

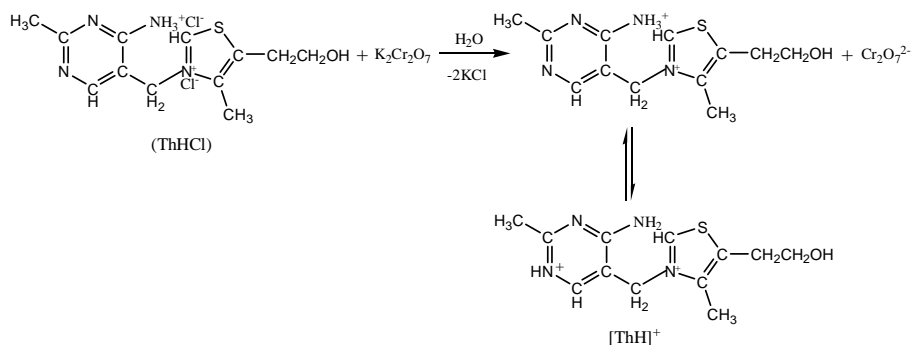
## INTERACTION OF THIAMINE.HCl WITH $\text{Cr}_2\text{O}_7^{2-}$ ION

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### ABSTRACT

The reaction of thiamine.HCl (ThHCl) with  $\text{K}_2\text{Cr}_2\text{O}_7$  has been studied in aqueous solution at room temperature. The compound obtained is ionic 1 : 1 in which thiamine is present as a cation and  $\text{Cr}_2\text{O}_7^{2-}$  as an anion. The chemical formula of the salt,  $(\text{C}_{12}\text{H}_{18}\text{N}_4\text{OS})(\text{Cr}_2\text{O}_7)$  (symbolically ThHCr<sub>2</sub>O<sub>7</sub>), has been established by elemental analysis, IR and UV/Vis spectra, magnetic measurement, thermal analysis, conductivity measurement, cyclic voltammetric study and X-ray diffraction analysis.



Key words: Thiamine, Thiazolium ion, Pyrimidine, Cyclic voltammetry, Glassy carbon electrode

### INTRODUCTION

Thiamine and its derivatives play an important role in many biological processes. The pyrophosphate ester of thiamine (Vitamin B<sub>1</sub>) is the coenzyme of many enzymes e.g. carboxylase, transketolase etc., catalyzing the decarboxylation of  $\alpha$ -ketoacids or the formation of  $\alpha$ -ketols (Hadjiliadis and Markopoulos 1981, Breslow and McNelis 1959). A detailed study showed that the mechanism of the enzymatic action of thiamine (vitamin B<sub>1</sub>) enzymes is based mainly on the bivalent transition metal complexes of thiamine, conformation of the ligand and its derivatives (Malandrinos *et al.* 2000). For many years attempts to prepare metal complexes of thiamine with bivalent metals resulted, in the formation of ionic salts of the type  $[\text{ThH}]^{2+}[\text{MX}_4]^{2-}$  ( $\text{M} = \text{Zn}^{2+}, \text{Co}^{2+}, \text{Cd}^{2+}, \text{Hg}^{2+}$ ) (Schellenberger 1967, Talbert *et al.* 1970, Richardson *et al.* 1975, Adegboye 1981),

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$[\text{ThH}]^{2+}([\text{MX}_3])_2$  ( $\text{M} = \text{Pt}^{2+}, \text{Pd}^{2+}$ ) (Hadjiliadis *et al.* 1977) and  $([\text{Th}]^+)_2[\text{MX}_4]^{2-}$  ( $\text{M} = \text{Pt}^{2+}, \text{Pd}^{2+}$ ) (Hadjiliadis *et al.* 1977, Hu *et al.* 2001, Louloudi *et al.* 1994) without direct metal-ligand bonding. This is due to the net positive charge on thiamine and to the easily protonation of the ring N1' site of pyrimidine (Louloudi *et al.* 1990). Nevertheless, in recent years a few metal complexes of thiamine with  $\text{M}^{2+}$  ( $\text{M} = \text{Mn}, \text{Zn}, \text{Cd}, \text{Pt}, \text{etc.}$ ) containing mainly a M-N1' direct bonding were prepared and their structures were determined (Louloudi *et al.* 1990). Delocalization of the net positive charge on N3 of the thiazolium moiety to the sulfur atom also favors the formation M-N1' bond for the bivalent metal complexes (Hadjiliadis *et al.* 1991, Louloudi and Hadjiliadis 1991, Louloudi *et al.* 1992, Pletcher and Sax 1972). Recently (Hu *et al.* 2005) it was found that thiaminium cation interact with the polymeric halogenocadmate anions and formed organic-inorganic hybrid compounds. It was also claimed (Hadjiliadis *et al.* 1977) that Pt(II) and Pd(II) formed metal complexes through M-S linkage of the thiazolium ring of thiamine. In our present study, attempt was taken to look at the course of the reaction of thiamine hydrochloride with aqueous solution of  $\text{K}_2\text{Cr}_2\text{O}_7$ .

#### MATERIALS AND METHODS

Thiamine hydrochloride was procured from BDH, England and used as obtained. Potassium dichromate ( $\text{K}_2\text{Cr}_2\text{O}_7$ ) used in this experiment was collected from Aldrich, USA. All solvents such as methanol, ethanol, acetone, benzene and hexane were procured from E. Merck, Germany.

A melting point apparatus (model SMP11) equipped with a thermometer of capacity of recording the temperature up to  $250^\circ\text{C}$  was used for the determination of melting point of the compound. The infrared spectrum (IR) of the compound was recorded on a Shimadzu Infrared Spectrometer, model IR-470, in the range of 400 – 4000/cm using KBr pallets. The UV-visible spectrum was recorded using a Shimadzu UV-visible recording spectrometer; model UV-160A, in the wavelength range of 200 - 1100 nm using water as the solvent. Magnetic susceptibility measurement was done by the Sherwood Scientific Magnetic Susceptibility Balance, model Magway MSB MK1. The quasi-static thermogravimetric analysis (QSTG) was carried out in a carbolite calibrated muffle furnace of the type CWF 11/5. Conductance of the compound was recorded using a conductivity meter, model CM-55. Cyclic voltammetric measurement was performed using Computerized Electrochemical System, Model HQ-2040, developed by Advanced Analytics, USA. The X-ray powder diffraction was recorded in a Philips PW-1830 X-ray generator with XDC-700 Gunier Hagg focusing camera using Nickel filtered  $\text{CuK}_\alpha$  radiation ( $\lambda = 1.54098 \text{ \AA}$ ).

Equimolar amounts of aqueous solutions of thiamine hydrochloride and  $\text{K}_2\text{Cr}_2\text{O}_7$  (2 mmol in 10 ml) were prepared separately. The two solutions were mixed together and

filtered to remove insoluble impurities. The clear mixed solution was left overnight at room temperature for crystallization. Orange-red needle shaped crystals of thiaminium dichromate were obtained. The product was filtered, washed and dried in air. Melting point 85-90°C (dec). Yield 59.6%.

IR bands,/cm: 3400(w), 3220 - 3020(w, br), 1675(w), 1640(s), 1604(s), 1530(s, br), 1470(w), 1420(w, br), 1380(s), 1240(s), 1224(s), 1200(m), 1070(m), 1045(s), 991(m), 935(s), 867(s, sh), 748(s), 580(m), 540(s), 461(s), 430(m).

## RESULTS AND DISCUSSION

The prepared compound was stable both in air and to light. It was soluble in water but insoluble in common organic solvents suggesting its ionic character. The chromium content of the compound, determined by iodometric method (20.05%) agreed well with the theoretically calculated value (21.58%) of the proposed formula,  $\text{C}_{12}\text{H}_{18}\text{N}_4\text{O}_8\text{Cr}_2\text{O}_7$ .

The **stoichiometry** of the above compound was studied by Job's method. In this method, absorbances of a series of thiamine.HCl- $\text{K}_2\text{Cr}_2\text{O}_7$  mixtures of continuously varied molar ratios were measured by keeping the total number of moles constant in the mixtures. Absorbances of the solutions of free thiamine, free metal salt, and the mixtures were measured at 238 nm (Table 1).

**Table 1. The absorbance data of thiamine.HCl,  $\text{K}_2\text{Cr}_2\text{O}_7$ , and their mixtures.**

Mixture ratio	Absorbance of ThHCl solution ( $A_L$ ), nm	Absorbance of $\text{Cr}_2\text{O}_7^{2-}$ solution ( $A_M$ ), nm	Absorbance of ThHCl- $\text{Cr}_2\text{O}_7^{2-}$ solution ( $A_{L+M}$ ), nm	Absorbance difference (A), nm	Mole fraction of ligand $X_L$
1:9	0.106	0.046	0.432	0.280	0.099
2:8	0.204	0.086	0.495	0.205	0.199
3:7	0.308	0.126	0.572	0.138	0.299
4:6	0.418	0.156	0.638	0.064	0.399
5:5	0.521	0.210	0.711	0.020	0.500
6:4	0.635	0.193	0.789	0.039	0.600
7:3	0.732	0.291	0.860	0.163	0.700
8:2	0.814	0.345	0.938	0.221	0.800
9:1	0.906	0.360	1.017	0.249	0.900

Subtraction of the absorbance of free ligand ( $A_L$ ) and free metal salt ( $A_M$ ) from the mixtures ( $A_{M+L}$ ) at various mole fractions yielded the absorbance difference, which were plotted against the mole fraction of thiamine.HCl in the mixtures. The stoichiometry of the compound was then determined from the plot (Fig. 1). The plot in Fig. 1 showed that the stoichiometry of the prepared salt is 1 : 1, i.e.  $[\text{ThH}]^{2+}[\text{Cr}_2\text{O}_7]^{2-}$ .

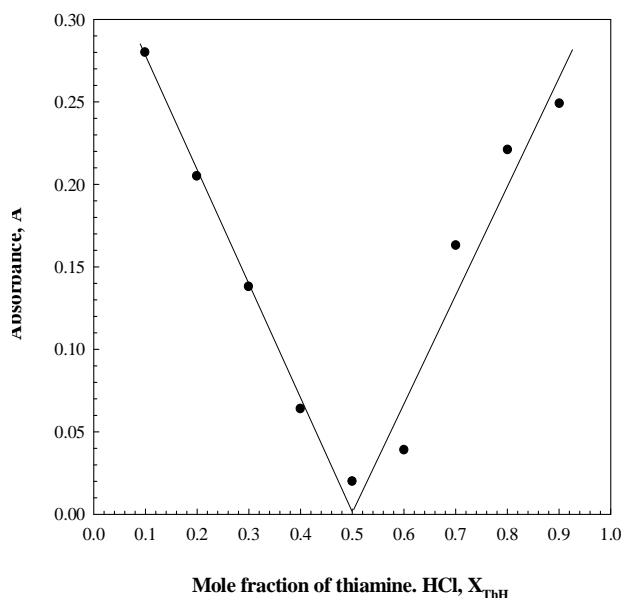


Fig. 1. A plot of absorbance vs. mole fraction of thiamine. HCl

Both ThHCl and ThHCr<sub>2</sub>O<sub>7</sub> compounds showed a broad absorption band in the region of 3475-2895 cm<sup>-1</sup> for -OH, -NH<sub>2</sub> and -CH stretching motions. Characteristic aromatic ring vibrations in the region of 1680-1380 cm<sup>-1</sup> were observed from the complete interactions of C=C, C=N and C=S vibrations. The bands due to the  $\nu(C=NH^+)$  stretching appeared at 1635 and 1640 cm<sup>-1</sup> for ThHCl and ThHCr<sub>2</sub>O<sub>7</sub> respectively which indicated that the N1' site of the pyrimidine ring nitrogen of thiamine moiety in both the compounds was protonated. In the thiaminium dichromate compound two strong peaks were observed at 580 and 430 cm<sup>-1</sup> due the Cr=O stretching and O-Cr-O deformation, respectively.

The UV-Visible spectrum of the compound was recorded in aqueous medium. Two strong characteristics bands at 286 and 345 nm were observed. The band at 286 nm is attributed to  $\pi \rightarrow \pi^*$  and  $n \rightarrow \pi^*$  electronic transitions of heteroaromatic moiety present in the thiaminium cation. Due to the charge transfer from O<sup>2-</sup> to Cr(VI), aqueous solution of dichromate(VI) ion is orange yellow in color. This transition appeared as a broad band at 345 nm in the spectrum of thiaminium dichromate.

The magnetic susceptibility of thiaminium dichromate was measured. It was negative, about  $-52.935 \times 10^{-8}$  cm<sup>3</sup>/g, suggesting the diamagnetic behavior of the compound. It was likely because Cr<sup>6+</sup> is a d<sup>0</sup> ion.

QSTG method was used to study the thermal behavior of the compound. Fig. 2 showed that the decomposition process started at temperature 100°C and about 34.5% of its original weight was lost up to 200°C. After that the decomposition process is nearly

continuous and the residue left at  $550^\circ\text{C}$  was identified as  $\text{Cr}_2\text{O}_3$  (green powder, observed wt. 30.06% and calculated wt. 31.51%).

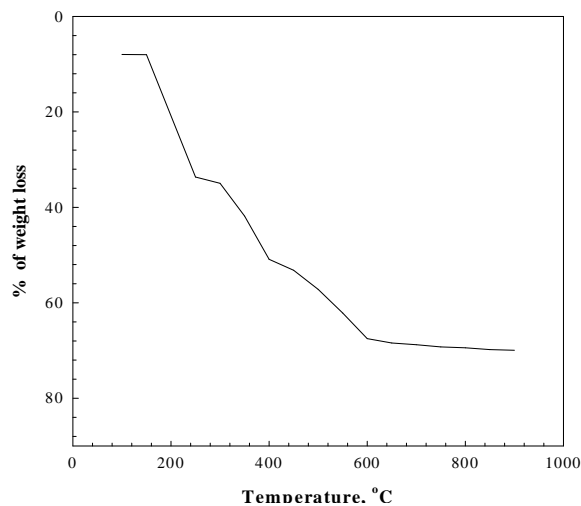


Fig. 2. QSTG for thiaminium dichromate.

The conductivity of thiaminium dichromate in aqueous medium at different concentrations was measured. The molar conductance of the compound increased with the increase of dilution as in Fig. 3 indicating that the compound underwent ionic dissociation in water.

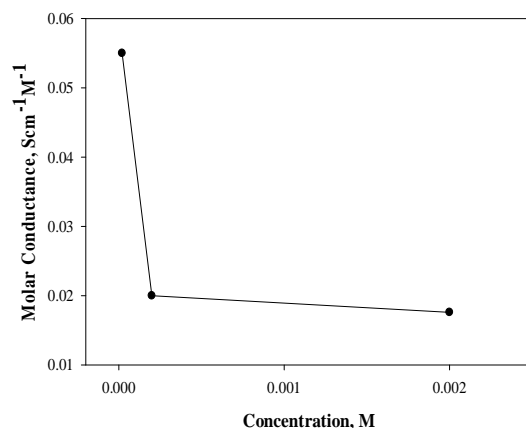


Fig. 3. Variation of molar conductance with concentration of thiaminium dichromate at  $24^\circ\text{C}$ .

The electrochemical behaviour of 2.00 mM  $\text{K}_2\text{Cr}_2\text{O}_7$  in 0.2 M HCl medium at GCE within the potential window of 1200 mV to - 600 mV was investigated. A typical voltammogram with a scan rate of 100 mV/s is shown in Fig. 4. It showed a cathodic peak, at about 240.51 mV. This corresponded to the reduction of Cr(VI) to Cr(III). A

broad hump also appeared at the cathodic region at higher scan rate. Absence of its anodic counterpart might suggest that Cr(VI) underwent electrochemically irreversible reduction in acidic solution at GCE.

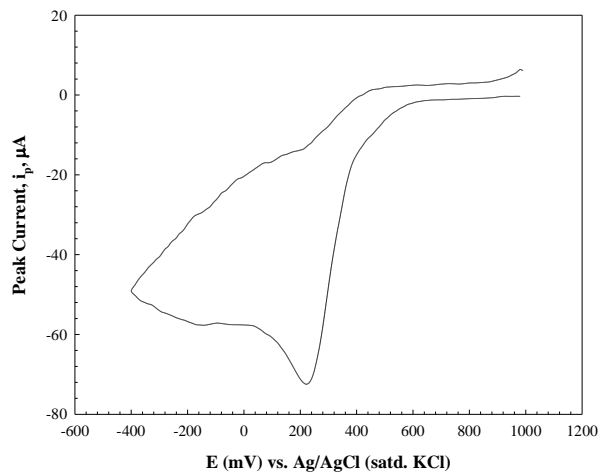


Fig. 4. Cyclic voltammogram of 2.0 mM  $K_2Cr_2O_7$  in 0.2 M HCl at GCE with scan rate of 100 mV/s.

A series of voltammograms of 2.0 mM  $K_2Cr_2O_7$  in HCl medium at various scan rates were recorded and it is shown in Fig. 5. The cathodic peak current linearly increases with the increase of scan rate.

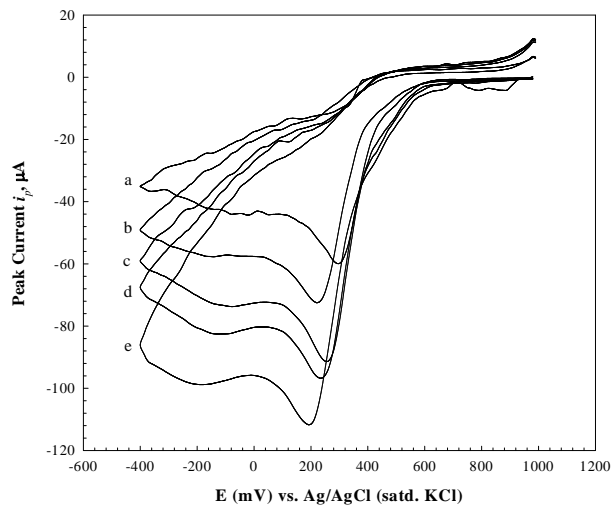


Fig. 5. Cyclic voltammograms of 2.0 mM  $K_2Cr_2O_7$  in HCl medium at GCE with scan rate of (a) 50, (b) 100, (c) 150, (d) 200 and (e) 300 mV/s.

The peak position of the cathodic peak slightly shifted towards the negative potential with the increase of scan rate. This result suggests that the electrode process is diffusion controlled in this medium.

Fig. 6 depicted the voltammogram of 2.0 mM  $\text{ThHCr}_2\text{O}_7$  solution with a scan rate 100 mV/s at GCE. It also showed a sharp cathodic peak at about 340.0 mV which resulted from the reduction of Cr(VI) to Cr(III). Whilst the absence of corresponding anodic peak in the potential range studied indicated an irreversible reduction reaction.

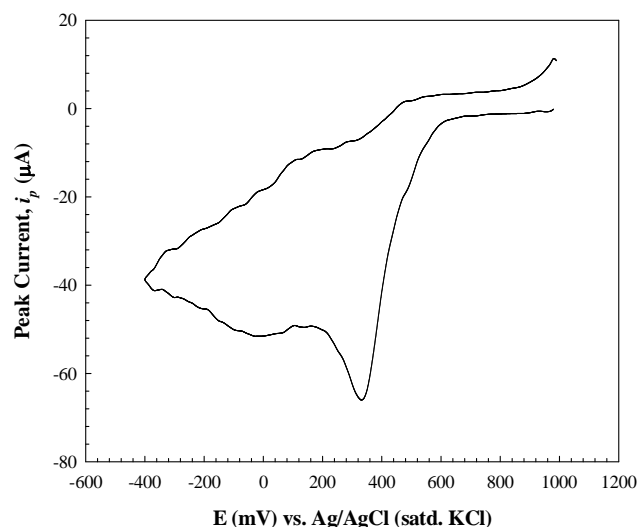


Fig. 6. Cyclic voltammogram of 2.0 mM  $\text{ThHCr}_2\text{O}_7$  in HCl at GCE with scan rate of 100 mV/s.

The presence of thiaminium cation might influence the rate of hexavalent chromium reduction, reorganized by the shifting of the peak potential from 240.51 mV in  $\text{K}_2\text{Cr}_2\text{O}_7$  to 340.0 mV in thiaminium dichromate. This could be explained by the fact that the adsorbed thiaminium cation on the electrode surface might inhibit the reduction process.

**Table 2. X-ray powder diffraction data for the thiaminium dichromate.**

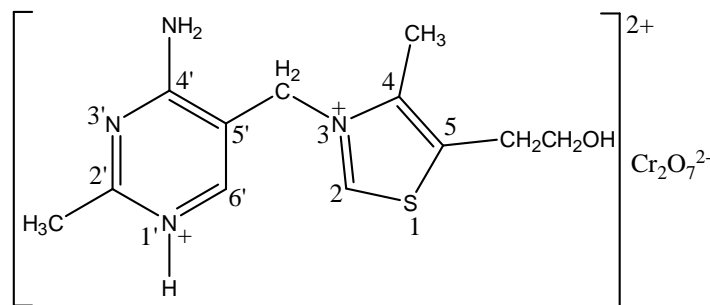
Compound	Relative intensity	$\ell$ , mm	$2\theta$ , degrees	d (calculated), Å
$(\text{C}_{12}\text{H}_{18}\text{N}_4\text{OS})(\text{Cr}_2\text{O}_7)$	m	25	14.1668	6.2470
	s	28	15.8668	5.5809
	w	35	19.8336	4.4728
	s	37	20.9670	4.2335
	vw	45	25.5004	3.4902
	w	47	26.6338	3.3442

m = medium, s = strong, w = weak, vw = very weak.

The X-ray powder diffraction of the prepared thiaminium dichromate compound was recorded photographically on a film and a series of lines were obtained from the primary beam. The interplanar spacing, d values were calculated and gathered in Table 2.

This compound showed only a few lines indicating that either it belongs to a high symmetry crystal system or it does not diffract well.

From the results described and discussed in this paper, the most probable structure suggested for the compound is given below:



Probable structure of thiaminium dichromate.

## CONCLUSION

The reaction of ThHCl and  $K_2Cr_2O_7$  yielded a salt like compound,  $ThHCr_2O_7$  with no direct metal-thiamine bonding. The net positive charge on the thiazolium nitrogen and to the easy protonation of the ring N1' site of pyrimidine in acid medium favors the formation of ionic salt rather than metal complexes of thiamine.

## REFERENCES

- Adegboye, A. O. 1981. Synthesis and characterization of novel vitamin B<sub>1</sub> metal complexes, *Inorg. Chem. Acta* **55**: 177.
- Breslow, R. and E. McNelis. 1959. Studies on model systems for thiamine action. Synthesis of reactive intermediates, and evidence on the function of the pyrimidine ring. *J. Am. Chem. Soc.* **81**: 3080.
- Hadjiliadis, N., J. Markopoulos, G. Pneumatikakis, D. Katakis and T. Theophanides. 1977. Interaction of thiamine and its phosphate esters with Pt(II) and Pd(II), *Inorg. Chim. Acta* **25**: 21.
- Hadjiliadis, N. and J. Markopoulos. 1981. "Vitamin B<sub>1</sub>", (Isolation, preparation, properties, mechanism of catalytic action). *Chim. Chron. (New Series)*. **10**: 1.
- Hadjiliadis, N., M. Louloudi and I. S. Butler. 1991. Infrared and Raman spectra of 2-( $\alpha$ -hydroxybenzyl)thiamine, 2-( $\alpha$ -hydroxycyclohexylmethyl)thiamine, their protonated forms and their complexes with zinc(II), cadmium(II) and mercury(II), *Spectrochim. Acta Part A: Molecular Spectroscopy* **47**(3-4): 445.
- Hu, N. -H., K. Aoki, A. O. Adeyemo and G. N. Williams. 2001. Metal ion and anion coordination in the thiamine- $[PtII(NO_2)_4]^{2-}$  system. Structures of a metal complex,  $Pt(thiamine)(NO_2)_3$ , and two salts,  $(H-thiamine)[Pt(NO_2)_4] \cdot 2H_2O$  and  $(thiamine\ monophosphate)_2[Pt(NO_2)_4] \cdot 2H_2O$ , *Inorg. Chim. Acta* **325**(1-2): 9.
- Hu, N. -H., H. -Q. Jia, J. -W. Xu and K. Aoki. 2005. Interactions of thiamine with polymeric halogenocadmium anions in the organic-inorganic hybrid compound (thiaminium)  $[Cd_3Br_{4.4}Cl_{3.6}]$ . *Acta Cryst.* **C61**: m538.



- Louloudi, M., N. Hadjiliadis, J. P. Laussac and R. Bau. 1994. Transition and group IIB metal complexes with active aldehyde derivatives of thiamine. *Metal Based Drugs* **1**: 221.
- Louloudi, M., N. Hadjiliadis, J. A. Feng, S. Sukumar and R. Bau. 1990. Interaction of Zn<sup>+2</sup>, Cd<sup>+2</sup> and Hg<sup>+2</sup> with 2-(hydroxybenzyl) thiamine and 2-(hydroxycyclohexylmethyl)thiamine. The crystal structure of the complex Hg(2-hydroxybenzyl)thiamine. *J. Am. Chem. Soc.* **112**(20): 7233.
- Louloudi, M. and N. Hadjiliadis. 1991. Interaction of Co<sup>II</sup>, Ni<sup>II</sup> and Cu<sup>II</sup> with the active aldehyde derivatives of thiamine, 2-(hydroxybenzyl) thiamine = HBT and 2-(hydroxycyclo-methyl) thiamine = HCMT. *J. Chem. Soc. Daltons Tans.* 1635.
- Louloudi, M., N. Hadjiliadis and I. S. Butler. 1992. Solution versus solid state conformation of IIB group metal complexes of the active aldehyde derivatives of thiamine, *J. Chem. Soc. Dalton Trans.* 1401.
- Malandrinos, G., K. Dodi, M. Louloudi and N. Hadjiliadis. 2000. On the mechanism of action of thiamin enzymes in the presence of bivalent metal ions. *J. Inorg. Biochem.* **79**: 21.
- Pletcher, J. and M. Sax. 1972. Crystal and molecular structure of thiamine pyrophosphate hydrochloride. *J. Am. Chem. Soc.* **94**(11): 3998.
- Richardson, M. F., K. Franklin and D. M. Thompson. 1975. Reactions of metals with vitamins. I. Crystal and molecular structure of thiaminium tetrachlorocadmate monohydrate. *J. Am. Chem. Soc.* **97**(11): 3204.
- Schellenberger, A. 1967. Structure and mechanism of action of the active center of yeast pyruvate decarboxylase. *Angew. Chem.* **6**: 1024.
- Talbert, P. T., J. A. Weaver and P. Hambright. 1970. Zinc(II) and cobalt(II) halide interactions with vitamin B<sub>1</sub> and certain N-substituted thiazolium salts. *J. Inorg. Nucl. Chem.* **32**(7): 2147.

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