Synthesis, characterization and bioassay of Cr(III), Mn(II), Fe(II), and Zn(II) complexes with (2E)-2-(4-methoxy benzylidene) hydrazine carboxamide

Sallal A.H. Abdullah

Chemistry division, Applied Science department, University of Technology ,Baghdad, Iraq

Abstract

The ligand (2*E*)-2-(4-methoxybenzylidene)hydrazine carboxamide [L] has been synthesized from the reaction of 4-methoxybenzyaldehyde with semicarbazide. This ligand was characterized by elemental analysis, ¹H-NMR spectra, FT-IR spectra and Uv-visible spectra.Metal complexes of this ligand were synthesized by reaction of metal ions [Cr(III), Fe(II), Mn(II) and Zn(II)] with this ligand [L]. All metal complexes were characterized by elemental analysis, Magnetic susceptibility, electrical conduc- tance, Uv-vis spectra and FT-IR spectra. The antimicrobial activity of the ligand and its metal complexes were investigated for their (*In-Vitro*) antibacterial on (*E. coli*) and (*Bacillusubtilis*) and antifungal (*A. niger*) and (*P. chrysogenum*) activities. The result indicates that the growth of the tested organism was inhibited by the most of this complexes.

المستخلص

يتضمن هذا البحث تحضير الليكاند (E.coli) وطيف الأشعة تحت الحمراء (FT-IR) وطيف الأشعة فوق تشخيص الليكاند (L) من خلال عدة تقنيات مثل طيف الأشعة تحت الحمراء (FT-IR) وطيف الأشعة فوق البنفسجية و المرئية (UV-Vis) وطيف الرنين النووي المغناطيسي (HNMR¹) والتحليل العناصر (C.H.N.O). حضر من هذا الليكاند مجموعة من معقدات الأيونات الفلزية الكروم(III) والمنغنيز(II) والحديد(II) والخارصين(II) والتي تم تشخيصها بإستخدام طيف الأشعة الحمراء وطيف الأشعة فوق البنفسجية والمرئية وتقنية تحليل العناصر الدقيق (C.H.N.O) وتقنية الإمتصاص الذري اللهيبي للعناصر إضافةً إلى قياسات الحساسية المغناطيسية والتوصيلية الكهربائية.وتم فحص الفعالية الحيوية لليكاند ومعقداته بإستخدام تراكيز مختلفة ضد البكتريا المغناطيسية والتوصيلية الكهربائية.وتم فحص الفعالية الحيوية لليكاند ومعقداته بإستخدام تراكيز مختلفة ضد البكتريا المغناطيسية والتوصيلية الكهربائية.وتم فحص الفعالية الحيوية للمركبات ضد الفطريات (A.niger) و المخاريات الفلزيات المخترام المغالية الحيوية المركبات مت المغناطيسية المراكية المعتراريات المغالية الحركيات المغالية الحرار المرئية وتقنية المركبات المغالية الحروية المركبات المغالم (E.coli) و المعانية الحساسية المغربائية.وتم فحص الفعالية الحيوية لليكاند ومعقداته بإستخدام تراكيز مختلفة ضد البكتريا و (E.coli) و (Bacillussubtili) و الغوية اليكاند المحضر ومعقداته فعاليه حيوية تجاه العزلات المختار

Key words: hydrazine carboxamide Schiff base compounds, coordination complexes of Schiff base, Semicarbazone, spectral data, antimicrobial activity.

Introduction

Hydrazine carboxamide compounds were obtained by condensation of semicarbazide with carbonyl compounds (ketones, aldehydes) [1]. Semicarbazones have very important nitrogen and oxygen donor atoms and can perform as neutral or charged ligand moieties^[2]. These compounds generally have been reacting with metal ions to produce metal complexes in which the semicarbazones act as chelating compounds[3]. Formation of a variety of metal complexes from these ligands is the great development in coordination and bioinorganic chemistry[4]. The complexes of semicarbazones participate an important role in agriculture[5], pharmaceutical[6], manufacturing

chemistry[7] and it was used as catalysts, in different biological system[8], and it used to prepare dyes and polymers [9]. The reported semicarbazone comp-ounds and their metal complexes were used and screened toward many biological functions such as antifungal[9,10], antitumor[11], antiviral[12], antimalarial and antiparasital activities[8-11]. They were observed for of some their derivatives[10]. The activity of semicarbazone complexes depend- ed on type and charge of metal ions[11]. This work study the Synthesis, characterization and bioassay of Cr(III), Mn(II), Fe(II), and Zn (II) metal complexes with (2E) -2- (4methoxy benzylidene) hydrazine carboxamide

Experimental

1. Instrumentation

Melting points were recorded on a GallenkampMF B600 melting point apparatus. Elemental analyses (C.H.N.O) were gained using EA-034.mth. for complexes and ligand. ¹H-NMR spectra were obtained with Bruker spectrophotometer model ultra-shield at 300MHz in d_6 DMSO solution with the TMS as internal standard. Metal contents of complexes were predicted

using Flame atomic absorption spectroscopy Shimadzu-670 AA Spectrophotometer. Infrared spectra restricted using FT-IR-8300 were Shimadzu with range (4000-350)cm⁻¹, the measured samples were recorded on (CsI) disc. Magnetic susceptibilities of metal complexes were calculated by using Magnetic Susceptibility Balance of Sherwood Scientific. The molar

conductivity was measured using Electrolytic Conductivity Measuring set Model MC-1-Mark V using platinum electrode (EDC 304), the cell constant was (1cm^{-1}) , the concentration of prepared compounds $was(10^{-3} \text{ M})$ in solvent (DMF) as a at room temperature. Electronic spectra were recorded using UV-1650PC-Shimadzu Spectrophotometer at room temperature and the concentration of the ligand and their complexes was $(10^{-3}M)$.

2. Materials and Methods

All chemical were of high purity and used as received.

Synthesis of ligand (L)

The synthesized ligand was prepared according to the literature with slight modification[13,14]. A 4methoxybenzaldehyde (0.009 mol, 1.225g in 25 ml ethanol (95%)) was added to the solution of semicarbazide hydrochloride (0.009 mol, 1.0g) and sodium acetate (0.009 mol, 1.102g). The reaction mixture was refluxed for 3 hrs, the product was washed and filtered off and recrystallized from ethanol[13-15]. Scheme(1).



Scheme (1): Synthesis of Ligand (L)

Synthesis of metal complexes (H₁-H₄)

An Ethanolic solution of each of the following metal ions salts (0.05 mmol) [CrCl₃.6H₂O, MnCl₂.4H₂O, FeCl₂.4H₂O, and ZnCl₂] was added to an ethanolic solution (0.193 g, 1 mmol) of the prepared ligand (L). The reaction mixture were refluxed for (2) hours, during this time a precipitate was formed. The product was filtered off, washed with hot ethanol, then by cold water[13-15]. Scheme (2)



Scheme (2): Synthesis of metal complexes

3. Biological bioassay for (L) ligand and its Complexes(H₁-H₄)

The ligand (L) and its complexes (H_1-H_4) were screened antagonistic toward two types of bacteria (*E. coli*) and (*Bacillusubtilis*). These bacteria were cultured in Nutrient agar medium. The control and the solvent is DMSO (dimethyl sulfoxide).The concentration of the ligand and its metal complexes were $(10^{-3}M)$.The new complexes (H_1-H_4)

H₄) were screened for their *in vitro* growth inhibitory activity against further pathogenic fungi, i.e., (*A. niger*) and (*P. chrysogenum*) on potato dextrose agar medium and incubated at 30 $^{\circ}$ C for 72 hours. The inhibition of fungal growth, expressed in percentage terms, compared to the respective control plates [13].

Results and Discussion

1. Elemental Analyses

The physical and analytical data of the ligand (L) and its metal complexes (H_1 - H_4) are given in Table (1). The results obtained from elemental analysis are consistent with the calculated values. The new complexes (H_1-H_4) were soluble in $(CH_2Cl_2, CHCl_3, DMF and DMSO)$. They are thermally stable and unaffected by moisture.

Table (1): Physical measurements, elemental analysis and melting points of ligand and their metal complexes (H_1-H_4)

Comp. symbol	General formula	Mwt g.mol ⁻¹	Color	M.P (°C)		Elemental analysis(%) Found(calc.)			
					С	Н	Ν	0	М
L	$C_9H_{11}N_3O_2$	193.2	yellow	152-154	55.95	5.74	21.75	16.56	
					(55.90)	(5.69)	(21.73)	(16.31)	
H ₁	[CrL ₂ Cl ₂] Cl	544.496	Light green	$340 \mathrm{dec}^*$	19.67	2.00	7.68	5.75	9.55
					(19.83)	(2.02)	(7.71)	(5.87)	(9.54)
H_2	[MnL ₂ Cl ₂]	511.93	Brown	220-222	20.99	2.20	8.17	6.23	10.72
					(21.09)	(2.14)	(8.20)	(6.25)	(10.74)
H ₃	[FeL ₂]Cl ₂	512.847	Light brown	210-212	21.04	2.16	8.13	6.21	10.69
					(21.05)	(2.14)	(8.18)	(6.23)	(10.88)
H.	$[7n L_{2}]C_{2}$	522 38	Off white	white $375 \mathrm{dec}^*$	20.66	2.06	8.01	6.11	12.54
114		522.50	on white		(20.67)	(2.10)	(8.04)	(6.12)	(12.51)

Where $dec^* = decomposition$

2. ¹H-NMR Spectrum of the prepared Ligand (L)

The ¹H-NMR spectrum of free ligand, Fiq (2),in DMSO-d₆ showes signal at (9.863 ppm, 2H) assigned to protons of NH₂ group of semicarbazone, while, signal at (9.363 ppm, 1H) may be attributed to (C-H) group proton of Schiff base, signals at (8.112 ppm, 2H,

7.472 ppm, 2H) belongs to protons of aromatic ring, while the signals at (4.663 ppm, 1H and 3.232 ppm, 3H) assigned to proton of NH group, and protons of CH_3 group of aromatic ring respectively[16].



Figure (2): ¹H-NMR spectrum of prepared ligand (L) in DMSO-d₆

3. FT-IR Spectra of ligand (L) and its Complexes (H₁-H₄)

The FT-IR spectral data of the ligand and its metal complexes were listed in Table (2).

FTIR spectrum of the free ligand showed band at (3454 cm⁻¹) in FTIR spectrum due to υ (N-H) vibration of semicarbazone, and bands at (3257 cm⁻¹, 3234cm⁻¹) attributed to υ (NH₂) vibration. These bands also observed at complexes spectra[14-16]. This mean that this group does not participate in the coordination process, The υ (C=O) amide vibration which observed at (1685 cm⁻¹) in free ligand shifted by (16-27) cm⁻¹ to a lower frequency. The band at (1645 cm⁻¹) in free ligand referred to (C=N) group of Schiff base. This band was shifted by (17-29) cm⁻¹ toward lower frequencies in the spectra of all complexes.These two different behaviors indicated the involvement the amide group (C=O) and azomethine group (C=N) of Schiff base in the coordination process with metal ions. In the lower frequencies, the stretching vibration bands of υ (M–N) and υ (M–O) in the spectra of complexes were observed at (462-454cm⁻¹) and (544-535cm⁻¹), respectively[17].

Com	L	H_1	H_2	H ₃	H_4
v(N-H)	3450	3452	3447	3449	3501
	3257(m)	3255(w)	3260(w)	3258(w)	3256(w)
$U(NH_2)$	3234(m)	3230(w)	3233(w)	3234(w)	3235(w)
v(C=O)	1685(s)	1666(s)	1669(s)	1662(s)	1658(s)
v(C=N)	1645(s)	1628	1633	1626	1631
v(M–N)		458(w)	462(w)	454(w)	461(w)
v(M-O)		544(w)	538(w)	540(w)	535(w)
v(M–Cl)		368	362		

Table (2): FT-IR spectral data (cm⁻¹) of the ligand and their complexes

Where : S=strong, W=weak, M=medium

4. Electronic spectra, Magnetic susceptibility, and Conductivity measurements

The UV spectrum of synthesized ligand (L), in absolute ethanol showed two absorption bands at 272 nm and at 354nm may be attributed to $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions,

respectively[13,14]. The maxim-um absorption of the ligand and its metal complexes (H_1-H_4) complexes in chloroform with their assignments, as shown in table (3).

Electronic spectraum of yellow complex (H₁) shows three allowed transitions in high spin state ${}^{4}A2g_{(F)} \rightarrow$ ${}^{4}T2g_{(F)}$ (v1), ${}^{4}A2g_{(F)} \rightarrow {}^{4}T1g_{(F)}$ (v2) and ${}^{4}A2g(F) \rightarrow {}^{4}T1g(P)$ (v3), at (467nm,21413cm⁻¹),(442nm, 22624cm⁻¹), and (275nm, 36363cm⁻¹) respectively[13,16]. These indicate the complex have an octahedral geometry. The magnetic susceptibility and molar conductivity showed that the metal complex is paramagnetic (3.74 B.M) and it have ionic behavior.

The spectrum of brown Mn(II) complex (H₂), shows three bands, attributed to ${}^{6}A1g \rightarrow {}^{4}T2g$ and ${}^{6}A1g \rightarrow {}^{4}E2g$, respectively (690nm,14492.75) and (445nm,22471.9cm⁻¹)[18] The bands shows an octahedral shape around Mn(II) ion [19,20]. The magnetic moment of this complex was (5.38B.M), this value refers to a high-spin (d⁵) complex[21], table (3). Conductivity measurement in (DMF) referred to a non-ionic behavior of this complex.

The electronic spectrum of light brown complex Fe (II) (H_3) , displays $(452 \text{nm}, 22123 \text{cm}^{-1})$ bands at and (325nm,30769 cm⁻¹) which corresponds to $({}^{5}T2g \rightarrow {}^{5}Eg)$ and charge transfer transition. The measured magnetic moment of complex was (5.08 B.M), this value referred to tetrahedral shape (II)complex[20-22]. for Fe The conductivity measured in DMF indicated that the metal complex was

conducting .According to the electronic spectra of Zn(II) off white complex (H₄), no absorption bands shown at rang (365-1000)nm. This indicate no transition is located which belongs to d^{10} in visible region that is a good result for Zn(II) tetrahedral complex[23,24]. The synthesized complexes was an off white in color with the diamagnetic character [21]. The U.V-Vis spectrum of (H_4) , in CHCl₃, confirm three bands at (256 nm, 38912 cm⁻¹), (294 nm, 34127 cm⁻¹) and (334 nm, 29851 cm⁻¹), respectively, belongs to $(\pi \rightarrow \pi^*),$ $(n \rightarrow \pi^*)$ and $(M \rightarrow LCT)$ transitions [13,23]. The measured conductivity indicate ionic behavior of the prepared complex.

Table (3): Uv-Vis spectra, Magnetic moment (B.M) and molar conductivity in(DMF) for (H1-H4) complexes

No.	Maximum absorption	Band assignment	Molar Cond. S.cm ² .mol ⁻¹	µeff.	Suggested geometry	
	$v_{max}(cm^{-})$			B' M	8	
	21413	${}^{4}\text{A2g}_{(F)} \rightarrow {}^{4}\text{T2g}_{(F)}(v1)$				
(H ₁)	22624	${}^{4}\text{A2g}_{(F)} \rightarrow {}^{4}\text{T1g}_{(F)}(v2)$	190.15	3.74	O.h	
	36363	${}^{4}\text{A2g}_{(F)} \rightarrow {}^{4}\text{T1g}_{(P)} (v3)$				
	14492.75	${}^{6}\text{A1g} \rightarrow {}^{4}\text{T2g}$	22.65	5 29	Oh	
(H ₂)	22471.9	${}^{6}\mathrm{A1g} \rightarrow {}^{4}\mathrm{E1g}$	22.03	5.58	0.11	
(II)	22123	${}^{5}\text{T2g} \rightarrow {}^{5}\text{Eg}$	179 22	5 08	Th	
(H ₃)	30769	$L \rightarrow M_{CT}$	178.55	5.08	1.11	
	38910	$\pi \rightarrow \pi^*$				
(H ₄)	34129	$n \rightarrow \pi^*$	188.6	Dia	T.h	
	29850	$M \rightarrow L_{CT}$				

Suggested chemical Structure of metal complexes (H₁-H₄)

According to the results obtained from elemental and spectral analysis as well as magnetic moment and conductivity measurements, the structure of the above mentioned compounds can be illustrated as follows, Fiq (4).



Figure (4): Suggested chemical structure of Metal complexes (H₁-H₄)

5. Biological assay

The synthesized ligand (L) and its complexes (H_1 - H_4) were screened *in vitro* for their ability to inhibit the growth of representative (*E. coli*) as gram negative becteria and (*Bacillusubtilis*) as gram positive bacteria, (Table 4). Also the study was done against ((*A. niger*) and (*P. chrysogenum*) fungus, in DMSO as a solvent,

Table(4). As an outcome from the on top of studies, the following points were concluded that the ligand (L) was active against *E.coli*. and it was inactive against Bacillusubtilis. All complexes (H1-H₄) showed highly effectiveness inhibition toward two types of bacteria compared with synthesized ligand(L).Results of the activity of antifungal of new prepared complexes, (Table 4) exhibit that the complexes (H_1-H_4) were extra poisonous compared with its prepared ligand (L) against the microorganism itself. The biological activity of Hydrazine carboxamide were associated to coordinated metal ion. Initially, lipophilicity, which hold the speed of entry into the cell, is modified by coordinated to metal ions[24].Furthermore, the complex create more active than the ligand. The mechanism of action content engage binding to a metal ion (in vivo) or the complex may be a medium for activation of the ligand as the cytotoxic agent[24]. The increasing activity of the antifungal metal complexes may be of attributed to the effect of the metal ion on the normal cell process[24-26].

Table (4): Antimicrobial activities for ligand (L) and its metal complexes (H₁-H₄) $(10^{-3} \,\mu gm.ml^{-1})$

Comp. No.	E. coli	Bacillusubtilis	A. niger	P. chrysogenum
Control DMSO	-	-	-	-
(L)	+	+	++	++
(H ₁)	++	++	++	++
(H ₂)	+++	++	+++	+++
(H ₃)	+++	+++	++	+++
(H ₄)	++	++	+++	+++

Where : + represent that inhibition zone equal to or less 6mm

++ represent that inhibition zone equal to or less 12mm

+++ represent that inhibition zone equal to 30mm

Conclusions

The (2E)-2-(4methoxybenzylidene) hydrazine carboxamide (L) and its complexes were synthesized and characterized. The geometrical structure of all metal complexes

specified throughout were physical, chemical and spectral methods. The prepared ligand (L) and its metal complexes confirm antibacterial significant and antifungal activity and all complexes were established more efficient than the ligand. transition activity of metal complexes of substituted benzoin

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