8)-C(9)-O(4), 0.37, -0.32, -0.08, 0.54, -0.23, -0.28. The pyridine ring is twisted from the plane of the MoO₂ group by 61.9°. The most unusual feature of the coordination geometry is the large Mo-O-C bond angles of 137.3 (3)° and 141.9 (3)°. The corresponding angles in **8** are 124.3 (2)° and 126.7 (2)°. The expanded angles are indicative of the large size of the chelate rings which, in view of the Mo-O-C and the small O-Mo-N angles (79.2 (1)° and (1)°), appear to be strained. The MoO₂ group has the general property of compressing bond angles involving other atoms to less than the octahedral values of 90° or 180°. This effect is also evident in, e.g., the O(3)-Mo-O(4) angle of 153.2 (1)°.

The *gem*-diphenyl groups project on the Mo-O(1,2) bonds in a manner desired to prevent μ -oxo dimerization. This is most readily quantitated in terms of distances from the least-squares O(2-5) and N-O(1,3,4) planes, which are essentially normal to the Mo-O(1) and Mo-O(2) bond vectors, respectively. For the first plane, the C(10-15) and C(22-27) rings extend along the Mo-O(1) bond. Selected atom deviations are 0.25, 1.93, 1.52, and 1.73 Å for Mo, O(1), C(13), and C(23), respectively. Similarly for the second plane, the C(16-21) and C(22-27) rings extend along the Mo-O(2) bond and deviations are 0.29, 1.98, 3.53, and 2.72 Å for Mo, O(2), C(18), and C(24), respectively. The carbon atoms cited are those of each ring which lie the furthest above the appropriate plane.

(b) MoO₂(LNS₂). Crystals of this compound are composed of discrete molecules. This property stands in contrast to the

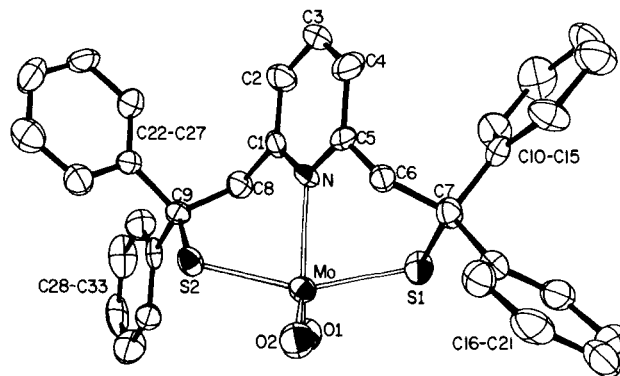


Figure 4. Structure of MoO₂(LNS₂) (**6**) showing the atom labeling scheme and 50% probability ellipsoids.

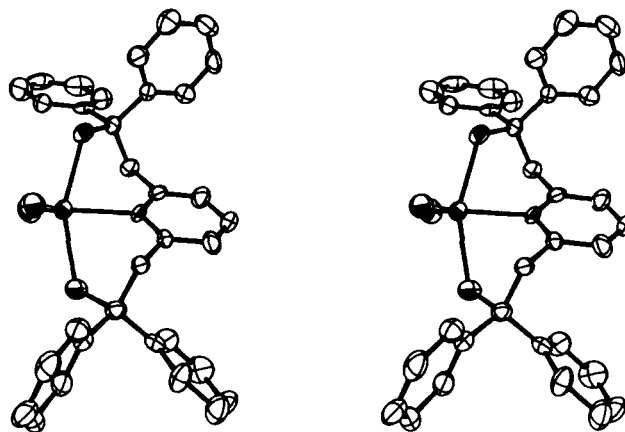


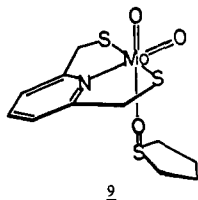
Figure 5. Stereoview of the structure of MoO₂(LNS₂) (**6**).

(47) (a) MoO₂Cl₂(Me₂SO)₂: 2.11, 2.23 Å, Florian, L. R. *Diss. Abstr. Int. B* 1970, B30, 3078. (b) Mo₃O₉·4Me₂SO: 2.245 Å; McCarron, E. M., III; Harlow, R. L. *Chem. Commun.* 1983, 90.

crystalline arrangement of other MoO₂(tridentate) complexes such as **8**²⁷ and MoO₂((OCH₂CH₂)₂O),⁴⁸ which involve linear polymers

with unsymmetrical Mo=O...Mo bridges between six-coordinate Mo atoms. Structurally uncharacterized species with low ν_{MoO} values⁴⁹ are presumably similarly polymerized. The structure of MoO₂(LNS₂) is presented in Figure 4; a stereoview is provided in Figure 5. Metric data are given in Table V. The coordination sphere consists of two oxo atoms, two thiolate sulfur atoms, and a pyridine nitrogen atom, affording the first example of a five-coordinate dioxo Mo(VI) complex. This is the form obtained from a crystallization solvent containing Me₂SO. The related complex derived from pyridine-2,6-dimethanethiol readily forms solvent adducts, and the six-coordinate structure of the tetramethylene sulfoxide adduct 9 has been established by X-ray analysis.²⁷

The geometry of the MoO₂S₂N coordination unit is best approximated by a trigonal bipyramid (TBP), with axial S(1,2) and equatorial O(1,2) and N ligands. The S(1)-Mo-S(2) angle is



156.4 (2)°; all other bond angles at the Mo atom are <126°. Furthermore, the S-Mo-(O,N) angles are 78–102° while angles involving equatorial ligands only are larger, 110–126°. Consideration of dihedral shape parameters⁵⁰ substantiates the assignment of a TBP geometry, which is, however, considerably distorted. The coordination unit closely approaches C₂ symmetry, with the twofold axis coincident with the Mo-N bond vector. The most nearly related structures are found with the μ -oxo Mo(V) dimers MoO₂(Y(CH₂CH₂S)₂)₂ (Y = O, S, and NMe), which have MoO₂S₂X coordination units. Here, however, the bridging oxo and Y ligands are axial, and the terminal oxo and sulfur atoms lie in the equatorial plane.

The Mo-ligand bond distances are quite similar to those found in MoO₂(SR)₂Y₂ complexes with distorted octahedral^{23,24,26-29} and the unusual skew trapezoidal²⁵ structures. In structures of the first type, thiolate groups are mutually trans and each is cis to an oxo atom. Dimensions of the MoO₂ group are normal. The tendency of this group to compress bond angles is evident in the mean value of 78.2° for the S(1,2)-Mo-N angles. The S(1)-Mo-S(2) angle is also subject to this effect and to constraints imposed by the ligand structure. The Mo-S distances are of prime significance, for these are the most securely evaluated structural parameters from EXAFS analysis of enzymatic Mo sites. The values of 2.412 (2) and 2.419 (2) Å fall within the narrow range of 2.40–2.44 Å found for MoO₂(SR)₂Y₂ complexes²³⁻²⁹ and 2.41–2.47 Å for enzyme sites.^{14,15} The few Mo-S(thioether) distances available, all for bonds trans to Mo=O groups, are much longer (2.71–2.81 Å^{24,26}). The Mo-N distance of 2.244 (7) Å is relatively short but is still within the range of values for this bond type when Y = N-ligand.²³⁻²⁹

Ligand bond distances and angles are conventional except for the somewhat long C-S distances of 1.844 (8) and 1.875 (8) Å. These values exceed the distance in the simplest alkyl sulfide, Me₂S (1.807 (2) Å^{52a}) but are less than those in the highly hindered sulfide Ph₃CSCPh₃ (1.892 (1) and 1.916 (1) Å^{52b}). The pyridine ring is considerably twisted from the MoO₂ and MoS₂ planes, the dihedral angles being 38.2° and 58.0°, respectively. This twist

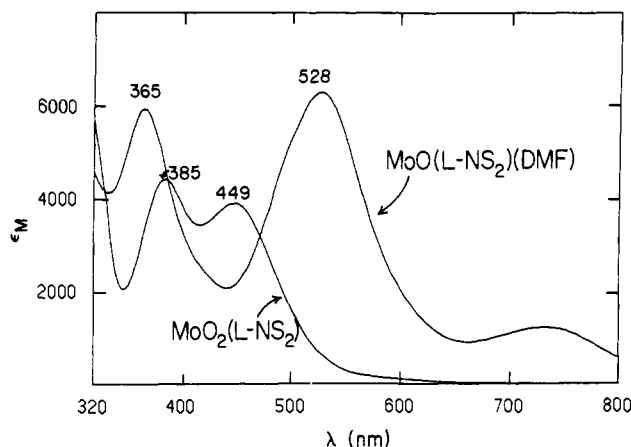


Figure 6. UV-visible absorption spectra of MoO₂(LNS₂) (6) and MoO(LNS₂)(DMF) (7) in DMF solutions.

reflects the large size of the six-membered chelate rings, which are substantially puckered in a twist-boat conformation with relatively unstrained Mo-S-C angles of 106.2 (2)° and 107.5 (2)°. Atom position deviations (in angstroms) for the indicated least-squares planes are the following: Mo-S(1)-C(7)-C(6)-C(5)-N, 0.61, -0.56, 0.02, 0.66, -0.27, -0.46; Mo-S(2)-C(9)-C(8)-C(1)-N, -0.60, 0.55, -0.02, -0.63, 0.24, 0.46. These observations provide a rationale for the five-coordinate structure of MoO₂(LNS₂) vs. a six-coordinate arrangement related to MoO₂(LNO₂)(Me₂SO) or 9. The large Mo-O-C angles were previously cited as evidence of ring strain in the alkoxide complex. The increased ring size caused by sulfur for oxygen substitution cannot be accommodated without the large amounts of twist and pucker observed. These effects direct the chelate arms with their *gem*-diphenyl substituents toward the sites that would be occupied by an additional monodentate ligand, thereby destabilizing adduct complexes. Complex 9 obviously is devoid of such a property.

The *gem*-diphenyl groups do provide the intended steric shielding along the Mo-O(1,2) bonds. This feature is described in terms of atom distances from planes normal to the Mo-O(1,2) bond vectors and containing the Mo atom. Thus, for the plane normal to Mo-O(1), the C(28-33) ring extends outward past O(1). Atom distances are 1.69, 2.00, 3.26, 4.02, 3.51, 2.25, and 1.50 Å for O(1), C(28), C(29), C(30), C(31), C(32), and C(33), respectively. For the plane normal to Mo-O(2), the distances are 1.70, 2.71, 3.82, 3.69, 2.45, 1.35, and 1.48 Å for O(2), C(16), C(17), C(18), C(19), C(20), and C(21), respectively. Each oxo atom experiences an extent of frontside steric protection, i.e., in the direction of potential Mo-O-Mo bond formation, by one phenyl group. The remaining phenyl groups are directed backward, toward the pyridine ring. The stereoview in Figure 5 is useful in visualizing the overall structure of MoO₂(LNS₂).

At this stage of evolution of the problem, the MoO₂S₂N coordination unit of MoO₂(LNS₂) is a credible approximation to those existing in the oxidized sites of oxo-transfer enzymes. The pyridine nitrogen atom is a simulator of O/N ligands suspected to be present but not securely identified by EXAFS analysis.^{14,15} Steric repression of the μ -oxo dimerization reaction 4 has been built in by the inclusion of *gem*-diphenyl groups on the C-(O,S) carbon atoms. The preparation of MoO(LNS₂)(DMF) (7) from MoO₂(LNS₂) in 65% yield is one indication that the steric features of the ligands achieve the desired result. Evidence of the absence of dimerization in oxo-transfer reactions involving these complexes is presented elsewhere. Complex 7 has not been obtained as yet in a form suitable for X-ray diffraction. Prior to consideration of oxo-transfer reactions in the following paper in this issue,³¹ two properties important for the monitoring and occurrence of these reactions are examined.

Absorption Spectra. The UV-visible spectra of MoO₂(LNS₂) and MoO(LNS₂)(DMF) in DMF are shown in Figure 6. The spectrum of the former complex, which forms orange solutions, consists of two intense bands with $\lambda_{\text{max}}(\epsilon_{\text{M}}) = 449$ (3900) and 385

(48) Wilson, A. J.; Penfold, B. R.; Wilkins, C. J. *Acta Crystallogr., Sect. C* **1983**, C39, 329.

(49) (a) Rajan, O. A.; Chakravorty, A. *Inorg. Chem.* **1981**, 20, 660. (b) Toplich, J.; Lyon, J. T., III. *Polyhedron* **1984**, 3, 55.

(50) Muettterties, E. L.; Guggenberger, L. J. *J. Am. Chem. Soc.* **1974**, 96, 1748.

(51) (a) Tsao, Y.-Y. P.; Fritchie, C. J., Jr.; Levy, H. A. *J. Am. Chem. Soc.* **1978**, 100, 4089. (b) Hyde, J. R.; Zubieta, J. *Cryst. Struct. Commun.* **1982**, 11, 929.

(52) (a) Iijima, T.; Tsuchiya, S.; Kimura, M. *Bull. Chem. Soc. Jpn.* **1977**, 50, 2564. (b) Jeffrey, G. A.; Robbins, A. *Acta Crystallogr., Sect. B* **1980**, B36, 1820.

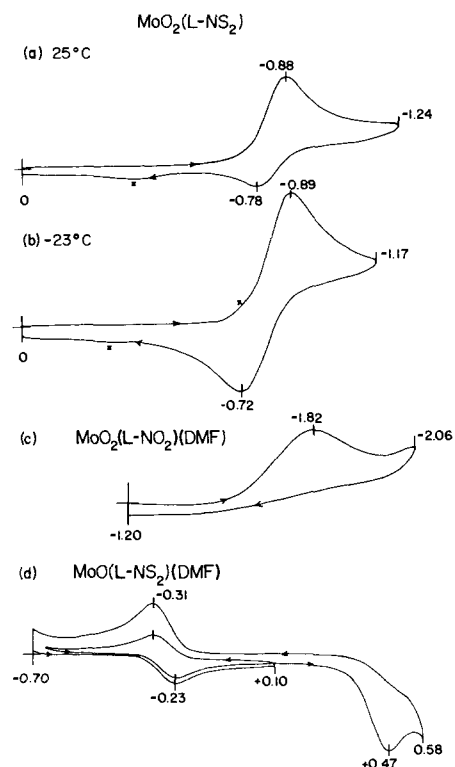
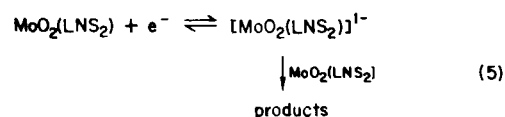


Figure 7. Cyclic voltammograms in DMF solutions: (a) $\text{MoO}_2(\text{LNS}_2)$, (b) $\text{MoO}_2(\text{LNS}_2)$ at -23°C , (c) $\text{MoO}_2(\text{LNO}_2)(\text{DMF})$; (d) $\text{MoO}(\text{LNS}_2)(\text{DMF})$. Voltammograms (a)–(c) were recorded at 500 mV/s; solutions contained 0.1 M (*n*- Bu_4N)(ClO_4). Voltammogram (d) was measured at 100 mV/s in the presence of 0.1 M Et_4NCl . Peak potentials vs. SCE are indicated; (a), (c), and (d) were recorded at $\sim 25^\circ\text{C}$ (x = unidentified feature).

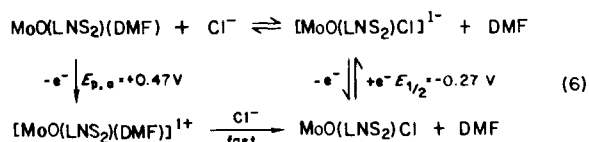
(4400 nm). Other dioxo Mo(VI) alkylthiolate complexes have their lowest energy features below ~ 390 nm.^{28,53} These absorptions are assigned to $\text{RS}^- \rightarrow \text{Mo(VI)}$ charge transfer. In this connection it is relevant to observe that the oxidized Mo fragment of rat liver sulfite oxidase also absorbs at relatively low energy, with features at ~ 475 and 350 nm.⁵⁴ Two or three thiolate ligands are indicated by EXAFS to be present in the oxidized holoenzyme,¹⁴ strongly suggesting that the foregoing bands have the same origin as those of $\text{MoO}_2(\text{LNS}_2)$. Conversion of this complex to $\text{MoO}(\text{LNS}_2)(\text{DMF})$ affords a purple chromophore with $\lambda_{\text{max}}(\epsilon_{\text{M}}) = 734$ (1200), 528 (6300), and 365 (5900) nm. Other oxo Mo(IV) thiolate complexes exhibit strong bands at ~ 370 – 500 nm.^{22a,53} The large differences between the two chromophores in Figure 6 allow for effective spectrophotometric monitoring of the forward and reverse oxo-transfer reaction 1.³¹

Electrochemistry. The electrochemical behavior of $\text{MoO}_2(\text{LNS}_2)$, $\text{MoO}(\text{LNS}_2)(\text{DMF})$, and $\text{MoO}_2(\text{LNO}_2)(\text{DMF})$ in DMF solutions has been surveyed. Cyclic voltammograms are shown in Figure 7. $\text{MoO}_2(\text{LNS}_2)$ exhibits an irreversible reduction which approaches chemical reversibility at -23°C ($i_{\text{p,c}}/i_{\text{p,a}} \approx 1$), where $E_{1/2} \approx -0.81$ V. Controlled potential coulometry at -1.20 V gave $n = 0.51$ e⁻/Mo (mean of three determinations) and essentially colorless solutions upon completion of electrolysis. These results indicate that the initial reduction product reacts with the starting complex in reaction 5 to produce, finally, species (unidentified) lacking Mo–thiolate ligation. Recently, the six-coordinate complex $\text{MoO}_2(o\text{-C}_6\text{H}_4(\text{S})\text{SCH}_2)_2$ has been reported to undergo a quasireversible reduction at -0.89 V in DMF.^{21b} In this case, controlled potential coulometry gave $n = 2\text{e}^-/\text{Mo}$ and an oxo



Mo(IV) product. $\text{MoO}_2(\text{TPP})$ in dichloromethane behaves similarly.⁵⁵ In the general case, because of possible electroactivity of initially generated species at the potentials employed and different experimental time scales, the final product of electrolysis is not necessarily the same as the first species detected by cyclic voltammetry. Reductions of dioxo Mo(VI) complexes in aprotic solvents are generally irreversible.^{21c,22b,49,56,57} It appears likely that the initial reduction product is a Mo^{VO}_2 species which, because of its high basicity, may be scavenged by protic impurities in a following step to a Mo^{VO} or $\text{Mo}^{\text{VO}}(\text{OH})$ complex. Inasmuch as the potential for reduction of this type of complex is usually less than that of the initial reduction, it is not surprising that in some cases the electrolysis product is a Mo^{VO} complex.^{21b,55} A corresponding sequence does not occur with $\text{MoO}_2(\text{LNS}_2)$ under the conditions used. Reaction of the monoanion and neutral complex is apparently dominantly fast, and the reaction products are not reducible on platinum at -1.20 V.

The redox behavior of a solution of $\text{MoO}(\text{LNS}_2)$ in DMF containing 0.1 M Et_4NCl includes a reversible oxidation at $E_{1/2} = -0.27$ V ($\Delta E_{\text{p}} = 80$ mV). Scans to higher potentials reveal a further oxidation process, at $E_{\text{p,c}} = +0.47$ V and irreversible. The cathodic scan shows that this process is coupled to the reversible redox step at lower potential. These results are consistent with reaction scheme 6, which is also supported by several additional



observations. (i) The potential of the reversible couple is quite comparable with those for the Mo(IV,V) couples $[\text{MoO}(\text{mpe})\text{Cl}]^{0,1-}$ (-0.37 V^{22a}) and $[\text{MoO}(o\text{-C}_6\text{H}_4(\text{S})\text{SCH}_2)_2]^{0,1-}$ (-0.18 V^{21b}), which contain N_2S_2 and S_4 ligand sets, respectively. (ii) With 0.1 M (*n*- Bu_4N)(ClO_4) present and chloride absent, the reversible couple does not appear but an irreversible oxidation, at $E_{\text{p,a}} = +0.52$ V, is retained. The rapid displacement of DMF from the cationic product by chloride is certainly a reasonable proposal based on charge considerations. These observations bode well for the stability of $\text{MoO}(\text{LNS}_2)\text{Cl}$ and analogous ligated Mo(V) species. Their synthesis by chemical or electrochemical means is under investigation. These complexes will be useful in confirming the above scheme. Such species may be related to the EPR-active sites of oxo-transfer enzymes observed under a variety of conditions.^{2–4,12} The failure to observe a reversible Mo(VI)/Mo(V) couple at ambient temperature is not considered a serious drawback to $\text{MoO}_2(\text{LNS}_2)$ as an enzyme site model. Reversible enzyme couples have been measured under (near) equilibrium conditions in aqueous solution, where the experimental time scale and the means of stabilization of Mo(V) by protonation reactions are obviously different from those in the experiments described here.

Lastly, the reduction of $\text{MoO}_2(\text{LNO}_2)(\text{DMF})$, the form derived from 5 in DMF solution, is irreversible at ambient temperature and below. Further, the cathodic peak potential $E_{\text{p,c}} = -1.82$ V is 0.94 V more negative than that of $\text{MoO}_2(\text{LNS}_2)$ under the same conditions. This result is consistent with the effect of

(55) Ledon, H.; Varescon, F.; Malinski, T.; Kadish, K. M. *Inorg. Chem.* **1984**, *23*, 261 (TPP = *meso*-tetraphenylporphyrinate dianion).

(56) (a) Spence, J. T. In "Proceedings of the Climax Third International Conference on the Chemistry and Uses of Molybdenum;" Barry, H. F., Mitchell, P. C. H., Eds.; Climax Molybdenum Company: Ann Arbor, MI, 1979; pp 237–244. (b) Spence, J. T.; Minelli, M.; Kroneck, P. J. *Am. Chem. Soc.* **1980**, *102*, 4538. (c) Taylor, R. D.; Street, J. P.; Minelli, M.; Spence, J. T. *Inorg. Chem.* **1978**, *17*, 3207.

(57) (a) Topich, J. *Inorg. Chem.* **1981**, *20*, 3704. (b) Ghosh, P.; Bandyopadhyay, P.; Chakravorty, A. *J. Chem. Soc., Dalton Trans.* **1983**, 401.

(53) (a) Topich, J.; Lyon, J. T., III. *Inorg. Chim. Acta* **1983**, *80*, L41. (b) Complexes with arenethiolate ligands are reported to absorb at ≤ 470 nm:^{21b} Topich, J.; Lyon, J. T., III. *Polyhedron* **1984**, *3*, 61. (c) Corbin, J. L.; Miller, K. F.; Pariyadath, N.; Wherland, S.; Bruce, A. E.; Stiefel, E. I. *Inorg. Chim. Acta* **1984**, *90*, 41.

(54) (a) Johnson, J. L.; Rajagopalan, K. V. *J. Biol. Chem.* **1977**, *252*, 2017. (b) Rajagopalan, K. V. In ref 4, pp 241–272.

O → S substitution on the potentials of Mo complexes containing otherwise identical ligands.^{22a,49b,56ac} This effect, which renders O-ligated complexes poorer oxidants than their S-ligated analogues, is very large compared to, e.g., the 0.22 V difference between MoO₂(tox)₂ and MoO₂(ox)₂ in DMF.^{56ac} Here the donor atom set also involves a 2S (tox = 8-mercaptoquinoline) → 2O (ox = 8-hydroxyquinoline) comparison. As will be seen,³¹ the comparatively negative potential of MoO₂(LNO₂)(DMF) (which may also derive from structural differences) renders it inert to oxidation by Ph₃P under conditions where MoO₂(LNS₂) stoichiometrically oxidizes this substrate. The oxo-transfer reactions of MoO₂(LNS₂) and MoO(LNS₂)(DMF) are described in the following paper in this issue.³¹

Acknowledgment. This research was supported by NSF Grant CHE 81-06017. X-ray equipment used in this research was obtained by NSF Grant 80-00670.

Registry No. 1, 89959-09-1; 2, 89959-03-5; 3, 89959-04-6; 4, 89959-05-7; 5, 89975-14-4; 6, 89959-07-9; 7, 89959-08-0; 2,6-lutidine, 108-48-5; benzophenone, 119-61-9; diphenylmethanethiol, 831-91-4; 2,3-dihydropyran, 110-87-2; 2,6-bis(bromomethyl)pyridine, 7703-74-4.

Supplementary Material Available: Anisotropic temperature factors, calculated hydrogen atom coordinates, and calculated and observed structure factors for MoO₂(LNO₂)(Me₂SO) and MoO₂(LNS₂) (33 pages). Ordering information is given on any current masthead page.

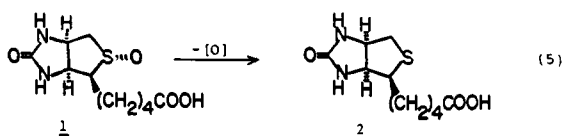
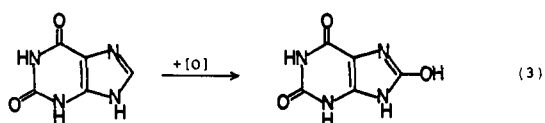
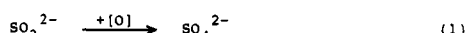
A Model for the Active Sites of Oxo-Transfer Molybdoenzymes: Reactivity, Kinetics, and Catalysis

Jeremy M. Berg¹ and R. H. Holm*

Contribution from the Department of Chemistry, Harvard University, Cambridge, Massachusetts 02138. Received August 10, 1984

Abstract: Oxidation-reduction reactions of substrates in systems containing the complexes Mo^{VI}O₂(LNS₂) and Mo^{IV}O(LNS₂)(DMF) (LNS₂ = 2,6-bis(2,2-diphenyl-2-mercaptoethyl)pyridine) in DMF solutions at 23 °C have been investigated as models for the activities of certain oxo-transfer molybdoenzymes. The MoO_{1.2}S₂N coordination units are reasonable representations of this class of enzymes. MoO₂(LNS₂) reacts with Ph₃P in a second-order process to yield MoO(LNS₂)(DMF) and Ph₃PO with the rate constant $k_1 = 7 (1) \times 10^{-3} \text{ M}^{-1} \text{ s}^{-1}$. MoO(LNS₂)(DMF) reduces sulfoxides in a two-stage reaction involving equilibrium formation of the R₂SO adduct ($K = 4.2\text{--}16 \times 10^3$) followed by R₂S formation ($k_1 = 1.36\text{--}1.70 \times 10^{-3} \text{ s}^{-1}$). The small dependence of K and k_1 on substrate structure suggests that the adduct is O-ligated to Mo(IV). These reactions exhibit the frequent enzymatic property of substrate saturation kinetics. One substrate is *d*-biotin *d*-(S-oxide), the natural substrate of the Mo-dependent enzyme biotin S-oxide reductase from *E. coli*, indicating the biological significance of the reactions. Evidence concerning this and other physiological sulfoxide reducing activities is summarized. Oxo transfers to and from substrate have been coupled to produce a catalytic system which turns over the reaction $\text{Me}_2\text{SO} + \text{Ph}_3\text{P} \rightarrow \text{Me}_2\text{S} + \text{Ph}_3\text{PO}$, in which Me₂SO serves as a model substrate. No reaction is observed in the absence of the Mo catalyst. The initial catalytic rate is given by $k[\text{MoO}_2(\text{LNS}_2)]$, with $k = 6 \times 10^{-3} \text{ M}^{-1} \text{ s}^{-1}$. This rate is limited by the rate of reduction of MoO₂(LNS₂) by Ph₃P. The sulfoxide reducing system developed here is characterized by substrate saturation kinetics, transformation of a biological substrate, and a well-defined catalytic cycle capable of turnover of hundreds of equivalents of a model substrate without intervention of a physiologically unrealistic μ -oxo Mo(V) dimer. This system joins others recently devised in a broad development of reactivity models of metalloenzymes.

With the exception of nitrogenase,² the known molybdenum-containing enzymes catalyze reactions that, at least formally, are oxygen atom transfer processes. These oxo-transfer reactions are of two types: oxidation, involving the addition of an oxygen atom to substrate, and reduction, involving the removal of an oxygen atom from substrate. Examples are given as reactions 1–5, written without mechanistic implication. The properties and reactions



of oxo-transfer molybdoenzymes, including sulfite and aldehyde oxidases, xanthine oxidase/dehydrogenase, and nitrate reductase, have been reviewed.^{3–6} *d*-Biotin *d*-(S-oxide) reductase, which catalyzes the reduction of the sulfoxide **1** to *d*-biotin (**2**) in reaction 5, is a more recently discovered Mo-dependent enzyme.^{7,8} As will become evident, it is of particular relevance to the present research.

One approach to an understanding of the fundamental chemistry underlying enzymatic oxo-transfer reactions requires the development of well-characterized systems of synthetic Mo complexes capable of executing these or related reactions. In order for the information obtained from such systems to be most relevant to the enzyme problem, several additional criteria, previously enumerated,^{9–11} must be met. First, the ligand environment should

(3) Bray, R. C. In "The Enzymes"; Boyer, P. C., Ed.; Academic Press: New York, 1975; Vol. XII, Part B, Chapter 6.

(4) Bray, R. C. *Adv. Enzymol. Relat. Areas Mol. Biol.* **1980**, *51*, 107.

(5) "Molybdenum and Molybdenum-Containing Enzymes"; Coughlan, M. P., Ed.; Pergamon Press: New York, 1980.

(6) "Molybdenum Chemistry of Biological Significance"; Newton, W. E., Otsuka, S., Eds.; Plenum Press: New York, 1980.

(7) del Campillo-Campbell, A.; Campbell, A. *J. Bacteriol.* **1982**, *149*, 469.

(8) del Campillo-Campbell, A.; Dykhuizen, D.; Cleary, P. P. *Methods Enzymol.* **1979**, *62*, 379.

(9) Berg, J. M.; Holm, R. H. *J. Am. Chem. Soc.* **1984**, *106*, 3035.

(10) Holm, R. H.; Berg, J. M. *Pure Appl. Chem.* **1984**, *56*, 1645.

(11) Berg, J. M.; Holm, R. H. *J. Am. Chem. Soc.*, preceding paper in this issue. This paper contains pertinent references to oxo-transfer molybdoenzymes and synthetic Mo complexes not cited here.

(1) National Science Foundation Predoctoral Fellow, 1980–1983.

(2) Mortenson, L. E.; Thorneley, R. N. F. *Annu. Rev. Biochem.* **1979**, *48*, 387.