Binding of Inorganic Mercury at Biological Sites: Crystal Structures of Hg^{2+} Complexes with Sulphur Amino-acids

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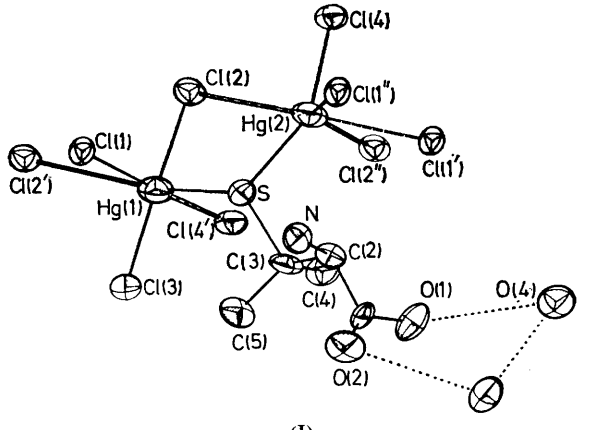
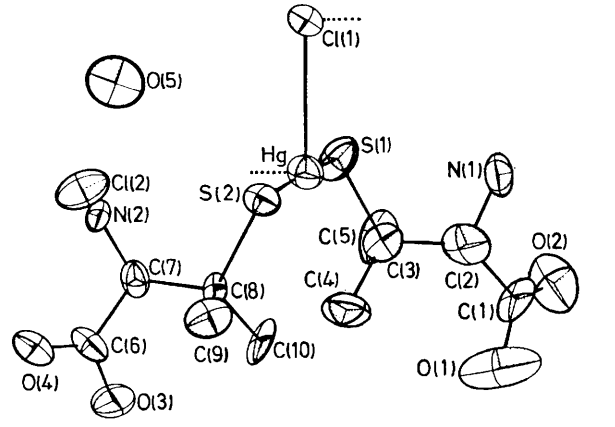
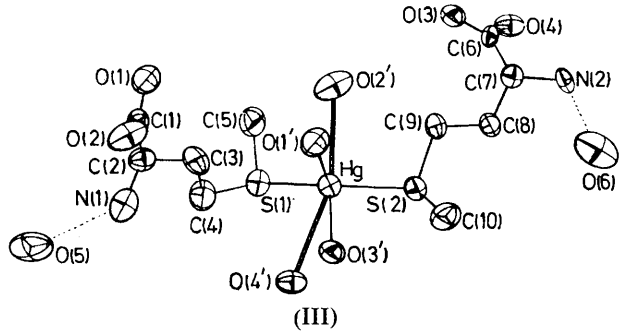
Summary Crystal structure analyses of three Hg^{2+}–sulphur aminoacid complexes relevant to the toxicology of Hg^{2+} have revealed polar, polymeric structures with chloride, sulphur and carboxylate bridges which are absent in the corresponding methylmercury derivatives.



(I)



(II)



(III)

FIGURE. Perspective drawings of the molecular structures of (I), (II) and (III). Important bond lengths and angles are: (I); Hg(1)–Cl(1), 2·687(5); Hg(1)–Cl(2), 2·380(5); Hg(1)–Cl(2′), 3·335(6); Hg(1)–Cl(3), 2·348(5); Hg(1)–Cl(4′), 3·410(5); Hg(2)–Cl(1′), 2·780(5); Hg(2)–Cl(1″), 3·091(4); Hg(2)–Cl(2), 3·426(5); Hg(2)–Cl(2″), 3·429(5); Hg(2)–Cl(4), 2·356(5) Å; Cl(2)·Hg(1)–Cl(3), 152·1(1); Cl(4)–Hg(2)–S, 152·7(1)°; (II); Hg–S(1), 2–335(5); Hg–S(2), 2·357(4); Hg–Cl(1), 2·850(5); Hg–Cl(1′), 3·323(5) Å; S(1)–Hg–S(2), 171·6(1)°; (III); Hg–S(1), 2·500(4); Hg–S(2), 2·475(4); Hg–O(1′), 2·27(1); Hg–O(2′), 2·82(1); Hg–O(3′), 2·32(1); Hg–O(4′), 2·86(1) Å; S(1)–Hg–S(2), 122·7(1)°. O(3) and O(4) in (I), O(5) in (II) and O(5) and O(6) in (III) are oxygen atoms of water of crystallisation. The ionic perchlorate groups in (III) are not shown.

THE toxicological effects of mercury compounds are highly specific, with unique patterns for the different forms of the metal.[1] Methylmercury, for example induces complex disturbances of the central nervous system whereas mercuric ion is primarily a nephrotoxic agent. The chemical nature and physical properties of Hg^{2+} and $MeHg^{+}$ complexes of sulphur amminoacids and sulphydryl containing proteins are highly relevant to biotransport mechanisms, membrane permeabilities and cell site specificities responsible for these toxicological differences.[2] Unfortunately structural data for Hg^{2+} compounds[3] are lacking for comparison with the well-characterised methylmercury complexes.[4] We have now solved the structures of $(HgCl_2)_2$·(pen).$2H_2O$ (I), $HgCl_2(pen)_2.H_2O$ (II) and $Hg(ClO_4)_2(met)_2.2H_2O$ (III) (where pen = D,L-penicillamine; met = D,L-methionine). The results illustrate the essential differences between aminoacid binding to $MeHg^{+}$ and Hg^{2+}. Some new and unexpected bonding features are apparent.

Reactions of Hg^{2+} [as $HgCl_2$ or $Hg(ClO_4)_2.3H_2O$] with the aminoacids in neutral (II) and (III) or slightly acid (I) aqueous solutions gave, after slow evaporation over several days, crystalline compounds. The molecular structures of (I)—(III), determined by *X*-ray diffraction are shown in the Figure.†

The penicillamine ligand in (I) is strongly bonded to Hg(2) [Hg(2)–S 2·356(5) Å] *via* a deprotonated sulphydryl group and simultaneously interacts with Hg(1) [Hg(1)–S 2·822(5) Å] in a weak thioether–metal type linkage. The inner co-ordination sphere of Hg(2) is completed by a strong bond to Cl(4) and two weaker interactions to chloride ligands [Cl(1′) and Cl(1″)] in adjacent molecules. Mercury atom Hg(1) has three interactions of significance with chloride ligands, two of these bonds [to Cl(2) and Cl(3)] being shorter than the other [to Cl(1)]. To a first approximation the structure can be considered as an assemblage of $[HgCl_3]^{-}$ anions and $[ClHgSCMe_2CH(NH_3)CO_2H]^{+}$ cations, bound in ribbons by chloride and sulphur bridges, with ribbons held together in one direction by hydrogen bonds between aminoacid residues and in the other by weak chloride bridges.

Compound (II) has a simpler polymeric structure. Two sulphur atoms of the aminoacids are bound to mercury in approximately linear fashion; these $Hg[SCMe_2CH(NH_3)CO_2H]_2$ units are linked into spirals by single asymmetric chloride bridges. Spirals are linked by hydrogen bonds. In addition the lattice contains essentially free chloride ions and water of crystallisation.

The principal structural features of the methionine complex (III) are the strong thioether–mercury bonding and the presence of two short intermolecular Hg–O (carboxylate) bonds. This result was unexpected since previous spectroscopic work[5] on methionine complexes suggested co-ordination through amine and carboxylate sites in the solid state and *via* thioether bonding only in acid solution.

These structures allow several important deductions concerning Hg_2^{2+} binding in biological media. (a) Whereas methylmercury complexes of small molecules (*e.g.* L-cysteine) are essentially monomeric and non-polar in the crystal[4], Hg^{2+} complexes are polymeric and highly polar.

† *Crystal data:* $(HgCl_2)_2[SCMe_2CH(NH_3)CO_2H].2H_2O$; triclinic $P\bar{1}$; $a = 12·335(18)$, $b = 7·671(6)$, $c = 9·708(9)$ Å; $\alpha = 117·67(7)$, $\beta = 107·22(4)$, $\gamma = 84·34(5)°$, $Z = 2$; $D_m = 3·08$, $D_c = 3·106$ g cm^{-3}; $R = 0·045$ on 1815 observed reflections (GE-XRD6). $HgCl_2[SCMe_2CH(NH_3)CO_2H]_2.H_2O$; tetragonal, $I4_{1/a}$, $a = 24·183(4)$, $c = 12·890(3)$ Å, $Z = 16$, $D_m = 2·05$, $D_c = 2·064$ g cm^{-3}; $R = 0·045$ on 1349 observed reflections. $Hg(ClO_4)_2[MeS(CH_2)_2CH(NH_3)CO_2].2H_2O$; monoclinic, $P2_{1/c}$; $a = 11·549(5)$, $b = 16·399(14)$, $c = 12·964(5)$ Å. $\beta = 110·21(6)°$, $Z = 4$, $D_m = 2·13$, $D_c = 2·115$ g cm^{-3}; $R = 0·051$ on 2256 observed reflections.

The nature of intermolecular interactions in the latter suggests that polymeric aggregates may well persist on dissolution. These observations may be particularly relevant to the biotransport of mercurials. (b) Chloride ion co-ordination to Hg^{2+} is appreciable even in the presence of strong mercury–sulphydryl bonding. (c) Thioether bonding to Hg_2^{2+} is favoured over amino group bonding and may be more important for Hg^{2+} than previously thought.

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