Metal Binding in Chelation Therapy: the Crystal Structure of D-Penicillaminatolead(II)

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Summary The crystal structure of the 1:1 complex formed by lead(II) and D-penicillamine at pH 2—7 has been determined; the amino-acid acts as a tridentate chelator with respect to the lead atom, and forms weaker bonds with the lead atoms of two neighbouring complexes in the crystal.

ONE of the applications of D-penicillamine (β,β-dimethyl-D-cysteine) in chelation therapy is the treatment of lead poisoning.[1] Potentiometric titration, u.v.-visible, and [1]H n.m.r. spectroscopic data indicate that penicillamine acts as a tridentate chelator for lead.[2,3] It has been suggested that the tridentate nature of the ligand accounts for its effectiveness in the removal of the toxic metal.

Crystals of D-penicillaminatolead(II), $Pb[SCMe_2CH(NH_2)CO_2]$, prepared from a solution of lead nitrate (0·01M) and D-penicillamine (0·01M) in water, are monoclinic with $a = 6·302(6)$, $b = 6·234(6)$, $c = 10·43(1)$ Å, $\beta = 108·0$-$(1)°$, $Z = 2$, $D_m = 3·0(1)$ g cm^{-3}, space group $P2_1$. A set of 2129 non-equivalent reflections, including 950 Bijvoet pairs, was recorded (equi-inclination diffractometer, Mo-K_α radiation). The structure was solved by standard heavy-atom methods. The final residual R is 0·047.

The Figure (A) shows the structure and some dimensions of the complex. The amino, carboxy, and sulphide groups from a single ligand form the base of a trigonal pyramid whose apex is occupied by the lead atom. In addition to these three strong interactions, each lead atom is weakly
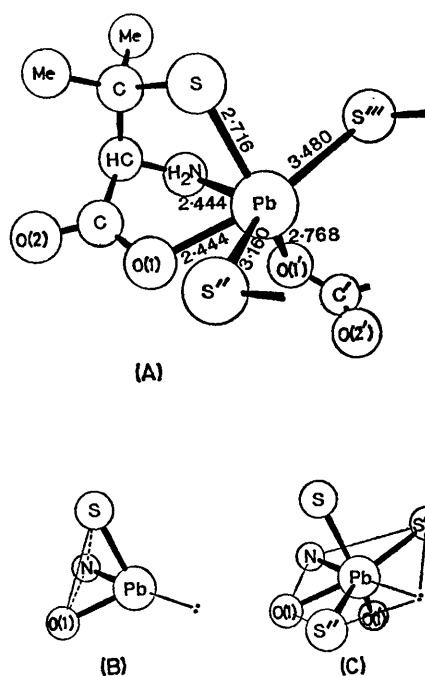

(A)

(B)   (C)

FIGURE. Crystal structure and stereochemistry around the lead atom in D-penicillaninatolead(II), distances in Å.

bonded to an oxygen [O(1)'] and a sulphur (S'') of neighbouring molecules. The next-nearest neighbour of the lead

atom is a third sulphur (S'''), but the inter-atomic distance [3·480(4) Å] exceeds the sum of the atomic radii of Pb and S according to the conventional definitions [sum of radii = 2·5 Å (covalent), 2·9 Å (ionic), 3·4 Å (covalent Pb plus non-bonding S)[4,5]].

When only the three strong interactions between the lead atom and a single ligand molecule are considered, the co-ordination geometry is tetrahedral provided that an inert electron pair occupies a metal orbital directed away from the ligand (Figure B). If the two weaker bonds Pb–S'' and Pb–O(1') are included, then the co-ordination geometry cannot be related to any regular polyhedron. Finally, if S''' is considered as part of the co-ordination sphere and the inert electron pair occupies the same position as previously, then the geometry is that of a distorted pentagonal bipyramid (Figure C). The latter geometry is known for lead(II).[6]

It is likely that the weak interactions between adjacent molecules contribute significantly to the stability of the crystals, for the same 1:1 compound is isolated under a wide range of conditions. The present crystals were grown under conditions where the species with a 1:1 ligand:metal ratio predominates ($\log\beta_1 = 13·5$, $\log\beta_2 = 3·9$).[7] However, identical crystals were formed from solutions which contained a 10:1 excess of ligand. All these solutions had pH $\leqslant$ 2. At physiological pH (obtained by raising the pH to 10 with NaOH, and then lowering it to ca. 7 with HNO₃) the same compound was invariably produced as a fine precipitate. The identity of all the products was established from their i.r. spectra in Nujol mulls between 400 and 4000 cm⁻¹.

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