X-Ray Structural Characterization of Molybdate-tripeptide Complex, $[Mo_4O_{12}(glycylglycylglycine)_2]\cdot 9H_2O$

Toshihiro Yamase,* Miyao Inoue, Haruo Naruke, and Keisuke Fukaya
Research Laboratory of Resources Utilization, Tokyo Institute of Technology, 4259 Nagatsuta, Midori-ku, Yokohama 226-8503

(Received March 4, 1999; CL-990146)

The first isolated polyoxomolybdate-tripeptide complex, $[Mo_4O_{12}(glycylglycylglycine)_2]$, is an infinite centrosymmetric complex of the Mo_4O_{12} unit in which a pair of Mo atoms is singly bridged by a glycylglycylglycine carboxylate group as a bidentate ligand resulted in four edge-shared MoO_6 octahedral linkage. $[Mo_4O_{12}]_n$ exhibits a corrugated sheet-belt structure of four co-planar Mo atoms linked by four triply-bridging O atoms with cis-configurated two terminal O atoms for each Mo atom.

The discovery that polyoxomolybdates exhibit antitumor activity *in vivo* has stimulated interest in the nature of binding to cellular metabolites and proteins.[1] Since the composition and structure of aqueous complexes are of direct relevance to the mechanism in which polyoxomolybdates interact in biological systems, characterization of such complexes is important for understanding the antitumoral mechanism. From this standpoint we have investigated the crystal structures of both the γ-type octamolybdates coordinated by amino acids and the pentamolybdates coordinated by nucleotides.[2] In the former amino acid ligands are coordinated via their monodentate carboxylate-oxygen atoms at the vacant sites on the two five-coordinate molybdenum for the centrosymmetric γ-$[Mo_8O_{26}]^{4-}$ anion to retain their configuration. In the latter, two nucleotide phosphate tetrahedra span either side of a ring of edge- and corner-linked MoO_6 octahedra with an isostructural mode with $[(OPO_3)_2Mo_5O_{15}]^{6-}$. Although proteins and peptides are polymers of amino acids, and all of the functionalities in amino acid side chains have the potential of forming complexes with polyoxometalates, there has been no structurally characterized polyoxomolybdate containing peptide ligands. The interaction of polyoxometalates with peptides has been investigated mainly for polyoxovanadates.[3] Especially revealing was the finding by Crans and co-workers that the dipeptide in the x-ray crystallographically characterized decavanadate-dipeptide complex, $(NH_4)_6(glycylglycine)_2[V_{10}O_{28}]\cdot 4H_2O$, bridges between decavanadate molecules by hydrogen bonding, thereby suggesting the importance of the noncovalent interactions between dipeptide and decavanadate.[3a,4] In the course of our work on polyoxomolybdate-glycylglycylglycine complex, we have found that the interaction with the tripeptide induces formation of an infinite complex $[Mo_4O_{12}(tripeptide)_2]$ and that a set of two Mo(VI) atoms in the Mo_4O_{12} moiety is chelated by bidentate carboxylate oxygen atoms of tripeptide.[5] Such a new coordination with two oxygen atoms in two terminal modes for the tripeptide carboxylate ligand may be characteristic of the polyoxomolybdate-tripeptide complexes, different from the cases of polyoxovanadate-tripeptide complexes. We describe here the structural identification of a $[Mo_4O_{12}(glycylglycylglycine)_2]\cdot 9H_2O$ complex which will become a useful model to the interaction between molybdenum(VI) and protein.

$[Mo_4O_{12}(glycylglycylglycine)_2]\cdot 9H_2O$ was prepared as follows: an aqueous solution of $Na_2MoO_4\cdot 2H_2O$ (0.50 g) in water (10 ml) was acidified by $HClO_4$ to pH 3.4 and then glycylglycylglycine (0.10 g) was added. The resultant solution was cooled at 5 °C for two weeks, to provide colorless needle-like single crystals of $[Mo_4O_{12}(glycylglycylglycine)_2]\cdot 9H_2O$. Yield: 0.18 g. Found: H, 3.37; C, 12.76; N, 7.59; Mo, 34.15; H_2O, 14.41 wt%. Calcd for $C_{12}H_{40}N_6O_{29}Mo_4$: H, 3.61; C, 12.91; N, 7.53; Mo, 34.38; H_2O, 14.53 wt%. IR spectrum of $[Mo_4O_{12}(glycylglycylglycine)_2]\cdot 9H_2O$ (Figure 1) displays

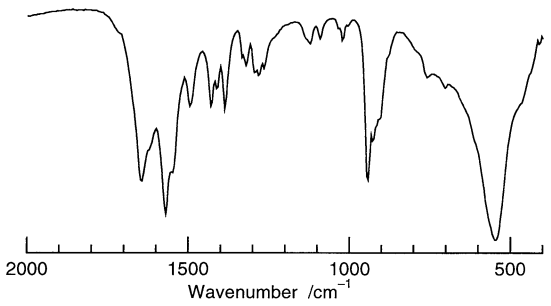

Figure 1. Infrared spectrum of $[Mo_4O_{12}(glycylglycylglycine)_2]\cdot 9H_2O$.

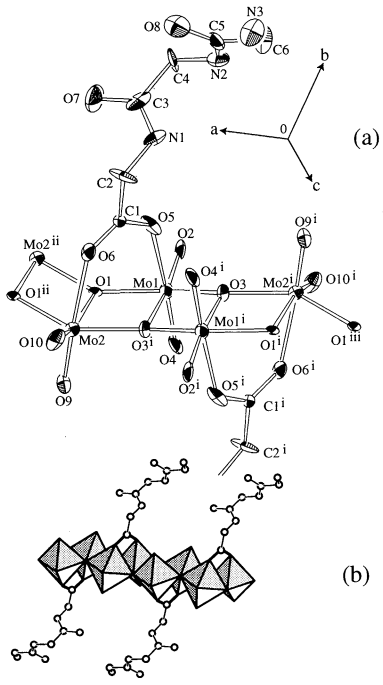

Figure 2. Molecular structure and numbering scheme for $Mo_4O_{12}(glycylglycylglycine)_2$ (a). The complex is also shown using the polyhedral representation (b). Symmetry equivalent positions: i) -x, 1-y, 1-z; ii) 1-x, 1-y, 1-z; and iii) -1+x, 2+y, z.

ν(Mo-$O_{terminal}$) and ν(Mo-O(μ_3)-Mo) peaks at 950 and 550 cm^{-1}, respectively. Crystal structure of $[Mo_4O_{12}(glycylglycylglycine)_2] \cdot 9H_2O$ was determined by X-ray crystallographic analysis.[6]

The structure and numbering scheme for Mo_4O_{12}(glycylglycylglycine)$_2$ are shown in Figure 2, where the polyhedral representation of compound is also shown. The compound is an infinite chain (parallel to the *a* axis) of the neutral complex of a zigzag edge-shared octahedral Mo_4O_{12} moiety chelated by two bidentate glycylglycylglycine ligands; a crystallographic inversion center is imposed on the molecule. Each Mo atom in Mo_4O_{12}(glycylglycylglycine)$_2$ is coordinated by two terminal oxygens O(2,4; 9,10; 2^i,4^i; 9^i,10^i) with *cis* configuration (in Mo-O distances 1.65(1)-1.70(2) Å)), three triply bridged oxygens O(1,3,3^i; 1,1^{ii},3^i; 1^i,3,3^i; 1^i,1^{iii},3) (in two kinds of Mo-O distances 1.94(2)-1.99(2) Å and 2.23(1)-2.28(1) Å), and one carboxyl-oxygen atom (in Mo-O distances 2.26(2) and 2.31(2) Å) of the glycylglycylglycine to achieve a saturated octahedral coordination sphere. The long Mo-O distances (2.23(1)-2.28(1) Å) occur *trans* to the terminal Mo-O bond, a feature which is typical of oxomolybdenum complexes.[7] The four Mo atoms are linked by four triply-bridging, O1, O3, $O1^i$, and $O3^i$ to form an eight-membered Mo_4O_4 ring with a corrugated sheet-belt of O1-Mo1-O3-$Mo2^i$/Mo2-$O3^i$-$Mo1^i$-$O1^i$ representing the parallel two sides of the belt (with an average width of 2.25 Å), as supported by IR spectrum (Figure 1). A set of Mo1 and Mo2 (or $Mo1^i$ and $Mo2^i$) is bridged by a terminal carboxyl group of the bidentate glycylglycylglycine ligand with the Mo•••Mo separation of 3.402(3) Å which is in good agreement with Mo•••Mo distances for the edge-shared $Mo^{VI}O_6$ octahedra.[2]

The glycylglycylglycine oxygen atoms are situated in distorted octahedral geometries about each molybdenum atom, with O-Mo-O bond angles varying from 71.4(6) to 108.0(7)°. The bidentate coordination mode singly bridged by glycylglycylglycine is identical to that found in a trimeric cluster complex $[Fe_3O(H_2O)_3$(glycylglycylglycylglycine)$]^{7+}$ where any set of two iron atoms is bridged by two cyclic glycylglycylglycine carboxylates with Fe•••Fe distance of 3.312(3) Å.[8] As well as the amido nitrogen atoms, the terminal amino nitrogen atoms of the glycylglycylglycine ligand are hydrogen bonded to terminal oxygen atoms of the neighboring Mo_4O_{12} layers, and lattice-water molecules also are hydrogen bonded to terminal O(2,4,9,10), carboxylate O(5,6), and caybonyl O(7,8) atoms. Furthermore, the hydrogen bonding between amino nitrogen N3 and amido carbonyl oxygen O8 atoms for glycylglycylglycine chains of the neighboring Mo_4O_{12} layers (in N•••O distance of 2.95(2) Å) occurs with a similarity to the antiparallel β-sheet structure in polypeptide solids.[9] Such hydrogen bondings together hold the corrugated sheet-belts of molybdenum and oxygen atoms by alternating glycylglycylglycine branches stacked approximately perpendicularly to the sheet-belts as shown in Figure 3.

The reaction between molybdate and tripeptides at weak acidic pH did indeed form a complex Mo_4O_{12}(tripeptide)$_2$ in which the bidentate carboxylate for the tripeptide ligand serves as bridge across two di μ-oxo molybdenum atoms in addition to the hydrogen-bonding functionalities in tripeptide side chains.

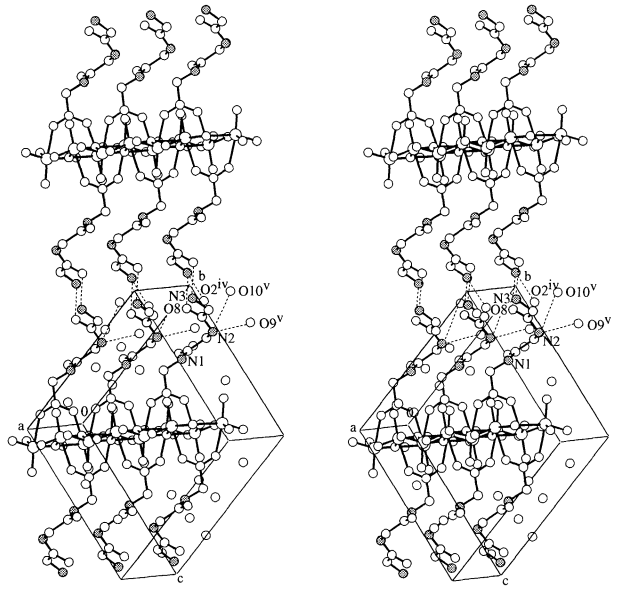

Figure 3. Stereoscopic view of the unit cell contents of $[Mo_4O_{12}$(glycylglycylglycine)$_2] \cdot 9H_2O$. Amino and amido nitrogen atoms are denoted by shaded circles. $O2^{iv}$, $O9^v$, and $O10^v$ are terminal oxygen atoms of neighboring Mo_4O_{12} layers. Hydrogen bonds among tripeptide-side chains and the terminal oxygen atoms are indicated by dashed lines. Symmetry equivalent positions: iv) x-1, y, z-1; and v) x, y+1, z.

References and Notes

1 a) T. Yamase, H. Fujita, and K. Fukushima, *Inorg. Chim. Acta*, **151**, 15 (1988). b) T. Yamase, "Polyoxometalates: From Platonic Solids to Anti-retroviral Activity," ed by M. T. Pope and A. Müller, Kluwer Acad. Pub., Dordrecht, the Netherlands (1994), pp. 337. c) T. Yamase, "Polymeric Materials Encyclopedia: Synthesis, Properties, and Applications," ed by J. C. Salamone, CRC Press, Inc., Boca Raton, Fla., (1996), pp. 365.

2 a) M. Inoue and T. Yamase, *Bull. Chem. Soc. Jpn.*, **68**, 3055 (1995). b) M. Inoue and T. Yamase, *Bull. Chem. Soc. Jpn.*, **69**, 2863 (1996).

3 a) D. C. Crans, M. M-Tahir, O. P. Anderson, and M. M. Miller, *Inorg. Chem.*, **33**, 5586 (1994). b) D. C. Crans, H. Chen, O. P. Anderson, and M. M. Miller, *J. Am. Chem. Soc.*, **115**, 6769 (1993). c) J. S. Jaswal and A. S. Tracey, *Can. J. Chem.*, **69**, 1600 (1991).

4 D. C. Crans, R. L. Bunch, and L. A. Theisen, *J. Am. Chem. Soc.*, **111**, 7597 (1989).

5 The paper for polyoxomolybdate-glycine ($Na_4[Mo_8O_{26}(glycine)_2] \cdot 8H_2O$) and -glycylglycine ($Na_4[Mo_8O_{26}(glycylglycine)_2] \cdot 12H_2O$) complexes is in preparation. Both complexes exhibited the same structural mode in the γ-type octamolybdates chelated by monodentate carboxylate-oxygen atoms of two glycine or two glycylglycine ligands. Crystal data and final discrepancy factors are as follows. $H_{26}C_4N_2O_{38}Na_4Mo_8$: M= 1569.72, space group $P\bar{1}$ (No. 2), a= 8.478(1) Å, b= 10.853(3) Å, c= 11.073(4) Å, α= 100.22(2)°, β= 98.58(2)°, γ= 110.44(2)°, Z= 1, D_c= 2.850 $g \cdot cm^{-3}$, F(000)= 748, $\mu(MoK_\alpha)$= 28.16 cm^{-1}, R_1= 0.042, and wR_2= 0.052. $H_{40}C_8N_4O_{44}Na_4Mo_8$: M=1755.88, space group $P\bar{1}$ (No. 2), a= 9.424(2) Å, b= 11.319(4) Å, c= 11.813(4) Å, α= 63.95(3)°, β= 74.21(2)°, γ= 110.44(2)°, Z= 1, D_c= 2.677 $g \cdot cm^{-3}$, F(000)= 848, $\mu(MoK_\alpha)$= 23.91 cm^{-1}, R_1= 0.039, and wR_2= 0.040.

6 A single crystal with 0.4 x 0.10 x 0.05 mm was sealed in a glass capillary and mounted on Rigaku AFC5S four-circle diffractometer with graphite-monochromatized MoK_α radiation (λ= 0.71069 Å). Crystal data for $[Mo_4O_{12}(glycylglycylglycine)_2] \cdot 9H_2O$: $H_{40}C_{12}N_6O_{29}Mo_4$, M= 1116.23, triclinic, space group $P\bar{1}$ (No. 2), a= 7.365(2) Å, b= 11.837(4) Å, c= 11.935(4) Å, α=110.49(2)°, β=105.06(3)°, γ=105.38(2)°, Z= 1, D_c= 2.142 $g \cdot cm^{-3}$, F(000)= 554, $\mu(MoK_\alpha)$=15.26 cm^{-1}. Of the 5369 total reflections collected, 5011 were independent. Structure was solved using direct method (DIRDIF92) and refined using a full-matrix least-squares procedure based on 1321 observed reflections with $I>3\sigma(I)$ and 225 variables. Absorption correction was applied using DIFABS with the transmission factors from 0.661 to 1.223. The final descrepancy factors were R_1= 0.070 and wR_2= 0.053. $2\theta_{max}$=55°. The site occupancy of the lattice water O15 was fixed at 0.5 throughout the structure refinements, since the distance (2.5(1) Å) between O15 and O15* (* indicates a symmetric code of -1-x, 1-y, -z) was short.

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

8 E. M. Holt, S. L. Holt, and N. W. Alcock, *Cryst. Struct. Commun.*, **11**, 505 (1982).

9 a) D. van der Helm and T. V. Willoughby, *Acta Crystallogr., Ser B*, **25**, 2317 (1969). b) P. R. Meulemans, P. Piret, and M. van Meerssche, *Acta Crystallogr., Ser B*, **27**, 1187 (1971).