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Metallothioneins: Zinc, Cadmium, Mercury, and Copper Thiolates and Selenolates Mimicking Protein Active Site Features – Structural Aspects and Biological Implications

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Contents

1. Introduction

Metallothioneins (MTs) define a superfamily of ubiquitous cysteine-rich low molecular weight proteins or polypeptides that contain polynuclear metal–sulfur coordination sites formed by metal ions with d^{10} configuration. The most prominent characteristics of these biomolecules, which have been discovered as a cadmium and zinc containing protein in horse kidney by Margoshes and Vallee in 1957,[1] are their extremely high metal and sulfur contents (up to 10% w/w).

Although MTs have been known as long as about half a century, their precise physiological function is still under debate. According to Kägi and Schäffer, they are thought to play roles both in the intracellular fixation of the essential trace elements zinc and copper, in controlling the concentrations of the free ions of these elements, in regulating their flow to their cellular destinations, in neutralizing the harmful influences of exposure to toxic elements such as cadmium and mercury, and in the protection from a variety of stress conditions.[2] More recently, it was concluded by Maret and Vallee that the long sought role of MT lies in the control of the cellular zinc distribution as a function of the energy state of the cell and not in the widely held belief that MT primarily scavenges radicals or detoxifies metals.[3] As can be learned by these speculations, investigations directed to explore the structure and chemistry of metallothioneins in greater detail are extremely important taking into account that nature makes use of them as multipurpose proteins. Several reviews covering this issue are available in the literature.[4]

Today, MTs are known to occur in all animal phyla examined so far as well as in certain fungi, plants, and cyanobacteria. Characterized by a low molecular mass of 6.000–7.000 amu, by 20 totally conserved cysteines out of a total of 61 or 62 amino acid residues (according to ca. 30% by number), without aromatic amino acids such as tyrosine or histidine, the apoprotein from rat liver (thionein) is able to bind a total of seven equivalents of divalent metal ions with d^{10} configuration such as Zn^{2+} or Cd^{2+} in two noninteracting domains. After demetalation, these proteins can be loaded with up to six Cu^{1+} ions in each domain.[5]

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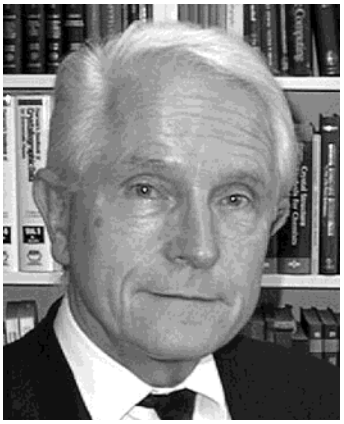
Gerald Henkel was born in Burow (Mecklenburg/Vorpommern, Germany) in 1948. He studied chemistry at the University of Kiel (1968–1973) and obtained his Ph.D. (Dr. rer. nat.) in chemistry in the group of B. Krebs at the University of Bielefeld in 1976. After work as a teaching and research assistant in Bielefeld (until 1977) and in Münster, he completed his habilitation (Münster, 1984) with work on coordination compounds of electron-rich transition metals with sulfur-containing ligands. Since 1988, he was Professor of Inorganic Chemistry at the University of Duisburg where he was Head of the Inorganic Chemistry/Solid State Chemistry division. In 2001, he moved to the University of Paderborn as a Full Professor of Inorganic Chemistry where he is presently Head of the Chemistry Department. The main areas of his research are in the fields of structural and solid-state chemistry, of synthetic coordination chemistry (complexes with sulfur, selenium, and tellurium ligands), and of bioinorganic chemistry with special emphasis on biomimetic model complexes of metallobiomolecules as well as on structural studies of metalloenzymes by means of XAS spectroscopy.



Bernt Krebs studied chemistry at the University of Göttingen (1958–1963) where he received his doctorate degree in chemistry with G. Gattow in 1965. From 1965 to 1966, he worked as a research assistant with W. C. Hamilton and D. F. Koenig at Brookhaven National Laboratory. After returning to Göttingen, he completed his habilitation in 1969 in O. Glemser's laboratory with the synthesis and structure of Mo, Tc, and Re oxo compounds. In 1971, he accepted an associate professorship at the University of Kiel, and in 1974 became the first Professor of Inorganic Chemistry at the newly established University of Bielefeld. Since 1977, he has been Professor of Inorganic Chemistry and Institute Director at the University of Münster. His wide-spread research interests reach from the synthesis and structural chemistry of inorganic sulfur, selenium, and tellurium compounds to transition metal oxo compounds and heteropolymetalates, and to the solid-state chemistry of ion-conducting chalcogenides. His special interest is in the field of bioinorganic chemistry, including synthesis and function of biomimetic transition metal complexes and crystal structure studies of metalloenzymes. He has received the International Max Planck Award and the Wilhelm Klemm Award of the German Chemical Society.

Another mammalian species that is almost exclusively expressed in the brain (known as metallothionein-3 or neuronal growth inhibitory factor (GIF)) contains four Cu(I) and three Zn(II) ions organized in homometallic thiolate clusters located in two independent protein domains. The situation is somewhat different for MTs originating from yeast and fungus, which possess only one metal binding site unable to incorporate zinc or cadmium. The MTs found in higher organisms are the sole proteins that are able to accumulate cadmium as a primary biological function.[6]

After discovery, the MTs were classified into families according to empirical aspects. Members of Class I are defined to include polypeptides related in the positions of the cysteine residues to the mammalian forms, while those of class II display none or very distant correspondence in this respect. Class I subsumes besides the vertebrate MTs all presently known crustacean and molluscan sequences. Class III MTs are polyisopeptides composed of atypical gamma-glutamylcysteinyl units and therefore are not direct gene products.[7] The growing number of known MT sequences, however, which show that their lengths, amino acid compositions, and the numbers and repartitions of their cys resisues are highly variable clearly demonstrates that this subdivision is inadequate. Binz and Kägi have therefore proposed a new classification system that is based on sequence similarities and phylogenetic relationships. According to this system, the MTs form a superfamily that is subdivided into families, subfamilies, subgroups, and isolated isoforms and alleles.[4c]

The superfamily itself is defined phenomenologically as comprising all polypeptides that resemble equine renal metallothionein in several of their aspects, whereas a MT family consists of MTs that share a particular set of sequence-specific characters. Members of a specific family cannot belong to other families and are thought to be evolutionary related. Each family is identified by a given specific number and its taxonomic range (for example, family 1, vertebrate MTs). Within a subfamily the MTs share not only the family characters but also a set of more stringent phylogenetic features such as specific monophyletic relationships among the sequences of proteins and/or of nucleotide segments in the genes. A subfamily is usually abbreviated with a letter character followed by an arabic number (for example, m1, mammalian MT-1). Specific members of a subfamily can belong to a subgroup if they share a branch of MT sequences that is clearly distinguishable in a tree by its monophyletic character (for example, m2U2, ungulate MT-2, subgroup of the m2 subfamily). Isoforms or allelic forms are specifiable as members of families, subfamilies, and subgroups. They are named according to the nomenclature of Kojima et al.[8] If a set of partial or total amino acid or polynucleotide sequences, subgroups, subfamilies, families, or combinations of them share characters not defined by the above classification criteria, a corresponding clan is defined that can be related to common spatial structure, thermodynamic properties, metal binding properties, functionally related characters, or other relevant features.

All vertebrates examined so far contain at least two distinct MT isoforms designated as MT-1 to MT-4.

Whereas MT-1 and MT-2 occur within all organs of mammalians, MT-3 is found in the brain (see above) and MT-4 in certain tissues. They are composed of two subunits, the C-terminal α domain and the N-terminal β domain, which are responsible for metal binding via S-Cys donor functions.

This review covers the thiolate chemistry of the metal ions zinc, cadmium, mercury, copper, and silver relevant to the metallothioneins, which means that ligands containing sulfur not bonded to carbon or ligands with abiotic sulfur donor functions such as thiourea, 1,1-dithio ligands (e.g., dithiocarbamates), or dithiolene-type systems have been excluded from the discussion. In addition, heteroleptic thiolate complexes containing additional non-sulfur donor functions have also been excluded. Prior to this contribution, review articles covering various aspects of metal−thiolate as well as of metal−sulfide−thiolate chemistry have appeared.[9]

2. Metal Binding Sites in Metallothioneins

In 1986, a crystal structure determination of Cd_5Zn_2-MT-2 isolated from cadmium-overloaded rat liver provided the first structural models for the metal−sulfur clusters within these domains.[10] However, results of multidimensional/multinuclear NMR investigations published in due course were unable to confirm this X-ray structure especially with respect to the metal-to-cystein coordination patterns in both clusters.[11] After finding out that the initial crystal structure needed to be revised due to errors in the Cd positions, a new crystal structure was published that was now in complete agreement with the NMR results.[12]

From both the solution NMR as well as the solid-state X-ray structure of native rat liver Cd_5Zn_2-MT-2 (crystals) and of rat,[13] rabbit,[14] and human liver[15] ^{113}Cd-reconstituted Cd_7-MT-2 (solution), it is now established that the α domain hosts a tetranuclear $\{M_4S_{11}\}$ cluster (cluster A, Figure 1), whereas a trinuclear $\{M_3S_9\}$ cluster (cluster B, Figure 2) is located in the β domain with Zn or Cd in (distorted) tetrahedral sulfur environments.[16] The identity of MT structures containing either Zn or Cd was proven by further comparative NMR as well as XAFS studies.[17]

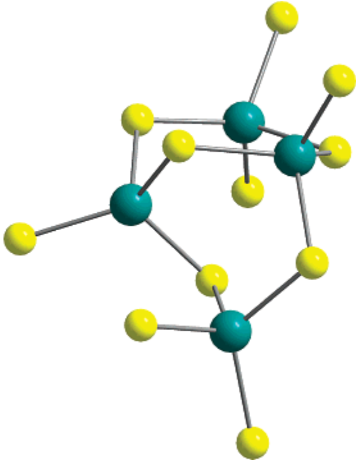


Figure 1. The tetranuclear $\{Cd_4S_{11}\}$ core portion of M_7-MT-2 from rat liver (cluster A).

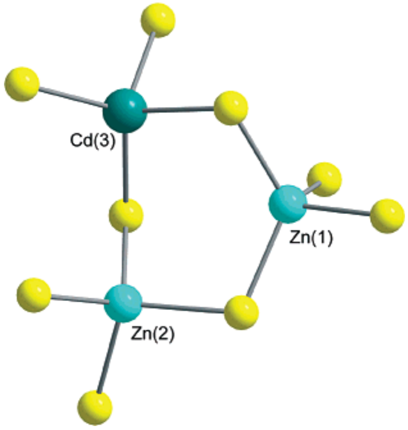


Figure 2. The trinuclear $\{CdZn_2S_9\}$ core portion of M_7-MT-2 from rat liver (cluster B).

Besides the NMR structures of these mammalian M_7-MT-2 derivatives, an NMR solution structure of recombinant mouse $^{113}Cd_7$-MT-1 has also been determined showing high similarities between these species.[18] Comparable $\{M_3S_9\}$ as well as $\{M_4S_{11}\}$ clusters have also been identified in recombinant human Zn_7- and Cd_7-MT-3[19] as well as in recombinant mouse Cd_7-MT-3.[20] Although it was not possible to determine their complete solution structures in the case of the human protein, the structure of the $\{Cd_4S_{11}\}$ cluster from the mouse Cd_7-MT-3 protein has successfully been elucidated showing a molecular architecture similar to that of the cluster within the α domain of the M_7-MT-2 species examined so far.

In contrast to these engineered proteins, naturally occurring MT-3 from bovine brain, however, has been shown to contain four Cu and three Zn ions. EXAFS Cu and Zn K-edge investigations are indicative of distinct homometallic {MS} clusters with trigonal and tetrahedral coordination geometries, respectively.[21] Although the location of both clusters in the protein structure is yet not exactly known, it has been suggested that the $\{Zn_3\}$ cluster is not located in the N-terminal β domain of the protein as in the Zn_7-MT-3 derivative but, untypically, in the α domain instead. The latest example of a vertebrate metallothionein whose solution structure has been determined by multinuclear/multidimensional NMR spectroscopy is Cd_7-MT-A from the antarctic fish Notothenia coriiceps. The $\{Cd_4S_{11}\}$ and $\{Cd_3S_9\}$ clusters within the α and β domains of the protein show striking structural similarities with the corresponding units found in mammalian M_7-MT-2. The close structural relationship between the $\{Cd_4S_{11}\}$ clusters from mammalian Cd_7-MT-2 and Cd_7-MT-A from Notothenia coriiceps can easily be recognized by inspection of Figure 3 which shows a superposition of both coordination sites fitted to match the atoms within the bicyclic $\{M_4S_5\}$ frames.[22]

Besides the NMR structures of these vertebrate proteins, complete NMR solution structures have also been determined for the invertebrate Cd_6-MT-1 proteins from crustacean blue crab (*Callinectes sapidus*)[23] and from lobster[24] and for Cd_7-MTA from equinodernal sea urchin (*Strongylocentrotus purpuratus*).[25] In all these cases, the structures consist of a monomeric protein that is composed of two globular

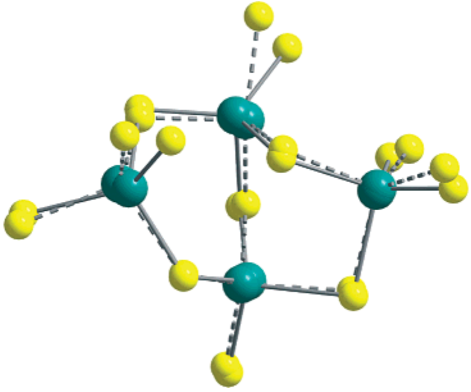


Figure 3. Superposition of the $\{Cd_4S_{11}\}$ clusters of M_7-MT-2 from rat liver (solid sticks) and Cd_7-MT-A from Notothenia coriiceps (broken sticks).

domains hosting a metal−thiolate cluster each. In this respect, there are similarities with the mammalian M(II) MTs. Significant differences, however, are found with respect to the chemical definitions of the metal−sulfur clusters itself. Within the Cd_6-MT-1 species of crustacean blue crab and of lobster, both the α and the β domains contain $\{Cd_3S_9\}$ clusters in distorted boat conformations, while Cd_7-MTA from equinodernal sea urchin contains $\{Cd_4S_{11}\}$ and $\{Cd_3S_9\}$ clusters in a reversed arrangement if compared with the cluster distribution of vertebrate M_7-MT-2: In the former system, the $\{Cd_4S_{11}\}$ cluster is located in the N-terminal domain of the protein, while the $\{Cd_3S_9\}$ cluster resides in the C-terminal domain. This modification leads to significantly different connectivity patterns of the Cd−S bonds as well as to novel local folds of the polypeptide backbone. Another remarkable aspect here is the fact that the topology of the $\{Cd_4S_{11}\}$ cluster observed in Cd_7-MTA from equinodernal sea urchin does not match the principal structural characteristics of the $\{M_4S_{11}\}$ units of identical composition present in the α domains of all vertebrate M_7-MTs investigated so far. The $\{Cd_3S_9\}$ cluster, however, is of conventional design. The structure of both clusters is shown in Figures 4 and 5, whereas a superposition of both is given in Figure 6.

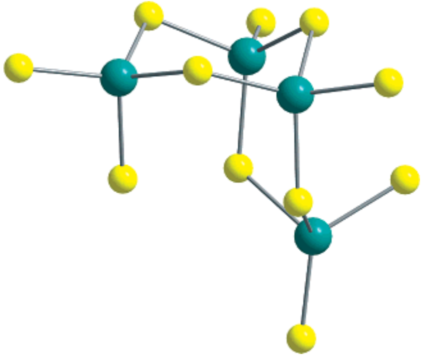


Figure 4. The tetranuclear $\{Cd_4S_{11}\}$ cluster of Cd_7-MTA from equinodernal sea urchin.

In contrast to the zinc- and cadmium-containing proteins discussed above, the architecture of metal−sulfur clusters in copper- and silver-containing MTs including all isoforms of higher organisms as well as yeast and fungal proteins is still unknown. The structures of the metal−thiolate clusters in Cu_{12}-MT, Ag_{12}-MT, and Ag_{17}-MT from rabbit liver have been investigated by sulfur K-edge X-ray absorption spectroscopy (XAS).[26] The sulfur EXAFS data provide the first direct evidence for mixtures of bridging and terminal sulfur atoms. They indicate that Cu(I) has three sulfur neighbors at distances of ca. 2.25 Å. Significant changes in the CD spectra observed between Ag_{12}-MT-1 and Ag_{17}-MT-1 indicate that a change of the three-dimensional structure occurs when Ag_{12}-MT-1 is transformed to Ag_{17}-MT-1 on addition of Ag(I). From the Ag−S bond distances it was concluded that Ag(I) in both Ag_{12}-MT-1 and Ag_{17}-MT-1 has only two sulfur neighbors and that the structures in Ag(I) and Cu(I) metallothioneins are probably quite different.

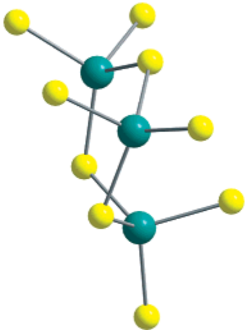


Figure 5. The trinuclear $\{Cd_3S_9\}$ cluster of Cd_7-MTA from equinodernal sea urchin.

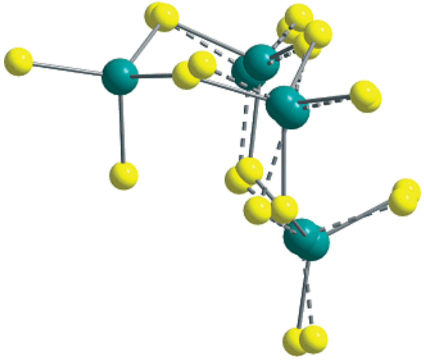


Figure 6. Superposition of the $\{Cd_4S_{11}\}$ and the $\{Cd_3S_9\}$ clusters of equinodernal sea urchin.

All attempts to crystallize copper- and silver-containing MTs failed so far. This is also true for truncated forms of the protein from yeast which have been prepared to facilitate possible crystallization.[27] MT-1 and MT-2 in their fully Cu-loaded forms contain 12 copper ions bonded to sulfur in two unidentified spacial arrangements. The mixed Cu/Zn derivative of MT-3, Cu_4Zn_3-MT-3, has been shown by copper K-edge EXAFS spectroscopy to contain homometallic metal−thiolate clusters.[21] The NMR structure of the M(I)-MT (M = Cu, Ag) of yeast (*Saccharomyces cerevisae*) shows the presence of a $\{Cu_7S_{10}\}$ cluster with unidentified distribution of the Cu atoms.[28,29] Attemps to fit the metal atoms to the well-resolved sulfur frame resulted in a variety of possible $\{Cu_7S_{10}\}$ cluster structures. Furthermore, from low-resolution NMR data of the fungal MT from *Neurospora crassa* the existence of a hexanuclear Cu-thiolate cluster of unknown structure has also been postulated.[30]

3. Synthetic and Chemical Aspects

The biologically important metal−chalcogenolate or metal−chalcogenide−chalcogenolate complexes discussed in this paper have usually been prepared by self-assembly reactions starting from suitable precursor compounds mostly in organic solvents. Molecular complexes usually appear as anionic species that have been crystallized in most cases as quaternary ammonium or phosphonium salts or in some instances as complex salts by using suitable complex cations as counterions. The detailed synthetic procedures as well as principal reactions, reactivities, solution equilibra, and kinetic, magnetic, spectroscopic, and chemical properties of the compounds discussed here are described in the original literature. In this work, the functionality of the metallothioneins as well as of model compounds mimicking relevant properties of the biological archetypes is discussed on a structural basis.

4. Zinc, Cadmium, Mercury: A Systematic Structural Approach

In this section, we will show that the structural features of the $\{M_3S_9\}$ and the $\{M_4S_{11}\}$ clusters (M = Zn, Cd) as well as most of the synthetic compounds with tetrahedral $\{MS_4\}$ coordination sites which may act as structural and/or functional models follow simple topological concepts. This approach has been chosen to highlight the underlying superior relationships and to prevent erroneous pictures made possible by inadequate descriptions of the structures of the clusters A and B in the literature which are often discussed (erroneously) in terms of adamantane-type rings and cages.

4.1 Mononuclear Complexes

This topological concept is based on the tendency of the sulfur atoms to order in space such that more or less regular fragments of three-dimensional infinite closed-packed arrays are formed. The driving force behind this is the fact that a tetrahedrally shaped $\{MS_4\}$ coordination site represents a minimal spatial portion of a closed-packed three-dimensional area of sulfur atoms. The fundamental $\{MS_4\}$ coordination unit is designated as unit A.

Its structure as well as that of the complex anion $[Zn(SC_6H_4\text{-}o\text{-}NC_6H_8)_4]^{2-}$ as a synthetic molecular thiolate system containing unit A as metal−sulfur frame are shown in Figures 7 and 8.[31] Other mononuclear complexes containing unit A include $[M(edt)_2]^{2-}$ (M = Zn, Cd),[32] $[M(SPh)_4]^{2-}$ (M = Zn, Cd),[33,34] $[M(SC_6H_4\text{-}o\text{-}Ph)_4]^{2-}$ (M = Zn, Cd, Hg),[35] $[M(SePh)_4]^{2-}$ (M = Zn, Cd),[34] $[Cd(SC_6H_4\text{-}o\text{-}NC_6H_8)_4]^{2-}$,[31] $[Cd(SC_6H_4\text{-}o\text{-}SiMe_3)_4]^{2-}$,[36] $[M(S_2C_6H_{10})_2]^{2-}$ (M = Cd, Hg)[37] and $[Hg(SC_6H_4\text{-}p\text{-}Cl)_4]^{2-}$.[38]

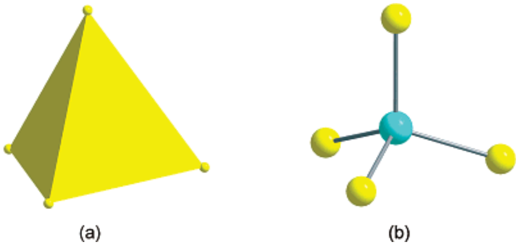


Figure 7. Unit A: the $\{MS_4\}$ tetrahedron; (a) schematic representation; (b) stick-and-ball model.

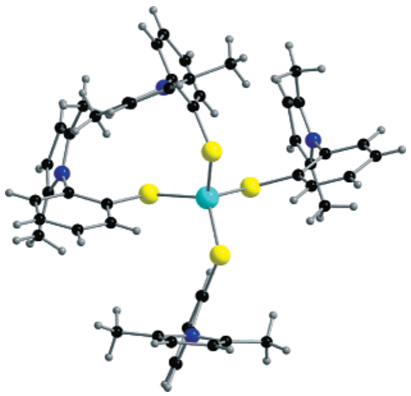


Figure 8. The complex anion $[Zn(SC_6H_4\text{-}o\text{-}NC_6H_8)_4]^{2-}$.

4.2 Tetranuclear Complexes

Having this in mind, we identify the other fundamental three-dimensional fraction of closed-packed areas in the order of increasing volume as a regular octahedron. Although not directly involved in interstitial metal-ion hosting if only $\{MS_4\}$ units are expressed, this octahedron consisting of eight trigonal $\{S_3\}$ faces can provide up to eight of them as bases for a corresponding number of $\{MS_4\}$ tetrahedra. In the most frequently observed case, four of them are used in an alternating manner. The resulting tetracapped $\{S_6\}$ octahedron can thus also be described as an ensemble of four metal-filled $\{S_4\}$ tetrahedra each of which are connected with the other ones by sharing common corners. A molecular unit of composition $\{M_4S_{10}\}$ defined in this way thus is a direct representation of a portion of the sphalerite-type (ZnS) lattice with M(II) in uniformely orientated tetrahedral holes (say the T^+ set) of a cubic closed-packed arrangement of sulfur atoms and adopts a heteroadamantane-like structure. This basic coordination unit is referred to as unit B. Its structure as well as that of the complex anion $[Zn_4(SPh)_{10}]^{2-}$ as a synthetic molecular system containing an adamantane-like $\{Zn_4S_{10}\}$ core are shown in Figures 9 and 10.[39]

Other tetranuclear complexes containing unit B include $[Zn_4(SCH_2Ph)_{10}]^{2-}$,[40] $[M_4(SePh)_{10}]^{2-}$ (M = Zn,[41,42] Cd[41]), $[Cd_4(SPh)_{10}]^{2-}$,[39,43] and $[Cd_4(SC_6H_4\text{-}p\text{-}^tBu)_{10}]^{2-}$.[44] Interesting variants containing adamantane-like $\{Cd_4S_6\}$ cages fused via thiolate bridges to form three-dimensional polymeric networks are condensation products of formula $[Cd_4(SPh)_8]_n$[45] or ring-substituted derivatives derived thereof. Adamantane-like $\{M_4S_6\}$ cages are also present in the molecular complex anions $[M_4(SPh)_6X_4]^{2-}$ (M = Zn, X = Cl,[46a,b] Br[46b], I;[46b] M = Cd, X = Cl,[46c] Br[46d]), $[Cd_4(S^iPr)_6Br_4]^{2-}$,[46e] $[Cd_4(SC_6H_4\text{-}p\text{-}tBu)_6Cl_4]^{2-}$,[44] and $[Hg_4(SEt)_6Br_4]^{2-}$,[46f] and the $\{M_4Se_6\}$ and $\{M_4Te_6\}$ cages are found in complex anions of the series $[Hg_4(EPh)_6X_4]^{2-}$ (E = Se, Te; X = Cl, Br, I).[46g]

4.3 Octanuclear Complexes

We now come back to our tetracapped $\{S_6\}$ octahedron and extend the remaining four trigonal faces

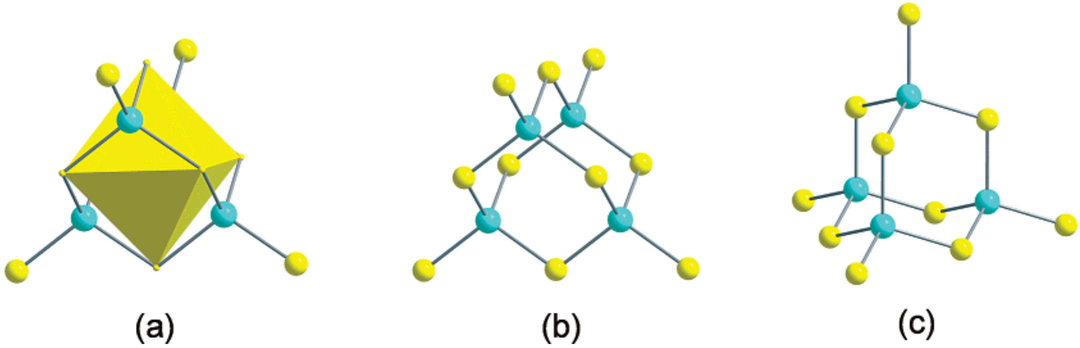


Figure 9. Unit B: the $\{M_4S_{10}\}$ framework containing a metal tetrahedron; (a) and (b) schematic representation and stick-and-ball model in identical orientation; (c) stick-and-ball model in a different orientation.

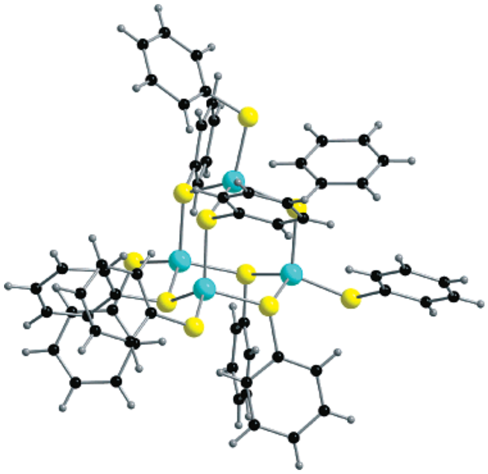


Figure 10. Structure of the complex anion $[Zn_4(SPh)_{10}]^{2-}$.

toward additional $\{MS_4\}$ tetrahedra. The resulting octacapped $\{S_6\}$ octahedron can be described as an ensemble of eight metal-filled $\{S_4\}$ tetrahedra each of which are connected to three nearest neighbors by one common edge and to three neighbors further apart by one common corner. Thus, molecular unit of composition $\{M_8S_{14}\}$ defined in this way is a direct representation of a portion of the anti-fluorite-type (anti-CaF_2) lattice with M(II) in both the T^+ and the T^- set of tetrahedral holes of a cubic closed-packed arrangement of sulfur atoms. The structure of this basic coordination unit which is referred to as unit C is shown in Figure 11. Actually, no metal thiolate complex of formula $[M_8(SR)_{14}]^{2+}$ containing the $\{M_8S_{14}\}$ core shown in Figure 11 is known so far.

Obviously, thiolate ligands are not suited to bind to four metal ions simultaneously in homoleptic polynuclear metal thiolate complexes. This restriction, however, does not apply to "naked" sulfide ions which are derived from thiolate ions by dealkylation. Consequently, corresponding mixed sulfide−thiolate complexes of divalent metal ions of formula $[M_8S_6(SR)_8]^{4-}$ should be stable chemical entities, and with $[Co_8S_6(SPh)_8]^{4-}$ shown in Figure 12 it was possible to obtain the first representative of this class of complexes.[47]

The tetracapped $\{S_6\}$ octahedron is not the only way to assemble four $\{MS_4\}$ coordination tetrahedra in such a way that sulfur frames are formed which are entities of the cubic closed-packed lattice. The other possibility is the sulfur-centered sulfur cuboctahedron. This fragment of the cubic closed-packed lattice is obtained if four $\{MS_4\}$ tetrahedra in identical orientations are fused such that they share one common corner. The structure of the resulting $\{M_4S_{13}\}$ frame shown in Figure 13 is referred to as unit D. The sulfur framework of unit D contains a total of eight tetrahedral holes of which one-half (say, the T^+ set) is occupied by metal ions. If the T^- set of holes is also occupied by metal ions, a unit of composition $\{M_8S_{13}\}$ (unit E, Figure 14) results which contains a metal cube identical to that present in unit C (Figure 11).

This congruency is based on the fact that both unit C and unit E are − different − portions of the anti-fluorite-type (anti-CaF_2) lattice with M(II) in both the T^+ and the T^- sets of tetrahedral holes of a cubic closed-packed arrangement of sulfur atoms. Tetra-

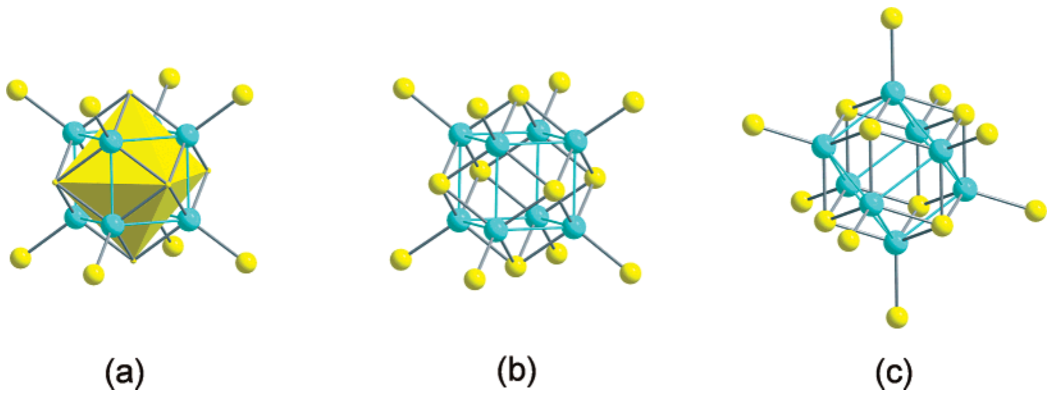


Figure 11. Unit C: the $\{M_8S_{14}\}$ framework containing a metal cube; (a) and (b) schematic representation and stick-and-ball model in identical orientation; (c) stick-and-ball model in a different orientation.

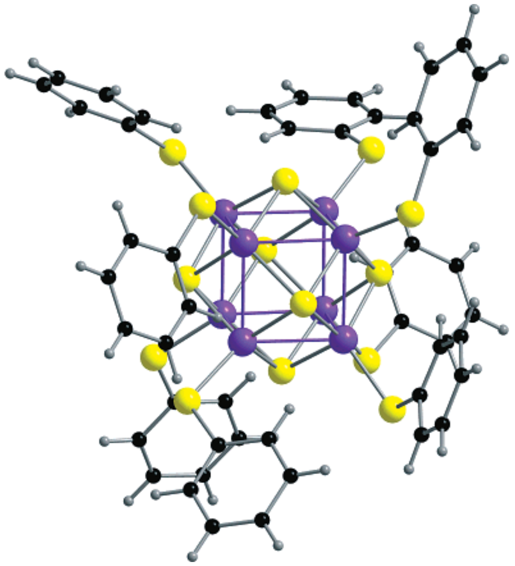


Figure 12. Structure of the complex anion $[Co_8S_6(SPh)_8]^{4-}$.

nuclear thiolate complexes of (hypothetical) formula $[M_4S(SR)_{12}]^{6-}$ containing unit D as metal−sulfur frameworks are expected to be unstable because of their high negative charges. Consequently, no examples are known in coordination chemistry. A similar situation is found if the corresponding octanuclear M(II) complexes of (hypothetical) formula $[M_8S(SR)_{12}]^{2+}$ containing unit E are considered. In this case, the positive charge of the complex presumably results in considerable destabilization. The charge problem, however, can be reduced by replacing the T^- set of M(II) ions by monovalent d^{10} ions, e.g., Cu(I). Following this strategy, the complex anion $[Zn_4Cu_4S(S^iPr)_{12}]^{2-}$ has been synthesized and characterized in its benzyltrimethylammonium salt.[48] Its structure is shown in Figure 15. The replacement of divalent metal ions by Cu(I) introduces significant structural changes of the $\{M(II)_4M(I)_4S_{13}\}$ core if compared with unit E. First, the monovalent copper ions are no longer within the centroids of the $\{CuS_4\}$ tetrahedra but are shifted toward the trigonal faces opposite to the sulfur atom within the metal cube. Second, the sulfur cuboctahedron of unit E has been rearranged such that an icosahedron is observed in $[Zn_4Cu_4S(S^iPr)_{12}]^{2-}$. The corresponding $\{M(II)M(I)S_{13}\}$ core portion referred to as unit F is depicted in Figure 16.

Starting from the structure of $[Zn_4Cu_4S(S^iPr)_{12}]^{2-}$, it is now only a minor step to arrive at complexes of general formula $[Zn_4Zn_4S(SR)_{16}]^{2-}$ which can be regarded as topological parents of the $\{M_3S_9\}$ and $\{M_4S_{11}\}$ clusters observed in vertebrate $M(II)_7S_{20}$-MTs (vide infra). From a structural point of view, this step includes further shifting of the {Cu(I)} ions away from the central sulfur atom into positions outside the $\{S_{12}\}$ icosahedron followed by their replacement by {Zn(II)SR} fragments (see Figure 18). In the case of the complex anion $[Zn_8S(SCH_2Ph)_{16}]^{2-}$ (= $[Zn_4Zn_4S(SCH_2Ph)_{16}]^{2-}$, Figure 17),[40,49] this transformation is accompanied by a rearrangement of the sulfur icosahedron which now converts into a cuboctahedron. The structural relationship between $[Zn_4Cu_4S(S^iPr)_{12}]^{2-}$ and $[Zn_4Zn_4S(SCH_2Ph)_{16}]^{2-}$ based on a cuboctahedral sulfur frame is shown in Figure 18. The replacement of {Cu(I)} by {Zn(II)SR} fragments extends the

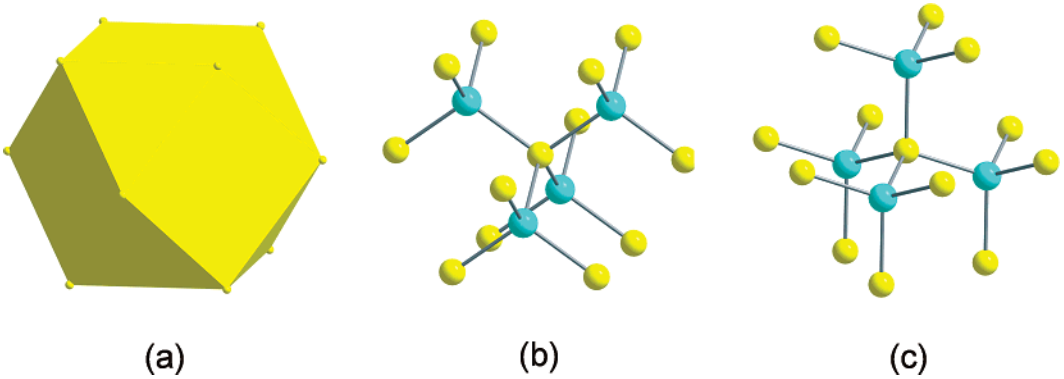


Figure 13. Unit D: the cuboctahedral $\{M_4S_{13}\}$ framework containing a metal tetrahedron; (a) and (b) schematic representation and stick-and-ball model in identical orientation; (c) stick-and-ball model in a different orientation.

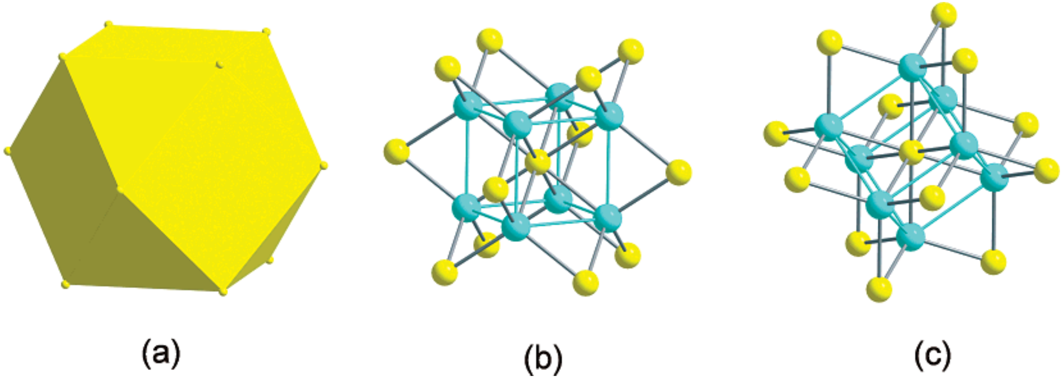


Figure 14. Unit E: the cuboctahedral $\{M_8S_{13}\}$ framework containing a metal cube; (a) and (b) schematic representation and stick-and-ball model in identical orientation; (c) stick-and-ball model in a different orientation.

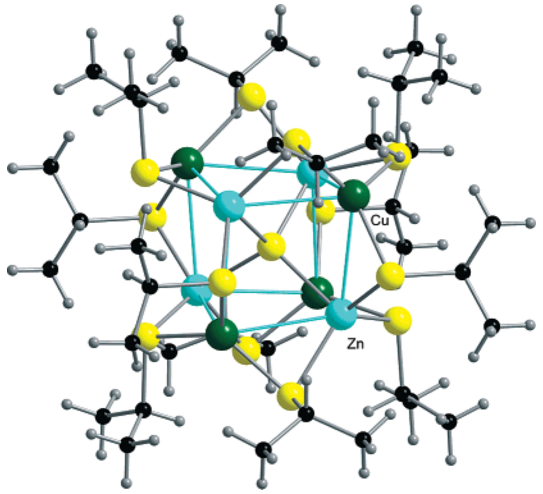


Figure 15. Structure of the complex anion $[Zn_4Cu_4S(S^iPr)_{12}]^{2-}$.

inner cuboctahedral $\{Zn_4S_{13}\}$ framework (unit D) of $[Zn_4Zn_4S(SR)_{16}]^{2-}$ by using the triangular faces formerly attached to $\{Cu(I)\}$ as bases for additional $\{ZnS_4\}$ tetrahedra. This extension does not match the topology of a cubic closed-packed array of sulfur atoms because now four $\{S_4\}$ tetrahedra occur at places were the cubic closed-packed array comprises $\{S_6\}$ octahedra. What we observe here is the termination of a portion of a cubic closed-packed sulfur lattice represented by the complete set of 12 neighbors surrounding a central sulfur atom in a cuboctahedral manner by structural elements of the corresponding homeotectic hcp lattice.

It is interesting to note that both complex anions $[Zn_8S(SCH_2Ph)_{12}S_4]^{2-}$ [50] and $[Zn_8Cl(SPh)_{16}]^{-}$ [51] described in the literature have $\{M_8X(SR)_{12}\}$ frameworks (X = S, Cl) comparable to that of $[Zn_8S(SCH_2Ph)_{16}]^{2-}$ with the only exception that the former ones contain $\{S_{12}\}$ icosahedra instead of the cuboctahedron observed in the latter case. In this respect, the complex anion described as $[Zn_8S(SCH_2Ph)_{12}S_4]^{2-}$ could be regarded as a direct topological extension of $[Zn_4Cu_4S(S^iPr)_{12}]^{2-}$ retaining its $\{S_{12}\}$ icosahedron (see Figure 15). At this stage, however, we run into problems with $[Zn_8S(SCH_2Ph)_{12}S_4]^{2-}$ because a complex anion comprising this composition is not compatible with divalent zinc. On the basis of the reported NMR properties which imply diamagnetic behavior of the complex anion, we assume that the chemical formula given in the literature is in error and may probably read $[Zn_8S(SCH_2Ph)_{12}Cl_4]^{2-}$ or $[Zn_8S(SCH_2Ph)_{12}(SH)_4]^{2-}$. Other octanuclear complexes containing the $\{M_8XE_{12}\}$ core (X = S, Cl, E = S, Se) include $[Zn_8Se(SePh)_{12}Cl_4]^{2-}$,[52] $[Cd_8Cl(SC_6H_{12}NH)_{16}]^{15+}$,[53] $[Cd_8S(SPh)_{12}Cl_4]^{2-}$,[54] $[Cd_8S(SePh)_{16}]^{2-}$ [55] and $[Cd_8Se(SePh)_{12}Cl_4]^{2-}$.[56]

4.4 $\{M_4S_{11}\}$ and $\{M_3S_9\}$ Clusters of the Vertebrate MTs

Before we extend our discussion toward complexes of higher nuclearities, we will show that the $\{M_4S_{11}\}$ cluster within the vertebrate $M(II)_7S_{20}$-MTs is neither a direct representation of the sphalerite- nor of the wurtzite-type structure. In its idealized geometry, the $\{M_4S_{11}\}$ cluster is a bicyclic system consisting of two six-membered nonplanar rings that adopt the boat conformation in both cases. The idealized structure (referred to as unit G) is shown in Figure 19. Its principal topological features are realized in the complex anion $[Zn_8S(SCH_2Ph)_{16}]^{2-}$ which contains two such $\{M_4S_{11}\}$ units perpendicular to each other and connected via common sulfur atoms (Figure 17). One of these $\{M_4S_{11}\}$ units is shown as a fragment of the $\{Zn_8S_{17}\}$ core of $[Zn_8S(SCH_2Ph)_{16}]^{2-}$ in Figure 20, and in Figure 21 a direct comparison of this fragment with cluster A observed in $Cd_5Zn_2S_{20}$-MT-2 is given. The trinuclear $\{M_3S_9\}$ cluster of the β domain of Cd_5Zn_2-MT-2 (Figure 2, cluster B) itself is a fraction of cluster A (Figure 1) and consists of a six-membered heterocycle adopting a distorted boat conformation. A superposition of both metal clusters is shown in Figure 22, and Figure 23 clearly demonstrates the distortions of cluster A from idealized symmetry if compared with unit G (Figure 19). Although the cluster B of Cd_5Zn_2-MT-2 is directly related with the wurtzite-type lattice, its extension to cluster A has no precedent in three-dimensional infinite lattices (Figures 19−23).

4.5 Complexes of Higher Nuclearities

4.5.1 Complexes with Seventeen Metal Atoms

The discussion has shown that the inner $\{Zn_4S(S)_{12}\}$ core portion (unit D, Figure 13) of the $[Zn_8S(SCH_2Ph)_{16}]^{2-}$ complex anion (Figure 17) is a sulfur-centered sulfur cuboctahedron hosting four zinc atoms in its T^+ holes. The inverted polyhedron,

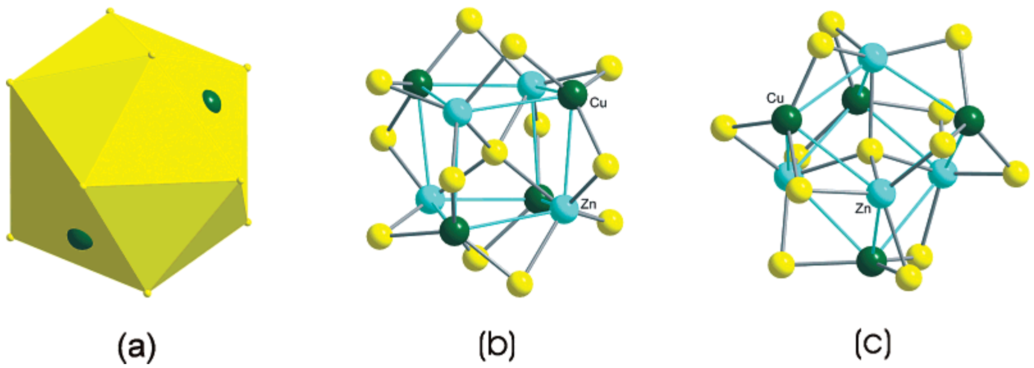


Figure 16. Unit F: the icosahedral $\{M_4S_{13}\}$ framework consisting of four $\{MS_4\}$ tetrahedra and four $\{MS_3\}$ triangles; (a) and (b) schematic representation and stick-and-ball model in identical orientation; (c) stick-and-ball model in a different orientation.

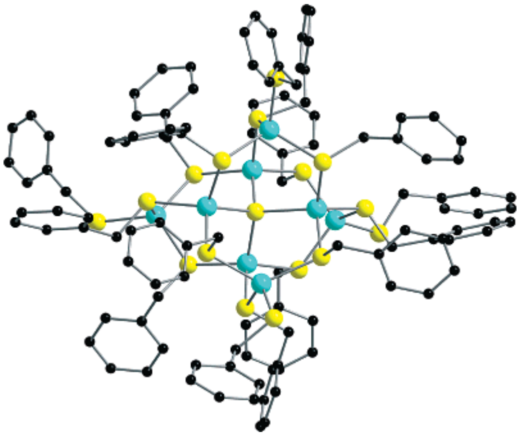


Figure 17. Structure of the complex anion $[Zn_8S(SCH_2Ph)_{16}]^{2-}$ (without H atoms).

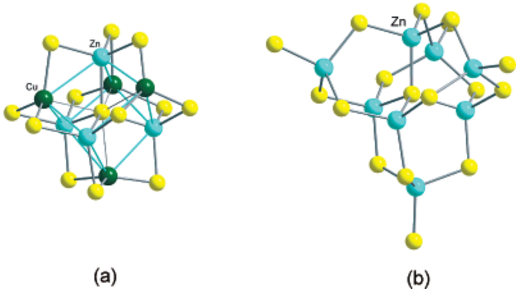


Figure 18. Structural relationship between $[Zn_8S(SCH_2Ph)_{16}]^{2-}$ and $[Zn_4Cu_4S(S^iPr)_{12}]^{2-}$: Replacement of Cu (a) ions by Zn−S groups (b).

namely, the $\{S_4Cd(Cd)_{12}\}$ framework (unit H, Figure 24), forms the base of the complex anion $[Cd_{17}S_4(SPh)_{28}]^{2-}$ (= $[S_4CdCd_{12}(SPh)_{12}(SPh)_{12}Cd_4(SPh)_4]^{2-}$) whose structure is shown in Figure 25.[57]

Within this molecule, 16 out of 32 sulfur atoms define a section of the cubic closed-packed lattice (unit I, Figure 26) consisting of a cadmium-centered central $\{S_4\}$ tetrahedron (say, T^+) sharing faces with four surrounding $\{S_6\}$ octahedra. This ensemble is extended by additional 12 sulfur atoms to be able to host 12 other cadmium atoms in equally orientated tetrahedral sites of the type T^+. The remaining four sulfur atoms extend four trigonal faces of the {28-S} polyhedron toward sulfur tetrahedra that host the remaining four Cd atoms. This extension, however, does not match the topology of a ccp lattice because these four $\{S_4\}$ tetrahedra occur at places where the cubic closed-packed array comprises $\{S_6\}$ octahedra. What we observe here is, in close analogy to the complex anion $[Zn_4S(SPr)_{12}Zn_4(SPr)_4]^{2-}$ (Figure 17), the termination of a portion of the ccp lattice by structural elements of the corresponding homeotectic hcp lattice.

4.5.2 Complexes Containing Ten Metal Atoms and the Relationship with Tetranuclear Complexes

The hexagonal termination necessary in $[Cd_{17}S_4(SPh)_{28}]^{2-}$ (= $[CdS_4Cd_{12}(SPh)_{12}(SPh)_{12}Cd_4(SPh)_4]^{2-}$) can be avoided if the T^+ set of tetrahedral holes within unit I (Figure 26) remains unoccupied and the T^- set is filled with six divalent metal atoms instead. In this case, the central $\{S_4\}$ tetrahedron which is now empty is surrounded by a set of six $\{S_4\}$ tetrahedra of the type T^-. The corresponding polyhedral representation is given in Figure 27. With four additional sulfur atoms it is now possible to develop four trigonal faces of the {16-S} polyhedron into sulfur tetrahedra of the type T^- which now may host four additional divalent metal atoms matching the topology of a ccp lattice (Figure 28).

Chemical examples reflecting these principles are the complex anions $[Zn_{10}S_4(SCH_2C_6H_4CH_2S)_8]^{4-}$ (Figure 29)[58] and $[Zn_{10}S_4(SPh)_{16}]^{4-}$.[59] In both cases, the metal atoms form tetracapped metal octahedra and thus follow exactly the same structural principles as the sulfur atoms of unit B shown in Figure 9. This means that the arrangement of the zinc atoms within $[Zn_{10}S_4(SCH_2C_6H_4CH_2S)_8]^{4-}$ or $[Zn_{10}S_4(SPh)_{16}]$,$^{4-}$ which is a portion of a face-centered cubic (fcc) lattice, matches exactly the arrangement of the sulfur atoms within $[Zn_4(SPh)_{10}]^{2-}$. The complementary substructures defined by the zinc atoms within $[Zn_4(SPh)_{10}]^{2-}$ and the sulfur atoms within $[Zn_{10}S_4(SPh)_{16}]$,$^{4-}$ however, are not congruent. They make use of complementary tetrahedral holes of the corresponding fcc lattice. Other complex anions containing the $\{M_{10}E_{16}\}$ coordination unit are $[Cd_{10}S_4(SPh)_{16}]^{4-}$[59−61] and $[Cd_{10}S_4(S\text{-}p\text{-}Tol)_{12}X_4]^{4-}$ (X = Br, I),[61] and with $[Zn_{10}S_4(SEt)_{12}(C_5H_5N)_4]$,[62] a neutral example is also known.

4.5.3 Relationship between Complexes of Nuclearity Eight and Seventeen

A structural relationship completely analogous to that found between $[Zn_{10}S_4(SPh)_{16}]^{4-}$ and $[Zn_4(SPh)_{10}]^{2-}$ is also observable for the complex anions $[Zn_8S(SCH_2Ph)_{16}]^{2-}$ and $[Cd_{17}S_4(SPh)_{28}]^{2-}$: The arrangement of the sulfur atoms within the former compound matches exactly that of the cadmium atoms within the latter, and the complementary

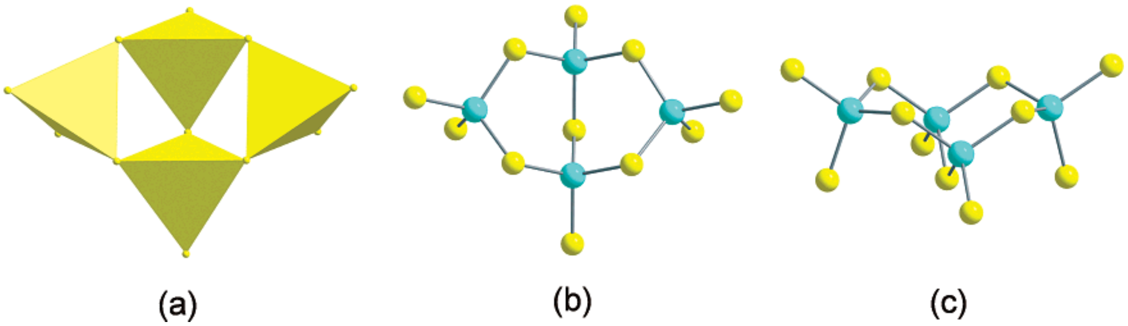


Figure 19. Unit G: the idealized $\{M_4S_{11}\}$ framework (cluster A) of the metallothioneins; (a) and (b) schematic representation and stick-and-ball model in identical orientation; (c) stick-and-ball model in a different orientation.

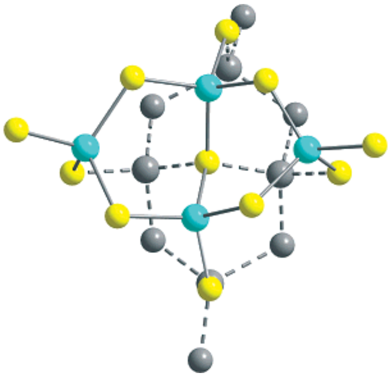


Figure 20. The $\{M_4S_{11}\}$ unit as a (colored) fragment of the $\{M_8S_{17}\}$ framework of the complex anion $[Zn_8S(SCH_2Ph)_{16}]^{2-}$.

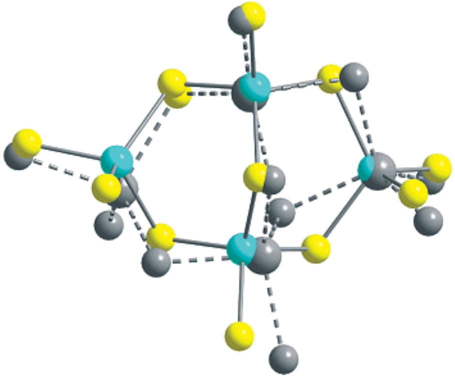


Figure 21. Superposition of the $\{M_4S_{11}\}$ framework of the complex anion $[Zn_8S(SCH_2Ph)_{16}]^{2-}$ and the $\{M_4S_{11}\}$ cluster (cluster A) of rat-liver M_7-MT-2.

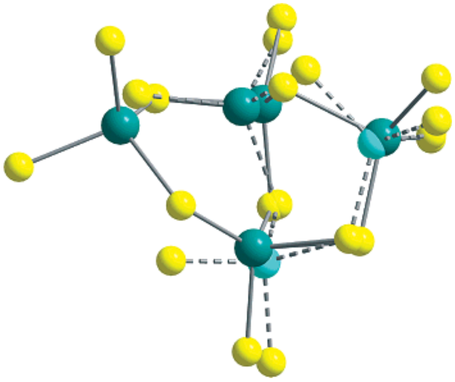


Figure 22. Superposition of the $\{M_4S_{11}\}$ (cluster A) and the $\{M_3S_9\}$ (cluster B) core portions of M_7-MT-2 from rat liver.

Figure 23. Real structure of cluster A from M_7-MT-2 (rat liver; schematic representation).

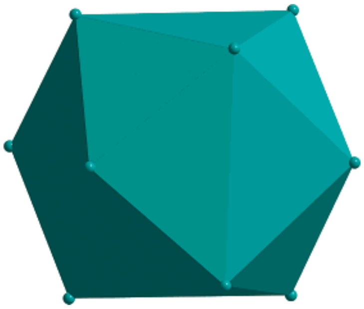


Figure 24. Unit H: the (distorted) cuboctahedral $\{M_{13}S_4\}$ framework of the complex anion $[Cd_{17}S_4(SPh)_{28}]^{2-}$ (see Figure 25).

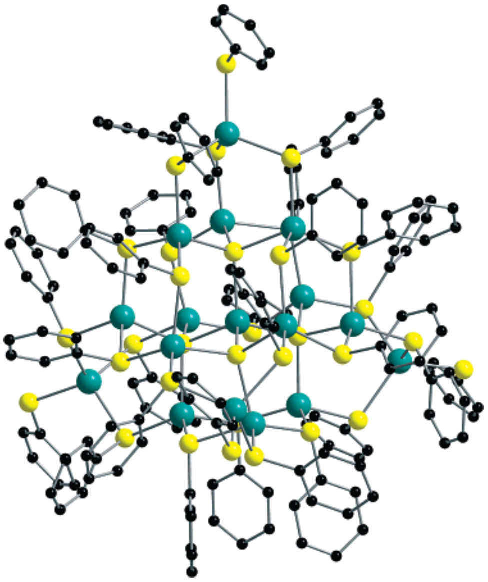


Figure 25. Structure of the complex anion $[Cd_{17}S_4(SPh)_{28}]^{2-}$ (without H atoms).

substructures defined by the zinc and sulfur atoms, respectively, are distinguished by different orientations of their $\{MS_4\}$ and $\{SM_4\}$ tetrahedra, respectively. On the basis of this principle, it should be possible to propose the existence of sulfide−thiolate complexes of unknown nuclearities containing metal−chalcogen tetrahedra sharing vertices. As an example, starting from $[Cd_{17}S_4(SPh)_{28}]^{2-}$ we arrive at a complex anion of hypothetical formula $[M_{32}E_{14}(ER)_{40}]^{4-}$ (M = Zn, Cd; E = S, Se, Te). Although no species with complete chalcogen ligand spheres are known so far, the cadmium thiolate derivatives $[Cd_{32}S_{14}(SPh)_{36}(DMF)_4]$ and $[Cd_{32}S_{14}(SCH_2CH(OH)Me_3)_{36}(H_2O)_4]$[63] containing four terminally bonded neutral solvent molecules instead of chalcogenolate ligands have been described. The structure of $[Cd_{32}S_{14}(SCH_2CH(OH)Me_3)_{36}(H_2O)_4]$ is given in Figure 30. It is interesting to note that the central $\{Cd_{32}S_{50}O_4\}$ framework of $[Cd_{32}S_{14}(SCH_2CH(OH)Me_3)_{36}(H_2O)_4]$ which is shown in Figure 31 hosts the complete $\{M_{10}S_{20}\}$ core of the complex anions $[Zn_{10}S_4(SPh)_{16}]^{4-}$ or $[Zn_{10}S_4(SCH_2C_6H_4CH_2S)_8]^{4-}$ (Figure 29). However, in contrast to the latter ones, the extension of the $\{M_{10}S_{20}\}$ core toward $\{Cd_{32}S_{50}O_4\}$ necessitates the hexagonal termination of the array of sulfur atoms—which represents a portion of the ccp lattice—by oxygen. In this respect, the compounds $[Cd_{32}S_{14}(SCH_2CH(OH)Me_3)_{36}(H_2O)_4]$, $[Cd_{17}S_4(SPh)_{28}]^{2-}$, and $[Zn_8S(SPr)_{16}]^{2-}$ behave

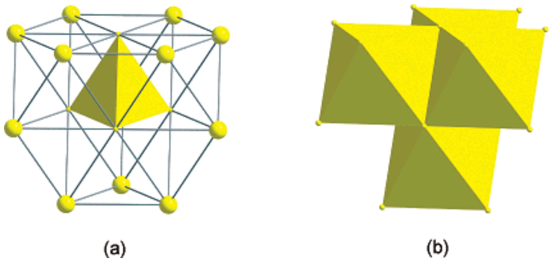


Figure 26. Unit I: the $\{MS_{16}\}$ framework of the complex anion $[Cd_{17}S_4(SPh)_{28}]^{2-}$ (a) schematic representation showing the central $\{MS_4\}$ tetrahedron; (b) schematic representation showing four $\{S_6\}$ octahedra sharing faces with the inner $\{MS_4\}$ tetrahedron.

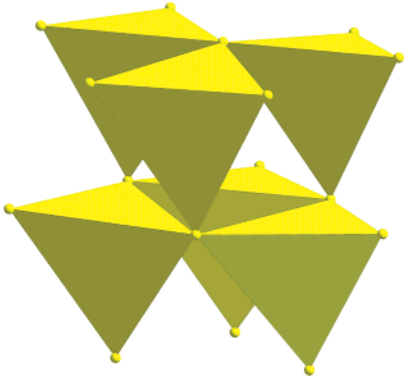


Figure 27. Polyhedral representation of the $\{S_{16}\}$ framework of unit I (see Figure 26) consisting of six T$^-$-$\{S_4\}$ tetrahedra which surround an inner T$^+$-$\{S_4\}$ tetrahedron.

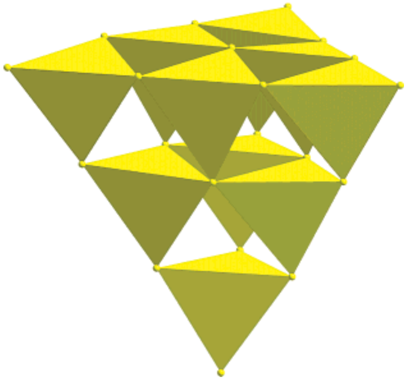


Figure 28. The extension of the $\{S_{16}\}$ framework shown in Figure 27: Schematic representation of the $\{M_{10}S_{20}\}$ framework of the complex anion $[Zn_{10}S_4(SCH_2C_6H_4CH_2S)_8]^{4-}$.

similarly emphasizing the unique structural properties of $[Zn_{10}S_4(SPh)_{16}]^{4-}$ as well as of $[Zn_{10}S_4(SCH_2C_6H_4CH_2S)_8]^{4-}$ within this class of sulfide–thiolate complexes containing tetrahedrally coordinated M(II) ions with d^{10} electron configurations.

4.5.4 Comparative Discussion

At this stage, we conclude that molecular M(II)–thiolate or M(II)–sulfide–thiolate complexes containing metal–sulfur frames which are representations of the sphalerite type structure either completely or predominantly have reached their maximal dimensions in the species $[Zn_8S(SCH_2Ph)_{16}]^{2-}$ (complex I, Figure 17), $[Cd_{17}S_4(SPh)_{28}]^{2-}$ (complex II, Figure 25), and $[Zn_{10}S_4(SCH_2C_6H_4CH_2S)_8]^{4-}$ (complex III, Figure 29). Complexes I–III are members of families that differ in the definition of their central cage units from which they derive in formal step-by-step condensation processes. Complex I contains a sulfur-centered sulfur cuboctahedron (unit D, Figure 13) which is replaced by a metal-centered metal cuboctahedron in complex II. The central part (unit I, Figure 26) of the corresponding sulfur polyhedron of complex II is a cadmium-centered $\{S_4\}$ tetrahedron sharing faces with four surrounding $\{S_6\}$ octahedra. A nearly identical sulfur polyhedron (unit I, Figure 27) is present in complex III. In contrast to complex II, however, the central sulfur tetrahedron is empty, and the metal atoms occupy the complementary set of tetrahedral holes (T$^-$) within unit I. The resulting metal octahedron is extended toward a tetracapped octahedron by adding the remaining four metal atoms. It is interesting to note that the cadmium complexes $[Cd_{32}S_{14}(SPh)_{36}(DMF)_4]$ and $[Cd_{32}S_{14}(SCH_2CH(OH)Me_3)_{36}(H_2O)_4]$ contain the complete metal–sulfur frame of complex III. The central metal-sulfur frame of $[Cd_{32}S_{14}(SPh)_{36}(DMF)_4]$ and $[Cd_{32}S_{14}(SCH_2CH(OH)Me_3)_{36}(H_2O)_4]$ is unit B (Figure 9) which is

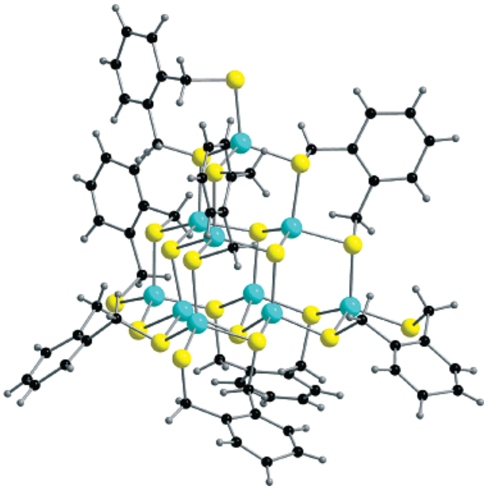


Figure 29. Structure of the complex anion $[Zn_{10}S_4(SCH_2C_6H_4CH_2S)_8]^{4-}$.

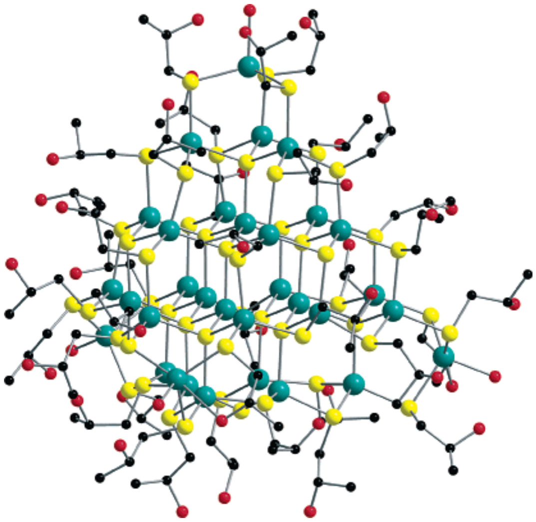


Figure 30. Structure of the neutral polynuclear complex $[Cd_{32}S_{14}(SCH_2CH(OH)Me_3)_{36}(H_2O)_4]$ (without H atoms).

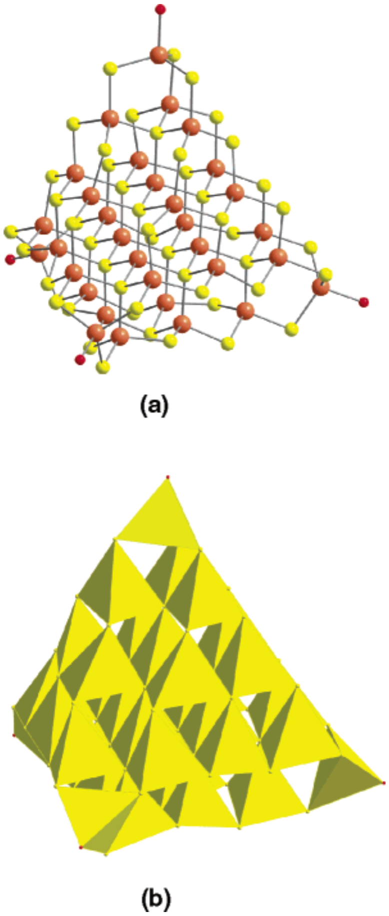


Figure 31. The $\{Cd_{32}S_{50}O_4\}$ framework of $[Cd_{32}S_{14}(SCH_2CH(OH)Me_3)_{36}(H_2O)_4]$; (a) stick- and-ball model; (b) schematic representation.

extended into three dimensions following the principles of the sphalerite type structure. The first three-dimensional extension product of unit B built up of tetrahedral $\{MS_4\}$ sites is the (hypothetical) complex anion $[Cd_{28}S_{14}(SR)_{36}]^{8-}$. Its $\{Cd-S\}$ frame is a portion of the sphalerite type lattice and contains a total of four triangular sulfur planes. These planes are extended toward $\{S_3N\}$ (for $[Cd_{32}S_{14}(SPh)_{36}(DMF)_4]$) and $\{S_3O\}$ tetrahedra (for $[Cd_{32}S_{14}(SCH_2CH(OH)Me_3)_{36}(H_2O)_4]$) which occur at places where the sphalerite-type lattice comprises $\{S_6\}$ octahedra.

4.6 Complexes that Can Be Derived from $[Co_8S_6(SR)_8]^{4-}$ by Degradation

4.6.1 Trinuclear Complexes

We now direct our attention to the complex anion $[Co_8S_6(SR)_8]^{4-}$ (Figure 12) which contains a metal cube inscribed into a sulfur octahedron with eight terminally bonded sulfur atoms (unit C, Figure 11). Unit C can be depleted to unit B (Figure 9) by removal of four metal and four sulfur atoms. Another degradation product of unit C containing three conserved metal sites is obtained if one complete metal square as well as one of the remaining metal atoms are removed. The corresponding $\{M_3S_8\}$ frame (unit J) as a fragment of unit C is shown in Figure 32. Unit J itself (Figure 33) has chemically been realized in the complex ion $[Hg_3(SCH_2C_6H_4CH_2S)_4]^{2-}$ whose structure is depicted in Figure 34.[64] In this context, it is interesting to note that the more symmetric trinuclear $\{M_3S_9\}$ unit (unit K, Figure 35) which can be derived from unit B by removal of one $\{MS\}$ fragment has not been observed in synthetic metal thiolate complexes as integral entity so far. The $\{M_3S_3\}$ core portion of unit K, however, can be identified as a heterocyclic six-membered chair within the bimetallic complex anion $[Zn_3(SC_3H_7)_6Cl_3Cu]^{2-}$ (Figure 36).[65]

Moreover, this entity has obviously been used as a structural model for both the $\{M_3S_9\}$ and the $\{M_4S_{11}\}$ coordination sites in the first X-ray structure report of the Cd_5Zn_2-MT-2 protein which in subsequent NMR and X-ray work was subject for major revision. The revised X-ray structure of Cd_5Zn_2-MT-2 now shows $\{M_3S_9\}$ coordination sites that are not fragments of the sphalerit-type lattice but derive from the wurtzite-type structure with six-membered $\{M_3S_6\}$ heterocycles in boat conformations (unit L, Figure 37) instead. Unit L (Figure 37) defined in this way is also a component of the $\{M_4S_{11}\}$ coordination site within this protein (Figure 22) which can be regarded as an extension toward a bicyclic unit consisting of two six-membered rings adopting the boat conformation. For a discussion of the structure of complex A observed in Cd_5Zn_2-MT-2, see the previous chapter.

An interesting modification of the structural motif shown in Figure 33 has been observed in the trinuclear complex anion $[Cd_3(SC_6H_2\text{-}2,4,6\text{-}{}^iPr)_7]^-$ (Figure 38).[66] The $\{Cd_3S_7\}$ core portion of this compound (Figure 39) derives from unit J (Figure 33) by an

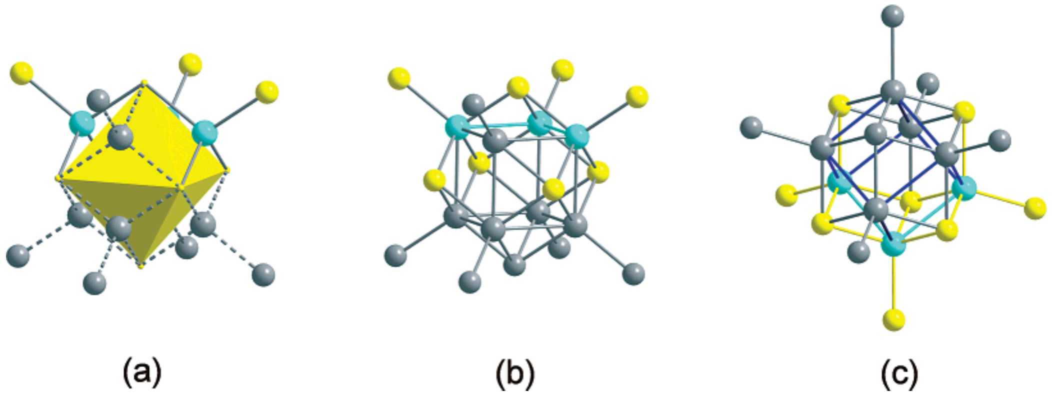


Figure 32. Unit J: the $\{M_3S_8\}$ frame as a section of Unit C; (a) and (b) schematic representation and stick-and-ball model in identical orientation; (c) stick-and-ball model in a different orientation.

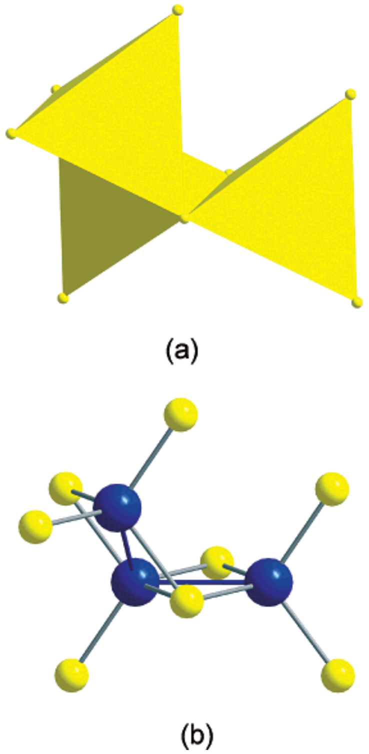


Figure 33. Unit J: the $\{M_3S_8\}$ core portion of the complex anion $[Hg_3(SCH_2C_6H_4CH_2S)_4]^{2-}$; (a) and (b) schematic representation and stick-and-ball model in identical orientation.

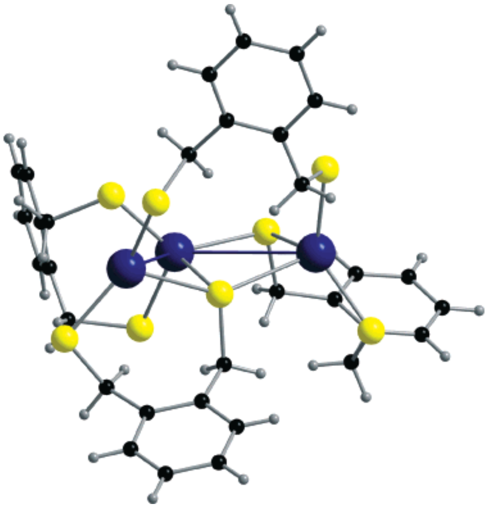


Figure 34. Structure of the complex anion $[Hg_3(SCH_2C_6H_4CH_2S)_4]^{2-}$.

additional condensation step resulting in the loss of two terminally bonded S atoms accompanied by the formation of a third u_2–S bridge. In the context of our topological approach, we conclude that the metal–sulfur framework of $[Cd_3(SC_6H_2\text{-}2,4,6\text{-}{}^iPr)_7]^-$ is based on a metal-deficient $\{M_4\}$ tetrahedron lacking one vertex that would fit both into the ccp and into the hcp type lattice, but the sulfur atoms do not.

4.6.2 Binuclear Complexes, Complexes Containing $\{M_2S_6\}$ Frameworks, and Compounds with Related Structural/Chemical Properties

If degradation of unit C continues and we remove one of the metal atoms attached to two terminal sulfur atoms from unit J, we arrive at the binuclear fragment $\{M_2S_6\}$ (unit M, Figure 40). This fragment which consists of a complete edge of the metal cube of unit C defines the metal–sulfur framework of a widely distributed class of complexes of general formula $[M_2(SR)_6]^{2-}$. Within these complexes, two $\{MS_4\}$ tetrahedra share a common edge. A characteristic section of the one-dimensional chain structure of $[\{Hg_2(SCH_2CH_2S)_3\}^{2-}]_n$ in crystals of $[Ph_4P]_2[Hg_2(SCH_2CH_2S)_3]$ containing bitetrahedral $\{M_2S_6\}$ coordination sites is shown in Figure 41 as a representative example.[67] $\{Hg_2S_6\}$ units similar to those found in the one-dimensional anionic chains of $[Ph_4P]_2[\{Hg_2(SCH_2CH_2S)_3]$ have also been observed in the cross-linked endless anionic $[\{Hg_2(SCH_2CH_2CH_2CH_2S)_3\}^{2-}]_n$ double chains of the homologous compound $[Et_4N]_2[Hg_2(SCH_2CH_2CH_2CH_2S)_3]\cdot 2MeOH$ (Figure 42).[68]

Other complexes hosting unit M as metal–chalcogen coordination sites are $[Hg_2(SMe)_6]^{2-}$,[69] $[M_2(SPh)_6]^{2-}$ (M = Hg,[70] Cd,[71,72] Zn[72,73]), $[Zn_2(SEt)_6]^{2-}$,[71] $[M_2(SC_6H_{11})_6]^{2-}$, (M = Zn,[71] Cd[74]), $[Zn_2(SCH_2Ph)_6]^{2-}$,[40] and $[Zn_2(SC_6H_4\text{-}p\text{-}{}^tBu)_6]^{2-}$.[75] An extension of unit M toward three $\{E_4\}$ tetrahedra sharing opposite edges (Figure 43) has been observed in $[Hg_3(edt)_4]^{2-}$ (Figure 44),[67] and complexes containing one-dimensional endless chains of edge-linked $\{E_4\}$ tetrahedra or three-dimensional networks of vertex-linked ones are also known. They comprise $\{[Hg(SC_6H_{11})_2]\}_n$,[76] $\{[Cd(SC_6H_{11}\text{-}NH)_2]\}_n$,[77] $\{[Cd(TeC_6H_2\text{-}2,4,6\text{-}Me_3)_2]\}_n$[78] and $\{[Hg_4(SeMe)_8]\}_n$.[79] Unit M is also a major component of the three-dimensional coordination polymer of composition $\{[Cd_8(SCH_2CH(OH)CH_2OH)_{16}]\}_n$[80] and represents one-half of the Cd atoms within this compound. The other ones form eight-membered $\{Cd_4S_4\}$ heterocycles which are folded such that a regular $\{S_4\}$ tetrahedron is formed with S···S distances ranging from 3.818 to

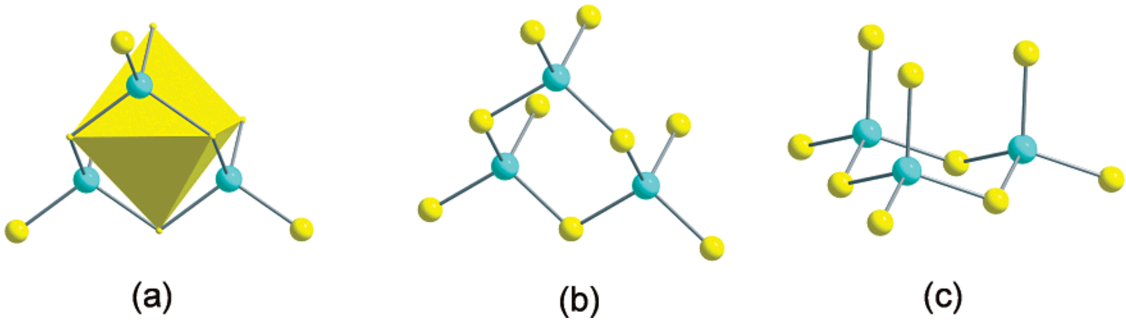


Figure 35. Unit K: the $\{M_3S_9\}$ frame; (a) and (b) schematic representation and stick-and-ball model in identical orientation; (c) stick-and-ball model in a different orientation.

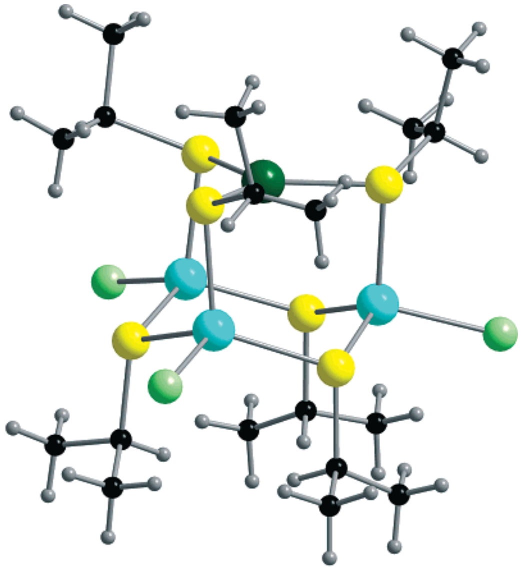


Figure 36. Structure of the complex anion $[Zn_3(S^iPr)_6Cl_3Cu]^{2-}$.

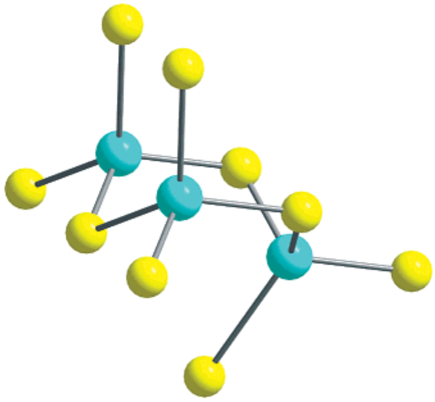


Figure 37. Unit L: the $\{M_3S_9\}$ frame as a fraction of the wurtzite-type lattice.

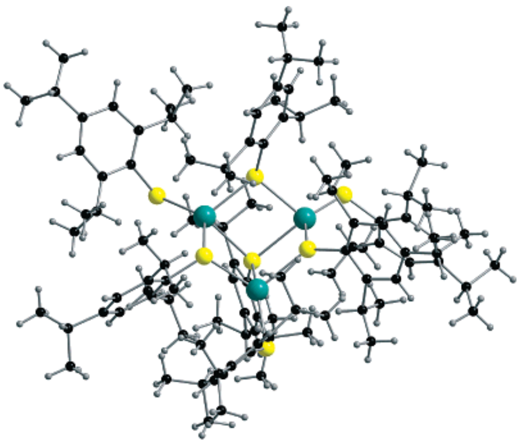


Figure 38. Structure of the complex anion $[Cd_3(SC_6H_2\text{-}2,4,6\text{-}^iPr)_7]^-$.

3.982 Å. The Cd atoms within this structural motif complete their ligand spheres by binding two sulfur donor functions from different $\{Cd_2S_6\}$ units each. A characteristic section of the three-dimensional polymeric structure is shown in Figure 45 together with the connectivity pattern of the $\{CdS_4\}$ tetrahedra.

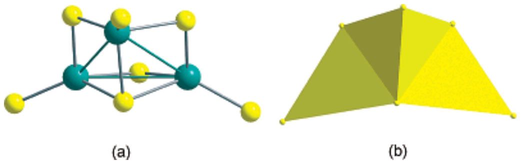


Figure 39. The $\{Cd_3S_7\}$ core portion of $[Cd_3(SC_6H_2\text{-}2,4,6\text{-}^iPr)_7]^-$; (a) stick-and-ball model; (b) schematic representation.

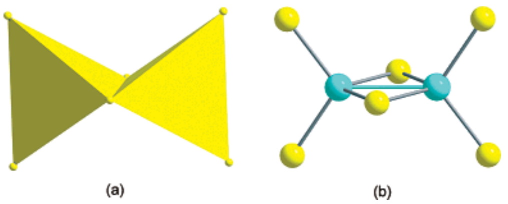


Figure 40. Unit M: the $\{M_2S_6\}$ frame; (a) stick-and-ball model; (b) schematic representation.

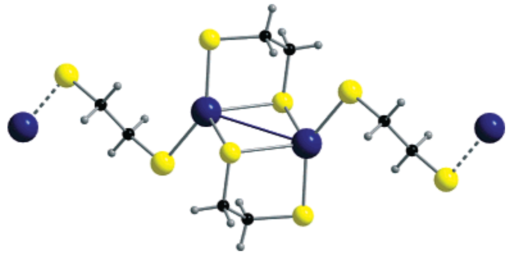


Figure 41. Section of the polymeric chain structure of $[\{Hg_2(SCH_2CH_2S)_3\}^{2-}]_n$ in crystals of $[Ph_4P]_2[Hg_2(SCH_2CH_2S)_3]$.

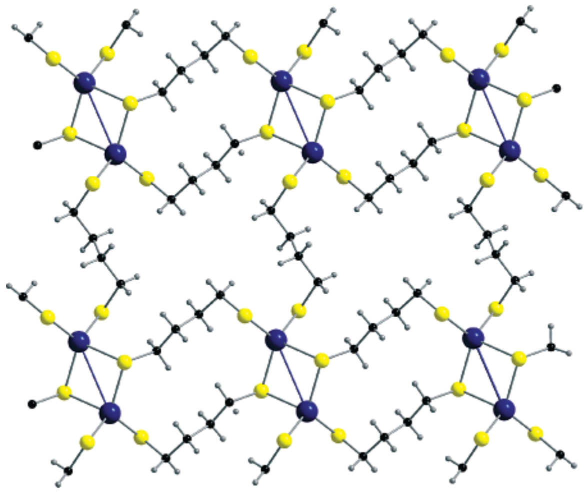


Figure 42. Section of the $[\{Hg_2(SCH_2CH_2S)_3\}^{2-}]_n$ double chains in crystals of $[Et_4N]_2[Hg_2(SCH_2CH_2CH_2CH_2S)_3]\cdot 2MeOH$.

Another complex containing three such $\{M_2S_6\}$ units condensed to form a $\{Hg_6Se_{14}\}$ framework is $[Hg_6(SePh)_{14}]^{2-}$ whose structure is shown in Figure 46.[81] The central $\{Hg_2S_6\}$ fragment of the complete $\{Hg_6Se_{14}\}$ core portion of the hexanuclear anion (Figure 47) resembles the analogues $\{Cd_2S_6\}$ fragment within $\{[Cd_8(SCH_2CH(OH)CH_2OH)_{16}]\}_n$ (Figure 45) in view of its binding properties toward four neighboring M(II) ions. Replacement of this fragment by a central tetrahedral $\{HgS_4\}$ unit leads to the $\{Hg_5Se_{12}\}$ core portion (Figure 48) which has chemically been realized in the pentanuclear spirocyclic complex anion $[Hg_5(SePh)_{12}]^{2-}$ shown in Figure 49.[82]

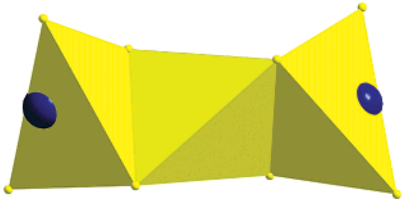


Figure 43. The $\{M_3S_8\}$ frame of the complex anion $[Hg_3(edt)_4]^{2-}$ (schematic representation).

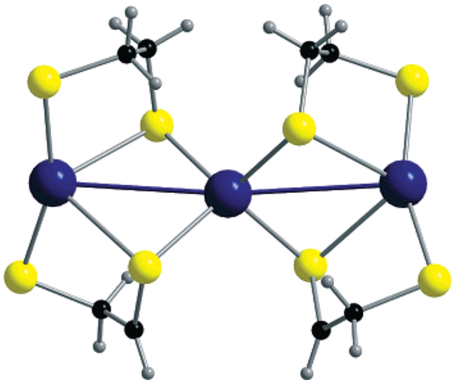
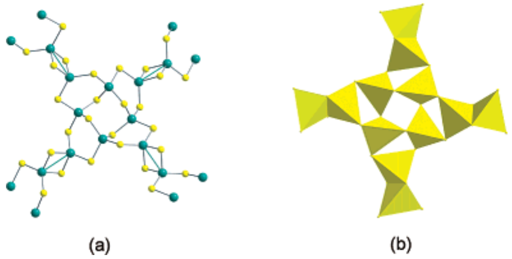


Figure 44. Structure of the complex ion $[Hg_3(edt)_4]^{2-}$.



(a) (b)

Figure 45. Characteristic section of the polymeric compound $\{[Cd_8(SCH_2CH(OH)CH_2OH)_{16}]\}_n$; (a) stick-and-ball model; (b) schematic representation.

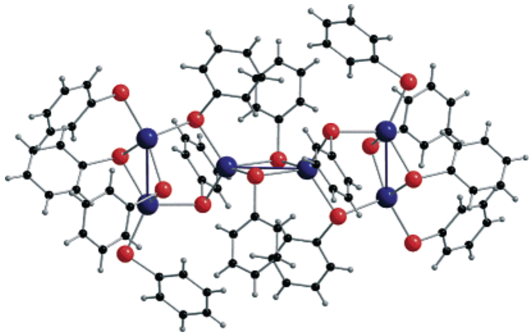


Figure 46. Structure of the complex anion $[Hg_6(SePh)_{14}]^{2-}$.

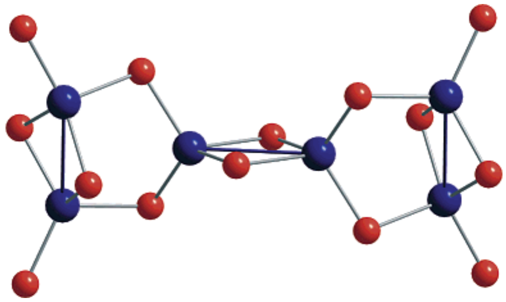


Figure 47. The $\{Hg_6Se_{14}\}$ core portion of the complex anion $[Hg_6(SePh)_{14}]^{2-}$.

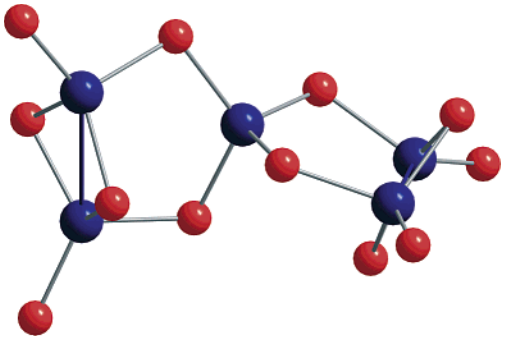


Figure 48. The $\{Hg_5Se_{12}\}$ core portion of the complex anion $[Hg_5(SePh)_{12}]^{2-}$.

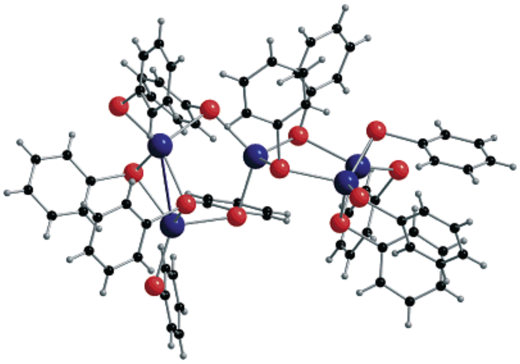


Figure 49. Structure of the complex anion $[Hg_5(SePh)_{12}]^{2-}$.

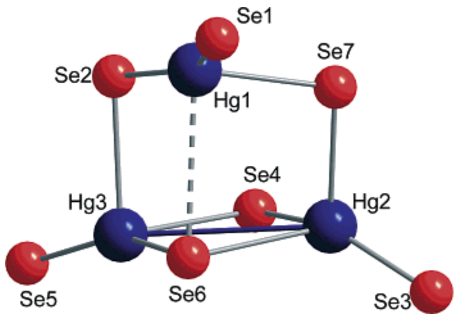


Figure 50. The $\{Hg_3Se_7\}$ core portion of the complex anion $[Hg_3(SePh)_7]^{-}$.

If one of the two $\{Hg_2S_6\}$ fragments of the $\{Hg_5Se_{12}\}$ core portion of $[Hg_5(SePh)_{12}]^{2-}$ is replaced by a terminally bonded selenium atom, one arrives at the Hg−S framework $\{Hg_3Se_7\}$ (Figure 50) which could be stabilized in the complex anion $[Hg_3(SePh)_7]^{-}$ (Figure 51).[83] The trinuclear species containing mercury and selenium is closely related with the cadmium- and sulfur-containing complex anion $[Cd_3(SC_6H_2\text{-}2,4,6\text{-}^iPr)_7]^{-}$ (Figure 38)[66] with respect to its overall structural principles. Significant differences, however, are obvious if the metal−chalcogen bond distances are compared.

Within $[Cd_3(SC_6H_2\text{-}2,4,6\text{-}^iPr)_7]^{-}$, all Cd−sulfur bonds are of comparable order, whereas in $[Hg_3(SePh)_7]^{-}$ one very long Hg−Se distance (Hg(1)−Se(6) 3.429 Å, indicated in Figure 50 as open stick) is observed besides six shorter (Hg(1)−Se(1)/Se(2) 2.476 and 2.507, Hg(2)−Se(3)/Se(4) 2.496 and 2.514, Hg(3)−Se(5)/Se(6) 2.479 and 2.508 Å) and five longer ones (Hg(1)−Se(7) 2.738, Hg(2)−Se(7)/Se(6) 2.738 and 3.153, Hg(3)−Se(2)/Se(4) 2.917 and 2.986 Å). These differences in the Hg−Se distances clearly show the preference of Hg(II) to form two short primary bonds

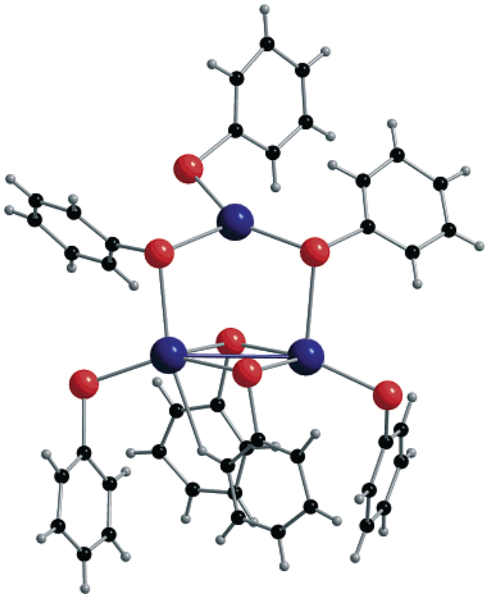


Figure 51. Structure of the complex anion $[Hg_3(SePh)_7]^-$.

with large Se−Hg−Se angles (range: 147.8−153.9°) each. These primary bonds are combined with two longer secondary ones in the case of Hg(2) and Hg(3), whereas only one secondary (Hg(1)−Se(7)) and one tertiary one (Hg(1)−Se(6)) is observed for Hg(1). As a consequence, the coordination characteristics of Hg within this complex anion should best be described as distorted tetrahedral for Hg(2) and Hg(3) and as distorted trigonal-planar for Hg(1). In this context, it is interesting to note that with the sole exception of Se(7), all other selenium atoms present in $[Hg_3(SePh)_7]^-$ are engaged in one primary Hg−Se bond, whereas Se(7) forms two secondary ones. A combination of the tetrahedral and the trigonal-planar Hg−E (E = S) coordination is also found in the pentanuclear complex anion $[Hg_5(edt)_4(SEt)_4]^{2-}$ (Figure 52) which contains the $\{[Hg_5S_{12}]\}$ core portion (Figure 53).[84] This structural unit resembles the $\{Hg_5Se_{12}\}$ core portion observed in $[Hg_5(SePh)_{12}]^{2-}$ (Figure 48) with the exception that the chalcogenolate ligands bridging the outer Hg ions within $\{[Hg_5Se_{12}]\}$ are transformed into terminal ones.

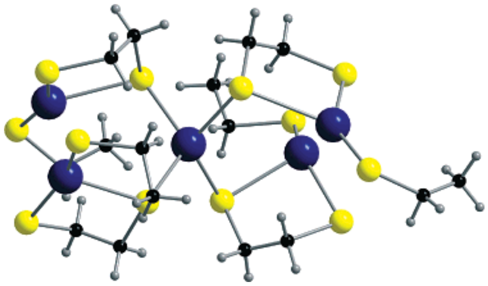


Figure 52. Structure of the complex anion $[Hg_5(edt)_4(SEt)_4]^{2-}$.

5. Copper and Silver

As indicated in the introduction much less explicit structural information is available in the field of copper thioneins from various physical methods than for the various forms of zinc and cadmium MTs. The experimental and computational results on the copper clusters in thioneins are still ambiguous. At present, no X-ray crystal structure of a copper thionein is known. The most detailed structural information is available from NMR studies,[29] among them a recent comprehensive two-dimensional ^1H study on the solution structure of the protein part of Cu7 metallothionein from *Saccharomyces cerevisiae*.[29d]

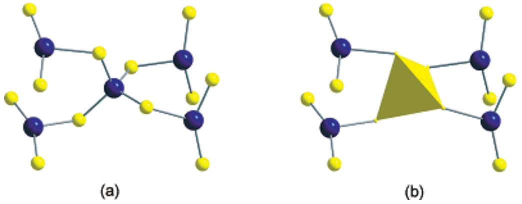


Figure 53. The $\{Hg_5Se_{12}\}$ core portion of the complex anion $[Hg_5(edt)_4(SEt)_4]^{2-}$; (a) ball-and-stick model; (b) schematic representation.

Cu-thionein from *S. cerevisiae* contains 12 cysteines. According to early EXAFS data a $\{Cu_8S_{12}\}$ system was postulated with trigonal planar coordination of the copper atoms.[85−88] From ^{109}Ag NMR (HMQC) studies on the Ag-exchanged copper thionein from *Saccharomyces* the group of Winge et al. proposed 10 of the 12 cysteines present to coordinate seven Ag atoms, out of them eight bridging, and two terminal. Thus, four of the Ag were proposed to have linear coordination, three being in trigonal planar coordination.[89,90] Accordingly, the earlier EXAFS data suggesting only trigonal planar copper were revised, and also linear coordination was taken into account for copper. The transcription factor ACE1 necessary for the biosynthesis of *Saccharomyces* thionein appears to have a structure similar to the thionein itself, with clusters of 6−7 Cu^+. Binding of the N-terminal domain to DNA is only possible in the presence of these copper ions.[91]

In the absence of more precise structural information, it appears to be appropriate to study the coordinational behavior of copper (and homologous silver and gold) in oligomeric complexes reaching from mononuclear to higher nuclearities. All of them might act as structural and spectroscopic models for copper thioneins and might contribute to the understanding of the thionein structure and function. The most useful model ligands for the cysteine bonding are without doubt thiolates of all kinds. Consequently, a large variety of mononuclear and oligomeric complexes have been prepared and characterized. Several aspects of this rich copper, silver, and gold coordination chemistry have been treated in various review articles, among them those by Dance,[9a,92] Blower and Dilworth,[9b] and Krebs and Henkel.[9d,e]

Copper is normally monovalent in its thiolate complexes and the coordination is normally trigonal planar, although a number of linearly coordinated examples are known. In the oligonuclear complexes, which are normally prepared from Cu^I or Cu^{II} salts and thiolates under various reaction conditions in solvents such as methanol, the ligands are normally bridging.

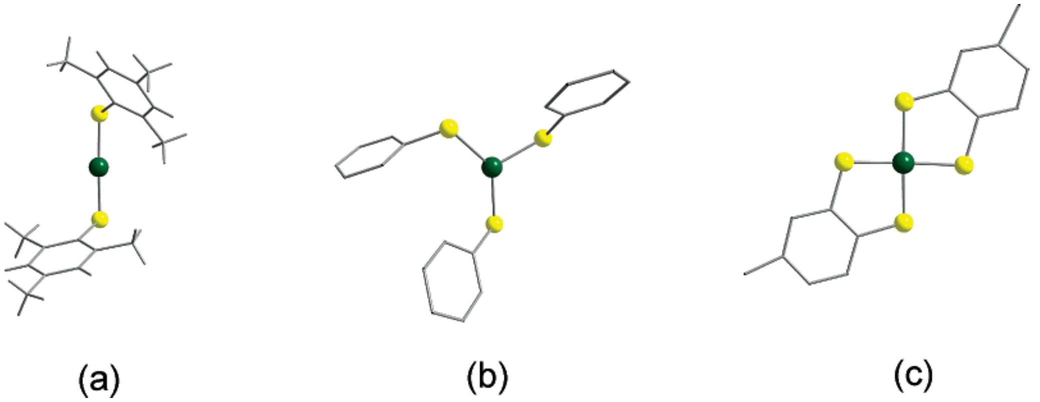


Figure 54. Coordination geometries in mononuclear copper thiolates: (a) $[Cu(SMes)_2]^-$; (b) $[Cu(SPh)_3]^{2-}$; (c) $[Cu(tdt)_2]^-$.

5.1 Mononuclear Complexes

In mononuclear thiolates of Cu, Ag, and Au coordination numbers of 2, 3, and 4 are observed. For monovalent copper and silver linear coordination is stabilized by sterically demanding ligands with voluminous substituents close to the thiol groups. The large ligands facilitate favorable packing of monomeric molecular $[M(SR)_2]^-$ ions in the crystal, whereas with smaller ligands higher aggregates of oligomeric or polymeric species are favored.[93] Examples for monomolecular species are $[{}^nPr_4N][Cu(SC_6HMe_4)_2]$ and the isomorphous silver compound[94] as well as $[Cu(SPh)_2]^-$ [95] and the mesityl complex $[Cu(SMes)_2]^-$ (Figure 54a).[96] $[Cu(SAd)_2]^-$ (HSAd = adamantanethiol) is the first structurally characterized two-coordinate aliphatic monothiolate Cu^I complex.[93] In Au^I compounds linear two-coordination is present in all known cases, as shown, e.g., by $[Au(SPh)_2]^-$,[97] $[Au(SC_6H_2{}^iPr_3)_2]^-$,[98] and $[Au(SC_6H_4\text{-}o\text{-}NH_2)_2]^-$.[99]

The formation of $[Cu(SPh)_3]^{2-}$ (Figure 54b) is in competition with oligomeric units. The anion is obtained from the reaction of KSPh with $[Ph_3PCuCl]_4$ or $[Ph_4P]_2[Cu(dts)_2]$.[95,100] Other interesting stable mononuclear tricoordinate species prepared recently are the dianions $[M(SC_6H_4\text{-}p\text{-}X)_3]^{2-}$ (M = Cu(I), Ag(I), X = Cl, Br).[101]

Especially interesting electronic properties are present in mononuclear complexes with electronically non-innocent ligands such as toluene-3,4-dithiolate (tdt). In $[{}^nBu_4N][Cu(tdt)_2]$ (Figure 54c) with square planar copper coordination[102,103] the anion is clearly monovalent, suggesting the presence of Cu^{III}; however, it is clear that d^9 Cu^{II} is produced by electron transfer from the ligand. Trivalent gold forms typical square planar complexes $[Au(SCH_2CH_2S)_2]^-$ [104] and $[Au(tdt)_2]^-$.[105] By electrochemical oxidation of $[{}^nBu_4N][Au(bdt)_2]$ with bdt = benzene-1,2-dithiolate the neutral species $[Au(bdt)_2]$ is formed.[106] Similar to the case of $[Cu(tdt)_2]^-$ above Au^{IV} was postulated to be present here, but here also the system has to be described as d^8 Au^{III} with the radical electron being delocalized in the ligand.

5.2 Dinuclear Complexes

In the series of dinuclear copper and silver thiolates only a few cases are known with a central four-membered $\{M_2S_2\}$ unit, probably because of M···M and ligand···ligand repulsions. Examples are $[Cu_2(mimtH)_6]^{2+}$ with mimtH = 1-methylimidazoline-2-thione (Figure 55),[107] the thione complex $[Cu_2(SNC_5H_5)_6]Cl_2$,[108] the thiolate complex $[Cu_2(SC_6H_4\text{-}o\text{-}Me)_2(1,10\text{-}phen)_2]$[109] with phenanthroline as coligand, and the silver polysulfide complex $[Ph_4P]_2[Ag_2(S_6)_2]$.[110] Different structural principles are observed with difunctional ligands which connect two metal centers through one or two chains. The anions $[Au_2(SCH_2CH_2CH_2S)_2]^{2-}$ [104] and $[Ag_2(SCH_2CH_2CH_2S)_2]^{2-}$ (Figure 56a)[99] contain linear S−M−S units linked through aliphatic C_3 chains. In $[Au_2(S_2\text{-}o\text{-}xyl)_2]^{2-}$ with S_2-o-xyl = o-xylene-α,α′-dithiolate the metals are kept at a distance of 5.4 Å by C_4 chains.[104] A large number of interesting structural topologies of such dinuclear units with possible relevance, in a wider sense, for thionein structural properties are present in various polychalcogenide complexes of copper, silver, and gold.[104,111−120] The examples $[(Se_4)Cu(Se_5)Cu(Se_5)]^{4-}$,[116] $[Au_2(Se_2)(Se_4)]^{2-}$,[112] $[(Se_4)AuSe_2Au(Se_4)]^{2-}$,[120] and $[(Te_5)Au(Te_2)Au(Te_5)]^{2-}$ [119] are shown in Figures 57a, 56b,c, and 57b.

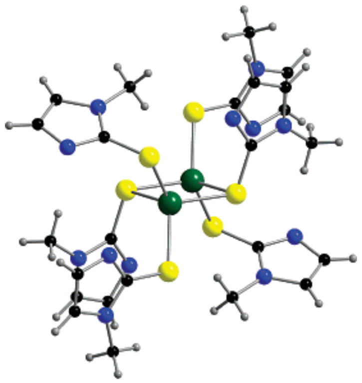


Figure 55. Structure of the dinuclear cation $[Cu_2(mimtH)_6]^{2+}$.

5.3 Trinuclear Complexes

The trinuclear anion $[Cu_3(SCH_2CH_2S)_3]^{3-}$ which has also been prepared in a modified structure as $\{Na(MeOH)[Cu_3(SCH_2CH_2S)_3]\}^{2-}$ (Figure 58)[32] contains three bridging and three terminal thiolates. The $\{Cu_3S_3\}$ ring has a chair configuration, as shown in Figure 59a.[32] This structural type had been observed before in the polysulfide complexes $[Cu_3(S_6)_3]^{3-}$ [121] and $[Cu_3(S_4)_3]^{3-}$.[122] The stereochemistry of this ring system is discussed by Dance et al.[123] on the basis of the novel related compound $[Cu_3(\mu\text{-}SPh)_3(PPh_3)_4]$. It

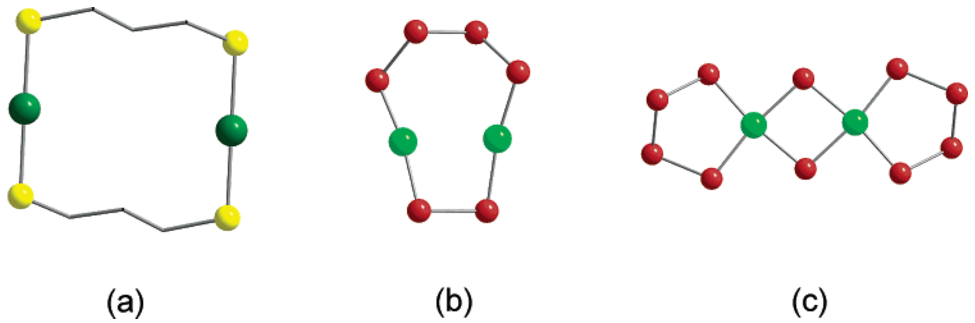


Figure 56. Core structures of bridged dinuclear complexes (a) $[Ag_2(SCH_2CH_2CH_2S)_2]^{2-}$; (b) $[Au_2(Se_2)(Se_4)]^{2-}$; (c) $[(Se_4)AuSe_2Au(Se_4)]^{2-}$.

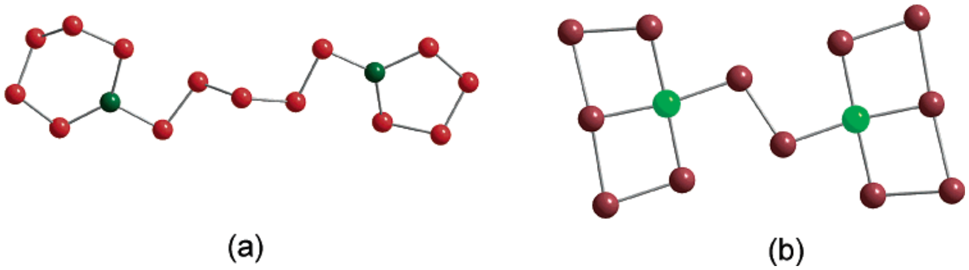


Figure 57. Dinuclear complexes bridged by polychalcogenide ligands: (a) $[(Se_4)Cu(Se_5)Cu(Se_5)]^{4-}$; (b) $[(Te_5)Au(Te_2)Au(Te_5)]^{2-}$.

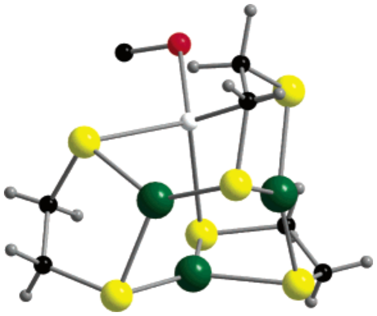


Figure 58. Core structure of $\{Na(MeOH)[Cu_3(SCH_2CH_2S)_3]\}^{2-}$.

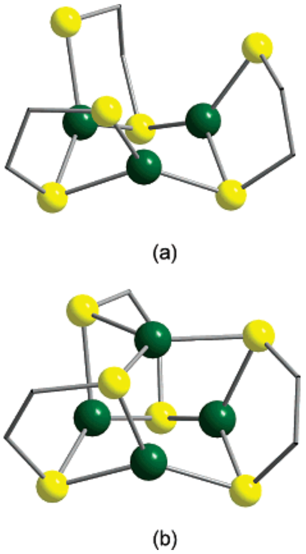


Figure 59. Comparison of the tri- and tetranuclear frameworks of $[Cu_3(SCH_2CH_2S)_3]^{3-}$ and $[Cu_4(SCH_2CH_2S)_3]^{2-}$.

is highly interesting to note that the terminal sulfur atoms are arranged in a way to leave a vacant metal position for a fourth copper atom with trigonal planar coordination. This position is indeed filled in the large and important class of tetranuclear copper thiolates.

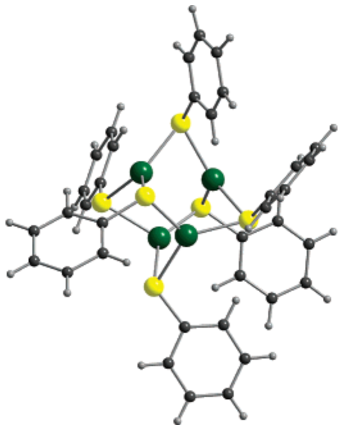


Figure 60. Molecular structure of the tetranuclear cluster anion $[Cu_4(SPh)_6]^{2-}$.

Figure 59 shows the comparison of the two trinuclear and tetranuclear frameworks as exemplified by the geometries of $[Cu_3(SCH_2CH_2S)_3]^{3-}$ [32] and $[Cu_4(SCH_2CH_2S)_3]^{2-}$.[124] One important factor for the stabilization of the tetranuclear unit compared to the trinuclear one is the lower negative charge of the latter by incorporation of the fourth copper atom.

5.4 Tetranuclear Complexes

The adamantane-like $\{M_4S_6\}$ polyhedron is the most frequently observed species in copper- and silver-thiolate chemistry. This *tetrahedro*-Cu_4-*octahedro*-$(\mu\text{-}S)_6$ structure[84,95,124−129] consists of a $\{M_4\}$ tetrahedron the edges of which are bridged by sulfur atoms; thus, the $\{S_6\}$ fragment forms an octahedron around the $\{M_4\}$ tetrahedron (Figures 59b and 62a). A selection of examples with monofunctional aliphatic and aromatic thiolate ligands are $[Cu_4(SPh)_6]^{2-}$ (Figure 60),[126,127,130] $[Cu_4(SMe)_6]^{2-}$,[125,131] $[Cu_4(SEt)_6]^{2-}$,[132] $[Cu_4(SC_6H_4\text{-}o\text{-}NH_2)_6]^{2-}$,[99] $[M_4(SC_6H_4\text{-}p\text{-}Cl)_6]^{2-}$, (M = Cu(I), Ag(I)),[101] and $[Ag_4(TeC_4H_3S)_6]^{2-}$.[84,133] If difunctional thiolate or polychalcogenide ligands are em-

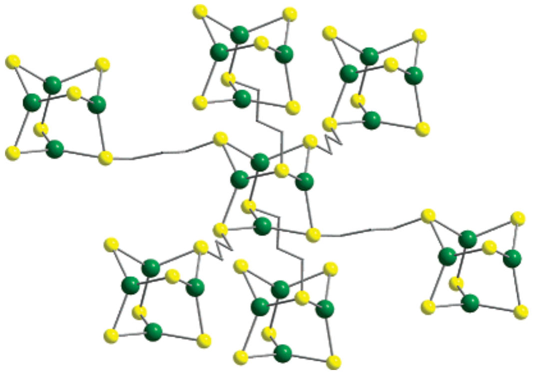


Figure 61. Connection of the $\{M_4S_6\}$ units in the crystal structure of $[Ag_4(SCH_2CH_2CH_2S)_3]^{2-}$.

ployed the $\{M_4S_6\}$ units are normally significantly distorted by the steric strain of the chelate effect. Some typical examples for this variety are $[Cu_4(SCH_2CH_2S)_3]^{2-}$,[124] $[Cu_4(SCH_2CH_2CH_2S)_3]^{2-}$,[99,134] $[Cu_4(S_2\text{-}o\text{-}xyl)_3]^{2-}$,[128] $[Cu_4(S_2C_6H_4)_3]^{2-}$,[99] $[Cu_4(S_4)_2(S_5)]^{2-}$,[135] $[Ag_4(SCH_2CH_2S)_3]^{2-}$,[99] $[Ag_4(SCH_2CH_2CH_2S)_3]^{2-}$,[99] $[Ag_4(S_2\text{-}o\text{-}xyl)_3]^{2-}$,[104] $[Cu_4L_3]^{2-}$ with L = 1,1-dicarbo-*tert*-butoxyethylene-2,2-thioperthiolate,[136] $[Cu_4(dmt)_4]^{2-}$ [137] with dmt = 1,2-dithiole-3-thione-4,5-dithiolate and $[Ag_4(Se_4)_3]^{2-}$.[138,139]

Interesting similar cluster geometries are present in complexes with five-membered chelating perthiocarboxylate ligands such as $[Cu(S_3C_6H_2Me_3)]_4$ with $(S_3C_6H_2Me_3)^- = 2,4,6$-trimethylperthiobenzoate,[140] $[Cu(S_3C\text{-}o\text{-}tolyl)]_4$ with $(S_3C\text{-}o\text{-}tolyl)^-$ = *o*-tolylperthiocarbonate,[141] and $[Ag(S_3C\text{-}o\text{-}tolyl)]_4$.[142]

In contrast to $[Cu_4(SCH_2CH_2CH_2S)_3]^{2-}$, the formally analogous $[Ag_4(SCH_2CH_2CH_2S)_3]^{2-}$ [99] has an interesting polymeric structure. The difunctional ligands do not shield the central molecular frameworks from each other but connect each $\{M_4S_6\}$ unit three-dimensionally to six neighboring units, as shown in Figure 61.

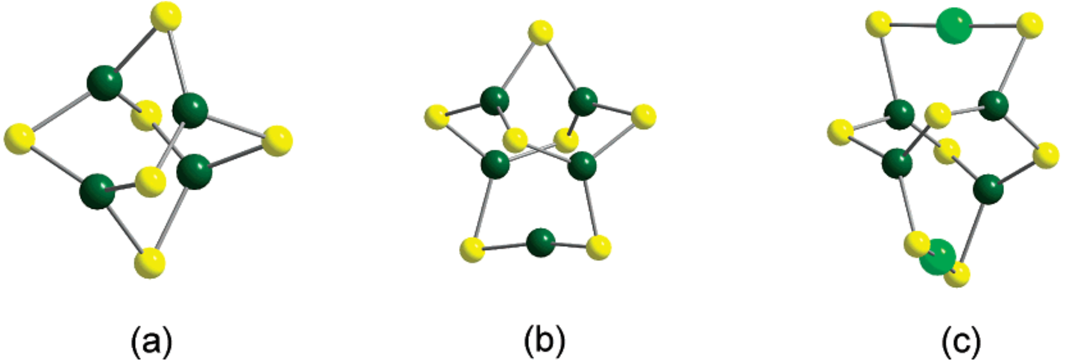
5.5 Penta- and Hexanuclear Complexes

Remarkable derivatives of the adamantane structure are produced by formally cleaving one or two thiolate bridges and replacing the bridging sulfurs by a S−M−S bridge each. The resulting species contain the two new types of framework, $[M_5(SR)_7]^{2-}$ and $[M_6(SR)_8]^{2-}$. They are shown in Figure 62 in comparison to the symmetrical adamantane-type $[Cu_4(edt)_3]^{2-}$.[125] The $[M_5(SR)_7]^{2-}$ structure type contains four metal ions in trigonal−planar and one in linear coordination and was first observed in $[Cu_5(SPh)_7]^{2-}$, $[Ag_5(SPh)_7]^{2-}$,[143,144] $[Ph_4P]_2[Cu_5(SMe)_7].HOCH_2CH_2OH$,[131] and $[Ag_5(S^iBu)_7]^{2-}$ [99] from preparations that also yielded tetranuclear $[M_4(SPh)_6]^{2-}$ compounds as secondary products.[143,144]

A rich variety of compounds and derivative structures has been synthesized for an alternative pentanuclear framework with a metal/sulfur ratio of 5:6. In the monovalent $[M_5(SR)_6]^-$ anionic framework (Figure 63)[93] three of the metal atoms have linear sulfur coordination. In the idealized symmetrical structure the metal atoms form a $\{M_5\}$ trigonal bipyramid that is incorporated into a $\{S_6\}$ trigonal prism. Again, it appears that this structure type with predominating two-coordination is favored especially for voluminous and sterically demanding ligands. A characteristic feature of this important structure type is its steric flexibility: As shown by various examples hitherto synthesized the trigonal $\{S_6\}$ prism can be tilted around the central vertical axis (Figures 63 and 64) up to the limit of a trigonal antiprism. In $[Ag_5(S(CH_2)_3NHMe_2)_3(S(CH_2)_3NMe_2)_3]^{2+}$ an ideally symmetric $\{M_5S_6\}$ trigonal prism is observed, possibly by simple packing arguments in the hexagonal crystal structure,[145] whereas in monoclinic $[Et_4N][M_5(S^tBu)_6]$ (M = Cu, Ag) the trigonal faces of the $\{S_6\}$ prism are tilted by 40°.[146,147] Only a slight tilt of the $\{CuS_3\}$ faces against each other is present in orthorhombic $[Ph_4P][Cu_5(SC_5H_{11})_6]$.[96] A more recent example of this structure type is the interesting complex anion $[Cu_5(SAd)_6]^-$ with adamantanethiolate (SAd) as a monodentate sterically demanding ligand (Figure 64).[93]

The first examples for oligomeric anions with the equally remarkable $[M_6(SR)_8]^{2-}$ core were the mixed-metal species $[Au_2Cu_4(SCH_2CH_2S)_4]^{2-}$ and $[Au_2Ag_4(SCH_2CH_2S)_4]^{2-}$.[105] Here (Figure 62c) two of the metal positions are two-coordinate. They are occupied by the gold atoms. Again, an interesting isomeric structure is reported for this formula type: In the nonlinear optical material $[Me_4N][Ag_6(SPh)_8]$ with the same metal/ligand ratio the structure is polymeric with three-dimensionally linked $[Ag_{12}(SR)_{16}]$ repeating units.[131,148]

Another variant of a hexanuclear unit could be prepared in the copper-polysulfide system: In $[Ph_4P]_2[Cu_6(S_4)_3(S_5)]$ the copper atoms are tetrahedrally coordinated with the edge-sharing $\{CuS_4\}$ tetrahedra linked together by $\{S_4\}$ and $\{S_5\}$ chains.[149−151]



(a) (b) (c)

Figure 62. Geometry of the metal-sulfur frameworks (a) $\{Cu_4S_6\}$; (b) $\{Cu_5S_7\}$; and (c) $\{Au_2Cu_4S_8\}$.

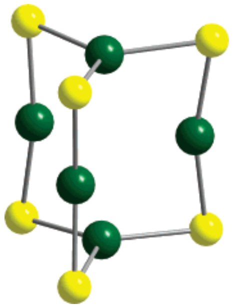


Figure 63. Structure of the $\{Cu_5S_6\}$ core in pentanuclear clusters of the $[M_5(SR)_6]^-$ type.

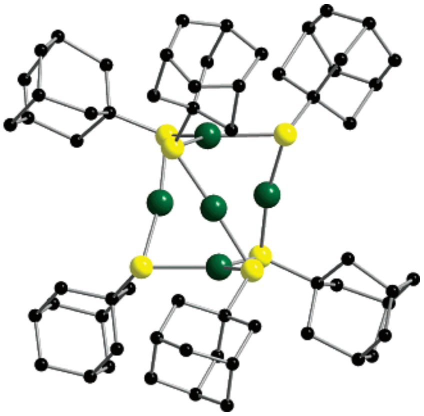
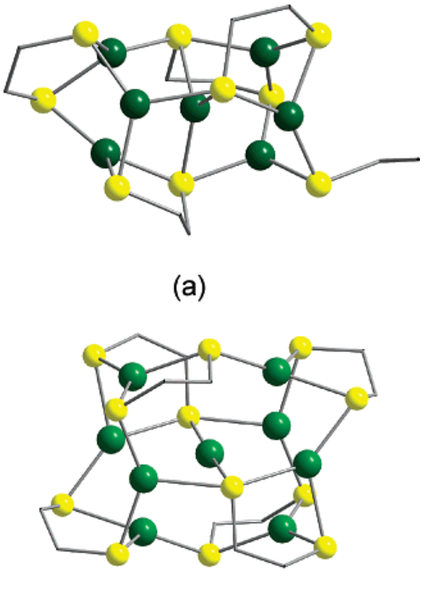


Figure 64. Molecular structure of the pentanuclear copper adamantane-thiolate $[Cu_5(SAd)_6]^-$.



(a)

(b)

Figure 65. The thiolate cluster anions $[Cu_7(SCH_2CH_2S)_4(SEt)]^{2-}$ and $[Ag_9(SCH_2CH_2S)_6]^{3-}$.

5.6 Heptanuclear Complexes and Complexes with Higher Nuclearities

Also the oligomeric complexes with higher nuclearities are expected to have structural features related to the copper cluster structures in thioneins. The topology of $[Cu_7(SCH_2CH_2S)_4(SEt)]^{2-}$ with dibesides monofunctional ligands (Figure 65a)[84] is determined by a framework of two corner-sharing Cu_4 tetrahedra with trigonal planar coordination of

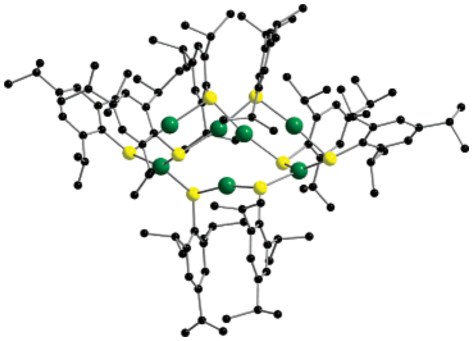


Figure 66. Molecular structure of the heptanuclear silver thiolate cluster $[Ag_7(SC_6H_2{}^iPr_3)_8]^-$.

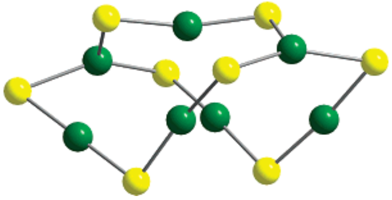
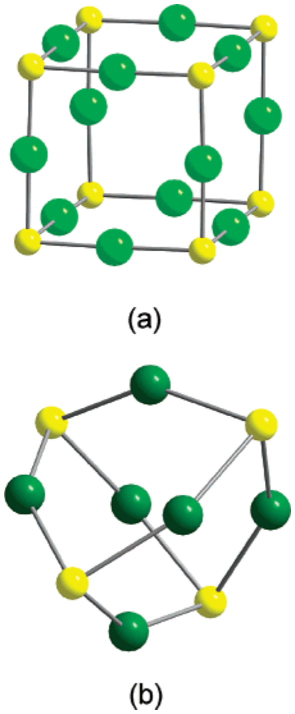


Figure 67. Silver−sulfur framework of $[Ag_7(SC_6H_2{}^iPr_3)_8]^-$.



(a)

(b)

Figure 68. Structural frameworks of the highly symmetrical clusters $[Au_{12}S_8]^{4-}$ and $[Ag_6S_4]^{2-}$.

all copper atoms. If the central metal atom is removed, the remaining $\{Cu_6S_9\}$ framework, which has a trigonal prismatic arrangement of the metal atoms and a face-sharing bioctahedral $\{S_9\}$ geometry, may serve as a model for the proposed metal−sulfur centers in copper metallothioneins such as the one from *Neurospora crassa*.[152−154]

In contrast, $[Ph_4P][Cu_7(SEt)_8]$ forms a polymeric chain structure that is composed of cage-like $\{Cu_7(SEt)_{10}\}$ units with trigonal planar coordination of the Cu atoms. They are linked via four S atoms to give one-dimensional infinite polymers.[155,156] Remarkably, the conditions of synthesis of this polymer are rather similar to those of $[Cu_4(SEt)_6]^{2-}$.[84,155] In $[Ag_7(SC_6$-

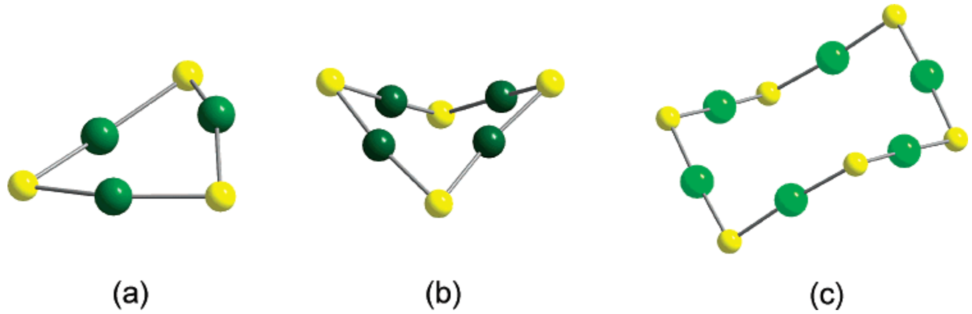


Figure 69. Metal-sulfur frameworks of the ring structures of (a) $[Ag(SC(SiPhMe_2)_3)]_3$; (b) $[Cu(SC_6H_2{}^iPr_3)]_4$; (c) $[Au(SC_6H_2{}^iPr_3)]_6$.

$H_2{}^iPr_3)_8]^-$ (Figure 66)[96] a $\{Ag_6S_6\}$ ring is bridged by two opposite Ag atoms through a {S−Ag−S} link (Figure 67). A similar reaction system in which thioxanthate is present as a coligand affords the octanuclear $[Cu_8(SC_5H_{11})_4(S_2CSC_5H_{11})_4]$, in which the $\{Cu_8S_{12}\}$ framework represents a new type of a cage; Cu is coordinated in a trigonal planar fashion and the cage consists of eight $\{Cu_3S_3\}$ rings in a boat form and two $\{Cu_4S_4\}$ rings.[157] A different kind of cluster structure was reported for the highly charged water-soluble anion $[Ag_8(mba)_{10}]^{12-}$, with H_2mba = 2-mercaptobenzoic acid, consisting of two butterfly-type $\{Ag_4S_4\}$ subunits bridged by two μ_3-S atoms.[158]

The interesting metal framework of the nonameric anion $[Ag_9(SCH_2CH_2S)_6]^{3-}$ (Figure 65b)[84] can be described as a tetragonal prism of eight Ag, centered by the ninth Ag. The latter has a linear AgS_2 coordination, whereas the other ones form approximately trigonal planar $\{AgS_3\}$ units. A structurally especially appealing cluster unit—however probably less closely related to the metal-sulfur structures in copper thioneins—could be prepared and structurally characterized in various dodecameric cubane structures. $[Cu_{12}S_8]^{4-}$,[159] $[Au_{12}S_8]^{4-}$,[160] and $[Au_{12}Se_8Na]^{3-}$ (Figure 68a),[161] which are examples of this type, consist of a cubelike arrangement of eight trigonal pyramidally coordinated sulfur atoms, the linearly coordinated 12 metal atoms sitting on the edges of this cube. No analogous silver complex could be prepared; however, in $[Ag_6S_4]^{2-}$ (Figure 68b)[162,163] the same metal/sulfur ratio is present, and the structure is topologically similar: The sulfur atoms form a tetrahedron, and the metal atoms occupy the centers of the six edges of the tetrahedron.

5.7 Neutral [M(SR)]*n* Compounds

The preference of univalent copper, silver, and gold has led to a highly interesting and relevant class of neutral molecules of composition $[M(SR)]_n$.[164] As neutral molecules, they may not only give clues on possible structural features in biomolecules but they are also interesting precursors for solid state and surface layer production from thermal methods from solution or by CVD.[164] The molecular species can be considered as fragments of polymers with the same general composition. The general structural principle is the formation of more or less large rings with linear two-coordination around the metals. In Figure 69 typical examples of tri-, tetra- and hexanuclear frameworks are shown. $[Ag(SC(SiPhMe_2)_3)]_3$ (Figure 69a)[165] is the only trinuclear species in this series. One of the S atoms in the $\{Ag_3S_3\}$ ring is out-of-plane, the S−Ag−S angles are 150°, thus far from linear. A tetrameric $\{M_4S_4\}$ ring minimizes geometric strain for a linear metal coordination and an angular coordination at sulfur. Quite a number of complexes have been reported, almost all of them with a folded geometry of the ring. Examples are $[Ag(SSi(O^tBu)_3)]_4$,[166] $[Cu(SSi(O^tBu)_3)]_4$,[167] $[Cu(SC_6H_3\text{-}2,6\text{-}(SiMe_3)_2)]_4$,[168] $[Cu(SC_6H_2{}^iPr_3)]_4$,[169] $[Au(SC(SiMe_3)_3)]_4$,[170] $[Au(SSi(O^tBu)_3)]_4$,[171] and $[Ag(SeC(SiMe_3)_3)]_4$ (Figure 69b).[172]

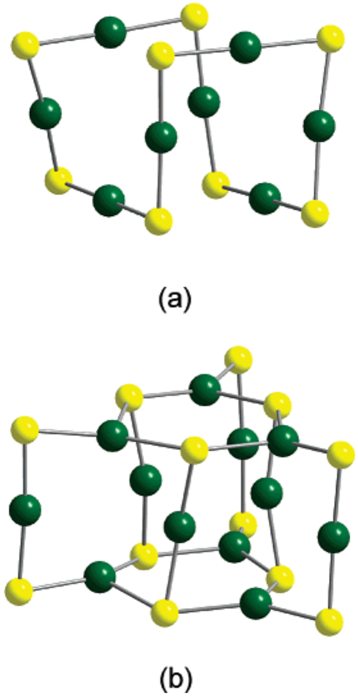


Figure 70. Comparison of the metal-sulfur framework structures of $[Cu(SC_6H_2{}^iPr_3)]_8$ and $[Cu(SC_6H_4\text{-}o\text{-}SiMe_3)]_{12}$.

The hexanuclear unit in $[Au(SC_6H_2{}^iPr_3)]_6$ (Figure 69c)[98] shows a $\{Au_6S_6\}$ ring with chair configuration. It is the first gold thiolate with bridging thiolate sulfur. Copper forms an octanuclear complex $[Cu(SC_6H_2{}^iPr_3)]_8$ (Figure 70a)[173] in which the twisted $\{Cu_8S_8\}$ ring is doubly folded such that the sulfur atoms are arranged formally at the corners of an idealized cube. A rather spectacular structure is formed by the $\{Cu_{12}S_{12}\}$ framework of $[Cu(SC_6H_4\text{-}o\text{-}SiMe_3)]_{12}$ (Figures 70b and 71).[36,174] It has the shape of a paddle wheel. The polyhedron contains two $\{Cu_3S_3\}$ rings in parallel stacking above each other,

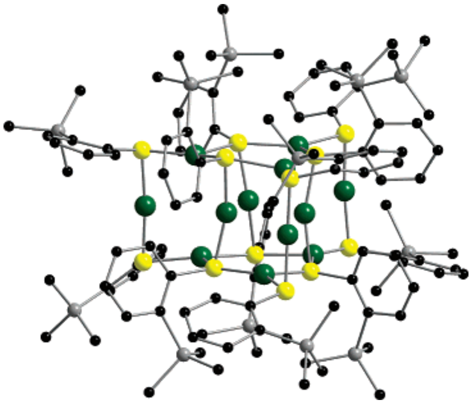


Figure 71. Molecular structure of the paddle-wheel cluster $[Cu(SC_6H_4\text{-}o\text{-}SiMe_3)]_{12}$.

with a slight tilt around the 3-fold axis. The two ring units are connected through six linear {S−Cu−S} links. Six of the Cu^{I} atoms in the [2$_3$](1,3,5)-cyclophane-like structure are almost trigonal planar, 6 S atoms are μ_2-bridging, 6 S are μ_3-bridging.

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