Models for the Methylmercury–Protein Interaction: a Comparison of the Molecular Structures of Methyl-L-cysteinatomercury(II) and Methyl-DL-methioninemercury(II)

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Summary X-ray crystal structure determinations have shown that the essential amino-acid L-cysteine is bound to methylmercury(II) *via* a deprotonated sulphydryl group, whereas methionine is co-ordinated *via* an amino group in their respective 1:1 complexes.

Complexes with amino-acids and peptides have been extensively utilised as models for the interaction of metal ions with protein and enzyme molecules. In this context the binding of heavy-metal ion pollutants such as Cd^{2+}, Hg^{2+}, and RHg^{+}, which pose environmental hazards has assumed significance. We describe a comparison of the molecular structures of methylmercury(II) complexes of the essential amino-acids L-cysteine and DL-methionine as determined by X-ray diffraction. The cysteine complex has been directly implicated in poisoning by methylmercury(II) and in metabolic processes leading to the synthesis of methylmercurythiomethyl in shellfish.[1] Although the essential features of methionine metabolism are established,[2] the rôle of methionine residues in complexing organomercury(II) poisons is currently unclear.

The L-cysteine complex $MeHgSCH_2CH(N^+H_3)CO_2^-,H_2O$ (I) was obtained from the reaction of MeHgOH with L-cysteine in aqueous ethanol.

Crystal data: $HgC_4H_9NO_2S,H_2O$, orthorhombic crystals, space group $P2_12_12_1$, $a = 6{\cdot}386(6)$, $b = 26{\cdot}026(13)$, $c = 5{\cdot}282(4)$ Å, $Z = 4$, $D_c = 2{\cdot}676$, $D_m = 2{\cdot}65$ g cm^{-3}. Crystals of the methionine complex $MeHgMeS(CH_2)_2CH(NH_2)CO_2^-$ (II) from aqueous ethanol are monoclinic, space group $P2_1/c$, $a = 7{\cdot}048(9)$, $b = 5{\cdot}826(4)$, $c = 25{\cdot}320(5)$ Å, $\beta = 93{\cdot}15\ (21)^\circ$, $Z = 4$, $D_c = 2{\cdot}34$, $D_m = 2{\cdot}38$ g cm^{-3}. The structures were solved by the heavy-atom method using 980 and 1027 observed reflections for (I) and (II) respectively measured on a GEXRD6 automatic diffractometer. Refinement by least-squares methods proceeded to R values of 0·065 for (I) and 0·099 for (II). ORTEP plots of the structures are shown in the Figure.

The principal structural features of (I) are the co-ordination of the amino-acid in the zwitterionic form $-SCH_2CH(N^+H_3)CO_2^-$ to $MeHg^+$ *via* a deprotonated sulphydryl group such that an almost linear C–Hg–S unit is formed. Both Hg–C(4) [2·09(4) Å] and Hg–S [2·352(12) Å] distances are normal for 2-co-ordinate Hg^{II}. However, a scan of intra- and inter-molecular contacts ($\leqslant 3{\cdot}5$ Å) revealed a weak intramolecular Hg–O(2) bond to a carboxylate oxygen atom. The Hg–O(2) distance [2·84(2) Å] is comparable to a value of 2·88 Å in *cis*-β-benzoylvinylmercuric chloride[3] and is shorter than the sums of van der Waals radii for mercury and oxygen (*ca.* 3·0 Å).[4]

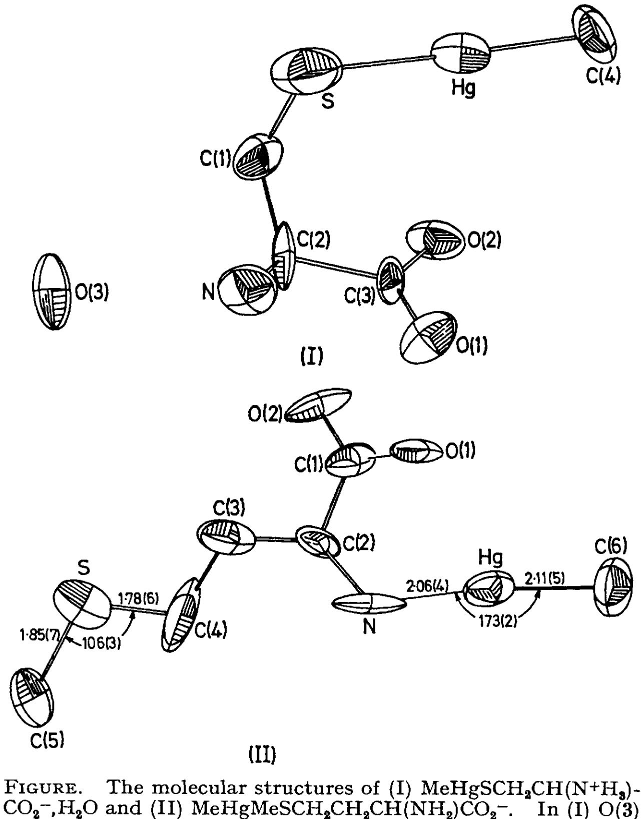

Figure. The molecular structures of (I) $MeHgSCH_2CH(N^+H_3)CO_2^-,H_2O$ and (II) $MeHgMeSCH_2CH_2CH(NH_2)CO_2^-$. In (I) O(3) is the oxygen atom of the solvent water molecule of crystallisation.

By contrast, in (II) the amino-acid is bound to $MeHg^+$ *via* the amino group with an Hg–N bond length of 2·06(4) Å similar to the Hg–N distance of 2·10 Å in H_2NHgCl.[5] That the mercury–nitrogen interaction in (II) is strong is evident from a comparison with the Hg–N bond lengths (av. 2·61 Å) in $Cl_3CHgCl,C_{12}H_8N_2$.[6] Apparently, free amino groups can interact strongly with the charged CH_3Hg^+ ion despite predictions to the contrary.[1] It is also noteworthy that the thioether group is not involved in complexation. Recent n.m.r. studies for Hg^{II}–methionine complexes in acidic aqueous solution have been interpreted in terms of mercury-(II) thio ether binding.[7] Although the C(1)–Hg-N angle is 173(2)°, the presence of two additional weak Hg–O (carboxylate) bonds is shown by the intramolecular Hg–O(1) distance of 2·67(3) Å and an intermolecular Hg–O(2) contact of 2·72(3) Å. These contacts presumably reflect ionic interactions resulting from the zwitterionic nature $[CH_3–Hg^+–NH_2CH(CO_2^-)CH_2CH_2SCH_3]$ of the complex.

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