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STRUCTURE OF Zn(II) COMPLEX WITH CYCLO(L-METHIONYL-L-HISTIDYL)

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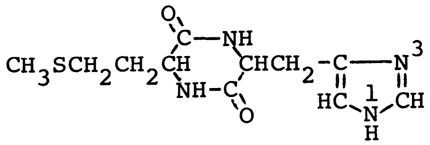
X-Ray structure analysis of a Zn(II) complex with cyclo(L-methionyl-L-histidyl) as a metalloprotein model shows tetrahedral coordination of Zn by each 1-N atom of four imidazole groups of histidine residues.

It is well known in metalloproteins (including metalloenzymes) that the functional groups in the side chains of the peptides, such as imidazole(Im) and thioether, coordinate to metal ions as ligating groups, but not their amide groups do.

The authors have used cyclo(L-histidyl-L-histidyl),[1a] cyclo(L-methionyl-L-methionyl),[1b] and cyclo(L-methionyl-L-histidyl)(CMH)[1c] as model compounds in order to examine metal-protein interactions at histidine and methionine residues. This paper reports on the structure of a Zn(II) complex with CMH.

Crystal Data: $Zn(C_{11}H_{16}N_4O_2S)_4SO_4\cdot 10H_2O$, $M=1414.7$, monoclinic, space group $P2_1$, $a=15.143(2)$, $b=20.586(4)$, $c=11.007(2)$ Å, $\beta=97.89(1)°$. $U=3398(1)$ Å^3, $Z=2$, $D_o=1.38$ g cm^{-3}, $D_c=1.38$ g cm^{-3}, μ(Mo $K\alpha$)$=5.9$ cm^{-1}.

CMH:



A prismatic crystal, grown from aqueous solution, was carefully sealed in a thin-wall glass capillary to avoid decomposition. All unique diffraction maxima with $2\theta \leq 44°$ were recorded on a four-circle diffractometer using graphite-monochromated Mo-$K\alpha$ radiation. Of the 4308 reflections surveyed, 2692 were judged as observed[$I>3\sigma(I)$]. The structure was solved using MULTAN.[2] Ten water molecules were located on difference syntheses. The positions of the non-hydrogen atoms were refined anisotropically to R=0.075.[3]

The structure of the complex ion is shown in Fig. 1,[4] together with the most important geometrical parameters. This is the first example of the X-ray structure analysis of a Zn(II) complex in which Zn(II) ion links to each 1-N atom of the Im groups of the histidine residues of peptides exclusively. The N-Zn-N angles are all within 3.5° of the 109.5° expected for a tetrahedral coordination. The average of the four Zn-N bond lengths is 2.01(1) Å in agreement with those of other tetrahedral complexes of zinc such as $Zn(Im)_4(ClO_4)_2$,[5] $Zn(L\text{-histidinato})_2\cdot 2H_2O$,[6] and $Zn(Im)_2Cl_2$.[7] The complex ion has an approximate D_2 symmetry except for terminal $-CH_2SCH_3$ groups, since there are three pseudo two-fold axes perpendicular to one another passing through the central Zn atom and bisecting N-Zn-N angles. Im rings A and D make angles of 74° and 90°, respectively, with the plane defined by N(2A), Zn, and N(2D) atoms, and rings B and C make angles of 88° and 86°, respectively, with the plane defined by N(2B), Zn, and N(2C) atoms. The Zn-N(2A) and Zn-N(2D) bonds form

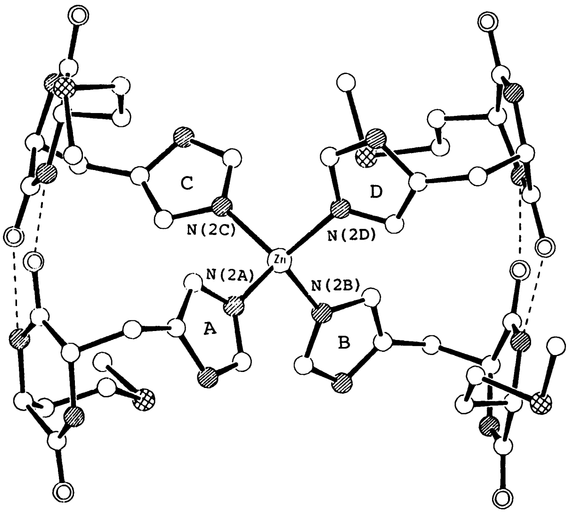


Fig. 1. Structure of the Zn(L-methionyl-L-histidyl)$_4^{2+}$ cation. ○ C atom, ▨ N atom, ◎ O atom, ▩ S atom. Important bond lengths(Å): Zn-N(2A) 1.97(1), Zn-N(2B) 2.01(1), Zn-N(2C) 2.01(1), Zn-N(2D) 2.04(1); angles(°): N(2A)-Zn-N(2B) 112.2 (5), N(2A)-Zn-N(2C) 106.6(5), N(2A)-Zn-N(2D) 110.8, N(2B)-Zn-N(2C) 112.9(5), N(2B)-Zn-N(2D) 108.2(5), N(2C)-Zn-N(2D) 106.1(6).

angles of 5° and 8° to Im rings A and D, respectively, to make the distal ends of these two rings approach. Similarly, the Zn-N(2B) and Zn-N(2C) bonds form angles of 6° and 6° to Im rings B and C, respectively.

In each CMH moiety, the Im ring is folded over the diketopiperazine ring. Such a conformation is common to several cyclic dipeptides[8)] and interpreted as the result of attractive force between aromatic rings which stabilize this conformation.[9)] Neighboring diketopiperazine rings are connected by two -NH---O=C- hydrogen bonds shown in Fig. 1 as dotted lines. These hydrogen bonds together with the folded conformations between Im and diketopiperazine rings appear to play important roles in determining the overall conformation of the complex ion.

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References

1) a) Y. Kojima, Transition Met. Chem., 4, 269(1979); b) Y. Kojima, T. Yamashita, Y. Ishino, T. Hirashima, and K. Hirotsu, Chem. Lett., 1983, 453; c) Y. Kojima, T. Yamashita, Y. Ishino, T. Hirashima, and T. Miwa, Bull. Chem. Soc. Jpn., submitted for publication.
2) G. Germain, P. Main, and M. M. Woolfson, Acta Crystallogr., Sect. B, 26, 274(1970)
3) W. R. Busing, K. O. Martin, and H. A. Levy, ORFLS, Oak Ridge National Laboratory Report ORNL-TM-305(1965).
4) C. K. Johnson, ORTEP-II, Oak Ridge National Laboratory Report ORNL-3794(2nd revision with supplemental instructions)(1971).
5) C. A. Bear, K. A. Duggan, and H. C. Freeman, Acta Crystallogr., Sect. B, 31, 2713 (1975).
6) T. J. Kistenmacher, Acta Crystallogr., Sect. B, 28, 1302(1972).
7) B. K. S. Lundberg, Acta Crystallogr., 21, 901(1966).
8) R. Ramani, K. Venkatesan, and R. E. Marsh, J. Am. Chem. Soc., 100, 949(1978); M. Cotrait and M. Ptak, Acta Crystallogr., Sect. B, 34, 528(1978); I. Tanaka, T. Iwata, N. Takahashi, and T. Ashida, Acta Crystallogr., 33, 3902(1977).
9) Y. Imanishi, Adv. Polym. Sci., 20, 1(1976).

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