Model Compounds for Metal Protein Interactions: ESR Study of the Cadmium(II) Chloride Complexes of Amino Acids

[1]IZHAR HUSSAIN* AND [2]MARGARET GOODGAME
[1]*Department of Pharmacy, University of Balochistan, Quetta, Pakistan*
[2]*Department of Chemistry, Imperial College of Science, Technology and Medicine, London, SW7 2AY, U.K.*

(Received 19th August, 1995, revised 21st October, 1995)

Summary: The model compounds for metal-protein interactions have been prepared by reacting cadmium(II) chloride with several amino acids. Esr spectra at both X- and Q-band frequencies are measured for manganese(II) ions doped in the lattices of these complexes and the zero field splitting parameters D and λ (=E/D) are deduced to see the effects of various environments around cadmium ion. The D and λ values observed for chloride bridged complexes, $Cd(L\text{-}Pro)Cl_2.H_2O$ and $Cd(4\text{-}Hyp)Cl_2$ [1-2], are consistent with the values previously found for corresponding acetamide complex [3]. In contrast to chloride-bridged complexes, the observed value of λ (0.32) for $Cd(Gly)_2Cl_2$ suggests meridional geometric structure in which three axes have different types of donor atoms sets i.e. Cl-Cd-Cl, Cl-Cd-O and O-Cd-O. The D and λ values found for $Cd(Gly\text{-}Gly)_2Cl_2$ are consistent with CdO_4Cl_2 chromophore and the negative sign of D observed for this complex is in agreement with the cis-arrangement found by X-ray diffraction [4].

Introduction

The role of metal ions in biochemical systems has long been established as being of essential significance, with almost all processes in living tissues requiring the presence of metals of one kind or another [5]. In order to understand the roles of metal ions in metalloproteins, it is first necessary to know the coordination sphere of complexed metal ions in their active sites. Such information is difficult to obtain since these active sites are buried in a large and complex protein backbone. To over come this difficulty, the active site is modeled by relatively simple coordination complexes. As the amino-acids contain the same type of donor groups as proteins therefore the amino-acids complexes act as models for the metal binding sites on proteins. The model compounds for metal-protein interactions studied in the present work, include the complexes of cadmium(II) chloride with several amino acids, such as L-Proline (L-Pro), 4-Hydroxy L-Proline (4-Hyp), Glycine (Gly) and Glycyl-Glycine (Gly-Gly) (Fig. 1).

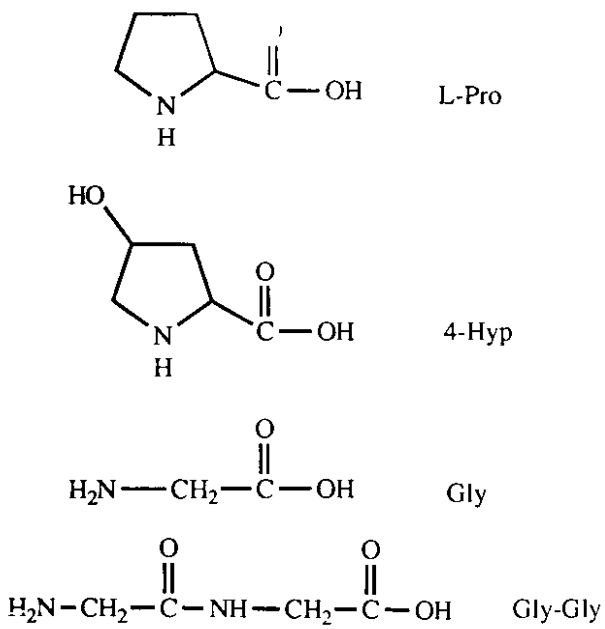

Fig.1: Amino acids structures and abbreviations.

The complexes of amino acids with cadmium(II) chloride are well known and the crystal structures of most of them have been studied [1-2,4,6]. The structure determinations of the complexes $Cd(L\text{-}Pro)Cl_2.H_2O$ and $Cd(L\text{-}Hyp)Cl_2$, by X-ray diffraction, revealed both structures to be that of chloride-ion bridged polymers with octahedral coordination of the cadmium [1-2]. Each cadmium ion has four chloride ions coordinating in a plane and from the trough

*To whom all correspondence should be addressed.

positions in the Zig-Zag folding structure, the two carboxyl oxygen atoms of ligands coordinate to the two cadmium atoms.

The structures of $Cd(Gly)_2Cl_2$ and $Cd(Gly\text{-}GLy)_2Cl_2$ have also been studied by X-ray diffraction [4,6]. In $Cd(Gly)_2Cl_2$, each cadmium atom co-ordinates octahedrally with three chloride atoms and three carboxyl oxygen atoms [6]. On the other hand, in $Cd(Gly\text{-}Gly)_2Cl_2$ each metal atom is surrounded octahedrally by two chlorine atoms and four carboxyl oxygen atoms from Gly-Gly [4].

Therefore, for these cadmium(II) chloride complexes of amino acids there are following three different environments around the cadmium atom.

CdO_2Cl_4 (Pro and 4-Hyp complexes)

CdO_3Cl_3 (Gly complex)

CdO_4Cl_2 (Gly-Gly complexes)

In order to see the effects of various environments around the cadmium, on the zero field splitting parameters, D and λ, the complexes $Cd(L\text{-}Pro)Cl_2.H_2O$, $Cd(4\text{-}Hyp)Cl_2$, $Cd(Gly)_2Cl_2$ and $Cd(Gly\text{-}Gly)_2Cl_2$ were prepared doped with 1% of manganese (II) ions and their e.s.r. spectra were measured at both the X- and Q-band frequencies.

Results and Discussion

At X-band frequency, the spectra of all these complexes are very complicated, with overlapping of transitions and therefore, difficult to interpret. The spectra of complexes $Cd(L\text{-}Pro)Cl_2.H_2O$ and $Cd(4\text{-}Hyp)Cl_2$ are very similar to one another but entirely different from that of $Cd(Gly)_2Cl_2$.

At Q-band frequency, all of these complexes gave good quality and very well resolved spectra (Fig. 2) which were therefore used to determine the precise values of zero-field splitting parameters D and λ in the Spin Hamiltonian (I)

$$\Re = g\,\beta\,BS + D(Sz^2 - 35/12) + E(Sx^2 - Sy2) \qquad (I)$$

Experimental resonance fields agreed well with those calculated, using the program ESRS [7], by exact diagonalization of the matrix derived from (I) $g_{iso} = 2.00$. Details are given in Table-1.

Like $Ca(L\text{-}Pro)_2Cl_2$ [8], in these amino acids complexes of cadmium (II) chloride, the variations

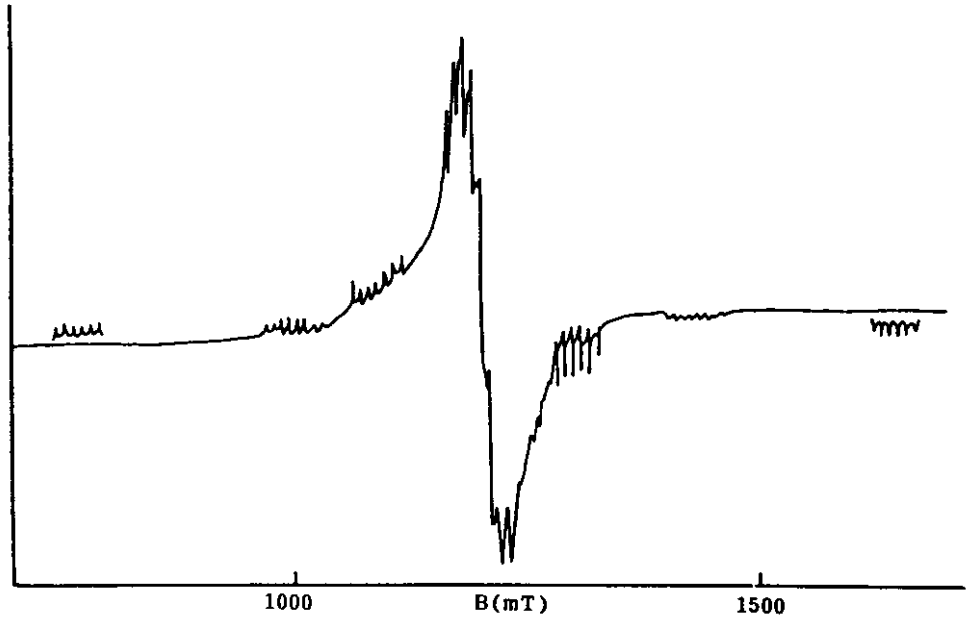

Fig. 2: Q-band ESR spectrum of $Cd(Mn)(4\text{-}Hyp)Cl_2$.

Table-1: Q-band ESR spectrum (mT) of Cd(Mn) (L-Pro)$Cl_2.H_2O$.

Observed (v=33.900 GHz)	Calculated for D= - 0.109 cm^{-1}, λ=0.033 B.	T.P.	Field Directon	Levels
441.2 W				
Region:				
616-687 W				
744.1 W	744.2	5.07	Z	6--5
968.6 W	968.2	4.10	Y	2--1
977.1 M	977.5	8.07	Z	5--4
1014.7 W/M	1015.5	4.05	X	2--1
1074.0 M	1073.2	7.12	Y	3--2
1092.8 M/S	1094.1	7.08	X	3--2
1187.8 S	1187.4	8.76	X	4--3
1190.9 S	1190.5	8.75	Y	4--3
Region:	1210.9	9.02	Z	4--3
1299.8 S/M	1298.3	8.62	X	5--4
1322.8 S/M	1323.1	8.56	Y	5--4
1432.6 M	1430.7	6.01	X	6--5
1445.7 M	1444.4	7.97	Z	3--2
1474.3 W	1475.4	5.94	Y	6--5
1677.9 W	1677.9	4.94	Z	2--1

in the average hyperfine spacing of the sextets were sufficient enough, at Q-band frequency, that the sign of D could be determined from the extreme Z-axis transitions. For the complexes Cd(L-Pro)$Cl_2.H_2O$, Cd(4-Hyp)Cl_2 and Cd(Gly-Gly)$_2Cl_2$, the spacing was greater on the lowest field than on the highest field transition, so D is negative. For the complex Cd(Gly)$_2Cl_2$, it was not possible to determine the sign of D, due to the overlapping of Z-axis transitions with those of the X- and Y-axes transitions (Fig. 3).

The values of D and λ, for these amino acids complexes are collected in Table-2. The closely similar values of D and λ observed for Cd(L-Pro)$Cl_2.H_2O$ and Cd(4-Hyp)Cl_2 are as expected, due to their very similar X-ray crystal structures. These figures are consistent with the values (D=0.100 cm^{-1}, λ = 0.030) found for the corresponding chloride-bridged acetamide complex Cd(acetamide)$_2Cl_2$ [3].

Table-2: Zfs parameters of Mn(II) in amino acids complexes.

Complex	D (cm^{-1})	λ
Cd(L-Pro)$Cl_2.H_2O$	- 0.109	0.033
Cd(4-Hyp)Cl_2	- 0.102	0.014
Cd(Gly)$_2Cl_2$	0.091	0.320
Cd(Gly-Gly)$_2Cl_2$	-0.119	0.050

The negative sign of D observed for both of these complexes suggest the tetragonal compression of an octahedron i.e. the ligand field on the z-axis is stronger than that on either the X- or Y-axes. This result is again consistent with the chloride bridged structure and the Z-axis Cd-O

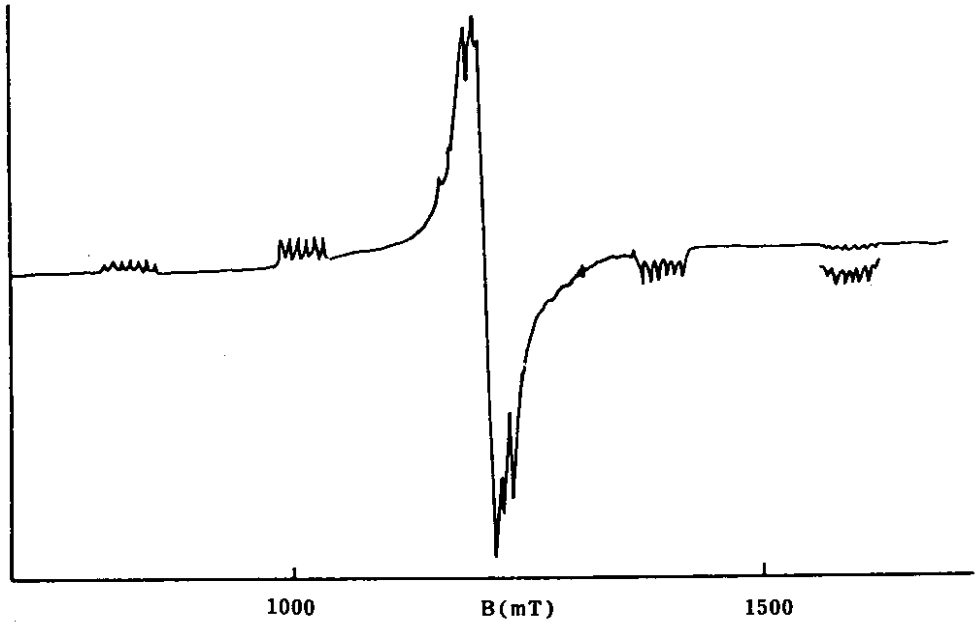

Fig. 3: Q-band ESR spectrum of Cd(Mn) (Gly)$_2Cl_2$.

bonds would have stronger ligand fields than the X- and Y-axes Cd-Cl bonds.

In contrast to the chloride-bridging complexes, $Cd(Gly)_2Cl_2$ has D=0.0905 cm^{-1} and λ=0.320. The value of λ (0.32) for this complex is extremely high, approaching the maximum of 1/3 and indicates considerable asymmetry in the X/Y plane, suggesting quite appreciable rhombic distortion. The higher values of D and λ observed for this complex are consistent with its meridional geometric structure, in which the three axes have different types of donor atoms sets i.e. Cl-Cd-Cl, Cl-Cd-O and O-Cd-O [6]. In a perfect meridional octahedron a value of 0.333 would be predicted. For a facial geometry each axis would have the same donor atoms set i.e. Cl-Cd-O, resulting in lower D and λ values.

The D values found for $Cd(Gly\text{-}Gly)_2Cl_2$ is slightly higher than for the chloride-bridged cadmium complexes but of the same order of magnitude. The negative sign of D observed for this complex is in agreement with the cis-arrangement found by X-ray diffraction. The unique axis has two oxygen donor ligands, and therefore a stronger crystal field than the X- and Y-axes. The octahedron is therefore compressed. The D value is lower than would be expected for a trans-arrangement.

Experimental

Preparation of complexes

All the chemicals used in the present work were pure analytical grade and were used without further purification.

$Cd(L\text{-}Pro)Cl_2.H_2O$

Cadmium(II) Chloride $2.5H_2O$ (0.02 mole) and L-Pro (0.02 mole) were dissolved in hot water (30 cm^3). The solution was stirred for six hours on a water bath at 70°C. The white precipitates thus formed were dried in vacuo at 50°C. Found:- C, 18.67, H, 3.26; N, 4.30 calculated for $Cd(L\text{-}Pro)Cl_2.H_2O$:- C, 18.96; H, 3.48; N, 4.30.

$Cd(4\text{-}Hyp)Cl_2$

To an aqueous solution of 4-Hyp (0.02 mole), $CdCl_2.2.5H_2O$ (0.02 mole) was added. The resulting solution was stirred for eight hours on a water bath at 60°C. The white precipitates thus formed were filtered off and dried in vacuo at 60°C. Found:- C, 18.98; H, 3.01; N, 4.44 calculated for $Cd(4\text{-}Hyp)Cl_2$:- C, 19.08; H, 2.86; N, 4.45.

$Cd(L)_2Cl_2$(L=Gly and Gly-Gly)

Both of these complexes were prepared by the same general method. The equimolar ratios of $CdCl_2.2.5H_2O$ and amino acid were dissolved separately in the minimum of water. The solutions were mixed and allowed to evaporate at room temperatures. The white precipitates thus formed were dried in vacuo over P_2O_5. Found:- C, 14.12, H, 2.72; N, 8.22 calculated for $Cd(Gly)_2Cl_2$:- C, 14.40; H, 3.00; N, 8.40. Found:- C, 21.54; H, 3.62; N, 12.55 calculated for $Cd(Gly\text{-}Gly)_2Cl_2$:- C, 21.46; H, 3.58; N, 12.52.

Elemental analysis for % composition of C, H and N were carried out by the Microanalytical Laboratory, Imperial College of Science, Technology and Medicine, London.

X-band spectra were obtained using a Varian E12 spectrometer. Q-band spectra were obtained with a Bruker ER200D-SRC spectrometer and an ER 078 15-inch electromagnet. All samples were measured as polycrystalline solids.

References

1. Y. Yukawa, Y. Inomata and T. Takeuchi, *Bull. Chem. Soc. Jpn.*, **56**, 2125 (1983).
2. Y. Yukawa, Y. Inomata, T. Takeuchi, M. Shimoi and A. Ouchi, *Bull. Chem. Soc. Jpn.*, **55**, 3135 (1982).
3. I. Hussain and M. Goodgame, To be publised.
4. R.J. Flook, H.C. Freeman, C.J. Moore and M.L. Scudder, *J. Chem. Soc. Chem. Comm.*, 753 (1973).
5. H.A.O. Hill, "Inorganic Biochemistry", Vol. 1, Bartholomew Press, Dorking, (1979).
6. R. Thulasidhass and J.K. Mohanarao, *Current Sci.*, **49**, 349 (1980).
7. D. Vivian and J.F. Gibson, *J. Chem. Soc., Faraday Trans, II*, 1640 (1975).