

SYNTHESIS AND CHARACTERIZATION AND STUDY OF THE BIOLOGICAL ACTIVITY OF SOME NEW METAL COMPLEXES OF 2-HYDROXY BENZYLEDENE-5-(2-ACETILOXYPHENYL)-1,3,4-THIADIAZOLE.

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Abstract

New metal complexes of the ligand 2-Hydroxy benzyledene-5-(2-acetyloxyphenyl)-1,3,4-thiadiazole with the metal ions Cr (III), Fe(III), Co(II), Ni(II) and Cu(II), were prepared in alcoholic medium.

The prepared complexes were characterized by FTIR and electronic spectroscopy, electric conductivity and magnetic susceptibility measurements. Formation complexes in solution were studies in Molar ratio and continuous variation methods, which gave comparable result with those obtained from solid state study. Monomer structures for the complexes were proposed. The newly metal complexes were subjected to *in vitro* testing against pathogenic microorganisms. The results obtained revealed that these complexes showed measurable activity against bacteria.

Introduction

Increasing physiological importance of nitrogen and sulphur donor organic compounds⁽¹⁾ and active role played by certain metal ions coordinated to them⁽²⁾ have been interested us in synthesizing and studying structural aspects of metal complexes with some sulphur and nitrogen donor ligands⁽³⁻⁸⁾.

The 1,3,4- thiadiazole nucleus is associated with a variety of pharmacological actions, such as fungicidal^(9,10), and leishmanicides⁽¹¹⁾ activities. These activities are probably due to the presence of the N=C-S group. In particular, the 1,3,4-thiadiazole derivatives showed these activities⁽¹²⁻¹⁸⁾. Substituted thiadiazoles have been reported to display diverse applications as oxidation inhibitor, cyanic dyes and metal complexing agents⁽¹⁹⁾. Metal complexes of 1,3,4-thiadiazole moiety have been used as antifungal⁽¹⁾, photographic layer stabilizers⁽²⁰⁾, and other applications.

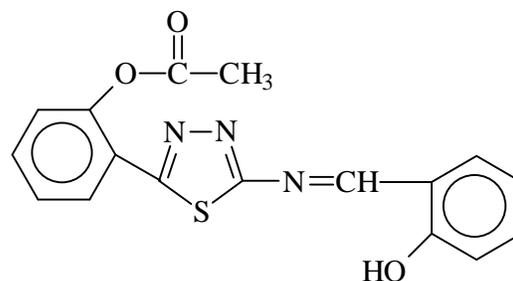
The wide range of application of the ligand and its metal complexes are used our interest to prepare a new series of some of those metal complexes.

Experimental

All chemical used were of reagent grade (supplied by either Merck or fluka) and used as supplied. The FTIR spectra in the range (4000-200) cm^{-1} were recorded as cesium

iodide disc on FTIR.8300 Shimadzu Spectrophotometer. The Uv-visible spectra were measured in ethanol using Shimadzu uv-vis. 160A, Ultra-violet Spectrophotometer in the range (200-1000) nm. Magnetic susceptibility measurements for complexes were obtained at room temperature using (Magnetic Susceptibility Balance) Johnson Matthey catalytic systems division. Gallencamp M.F.B600.01F melting point apparatus were used to measure the melting point of all the prepared compounds. Conductivity measurement by using Coring Conductivity Meter 220. Elemental microanalysis was carried out using CHNOS elemental analyzer model 5500Carlo-Erba instruments (Italy).

Synthesis of the ligand: 2-Hydroxy benzyledene -5- (2-acetyloxyphenyl)-1,3,4 -thiadiazole (L):



(L)

A mixture of 2-acetyl salicylic acid (0.01 mol), thiosemicarbazide (0.01 mol), and phosphorus oxychloride (5 ml), was refluxed for five hour. After cooling, water was added (25 ml). The mixture then was refluxed for (4 hr) and filtered. The solution was neutralized with potassium hydroxide after that the product was dissolve in absolute ethanol and refluxed for (3 hr) after adding *ortho*-hydroxyl formaldehyde in presences of two drop of glacial acetic acid. The precipitate was filtered and washed with distilled water and recrystallized from ethanol to give the ligand (L).

Preparation of complexes

Addition of an aqueous solution of the metals salt ($\text{NiSO}_4 \cdot 6\text{H}_2\text{O}$, $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$, $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$, $\text{CrCl}_3 \cdot 6\text{H}_2\text{O}$ & $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$) to an ethanol solution of (L) in 2:1 (ligand: metal) molar ratios. After stirring for half an hours, crystalline different colored precipitates and formed at room temperature, the resulting solid was filtrated off, washed with distilled water and recrystallized from ethanol and dried at 50°C .

Results and Discussion

able (1) shows the decomposition point, color, metal percentage by atomic absorption and electronic absorption bands for ligand and complexes. The bands are classified into three distinct groups: The intermolecular transitions appear in the uv region, charge transfer from ligand to metal, and d-d transitions appear in the visible region. These transitions are assigned in relevant to the structures of complexes, and also shown in Table (1).

The infrared data are shown in Table (2). The Table lists the stretching frequency (ν) for some of the characteristics groups exhibited by the ligand and complexes.

The formation of these complexes was confirmed by monitoring the changes both in location and intensity of the certain bands. In the free ligand, the band at $(1614)\text{ cm}^{-1}$ is assigned to the stretching of C=N. On complexation, this band is shifted to a lower frequency region. This shift is probably due to the lowering of bond order of the carbon-nitrogen bond resulted from complexation of the metal to the ligand through nitrogen. A

broad band appeared in range of $(3400-3500)\text{ cm}^{-1}$ assigned to -OH stretching of outer sphere water molecules. Stretching of metal nitrogen bonds of the complexes appeared in low frequency region $(362-437)\text{ cm}^{-1}$.

The molar ratio method and method of continuous variation were followed to detect the ratio of metal ion to ligand of complex. Ethanol was used as a solvent. The [M]/ [L] ratio was found 1:2 to all complexes. The values of magnetic moment in Table (4) supported the suggested structures.

Biological Activity

With a view to explore the possibility of obtaining biologically useful compounds that contain 1,3,4- thiadizole ring system⁽²⁰⁻²³⁾, such biological activity prompt us to prepare some new series containing the above mentioned unite. The antimicrobial activity of these compounds was determined by the agar diffusion method⁽²⁴⁾ used were *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa* and *Candida albicans*.

In this method a standard 5mm diameter sterilized filter paper disc impregnated with the compound (1 mg per 1 ml of acetone) was placed on an agar plate seeded with the test organism. The plates were incubated for 24 hours at 37°C . The zone of inhibition formed was measured in mm and are represented by (+). (+ +), (+ + +) depending upon the diameter and clarity, Table (5).

Table (1)
Some physical data and electronic spectra for ligand and complexes in ethanol solvent.

No.	Symbol	Dec. Point ^o C	Color	M% Calc	M% Found	Absorption Bands (nm)	Assigned Transition
1	L	208	White	-	-	260	$\pi \rightarrow \pi^*$
						285	$n \rightarrow \pi^*$
2	CuL	185	Green	8.39	8.11	250	$\pi \rightarrow \pi^*$
						271	$n \rightarrow \pi^*$
						305	Charge Transfer
						660	${}^2E_g \rightarrow {}^2T_{2g}$
3	CoL	236	blue	7.83	7.6,0	225	$\pi \rightarrow \pi^*$
						243	$n \rightarrow \pi^*$
						299	Charge Transfer
						342	${}^4T_{1g}^{(F)} \rightarrow {}^4T_{1g}^{(P)}$
4	NiL	244	Pale green	7.80	7.88	920	${}^4T_{1g} \rightarrow {}^4A_{2g}$
						244	$\pi \rightarrow \pi^*$
						285	$n \rightarrow \pi^*$
						308	Charge Transfer
5	CrL	291	Gray	6.36	6.12	835	${}^3A_{2g} \rightarrow {}^3T_{1g}^{(P)}$
						918	${}^3A_{2g} \rightarrow {}^3T_{1g}^{(F)}$
						241	$\pi \rightarrow \pi^*$
						264	$n \rightarrow \pi^*$
6	FeL	126	Brown	6.80	6.50	305	Charge Transfer
						475	${}^4A_{2g} \rightarrow {}^4T_{1g}$
						595	${}^4A_{2g} \rightarrow {}^4T_{1g}$
						690	${}^4A_{2g}^{(F)} \rightarrow T_{1g}^{(P)}$
						225	$\pi \rightarrow \pi^*$
						290	$n \rightarrow \pi^*$
						304	Charge Transfer
						503	${}^5T_{2g} \rightarrow {}^5E_g$

Table (2)
The characteristic IR bands for ligand and its complexes.

No.	Symbol	$\nu(C=N)$	$\nu(O-H)$	$\nu(M-N)$
1	L	1614(s)	3500(s)	-
2	CuL	1608(s)	3300(b)	362(s)
3	CoL	1607(s)	3310(b)	432(s)
4	NiL	1606(s)	3374(b)	433(s)
5	CrL	1605(s)	3390(b)	431(s)
6	FeL	1606(s)	3380(b)	437(s)

Table (3)
Conductivity measurement in DMF solvent.

No.	Symbol	Conductivity $\mu\text{s.cm}^{-1}$
1	L	12
2	CuL	22
3	CoL	19
4	NiL	30
5	CrL	25
6	FeL	29

Table (4)

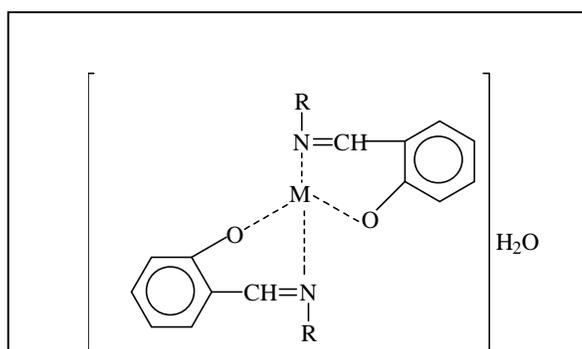
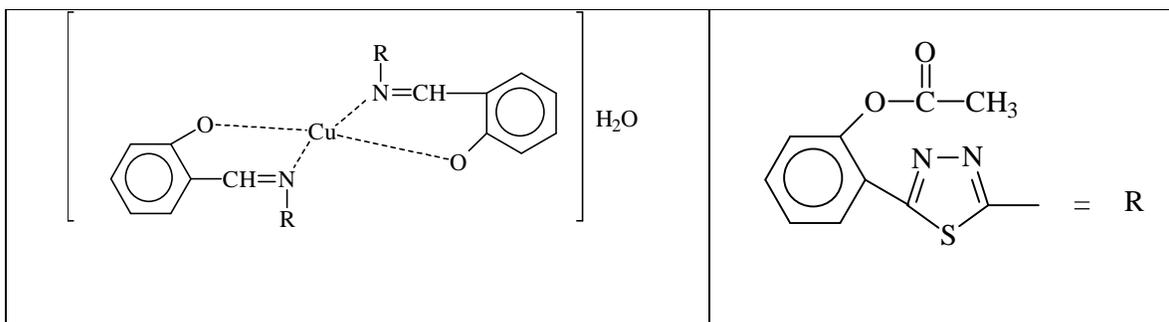
No.	Symbol	Suggested Molecular Formula	Name	Magnetic Moment (B.M)	Suggested Structure
1	L	$\text{C}_{17}\text{H}_{13}\text{N}_3\text{SO}_3$	2-Hydroxy benzylidene-5-(2-acetyloxyphenyl)-1,3,4-thiadiazole	-	-
2	CuL	$[\text{Cu}(\text{L})_2]\cdot\text{H}_2\text{O}$	[Bis(2-Hydroxy benzylidene -5- (2-acetyloxyphenyl)-1,3,4 -thiadiazole)Copper(II)] Hydrate	0.85	Square Planner
3	CoL	$[\text{Co}(\text{L})_2]\cdot\text{H}_2\text{O}$	[Bis(2-Hydroxy benzylidene -5- (2-acetyloxyphenyl)-1,3,4 -thiadiazole) Cobalt(II)] Hydrate	5.15	Tetrahedral
4	NiL	$[\text{Ni}(\text{L})_2]\cdot\text{H}_2\text{O}$	[Bis(2-Hydroxy benzylidene -5- (2-acetyloxyphenyl)-1,3,4 -thiadiazole) Nickel(II)] Hydrate	4.44	Tetrahedral
5	CrL	$[\text{Cr}(\text{L})_2\text{Cl}_2]\cdot\text{H}_2\text{O}$	[Bis(2-Hydroxy benzylidene -5- (2-acetyloxyphenyl)-1,3,4 -thiadiazole)dichloro Chromium(III)] Hydrate	5.65	Octahedral
6	FeL	$[\text{Fe}(\text{L})_2\text{Cl}_2]\cdot\text{H}_2\text{O}$	[Bis (2-Hydroxy benzylidene -5- (2-acetyloxyphenyl)-1,3,4 -thiadiazole)dichloro Ferric(III)] Hydrate	4.10	Octahedral

Table (5)
Antibacterial activity of the ligand and their complexes.

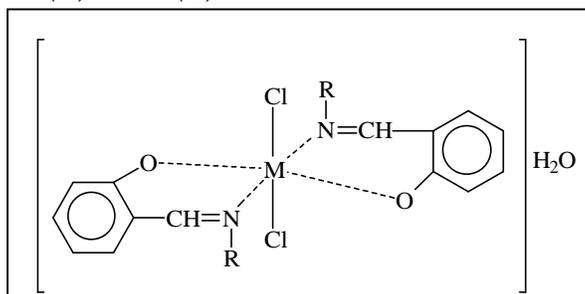
Comp. Symbol	Staphylococcus aureus	Escherichia coli	Pseudomonas aeruginosa	Candida albicans
L	+	+++	-	-
CuL	+	+++	+	++
CoL	+	+++	++	+
NiL	++	++	++	+
CrL	+	+++	+++	++
FeL	++	+++	++	+

Note (-) = no inhibition, (+) = (5-10) mm, (++) = (11-20) mm, (+++) = more than (20)mm.

On the basis of the preceding discussion, the structure of the complexes may be suggested as follows:



Where $M = Ni(II)$ and $Co(II)$



Where $M = Cr(III)$ and $Fe(III)$

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الخلاصة

تم تحضير معقدات جديدة لليكاند 2-هيدروكسي بنزليدين-5-(2-اسيتوكسيفنيل)-4,3,1- ثايودايازول مع الايونات الفلزية التالية: الكروم والحديد والكوبلت والنحاس والنيكل وفي وسط كحولي.

شخصت المعقدات المحضرة بتقنية الاطياف تحت الحمراء المعززة بتحويلات فورير (FTIR) والامتصاصات الإليكترونية والتوصيلية الكهربائية والحساسية المغناطيسية. تم قياس النسب المولية المستمرة والمتغيرة في المحلول فأعطت نتائج مطابقة مع تلك التي تم الحصول عليها في الحالة الصلبة. حيث تم اقتراح شكل هندسة الوحدة الأساسية للمعقدات المحضرة.

تم تقييم الفعالية البايولوجية للمعقدات الجديدة المحضرة ضد انواع منتخبة من البكتريا (خارج الجسم) وقد دلت النتائج المستحصلة بان لهذه المعقدات فعالية جيدة ضد البكتريا.