Metal Binding by D-Penicillamine: Crystal Structure of D-Penicillaminatocadmium(II) Hydrate

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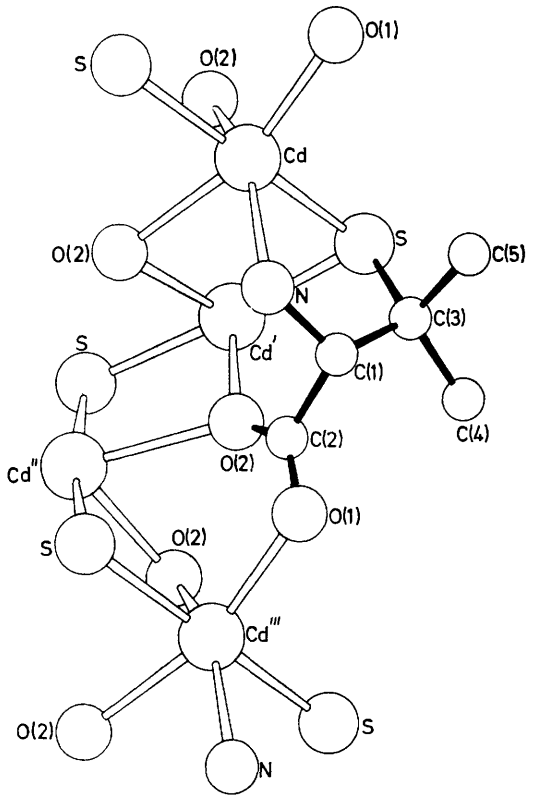
Summary The crystal structure analysis of a 1 : 1 complex of cadmium(II) and D-penicillamine shows that the metal atoms are bonded to the amino, carboxylate, and thiol groups of the ligand, but that the complex cannot be described in terms of discrete monomeric subunits.

THE amino-acid, D-penicillamine, $^{+}NH_3CH(CO_2^{-})C(Me_2)SH$, is used in chelation therapy for lead and mercury poisoning[1] but is ineffective in the treatment of cadmium poisoning.[2] Instead of promoting the excretion of cadmium from cadmium-intoxicated mice, D-penicillamine causes mobilisation of the metal and its re-distribution to other tissues.[3] We have determined the crystal structure of D-penicillaminatocadmium(II) hydrate to gain an insight into the reason for this behaviour. The structure analysis complements earlier work on Cd–amino-acid and Cd–peptide complexation[4] by providing the first structural data for the binding of Cd atoms at amino-acid thiol groups. The biological effects of cadmium, like those of lead and mercury, are believed to involve metal-binding at the thiol groups of cysteine residues in proteins.[5]

D-Penicillaminatocadmium(II) hydrate was obtained as hexagonal prisms by the slow evaporation of an aqueous solution containing stoicheiometric quantities of $CdCl_2$ and D-penicillamine at pH 6. The complex crystallises as a one-dimensional polymer in which each penicillamine molecule is bonded to four cadmium atoms. The first of these (labelled simply Cd in the Figure) is involved in a 5-membered chelate ring with S and N as the donor atoms. The second cadmium atom (Cd′) is part of a 6-membered

chelate ring in which the donor atoms are S and O(2). The third cadmium atom (Cd'') is bonded only to O(2), and the fourth (Cd''') is bonded only to the second carboxylate



FIGURE

oxygen O(1). The cadmium atoms Cd, Cd', Cd'', and Cd''' lie along a left-handed helix (*i.e.*, they are related by one of the 3_2 screw axes required by the crystal symmetry). Adjacent cadmium atoms, *e.g.* Cd'' and Cd''', are triply bridged *via* the thiol S atom, the carboxylate O(2) atom, and the carboxylate O(2)–C(2)–O(1) group of three ligand molecules. Each Cd atom is surrounded by a distorted octahedron of two S atoms, three O(carboxylate) atoms, and one N(amino) atom of four ligand molecules. The metal–ligand bond-lengths are Cd–S 2·563(7), Cd'–S 2·567(7), Cd–NH_2 2·38(2), Cd'–O(2) 2·57(2), Cd''–O(2) 2·51(2), and Cd'''–O(1) 2·40(2) Å. These values correspond to relatively weak metal–ligand interactions. They all lie near the upper limits of the ranges most commonly found in octahedral Cd complexes with comparable ligands (Cd–S 2·52—2·54, Cd–NH_2 2·27—2·32,[4] and Cd–O 2·27—2·52 Å[4]).

The water molecules in the crystal are also arranged along left-handed helices. They occupy interstices between the penicillaminatocadmium chains. Each water molecule is hydrogen bonded to one amino group, one carboxylate O(1) atom, and two other water molecules.

The relatively weak and non-specific interactions between cadmium and D-penicillamine are in contrast with the strong tridentate chelation in D-penicillaminatolead(II).[6] The structures in the solid state are consistent with the relative thermodynamic stabilities of the complexes in solution ($Pb^{II} > Cd^{II}$)[7] and with the relative therapeutic efficacies of the ligand with respect to the two metals.

Crystal data: $[Cd\{NH_2CH(CO_2)C(Me_2)S\}].H_2O$, trigonal, $a = b = 10{\cdot}509(10)$, $c = 7{\cdot}093(7)$ Å, $Z = 3$, $D_m = 2{\cdot}13(3)$ g cm^{-3}, space group $P3_2$. A set of 1287 non-equivalent reflections, including 294 whose intensities were below the observable threshold, was recorded (equi-inclination diffractometer, ω-scans, Mo-K_α radiation). The structure was solved by standard heavy-atom methods and refined by full-matrix least-squares. The final residual R is 0·063.

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