Tetrahydropterin Reactions of Dioxo-Molybdenum(6+) Complexes: Does Redox Occur?

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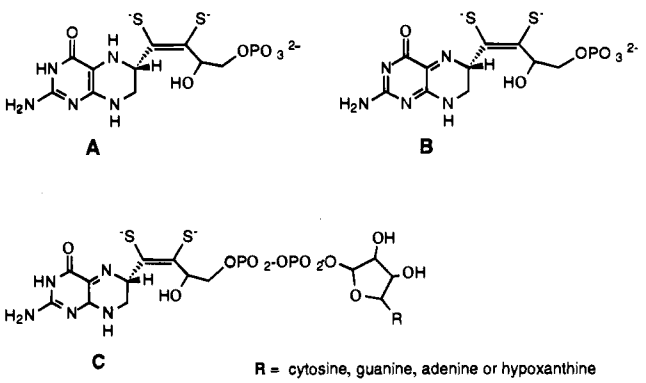
Abstract: This report describes our continued investigation of reactions between tetrahydropterins and dioxo-molybdenum complexes. We report the results of structural, reactivity, and theoretical experiments that indicate these reduced molybdenum-pterin complexes are better described as Mo(6+)-H_4pterin rather than Mo(4+)-H_2-pterin as previously assigned. Both Mulliken charges calculated using the extended Hückel molecular orbital method and the bond valence sum method predict a formal molybdenum oxidation state midway between 5+ and 6+. The complexes $Mo_2O_4Cl_2$(tetrahydro-6,7-dimethylpterin)$_2$, $MoOCl_3$(tetrahydro-6,7-dimethylpterin), and $MoOCl_2$(tetrahydro-6-(hydroxymethyl)pterin)(diethyldithiocarbamate) have been characterized by ^{1}H NMR, IR, UV/vis, and conductivity measurements. The X-ray crystal structure is reported for $Mo_2O_4Cl_2$(tetrahydro-6,7-dimethylpterin)$_2$·4DMF. Inner coordination sphere bond distances indicate substantial electron density is donated from the pterin N(5) to Mo. These complexes undergo solvation and ligand substitution reactions. It is shown that solvation is associated with acid-base reactions at the tetrahydropterin ligands. The molybdenum-tetrahydropterin complexes show a variety of reactivities toward the oxidants O_2, 2,6-dichloroindophenol, and dimethyl sulfoxide. This study shows that tetrahydropterin has a high affinity to chelate Mo(6+) if one of the two oxo ligands is removed and that coordination to molybdenum stabilizes tetrahydropterins toward oxidation. Results from this study also suggest that dioxo-Mo(VI) coordination to tetrahydropterin is unlikely.

Introduction

The function of the pterin component (molybdopterin) of the molybdenum cofactor (Mo-co) that is common to all oxo-molybdenum enzymes remains a mystery.[1] In his initial proposal for the structure of molybdopterin (**A**), Rajagopalan favored the dithiolene site for molybdenum binding but added that the pterin might also interact with Mo.[2] His revised structure (**B**) incorporated a different reduction level for the pterin based on redox titrations;[3] structure **B** represents one of several possible tautomeric structures. These experiments encouraged further speculation on how a redox role might be assigned to molybdopterin in Mo-co that would parallel the redox roles demonstrated by pterin cofactors in other biochemical processes such as phenylalanine hydroxylase and methyl transfer by tetrahydrofolate.[4] The mystery of molybdopterin function has more recently been complicated by the discovery of a new class of molybdopterin structures (C) in many bacterial forms of Mo-co that are distinguished by nucleotide side chains.[5]



The possible combination of a tetrahydropterin (as shown in **A**) and a dioxo-Mo(6+) group in Mo-co prompted us to investigate the reactions of tetrahydropterins with dioxo-molybdenum model complexes. Our initial report from this study described the reaction of MoO_2(diethyldithiocarbamate)$_2$ and 6,7-dimethyltetrahydropterin as a two-electron redox reaction producing Mo(4+) coordinated to the quinonoid isomer of dihydropterin (quin-H_2pterin).[6] Later, the same two-electron redox reaction was reported for $Mo^{VI}O_2Cl_2$ and tetrahydrobiop-

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(1) (a) Enemark, J. H.; Young, C. G. *Adv. Inorg. Chem.* **1994**, *40*, 1. (b) Rajagopalan, K. V. In *Advances in Enzymology and Related Areas of Molecular Biology*; Meister, A., Ed.; John Wiley & Sons: New York, 1991; Vol. 64; pp 215-289. (c) Stiefel, E. I. In *Molybdenum Enzymes, Cofactors and Model Systems*; Stiefel, E. I., Coucouvanis, D., Newton, W. E., Eds.; ACS Symposium Series No. 535; American Chemical Society: Washington, DC, 1993; p 1. (d) Pilatc, R. S.; Stiefel, E. I. In *Bioinorganic Catalysis*; Reedjik, J., Ed.; Marcel Dekker: New York, 1993; p 131. (e) Burgmayer, S. J. N.; Stiefel, E. I. *J. Chem. Educ.* **1985**, *62*, 943.

(2) (a) Johnson, J. L.; Hainline, B. E.; Rajagopalan, K. V.; Arison, B. H. *J. Biol. Chem.* **1984**, *259*, 5414. (b) Johnson, J. L.; Hainline, B. E.; Rajagopalan, K. V. *J. Biol. Chem.* **1980**, *255*, 1783. (c) Kramer, S. P.; Johnson, J. L.; Ribiero, A. A.; Millington, D. S.; Rajagopalan, K. V. *J. Biol. Chem.* **1987**, *262*, 16357.

(3) Rajagopalan, K. V.; Kramer, S.; Gardlik, S. *Polyhedron* **1986**, *5*, 573.

(4) Benkovic, S. J.; Slieker, L. J.; Daubner, L. F.; Courtney, L. F.; Dix, T. A.; Pember, S. O.; Bloom, L. M.; Fierke, C. A.; Mayer, R. J.; Chen, J.; Taira, K. In *Chemistry and Biology of Pteridines-Pteridines and Folic Acid Derivatives*; Cooper, B. A., Whitehead, V. M., Eds.; de Gruyter: Berlin, 1986; p 13.

(5) (a) Johnson, J. L.; Bastian, N. R.; Rajagopalan, K. V. *Proc. Natl. Acad. Sci. U.S.A.* **1990**, *87*, 3190. (b) Meyer, O.; Frunzke, K.; Tachil, J.; Volk, M. In *Molybdenum Enzymes, Cofactors and Model Systems*; Stiefel, E. I., Coucouvanis, D., Newton, W. E., Eds.; ACS Symposium Series No. 535; American Chemical Society: Washington, DC, 1993; p 50.

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terin.[7] However, our continued investigation of both reactions leads us to believe that the Mo(4+)−(quin-H_2pterin) assignments are inaccurate and that *no net* two-electron transfer from pterin to molybdenum occurs.[8] Herein we report the results of structural, reactivity, and theoretical experiments that indicate these reduced molybdenum−pterin complexes are better described as Mo(6+)−tetrahydropterin than as Mo(4+)−dihydropterin complexes. The results of this study suggest additional roles for molybdopterin in molybdoenzymes. These roles include reversible molybdenum chelation by tetrahydropterin where chelation stabilizes tetrahydropterin to oxidation. Results from our study also suggest that dioxo−Mo(VI) coordination to tetrahydropterin is unlikely.

Experimental Section

All reagents used in this work were purchased from Aldrich Chemical Co. except as noted below. MoO_2Cl_2 was purchased from Alfa Inorganics. MoO_2(acetylacetonate)$_2$ (MoO_2(acac)$_2$) and MoO_2(diethyldithiocarbamate)$_2$ (MoO_2(detc)$_2$) were synthesized according to literature procedures.[9] Tetrahydropterins H_4dmp and H_4hmp were synthesized by previously published methods.[10] Solvents were HPLC grade, stored over 4 Å molecular sieves and not further purified. Dimethylformamide was stored under nitrogen. All molybdenum reactions were performed in standard laboratory glassware under a nitrogen atmosphere in a Vacuum Atmospheres drybox. NMR spectra were obtained using an IBM 300 MHz FT-NMR, and chemical shifts are reported in parts per million referenced to internal TMS or solvent. Infrared spectra of samples of KBr disks were recorded on a Perkin-Elmer Model 283 instrument and are referenced to the 1601.2 cm^{-1} absorption of polystyrene. Electronic spectra were recorded using a Hewlett-Packard 8452A spectrophotometer. Solution conductivities were measured using a Barnstead PM-70CB conductivity bridge equipped with a Yellow Springs Instruments 3403 dip cell. Microanalyses were performed by Robertson Microanalytical Labs, Madison, NJ. The following abbreviations are used in this paper: acac, acetylacetonate; detc, diethyldithiocarbamate; ssp, saliciminothiophenolate; sap, saliciminophenolate; dmp, 6,7-dimethylpterin; hmp, 6-(hydroxymethyl)pterin; DCIP, 2,6-dichloroindophenol; hq, 8-hydroxyquinoline; piv-H_4dmp, 2-(*N*-pivalamido)-5,6,7,8-tetrahydro-6,7-dimethylpterin.

Syntheses. $Mo_2O_4Cl_2(H_4dmp)_2$ (1). MoO_2(acac)$_2$ (2.0 mmol, 0.65 g) dissolved in dimethylformamide (10 mL) was added dropwise to H_4dmp·2HCl (0.57 g, 2.0 mmol) in dimethylformamide (20 mL). Within a minute after the addition was complete, the color of the reaction solution changed from pale yellow through orange to red-purple. Diethyl ether (55 mL) was added to induce precipitation which produced dark purple microcrystalline solid after four days (0.31 g, 30% yield). Anal. Calcd for $Mo_2Cl_2O_{10}N_{14}C_{28}H_{52}$ ($Mo_2O_4Cl_2(H_4dmp)_2$·4DMF (**1**): Mo, 19.04; Cl, 7.04; N, 19.46; C, 33.38; H, 5.20. Found: Mo, 18.93; Cl, 7.31; N, 19.29; C, 33.44; H, 4.79. Crystals of suitable quality for X-ray diffraction were obtained by transferring portions (5 mL) of the reaction solution to scintillation vials and letting these stand undisturbed in the glovebox or on a lab bench.

$MoOCl_2(H_4dmp)$·2MeOH (2a). MoO_2(acac)$_2$ (0.7 mmol, 0.234 g) dissolved in methanol (5 mL) was added to H_4dmp·2HCl (0.162 g, 0.7 mmol) in MeOH (10 mL). The color of the reaction solution changed to dark orange-red. Addition of equal volumes of chloroform (15 mL) and diethyl ether (15 mL) caused the precipitation of red-purple microcrystalline solid (0.227 g, 82% yield). Anal. Calcd for $MoCl_2O_5N_5C_{10}H_{21}$ ($MoOCl_2(H_4dmp)$·2MeOH (**2**): Mo, 21.03; Cl, 15.54; N, 15.35; C, 26.33; H, 4.20. Found: Mo, 18.19; Cl, 15.25; N, 16.81; C, 27.07; H, 3.79.

$MoOCl_2(H_4hmp)$·2MeOH (2b) was synthesized following the above procedure for **2a**.

$MoOCl_3(H_4dmp)$ (3). MoO_2Cl_2 (0.199 g, 1.00 mmol) dissolved in MeOH (4 mL) was added dropwise to a solution of H_4dmp·2HCl (0.269 g, 1.00 mmol) in MeOH (24 mL). The color of the reaction solution changed from pale yellow to violet-red. After three days the dark purple microcrystalline precipitate was isolated by vacuum filtration and then washed twice with ethyl ether (0.307 g, 74% yield). Anal. Calcd for $MoCl_3O_2N_5C_8H_{11}$ ($MoOCl_3(H_4dmp)$ (**3**)): Mo, 21.58; Cl, 23.92; N, 15.75; C, 23.92; H, 3.63. Found: Mo, 21.94; Cl, 24.29; N, 15.98; C, 24.44; H, 3.79.

$MoOCl_2$(detc)(H_4hmp) (4). MoO_2(detc)$_2$ (0.339 g, 0.8 mmol) dissolved in $CHCl_3$ (6 mL) was added dropwise to H_4hmp·2HCl (0.221 g, 0.8 mmol) in MeOH (14 mL), causing a solution color change from orange to red within 5 min. Dark red microcrystals precipitated after four days (0.221 g, 56% yield). Anal. Calcd for $MoCl_2S_2O_3N_6C_{12}H_{19}$ ($MoOCl_2$(detc)(H_4hmp) (**4**)): Cl, 13.47; S, 12.18; N, 15.97; C, 27.39; H, 3.64. Found: Cl, 12.94; S, 12.08; N, 16.27; C, 27.99; H, 3.67.

Reaction of 1, 3, and 4 with 8-Hydroxyquinoline. In a typical experiment, **1** (0.0109 g, 0.01 mmol) was dissolved in DMF-d_7 (0.5 mL) and a ^{1}H NMR spectrum recorded. This sample was returned to the drybox where it was mixed with a solution of 8-hydroxyquinoline (0.0031 g, 0.02 mmol) dissolved in DMF-d_7 (0.5 mL). The reaction was monitored by ^{1}H NMR. The reaction of **3** and 8-hydroxyquinoline was performed in DMF-d_7, and the reaction of **4** and hq was performed in MeOH-d_4.

Reaction of 1 and 4 with DCl. In a typical experiment, **1** (0.0109 g, 0.01 mmol) was dissolved in MeOH-d_4 (0.5 mL) and a ^{1}H NMR spectrum recorded. In the drybox, 3 μL of DCl in D_2O (30%) was added by syringe. The reaction was monitored by ^{1}H NMR.

Reaction of 1, 3, and 4 with 2,6-Dichloroindophenol (DCIP). Solutions of complexes **1**, **3**, and **4** in DMF or MeOH (0.05 mM) were mixed with 0.25, 0.5, 0.75, and 1.0 equiv DCIP. The extent of DCIP reduction or protonation was monitored by UV/vis spectrophotometry. DCIP is blue in methanol (λ_{max} = 628 nm; ϵ = 23 400 cm^{-1} M^{-1}) and red in acidic methanolic solutions (λ_{max} = 525 nm; ϵ = 5500 cm^{-1} M^{-1}). Reduced $DCIP^{2-}$ is colorless in methanol (λ_{max} = 212, 274 nm).

Reaction of MoO_2ssp with Tetrahydropterin in Basic Solution. Triethylamine (0.28 mL) was added to H_4dmp (0.268 g, 1.0 mmol) dissolved in DMF (20 mL). This colorless solution was added slowly to an orange solution of MoO_2ssp (0.358 g, 1.0 mmol) in DMF (30 mL). Over the next 24 h the solution color changed from red-orange to red-purple. After one week dark brown crystals of Mo_2O_3(ssp)$_2$(DMF)$_2$ were isolated (70%) followed by precipitation and isolation of dimethylpterin (25%). A control reaction of MoO_2ssp and triethylamine in dimethylformamide after a much longer reaction period (two weeks) produced Mo_2O_3(ssp)$_2$(DMF)$_2$ in much lower yields (29%).

Preparation of 2-(*N*-Pivalamido)-5,6,7,8-tetrahydro-6,7-dimethylpterin (piv-H_4dmp). 6,7-Dimethylpterin (3.82 g, 20 mmol) and trimethylacetic (pivalic) anhydride (20 mL) were placed in a 100 mL round bottom flask with a condensor and heated at reflux in an oil bath for 2 h. The formation of a pale brown precipitate resulted as the flask cooled to room temperature. Diethyl ether was added to break up the solid, and the resulting slurry was vacuum filtered. The yellow product 2-(*N*-pivalamido)-6,7-dimethylpterin (piv-dmp) (73% yield) was dried over P_2O_5 and recrystallized from ethanol if necessary (31% yield). ^{1}H NMR: δ 1.34 (s, 9H, *t*-Bu); 2.69, 2.71 (s, 3H, Me(6), Me(7)). Piv-dmp (0.5 g, 1.8 mmol) was dissolved in methanol (50 mL) and bubbled with nitrogen for 5 min. 10% Pd/C catalyst (0.2 g) was added and the solution again purged with nitrogen for 3 min. The pterin was hydrogenated on the Parr hydrogenator at 46 psi for a minimum of 48 h. The catalyst was removed by filtration. Evaporation to dryness gave a pale yellow solid (90% yield). The product piv-H_4dmp was stored under nitrogen. ^{1}H NMR: δ 1.11, 1.14 (d, 3H, Me(6), Me(7), 1.30 (s, 9H, *t*-Bu), 3.35, 3.60 (dq, 1H, H(6), H(7)).

Reaction of MoO_2(acac)$_2$ with piv-H_4pterin. A pale yellow solution of MoO_2(acac)$_2$ (0.326 g, 1.0 mmol) dissolved in CH_2Cl_2 (10

(6) Burgmayer, S. J. N.; Baruch, A.; Kerr, K.; Yoon, K. *J. Am. Chem. Soc.* **1989**, *111*, 4982.

(7) Fischer, B.; Strahle, J.; Viscontini, M. *Helv. Chim. Acta* **1991**, *74*, 1544.

(8) Burgmayer, S. J. N.; Everett, K. M.; Bostick, L. In *Molybdenum Enzymes, Cofactors and Model Systems*; Stiefel, E. I.; Coucouvanis, D., Newton, W. E., Eds.; ACS Symposium Series No. 535; American Chemical Society: Washington, DC, 1993; p 114.

(9) (a) Moore, F. W.; Larson, M. L. *Inorg. Chem.* **1967**, *6*, 998. (b) Chen, G.; McDonald, J. W.; Newton, W. E. *Inorg. Chem.* **1976**, *15*, 2612.

(10) Mager, H. I. X.; Addink, R.; Berendo, W. *Recl. Trav. Chim. Pays-Bas* **1967**, *86*, 833. This procedure was followed for the reduction of H_4hmp with the substitution of methanol as solvent.

Table 1. Crystallographic Data for $Mo_2O_4Cl_2(H_4dmp)_2$·4DMF (**1**)

(a) Crystal Data	
formula	$C_{28}H_{52}Cl_2Mo_2N_{14}O_{10}$
formula weight	1007.6
crystal color and habit	purple plate
crystal size, mm	0.06 × 0.36 × 0.36
crystal system	orthorhombic
space group	*Pbcn*
a, *b*, *c*, Å	19.931(5), 20.699(4), 20.477(7)
V, Å^3	8448(4)
Z	8
D(calcd), g cm^{-3}	1.584
μ (Mo Kα), cm^{-1}	7.87
(b) Data Collection	
diffractometer	Siemens P4 (Mo Kα)
no. of reflections collected	7965 (max $2\theta = 50°$)
no. of independent reflections	7497
no. of observed reflections	4531 ($4\sigma F$)
min/max transmission	0.623/0.683
(c) Refinement	
R(*F*), *R*(*wF*), %	5.06, 5.83
no. of data/parameter	9.0
$\Delta\rho$(max), e Å^3	0.73

mL) was added dropwise to piv-H_4pterin (0.280 g, 1.0 mmol) in MeOH (8 mL). During the addition the solution color changed from yellow to purple to dark red. Dilution of the reaction solution into methylene chloride showed an absorption at 546; dilution into methanol produced a low-intensity absorption at 504 nm. Addition of the reaction solution to >5 volumes of methylene chloride induced precipitation of a dark purple powder (0.200 g). IR: $\nu_{C=N,O}$ 1640, 1590 and $\nu_{Mo=O}$ 945, 910 cm^{-1}. Vis: (MeCN) 546 nm, (Me_2SO) 542 nm, (DMF) 544 nm, (MeOH) 516 nm.

Reaction of $MoO_2(detc)_2$ with piv-H_4pterin. $MoO_2(detc)_2$ (0.424 g, 1.0 mmol) dissolved in CH_2Cl_2 (15 mL) was added dropwise to piv-H_4pterin (0.212 g, 1.0 mmol) in MeOH (10 mL). During the addition of $MoO_2(detc)_2$ the solution color changed from yellow to red-purple. Monitoring the reaction by UV/vis showed the growth of two absorptions at 506 and 740 nm. After one day a dark purple powder precipitated that was identified as $Mo_2O_3(detc)_4$ by both IR and UV/vis spectroscopy.

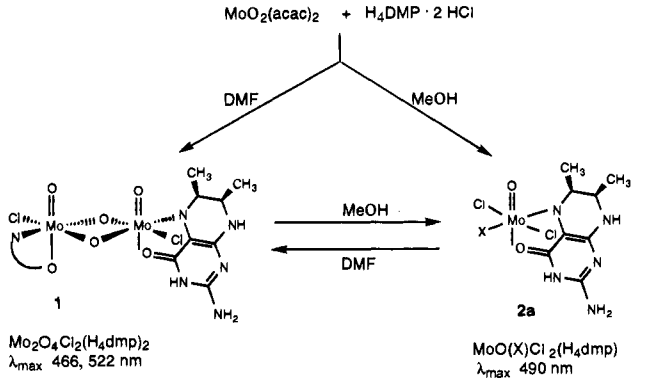
Extended Hückel Molecular Orbital (EHMO) Calculations. Fractional atomic coordinates and cell parameters were taken from the literature and used to obtain atomic positions in Cartesian coordinates. The molybdenum parameters were taken from ref 11.

Bond Valence Sum (BVS) Calculations. The r_o parameters for Mo−O, Mo−N, and Mo−S bonds in oxidation states Mo(6+), Mo(5+), and Mo(4+) were taken from the literature[12a,b] while r_o parameters for Mo−Cl bonds were for Mo(6+)−Cl 2.11, for Mo(5+)−Cl 2.11, and for Mo(4+)−Cl 2.17.[12c] The calculated molybdenum oxidation state listed for each of the complexes in Table 5 represents the value most consistent with the r_o set used. For example, using the bond distances of $MoO_2(ssp)(MeOH)$ with the r_o values assigned to Mo−O, Mo−N, and Mo−S bonds in Mo(6+) gives a calculated oxidation state of +5.99 while the r_o values for Mo−O, Mo−N, and Mo−S bonds in Mo(5+) and Mo(4+) give calculated oxidation states of +6.03 and +5.36, respectively; the most consistent value is therefore +5.99 from the r_o set for Mo(6+).

X-ray Structure Determination. Crystallographic data are collected in Table 1. A specimen mounted on a glass fiber was determined photographically to possess *mmm* Laue symmetry. Systematic absences in the diffraction data uniquely indicated the space group. A semiempirical correction for absorption used 216 ψ-scan reflections. The structure was solved by direct methods. Four molecules of dimethylformamide reside in the lattice for each Mo_2 complex. All nonhydrogen atoms were refined anisotropically, and hydrogen atoms were treated as idealized, updated contributions. All computations used the SHELXTL (4.2) program library (G. Sheldrick, Siemens XRD, Madison, WI).

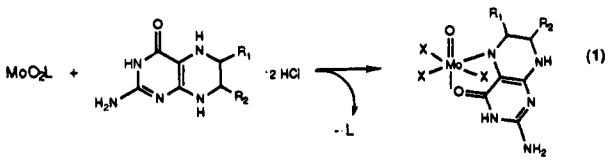
(11) Hoffmann, R.; Kubacek, P. *J. Am. Chem. Soc.* **1981**, *103*, 4320.
(12) (a) Liu, W.; Thorp, H. H. *Inorg. Chem.* **1993**, *32*, 4102. (b) Thorp, H. H. *Inorg. Chem.* **1992**, *31*, 1585. (c) Thorp, H. H. Personal communication.

Scheme 1



Results

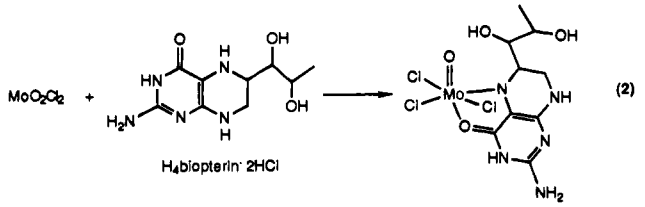
Syntheses. Tetrahydropterins react with a variety of molybdenum(6+)−dioxo reagents, MoO_2L, to give pterin complexes. Many of these reactions proceed by dissociation of the ancillary ligand L (L = acetylacetonate, saliciminothiophenolate, hydrotris(3,5-dimethylpyrazolyl borate)), a process that is promoted by the presence of HCl associated with the pterin reagents (eq 1, X = Cl or solvent).



(1)

The reaction of $MoO_2(acac)_2$ and 6,7-dimethyltetrahydropterin dihydrochloride (H_4dmp·2HCl) yields two different products depending on the solvent (Scheme 1). In dimethylformamide this reaction yields dark purple crystals identified as the dimer $Mo_2O_4Cl_2(H_4dmp)_2$·4DMF (**1**) by X-ray crystallography. In contrast, a red-purple solid (**2a**) precipitates from the same reaction performed in methanol. Although **1** and **2a** display nearly identical IR spectra, their electronic spectra are markedly different. Furthermore, **1** and **2a** interconvert slowly (1−5 h) when dissolved in methanol and dimethylformamide, respectively (Scheme 1). Microanalytical data for **2a** indicate a molybdenum:chloride:tetrahydropterin ratio of 1:2:1. On the basis of this last information and the close similarity between the UV/vis and ^{1}H NMR spectra from **2a** and $MoOCl_3(H_4dmp)$ (**3**) (below) we tentatively formulate **2a** as the monomeric complex "$MoO(X)Cl_2(H_4dmp)$" where X may be methanol solvent or water resulting from the protonation of bridging oxide ligands of **1**.

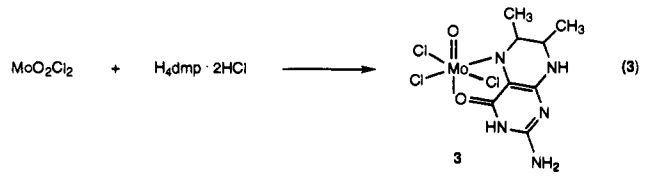
The facile cleavage of dimeric **1** to form a monomeric complex (Scheme 1) led us to suspect that **1** was chemically related to the recently reported Mo complex of reduced biopterin $MoOCl_3(H_2biopterin)$ (eq 2).[7] In order to study this relationship,



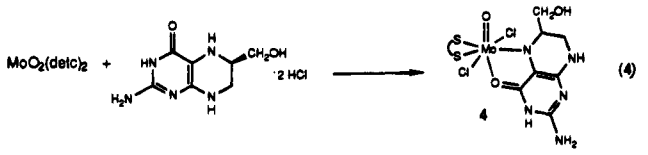
(2)

a synthesis of the 6,7-dimethylpterin analog $MoOCl_3(H_4dmp)$

(**3**) was accomplished using an adaptation of the published procedure (eq 3).

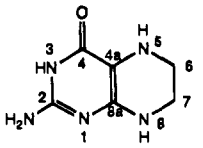


We previously reported that $MoO_2(detc)_2$ reacts with H_4dmp, resulting in pterin coordination as indicated spectroscopically (NMR); unfortunately the product of this reaction has defied isolation in pure form.[6] The reaction of an alternate pterin reagent, 6-(hydroxymethyl)tetrahydropterin (H_4hmp), with $MoO_2(detc)_2$ gives an easily isolated red crystalline product, $MoOCl_2(detc)(H_4hmp)$ (**4**) (eq 4). Equation 4 differs from the



general eq 1 where the ancillary ligand L dissociates because **4** retains one dithiocarbamate ligand in addition to the pterin chelate. Although 7-coordinate Mo(6+) complexes are rare, **4** may be considered a derivative of the known complex $MoOCl_2(detc)_2$ where an anionic tetrahydropterin chelate substitutes for a dithiocarbamate chelate.[13]

We formulate **1**, **2a**, **3**, and **4** as Mo(6+) complexes coordinated by bidentate anionic tetrahydropterin ligands where the pterin is deprotonated at the N(5) site in the pyrazine ring, the nitrogen involved in chelating molybdenum.[14] We prefer



this formulation to the Mo(4+)−dihydropterin choice made by other researchers.[7] This preference is based on structural features, reactivity behavior, and theoretical analysis of the charge on molybdenum as will be discussed below.

X-ray Structure of $Mo_2O_4Cl_2(H_4dmp)_2$·4DMF (1). The dimeric structure of $Mo_2O_4Cl_2(H_4dmp)_2$·4DMF (**1**) was proved by a single-crystal diffraction analysis. An ORTEP drawing of **1** is given in Figure 1. Experimental details from X-ray data collection, structure isolation, and refinement are in Table 1. Selected intramolecular bond distances and selected angles are in Table 2. A molecular 2-fold symmetry axis coincident with a crystallographic 2-fold axis bisects the Mo−Mo vector. The asymmetric unit contains two "$MoO_2Cl(H_4dmp)$" halves of two unique molecules and four molecules of dimethylformamide,

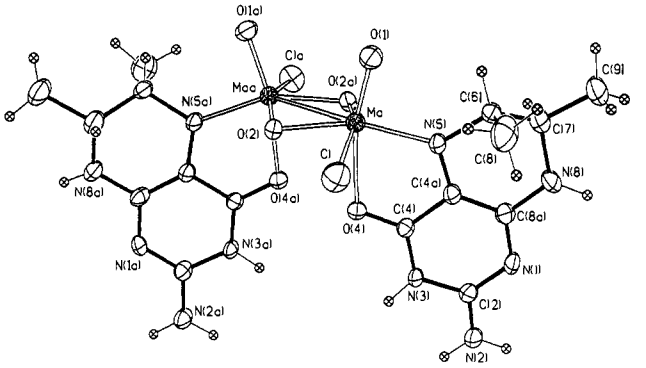


Figure 1. Ortep drawing of $Mo_2O_4Cl_2(H_4dmp)_2$·4DMF (**1**). Atoms labeled "a" are generated from the other half of the dimer by a crystallographic 2-fold axis perpendicular to the $Mo(O_{br})_2Mo$ plane.

Table 2. Selected Bonds and Angles in $Mo_2O_4Cl_2(H_4dmp)_2$·4DMF (**1**)[a]

atoms	distance	atoms	distance
Mo−Cl	2.417(2)	Mo′−O(1′)	1.670(5)
Mo−O(2)	1.966(4)	Mo′−O(4′)	2.287(4)
Mo−N(5)	1.997(5)	Mo′−Mo′A	3.007(2)
O(4)−C(4)	1.266(8)	O(2′)−Mo′A	1.947(4)
N(1)−C(8A)	1.368(9)	N(1′)−C(2′)	1.333(9)
N(3)−C(2)	1.370(9)	N(2′)−C(2′)	1.332(9)
N(5)−C(4A)	1.375(9)	N(3′)−C(4′)	1.365(8)
N(8)−C(7)	1.488(9)	N(5′)−C(6′)	1.497(9)
C(4)−C(4A)	1.401(9)	N(8′)−C(8A′)	1.3379(9)
C(6)−C(7)	1.502(12)	C(4A′)−C(8A′)	1.407(10)
C(7)−C(9)	1.532(11)	C(6′)−C(7′)	1.475(11)
Mo−O(1)	1.674(4)	Mo′−Cl′	2.421(2)
Mo−O(4)	2.269(4)	Mo′−O(2′)	1.957(4)
Mo−MoA	3.037(2)	Mo′−N(5′)	2.013(5)
O(2)−MoA	3.037(2)	Mo′−O(2′A)	1.947(4)
N(1N(1)−C(2)	1.320(9)	O(4′)−C(4′)	1.243(8)
N(2)−C(2)	1.313(8)	N(1′)−C(8A′)	1.347(9)
N(3)−C(4)	1.365(8)	N(3′)−C(2′)	1.372(9)
N(5)−C(6)	1.509(9)	N(5′)−C(4A′)	1.384(8)
N(8)−C(8A)	1.341(9)	N(8′)−C(7′)	1.491(10)
C(4A)−C(8A)	1.383(10)	C(4′)−C(4A′)	1.389(9)
C(6)−C(8)	1.541(13)	C(6′)−C(8′)	1.535(11)
		C(7′)−C(9′)	1.510(12)

atoms	angle	atoms	angle
Cl−Mo−O(1)	95.6(2)	Cl−Mo−O(2)	85.3(1)
O(1)−Mo−O(2)	110.4(2)	Cl−Mo−O(4)	80.7(1)
O(1)−Mo−O(4)	165.6(2)	O(2)−Mo−O(4)	83.3(2)
Cl−Mo−N(5)	95.0(2)	O(1)−Mo−N(5)	92.6(2)
O(2)−Mo−N(5)	156.9(2)	O(4)−Mo−N(5)	74.0(2)
Mo−O(4)−C(4)	112.5(4)	C(2)−N(1)−C(8A)	116.8(6)
C(2)−N(3)−C(4)	120.0(5)	Mo−N(5)−C(4A)	120.4(4)
Mo−N(5)−C(6)	127.7(4)	C(4A)−N(5)−C(6)	111.5(5)
C(7)−N(8)−C(8A)	116.9(6)	N(1)−C(2)−N(2)	119.8(6)
N(1)−C(2)−N(3)	123.7(6)	N(2)−C(2)−N(3)	116.5(6)
O(4)−C(4)−N(3)	122.7(6)	O(4)−C(4)−C(4A)	118.9(6)
N(3)−C(4)−C(4A)	118.4(6)	N(5)−C(4A)−C(4)	114.0(6)
N(5)−C(4A)−C(8A)	128.0(6)	C(4)−C(4A)−C(8A)	118.0(6)
N(5)−C(6)−C(7)	110.9(6)	N(5)−C(6)−C(8)	107.2(6)
C(7)−C(6)−C(8)	114.8(6)	N(8)−C(7)−C(6)	110.6(7)
N(8)−C(7)−C(9)	108.8(6)	C(6)−C(7)−C(9)	113.6(7)
N(1)−C(8A)−N(8)	118.2(6)	N(1)−C(8A)−C(4A)	123.0(6)
N(8)−C(8A)−C(4A)	118.7(6)		

[a] Estimated standard deviations in parentheses.

the crystallization solvent. Because bond distances in the two unique molecules are not significantly different (all but six differ by 2 standard deviations or less) in all subsequent discussion the average bond distance between any two atoms will be used. The dimer may be considered a conlateral bioctahedron where the vector between the two bridging oxide ligands defines the fused edge. The actual geometry at each molybdenum atom is

(13) Dirand, J.; Ricard, L.; Weiss, R. *J. Chem. Soc. Dalton Trans.* **1976**, 278.

(14) Other examples of chelated pterin ligands are reported in the following: (a) Perkinson, J.; Brodie, S.; Yoon, K.; Mosny, K.; Carroll, P. J.; Morgan, T. V.; Burgmayer, S. J. N. *Inorg. Chem.* **1991**, *30*, 719. (b) Burgmayer, S. J. N.; Trofimenko, S.; Schwartz, J. *J. Inorg. Biochem.* **1993**, *51*, 138. (c) Burgmayer, S. J. N.; Stiefel, E. I. *J. Am. Chem. Soc.* **1986**, *108*, 8310. (d) Burgmayer, S. J. N.; Stiefel, E. I. *Inorg. Chem.* **1988**, *27*, 4059. (e) Abelleira, A.; Galang, R. D.; Clarke, M. J. *Inorg. Chem.* **1990**, *29*, 633. (f) Kohzuma, T.; Masuda, H.; Yamauchi, O. *J. Am. Chem. Soc.* **1989**, *111*, 3431. (g) Kohzuma, T.; Odani, A.; Morita, Y.; Takani, M.; Yamauchi, O. *Inorg. Chem.* **1988**, *27*, 3854. (h) Bessenbacher, C.; Vogler, C.; Kaim, W. *Inorg. Chem.* **1989**, *28*, 4645. (i) Jacobson, K. B.; Ferre, J.; Caton, J. E. *Bioorg. Chem.* **1985**, *13*, 296.

distorted from ideal octahedral structure primarily due to the >90° angle for the O=Mo—O_{br} angle of 110.4°. Also contributing to the distortion from ideal angles is the small bite angle (74°) of the coordinated pterin atoms N(5)—Mo—O(4).

Bond distances within the inner coordination sphere of molybdenum are typical of Mo(6+) complexes. The Mo—Mo separation of slightly greater than 3.00 Å indicates no Mo—Mo bond consistent with our oxidation state assignment of Mo(6+). Only one other example of a $Mo_2O_4^{4+}$ core exists for comparison. In $Mo_2O_4(Et_2NO)_2(C_2O_4)_2$ the Mo_2O_4 core is defined by structural parameters nearly identical with those in **1**.[15] Significant multiple bond character between Mo and N(5) of H_4dmp is indicated by the short Mo—N distance.[16] This Mo=N bond seems responsible for the longer Mo—O_{br} bond for the bridging oxide ligand trans to N(5) (1.961 Å) as compared to the bridging oxide trans to chloride (1.946 Å). Distances within the coordinated pterin confirm that N(5) is the site of deprotonation rather than N(3) as has been frequently observed.[14] The short C(4)—O(4) distance of 1.254 Å is consistent with considerable double bond character.[17] The saturation at C(6) and C(7) is apparent from the structural details in the N(5)—C(6)—C(7)—N(8) region of **1** that are typical of tetrahedral quaternary carbon atoms.[18] The reduced pyrazine ring in H_4dmp defined by C(4a)—N(5)—C(6)—C(7)—N(8)—C(8a) is in a half-chair conformation where the methyl groups at C(6) and C(7) are axial and equatorial, respectively. Despite the favored equatorial, equatorial conformation observed for uncoordinated 6,7-dimethyltetrahydropterin, it appears that steric repulsion between the oxo ligand O(1) and Me(6) is better relieved when Me(6) is axial.

Inspection of the packing adopted by the two unique dimers in the asymmetric unit reveals several interesting points. The two dimers appear to optimize a stacking interaction by interleaving the planar portions of pterin ligands. Figure 2 shows a view of the asymmetric unit perpendicular to the Mo-(O_{br})$_2$Mo plane. A hydrogen bonding interaction can be detected between N(2) on one dimer and O(2′) on the other dimer, leading us to speculate that this H bond may be responsible for the facile dimer cleavage. The N(2)—O(2′a) and N(2′a)—O(2) distances average 2.84 Å.

The structure of **1** is compared with that of $MoOCl_3(H_4$biopterin)[7] as one basis for proving that the molybdenum and pterin in these two complexes should be assigned the same oxidation states. Figure 3 shows the bond distances for each Mo—pterin complex to aid comparison. With the exception of the two additional chloride ligands in $MoOCl_3(H_4$biopterin), the inner coordination spheres are very similar and comprise a short Mo=O bond, a short Mo—N(5) bond with considerable multiple bond character, a long Mo—O(4) bond trans to the oxo group, and a Mo—Cl bond of average length. Bond distances within the two coordinated pterins shows considerable delocalization around the ring system and the same alternation of short and long bonds.

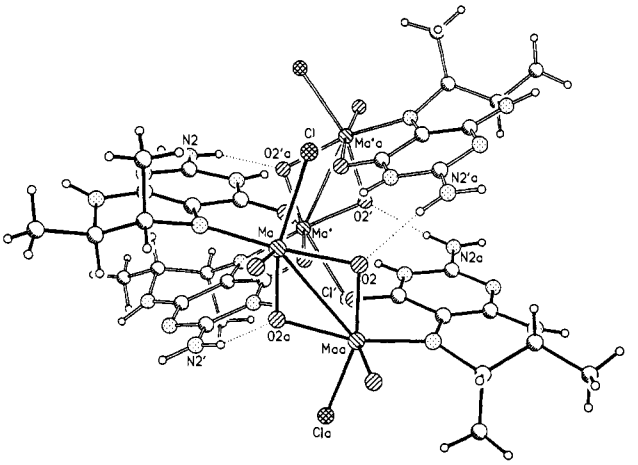


Figure 2. Ortep drawing of the asymmetric unit of $Mo_2O_4Cl_2(H_4$dmp)$_2$·4DMF (**1**). The view is perpendicular to the Mo(O_{br})$_2$Mo plane. The N(2)—O(2′a) and N(2′a)—O(2) distances average 2.84 Å.

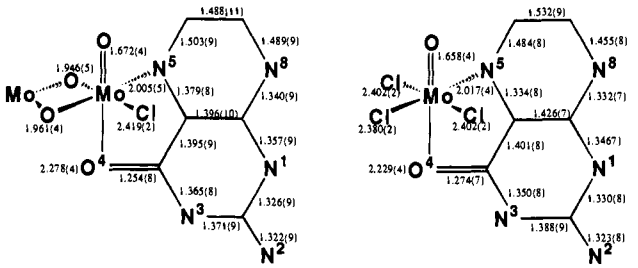


Figure 3. Comparison of bond distances in **1** and $MoOCl_3(H_4$biopterin).[7]

Spectral Properties of Reduced Molybdenum—Pterin Complexes. Molybdenum coordination by tetrahydropterin is most clearly indicated in the ^{1}H NMR spectrum where signals of tetrahydropterin protons H(6) and H(7) exhibit a large downfield shift. For example, H(6) of H_4dmp shifts more than 2 ppm (from 3.4 to 5.6 ppm) on molybdenum coordination while H(7) shows a less dramatic 0.6 ppm downfield shift (from 3.6 to 4.2 ppm). NMR data for complexes **1**, **2a**, **2b**, **3**, and **4** are listed in Table 3. In methanol-d_4 the protons bound to nitrogen atoms N(2), N(3), and N(8) are not detected due to proton exchange with the solvent. Broad signals from these protons are generally observed in dimethyl sulfoxide and dimethylformamide, but only the solution of **1** in DMSO-d_6 clearly revealed resolved resonances for all four protons.

Other spectroscopic properties for **1**, **2a**, **2b**, **3**, and **4** are listed in Table 4. In the infrared spectra $\nu_{Mo=O}$ vibrations are observed in the range 962—972 cm^{-1}. This range of values is high for molybdenum(6+)—oxo complexes where the common MoO_2^{2+} core exhibits two $\nu_{Mo=O}$ vibrations between 890 and 930 cm^{-1} and more typical of monooxo—Mo(5+) or —Mo(4+) species whose single strong $\nu_{Mo=O}$ occurs from 980 to 940 cm^{-1}.[19] It is, however, useful to compare the data in Table 4 with those from other monooxo—Mo(6+) complexes: $MoOX_2$(detc)$_2$ (X = Cl, Br) display $\nu_{Mo=O}$ at 950 (Cl) and 960 (Br) cm^{-1}.[13] It can be rationalized that the elevated $\nu_{Mo=O}$ frequency in **1**, **2a**, **2b**, **3**, and **4** results from an unusually strong π-donation by the single oxo ligand to Mo. The poorer π-donor ability of

(15) Wieghardt, K.; Hahn, M.; Swiridoff, W.; Weiss, J. *Inorg. Chem.* **1984**, *23*, 94.

(16) Typical Mo(6+)—N(amine) distances (*trans*-N—Mo=O): 2.441, 2.460 Å in Dowerah, D.; Spence, J. T.; Singh, R.; Wedd, A. G.; Wilson, G. L.; Farrchione, F.; Enemark, J. H.; Kristofzski, J.; Bruck, M. *J. Am. Chem. Soc.* **1987**, *109*, 5655. 2.385—2.481 Å in Hinshaw, C.; Peng, G.; Singh, R.; Spence, J. T.; Enemark, J. H.; Kristofzski, J.; Merbs, S. L.; Ortega, R. B.; Wexler, P. A. *Inorg. Chem.* **1989**, *28*, 4483. Typical Mo(6+)—N(amido) distances: 2.043, 2.056 Å in Rajan, O. A.; Spence, J. T.; Leman, C. Minelli, M.; Sato, M.; Enemark, J. H.; Kroneck, P. M.; Sulgar, K. *Inorg. Chem.* **1983**, *22*, 3065. Typical Mo—N(imine) distances: Mo(6+) 2.69—2.299, 2.363—2.411 (*trans*-N—Mo=O); Mo(5+) 2.164—2.162; Mo(4+) 2.145—2.299, 2.173, 2.175 (*cis*-N—Mo=O) in Craig, J. A.; Harlan, E. W.; Snyder, B. S.; Whitener, M. A.; Holm, R. H. *Inorg. Chem.* **1989**, *28*, 2082. Schultz, B. E.; Geller, S. F.; Meutterties, M. C.; Scott, M. J.; Holm, R. H. *J. Am. Chem. Soc.* **1993**, *115*, 2714.

(17) (a) Bieri, J. H. *Helv. Chim. Acta* **1977**, *60*, 2303. (b) Bieri, J. H.; Hummel, W.-P.; Viscontini, M. *Helv. Chim. Acta* **1976**, *59*, 2374.

(18) (a) Bierei, J. H.; Viscontini, M. *Helv. Chim. Acta* **1977**, *60*, 447. (b) Antoulas, S.; Prewo, R.; Bieri, J. H.; Viscontini, M. *Helv. Chim. Acta* **1986**, *69*, 210. (c) Bieri, J. H.; Viscontini, M. *Helv. Chim. Acta* **1977**, *60*, 1926.

(19) Stiefel, E. I. *Prog. Inorg. Chem.* **1977**, *22*, 1.

Table 3. NMR Spectral Data for **1**, **2**, **3**, and **4**

6,7-dimethyltetrahydropterin and its complexes		H(6), dq ^3J = 3.3, 6.7 Hz	H(7), dq ^3J = 3.3, 6.7 Hz	Me(6), Me(7), d ^3J = 6.7 Hz	NH, s
H_4dmp·2Cl[a]	DMSO-d_6	3.43	3.64	1.11, 1.08	10.8 br, 9.74 br, 7.54, 6.90
$Mo_2O_4Cl_2(H_4dmp)_2$ (**1**)	DMF-d_7	5.88, 5.75	4.24, 4.03	1.51, 1.33	
		5.68[d]	4.22[d]	1.56,[d] 1.40	9.2, 8.5 br, 7.9 br
	DMSO-d_6	5.60 br	4.03 br	1.42, 1.23	10.5, 8.62, 8.15, 7.96
$MoOCl_2(H_4dmp)$·2MeOH (**2a**)	DMF-d_7	5.66	4.22	1.56, 1.40	9.2, 8.5 br
$MoOCl_3(H_4dmp)$ (**3**)	DMF-d_7	5.69	4.25	1.57, 1.41	9.41, 8.72 br, 7.84 br
	DMSO-d_6	5.56	4.09	1.42, 1.25	9.3, 8.5 br, 7.6 br
	MeOH-d_4	6.0, 5.94, 5.58, 3.55[b]	4.13, 4.09, 3.97, 3.65[b]	1.45, 1.44, 1.39, 1.26, 1.24, 1.19, 1.17,[4]b 1.13[b]	

6-(hydroxymethyl)tetrahydropterin and its complexes		H(6), dd ^3J = 4.1, 8.9 Hz	$H(7_{eq})$, dd[c] ^3J = 4.1, 10.8 Hz	$H(7_{ax})$, dd[c] ^3J = 8.9, 10.8 Hz	$-CH_2-$, m (H_4hmp, detc)	−Me, t (detc)	NH, s
H_4hmp·2HCl	DMSO-d_6	3.56−3.50		3.33	3.81, 3.68 dd		
$MoOCl_2$(detc)(H_4hmp) (**4**)	MeOH-d_4	5.78	4.36	3.77	4.0−3.8	1.37, 1.36	
	DMF-d_7	5.75	4.36	3.75	4.0−3.8	1.64, 1.37	9.52, 8.67 br, 8.58 br
$MoOCl_2(H_4hmp)$·2MeOH (**2b**)	DMF-d_7	5.76	4.49	3.67	4.10, 3.95 dd ^3J = 4.1, 14 Hz		

[a] Assignment based on ref 6. [b] Uncoordinated H_4DMP. [c] Assigned on the basis of 6-MeH_4pterin. [d] These resonances grow in over time and become prominent.

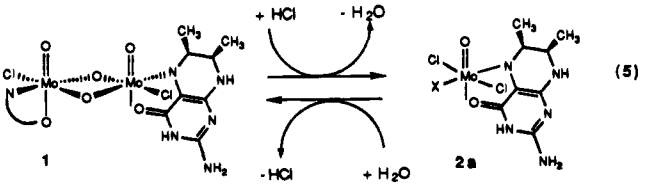
Table 4. Electronic and IR Spectral Data for **1**, **2**, **3**, and **4**

	λ_{max}, nm (ϵ, M^{-1} cm^{-1})	$\nu_{Mo=O}$	ν_{Mo-S}	ν_{Mo-Cl}	$\nu_{C=O,C=N}$
$Mo_2O_4Cl_2(H_4dmp)_2$ (**1**)	MeOH: 306, 492	962		320	1660, 1595
	DMF: 306 (13 600), 466(10 100), 522 (9900)				
	DMSO: 466, 525				
$MoOCl_2(H_4dmp)$·2MeOH (**2a**)	MeOH: 264 (11 300), 306 (5200) 486 (7300)	962		320	1660, 1595
	DMF: 270 (11 600), 310 (8800) 490(10 100)[c]				
$MoOCl_2(H_4hmp)$·2(MeOH) (**2b**)	MeOH: 272, 306, 490	968		340, 327	1660, 1620, 1596
	DMF: 310, 494				
	DMSO: 312, 504				
$MoOCl_3(H_4dmp)$ **3**	MeOH: 482[b]	972		326, 320	1679, 1645, 1595, 1578
	DMF: 306 (6200), 490 (12 800)				
	DMSO: 508				
$MoOCl_2$(detc)(H_4hmp) **4**	MeOH: 246 (19 300) 502 (13 900)	971	377	344, 315	1655, 1623, 1597, 1575, 1520, 1495
	DMF: 2744 (12 200), 322 (5820)				
	522 (10 900), 580 (9200)				
	DMSO: 262, 340 (sh), 524, 588[a]				

[a] Slow oxidation of the complex in DMSO occurs. [b] $MoOCl_3(H_4dmp)$ is unstable toward pterin dissociation in methanol. [c] Spectrum slowly equilibrates to show 306, 466, and 522 nm.

N(5) of coordinated pterin evidently offers little π-competition. No bridging vibrations $\nu_{Mo-O-Mo}$ can be definitively assigned in **1** since H_4dmp like all tetrahydropterins has absorptions in the 800−750 cm^{-1} region. All of these pterin complexes exhibit pterin $\nu_{C=O,C=N}$ absorptions at lower energy than in free tetrahydropterin, a trend previously noted for metal−pteridine complexes.[14]

Molybdenum−tetrahydropterin complexes have colors that range from red through purple due to intense absorptions in the region 480−520 nm. The magnitude of the extinction coefficients (ϵ = ca. 10 000 M^{-1} cm^{-1}) indicates these absorptions are charge transfer in origin, probably of the type pterin to Mo. These spectral features are unusual for dioxo−Mo(6+) complexes that are frequently yellow or yellow-orange but do find precedence in the few examples of monooxo−molybdenum(6+) catecholate complexes which display purple and blue colors from absorptions between 500 and 560 nm.[20] The electronic spectral properties of the molybdenum−tetrahydropterin complexes are difficult to interpret because they are highly dependent on solvent. For example, compare the data in Table 4 for **1** and **2a** dissolved in methanol, dimethylformamide, and dimethyl sulfoxide. Furthermore, an inspection of both the UV/vis and ^{1}H NMR data suggests that complexes **1**, **2a**, and **3** interconvert in solution. This interconversion was first observed for **1** and **2a** dissolved in methanol and dimethylformamide (Scheme 1). The cleavage of the dimeric structure of **1** forming monomeric **2a** may be considered a reversible acid−base reaction where **1** and **2a** are a conjugate acid−base pair (eq 5).



(5)

This reversible acid−base reaction has been demonstrated experimentally for the interconversion of **1** and **3**. Figure 4 shows the spectroscopic changes that result from sequential addition of hydrochloric acid and triethylamine to **1**. The addition of HCl causes the disappearance of the twin absorptions at 466 and 522 nm and the growth of a single absorption at 484 nm of approximately twice the intensity. The addition of triethylamine reverses the spectroscopic change. These results

(20) (a) Bradbury, J.; Schultz, F. A. *Inorg. Chem.* **1986**, *25*, 4461. (b) Mondal, J.; Schultz, F. A.; Brennan, T.; Scheidt, W. *Inorg. Chem.* **1988**, *27*, 3950. (c) Geller, S.; Newton, B.; Majig, L.; Bradbury, J.; Schultz, F. A. *Inorg. Chem.* **1988**, *27*, 359.

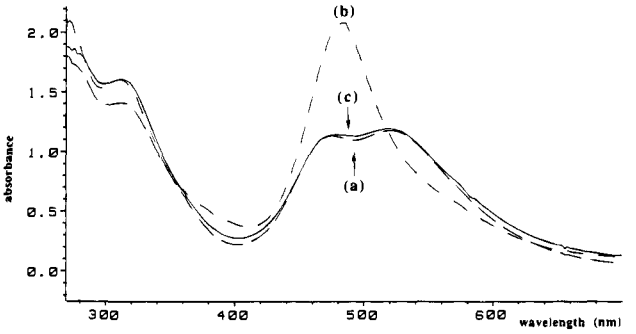


Figure 4. Electronic spectra showing the effect of addition of hydrochloric acid and triethylamine to $Mo_2O_4Cl_2(H_4dmp)_2$·4DMF (**1**): (a) **1** in dimethylformamide, (b) addition of HCl to **1**, (c) subsequent addition of NEt_3.

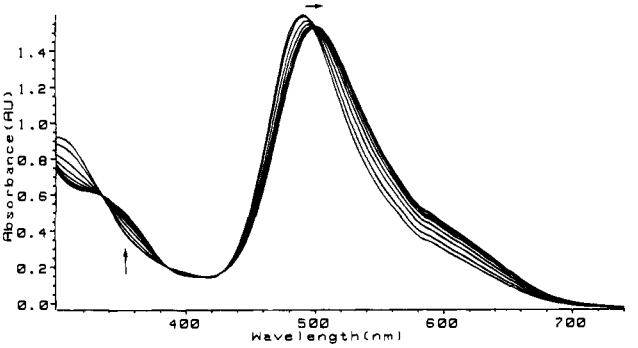
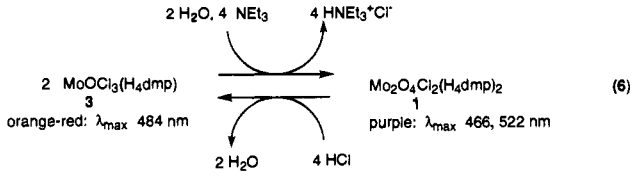


Figure 5. Spectral changes recorded over 5 min when $MoOCl_3(H_4dmp)$ (**3**) is dissolved in dimethyl sulfoxide. The arrows point to the red shift of the absorption at 486 nm and the increase in absorption at 340 nm.

are interpreted as described in eq 6. Equilibria among **1**, **2a**,

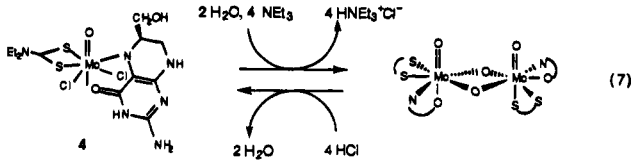


(6)

and **3** are most easily detected by UV/vis spectroscopy, but ^1H NMR data confirm this behavior. Samples of **2a** and **3** in DMF-d_7 and of **1** equilibrated in DMF-d_7 for several days display identical chemical shifts, suggesting that all consist of the same species. The ^1H NMR spectra of **3** in the presence of triethylamine slowly change (24 h) to give a spectrum identical to that from **1** freshly dissolved in DMF-d_7. Likewise, samples of **1** and **3** in DMSO-d_6 give nearly identical spectra.

Similar spectroscopic changes are observed for solutions of **4** treated with triethylamine and then hydrochloric acid. NEt_3 addition causes the absorption at 504 nm to shift to two unresolved absorptions at 522 and 582 nm, and subsequent HCl addition regenerates the single absorption at 504 nm. This suggests that a dimerization similar to eqs 5 and 6 may occur for complex **4** under basic conditions. When ^1H NMR is used to monitor the reaction of NEt_3 and **4** in DMF-d_7, two resonances in a 1:1 ratio are observed for H(6). This is consistent with formation of an unsymmetrical dimer (eq 7).

The complicated solution behavior demonstrated by molybdenum–tetrahydropterin complexes is due to two processes, acid–base reaction and solvation. The equilibria described above (eqs 5 and 6) that interconvert **1**, **2a**, and **3** involve protonation and deprotonation of oxo ligands. Because pterins are amphiphoteric molecules, they may also participate in acid–



(7)

base reactions. Such reactions have been deduced for **3** by a combination of NMR, UV/vis, and conductivity experiments (Scheme 2). Dissolution of **3** in DMSO appears to cause chloride dissociation and coordination of DMSO. This can be observed spectrophotometrically (Figure 5) where a shift of the λ_{max} at 486 to 508 nm occurs within minutes of dissolution. A molar conductivity value of 25 Ω^{-1} M^{-1} for **3** dissolved in DMSO is consistent with the formation of a 1:1 salt.[21] Surprisingly, *exactly* the same spectroscopic change is observed when triethylamine is added to **3** in dimethylformamide. Scheme 2 offers an explanation for how the same species is formed in both reactions. Substitution of chloride by dimethyl sulfoxide (reaction A) would form a cationic DMSO complex where the positive charge increases the acidity of pterin protons. Deprotonation of pterin, most likely at the amide N(3), would reform a neutral complex (reaction B). Deprotonation of pterin by triethylamine (reaction C) would generate an anionic complex that would be more susceptible to chloride dissociation and DMSO substitution (reaction D). Consistent with this scheme is the observation that the pterin-based absorption at 306 nm in **3** shifts to longer wavelength (approximately 340 nm), a behavior previously documented for pterins deprotonated at N(3).[14a]

When $MoO_2(acac)_2$ or Na_2MoO_4 is titrated with H_4dmp·2HCl in methanol, the sequential formation of several complexes is observed visually and spectroscopically. The solution color change from purple to red to orange-red parallels the increase in λ_{max} from 500 to 490 and then 482 nm. Assignment of the species formed in this titration may be made on the basis of the spectroscopic properties discussed above for isolated complexes (Scheme 3). Therefore, the specific conditions, such as chloride and proton concentration, present during reaction of various reagents MoO_2L with tetrahydropterins determine whether the product obtained corresponds to **1**, **2a**, or **3**.

Reactions of Reduced Molybdenum–Pterin Complexes. The reactivity of molybdenum–tetrahydropterin complexes has been studied for several reasons. The first goal was to assign oxidation levels to both pterin and molybdenum. Secondly, the reactivity at molybdenum was studied to ascertain the effect of reduced pterin coordination on known molybdenum chemistry.

Ligand substitution reactions were used to reveal the pterin reduction level. In these experiments, the strong chelant 8-hydroxyquinoline (hq) was added to solutions of **1**, **3**, or **4** to displace the reduced pterin ligand. Equations 8 and 9 indicate

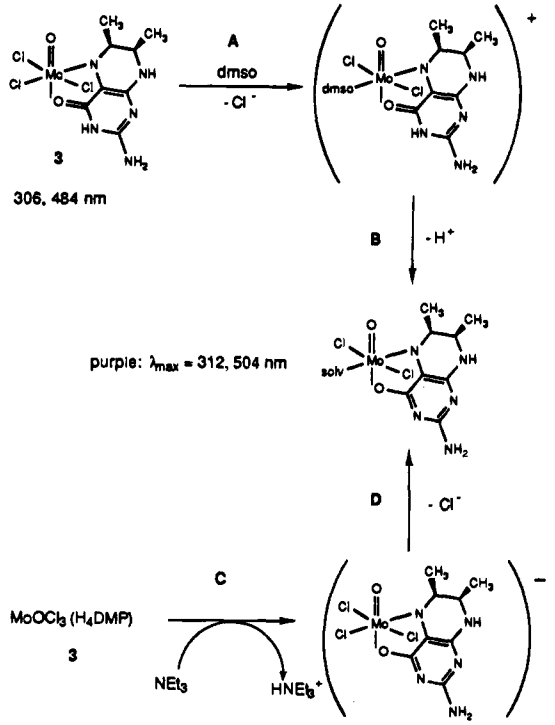
$$Mo^{IV}OCl_3(quin\text{-}H_2dmp) + 8\text{-hydroxyquinoline} \rightarrow MoOCl_3(hq) + 7,8\text{-}H_2dmp \quad (8)$$

$$Mo^{VI}OCl_3(H_4dmp) + 8\text{-hydroxyquinoline} \rightarrow MoOCl_3(hq) + H_4dmp \quad (9)$$

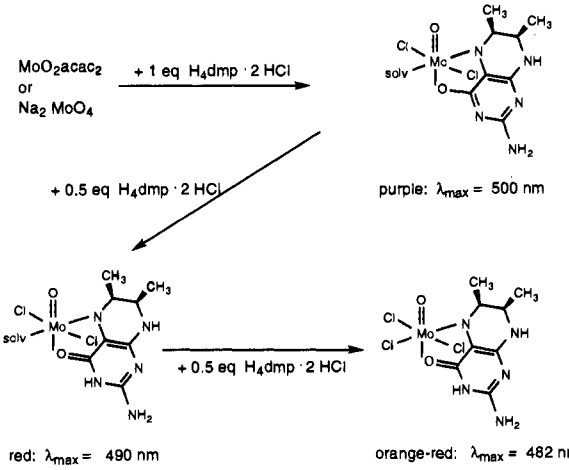
the expected chemistry for the two limiting forms of the reduced Mo–pterin complex **3**, that is, for pterin coordinated as the quinonoid–dihydropterin (eq 8) and as tetrahydropterin (eq 9). The key fact that allows eq 8 to be distinguished from eq 9 is that uncoordinated quinonoid–H_2dmp is unstable in solution at room temperature and rapidly rearranges to the isomeric

(21) Geary, W. J. *Coord. Chem. Rev.* **1971**, *7*, 81.

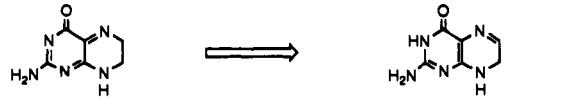
Scheme 2



Scheme 3



structure 7,8-H_2dmp (eq 10).[22] ^{1}H NMR can distinguish 7,8-



(10)

H_2dmp and H_4dmp[6] and provides an easy method to monitor this reaction. In experiments where 1 equiv of hydroxyquinoline was added to solutions of **1**, **3**, and **4**, ^{1}H NMR indicated that only eq 9 occurred; i.e., the coordinated pterin was displaced as the tetrahydropterin. We interpret this result as an indication that oxo–molybdenum–pterin complexes **1**–**4** are more accurately viewed as Mo(6+)–tetrahydropterin complexes rather than Mo(4+)–dihydropterin complexes. It should be noted that addition of a proton source accomplishes the same result—dissociation of the pterin ligand that is identified as tetrahydropterin by ^{1}H NMR.

(22) Kaufman, S. *J. Biol. Chem.* **1961**, *236*, 804.

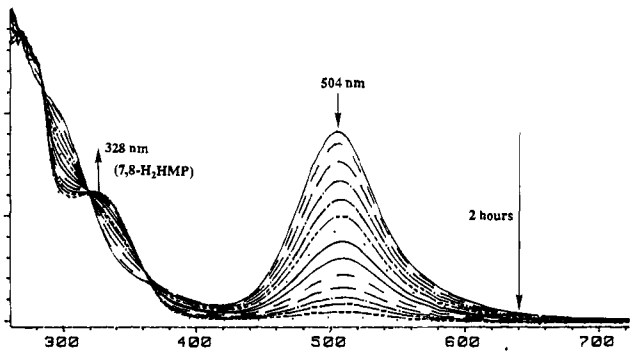


Figure 6. Spectral changes recorded during the oxidation of $MoOCl_2$(H_4-hmp)(detc) (**4**) by O_2 in methanol. The characteristic absorption at 504 nm is bleached as the absorption at 328 nm due to 7,8-H_2dmp grows in.

Table 5. Solution Molar Conductivities (Λ_M, Ω^{-1} M^{-1}) of **1**, **3**, and **4**

	MeOH	DMF	DMSO
$Mo_2O_4Cl_2(H_4dmp)_2$ (**1**)	*a*	30 (<1:1)	
$MoOCl_3(H_4dmp)$ (**3**)	280 (3:1)	7(<1:1)	25(1:1)
$MoOCl_2$(detc)(H_4hmp) (**4**)	130(1:1)	39(<1:1)	33(1:1)

[a] **1** is insufficiently soluble.

The reduced molybdenum–pterin complexes **3**, **4**, and $MoOCl_3(H_4$biopterin) are unstable to the atmosphere, a behavior that initially was interpreted as evidence for the Mo^{IV}(=O) core. Figure 6 shows the UV/vis spectroscopic changes over 2 h accompanying the decay of MoO(H_4hmp)(detc)Cl_2 in methanol exposed to oxygen. The steady decay of the intense visible absorptions at 504 and 304 nm signals the decompositions of the complex while the parallel growth of the absorption at 328 nm is due to the formation of 7,8-H_2dmp. The observed isosbestic points prove that there are no intermediates formed. Methanol solutions of **1**, **2a**, and **3** behave similarly. In dimethylformamide solution **3** undergoes air oxidation within 30 min. $MoOCl_2$(detc)(H_4hmp) and $Mo_2O_4Cl_2(H_4dmp)_2$ are more resistant to oxidation by O_2 in dimethylformamide than in methanolic solution; for example, less than 25% decay is observed for **1** after seven days of exposure to atmospheric oxygen.

In dimethyl sulfoxide solution the complexes exhibit a range of reactivities. Complex **1** shows little oxidation (<10%) by dimethyl sulfoxide after four days. Complex **3** exhibits a shift in its visible absorption that is interpreted as the result of solvent exchange (see above, data in Table 5 and Figure 5). Complex **4** undergoes a pterin oxidation reaction in dimethyl sulfoxide. The red color of an anaerobic dimethyl sulfoxide solution of MoO(H_4hmp)(detc)Cl_2 gradually fades to yellow over several days. Resonances due to coordinated H_4hmp disappear from the ^{1}H NMR spectrum while new signals appear that are assigned to uncoordinated detc and oxidized hmp.

2,6-Dichloroindophenol (DCIP) is a two-electron oxidant that has been used in studies of pterin redox reactions and to assign pterin oxidation states in molybdenum enzymes.[1,3] DCIP, a highly colored dye, is blue in dimethylformamide and methanol (λ_{max} = 628 nm), red in protic or acidic solutions (λ_{max} = 525 nm), and colorless when reduced. H_4dmp·2HCl reacts with 1 equiv of DCIP in methanol within seconds, as indicated by the rapid bleaching of a blue solution of DCIP. Previously it has been shown that 7,8-H_2pterin has no reaction with DCIP while quinonoid–H_2pterin reacts slowly.[22]

We have investigated the behavior of **1**, **3**, and **4** with the oxidant DCIP. None of these complexes react with DCIP in dimethylformamide solution. Addition of 0.25 equiv aliquots

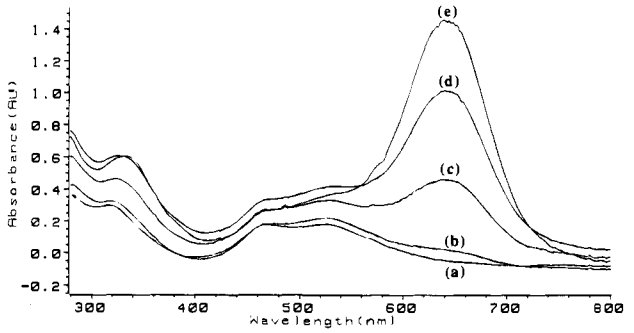


Figure 7. Spectral changes recorded during the titration of $Mo_2O_4Cl_2(H_4dmp)_2$·4DMF (**1**) by 2,6-dichloroindophenol (DCIP) in dimethylformamide: (a) **1** in DMF. (b), (c), (d), and (e) show the effect of adding 0.25, 0.5, 0.75, and 1.0 equiv of DCIP.

of DCIP to **4** or **1** (Figure 7) in methanol or dimethylformamide causes an absorption increase at 620 nm due to increasing concentrations of unreacted DCIP, verifying no reduction of coordinated pterin or molybdenum occurs (eq 11). When **3** is combined with DCIP in dimethylformamide, the initial absorption at 486 nm increases in intensity, shifts to 490 nm, and becomes distinctly asymmetric due to a shoulder on the low-energy side. Subtraction of the initial spectrum from the final spectrum shows that a new absorption at 525 nm is responsible for the spectral changes; this absorption corresponds to protonated DCIP. Therefore, **3** is not oxidized by DCIP in dimethylformamide but does behave as an acid to transfer a proton to DCIP (eq 12). In contrast, when a red methanolic solution of **3**

$MoOCl_2(H_4hmp)(detc)$ or

$$Mo_2O_4Cl_2(H_4dmp)_2 + DCIP \xrightarrow{DMF} \text{no reaction} \quad (11)$$

$$MoOCl_3(H_4dmp) + DCIP \xrightarrow{DMF} [MoOCl_3(H_3hmp)]^- + DCIPH^+ \quad (12)$$

is combined with a blue solution of DCIP, all solution color fades as bleaching of the dye and decomposition of the complex occur. These observations indicate a redox reaction has occurred wherein DCIP has been reduced by tetrahydropterin. However, it is important to recognize that **3** is unstable toward tetrahydropterin dissociation in methanol, a behavior identical to that reported for $MoOCl_3(H_2biopterin)$ (eq 13).[7] Therefore, in this last experiment it is likely that DCIP is reacting with uncoordinated, not coordinated, tetrahydropterin.

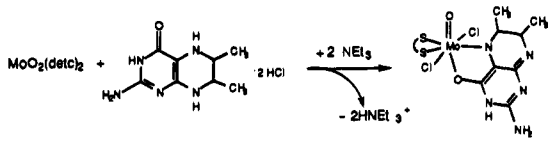
$$MoOCl_3(H_4dmp) \xrightarrow{MeOH} MoOCl_3(MeO) + H_4dmp \quad (13)$$

Reactions of Tetrahydropterins with Molybdenum–Dioxo Complexes in Basic and Neutral Solutions. The general reaction conditions described in eqs 1–4 were altered by removing the hydrochloric acid introduced into the media by the tetrahydropterin reagents. HCl was eliminated in two ways: (1) by addition of triethylamine and (2) through the use of a soluble neutral pterin, 2-(*N*-pivalamido)-6,7-dimethyltetrahydropterin (piv-H_4dmp). Equations 14–16 summarize the results from this change in procedure. Equation 14 shows that the reaction of MoO_2ssp and H_4dmp in the presence of hydrochloric acid leads to dissociation of the ssp ligand and the subsequent chelation of H_4dmp. When 2 equiv of triethylamine was added to neutralize the HCl, no molybdenum–pterin complexes were obtained. The recovery of the Mo(5+) dimer $Mo_2O_3(ssp)_2$ and oxidized dimethylpterin indicates that a redox reaction occurred (eq 15). When triethylamine was added to

$$2MoO_2ssp + H_4dmp{\cdot}2HCl \rightarrow Mo_2O_4Cl_2(H_4dmp)_2 + 2H(ssp) \quad (14)$$

$$MoO_2ssp + H_4dmp{\cdot}2HCl + 2NEt_3 \rightarrow Mo_2O_3(ssp)_2\ (70\%) + dmp\ (25\%) \quad (15)$$

the reaction of $MoO_2(detc)_2$ and H_4dmp·2HCl (eq 16), an immediate reaction color change (yellow-orange to purple; λ_{max} = 504 nm) was observed. A ^{1}H NMR spectrum of the reaction



(16)

solution showed two double quartet signals at 5.64 and 5.47 ppm with one-third the intensity of two doublets at 1.57 and 1.49 ppm. The 2 ppm downfield shift of resonances from *both* H(6) and H(7) suggested that N(8) as well as N(5) might be deprotonated to give a species such as the product in eq 16. Unfortunately when this reaction was repeated on a large scale, only small amounts of an impure Mo–pterin complex could be isolated. The Mo(5+) dimer $Mo_2O_3(detc)_4$ was also isolated from this reaction.

Reaction of tetrahydropterin and dioxo–Mo(6+) complexes in neutral media follows yet a different course. When piv-H_4dmp is combined with $MoO_2(acac)_2$ in a mixture of methylene chloride and methanol, a highly unstable purple compound can be isolated. Dissolving this product in methanol is accompanied by a change in color from purple to red, spectroscopically reported as a shift from 514 to 492 nm, that ultimately fades to a pale pink hue, indicating decomposition of the isolated species. A similar result occurs in dimethylformamide: the intense absorption at 544 shifts to 518 nm with dramatically decreased intensity. The isolated purple solid displays two strong $\nu_{Mo=O}$ at 945 and 910 cm^{-1} in addition to absorptions at 1640 and 1590 cm^{-1} that are characteristic of chelated pterin. A ^{1}H NMR spectrum shows unresolved resonances at chemical shifts characteristic of coordinated tetrahydropterin. From this spectroscopic data, the product appears to be a $Mo^{VI}O_2$(H_4pterin) complex (eq 17).

$$MoO_2(acac)_2 + piv\text{-}H_4dmp \rightarrow MoO_2(piv\text{-}H_4dmp) \quad (17)$$

When piv-H_4dmp is combined with $MoO_2(detc)_2$ in chloroform, no reaction is observed by electronic or ^{1}H NMR spectroscopy (eq 18). If the reaction is performed with addition of protic solvent (MeOH), NMR detects a small amount of pterin coordination as well as the formation of free diethyldithiocarbamate (eq 19).

$$MoO_2(detc)_2 + piv\text{-}H_4dmp \xrightarrow{CH_2Cl_2} \text{no reaction} \quad (18)$$

$$MoO_2(detc)_2 + piv\text{-}H_4dmp \xrightarrow{MeOH/CH_2Cl_2} \text{small amount of pterin coordination} + detc^- \quad (19)$$

Theoretical Calculations on Reduced Molybdenum–Pterin Complexes. Two computational methods were used to assign the oxidation state of the molybdenum and the coordinated pterin. Mulliken atomic charges[23] on molybdenum were computed by the extended Hückel molecular orbital (EHMO)

(23) Mulliken, R. S. *J. Chem. Phys.* **1955**, *23*, 1833.

Table 6. Formal Oxidation States and Mulliken Atomic Charges[a]

molecule	formal Mo oxidatn state	calcd Mulliken charge on Mo	ref
MoO_2(5-*t*-Bu(sap))(MeOH)	6	4.42	24a
MoO(naph-cat)(sap)	6	4.41	24b
MoO_2(HB(Me_2prz)$_3$)(NCS)	6	3.98	24c
MoO_2(HB(Me_2prz)$_3$)(S_2P(OEt)$_2$)	6	3.96	24d
$MoO_2(N_2S_2)$	6	3.82	24g
MoO(detc)$_2Cl_2$	6	3.70	13
MoO(HB(Me_2prz)$_3$)(N_3)$_2$	5	3.95	24e
MoO(HB(Me_2prz)$_3$)(NCS)$_2$	5	3.98	24e
Mo_2O_3(3-OEtBu(sap))$_2$(dmf)$_2$	5	3.60	24a
MoOCl(HB(Me_2prz)$_3$)(NCS)	5	3.58	24c
Mo_2O_3(3-*t*-Bu(sap))$_2$(dmf)$_2$	5	3.50	24a
MoO(HB(Me_2prz)$_3$)(S_2P(OEt)$_2$)	4	4.05	24d
MoO(HB(Me_2prz)$_3$)(detc)	4	3.88	24f
MoS(HB(Me_2prz)$_3$)(detc)	4	3.87	24f
MoO(3-*t*-Bu(sap))(bipy)	4	3.36	24a
MoOCl(HB(Me_2prz)$_3$)(py)	4	2.90	24c
$Mo_2O_4Cl_2$(H_4dmp)$_2$ (**1**)		4.25	this work
$MoOCl_3$(H_4biopterin)		3.9	7

[a] Ligand abbreviations are defined in the Experiment Section.

method, and the molybdenum oxidation state was approximated using the bond valence sum (BVS) method. These two methods were applied to **1** and to $MoOCl_3$(H_4biopterin) that have atomic positions determined by X-ray diffraction analysis. For purposes of comparison, a set of molybdenum−oxo complexes which, according to conventional assignments, have no oxidation state ambiguity were also treated by EHMO and BVS methods.[24]

The EHMO results are summarized in Table 6 and graphically depicted in Figure 8. Inspection of the Mulliken charges on molybdenum in model compounds shows that there is no discrete range of charges that correlates to a particular oxidation state. For example, molybdenum charges calculated for formally Mo(6+) complexes range from +4.42 to +3.70 while the values calculated for Mo(5+) and Mo(4+) complexes span the ranges +3.95 to +3.50 and +4.05 to +2.90, respectively. A trend is revealed, however, if the data are separated into groups according to the ligand donor set. Figure 8 is a plot of formal oxidation state versus Mulliken charge. The lines represent the best fit for the correlation of formal oxidation state and Mulliken charge for complexes having predominantly oxygen donors (O_4X_2 or O_5X), nitrogen donors (N_4X_2 or N_5X), or multiple sulfur donors (S_2X_4 or S_3X_3). Data for complexes with the electronegative "hard" oxygen and nitrogen donors produce the expected trend: a steady increase in Mo charge with an increase in formal oxidation state. In contrast, the peculiar bonding abilities of the "softer" sulfur donors result in molybdenum charges that are nearly constant for formal Mo charges of +4 to +6.

The molybdenum charge calculated for Mo_2O_4(H_4dmp)$_2$-Cl_2·4DMF (**1**) is +4.26. Since the molybdenum has an O_4NCl coordination sphere, this value is best considered with other data for Mo in predominantly oxygen donor sets. On the basis of the correlation for O_4X_2 or O_5X donor atoms plotted in Figure 8, a Mulliken charge of +4.26 corresponds to a formal Mo oxidation state of 5.85+. Therefore, Mo_2O_4(H_4dmp)$_2Cl_2$ appears to be most like a Mo(6+) dimer. $MoOCl_3$(H_4biopterin) produces a computed Mulliken charge of +3.9 for an O_2NCl_3 coordination sphere. Although no comparable donor set is available,[25] a computed charge of +3.9 corresponds to the range 5.4+ to 5.6+ for predominantly oxygen and nitrogen donors, respectively. $MoOCl_3$(H_4biopterin) seems to have an intermediate formal Mo oxidation level between 5+ and 6+, making the pterin ligand somewhat more oxidized than the tetrahydro level, but certainly not as oxidized as a dihydropterin.

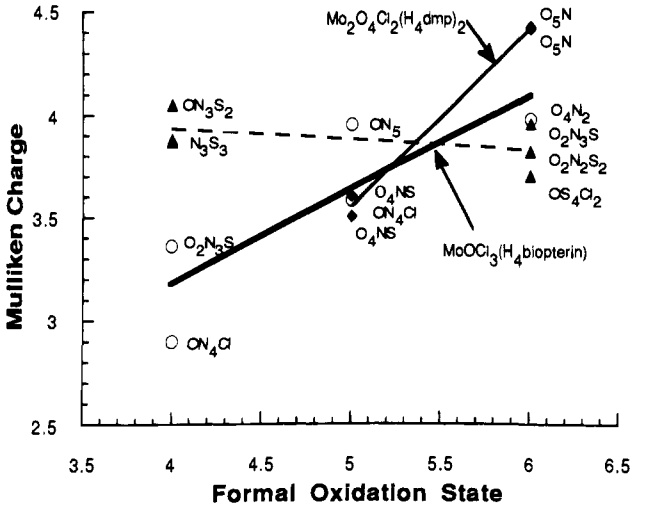


Figure 8. Calculated Mulliken charge versus the formal oxidation state assigned to molybdenum in other model compounds. The lines indicate the trends observed for complexes of similar inner coordination sphere. ◆ designates complexes having four or five oxygen atoms in the inner cordination sphere, and the trend in these data are indicated by the fine line. ○ designates complexes having three or four nitrogen atoms in the coordination sphere, and these generate the heavy line. ▲ designates complexes having two or three sulfurs atoms, and the dashed line shows the trend in these data. The arrows point to the calculated Mulliken charges for the molybdenum−pterin complexes $Mo_2O_4Cl_2$(H_4-dmp)$_2$·4DMF (**1**) and $MoOCl_3$(H_4biopterin).[7]

The bond valence sum (BVS) method using parameters recently published by Thorp[11] has been applied to Mo_2O_4(H_4-dmp)$_2Cl_2$, $MoOCl_3$(H_4biopterin), and the same set of model molybdenum complexes used for reference in the Mulliken charge calculations. The results are listed in Table 7. For the model complexes in oxidation states 6+ and 5+, the BVS method computes oxidation states close to the formally assigned integral value within ±0.25 unit. The BVS treatment of the Mo(4+) complexes is generally less successful in predicting a value near 4.0+, but it does produce a cluster of values within a significantly lower range than seen for 6+ and 5+. The molybdenum oxidation states computed by the BVS method for Mo_2O_4(H_4dmp)$_2Cl_2$ and $MoOCl_3$(H_4biopterin) are 5.5+ and 5.2+, respectively. These values are reasonably close (±0.3) to the estimates from the Mulliken charge correlation described above. Both methods indicate an intermediate oxidation state between 5+ and 6+ where the charge on Mo in Mo_2O_4(H_4-DMP)$_2Cl_2$ is slightly higher.

Discussion

Tetrahydropterins readily react with dioxo−molybdenum(6+) complexes, producing chelated pterin complexes. Although we and other researchers initially formulated these products as Mo-(4+)−quinonoid−dihydropterin complexes,[6,7] further analysis of the structures, bonding, and reactivity of these complexes

(24) Complexes used to establish the oxidation state yardstick are (a) $Mo^{VI}O_2$(ssp), $Mo^{V}_2O_3$(ssp)$_2$, and $Mo^{IV}O$(ssp)(bipy): *Inorg. Chem.* **1989**, *28*, 2082. (b) $Mo^{VI}O$(ssp)(catecholate): *Inorg. Chem.* **1988**, *27*, 3950. (c) $Mo^{VI}O_2$(NCS)(L-N_3), $Mo^{V}OCl$(NCS)(L-N_3), and $Mo^{IV}OCl$(py)(L-N_3): *Inorg. Chem.* **1990**, *29*, 3650. (d) $Mo^{IV}O(S_2P(OR)_2)$(L-N_3) and $Mo^{VI}O_2(S_2P$-$(OR)_2)$(L-N_3): *Inorg. Chem.* **1988**, *27*, 3044. (e) $Mo^{V}O(N_3)_2$(L-N_3) and $Mo^{V}O$(NCS)$_2$(L-N_3): *Acta Crystallogr.* **1987**, *C43*, 51. (f) $Mo^{IV}O$(detc)-(L-N_3) and $Mo^{IV}S$(detc)(L-N_3): *J. Am. Chem. Soc.* **1987**, *109*, 2938. (g) $Mo^{VI}O_2$(L-S_2N_2): *J. Am. Chem. Soc.* **1987**, *109*, 5655. (h) $Mo^{V}O(SPh)_2$-(L-N_3): *Inorg. Chem.* **1987**, *26*, 1017.

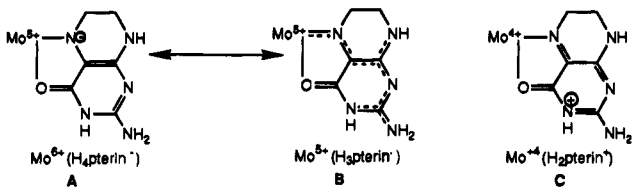
(25) A search of the Cambridge Crystallographic Structure Database revealed no molybdenum complexes having an O_2NCl_3 inner coordination sphere.

Table 7. Formal Oxidation States and BVS Calculated Oxidation States

molecule	formal Mo oxidatn state	BVS calcd oxidatn state	ref
MoO_2(5-*t*-Bu(sap))(MeOH)	6	5.99	24a
MoO(naph-cat)(sap)	6	5.87	24b
MoO_2(HB(Me_2prz)$_3$)(NCS)	6	6.12	24c
MoO_2(HB(Me_2prz)$_3$)(S_2P(OEt)$_2$	6	5.79	24d
MoO_2(N2S2)	6	5.73	24g
MoO(detc)$_2$$Cl_2$	6	5.32	13
MoO(HB(Me_2prz)$_3$)(N_3)$_2$	5	5.15	24e
MoO(HB(Me_2prz)$_3$)(N_3)$_2$	5	5.03	24e
MoOCl(HB(Me_2prz)$_3$)(NCS)	5		
Mo_2O_3(3-*t*-Bu(sap))$_2$(dmf)$_2$	5	5.43	24a
MoO(HB(Me_2prz)$_3$)(SPh)$_2$	5	5.09	24h
MoO(HB(Me_2prz)$_3$)(S_2P(OEt)$_2$)	4	4.57	24d
MoO(HB(Me_2prz)$_3$)(detc)	4	4.55	24f
MoS(HB(Me_2prz)$_3$)(detc)	4	4.22	24f
MoO(3-*t*-Bu(sap))(bipy)	4	4.78	24a
MoOCl(HB(Me_2prz)$_3$)(py)	4	4.57	24c
$Mo_2O_4Cl_2$(H_4dmp)$_2$ (**1**)		5.42,[a] 5.52,[b] 5.05[c]	this work
$MoOCl_3$(H_4biopterin)		5.18,[a] 5.24,[4]b 4.84[b]	7

[a] Calculated using VBS parameters for Mo(6+). [b] Calculated using VBS parameters for Mo(5+). [c] Calculated using VBS parameters for Mo(4+). [d] Ligand abbreviations are defined in the Experimental Section.

Scheme 4



leads us to conclude that they are best considered as Mo(6+)–tetrahydropterin complexes with substantial electron donation from pterin N(5) to Mo.[8] We prefer the resonance description involving partial structures **A** and **B** (Scheme 4) to the alternative structure C which implies a complete transfer of two electrons.

Thus, the reported behavior of "$MoOCl_3$(H_2biopterin) in methanol" [7] where the redox reaction was mysteriously reversed (eq 20) is viewed by us as simply a facile dissociation of coordinated anionic tetrahydropterin in a protic solvent (eq 21). This reaction is conceptionally identical to our experiments where addition of the potent chelant 8-hydroxyquinoline displaced the coordinated pterin (eq 22). It is emphasized that these last two reactions show that *no net* transfer of electron density is accomplished.

$$Mo^{IV}OCl_3(\text{quin-}H_2\text{biopterin}) + MeOH \rightarrow Mo^{VI}OCl_3(OMe) + H_4\text{biopterin} \quad (20)$$

$$Mo^{VI}OCl_3(H_4\text{biopterin}) + MeOH \rightarrow Mo^{VI}OCl_3(OMe) + H_4\text{biopterin} \quad (21)$$

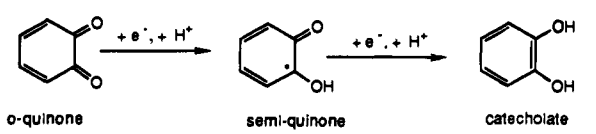
$$Mo^{VI}OCl_3(H_4\text{dmp}) + \text{hydroxyquinoline} \rightarrow MoOCl_3(\text{hydroxyquinoline}) + H_4\text{dmp} \quad (22)$$

Computation of Mulliken charges and bond valence sum oxidation states were used to verify the above interpretation for tetrahydropterin bound at molybdenum(6+). Despite the wide range of computed Mulliken charges on molybdenum in a variety of oxo–molybdenum complexes having 6+, 5+, and 4+ oxidation states, the Mulliken charges computed for dimer **1** and $MoOCl_3$(H_4biopterin) clearly favor an oxidation state midway between 5+ and 6+ (5.4+ to 5.8+) rather than 4+. The BVS method is in agreement with a prediction of a mid-5+ oxidation state (5.5+ and 5.2+) for both **1** and $MoOCl_3$(H_4biopterin).

The short Mo–N(5) distances in both **1** and $MoOCl_3$(H_4biopterin) indicate multiple bond character in a robust bond that must be responsible for the stability of Mo–H_4pterin complexes. Another role of the Mo=N bond is a replacement for the "missing" second oxo ligand that is characteristic of oxo–Mo(6+) chemistry.[19] In the case of dimeric **1** there are bridging oxo groups in addition to the pterin N(5) that can supply some π-electron density to the Mo(6+), but in monomeric $MoOCl_3$(H_4biopterin) the pterin alone must compensate for the missing second oxo ligand. Hence, the pterin is likely a stronger π-donor in $MoOCl_3$(H_4biopterin) than **1**, a conclusion supported by the marginally lower molybdenum charge calculated by both EHMO and BVS methods. Furthermore, we believe that a MoO_2 core would be incompatible with an anionic H_4pterin ligand since π-base competition between the MoO_2 group and the deprotonated N(5) could prevent formation of the Mo=N(5)(pterin) interaction. This expectation is consistent with the results of experiments where MoO_2L complexes are reacted with tetrahydropterins in aprotic and basic media. Under aprotic conditions tetrahydropterin coordinates only weakly and is easily displaced by solvent. Under basic conditions that should favor pterin deprotonation at N(5), the MoO_2 core persists and tetrahydropterin does not coordinate. This is presumably because the low proton concentration fails to protonate and remove one of the oxo ligands.

A complete characterization of the new Mo–tetrahydropterin complexes, including reactivity studies, required us to understand the complicated solution behavior of these species. Both ligand substitution reactions, largely involving chloride, and acid–base reactions, involving both oxo ligands and the coordinated pterin, are observed spectroscopically. Consistent with our assignment of **3** as a Mo(6+)–tetrahydropterin complex, rather than a Mo(4+)–dihydropterin complex, is the lack of oxo transfer reactivity with DMSO (Scheme 2), a reaction typical of Mo(4+) complexes.[26] More surprising is the lack of reactivity of the oxidant 2,6-dichloroindophenol with the molybdenum–tetrahydropterin complexes. Adopting the resonance view presented above (Scheme 4) leads to the suggestion that molybdenum is attenuating the reducing capability of tetrahydropterin. One lesson from these studies is that coordinated tetrahydropterin survives a changing molybdenum coordination sphere. A second message is that changes in ligand environment and overall charge can influence the acidity of pterins.

The emerging picture of metal–pterin coordination chemistry begins to resemble the chemistry of metal–quinone and metal–catecholate complexes.[27] Orthoquinone and catecholate ligands are related by proton-assisted redox couples similar to pterin redox reactions. The pattern



established for metal coordination chemistry by this series of

(26) Holm, R. H. *Coord. Chem. Rev.* **1990**, *100*, 183.
(27) Pierpont, C. *Prog. Inorg. Chem.* **1994**, *41*, 331.

redox related ligands is that quinone ligands are favored by low oxidation state "soft" metals, catecholate ligands are preferred by high oxidation state "hard" metals, and semiquinone ligands coordinate to metals intermediate between the two extremes. The softness of a metal can be adjusted by varying the ancillary ligands to effectively cause electron density flow from ligand to metal. Pterin coordination chemistry, though not as completely developed, thus far follows the same trends. Oxidized pterins and flavins prefer to coordinate soft metals (Re(+),[14h] Mo(0), and W(0),[28] Mo(4+),[29] Ru(2+),[14e] Mn(2+),[14a] Fe(2+),[14a,b] Co(2+),[14a,d] Ni(2+),[14a,i] Cu(2+),[14a,f,g] Cu(+),[30] Ag(+),[31] and reduced pterins coordinate to hard metals (Mo(6+)[8], W(6+)[32]). A consequence of this trend is that dihydropterins would be expected to best coordinate Mo in an intermediate oxidation state.

The implications of this study for molybdenum enzymes regard mainly the importance and feasibility of pterin coordination. On the basis of our synthetic experience, tetrahydropterin has a high affinity to chelate Mo(6+) if one of the two oxo ligands is removed. The electron-rich reduced pterin ligand behaves like an oxo ligand to stabilize the high oxidation state of molybdenum. Tetrahydropterin seems content to coordinate Mo in a variety of coordination environments. Extrapolating from what is known about Mo−oxo chemistry and from the parallels with quinone/catecholate coordination chemistry, tetrahydropterin is unlikely to strongly bind to Mo(4+). It is possible that a dihydropterin would be the favored partner for Mo(4+). Given the close proximity of molybdopterin to the molybdenum atom that is undergoing variable oxo ligation in Mo-co, if pterin coordination does not occur, it must be prevented by a considerable prohibitive force. We also note that the failure of DCIP to react with the Mo−tetrahydropterin complexes presented here may be important to interpreting results from biochemical experiments where DCIP also fails to oxidize molybdopterin in the presence of Mo[3]. As we and others continue to clearly define a role for the unusual pterin piece of Mo-co, our model studies provide examples of what chemistry is possible.

Conclusion

On the basis of structural and reactivity information, we conclude that the products isolated from reactions between tetrahydropterins and dioxo−molybdenum complexes are *not* Mo(4+) complexes of dihydropterin. We prefer to formulate these compounds as Mo(6+)−tetrahydropterinate compounds while keeping in mind that substantial electron donation from pterin to Mo is best described by the delocalized resonance structures in Scheme 4. The implications for molybdenum enzymes are that tetrahydropterin has a high affinity to chelate Mo(6+) if one of the two oxo ligands is removed and that coordination to molybdenum stabilizes tetrahydropterins toward oxidation by mild external oxidants like 2,6-dichloroindophenol.

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Supplementary Material Available: Tables listing positional parameters, anisotropic displacement coefficients, all bond distances and angles, and hydrogen atom positions and isotropic displacement coefficients (7 pages); table listing observed and calculated structure factors (17 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, can be ordered from the ACS, and can be downloaded from the Internet; see any current masthead page for ordering information and Internet access instructions.

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(28) Burgmayer, S. J. N.; Momoyama, Y.; Tadayyon, L. Unpublished results for Mo(0)− and W(0)−(pterin)$_3$.

(29) Burgmayer, S. J. N.; Rogge, C.; Everett, K.; Kerr, K. Unpublished results for Mo^{IV}(O)(ssp)(pterin).

(30) Yu, M. W.; Fritchie, C. J. *J. Biol. Chem.* **1975**, *250*, 946. (b) Fritchie, C. J. *J. Biol. Chem.* **1973**, *248*, 7516.

(31) Wade, T. D.; Fritchie, C. J. *J. Biol. Chem.* **1973**, *248*, 2337.

(32) Burgmayer, S. J. N.; Heising, J. Unpublished results for $W^{VI}(O)Cl_3(H_4$-pterin).