

SYNTHESIS, STRUCTURAL AND BIOLOGICAL ACTIVITY OF Cr(III), Mn (II), Cd(II) AND Hg(II) COMPLEXES OF 2-N(4,N,N-DIMETHYLBENZYLIDEN) 5(P-METHOXY PHENYL) 1,3,4-THIODIAZOLE

M.F.Alis, S.M.Khamas and M.K.Salman

**Department of Chemistry, College of Science for Women, University of Baghdad
Baghdad–Iraq.**

Abstract

The Schiff base, 2N-(4,N,N-dimethylbenzyliden) 5(P-methoxy phenyl)-1,3,4-thiodiazole, and their metal complexes Cr(III), Mn (II), Cd(II), and Hg(II), were synthesized. The prepared complexes were identified and their structural geometries were suggested by using flame atomic absorption technique, FTIR, and Uv-Vis spectrophotometry, in addition to magnetic susceptibility and conductivity measurements. The study of the nature of the complexes formed in ethanol solution, following the mole ratio method, gave results which were compared successfully with those obtained from isolated solid state studied. The antibacterial activity for the ligand and its metal complexes were studied against two selected micro – organisms (*Staphylococcus aureus*) as gram positive and (*Pseudomonas aeruginosa*) as gram negative.

Introduction

Schiff bases and their metal complexes have received a great deal of attention during the last decade from many workers to prepare new sets of these bases and their transition metal complexes [1,2]. These complexes have proven to be antitumor and have carcinostatic activity [2,3]. The pathway of Schiff bases is involved in the metabolism of Aflatoxin, produced by the fungi *Aspergillus flavus*, which grows on peanuts, is an extremely potent carcinogen capable of inducing liver cancer. It inhibits both replication and transcript of DNA [4]. Schiff bases are well known to have pronounced biological activities [5]. And, on the other side, have a great importance in biological reaction like visual process [6], and in the reaction that involve removing the amine group by enzyme effect (enzymatic transition reaction) and some B₆-catalysed reaction [7]. Many of the physiologically active compounds of Schiff base found applications in treatment of several diseases [8,9]. The biological activity of Schiff bases is attributed to the formation of stable chelates with transition metal ions presents in cells [10].

Experimental

A-Materials, Physical Measurements and Analysis

All chemicals were of highest purity and were used as received. Melting points were recorded on Gallenkamp melting point apparatus and were uncorrected. FTIR spectra were recorded using FTIR (IR 8400 shimadzu) in the range of 4000-200cm⁻¹ and samples were measured as CsI disc. Electronic spectra were obtained using (UV-160 shimadzu) spectrophotometer at room temperature, using ethanol as a solvent. The metal content was estimated using atomic absorption spectrophotometer. Conductivity measurement were obtained using (HANNA EC (214)) conductometer, these measurements were obtained in DMSO solvent using 10⁻³M concentration at 25°C. Magnetic susceptibility measurements were performed at 25°C on the solid state applying Faraday's method using Bruker BM₆ instrument.

B-Preparation the Compounds

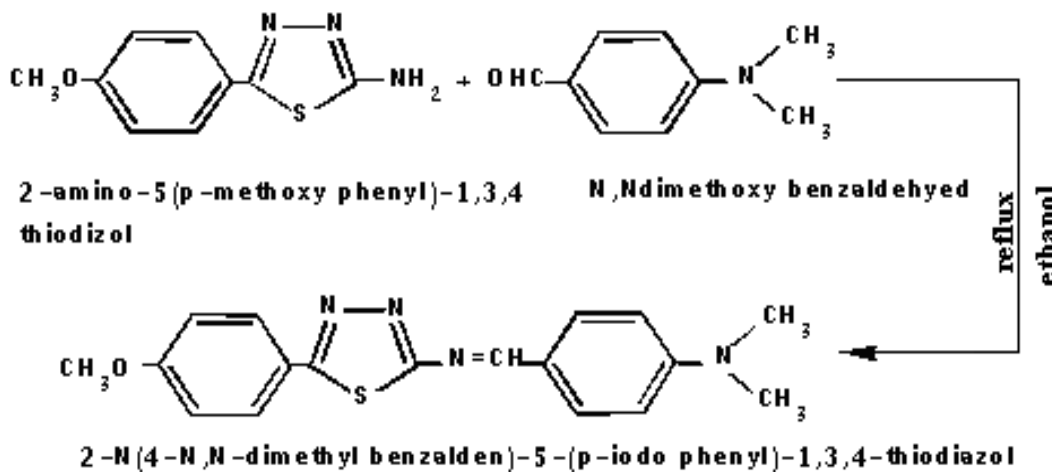
1-Preparation of the Ligand

The method that was used to prepare the 2-amino -5 (P-methoxy phenyl)-1,3,4-thiodiazole was reported elsewhere [11]. The Schiff base (L) was prepared according to the following:-

(5.17g ,0.05 mmole) from above starting material compound was dissolved in 15 ml of absolute ethanol and N,N-dimethyl benzyldehyde (3.7g,0.05 mmole) in 10 ml of the same solvent was added ,with drop of glycial acetic acid, the reaction mixture was refluxed for four hours ,after that ,the mixture was cooling at room temperature, then ,left

overnight in a refrigerator ,the separated solid was filtered and crystallized from ethanol. The physical properties of this ligand was listed in Table (1).

The suggested structural of the ligand can be shown in this scheme.



2-Preparation of Complexes

One general procedure was adoped,as follows: The salts of ($\text{CrCl}_3 \cdot 6\text{H}_2\text{O}$, $\text{Cd}(\text{NO}_3)_2 \cdot 4\text{H}_2\text{O}$, $\text{MnCl}_2 \cdot 4\text{H}_2\text{O}$ and HgCl_2) were dissolved in ethanol and added to ethanolic solution of Schiff base in (1:2) mole ratio with stirring .The mixture was heated under reflux for four hours. During this period the precipitation was completed form. The precipitate was then collected by filtration, washed with ethanol and dried under vaccum.All these complexes were analyzed by using different available techniques; the physical properties of these compounds are listed in Table (1).

C-Study ofComplex Formation in Solution

Complexes of the Schiff base with metal ions were studied in solution using ethanol as a solvent ,in order to determined [M:L] ratio in the complex following molar ratio method [12].A series of solution were prepared having a constant concentration 10^{-4}M of metal ion and the ligand. The [M: L] ratio was determined from the relationship between the absorption of the absorbed light and the mole ratio of [M/L].The results of complexes formation in solution were listed in Table (1).

D-Bacteriological Method

Bactericidal activity of the Schiff base and its chromium, manganese, cadmium and mercury complexes were evaluated against representative gram-positive and gram-negative bacteria by agar-plate method[13]. All the drugs were prepared freshly by dissolving them in DMSO to obtain a final concentration of 10 mM and 5 mM .All bacteria were cultivated in nutrient agar. The results are shown in Table (4).

Results and Discussion

A-Chemistry

Stable complexes were isolated in all cases, based on the metal analytical data, spectroscopic study, conductivity and magnetic moments measurements ,the general formula of the complexes can be depicted as $[\text{ML}_n\text{Cl}_m]\text{Y} \cdot \text{H}_2\text{O}$, where, $n = 2,2$ - $m = 0,2$ and $\text{Y} = 2\text{NO}_3, \text{Cl}$ for both Cd and Cr ions respectively and $[\text{M}_2\text{L}_4\text{Cl}_n]\text{Cl}_x$, where $n = 4,2$ - $x = 0,2$ for Mn and Hg ions respectively.

Schiff base (L) is a potential ligand which may act as mono or bidentate as it is illustrated by its structure shown in the scheme .So it expected that IR measurements are highly information with respect to in the complexation behavior with various metal

ions. The characteristic frequencies of the free ligand and its metal complexes were readily assigned based on comparison with literature references [14-17]. A broad band was observed around 3400-3430 cm^{-1} in the spectra of chromium, manganese and cadmium complexes, assigned as ν_{OH} suggested the presence of water molecule. The IR spectral data of all complexes are listed in Table (2).

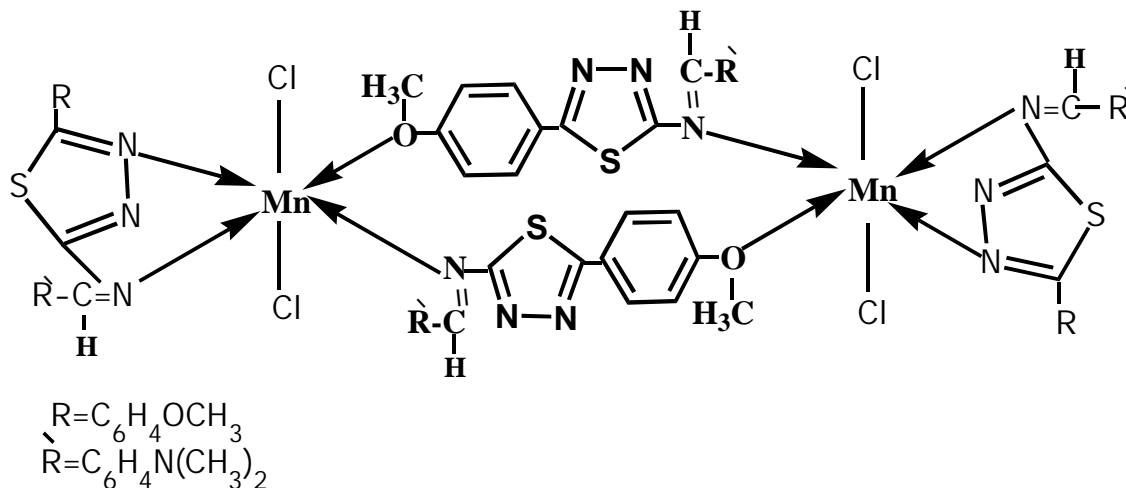
There is no appreciable change took place in the absorption of $\nu_{\text{s}}(\text{COC})$ and $\nu_{\text{as}}(\text{COC})$ modes and $\nu(\text{Ar-N})$ mode in the monomeric cadmium and chromium complexes, and dimeric mercury complex, which excluded the possibility oxygen and nitrogen atoms of the methoxy and aryl amine groups participation in coordination. Furthermore there is a change in frequency and intensity of $\nu_{\text{C=N}}$ and $\nu_{\text{N-N}}$ bonds, this behavior refers to coordinate modes of the ligand through nitrogen of isothane group and nitrogen moiety of the thiodiazole ring. Another behavior coordinate of this ligand can be shown in dimeric manganese complex, i. e through oxygen of methoxy group and nitrogen of isomethane as

a bridge, and other behavior of the ligand took place as a bidentate through nitrogen of isomethane and nitrogen of thiodiazole ring with this complex.

These observations were further supported by the appearance frequencies of $\nu_{\text{M-N}}$, $\nu_{\text{M-Cl}}$ respectively.

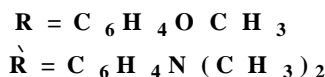
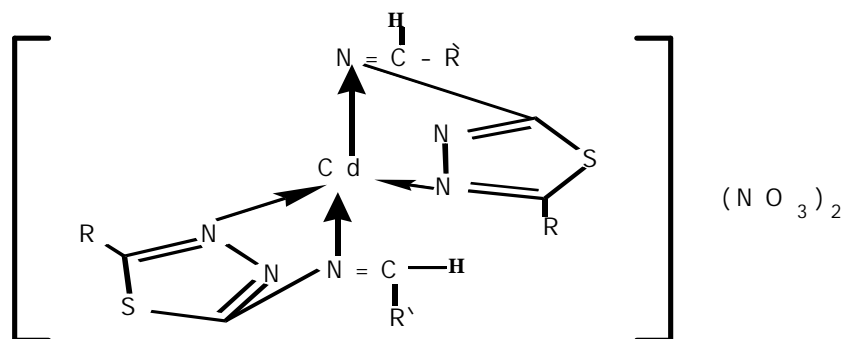
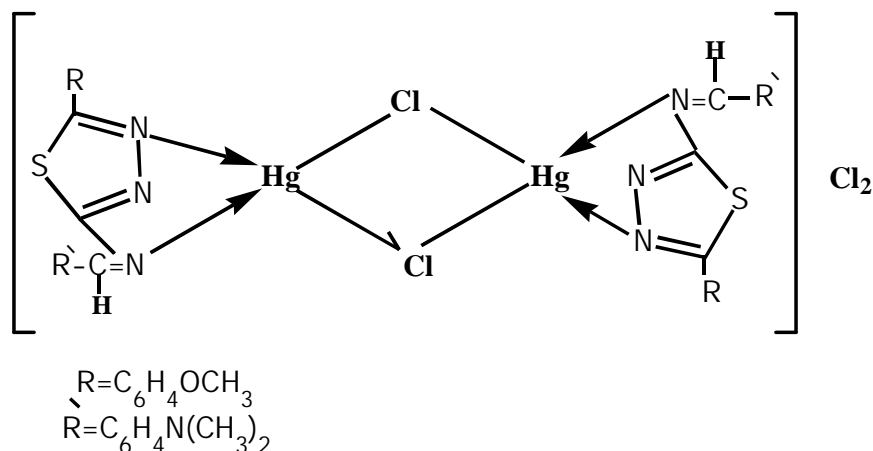
The manganese (II) complex showed a series of very weak and narrow bands have been observed spectra, this is expected because the only sextet term of the d^5 configuration in octahedral stereochemistry is the 6A_1g . Consequently, there can be no spin-allowed transition [18, 19], and were assigned to ${}^6A_1g \rightarrow {}^4T_1g(G)$, ${}^6A_1g \rightarrow {}^4T_2g(G)$ and ${}^6A_1g \rightarrow {}^4T_1g + {}^4Eg$ respectively [20].

The value of ligand field, Racah parameters have been calculated based on T.S. diagram, Table (3), the value of β (0.94) signifies a fair amount of ionic character [21]. Magnetic moment of the solid complex (5.79 BM) showed a high spin Mn(II) complex [20, 22]. Conductivity measurement showed the complex was non ionic. The proposed structure can be shown as follow:-



While cadmium and mercury ions behave similarly with respect to their coordination number, which may be to 2, 4, 5 or 6, and the most probable is the 4 coordination number [23, 20]. Since the metal d^{10} orbital for Zn group is completely filled, the complexes containing these metals are expected to be diamagnetic with zero magnetic moment value. The conductivity measurement showed

that these complexes were ionic. The proposed structures of the prepared these complexes are as follow:-



B-Solution Study

Molar ratio method was carried out to determine the M: L ratio. The result of complexes in ethanol solution, suggest that the metal to ligand ratio was (1:2), which are dimeric in nature for manganese complexes and (1:1) for dimeric mercury, and then which were comparable to these obtained from isolated solid study, Table (1).

C-Bactericidal activity

Preliminary screening experiments to detect the in vitro activity of the ligand and its metal complexes Table (4) the following points were concluded:-

1. The result reflected that the donor base, showed that there is no significant activity against *Pseudomonas aeruginosa* and *Staphylococcus aureus* bacteria, when we used high and low concentrations.
2. The result of antibacterial activities of manganese complex, showed that there's no effect toward the studied bacteria when we used high and

low concentrations, while the chromium complex, exhibited anti bacterial activity only toward *Staphylococcus aureus* bacteria when we used high and low concentrations.

3. Generally, the study of antibacterial activities revealed that the d^{10} configuration (Cd and Hg) complexes, exhibited highly significant activity against the studied bacteria rather than that observed for any of the remainder complexes especially for mercury complex, when we used high and low concentrations.
4. Biological evaluation of considerable number of these compounds have been maintained, and they were found to exhibit the expected synergic effect of activity, this attributed to the impact of the compound and the metal present in these complexes.

Table (1)
Physical data for the ligand and its metal complexes.

Comp.	Colour	M.P. °C	Yield	Atomic Abs.found (cal.)	Molar Ratio M:L	Formula Structure
L	Orange	114	90%	-	-	C ₁₈ H ₈ N ₄ SO
CrL	Brown	284d	62%	6.00 (6.37)	1:2.2	[CrL ₂ Cl ₂].H ₂ O
MnL	Brick-red	200d	55%	7.38 (7.06)	1:2.2	[Mn ₂ L ₄ Cl ₄].H ₂ O
CdL	orange	220	85%	10.43 (10.91)	1:2	[CdL ₂](NO ₃) ₂ .H ₂ O
HgL	orange	140	77%	-	1:1	[Hg ₂ L ₂ Cl ₂]Cl ₂

d:decomposed

Table (2)
most diagnostic FT-IR bands for the Ligand and its metal complexes.

Comp.	ν_{OH}	$\nu_{(C=N)}$ iso	ν_{NCS}	ν_{CSC}	ν_{CS}	$\nu_{(C=N)r}$ ing	ν_{NCN}	ν_{N-N}	ν_{Ar-N}	ν_{COC}	ν_{M-N}	ν_{M-Cl}
L	-	1658	1051 1120	1164	732	1589 1527	1373	1442	1311	1249 1033	-	-
CrL	3400	1650	1064 1112	1168	732	1604 1535	1373	1481	1310	1252 1029	-	-
MnL	-	1620	1049 1112	1168	732	1595 1535	1368	1485	1310	1262 1025	510	472
CdL	3430	1650	1060 1118	1166	733	1604 1542	1373	1460	1311	1250 1029	525	-
HgL	-	1648	1060 1110	1168	732	1598 1530	1373	1481	1310	1250 1030	350	310

Table (3)
Electronic spectra, conductance and magnetic moment, for metal complexes of schiff base.

Comp.	Band cm ⁻¹	Assignment	B	B'	β	10Dq	μ_{eff} B.M	μ_s cm ⁻¹
CrL	17.543 22.727 26.315	${}^4A_2g \rightarrow {}^4T_2g(F)$ ${}^4A_2g \rightarrow {}^4T_1g(F)$ ${}^4A_2g \rightarrow {}^4T_1g(P)$	918	840	0.91	16.355	3.30	42
MnL	18.181 22.624 26.178	${}^6A_1g \rightarrow {}^4T_1g(G)$ ${}^6A_1g \rightarrow {}^4T_2g(G)$ ${}^6A_1g \rightarrow {}^4T_1g + {}^4Eg$	860	810	0.94	11.055	5.79	31
CdL	25.125 27.173 31.347	ILCT					0.00	20
HgL	24.390 16.526 32.679	ILCT					0.00	58

ILCT: Internal Ligand Charge Transfer

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Table (4)
Antibacterial activities for the Schiff base and its metal complexes.

Comp.	<i>Staphylococcus aureus</i>		<i>Pseudomonas aeruginosa</i>	
	5mM	10mM	5mM	10mM
L	-	-	-	-
CrL	+	+	-	-
MnL	-	-	-	-
CdL	+	+	+	+++
HgL	++++	++++	++++	++++

(-) = No inhibition = inactive

(+) = (0.4-1)mm=Slightly active

(++) = (1- 1.6)mm= Moderately active

(+++)= (1.6- 2.2)mm= active

(++++)= (2.2-2.8)mm= Highly active

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الخلاصة

يتضمن البحث تحضير قاعدة شف N,N_4N-2 ثنائي مثيل بنزولين (5 (1,4-ميثوكسي فنيل) 4,3,1-ثايوديازول كالكاند لتحضير عدد من المعقدات الجديدة مع بعض الايونات الانتقالية الثنائية التكافؤ (كادميوم، منغنيز، الزئبق) وثلاثية التكافؤ كالكروم . تم عزل المعقدات المحضرة وتشخيصها باستخدام التقنيات الطيفية كالامتصاص الذري اللهي والاشعة تحت الحمراء والاشعة فوق البنفسجية- المرئية فضلا عن قياسات التوصيلية الكهربائية والحساسية المغناطيسية. تم كذلك دراسة طبيعة المعقد المتكون في محلول الايثانول باتباع طريقة النسبة المولي، وقد اعطت هذه الدراسة نتائج متطابقة تقريبا مع تلك التي تم الحصول عليها في الحالة الصلبة المعزولة. تم تقويم الفعالية المضادة للبكتريا للكاند ومعقداته واختير نوعان من البكتريا (*Staphylococcus aureus*) موجبة الصبغة و (*Pseudomonas aeruginosa*) سالبة الصبغة في وسط زراعي متعادل.