Difference in the Antagonistic Behaviour of Tetrathiomolybdate & Tetrathiotungstate towards Copper

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Freshly precipitated CuS can be solubilized by allowing it to stand in aqueous medium containing MoS\(^{2-}\). Discrete compounds \([\text{PPh}_3]^3_2\text{Cu}_2\text{MoS}_4\) and \([\text{o-phen}^3_2\text{Cu}_2\text{MoS}_4]\) have been isolated by reaction of the resultant solution with \text{PPh}_3 and \text{o-phenanthroline which indicate the in situ generation of \text{Cu}_2\text{MoS}_4\) species. The reaction has been carried out to mimic a possible reaction in the rumen and to rationalize the chemical implications of copper-molybdenum antagonism. A dramatic difference in the antagonistic behaviour of MoS\(^{2-}\) and WS\(^{2-}\) towards copper has been demonstrated.

The chemical implications of 'copper-molybdenum antagonism' have been a subject of much interest\(^1\), MoS\(^{2-}\) has been shown to be the strongest antagonist of copper\(^3\) and the finding that a Cu-Mo-S system in which copper is flanked by N-donor ligands could serve as a model for the study of such interactions has led to the synthesis of a number of model compounds to represent the highly insoluble species responsible for the depletion of copper in biological systems. Experiments have been carried out to show that in several respects the inhibitory action of WS\(^{2-}\) on copper metabolism is similar to that of tetrathiomolybdate\(^4\). However, in some respects the results show substantial differences\(^5\). Experiments on the inhibitory effects of thio and oxythio anions of Mo and W on copper metabolism indicate that whereas the fully substituted tetrathio derivatives are extremely potent antagonists, their oxothio analogs neither inhibit copper absorption nor induce clinical and biochemical signs of copper deficiency\(^6\).

In the present studies an in vitro experiment has been carried out to demonstrate the dramatic difference in the chemical and, hence, antagonistic behaviour of tetrathiomolybdate and tetrathiotungstate towards copper. The results may explain as to why molybdenum is preferred to tungsten in biological systems where it performs several important roles concerning electron transfer, redox reactions and substrate catalysis.

Freshly precipitated CuS was added to an aqueous solution of MoS\(^{2-}\) in 1:1, 2:1, 3:1 and 4:1 (CuS:MoS\(^{2-}\)) ratios and the contents kept for 16 hr when in all four sets a red solution was obtained indicating the dissolution of CuS in MoS\(^{2-}\). The solutions were filtered and divided into two parts: A and B. Part A was treated with triphenylphosphine (in DMF) and part B with \text{o-phenanthroline (in DMF) in each case. In all four sets, compound \([\text{PPh}_3]^3_2\text{Cu}_2\text{MoS}_4\) was obtained from Part A and \([\text{o-phen}^3_2\text{Cu}_2\text{MoS}_4]\) was obtained from part B indicating the existence of only one type of core, \text{Cu}_2\text{MoS}_4, in all the four sets of red solutions.

To demonstrate the 'spontaneous self assembly' of \text{Cu}_2\text{MoS}_4 core and also the in situ generation and interaction of CuS and MoS\(^{2-}\), which probably may occur in ruminants, Cu\(^{2+}/\text{MoO}_4^{2-}/\text{H}_2\text{S}\) system was also studied with varying ratios of Cu\(^{2+}\) and MoO\(^{2-}\) namely 1:1, 2:1, 3:1 and 4:1. A typical experiment is described below.

0.55 g of (NH\(_4\))\(_6\)Mo\(_7\)O\(_{24}\).24H\(_2\)O (0.5 mmol) and 1.2 g of CuCl\(_2\).2H\(_2\)O (7 mmol) were dissolved in a mixture of water (15 ml) and ammonia (50 ml, \(d=0.9\)). A continuous current of H\(_2\)S was passed into the solution. CuS was precipitated immediately and stepwise replacement of oxo group of MoO\(^{2-}\) by S\(^2-\) resulted in the ultimate formation of MoS\(^{2-}\) when the passage of H\(_2\)S was stopped (45 min). The contents were kept for 16 hr when most of the precipitated CuS went into solution. The resultant solution was filtered and divided into two parts (parts A and B).

Part A was poured into a solution of triphenylphosphine (2.65 g, 10.5 mmol) in DMF (30 ml) whereby a red microcrystalline compound separated out. It was filtered, washed with acetone, carbon disulphide and ether and dried in vacuo.

The compound was characterised as \([\text{PPh}_3]^3_2\text{Cu}_2\text{MoS}_4\), which had earlier been synthesised in non-aqueous medium and characterised\(^7\). The salient feature of the structure of this known complex is the unsymmetrical environment of copper centres where one of the copper is tetrahedrally coordinated (two PPh\(_3\) and two S centres of MoS\(^{2-}\)).

Part B was poured into a solution of \text{o-phenanthroline (1.4 g, 7 mmol) in DMF (30 ml).}
Addition of acetone (20 ml) resulted in the precipitation of a red compound which was filtered, washed with acetone, carbon disulphide and ether and dried in vacuo. Analysis and spectroscopic results suggest it to be \([\text{[(o-phen)}_2\text{Cu}_2\text{MoS}_4]\)\(^6\). Thus, a tetrahedral arrangement around both copper centres could be achieved which could be proved by various spectroscopic techniques like electronic, Raman, resonance Raman and XPS\(^8\).

A parallel attempt to solubilize CuS in WS\(^2\)_\(-\) and hence to isolate the parallel tungsten compounds namely \([\text{[(PPh}_3)_3\text{Cu}_2\text{WS}_4]\) and \([\text{[(o-phen)}_2\text{Cu}_2\text{WS}_4]\] using an identical procedure failed. This reflects the specific role of molybdenum in such interactions since Mo and W are supposed to have a parallel chemistry.

It is interesting, however, that the above two compounds of tungsten could be isolated in a non-aqueous solvent (DMSO) by the following procedure:

Two equivalents of cuprous chloride and two equivalents of \(\alpha\)-phenanthroline (or three equivalents of triphenylphosphine) were taken together in DMSO. One equivalent of WS\(^2\)_\(-\) dissolved in DMSO was added to the above solution. The resulting compounds, red in both cases, were filtered, washed with DMSO, ethanol and ether and dried in vacuo. Analytical results conformed to the formulae \([\text{[(PPh}_3)_3\text{Cu}_2\text{WS}_4]\) and \([\text{[(o-phen)}_2\text{Cu}_2\text{WS}_4]\].

The molybdenum analogues \([\text{[(PPh}_3)_3\text{Cu}_2\text{MoS}_4]\) and \([\text{[(o-phen)}_2\text{Cu}_2\text{MoS}_4]\] could also be synthesised in DMSO using the above procedure and adding MoS\(^2\)_\(-\) in place of WS\(^2\)_\(-\). The analytical spectroscopic results were in conformity with those reported earlier\(^5\)\(^6\).

Several copper thiomolybdate complexes in which Cu is flanked by P-donor ligands have been synthesised to serve as models\(^1\). But P-donor ligands may not be taken as true representatives of protein moiety. Copper thiomolybdate complexes like \([\text{[(o-phen)}_2\text{Cu}_2\text{MoS}_4]\) in which Cu is flanked by N-donor ligands would serve as more appropriate models for the biological systems. Moreover, the present compound could be isolated from aqueous medium which is also an exception to previous models.

It is significant to note that previous attempts to react copper compounds with MoS\(^2\)_\(-\) in aqueous medium resulted in the formation of the polymeric species\(^8\). Thus, dissolution of CuS in MoS\(^2\)_\(-\) in aqueous medium does represent a unique behaviour and may be thought to be relevant to the Cu-Mo-S interaction.

Further, all earlier attempts to rationalize Cu-Mo interaction have ignored the interaction between Cu\(^{\text{n+}}\) and S\(^{\text{2-}}\) prior to the interaction of Cu\(^{\text{n+}}\) and MoS\(^2\)_\(-\). It is not logical to propose the interaction of MoO\(^3\)_\(-\) and S\(^{\text{2-}}\) to give MoS\(^2\)_\(-\) in preference to the interaction of Cu\(^{\text{n+}}\) and S\(^{\text{2-}}\) where Cu\(^{\text{n+}}\) is present \textit{in situ}. In fact, according to simple solubility product criterion, CuS would be formed first in preference to MoS\(^2\)_\(-\). Hence, keeping in view the formation of CuS prior to that of MoS\(^2\)_\(-\), it is reasonable to study carefully the interaction of CuS and MoS\(^2\)_\(-\).

References
7 Without copper, a 30 min passage of H\(_2\)S is enough to transform MoO\(^3\)_\(-\) to MoS\(^2\)_\(-\) (monitored by 467 nm peak in the electronic spectra).