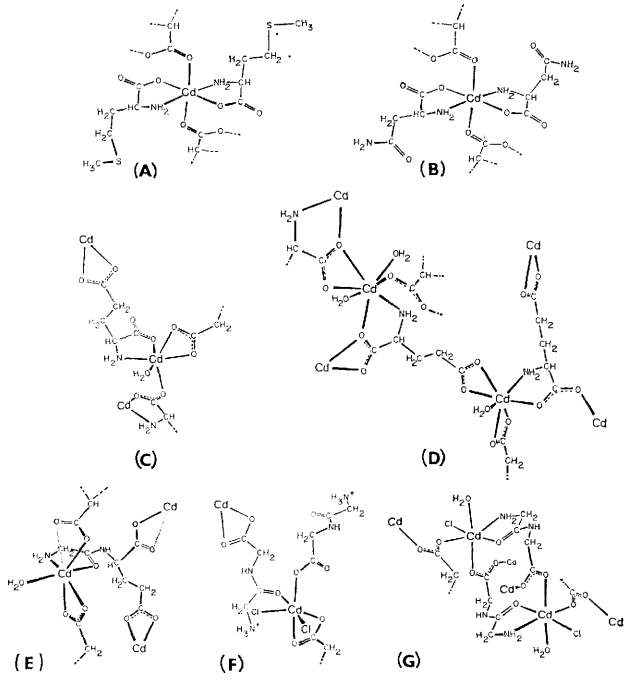
Model Compounds for Metal–Protein Interaction: Crystal Structures of Seven Cadmium(II) Complexes of Amino-acids and Peptides

By RICHARD J. FLOOK, HANS C. FREEMAN,* CHRISTOPHER J. MOORE, and MARCIA L. SCUDDER
(*School of Chemistry, University of Sydney, Sydney* 2006, *Australia*)

Summary The *X*-ray crystal structure analyses of bis-(L-methioninato)cadmium(II), bis-(L-asparaginato)cadmium(II), triaquabis-(L-glutamato)dicadmium(II) hydrate, aqua-(glycyl-L-glutamato)cadmium(II) hydrate, dichlorobis-(glycylglycine)cadmium(II), and aquachloro(glycylglycinato)cadmium(II) are reported; the crystal structure of aqua-(L-glutamato)cadmium(II) hydrate has been determined by *X*-ray and neutron diffraction.

WE report here the *X*-ray crystal structure analyses of the seven complexes named above. The abbreviations and symbols used in this paper are:† Cd(L-Met)$_2$, (A); Cd(L-Asn)$_2$, (B); Cd(L-Glu)(OH$_2$)·H$_2$O, (C); Cd(L-Glu)(OH$_2$)·Cd(L-Glu)-(OH$_2$)$_2$·H$_2$O, (D); Cd(Gly-L-Glu)(OH$_2$)·H$_2$O, (E); Cd(HGly-Gly)$_2$Cl$_2$, (F); and Cd(GlyGly)(OH$_2$)Cl, (G). The structure



of (C) was confirmed by a neutron structure analysis which took advantage of the anomalous dispersion effect of ^{113}Cd for neutrons.

The complexes (A)—(E) were crystallised by the slow evaporation of 0·1M-solutions containing $CdCl_2$ and the ligand in stoicheiometric proportions, together with sufficient NaOH to adjust the pH to 7—8. Crystals of the glutamate complexes (C) and (D) grew in different parts of a single solution. Both the glycylglycine complexes (F) and (G) were obtained from solutions containing $CdCl_2$ (0·1M) and glycylglycine (0·2M); crystals of (F) were formed at pH 6 and crystals of (G) at pH 8.

Structural formulae of the complexes are shown in the Figure. In the only complex (F) which was obtained at a low pH, the terminal amino-group of the peptide is protonated and the metal is bound at O(peptide) and O(carboxy) atoms. At higher pH's, a 5-membered chelate ring is formed between the amino-group and the adjacent O(peptide) [in a peptide] or O(carboxy) [in an amino-acid]. The terminal carboxy-groups of the amino-acid and peptide ligands, and the side chain carboxy-groups of glutamate residues, are involved in metal binding in all the complexes where they occur. They can form Cd–O=C=O–Cd bridges [as in (G)], take part in 5-membered chelate rings in addition to providing bridges between Cd atoms [in (A)—(D)], act as bidentate functional groups forming 4-membered chelate rings [in (C)—(F)], combine all of the preceding functions [in (D)], or bind a single Cd at one oxygen atom [in (F)]. All but one of the O(peptide) atoms in the three complexes which have peptide ligands, (E)—(G), are likewise bonded to Cd atoms. As expected for a metal where crystal field stabilisation is absent,[1] there is no evidence for Cd binding at the N(peptide) atoms. The metal–ligand interactions include those which were deduced from n.m.r. measurements of Cd–peptide complexes in solution.[2] The n.m.r. data also provide evidence that polymeric –Cd–ligand–Cd– aggregates such as those which characterise all these crystalline structures persist in solution. The types and lengths of the metal–ligand bonds which occur in the structures are shown in the Table. Structural analyses of related complexes are listed in ref. 3.

The Cd atoms in complexes (A)—(C) and (F)—(G) are 6-co-ordinate, and those in (D) and (E) are 7-co-ordinate. In the complexes where 6-co-ordinate Cd atoms are bonded to non-chelating groups, the bonds generally lie within 5° of the directions required for octahedral co-ordination. In (A), (B), and (G) the octahedral geometry is slightly distorted.

† Met = $NH_2CH(CH_2CH_2SCH_3)CO_2^-$, Asn = $NH_2CH(CH_2CONH_2)CO_2^-$, Glu = $NH_2CH(CH_2CH_2CO_2^-)CO_2^-$, HGly-Gly = $^+NH_3$-$CH_2CONHCH_2CO_2^-$.

TABLE. Summary of cadmium(II)–ligand bond lengths (in Å)
(E.s.d.'s of bond lengths *ca.* 0·005 Å)

Complex	(A)	(B)	(C)	(D)		(E)	(F)	(G)
Bond type								
Cd–O(carboxy)[a] ..	2·269[b]	2·291[b]	2·288[b]	2·311[b]	2·335[b]	2·277[c]	2·255[c]	2·267[f]
	2·445[b]	2·369[b]	2·252[b]	2·619[d]	2·502[c]	2·867[c]	2·602[c]	2·278[f]
	2·276[b]	2·277[b]	2·317[c]	2·326[d]	2·361[c]	2·331[c]	2·289[e]	
	2·524[b]	2·441[b]	2·458[c]	2·440[d]	2·368[c]	2·435[c]		
					2·499[c]			
Cd–O(peptide) ..	—	—	—	—	—	2·407	2·430	2·324
Cd–O(water) ..	—	—	2·258	2·438	2·338	2·290	—	2·452
				2·389				
Cd–N(amino) ..	2·270	2·277	2·299	2·318	2·361	2·269	—	2·322
	2·301	2·307						
Cd–Cl	—	—	—	—	—	—	2·558	2·564
							2·568	

[a] Superscripts denote bonding of carboxy-groups as shown below. Cd–O bonds from the same carboxy-group are bracketed. [b] Cd–O bond in a 5-membered chelate ring as well as in a Cd–O=C=O–Cd bridge. [c] Cd–O bond in a 4-membered chelate ring. [d] Combination of b, c, d. [e] Cd–O bond from a unidentate carboxy-group. [f] Cd–O bond in a Cd–O=C=O–Cd bridge.

The angles subtended at the Cd atoms by the bidentate ligands have an average value of 73°. The ligands in (C) and (F) include bidentate carboxy-groups. These groups cause further distortions from octahedral geometry because the O–Cd–O angles are about 54°.

The complexes (D) and (E) include three crystallographically independent examples of 7-co-ordinate Cd atoms. In (D), one of the Cd atoms (shown towards the right of the formula in the Figure) has a distorted square-based trigonal-capped co-ordination polyhedron. The bond configuration is almost identical with that in diaquabisacetatocadmium(II), $Cd(OAc)_2(OH_2)_2$.[4] The second Cd in (D) and the Cd in (E) have distorted pentagonal bipyramidal geometries with the axial directions along H_2O–Cd–O(carboxy) and H_2O–Cd–O(peptide), respectively.

Several of the present complexes of Cd^{II} are structurally similar to (but not isostructural with) the Cu^{II} complexes of the same ligands.

X-Ray diffraction data were recorded on a computer-controlled equi-inclination diffractometer.[5] The neutron diffraction data for (C) were measured on a four-circle diffractometer. The neutron flux at the specimen was 8×10^5 neutrons cm^{-2} s^{-1}, with $\lambda = 0{\cdot}981$ Å. The structure was solved *via* the sine-Patterson function, taking advantage of the anomalous scattering of ^{113}Cd.[6] *Crystal data:* (A) $a = 15{\cdot}53(1)$, $b = 5{\cdot}157(5)$, $c = 9{\cdot}73(1)$ Å, $\beta = 105{\cdot}8(1)°$, $D_m = 1{\cdot}80(2)$ g cm^{-3}, $Z = 2$, space group $P2_1$. (B) $a = 12{\cdot}42(1)$, $b = 5{\cdot}081(5)$, $c = 9{\cdot}84(1)$ Å, $\beta = 101{\cdot}4(1)°$, $D_m = 2{\cdot}02(2)$ g cm^{-3}, $Z = 2$, space group $P2_1$. (C) $a = 11{\cdot}61(1)$, $b = 10{\cdot}79(1)$, $c = 7{\cdot}286(7)$ Å, $D_m = 2{\cdot}14(2)$ g cm^{-3}, $Z = 4$, space group $P2_12_12_1$. (D) $a = 12{\cdot}30(1)$, $b = 8{\cdot}45(1)$, $c = 9{\cdot}12(1)$ Å, $\beta = 95{\cdot}8(1)°$, $D_m = 2{\cdot}10(2)$ g cm^{-3}, $Z = 2$, space group $P2_1$. (E) $a = 11{\cdot}87(1)$, $b = 12{\cdot}28(1)$, $c = 8{\cdot}130(8)$ Å, $D_m = 1{\cdot}97(2)$ g cm^{-3}, $Z = 4$, space group $P2_12_12_1$. (F) $a = 7{\cdot}357(7)$, $b = 8{\cdot}951(9)$, $c = 23{\cdot}11(2)$ Å, $\beta = 100{\cdot}3(1)°$, $D_m = 2{\cdot}01(2)$ g cm^{-3}, $Z = 4$, space group $P2_1/c$. (G) $a = 8{\cdot}226(8)$, $b = 9{\cdot}63(1)$, $c = 22{\cdot}30(2)$ Å, $D_m = 2{\cdot}23(2)$ g cm^{-3}, $Z = 8$, space group *Pbca*.

This work was supported by grants from the Institute of General Medical Sciences, United States Public Health Service, and the Australian Research Grants Committee, and by an Australian Institute of Nuclear Science and Engineering Studentship (M.L.S.).

(*Received*, 21*st May* 1973; *Com.* 736.)

[1] H. C. Freeman, *Adv. Protein Chem.*, 1967, **22**, 376.
[2] D. L. Rabenstein and S. Libich, *Inorg. Chem.*, 1972, **11**, 2960.
[3] R. J. Flook, H. C. Freeman, F. Huq, and J. M. Rosalky, *Acta Cryst.*, 1973, **B29**, 903.
[4] W. Harrison and J. Trotter, *J.C.S. Dalton*, 1972, 956.
[5] H. C. Freeman, J. M. Guss, C. E. Nockolds, R. Page, and A. Webster, *Acta Cryst.*, 1970, **A26**, 149.
[6] R. Pepinsky and Y. Okaya, *Proc. Nat. Acad. Sci. U.S.A.*, 1956, **42**, 286.