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 4000-200 cm\(^{-1}\) 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\(^{-3}\) M concentration at 25\(^\circ\)C. Magnetic susceptibility measurements were performed at 25\(^\circ\)C on the solid state applying Faraday's method using Bruker BM\(_6\) 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:-
(5.17 g, 0.05 mmole) from above starting material compound was dissolved in 15 ml of absolute ethanol and N,N-dimethyl benzyldehyde (3.7 g, 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-Prepartion of Complexes

One general procedure was adopted, as follows: The salts of (CrCl$_3$, 6H$_2$O, Cd(NO$_3$)$_2$.4H$_2$O, MnCl$_2$.4H$_2$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 of Complex 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 [ML$_n$Cl$_m$]Y. H$_2$O, where, n = 2, m = 0.2 and Y = 2NO$_3$Cl for both Cd and Cr ions respectively and [M$_2$L$_4$Cl$_n$]Cl$_x$, where n = 4, 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 \(\nu\)\(_{\text{OH}}\) suggested the presence of water molecule. The IR spectral data of all complexes are listed in Table (2).

There is no appreciable change that took place in the absorption of \(\nu\)\(_{\text{as}}\)(COC) and \(\nu\)\(_{\text{as}}\)(COC) modes and \(\nu\) (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 \(^6A_1g \rightarrow ^4T_1g\), \(^6A_1g \rightarrow ^4T_2g\), \(^6A_1g \rightarrow ^4T_1g\) + \(^4Eg\) respectively [20].

The value of ligand field, Racah parameters have been calculated based on T.S.digram, Table (3). The value of \(\beta\) (0.94) signifies a fair amount of ionic character [21]. Magnetic moment of the solid complex (5.79BM) 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:-

![Diagram](image_url)

\[R = \text{C}_6\text{H}_4\text{OCH}_3\]
\[\hat{R} = \text{C}_6\text{H}_4\text{N(CH}_3)_2\]

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 form isolated solid study, Table (1).

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 significate 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 effected towarded the studied bacteria when we used high and low concentrations, while the chromium complex, exhibited anti bacterial activity only towarded 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 signification 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 compound 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.

<table>
<thead>
<tr>
<th>Comp.</th>
<th>Colour</th>
<th>M.P. °C</th>
<th>Yield</th>
<th>Atomic Abs. found (cal.)</th>
<th>Molar Ratio M:L</th>
<th>Formula Structure</th>
</tr>
</thead>
<tbody>
<tr>
<td>L</td>
<td>Orange</td>
<td>114</td>
<td>90%</td>
<td>-</td>
<td>-</td>
<td>C_{18}H_{20}N_{4}SO</td>
</tr>
<tr>
<td>CrL</td>
<td>Brown</td>
<td>284d</td>
<td>62%</td>
<td>6.00 (6.37)</td>
<td>1:2.2</td>
<td>[CrL_{2}Cl_{2}Cl.H_{2}O]</td>
</tr>
<tr>
<td>MnL</td>
<td>Brick-red</td>
<td>200d</td>
<td>55%</td>
<td>7.38 (7.06)</td>
<td>1:2.2</td>
<td>[Mn_{2}L_{4}Cl_{4}].H_{2}O</td>
</tr>
<tr>
<td>CdL</td>
<td>orange</td>
<td>220</td>
<td>85%</td>
<td>10.43 (10.91)</td>
<td>1:2</td>
<td><a href="NO_%7B3%7D">CdL_{2}</a><em>{2}.H</em>{2}O</td>
</tr>
<tr>
<td>HgL</td>
<td>orange</td>
<td>140</td>
<td>77%</td>
<td>-</td>
<td>1:1</td>
<td>[Hg_{2}L_{2}Cl_{2}]Cl_{2} d:decomposed</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Comp.</th>
<th>V_{OH}</th>
<th>V_{(C\equiv N)}</th>
<th>V_{NCS}</th>
<th>V_{CSC}</th>
<th>V_{CS}</th>
<th>V_{(C\equiv N)_{ir}}</th>
<th>V_{NCN}</th>
<th>V_{N-N}</th>
<th>V_{Ar-N}</th>
<th>V_{OC}</th>
<th>V_{M-N}</th>
<th>V_{M-Cl}</th>
</tr>
</thead>
<tbody>
<tr>
<td>L</td>
<td>-</td>
<td>1658</td>
<td>1051 1120</td>
<td>1164</td>
<td>732</td>
<td>1589 1527</td>
<td>1373</td>
<td>1442</td>
<td>1311</td>
<td>1249 1033</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>CrL</td>
<td>3400</td>
<td>1650</td>
<td>1064 1112</td>
<td>1168</td>
<td>732</td>
<td>1604 1535</td>
<td>1373</td>
<td>1481</td>
<td>1310</td>
<td>1252 1029</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>MnL</td>
<td>-</td>
<td>1620</td>
<td>1049 1112</td>
<td>1168</td>
<td>732</td>
<td>1595 1535</td>
<td>1368</td>
<td>1485</td>
<td>1310</td>
<td>1262 1025</td>
<td>510</td>
<td>472</td>
</tr>
<tr>
<td>CdL</td>
<td>3430</td>
<td>1650</td>
<td>1060 1118</td>
<td>1166</td>
<td>733</td>
<td>1604 1542</td>
<td>1373</td>
<td>1460</td>
<td>1311</td>
<td>1250 1030</td>
<td>350</td>
<td>310</td>
</tr>
<tr>
<td>HgL</td>
<td>-</td>
<td>1648</td>
<td>1060 1110</td>
<td>1168</td>
<td>732</td>
<td>1598 1530</td>
<td>1373</td>
<td>1481</td>
<td>1310</td>
<td>1250 1030</td>
<td>350</td>
<td>310</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Comp.</th>
<th>Band cm^{-1}</th>
<th>Assignment</th>
<th>B</th>
<th>B'</th>
<th>β</th>
<th>10Dq</th>
<th>μ_{eff} B.M</th>
<th>μ s cm^{-1}</th>
</tr>
</thead>
<tbody>
<tr>
<td>CrL</td>
<td>17.543 22.727 26.315</td>
<td>4 A_{2}g \rightarrow 4 T_{2}g_{(F)}</td>
<td>918</td>
<td>840</td>
<td>0.91</td>
<td>16.355</td>
<td>3.30</td>
<td>42</td>
</tr>
<tr>
<td>MnL</td>
<td>18.181 22.624 26.178</td>
<td>6 A_{1}g \rightarrow 4 T_{1}g_{(G)}</td>
<td>860</td>
<td>810</td>
<td>0.94</td>
<td>11.055</td>
<td>5.79</td>
<td>31</td>
</tr>
<tr>
<td>CdL</td>
<td>25.125 27.173 31.347</td>
<td>ILCT</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HgL</td>
<td>24.390 32.679</td>
<td>ILCT</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ILCT: Internal Ligand Charge Transfer
Table (4)

Antibacterial activities for the Schiff base and its metal complexes.

<table>
<thead>
<tr>
<th>Comp.</th>
<th>Staphylococcus aureus 5mM</th>
<th>Staphylococcus aureus 10mM</th>
<th>Pseudomonas aeruginosa 5mM</th>
<th>Pseudomonas aeruginosa 10mM</th>
</tr>
</thead>
<tbody>
<tr>
<td>L</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>CrL</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>MnL</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>CdL</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td>HgL</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
</tr>
</tbody>
</table>

(-) = 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

References

الخلاصة

يتنتم البحث تحضير قاعدة شف-2)N,N(N4)-N(ثنائي ميثيل بنزيلين (5 (1,4- ميثوكسي فنيل)3,4- ثيوديزول كالياكاد لتحضير عدد من المعقدات الجديدة مع بعض الأيونات الانتقالية الثنائية الكافؤ (كوديميوم، مغنيزيوم، الزئبق) وثلاثية الكافؤ كالكروم. تتم عزل المعقدات المحضرة وتشخيصها باستخدام التقنيات الطيفية كالامتصاص الذري الليلي والاشعة تحت الحمراء والأشعة فوق البنفسجية. 

المتطلبة: قضاة قياسات التوصيلية الكهربائية والحساسية المغناطيسية. تم كذلك دراسة طبيعة المعقد المتكون في حلول الالثانول باتباع طريقة النسبة المولية. وقد أعطت هذه الدراسة نتائج متطابقة تتراوح بين تلك التي تم الحصول عليها في الحلحة الصلبة المعززة. تم تكوين الفعالية المضادة للكرياناميد ومعادتاته واختبار نوعان من البكتيريا (Staphylococcus aureus) و (Pseudomonas aeruginosa) وسالبة الصبغة في وسط زراعي متعادل.