

Synthesis, Spectroscopic, Thermodynamic and Biological Activity Studies of Schiff base and Metal Complexes derived from 2-[(1H-Pyrrol-2-ylimino methyl)]- 5-(2-hydroxy-phenyl)-[1,3,4-thiadiazol]

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Abstract

New metal complexes of type $M_2(HL)_2 \cdot 4H_2O$ ($M = Co(II), Ni(II)$ and $Cu(II)$) were prepared using the ligand (HL) = 2-[(1H-Pyrrol-2-ylimino methyl)]- 5-(2-hydroxy-phenyl)-[1,3,4-thiadiazol]. The Schiff bases were condensed from [1H-Pyrrole-2-carbaldehyde] with [2-amino-5-(2-hydroxy-phenyl)-1,3,4-thiadiazole] in alcoholic medium. The prepared complexes were characterized by FTIR, UV-vis, 1H -NMR and mass spectra as well as magnetic susceptibility measurements, thermal analysis. The activation thermodynamic parameters, such as ΔE^* , ΔH^* , ΔS^* and ΔG^* are calculated from the TGA curve using Coats-Redfern method. From the spectral measurements, structures for the complexes were proposed. Preliminary in vitro tests for antimicrobial activity show that all prepared compounds display good activity to *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa* and *Candida albicans*.

Keywords:- Schiff base , Microwave irradiation, Thermodynamic Parameters, biological activity.

Introduction

Increasing physiological importance of nitrogen and sulphur donor organic compounds [1] and active role played by coordination certain metal ions to them[2]. Have interested use in synthesizing and studying structural aspects of metal complexes with some sulphur and nitrogen donor ligands[3].

The aromatic thiadiazole nucleus is associated with a variety of pharmacological actions, such as fungicidal, and leishmanicidal activities. These activities are probably due to the presence of the $-N=C-S$ group [4]. Pyrrole; thiadiazole and its derivatives form an important class of organic compounds due to their structural chemistry and biological activities as analgesic, antipyretics and anti-inflammatory [5]. Even the simplest Pyrrole derivatives are widely used analgesic medicines. Pyrrole are efficient extractants of metal ions and they have potential to form different types of coordination compounds. In addition pyrrole can form a variety of Schiff bases and are reported to be superior reagents in biological, clinical and analytical applications [6,7]. In continuation of our work on the metal complexes of Schiff bases, we report here the study of some new, $Co(II)$, $Ni(II)$ and $Cu(II)$, complexes of Schiff bases

derived from Pyrrole and 2-amino-5-(2-hydroxy-phenyl)-1,3,4-thiadiazole. Preparation, characterization and antibacterial activity of above metal complexes with this Schiff bases are reported here. Where, HL is a Schiff base of 2-amino-5-(2-hydroxy-phenyl)-1,3,4-thiadiazole with Pyrrole. Metal complexes with some oxygen and nitrogen donor ligands [8]. From the TGA curves recorded for the successive steps in the decomposition process of these ligand and complexes it was possible to determine the following characteristic thermal parameters for each reaction step: Initial point temperature of decomposition (T_i): the point at which TG curve starts deviating from its base line. Final point temperature of decomposition (T_f): the point at which TG curve returns to its base line. Peak temperature, i.e. temperature of maximum rate of weight loss: the point obtained from the intersection of tangents to the peak of TG curve. Mass loss at the decomposition step (D_m): it is the amount of mass that extends from the point T_i up to the reaction end point T_f on the TG curve, i.e. the magnitude of the ordinate of a TG curve. The material released at each step of the decomposition is identified by attributing the mass loss (D_m) at a given step to the component of similar weight calculated from the molecular formula of the

investigated complexes, comparing that with literatures of relevant compounds considering their temperature. This may assist identifying the mechanism of reaction in the decomposition steps taking place in the complexes under study. Activation energy (E) of the composition step: the integral method used is the Coats-Redfern equation [9]. for reaction order $n \neq 1$ or $n = 2$, which when linearised for a correctly chosen n yields the activation energy from the slop;

$$\log \left[\frac{1-(1-\alpha)^{1-n}}{T^2(1-n)} \right] = \log \frac{ZR}{qE} \left[1 - \frac{2RT}{E} \right] - \frac{E}{2.303RT} \dots n \neq 1$$

$$\log \left[\frac{-\log(1-\alpha)}{T^2} \right] = \log \left[\frac{AR}{\beta E} \left(1 - \frac{2RT}{E} \right) \right] - \frac{E}{2.303RT} \dots n = 1$$

$\Delta S^* = 2.303R [\text{Log}(Ah/K T_{\max})]$, $\Delta H^* = E - RT_{\max}$, $\Delta G^* = \Delta H^* - T_{\max} \Delta S^*$ where: α = fraction of weight loss, T = temperature ($^{\circ}\text{K}$), n = order of reaction, A or Z = pre-exponential factor, R = molar gas constant, E = activation energy and q = heating rate. Order of reaction (n): it is the one for which a plot of the Coats-Redfern expression gives the best straight line among various trial values of n that are examined relative to that estimated by the Horovitz-Metzger method [10].

Experimental

All chemical used were of reagent grade (supplied by either sigma Aldrich or fluka) and used as supplied. The FTIR spectra in the range (4000-400) cm^{-1} cut were recorded as KBr disc on FTIR.4200 Jasco Spectrophotometer. The UV-Visible spectra were measured in ethanol using Shimadzu UV-Vis. 160 A-Ultra-violet Spectrophotometer in the range (200-1000) nm. Magnetic Susceptibility measurement for complexes were obtained at room temperature using (Magnetic Susceptibility Balance) Jhonson Matthey Catalytic Systems Division. Gallencamp M.F.B600.010 F melting point apparatus were used to measure the melting point of all the prepared compounds. Elemental microanalysis was carried out using CHNOS Elemental Analyzer Model 5500 Carlo-Erba Instruments (Italy).

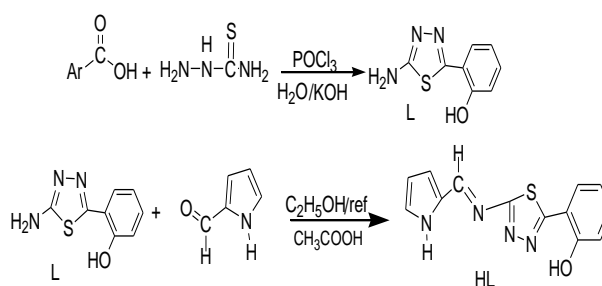
1- Synthesis of [2-amino-5-(2-hydroxy-phenyl -1,3,4- thiadiazole) [L]

A mixture of Salicylic acid (0.1 mol 12.2g), thiosemicarbazide (0.1 mol 9.1 g) and (40ml) of POCl_3 was heat gentle for 3 hours. After cooling (250 ml) of water was added reflux for (4) hours. The mixture was cooled filtered the filtrate neutralized with KOH conc and recrystallization solvent ethanol. M.p, yield, C.H.N.S analysis in Table (1).

2-[2-[(1H-Pyrrol-2-ylimino methyl)- 5-(2-hydroxy-phenyl)-[1,3,4-thiadiazol] [HL]

Method (1) A mixture of equimolar amounts (0.09 mol) of appropriate [1H-Pyrrole-2-carbaldehyde] and the (2-amino-5-(2-hydroxy- phenyl- 1,3,4- thiadiazole), in absolute ethanol (15 ml) with (2) drops of glacial acetic acid was refluxed (3) hours. The reaction mixture was then allowed to cool at room temperature, and the precipitate was filtered dried, and recrystallized from ethanol to give yellow powder.

Method (2): A mixture of equimolar amounts (0.09 mol) of appropriate [1H-Pyrrole-2-carbaldehyde] and the (2-amino-5-(2-hydroxy-phenyl-1,3,4-thiadiazole), were ground with a mortar, mixed, dried and subjected to microwave irradiation 250W for (15) minutes, after completion the reaction mixture was cooled to room temperature the solid obtained was recrystallized twice from absolute ethanol, some of physical data for these four compounds are listed in Table (1).



Scheme (1) Synthesis of Schiff base ligand.

Preparation of complexes

Method (1): An ethanol solution of the metal salte of Co(II), Ni(II) and Cu(II) were added to an ethanolic solution of (HL) in 1:1 (metal: ligand) molar ratios. After stirring for 2 hours with heating 50°C , crystalline colored precipitates formed cooling at room

temperature, the resulting solids were filtered off, washed with distilled water, dried and recrystallized from ethanol and dried at 50 °C
 Method (2): An ethanol solution of the metal salts of Co(II), Ni(II) and Cu(II) were added to an ethanolic solution of (HL) in 1:1 (metal: ligand) molar ratios. And put in ultrasonic bath heating 50°C After 30 mins crystalline colored precipitates formed, cooling at room temperature, the resulting solids were filtered off, washed with distilled water, dried and recrystallized from ethanol and dried at 50 °C. yield, C.H.N.S analysis in Table (1).

Table (1)
The characterization data of the prepared compounds.

Compound Formula,	Yield%	C	H	N	S	O	M	Cl
L C ₈ H ₇ N ₃ OS	76%	49.70 (49.73)	3.62 (3.65)	21.77 (21.75)	16.55 (16.59)	8.28 (8.28)	--	---
HL C ₁₃ H ₁₀ N ₄ O ₅	73%	57.59 (57.76)	3.82 (3.73)	20.91 (20.73)	11.77 (11.86)	5.91 (5.92)		
[Co ₂ (HL) ₂ (H ₂ O) ₄]Cl ₂	75	48.91 (49.40)	3.16 (3.29)	17.55 (17.28)	10.04 (10.00)	17.55 (17.28)	9.23 (9.03)	11.11 (10.95)
[Ni ₂ (HL) ₂ (H ₂ O) ₄]Cl ₂	58	48.93 (49.30)	3.16 (3.23)	17.56 (17.35)	10.05 (9.95)	17.56 (17.35)	9.20 (9.13)	11.11 (10.94)
[Cu ₂ (HL) ₂ (H ₂ O) ₄]Cl ₂	79	48.56 (48.93)	3.13 (3.24)	17.42 (17.21)	9.97 (9.90)	17.42 (17.21)	9.88 (9.76)	11.03 (10.95)

Result and discussion

The synthetic procedure of Schiff base ligand are presented in Scheme (1). The reactions of divalent transition metal ions *viz.*, Co(II), Ni(II) and Cu(II). The composition of the complexes formed in solution has been established by mole ratio and job methods. In both cases the results reveals (1:1) metal to ligand ratio yielded the corresponding metal chelates. Shows the decomposition point, color and electronic absorption bands for ligand and complexes in Table(2). 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 UV-Visible region.

1-[2-amino-5-(2-hydroxy-phenyl-1,3,4-thiadiazole)] [L]

The reaction of Thiosemicarbazide with Salicylic acid in presence of phosphorus oxychloride afforded 2-amino-5-phenyl-1,3,4-thiadiazole[11]. The structural assignment of the product was based on its melting point and spectral (FT-IR, ¹H-NMR and UV/Vis.) data. Besides the C.H.N.S. analysis Table (1). The FT-IR spectrum of compound (L) exhibited significant two band in the range (3396–3283)cm⁻¹ which could be attributed to asymmetric and symmetric stretching vibrations of NH₂ group. band in the (3101) cm⁻¹ stretching vibrations of (OH). Besides this, band at about (1626 cm⁻¹) due to cyclic (C = N) stretching is also observed. Bands at (1518 cm⁻¹) and (1484 cm⁻¹) are due

to the (N-H) bending and (C-N) stretching vibrations, respectively [12].

¹H-NMR spectrum of compound (HL) shows the following characteristic chemical shifts (DMSO-d₆, ppm). The signals at: (δ 7.40-7.94) were due to aromatic protons. Amino protons (NH₂) absorbed at (δ 3.38). Furthermore, the small peak at (δ 2.5) was due to DMSO-d₆.

2) [2-[(1H-Pyrrol-2-ylimino methyl)-5-(2-hydroxy-phenyl)-1,3,4-thiadiazol] [HL]

The FT-IR spectra show the disappearance of the two absorption bands due to (-NH₂) stretching of amino thiadiazole [HL] showed all the suggested bonds for olefinic (C-H), (C=C) aromatic, endocyclic (C=N) and exocyclic imine group. Stretching vibrations in addition to out of plane bending of substituted aromatic ring. All the prepared compounds (Schiff bases) exhibited the stretching band

near the region (1213-1253) cm⁻¹ this due to (=N-N=C-) cyclic group; 3426 cm⁻¹ (ν OH Stretching), a band at 3150 cm⁻¹ attributed to NH stretching (pyrrole ring), 1593cm⁻¹ (ν C=N Stretching of amine), 1229 cm⁻¹, 1468 cm⁻¹ (Characteristic bands of thiazole ring). All the spectral data for other compounds are listed in Table (3).

¹H-NMR spectrum of compounds [HL], shows the following characteristic chemical shift, (CDCL₃-d₆) ppm. The four aromatic ring protons of phenyl and three pyrrole ring appeared at (δ 6.124–7.494) ppm, the signal at (δ 8.66) attributed to (N=C-H) proton (azomethine), the signal at (δ 9.611) ppm, attributed to (N-H) proton, δ=11.7(s, 1H, OH).

The positive ion mass spectral analysis of (HL) observe at m/z 271.2 (M+1) (Fig.(5)), confirms the theoretical molecular weight i.e. 270.31.

Table (2)
Some physical data electronic spectra for ligand and complexes in ethanol.

Symbol	Dec. Point ⁰ C	Conductivity ohm ⁻¹ cm ² mol ⁻¹	Magnetic Moment (B.M)	Color	Absorption Bands (nm)	Assigned Transition
L	238	-	-	White-pink	295	π → π*
					320	n → π*
HL	280	-	-	yellow	215	π → π*
					390	n → π*
Co(II)	310d	11.73	4.82	Pale -Red	225	π → π*
					290	n → π*
					330	Charge Transfer
					375	⁴ T _{1g} ^(F) → ⁴ t _{1g} ^(P)
					915	⁴ T _{1g} → ⁴ A _{2g}
Ni(II)	320d	17	3.10	Pale green	225	π → π*
					290	n → π*
					370	Charge Transfer
					645	⁷ A _{2g} → ³ t _{1g} ^(P)
					934	⁷ A _{2g} → ³ t _{1g} ^(F)
Cu(II)	320d	13	1.89	Light Brawn	220	π → π*
					295	n → π*
					365	Charge Transfer
					420	¹ E _g → ² T _{2g}
					600	⁴ A _{2g} → ⁴ t _{1g}
					640	⁴ A _{2g} ^(F) → ⁴ t _{1g} ^(P)

Infrared spectral analysis of metal complexes

The infrared spectra of the ligands shows (ν O-H) (weakly H-bonded) at 3429 cm^{-1} and (ν N-H) at 3151 cm^{-1} . The absence of this band in all the metal complexes indicates the removal of proton of hydroxyl group of benzene ring and proton of NH group of pyrrole ring during the chelation. The sharp intense band at 1593 cm^{-1} in the ligands can be assigned to ν C=N (azomethine). A shift ($\Delta\nu = 7\text{-}15\text{ cm}^{-1}$) in ν C=N (azomethine) is observed upon coordination indicating that the nitrogen of azomethine group is involved in coordination. All the complexes show broad band in the region ($3285\text{-}3378$) cm^{-1} which may be assigned to (ν O-H) of coordinated water [13]. To account for the octahedral stereochemistry of the metal complexes, the coordination of two water molecules is expected.

The bands at 514 cm^{-1} in Co(II) complexes, 591 cm^{-1} in Ni(II) complexes and 590 cm^{-1} in Cu(II) complexes may be due to metal-nitrogen stretching vibration [14,15]. All the metal complexes involved in coordination. In the free ligand, the band at 1606 cm^{-1} is assigned to the stretching of C=N (thiazole ring). On complexation, this band was 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 in (ν C=N) compared to its respective ligands. This suggests that the nitrogen atom of the ring has not participated in the chelation. However, in water containing chelates, this band is observed as a broad with structure this may be due to coupling of the bending mode of coordinated [16].

Table (3)
Infrared data of Ligand and its metal complexes (cm^{-1}).

Symbol	ν (C=N)	ν (N-H)	ν (C-N=N-C)	ν (M-O)	ν (O-H) H ₂ O	ν (O-H)	ν (M-N)
HL	1593(s)	3151	1202-1229	-	-	3426	-
Co(II)	1608(s)	-----	1243-1304	473(s)	3285	-	541(s)
Ni(II)	1607(s)	-----	1229-1323	435(s)	3289	-	591(s)
Cu(II)	1600(s)	-----	1241-1304	434(s)	3433	-	590(s)

Thermal analysis

To understand thermal decomposition process, Schiff and its metal complexes were examined by thermo gravimetric analysis in the temperature range of $35\text{-}700\text{ }^{\circ}\text{C}$. The obtained thermo analytical results from TGA curves for all these compounds are given in Table (4). The decomposition was complete at $693\text{ }^{\circ}\text{C}$ for all the complexes. The data from the thermo gravimetric analyses indicated that the decomposition of the complexes and the ligand proceeds in (two – four) steps. The final decomposition products were metal oxide mixture formed above 598°C for the metal [17].

Table (4)
Thermodynamic parameters of the ligand and metal complexes.

Sample (step)	T.range °C	N	R ²	T _{max} °K	E _a K.J mol ⁻¹	ΔH* KJ mol ⁻¹	ZSec ⁻¹ x10 ⁵	ΔS* J mol ⁻¹ K ⁻¹	ΔG* KJ mol ⁻¹
L ₁ (1)	37-300	1	0.99	512.79	170.4906	166.2344	1.7762	-34.0617	183.700
L ₁ (2)	300-700	0.9	0.99	780.77	-7.87418	-14.3548	4.82	-354.698	262.5828
Co(1)	37-368	0.9	0.99	476.4	31.57044	27.61632	7.25	-289.758	165.6572
Co(2)	368-467	0.9	1	643.09	-6.84804	-12.1857	5.6	-351.864	214.094
Co(3)	368-700	0.9	0.99	766.6	-6,58243	-13.0282	6.35	-352.37	260.6221
Ni(1)	37-150	0.9	0.99	384	19.3764	16.1892	0.00381	-312.457	136.1727
Ni(2)	150-390	0.9	0.99	507	36.5	32.2919	0.017	-283.109	175.828
Ni(3)	390-700	0.9	0.99	775.12	-11.19	-17.6235	35.4	-257.205	259.2532
Cu(1)	37-180	0.9	0.99	423	125.9	46.49	7.68	-222.79	135.39
Cu(2)	180-395	0.9	0.99	554	54.214	121.04	0.5357	-100.31	169.81
Cu(3)	395-700	0.9	1	726.35	12.696	-5.734	4.91	-359.81	306.7

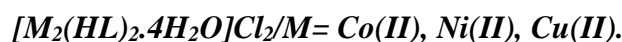
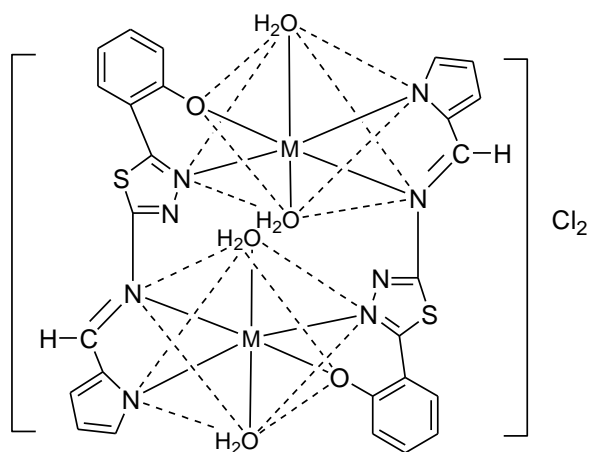
Biological Activity

With a view to explore the possibility of obtaining biologically useful complexes that contain 1,3,4- thiazole and pyrrole ring system, 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⁽¹⁸⁾.used were Staphylococcus aureus, Escherishia coli, Pseudomonas aeruginosa and Cndida 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 37⁰C. The zone of inhibition formed was measured in mm and are represented by (+), (+ +) and (+ + +) depending upon the diameter and clarity, Table (5). The preliminary screening result reveal that compound contained thiazole and pyrrole complexes exhibits highest antibacterial activity against Escherishia coli.

Table (5)
Antibacterial activity of the prepared compounds.

Symbol	<i>Staphylococcus aureus</i>	<i>Escherichia coli</i>	<i>Pseudomonas aeruginosa</i>	<i>Candida albicans</i>
HL	+	+++	-	-
Co(II)	+	+++	+	++
Ni(II)	+	+++	++	+
Cu(II)	++	++	++	++

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



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حضرت معقدات جديدة نوع $M, M_2(HL)_2 \cdot 4H_2O$ حيث $[M = Co(II), Ni(II), \text{ and } Cu(II)]$ باستخدام الليكاند $2-[(1H\text{-}Pyrrol\text{-}2\text{-ylimino methyl})\text{-} =HL$ والتي $5\text{-}(2\text{-hydroxy-phenyl})\text{-}[1,3,4\text{-thiadiazol}]$. حضرت من تفاعل ٥- (٢-هيدروكسي فنيل) ١،٣،٤- ثايودايازول مع ٢- بيرول كربوكسي الدهيد في الكحول النقي. شخصت المعقدات المحضرة بتقنية أطياف الأشعة تحت الحمراء وأطياف الإليكترونية وطيف الكتلة و النووي المغنطيسي البروتوني والتحليل الحراري وكما حددت البارامترات الترموديناميكية ΔE^* , ΔH^* , ΔS^* , ΔG^* باعتماد معادلة Coats-Red fern من أطياف التحلل الحراري الوزني للمركبات ولكل مرحلة من مراحل التحلل. فضلاً عن قياس الحساسية المغناطيسية. كما استخدم التحليل العنصري للمساعدة في عملية التشخيص، حيث تم اقتراح شكل البنية الأساسية للمعقدات. تم قياس النسب المولية المتغيرة في المحلول فأعطت نتائج مطابقة مع تلك التي تم الحصول عليها في الحالة الصلبه ومن نتائج الاطياف تم اقتراح شكل المعقدات المحضرة. كما دُرست الفعالية البيولوجية للمركبات ضد أنواع منتخبة من البكتريا.