

Synthesis and Biological Studies of Co(II),Ni(II),Cu(II) and Zn(II)Complexes with New Compound N-[(2,3-dioxoindolin-1-yl)-Nmethylbenzamide].

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Abstract

The N-[(2,3-dioxoindolin-1-yl)-N-methylbenzamide] was prepared by the reaction of acetanilide with isatin then in presence of added paraformaldehyde, the prepared ligand was identified by microelemental analysis, FT.IR and UV-Vis spectroscopic techniques. Treatment of the prepared ligand with the following selected metal ions (Co^{II}, Ni^{II}, Cu^{II} and Zn^{II}) in aqueous ethanol with a 1:2 M:L ratio, yielded a series of complexes of the general formula [M(L)₂Cl₂]. The prepared complexes were characterized using flame atomic absorption, (C.H.N) analysis, FT.IR and UV-Vis spectroscopic methods as well as magnetic susceptibility and conductivity measurements. Chloride ion content was also evaluated by (Mohr method). From the obtained data the octahedral structure was suggested for all prepared complexes. In addition biological activity of the ligand and complexes against three selected type of bacteria were also examined. Some of the complexes exhibit good bacterial activities.

Keywords:- Mannich base, biological activity, spectral studies.



تحضير ودراسة بايولوجية لمعقدات الكوبالت (II) ، النيكل(II) ، النحاس (II) والزنك(II) مع المركب الحديد (II) الجديد N_((12 داي اوكسواندولين -1- يل))-N- مثيل بنزامايد.

*هيام هادي عاكم، مهند عبد اللطيف محمود، روزى محمد ضيدان، *عمار جبار جراد، **ز هراء رشيد عبدالمجيد، **رنا عيسى عمران قسم الكيمياء- كلية التربية (ابن الهيثم)- جامعة بغداد قسم الكيمياء- كلية العلوم للبنات- جامعة بغداد **قسم التحليلات المرضية- كلية التقنيات الصحية والطبية- هيئة التعليم التقني

الخلاصة

حضرت الليكاند من تفاعل اسيتانالايد مع الاساتين بوجود بارافور مالديهايد. شخص الليكاند المحضر بواسطة اطياف الأشعة تحت الحمراء وفوق البنفسجية – المرئية والتحليل الدقيق للعناصر (C.H.N). تمت مفاعلة الليكاند مع ايونات ((II) and Zn(II) مرارع) وفوق البنفسجية – المرئية والتحليل الذيق للعناصر (C.H.N). تمت مفاعلة الليكاند مع ايونات الدقيق للعناصر (C.H.N) ما معقدات المحضرة بوساطة التحليل الدقيق للعناصر (C.H.N) ما معقدات المحضرة بوساطة التحليل الذيق للعناصر (C.H.N) ما معقدات المحضرة بوساطة التحليل الذيق للعناصر (C.H.N) ما معقدات المحضرة بوساطة التحليل الدقيق للعناصر (C.H.N) معقدات المحضرة بوساطة التحليل الدقيق للعناصر (C.H.N)؛ تقنية الإمتصاص الذري اللهبي واطياف الأشعة تحت الحمراء وفوق البنفسجية - المرئية، الدقيق للعناصر (C.H.N)؛ تقنية الإمتصاص الذري اللهبي واطياف الأشعة تحت الحمراء وفوق البنفسجية المرئية، الما من عن عياسات الحمراء وفوق البنفسجية من المعقدات المعقدات المحضرة بوساطة التحليل المقترح للمعقدات المحضرة من المعقدات المعقدات المعقدات المقترح للمعقدات المحضرة ما معقدات المحضرة ما مرئية، من البكتريا، حما ما معقدات المعقدات المعقدات المعقدات المعتما ما من ما ما من ما ما من ما معقدات المعامية المعالية الكهربائية، النبية التمرية التي تم الحصول عليها ان الشكل الهندسي المقترح للمعقدات المحضرة هو ثنائي السطوح. كما تم در اسة الفعالية البايولوجية لليكاند ومعقداته ضد ثلاثة انواع منتخبة من البكتريا، حيث اضهرت النتائج ان لهذه المعقدات قابلية متباينة على قتل الانواع المنتخبة من البكتريا.

الكلمات المفتاحية: قواعد مانخ ، الفعالية البايولوجية، الدر اسات الطيفية.



Introduction

Mannich reaction is one of the most important carbon-carbon bond formation reactions in organic synthesis^(1–3) and very useful compounds as building blocks in the synthesis of pharmaceuticals and natural products^(4,5). With their advantages of atom-efficient transformations, readily available materials, and various products, multicomponent reactions (MCRs) have received significant research interest from chemical and medicinal communities^(6,7). As one of the mostly studied MCRs, discovered in 1912, Mannich reaction is an aminoalkylation reaction of aldehyde⁽⁸⁾, It is an important basic reaction in organic synthesis. Mannich bases have several biological activities such as antimicrobial, cytotoxic, anticancer and analgesic activity. Morpholine derivative plays important role in the treatment of several diseases. Heterocyclic ring system having morpholine nucleus have aroused great interest in recent years due to their varity of biological activities⁽⁹⁾. The present paper reports the synthesis and characterization of new Co(II),Ni(II),Cu(II) and Zn(II) complexes.

Experimental

Instrumentation

UV-Vis spectra were recorded on a (Shimadzu UV-160 A) Ultra Violet-Visble Spectrophotometer. I.R-spectra were taken on a (Shimadzu, FTIR-8400 S) Fourier Transform Infrared. Spectrophotometer (4000-400) cm⁻¹ with samples prepared as KBr discs. Atomic Absorption was obtained by using a (Shimadzu A.A-160A) Atomic Absorption / Flame Emission Spectrophotometer. Microelemental analysis (C.H.N) was performed in AL-al- Bayt University, Jordan by using (Euro Vector EA 300 A Elemental Analyser). Conductivities were measured for 10⁻³M of complexes in DMF at 25°C by using (Philips PW- Digital Conductimeter). Magnetic susceptibilities were performed by using (Brucker Magnet B.M.6) instrument at 25°C. In addition, melting points were obtained by using (Melting Point Apparatus).

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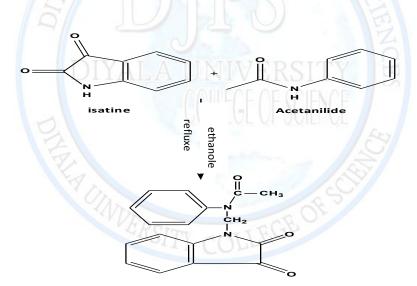
Synthesis and Biological Studies of Co(II),Ni(II),Cu(II) and Zn(II) Complexes with New Compound N-[(2,3-dioxoindolin-1-yl)-N-methylbenzamide]. *Heam H.Alkam, Muhanned A.Mahmood, Ruaa M.Dedan, ,*Amer J.Jarad **Zahraa R.Abdulmageed, Rana I.Omran***

<u>Materials</u>

The following chemicals were used as received from suppliers; acetanilide, isatine, paraformaldehyde, cobalt(II) chloride hexahydrate 98.8%, nickel(II) chloride hexahydrate 99.9%, copper(II) chloride dihydrate 98% and zinc(II) chloride 98.8% (Merck) , Dimethylsulphoxide) 99%, Ethanol 99.8%.

Synthesis of the Ligand

Acetanilide (0.005mol) in (25ml) absolute ethanol was added to isatine (0.005mol) with paraformaldehyde (0.006mol) and refluxed four hours, then(100ml) of ice distilled water was added, the precipitate was filtered, dried and recrystallized from ethanol. ⁽¹⁰⁾



N-((2,3-dioxoindolin-1-yl)-N-methylbenzamide).

Preparation of Metal Complexes (general procedure)

An aqueous solution of the metal salts containing 0.118g, 0.118g, 0.085g and 0.068g (1mmole) of CoCl₂.6H₂O, NiCl₂.6H₂O, CuCl₂.2H₂O and ZnCl₂ respectively was added gradually with stirring to ethanolic solution (0.25g,2mmol) of the ligand by using



stichiometric amount (1:2) Metal to Ligand molar ratio. The mixture was refluxed with constant stirring for two hours. The mixture was cooled at room temperature dark precipitate was formed, filtered and recrystillized from ethanol.

Study of Biological Activity

Three selected types of bacteria were used includes, *Esherichia Coli (E. Coli)* as Gram Negative Bacteria, *Staphylococcus Aureus (Staph. Aureus)* as Gram Positive Bacteria and *Psedomonas Aeruginosa (Ps. Aeruginosa)* in Neutrient Agar medium, using (DMSO) as a solvent and as a control, the concentration of the compounds in this solvent was 10⁻³M, using disc sensitivity test. This method involves the exposure of the zone of inhibition toward the diffusion of micro- organism on agar plate. The plates were incubated for 24hr. at 37C^o.

Results and Discussion

The solid complexes were prepared by reaction of alcoholic solution of the ligand with the aqueous solution of the metal ions in a (M:L) of (1:2). The (C.H.N) analysis with metal contents of these complexes were in good agreements with the calculated values (Table-1) includes some physical properties and elemental analysis.

Table(1):- Some Physical Properties and Elemental Analysis of the Ligand and It's Metal Complexes.

Compounds	Color	M.P°C	Yield%	Analysis Calc (Found)				M.Wt	
				Cl%	M%	С%	Н%	N%	gm/mol
Ligand	Orange	178	78	-	-	69.38 (68.74)	4.76 (3.87)	9.52 (8.17)	294
$[Co(L)_2Cl_2]$	Reddish Brown	235	72	9.88 (8.74)	8.21 (7.48)	56.82 (55.74)	3.89 (3.13)	7.79 (6.75)	718
$[Ni(L)_2Cl_2]$	Green	227	65	9.90 (9.03)	8.08 (7.35)	56.90 (56.02)	3.90 (3.07)	7.81 (6.58)	718
$[Cu(L)_2Cl_2]$	Green	243	71	9.82 (8.58)	8.85 (7.66)	56.43 (55.87)	3.87 (2.96)	7.74 (6.66)	723
$[Zn(L)_2Cl_2]$	Yellow	253	78	9.80 (8.73)	8.97 (7.36)	56.35 (55.93)	3.86 (2.88)	7.73 (6.76)	724



The molar conductance of the complexes as (10^{-3} M) in ethanol indicating their nonelectrolytic nature(11), the data were recorded in (Table- 2).

The effective magnetic moments (Table-2) of the complexes lie in the range (1.73-4.57) B.M. This value refers to a paramagnetic (high spin) which has been reported for most octahedral geometry. In case of Zn(II) complex because of filled-d orbital, therefore the magnetic moment (μ =0) is diamagnetic⁽¹²⁾.

The UV-Vis spectra data for the free ligand and all metal complexes are listed in (Table-2).

Compounds	λ _{max} (nm)	ABS	Wave number (cm ⁻¹)	$\frac{\mathcal{E}_{\max}}{(\mathbf{L}.\mathbf{mol}^{-1}.\mathbf{cm}^{-1})}$	Λ _m (S.cm ² .moΓ ¹) in ethanol(10 ⁻³ M)	μ _{eff} (B.M)	Assignment
Ligand(L)	262	0.404	38167	404	TDOIT	S// -	$\pi - \pi^*$
	345	1.318	28985	1318	EKDII	I	$n-\pi^*$
$[Co(L)_2Cl_2]$	305	1.832	32786	1832	21.87	4.57	C.T
	609	0.227	16420	227	LVIUVILIN		${}^{4}\mathrm{T}_{1g(F)} \rightarrow {}^{4}\mathrm{T}_{1g(P)}$
	673	0.334	14858	334		14	${}^{4}T_{1g(F)} \rightarrow {}^{4}A_{2g(F)}$
	827	0.019	12091	19	Come is		${}^{4}T_{1g(F)} \rightarrow {}^{4}T_{2g(F)}$
[Ni(L) ₂ Cl ₂]	268	1.390	37313	1390	18.83	3.05	C.T
	421	0.378	23752	378	C	S/	${}^{3}A_{2g(F)} \rightarrow {}^{3}T_{1g(P)}$
	611	0.102	16366	102	4		${}^{3}A_{2g(F)} \rightarrow {}^{3}T_{1g(F)}$
	795	0.061	2578	61	ECE		${}^{3}A_{2g(F)} \rightarrow {}^{3}T_{2g(F)}$
$[Cu(L)_2Cl_2]$	337	1.397	29673	1397	23.65	1.73	C.T
	421	0.559	23752	559			$^{2}E_{g} \rightarrow ^{2}T_{2g}$
$[Zn(L)_2Cl_2]$	311	1.827	32154	1827	19.77	0.00	C.T

Table(2):- UV-Vis, Magnetic Susceptibility and Conductance Measurements Data.

The UV-Vis spectrum of the ligand (L) (Fig-1) shows two peaks at 262 nm and 345 nm assigned to $(\pi - \pi^*)$ and $(n - \pi^*)$ electronic transitions respectively ^(13,14). The electronic spectrum of Co(II) complex (Fig-2) showed peak at 305 nm due to charge transfer. Other three peaks at 609 nm, 673 nm and 827 nm were found to be caused by (d-d) electronic transition type ${}^{4}T_{1g}$ (F) $\rightarrow {}^{4}T_{1g}$ (P), ${}^{4}T_{1g}$ (F) $\rightarrow {}^{4}A_{2g}$ (F) and ${}^{4}T_{1g}$ (F) $\rightarrow {}^{4}T_{2g}$ (F) respectively⁽¹⁵⁾. The spectrum of Ni(II) complex appeared absorption peak at 268 nm was related to charge



transfer, then other three peaks at 421 nm, 611 nm and 795 nm were assigned to electronic transition type ${}^{3}A_{2g(F)} \rightarrow {}^{3}T_{1g(P)}, {}^{3}A_{2g(F)} \rightarrow {}^{3}T_{1g(F)}$ and ${}^{3}A_{2g(F)} \rightarrow {}^{3}T_{2g(F)}$ respectively⁽¹⁶⁾. The spectrum of Cu(II) complex gave absorption peak at 337 nm due to charge transfer. The peak at 421 nm was caused by electronic transition^{(17) 2}E_g $\rightarrow {}^{2}T_{2g}$. The spectrum of Zn(II) complex showed absorption peak at 311 nm due to charge transfer. The absence of absorption peaks in the visible region indicated no (d-d) electronic transition happened; this is a good result for octahedral complex ⁽¹⁸⁾.

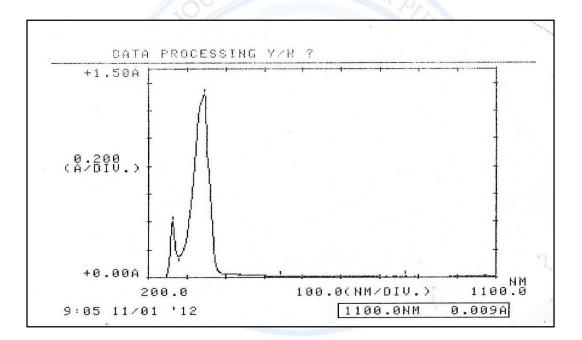


Fig.(1):- UV-Vis Spectrum of the Ligand.



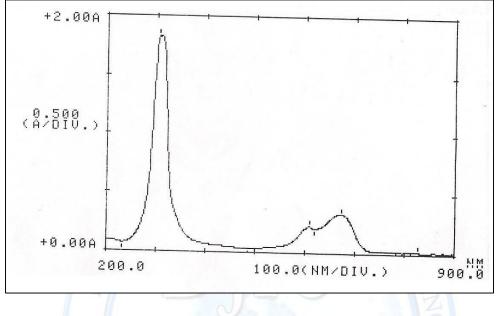


Fig.(2):- UV-Vis Spectrum of the [Co(L)₂Cl₂] Complex.

In order to study the binding mode of the ligand with the metal ions, a comparison was made for the FT.IR spectra of the free ligand and those of the prepared complexes and the data was tabulated in (Table-3). The IR spectrum of the ligand (L) (Fig-3) exhibited band at 1728 cm⁻¹ was assigned to v(C=O) for acetanilide stretching frequency⁽¹⁹⁾. This band remained unaltered in the complexes spectra, indication that is no coordination from main band. The band at 1666 cm⁻¹ in the ligand spectrum ascribed to v(C=O) of five member ringe ⁽²⁰⁾, on complexation a shifting with change in shape was observed from this band, while increasing in intensity were noticed. The significant may be a result of coordination with metal ion (Fig-4). The bands at 1616 cm⁻¹ and 1558 cm⁻¹ in the ligand spectrum due to v(C=C) aromatic . Since no change in this band was noticed, the possibility that coordination occur via the donation atom(N) in this group was excluded⁽²¹⁾. The new bands observed at (576-430) cm⁻¹ are tentatively assigned to v(M-O) (Metal-Ligand) stretching bands^(22,23).

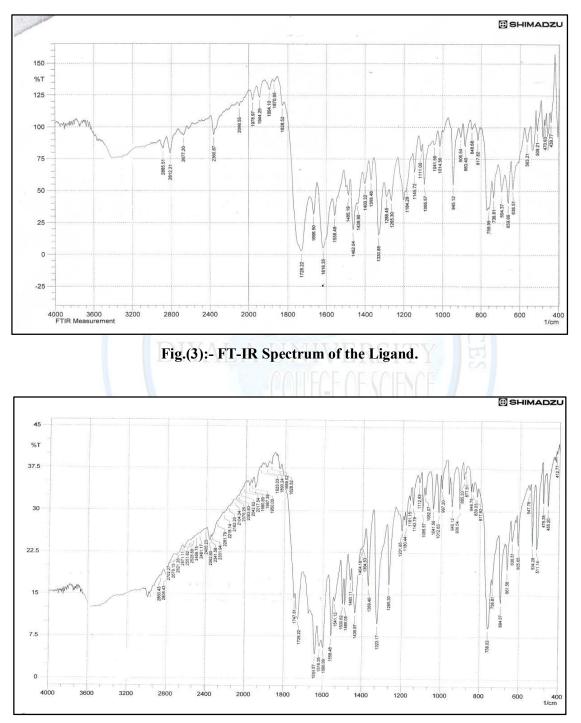


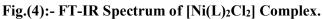
Table(3):- The Main Frequencies of the Ligands and It's Complexes(cm⁻¹).

Compounds	v(C=O)	v(C=O) five member ringe	v(C=C)	υ(M-O)
Ligand(L)	1728 s.	1666 sho.	1616 s. 1558 sho.	-
$[Co(L)_2Cl_2]$	1728 sh.	1654 sh.	1616 s. 1558 sh.	534 w. 511 w.
[Ni(L) ₂ Cl ₂]	1727 s.	1590 s.	1614 s. 1556 sh.	552 w. 521 w.
$[Cu(L)_2Cl_2]$	1727 sh.	1634 s.	1616 s. 1557 sh.	543 w. 527 w.
$[Zn(L)_2Cl_2]$	1728 s.	1643 sh.	1617 sh. 1558 s.	528 w. 511 w.

sh =sharp, sho=shoulder, s = strong, w =weak



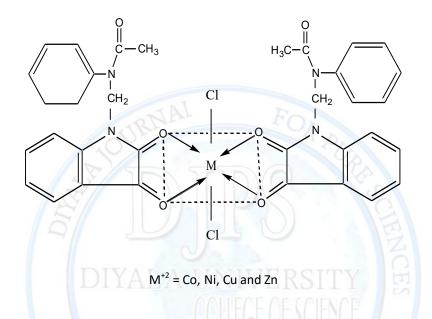




amide].

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According to the results obtained and spectral analysis an octahedral structure has been suggested to these complexes.



Finally, the biological activities of the ligand and their complexes have also been tested against selected type of bacteria, (Table-4) show the deactivation capacity against the bacteria specimen of the prepared compounds under study.

Table(4):- Diameters (mm) of Deactivation of Bacteria for the Phenylalanine and It's Complexes.

Compounds	Staphylococcus Aureus	Escherichia Coli	Psedomonas Aeruginosa	
Ligand(L)	-	-	++	
$[Co(L)_2Cl_2]$	+	++	-	
[Ni(L) ₂ Cl ₂]	-	-	+	
$[Cu(L)_2Cl_2]$	-	++	-	
$[Zn(L)_2Cl_2]$	+	+	+	



(-) =No inhibition.

- (+) =Inhibition diameter (6-8) mm.
- (++) =Inhibition diameter (8-10) mm.

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