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# Complexes of Vitamin $B_1$ with Transition Metal Ions. Crystal and Molecular Structure of Zn(thiamine)$Cl_3 \cdot 0.4H_2O$

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## Abstract

The reaction of zinc acetate with thiamine hydrochloride (Vitamin $B_1$) in water produced the complex Zn(thiamine)$Cl_3 \cdot 0.4H_2O$, whose structure has been determined by X-ray diffraction. The compound crystallizes with eight molecules in space group *C2/c* of the monoclinic system. The cell has dimensions at 20 °C of $a = 25.747(8)$, $b = 8.453(3)$, $c = 17.402(4)$ Å, $\beta = 105.8(1)°$, $V = 3644.3$ Å$^3$, $D_{calc} = 1.602$ g cm$^{-3}$. The structure has been refined by least-squares methods to a final *R* value of 0.037 for the 249 variables and the 2320 data. The crystal structure of the complex is composed of discrete Zn(thiamine)$Cl_3$ molecules and 0.4 disordered crystallization water molecule in the asymmetric unit. The three chlorine atoms and the $N_{1'}$ atom of the pyrimidine ring are bound to the zinc atom. The thiamine ligand is in the uncommon *S* conformation with torsional angles $\phi_T = 113.4°$, $\phi_P = 130.4°$. This new structure is the third example of binding of thiamine to a transition metal ion, and the first example of coordination to a first row transition metal in the +2 oxidation state.

## Introduction

The pyrophosphate ester of vitamin $B_1$ (thiamine hydrochloride) is a cofactor for several metabolic enzymes. In the presence of a divalent metal ion such as Mg(II) or Mn(II) it allows the decarboxylation of α-ketoacids and the transfer of aldehyde or acyl groups [1,2]. The metal ion is suggested to be involved in the formation of the enzyme–coenzyme complex and the pyrimidine part of thiamine is believed to be a primary site for metal interactions [3,4].

NMR data in solution suggested that transition paramagnetic metal ions interact, directly [5] or through a water molecule [6–8] at $N_{1'}$ site of the pyrimidine ring, whereas the $N_{3'}$ donor [9] of the pyrimidine ring has been proposed for IIB metal ions group.

In recent years some papers have characterized the structure of compounds containing a transition metal and vitamin $B_1$ or its pyrophosphate ester in order to investigate the nature of the interactions between the metal ion and thiamine.

In only three of the eight compounds [10–17] reported so far, namely in Cd(thiamine)$Cl_3$ [14], Cu(thiamine)$Cl_2$ [15] and $Rh_2$(acetato)$_4$(thiamine pyrophosphate)$_2$ [17], is the thiamine molecule coordinated to the metal. In the other compounds thiamine$^{2+}$ and $MCl_4^{2-}$ (M = Co [13], Cu [11], Cd [12], Hg [10]) groups are present, interacting through hydrogen bonds in the solid state, or the metal ion is bound to the pyrophosphate group like in Cu(thiamine pyrophosphate)(1,10-phenantroline)-$H_2O$ [16].

In the reaction with cadmium acetate, thiamine bound the metal in the +2 oxidation state [14], while with copper acetate it formed Cu(thiamine)$Cl_2$ [15], a complex containing the copper in the +1 oxidation state. These results prompted us to investigate the reaction of thiamine with other acetates of the first row transition metal ions, since most of these ions are known to have important biological roles [18]. Zinc appeared particularly tempting to us since it can easily replace magnesium as the activator in thiamine dependent enzymic catalyzed reactions [19]. Zinc is an essential element – necessary for the metabolic processes of living organisms – and appears to be one of the most important metals biologically, second only to iron among the transition metals. Zinc forms four-, five-, and six-coordinated complexes with comparable stability and the ligands are kinetically labile. In nature is often four- or five-coordinated. Zinc is stable only in the oxidation number +2, therefore cannot perform redox reactions and its Lewis acid properties, referred to the formation of tetrahedral compounds, are relatively better than those of the bipositive 3d metal ions. All of these reasons make zinc the best catalyst when the role of the metal ion is that of being a Lewis acid necessary to bind the substrate and activate it.

Reaction of vitamin $B_1$ with zinc acetate yielded a complex of formula Zn(thiamine)$Cl_3 \cdot 0.4H_2O$. Since

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this complex seems to be the first example of binding of a first row transition metal in the +2 oxidation state to thiamine, we determined its crystal and molecular structure by X-ray diffraction. We report here the crystal and molecular structure of the complex and compare it with the structures of other complexes of thiamine.

## Experimental

Crystals of the complex Zn(thiamine)$Cl_3 \cdot 0.4H_2O$ were prepared by slow evaporation of aqueous solutions containing $Zn(CH_3CO_2)_2 \cdot 2H_2O$ and thiamine hydrochloride in a one to two molar ratio at room temperature. The crystals were collected by suction filtration and washed with small amounts of water and acetone. *Anal.* Calc. for $C_{12}H_{17}Cl_3N_4OSZn$: C, 33.0; H, 3.92; N, 12.82; Zn, 14.96. Found: C, 33.0; H, 3.99; N, 12.78; Zn, 15.56.

### *X-ray Structure Determination*

A crystal of the compound Zn(thiamine)$Cl_3 \cdot 0.4H_2O$ shaped as a rhombic prism with dimension 0.08 × 0.22 × 0.25 mm was used for crystal data and intensity data collection. A Philips PW 1100 automated diffractometer with graphite-monochromated Mo K$\alpha$ radiation ($\lambda = 0.71069$ Å) was used for all operations. Lattice constants were determined at 20 °C from the setting angles of 20 reflections with $7° < \theta < 10°$. Details of crystal data and collection are listed in Table I. No systematic variation in the intensities of three standard reflections measured every 120 min was observed. The data were corrected for Lorentz and polarization effects as well as for absorption. The principal computer programs used in the crystallographic calculations are listed in ref. 20. The positions of the zinc and chlorine atoms were determined by direct methods, and those of all the other non-hydrogen atoms were found in subsequent Fourier maps. The structure was refined with use of a full-matrix least-squares method based on minimization of the function $\Sigma w(|F_o| - |F_c|)^2$ with weights $w = 1/\sigma^2(F_o)$. Anisotropic thermal parameters were used for all the non-hydrogen atoms. Hydrogens bound to N and C atoms were located in the last difference Fourier maps and were refined isotropically with assigned temperature factors 20% larger than the isotropic equivalent of the respective nitrogen or carbon atoms. The hydrogen bound to 053 was not found in the difference Fourier map and was not included in the refinement. The hydrogens of the methyl groups appeared to be disordered and the methyl were refined as rigid groups (C–H = 0.95 Å). Two extra peaks around 1 e Å$^{-3}$ remained in the last Fourier maps, one of them lying on a $C_2$ crystallographic axis. These were assigned to oxygen atoms of two water molecules. The introduction of the oxygens in the least-squares procedure led to a significant improvement of the agreement indices, but the fitting procedure converged to high thermal parameters for the oxygens which were found less than 1.1 Å apart. This was assumed as indicative of some disorder in the water molecule. The occupancies of the two independent water molecules giving the best *R* value were found to be 0.1 and 0.30 for OW1 and OW2 respectively and this establishes that the crystal examined contained 0.4 water molecule for zinc ion. It must be noted, however, that the large thermal parameters for the water molecule precludes a safe conclusion.

TABLE I. Summary of Crystal Data and Intensity Data Collection

| | |
|---|---|
| Formula | $C_{12}H_{17.8}Cl_3N_4O_{1.4}SZn$ |
| Cryst. system, space group | monoclinic, *C*2/*c* |
| *a* (Å) | 25.747(8) |
| *b* (Å) | 8.453(3) |
| *c* (Å) | 17.402(4) |
| $\beta$ (deg) | 105.8(1) |
| *V* (Å$^3$) | 3644.3 |
| *Z* | 8 |
| $D_{calc}$ (g cm$^{-3}$) | 1.602 |
| $\mu$(Mo K$\alpha$) (cm$^{-1}$) | 18.2 |
| Transmission factors, max–min | 0.87–0.72 |
| Scan type | $\omega$–2$\theta$ |
| Scan speed (deg min$^{-1}$) | 3 |
| Scan width ($\Delta\omega$) (deg) | 1.0 + 0.30 tan $\theta$ |
| Background | stationary counter-stationary crystal symmetric, at each end of scan |
| Collection range | $\pm h, k, l$ $5° < 2\theta < 50°$ |
| Number of data | 3370 |
| Number of data, $I > 3\sigma(I)$ | 2320 |
| Number of variables | 249 |
| $R$ [a] | 0.037 |
| $R_w$ [a] | 0.034 |

[a] $R = \Sigma||F_o| - |F_c||/\Sigma|F_o|$; $R_w = [\Sigma w(|F_o| - |F_c|)^2/\Sigma w(F_o)^2]^{1/2}$.

Disordered water molecules were observed also in the crystal structure of Cd(thiamine)$Cl_3 \cdot 0.6H_2O$ [14]. In that case some *h*0*l* reflections were observed with weak intensity suggesting that the actual arrangement of the water molecules violates the symmetry conditions of *C*2/*c* or *Cc* space groups. In the present complex all the *h*0*l* reflections were unobserved. This can be due to the smaller number of water molecules contained in the present complex or to a higher order of the water molecules in the crystal.

In order to investigate if the observed disorder in the water molecules could be due to an incorrect assignment of the space group we performed a refinement of the structure in the acentric *Cc* space group. The *R* value was slightly worse than in the *C*2/*c* space

TABLE II. Positional Parameters for the Atoms of Zn(thiamine)$Cl_3$·$0.4H_2O$[a]

| Atom | *x* | *y* | *z* |
|---|---|---|---|
| Zn | 3337(1) | 6737(1) | 3410(1) |
| Cl1 | 3248(1) | 4064(1) | 3393(1) |
| Cl2 | 2772(1) | 7955(1) | 4009(1) |
| Cl3 | 4191(1) | 7376(2) | 4069(1) |
| S | 5806(1) | 1520(1) | 3686(1) |
| N1′ | 3227(1) | 7343(4) | 2242(2) |
| C6′ | 3238(2) | 6176(4) | 1715(2) |
| C2′ | 3196(2) | 8836(4) | 1947(2) |
| C21′ | 3199(2) | 164(5) | 2506(3) |
| H21′1 | 3115(2) | 1167(5) | 2257(3) |
| H21′2 | 3548(2) | 246(5) | 2870(3) |
| H21′3 | 2951(2) | −22(5) | 2811(3) |
| N3′ | 3178(1) | 9195(3) | 1201(2) |
| C4′ | 3189(2) | 8019(4) | 687(2) |
| N41′ | 3160(2) | 8438(5) | −64(2) |
| H41′1 | 314(2) | 783(5) | −43(3) |
| H41′2 | 318(2) | 936(5) | −13(3) |
| C5′ | 3230(2) | 6424(4) | 940(2) |
| C35′ | 3254(2) | 5067(5) | 395(2) |
| H35′1 | 295(2) | 446(5) | 29(2) |
| H35′2 | 328(1) | 537(5) | −11(2) |
| N3 | 3703(1) | 3982(4) | 751(2) |
| C2 | 3620(2) | 2512(5) | 954(3) |
| H21 | 326(2) | 210(5) | 90(2) |
| C4 | 4245(2) | 4368(5) | 876(3) |
| C41 | 4396(2) | 5935(5) | 632(3) |
| H411 | 4771(2) | 5999(5) | 666(3) |
| H412 | 4318(2) | 6776(5) | 946(3) |
| H413 | 4205(2) | 6148(5) | 93(3) |
| C5 | 4569(2) | 3140(5) | 1188(3) |
| C51 | 5177(2) | 3077(7) | 1380(4) |
| H511 | 532(2) | 319(5) | 194(3) |
| H512 | 525(2) | 402(5) | 118(3) |
| C52 | 5388(2) | 1646(7) | 1078(4) |
| H521 | 577(2) | 174(5) | 116(2) |
| H522 | 520(2) | 113(5) | 54(3) |
| O53 | 5270(2) | 327(5) | 1519(3) |
| OW1 | 0 | 262(5) | 2500 |
| OW2 | 41(2) | 237(7) | 259(2) |

[a] The coordinates are multiplied by $10^4$.

group and it was not possible to rationalize the disorder of the water molecule. The scattering factors for the neutral atoms were taken from ref. 21 and the anomalous correction terms from ref. 22. The final $R$ values were $R = 0.037$ and $R_w = 0.034$. The highest peaks in the final difference map were less than 0.3 e $Å^{-3}$. The final atomic coordinates are given in Table II.

### *Description of the Structure of Zn(thiamine)$Cl_3$·$0.4H_2O$*

The crystals of Zn(thiamine)$Cl_3$·$0.4H_2O$ are isomorphous with those of Cd(thiamine)$Cl_3$·$0.6H_2O$ (space group *C2/C*, $a = 25.86(1)$, $b = 8.528(4)$, $c = 17.779(8)$ Å, $\beta = 107.20(2)°$) [14]. Including the present work only 4 structures of complexes in which thiamine is bonded to a metal atom have been reported [14, 15, 17]. A comparison between the most relevant structural and bonding parameters observed in these complexes is shown in Table III. The crystal structure of the complex is composed of discrete Zn(thiamine)$Cl_3$ molecules and 0.4 disordered crystallization water molecules in the cell. An ORTEP view of the zinc complex is shown in Fig. 1. Bond distances and angles are reported in Tables IV and V. The coordination around zinc is distorted pseudotetrahedral with the largest angle Cl2–Zn–N1′ of 114.43(9)°, to be compared with the value 117.45(5)° measured in the cadmium derivative. The zinc–chlorine bond distances are in the normal range usually observed in other $ZnNCl_3$ complexes [23–28]. The zinc nitrogen bond distance (2.040(3) Å) is the shortest observed in $ZnNCl_3$ complexes a more common value being 2.08 Å. Only in Zn(purinium)$Cl_3$ [24] and Zn(*N*-(4′pyridyl)-4-ethoxypyridinium)$Cl_3$ [28] were zinc nitrogen distances as short as 2.05 Å observed. All of these distances are significantly shorter than those measured in the cadmium complex.

The packing of the 8 formula units forming the unit cell is shown in Fig. 2. There exists several interactions between the molecules in the unit cell. They include dipolar interactions between each of the atoms of the thiazolium ring, which is positively charged, and the chloride atoms and hydrogen bonds. Short intermolecular distances are reported in Table VI. The strongest hydrogen bonds occur between O53 and Cl3 and between Cl2 and N3′. The observed O53–Cl3 distance (3.16(2) Å) is in the range observed in other structures (3.12–3.44 Å). The observed C2–N3′ distance (3.10(1) Å) is in an extremely good agreement with that predicted by Pletcher and Sax, 3.12 Å, for the hydrogen bonding interaction of the acidic C2–H group [29].

The pyrimidine and thiazolium ring of thiamine are planar. The least-square planes passing through these groups are reported in Table VII. Pyrimidine residues from two molecules related by inversion and centering operation stack one over the other along the a axis, the amino, N41′, group of one molecule overlapping the pyrimidine group of the other. This type of stacking has been already observed and seems to be common to the metal complexes of thiamine. The distance between two parallel planes is 3.47 Å, which is 0.05 Å shorter than in the cadmium complex.

The angle between the pyrimidine and thiazolium planes is 82.2° near to the value observed in Cd(thiamine)$Cl_3$ (88.4°) [14]. Kraut and Reed [30] suggested that this angle can be of importance in the oxidation of thiamine to thiochrome and have influence on the biological function of thiamine. In

TABLE III. Relevant Structural Parameters in Metal Thiamine Complexes

| Bond distances (Å)<br>Angles (deg) | $Zn(thiamine)Cl_3$[a]<br>M = Zn | $Cd(thiamine)Cl_3$[b]<br>M = Cd | $Cu(thiamine)Cl_2$[c]<br>M = Cu |
|---|---|---|---|
| M–Cl1 | 2.270(1) | 2.444(1) | 2.2002(6) |
| M–Cl2 | 2.255(1) | 2.451(1) | 2.3366(6) |
| M–Cl3 | 2.253(1) | 2.457(1) | |
| M–N1 | 2.040(3) | 2.239(1) | 1.993(2) |
| $\phi_T$[d] | 113.4 | 112.6 | −10.1 |
| $\phi_P$[d] | 130.4 | 129.8 | −83.8 |
| Conformation[d] | *S* | *S* | *F* |
| $\phi_{5\alpha}$[d] | 45.0 | 46.5 | 14.2 |
| $\phi_{5\beta}$[d] | −67.6 | −68.8 | −60.2 |
| S–O1 | 2.878(4) | 2.879(3) | 2.913(3) |

[a]This work. [b]Ref. 14. [c]Ref. 15. [d]The conformation follows the definitions of Pletcher and Sax [30, 31].

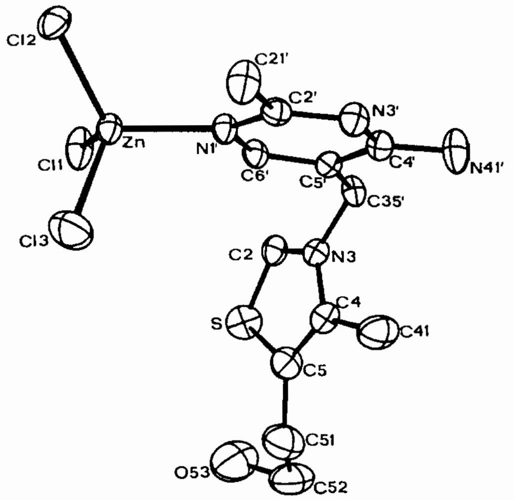

Fig. 1. ORTEP view of $Zn(thiamine)Cl_3$.

TABLE IV. Bond Distances (Å) in $Zn(thiamine)Cl_3 \cdot 0.4H_2O$

| | |
|---|---|
| Zn–Cl1 | 2.270(1) |
| Zn–Cl2 | 2.255(1) |
| Zn–Cl3 | 2.253(1) |
| Zn–N1′ | 2.040(3) |
| N1′–C6′ | 1.353(5) |
| N1′–C2′ | 1.357(5) |
| C2′–N3′ | 1.321(5) |
| C2′–C21′ | 1.483(6) |
| N3′–C4′ | 1.343(5) |
| C4′–N41′ | 1.336(6) |
| C4′–C5′ | 1.413(5) |
| C5′–C6′ | 1.360(6) |
| C5′–C35′ | 1.501(6) |
| N3–C2 | 1.323(5) |
| N3–C4 | 1.391(5) |
| N3–C35′ | 1.474(5) |
| C2–S | 1.666(4) |
| C5–S | 1.723(5) |
| C4–C41 | 1.476(6) |
| C4–C5 | 1.349(6) |
| C5–C51 | 1.511(7) |
| C51–C52 | 1.480(9) |
| C52–O53 | 1.431(8) |

the $Cu(thiamine)Cl_2$ [15] complex a much smaller angle (75.3°) was observed. Pletcher and Sax [31] suggested the use of the torsion angles $\phi_T$ and $\phi_P$ to describe the relative orientation of thiazolium and pyrimidine rings. In this structure the $\phi_T$ and $\phi_P$ angles are 113.4° and 130.4°, respectively. The conformation adopted by thiamine in this structure is quite uncommon and it is called *S* conformation. Including this work only 5 of 23 thiamine-related structures [10, 13–15, 17] so far determined are in the *S* conformation. It has been suggested that the *S* conformation should be favoured over the more common *F* conformation by the presence of substituents on C2. The present results together with the structure of $Cd(thiamine)Cl_3$ [14] and of the thiamine salt of $[CdCl_4]^{2-}$ [12] show that this is not the case.

Recently the X-ray crystal structures of $Cu(thiamine)Cl_2$ [15] and $Rh_2(acetato)_4(thiamine\ pyrophosphate)_2$ [17] have been determined. In both complexes the thiamine moieties are in *F* conformation. This can be indicative that complexation is not the leading effect in determining the *S* or *F* conformation, but that, as already suggested by Richardson [12], cooperative effects due to intermolecular interactions are of major importance.

The torsion angles defining the conformation of the β-hydroxyethyl side chain [32] are $\phi_{5\alpha} = 45.0°$ and $\phi_{5\beta} = -67.6°$, very similar to those observed in the cadmium complex. In both complexes the S–O53 contact is short and this interaction is responsible for the folding of the side chain.

Bond lengths and angles within the thiamine residue compare well with those reported for the cadmium and copper derivatives. A feature which received much attention is the C4′–N41′ bond length which was found to vary upon protonation or com-

TABLE V. Bond Angles (deg) in Zn(thiamine)$Cl_3 \cdot 0.4H_2O$

| | |
|---|---|
| Cl1–Zn–Cl2 | 112.68(5) |
| Cl1–Zn–Cl3 | 109.02(5) |
| Cl2–Zn–Cl3 | 108.59(5) |
| Cl1–Zn–N1′ | 104.51(9) |
| Cl2–Zn–N1′ | 114.43(9) |
| Cl3–Zn–N1′ | 107.4(1) |
| C2′–N1′–C6′ | 115.6(3) |
| N1′–C2′–N3′ | 124.6(4) |
| N1′–C2′–C21′ | 117.8(4) |
| C21′–C2′–N3′ | 117.6(4) |
| C2′–N3′–C4′ | 118.9(3) |
| N3′–C4′–C5′ | 120.7(4) |
| N3′–C4′–N41′ | 116.7(4) |
| N41′–C4′–C5′ | 122.5(4) |
| C4′–C5′–C6′ | 115.9(3) |
| C4′–C5′–C35′ | 123.0(4) |
| C5′–C6′–N1′ | 124.2(4) |
| C5′–C35′–N3 | 111.8(3) |
| C35′–N3–C4 | 123.9(3) |
| C35′–N3–C2 | 122.0(3) |
| C4–N3–C2 | 114.0(3) |
| N3–C4–C5 | 111.4(4) |
| N3–C4–C41 | 119.8(4) |
| C41–C4–C5 | 128.6(4) |
| C4–C5–S | 110.9(3) |
| C4–C5–C51 | 127.3(4) |
| C51–C5–S | 121.7(3) |
| C5–S–C2 | 93.3(2) |
| S–C2–N3 | 112.4(3) |
| C5–C51–C52 | 114.1(4) |
| C51–C52–O53 | 107.1(6) |

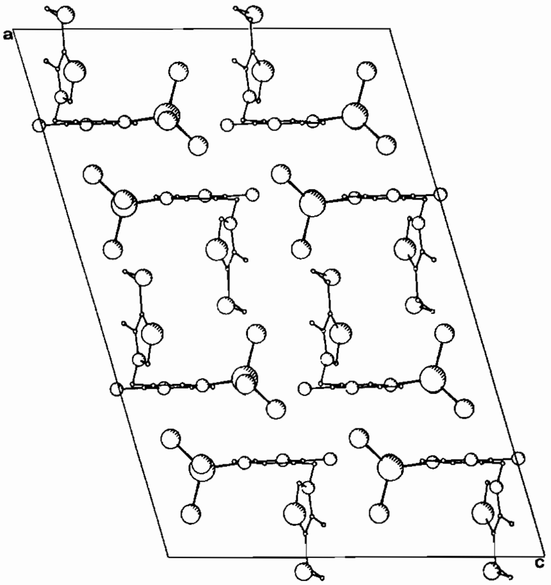

Fig. 2. Schematic view of the contents of a unit cell of Zn(thiamine)$Cl_3 \cdot 0.4H_2O$. The view is down $b$. The disordered water molecules are not shown for clarity purposes.

plexation. In the present structure this distance is 1.336(6) Å comparable with that found in the free base and in the copper complex (1.334(5) Å and 1.339(3) Å respectively) and slightly shorter than those observed in the cadmium complex (1.346(3) Å). This result definitely shows that the effect of

TABLE VI. Possible Hydrogen Bonding Interactions, A–H···B, and other Short Contacts

| A | B | Equivalent position for B | A–B (Å) | A–H–B (deg) |
|---|---|---|---|---|
| Hydrogen bonds | | | | |
| N41′ | Cl1 | $x, 1-y, z-1/2$ | 3.473(4) | 170(4) |
| N41′ | Cl2 | $x, 2-y, z-1/2$ | 3.468(4) | 149(3) |
| C2 | N3′ | $x, y-1, z$ | 3.10(1) | 118(2) |
| Other interactions | | | | |
| C21′ | Cl1 | $x, y, z$ | 3.628(5) | |
| C6′ | Cl1 | $x, y, z$ | 3.416(4) | |
| C35′ | Cl1 | $x, 1-y, z-1/2$ | 3.556(5) | |
| C21′ | Cl1 | $1/2-x, y-1/2, 1/2-z$ | 3.74(8) | |
| C21′ | Cl2 | $x, y, z$ | 3.62(4) | |
| N3 | Cl2 | $x, 1-y, z-1/2$ | 3.70(9) | |
| C35′ | Cl2 | $x, 1-y, z-1/2$ | 3.50(4) | |
| C2 | Cl2 | $x, 1-y, z-1/2$ | 3.52(3) | |
| C6′ | Cl2 | $1/2-x, -1/2+y, 1/2-z$ | 3.74(4) | |
| C35′ | Cl2 | $1/2-x, -1/2+y, 1/2-z$ | 3.57(4) | |
| C2 | Cl2 | $1/2-x, -1/2+y, 1/2-z$ | 3.620(6) | |
| O53 | Cl3 | $1-x, y-1, 1/2-z$ | 3.17(2) | |
| C41 | Cl3 | $1-x, y, 1/2-z$ | 3.73(3) | |
| C52 | Cl3 | $1-x, y-1, 1/2-z$ | 3.797(7) | |
| N3 | Cl3 | $x, 1-y, z-1/2$ | 3.67(5) | |

*(continued)*

TABLE VI. *(continued)*

| A | B | Equivalent position for B | A–B (Å) | A–H–B (deg) |
|---|---|---|---|---|
| C4 | Cl3 | $x, 1 - y, z - 1/2$ | 3.441(8) | |
| C41 | Cl3 | $x, 1 - y, z - 1/2$ | 3.84(2) | |
| C5 | Cl3 | $x, 1 - y, z - 1/2$ | 3.57(5) | |
| S | O53 | $x, y, z$ | 2.88(2) | |
| OW1 | O53 | $x - 1/2, 1/2 + y, z$ | 3.05(3) | |
| OW2 | O53 | $x - 1/2, 1/2 + y, z$ | 3.08(4) | |

TABLE VII. Best Weighted Least-Squares Planes

| Plane 1 | | Plane 2[a] | |
|---|---|---|---|
| Deviation from planes (Å) | | | |
| N1′ | −0.001(2) | S | −0.0003(6) |
| N3′ | 0.001(2) | N3 | 0.001(1) |
| C2′ | 0.003(2) | C2 | −0.001(1) |
| C4′ | −0.008(2) | C4 | −0.001(1) |
| C5′ | 0.009(2) | C5 | 0.001(1) |
| C6′ | −0.007(2) | C35′ | −0.02 |
| C21′ | 0.05 | C41 | −0.03 |
| C35′ | 0.03 | | |
| N41′ | 0.03 | | |

Parameters defining planes

| | Plane 1 | Plane 2 |
|---|---|---|
| $\sigma^b$ | 0.007 | 0.001 |
| A[c] | 25.039 | −2.529 |
| B | 0.465 | 1.151 |
| C | −0.349 | 7.219 |
| D | 8.343 | 0.063 |

[a] The angle between planes 1 and 2 is 82.2°. [b] Mean deviation from the plane. [c] The equation of the plane is $Ax + By + Cz = D$ in monoclinic coordinates as defined in ref. 33.

complexation contrast with those of protonation which causes a shortening of the C4′–N41′ bond.

## Conclusions

The thiamine molecule forms a stable complex with zinc(II). This complex is the first one so far reported with thiamine coordinated to a first row transition metal complex in the +2 oxidation state. This result supports the postulated mechanism of action of thiamine which requires the formation of a complex with divalent metal ions like magnesium(II) or manganese(II) [1, 2].

The present complex confirms that zinc(II) is bound to thiamine. This result is important since zinc(II) is one of the most common essential elements in nature, it serves as required prostetic groups in active sites and/or as coenzymes for indispensable metalloenzymes or metal-ion actived enzymes. The zinc complex is rather similar to the cadmium one, the main differences being in the Zn–Cl and Zn–N bond distances which are shorter than those observed in the Cd complex. In both complexes the thiamine assumes the *S* conformation. In this conformation the active site on the thiazolium ring is in one of the most exposed positions possible for reaction with the substrate. In the generally more stable *F* form the active site is shielded by the pyrimidine ring.

The *S* conformation of thiamine in the present complex is quite uncommon since it is found only in 5 of the 23 thiamine related structures [10, 13–15, 17]. The understanding of the factors which determine the conformation of thiamine could play a key role in the clarification of enzymic processes. Clearly more crystallographic studies are necessary to understand the nature of the metal coordination and to clarify the electronic effects on the thiamine base.

## Supplementary Material

Listings of the thermal parameters for the non-hydrogen atoms and of hydrogen atom coordinates (Table SI) and of observed and calculated structure factors are available as Supplementary Material.

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