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The Crystal Structure of Hexaimidazole Zinc(II) Dichloride Tetrahydrate, $Zn(C_3H_4N_2)_6Cl_2 \cdot 4\ H_2O$

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The crystal structure of hexaimidazole-zinc(II)-dichloride tetrahydrate has been determined and refined from three-dimensional X-ray data. The crystals are triclinic (space-group $P\bar{1}$) with one formula unit $Zn(C_3H_4N_2)_6Cl_2 \cdot 4\ H_2O$ in a unit cell with the dimensions $a = 10.7$ Å, $b = 9.4$ Å, $c = 8.8$ Å, $\alpha = 120°$, $\beta = 97°$ and $\gamma = 98°$. The structure contains discrete hexaimidazole-zinc(II)-ions linked together by hydrogen bonds to chloride ions and water molecules. The zinc atoms are octahedrally coordinated to the free nitrogen atoms of six imidazole molecules with Zn—N bond distances 2.15—2.26 Å.

In order to understand the function of metal ions in metallo-enzymes it is essential to know the mode of binding between possible ligands of the protein and the metal ion. As part of the structural investigation in Uppsala of the two zinc-enzymes carbonic anhydrase [1] and horse liver alcohol dehydrogenase [2] we became interested in the structure of model compounds for zinc-protein interactions. Potential binding sites for zinc in these two enzymes are the two ends of the main chain, sulfhydryl groups and the imidazole side-chains of the histidine residues. Since imidazole-groups have been shown to be involved in the specific binding site for zinc in myoglobin [3,4] it was decided to study the structure of possible complexes between zinc and imidazole. These compounds [5] as well as complexes with methyl-substituted imidazole [6] have been studied in solution.

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EXPERIMENTAL

Colourless crystals of hexaimidazole zinc(II) dichloride tetrahydrate were prepared by slow evaporation of an aqueous solution of imidazole and zinc(II) chloride in molar concentrations 10:1. The pH of this solution was adjusted to 6.9 with concentrated HCl. Zinc and nitrogen analysis of the crystals gave the following values: Zn 10.85 % and N 28.75 %. Calculated values for the formula $Zn(C_3H_4N_2)_6Cl_2 \cdot 4\ H_2O$ are: Zn 10.59 % and N 27.24 %. The structure determination has shown that this formula is correct in spite of the slight discrepancy between observed and calculated values. (We are very grateful to Mrs. K. Fridborg for help with the preparation and analysis of the crystals.)

A crystal with dimensions 0.11 × 0.20 × 0.33 mm was mounted in a capillary tube in equilibrium with its mother liquor, since the compound slowly decomposes in air. Equi-inclination Weissenberg photographs for eight zones were recorded using Cu$K\alpha$ radiation and with the [011] line as rotation axis. Unit cell dimensions of the triclinic crystals were determined from Weissenberg and oscillation photographs.

2127 independent intensities were estimated visually using the multiple-film tehnique and comparison with a calibrated intensity scale. The data were corrected for Lorentz and polarization effects.

Structure data

Cell symmetry: Triclinic; space-group $P\bar{1}$
Dimensions: $a = 10.7$ Å, $b = 9.4$ Å, $c = 8.8$ Å, $\alpha = 120°$, $\beta = 97°$, $\gamma = 98°$
Density (observed by the flotation method): 1.4 g/cm³
Density: (calculated) 1.37 g/cm³ for a cell content of one formula unit
$Zn(C_3H_4N_2)_6Cl_2 \cdot 4\ H_2O$.

DETERMINATION AND REFINEMENT OF ATOMIC PARAMETERS

The origin of the unit cell was arbitrarily chosen to coincide with the position of the zinc atom since there is only one zinc in the unit cell. An inspection of the three dimensional Pattersson function revealed the existence of only one peak considerably higher than the remaining peaks. It was assumed that this peak corresponded to vectors from zinc to two centrosymmetrically related chlorine atoms. The positions of the atoms of four of the six imidazole-rings could then be located from this function assuming the structure to possess a centre of symmetry. These positions as well as individual isotropic temperature-factors and scale-factors were refined by the method of least-squares. Using these refined parameters a three-dimensional difference-synthesis was calculated within bounded Fourier projections along the b-axis, each projection comprising one tenth of the b-axis. The remaining two imidazole-rings of the unit cell as well as two water molecules could be located from this function. Another least-squares refinement of all the parameters located at this stage was carried out and a difference synthesis was then computed. There were only two main peaks in the unit cell the height of which were three times the general background. These peaks were assumed to correspond to the remaining water molecules.

All Fourier and structure-factor calculations were made on the Swedish computer FACIT EDB using programmes devised by Liminga and Olovsson.[7]

The atomic coordinates (hydrogen atoms excluded), individual isotropic temperature-factors, and fifteen scale factors, one for each set of multiple-films were then refined by the method of least-squares employing the pro-

gramme devised by Åsbrink and Brändén [8] for FACIT. Since the final R-value of this refinement was as high as 0.163 it was assumed that there might be small deviations from a centre of symmetry in the structure. A full-matrix least-squares refinement was then made assuming a non-centric structure using a set of programmes adapted to the computer CD 3600 by R. Liminga and J. O. Lundgren at the Institute of Chemistry, Uppsala. The basic routines of these programmes were devised by Zalkin, Berkeley, Calif., U.S.A. The weights, w, were calculated according to an equation suggested by Cruickshank *et al.*[9]

$$w = 1/(a + |F_o| + c|F_o|^2 + d|F_o|^3)$$

final constants being $a = 5.0$, $c = 0.05$ and $d = 0.001$.

Table 1. Final atomic parameters and their estimated standard deviations.

Atom	x/a	$\sigma(x)$ Å	y/b	$\sigma(y)$ Å	z/c	$\sigma(z)$ Å	B Å^2	$\sigma(B)$ Å^2
Zn(1)	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	2.13	0.04
N (2)	0.1182	0.0018	0.2423	0.0024	0.2308	0.0027	2.16	0.34
C (3)	0.2270	0.0025	0.3338	0.0033	0.2233	0.0037	3.34	0.47
N (4)	0.2687	0.0022	0.4713	0.0032	0.4075	0.0035	3.64	0.46
C (5)	0.2029	0.0038	0.4578	0.0050	0.5095	0.0055	5.41	0.83
C (6)	0.1019	0.0021	0.3115	0.0030	0.3960	0.0033	3.22	0.39
N (7)	0.1234	0.0012	0.0395	0.0018	0.8332	0.0019	2.55	0.22
C (8)	0.2169	0.0022	0.9610	0.0030	0.7782	0.0032	3.04	0.42
N (9)	0.2819	0.0018	0.0379	0.0025	0.6922	0.0028	3.32	0.36
C (10)	0.2202	0.0028	0.1580	0.0037	0.6891	0.0041	5.23	0.59
C (11)	0.1148	0.0026	0.1534	0.0035	0.7665	0.0039	3.65	0.55
N (12)	0.1289	0.0019	0.8475	0.0025	0.0473	0.0029	2.02	0.34
C (13)	0.2298	0.0020	0.9081	0.0029	0.1824	0.0032	2.49	0.37
N (14)	0.2945	0.0021	0.8016	0.0027	0.1770	0.0030	3.72	0.42
C (15)	0.2057	0.0029	0.6347	0.0039	0.0348	0.0042	4.17	0.59
C (16)	0.1055	0.0022	0.6740	0.0031	0.9724	0.0032	3.19	0.44
N (17)	0.8825	0.0019	0.7730	0.0025	0.7655	0.0028	2.85	0.38
C (18)	0.7811	0.0023	0.6688	0.0031	0.7586	0.0034	2.65	0.44
N (19)	0.7266	0.0023	0.5301	0.0032	0.6115	0.0034	3.65	0.46
C (20)	0.8110	0.0030	0.5363	0.0041	0.4954	0.0044	4.44	0.58
C (21)	0.8992	0.0031	0.6663	0.0042	0.5723	0.0046	4.83	0.75
N (22)	0.8802	0.0012	0.9701	0.0018	0.1724	0.0019	2.63	0.22
C (23)	0.7658	0.0024	0.0160	0.0033	0.1956	0.0035	3.30	0.50
N (24)	0.7186	0.0020	0.9951	0.0027	0.3116	0.0031	4.05	0.42
C (25)	0.7951	0.0018	0.8893	0.0027	0.3460	0.0028	2.79	0.33
C (26)	0.8916	0.0023	0.8814	0.0032	0.2576	0.0035	2.88	0.45
N (27)	0.8735	0.0023	0.1441	0.0029	0.9504	0.0033	3.03	0.42
C (28)	0.7675	0.0024	0.0668	0.0032	0.8163	0.0036	3.36	0.46
N (29)	0.7236	0.0018	0.2143	0.0024	0.8132	0.0026	2.78	0.35
C (30)	0.7864	0.0030	0.3522	0.0040	0.9399	0.0043	4.52	0.62
C (31)	0.8780	0.0023	0.3185	0.0031	0.0420	0.0032	3.33	0.44
Cl (32)	0.4953	0.0007	0.7919	0.0009	0.4881	0.0010	3.08	0.12
Cl (33)	0.5036	0.0007	0.2040	0.0009	0.5050	0.0010	3.22	0.12
O (34)	0.5136	0.0020	0.1655	0.0025	0.1263	0.0029	4.99	0.42
O (35)	0.4615	0.0020	0.8184	0.0025	0.8604	0.0028	4.98	0.42
O (36)	0.5135	0.0022	0.4643	0.0029	0.1390	0.0031	6.67	0.50
O (37)	0.5318	0.0016	0.5444	0.0020	0.8828	0.0022	4.10	0.29

Table 2. Final weight-analysis.

Sin θ-interval	$w\Delta^2$	Number of reflexions	F_o-interval	$w\Delta^2$	Number of reflexions
0.00—0.46	1.91	311	0.0— 4.4	0.74	212
0.46—0.58	0.85	304	4.4— 5.9	0.89	213
0.58—0.67	0.68	289	5.9— 7.3	0.94	213
0.67—0.74	0.64	233	7.3— 8.7	0.84	213
0.74—0.79	0.90	232	8.7—10.5	0.89	212
0.79—0.84	0.94	212	10.5—12.6	0.86	213
0.84—0.89	0.91	176	12.6—15.3	1.04	212
0.89—0.93	0.90	169	15.3—19.8	0.83	213
0.93—0.97	1.14	142	19.8—26.3	1.12	213
0.97—1.00	1.13	59	26.3—79.2	1.86	213

After four cycles of refinement the final R-value was 0.116 and all shifts were less than the standard deviations. Final atomic parameters are listed in Table 1, and the weight-analysis for the last cycle of refinement is given in Table 2. Lists of the observed and calculated F-values can be obtained from this Institute on request.

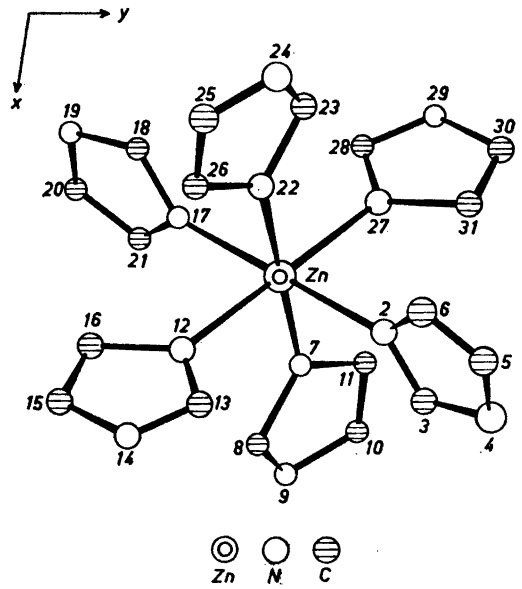

Fig. 1. The structure of the hexaimidazole-zinc(II)-ion.

DESCRIPTION AND DISCUSSION OF THE STRUCTURE

The structure of hexaimidazole-zinc(II) dichloride tetrahydrate is built up from discrete hexaimidazole-zinc(II)-ions linked together by hydrogen bonds to chloride ions and water molecules. The zinc atoms are octahedrally coordinated to the free nitrogen atoms of six imidazole molecules as is shown in Fig. 1. Within the limits of error there is no deviation from regular octahedral bond angles which is in agreement with Kretsingers [10] observations that zinc usually exhibits regular coordination when coordinated to identical monodentate ligands. The Zn—N bond lengths listed in Table 3 together with bond angles subtended at the zinc atom vary from 2.15 to 2.26 Å. The increase in the zinc-nitrogen bond lengths compared to those of tetrahedrally coordinated zinc (1.99—2.01 Å) is of the expected order of magnitude.[11]

The bond lengths and bond angles of the imidazole rings are listed in Table 4. The atoms of the imidazole rings are coplanar, the equations of their mean planes being given in Table 5 together with the mean deviations of the atoms including the zinc atom from their planes. The deviation from centrosymmetry in the hexaimidazole-zinc(II) ion is mainly due to differences in orientation of opposite imidazole rings. The angles between the normals to these opposite rings vary from 6° to 15°.

The hydrogen bond distances, linking imidazole-nitrogen, chloride ions, and water molecules are listed in Table 6. The six NH···Cl bond lengths of

Table 3. Zn—N bond distances and N—Zn—N bond angles.

Atoms	Distance Å	σ Å
Zn(1)—N(2)	2.210	0.035
Zn(1)—N(7)	2.214	0.021
Zn(1)—N(12)	2.264	0.025
Zn(1)—N(17)	2.153	0.035
Zn(1)—N(22)	2.193	0.021
Zn(1)—N(27)	2.192	0.028
Atoms	**Angle (°)**	**σ (°)**
N(2)—Zn(1)—N(7)	87.2	1.0
N(2)—Zn(1)—N(12)	92.9	1.1
N(2)—Zn(1)—N(17)	176.0	0.7
N(2)—Zn(1)—N(22)	91.0	1.0
N(2)—Zn(1)—N(27)	88.0	1.1
N(7)—Zn(1)—N(12)	90.6	0.9
N(7)—Zn(1)—N(17)	90.5	1.0
N(7)—Zn(1)—N(22)	178.0	0.5
N(7)—Zn(1)—N(27)	89.3	0.9
N(12)—Zn(1)—N(17)	90.4	1.1
N(12)—Zn(1)—N(22)	90.0	0.9
N(12)—Zn(1)—N(27)	179.1	0.8
N(17)—Zn(1)—N(22)	91.4	1.0
N(17)—Zn(1)—N(27)	88.8	1.1
N(22)—Zn(1)—N(27)	90.1	0.9

Table 4. Bond distances in the imidazole-rings.

Atoms	Distance Å	Atoms	Distance Å	Atoms	Distance Å
N(2)–C(3)	1.38(0.03)	N(7)–C(8)	1.32(0.03)	N(12)–C(13)	1.33(0.03)
C(3)–N(4)	1.44(0.04)	C(8)–N(9)	1.45(0.03)	C(13)–N(14)	1.28(0.03)
N(4)–C(5)	1.25(0.05)	N(9)–C(10)	1.39(0.04)	N(14)–C(15)	1.51(0.04)
C(5)–C(6)	1.42(0.05)	C(10)–C(11)	1.39(0.04)	C(15)–C(16)	1.33(0.04)
C(6)–N(2)	1.31(0.03)	C(11)–N(7)	1.46(0.03)	C(16)–N(12)	1.39(0.03)
N(17)–C(18)	1.33(0.03)	N(22)–C(23)	1.36(0.03)	N(27)–C(28)	1.35(0.04)
C(18)–N(19)	1.28(0.04)	C(23)–N(24)	1.28(0.04)	C(28)–N(29)	1.53(0.03)
N(19)–C(20)	1.46(0.04)	N(24)–C(25)	1.49(0.03)	N(29)–C(30)	1.23(0.04)
C(20)–C(21)	1.24(0.05)	C(25)–C(26)	1.36(0.03)	C(30)–C(31)	1.43(0.04)
C(21)–N(17)	1.53(0.04)	C(26)–N(22)	1.38(0.03)	C(31)–N(27)	1.41(0.04)

Table 5. Least-squares planes.

Atoms	Equations	Mean displacement	Distance to Zn
2–6	$-0.6521X+0.7397Y-0.1664Z+0.1257=0$	0.02 Å	−0.12 Å
7–11	$-0.3717X-0.3053Y-0.8767Z+4.4991=0$	0.03	−0.25
12–16	$0.6109X+0.4261Y-0.6672Z+3.0783=0$	0.05	0.08
17–21	$-0.6515X-0.7075Y-0.2739Z-3.9683=0$	0.01	−0.20
22–26	$-0.3045X-0.5405Y-0.7843Z-7.7874=0$	0.08	−0.09
27–31	$0.6125X+0.3025Y-0.7303Z-0.9390=0$	0.12	0.06

Table 6. Hydrogen bond distances.

Atoms	Distance Å	Atoms	Distance Å
Cl(32)–N(4)	3.30	Cl(33)–N(29)	3.33
Cl(32)–N(9)	3.48	Cl(33)–O(34)	3.18
Cl(32)–N(14)	3.32	Cl(33)–O(37)	3.20
Cl(32)–O(35)	3.23	O(34)–O(35)	2.82
Cl(32)–O(36)	3.13	O(34)–O(36)	2.74
Cl(33)–N(19)	3.24	O(35)–O(37)	2.86
Cl(33)–N(24)	3.30	O(36)–O(37)	2.72

3.24–3.48 Å agree well with corresponding hydrogen bond lengths in the structure of diimidazole-zinc(II) dichloride.[12] The OH···O distances vary from 2.72 to 2.86 Å and the OH···Cl distances are within the values 3.07–3.24 Å given by Pimentel *et al.*[13] for hydrogen bond distances between chloride ions and water molecules.

The present structure determination is part of an investigation of three zinc-imidazole complexes. At high pH (9.5) it was possible to isolate a di-imidazolate-zinc(II) complex in which the proton of imidazole has been split off and both nitrogen atoms coordinate to zinc. The structure of this complex [14] consists of an infinite three-dimensional net-work in which each zinc-atom is tetrahedrally coordinated to four nitrogen atoms of four different imidazole units and each imidazole is covalently bonded to two different zinc-atoms. Two complexes, di-imidazole-zinc(II) dichloride and hexa-imidazole-zinc(II)

dichloride tetrahydrate have been isolated at pH 6.7—7.1. The two nitrogen atoms of imidazole are not equivalent in these two complexes since a hydrogen atom is bonded to one of the nitrogen atoms. In the structure of di-imidazole-zinc(II) dichloride[12] each zinc-atom is tetrahedrally coordinated to two chlorine atoms and to the free nitrogen atoms of two imidazole molecules, whereas in the present structure zinc is octahedrally coordinated to six imidazole molecules.

These structure determinations have thus shown that zinc may be either tetrahedrally or octahedrally coordinated when bound to imidazole groups. This flexibility of coordination may be one of the reasons for the specific requirement of zinc for the catalytic activity of so many enzymes.

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