Dendrimer Encapsulation of $[Mo^{V}OS_4]$ Cores: Implications for the DMSO Reductase Family of Enzymes

Sujit Mondal and Partha Basu*,†

Department of Chemistry and Biochemistry, Duquesne University, Pittsburgh, Pennsylvania 15282

Received October 27, 2000

Pyranopterin-containing mononuclear molybdenum enzymes such as nitrate reductases and dimethylsulfoxide reductases (DMSOR) play important roles in global nitrogen and sulfur cycles.[1] Substantial evidence from crystallography[2−5] and spectroscopy[6,7] now exists for description of the molybdenum active center, e.g., in the fully oxidized state the oxo−molybdenum(VI) centers are coordinated by four sulfur donors. The oxidized state undergoes two one-electron reductive steps to regenerate the catalytically competent Mo(IV) state and, thus, passes through a molybdenum(V) state. Fundamental understanding of the electron transfer process is a key step to comprehend the function of these enzymes.

In addition to describing the details of the active center, crystallography also reveals that in all cases the Mo centers are deeply buried (∼15 Å) inside the protein matrix, and the coordinating ligands are not exposed to the surface. Taken together, the consistent minimal picture of molybdenum(V) centers emerges as a $[Mo^{V}OS_4]$ core buried inside the protein. Biologically important metal centers such as hemes and iron−sulfur clusters exhibit a significant modulation of the reduction potentials upon encapsulation.[8] However, the effect of encapsulation on the reduction potential of any oxo−molybdenum center is unknown, which prompted us to initiate this investigation with $[Mo^{V}OS_4]$ cores. Over the past two decades several $[Mo^{V}OS_4]$ cores have been reported in the literature; those provide a starting point for our investigation.[9−13] This report focuses on $[Mo^{V}OS_4]^{-}$ cores derived from tetrathiophenolate ligands.[14] Here, we disclose for the first time a new class of thiol-containing ligands and their use toward encapsulating $[Mo^{V}OS_4]^{-}$ cores.

The thiol group in 4-mercaptobenzoic acid is protected by oxidizing the thiols to disulfide by iodine, and the synthesis of polyether amine dendritic units following the literature.[15] The amine groups of these units have been linked with the carboxylato groups of 4,4′-dithiobenzoic acid, and the resulting materials have been purified in excellent yields (82−98%) by chromatography on silica gel. The G0 disulfide (**4a**) has been isolated as a white solid, whereas first generation nitrile terminated (**4b**) and ester terminated (**4c**) disulfides have been isolated as yellow liquids. The disulfides (**4b** and **4c**) have been reduced to dendritic thiols (**5a** and **5b**) with $NaBH_4$, and the corresponding thiols have been isolated as light yellow liquids (yield: 90−95%). All ligands and their precursors have been characterized by NMR and IR spectroscopy and mass spectrometry (Supporting Information).

Tetraphenylphosphonium salts of dendritic oxomolybdenum(V) tetrathiolate complexes, $[PPh_4][MoO(p\text{-}SC_6H_4CONHCH_3)_4]$ (**7a**), $[PPh_4][MoO(p\text{-}SC_6H_4CONHC(CH_2O(CH_2)_2CN)_3)_4]$ (**7b**), and **7c** have been synthesized from **6** (Scheme 1) via ligand exchange reactions[11a] either with dendritic thiols (**5a**, **5b**) or the disulfide (**4a**). Compound **7a** has been prepared by exchanging the thiophenolato groups of **6** using the disulfide **4a** via redox-coupled ligand exchange reaction in THF[11a,16] and has been isolated as a blue solid. Compounds **7b** and **7c** have been synthesized directly from the corresponding thiols by exchanging dendritic thiophenols with **6** in THF. Both **7b** and **7c** compounds have been purified by size exclusion chromatography in good yields (60−70%).

The molecular mass for compounds **6** and **7a**−**c** has been determined by negative ion electrospray ionization mass spectrometry (ESIMS) from their acetonitrile solutions (Table 1). The oxo−molybdenum(V) complexes **6** and **7a**−**c** exhibit an intense low-energy absorption at ∼600 nm ($\epsilon \sim 6000\ M^{-1}\ cm^{-1}$) due to S → Mo charge transfer (CT) transitions which obscures any d−d transition. Importantly, the position of the low-energy CT transition is not affected by the architecture of ligands. In contrast peripherally substituted thiophenolato complexes show significant variation in the CT transition as a function of substituents.[17] Even for the more structurally rigid trispyrazolylborate system, change in the reduction potential is accompanied by concomitant change in the low-energy CT transition.[18] Thus, the insensitivity of the

† E-mail: basu@duq.edu.

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10.1021/ic0011866 CCC: $20.00
Published on Web 12/15/2000

Scheme 1

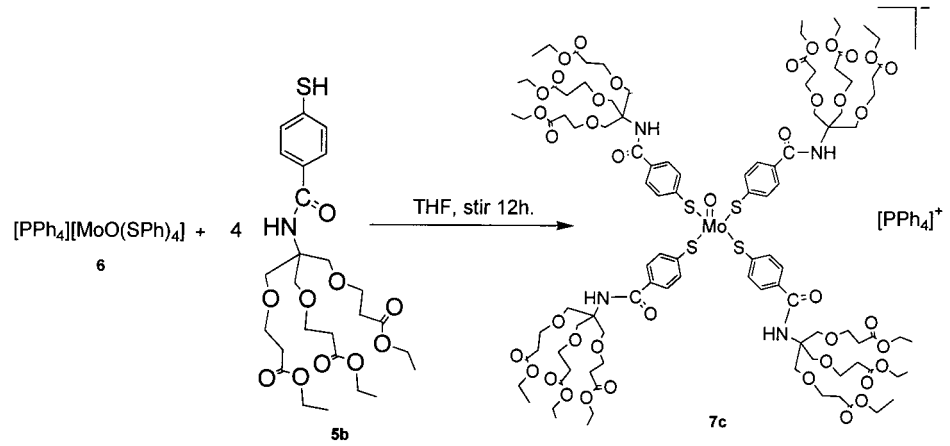

Table 1. Molecular Ion Peaks and Redox Potentials (vs Fc^+/Fc)

	M^-		
complexes	calcd base peak	obsd base peak[a]	$E_{1/2}$,[b] mV (ΔE_p,[b] mV)
6	550	550.7	−1151 (63)
7a	778	778.7	−993 (71)
7b	1775	1774	−1063 (136)
7c	2339	2339	−1092 (172)

[a] By electrospray ionization mass spectrometry (ESIMS). [b] Conditions: $\sim 10^{-3}$ M solutions of the complex in MeCN at 25 °C; scan rate, 100 mV/s; Pt working and reference electrodes; supporting electrolyte, $[NEt_4][BF_4]$; $E_{1/2} = {}^1/_2(E_{pa} + E_{pc})$ and $\Delta E_p = (E_{pc} - E_{pa})$.

CT transition in current molecules demonstrates a similar electronic structure of the metal center. For molybdenum complexes, the Mo═O^t vibrations have also been probed. The Mo═O^t vibration has been observed at the same position as other tetrathiophenolato complexes.[17] No variation in the Mo═O^t stretching frequency (941−943 cm^{-1}) has been observed within the complexes **6**, **7a**−**c**, suggesting that the bond strength of Mo═O^t in these molecules is essentially the same.

The d^1 oxo−molybdenum(V) complexes (**7a**−**c**) are paramagnetic with an $S = {}^1/_2$ ground state and are amenable to electron paramagnetic resonance (EPR) spectroscopy. EPR spectra of complexes **7a**−**c** have been recorded in frozen (20 K) acetonitrile−toluene (1:1) solutions. The molybdenum complexes exhibit axial EPR spectra similar to those observed for $[Mo^VO(SPh)_4]^-$ with characteristic molybdenum hyperfine structures.[19] No significant variation in the *g* values has been observed in these complexes; this indicates that the integrity of the square pyramidal $[Mo^VOS_4]^-$ core (C_{4v} local symmetry) is retained. Taken together, in the present case, the addition of bulky and symmetric dendritic architecture does not impose any further distortion at the metal center; therefore the electronic structure remains unaltered.

The redox property of tetraethylammonium salts of $[Mo^VO(SPh)_4]^-$ has been investigated in detail.[20] The anion displays a well-defined couple due to the reduction of Mo(V) to Mo(IV). The room-temperature cyclic voltammograms of **6** and **7a**−**c** in acetonitrile exhibit a well-defined one-electron couple (Table 1); however, no reversible oxidation couple has been observed within the solvent window. Several conclusions can be made from cyclic voltametry. First, introduction of electron-withdrawing amide functionality facilitates the reduction of the metal center by ∼150 mV as compared to **6**. Second, molecules **7a**−**c** display an increasingly larger potential difference between the current maxima of the reduction and return oxidation waves (ΔE), indicative of increasing kinetic difficulty of reduction and oxidation processes. The electrochemical data suggests that increasing the steric bulk of the ligand far from the metal center induces sluggish redox chemistry.[8c,21] Third, the reduction becomes increasingly difficult (by ∼100 mV for **7a** to **7c**; by 70 mV for **7a** to **7b)** for more sterically demanding ligands. Interestingly, the shift in the reduction potential in our molecules is larger than that reported for encapsulated iron−sulfur clusters (19−25 mV).[8c] The trend shows that by increasing the ligand bulk, reduction becomes increasingly difficult. Because accurate reporters of electronic structures of the molybdenum center such as the position of the charge transfer transition and the EPR *g* values show little variation, we suggest that, for molecules of the present study, the reduction potential is modulated by solvent accessibility to the electroactive metal center. Differential solvent accessibility conceivably could result in changing the effective dielectric constant at the metal center.

Interestingly, the Mo(V/IV) reduction potential for DMSOR isolated from different sources varies widely from −90 mV for *Escherichia coli*[22] (membrane-bound protein) to +140 mV for *Rhodobacter sphaeroides* (water-soluble protein).[23] The results of the present investigation led us to suggest that the variation in the Mo(V/IV) reduction potential in different DMSO reductases may be modulated by solvent.

Acknowledgment. We are grateful to Prof. M. Hendrich for recording EPR spectra. We also thank Drs. M. Bier and K. Somyatullya, Mr. A. Ghosh, and Mr. S. Sengupta for experimental assistance. Stimulating discussions with Profs. D. Wright and J. Stolz are acknowledged. Financial support from Research Corporation (RI 249), Noble J. Dick Foundation, and National Institutes of Health (GM 6155501) is acknowledged.

Supporting Information Available: Characterization data and cyclic voltammograms. This material is available free of charge via the Internet at http://pubs.acs.org.

IC0011866

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