Synthesis , Structural study and anti bacterial activity of Mannich base complexes [Cu (II), Pd(II) , Ru (III) and Pt(IV)].

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الخلاصة

تم في هذا البحث تحضير قاعدة مانخ الجديد ةZ)
(2-diphenyl amino methyl-2- thion -5-phenyl -1,3,4-oxadiazole) في محاولة لادخال مجموعة الامينو مثيل ضمن تركيب حلقة الاوكساديازول المعروفة بامتلاكها العديد من الصفات الدوائية لغرض التعرف على السلوك التناسقي للمركب الجديد تجاه بعض ايونات العناصر الانتقالية ومن ثم استقصاء الفعالية الحيوية.

تم تحضير المركب (Z) وذلك بتكاثف كل من الفورمالديهايد وثاني فينايل امين مع المشتق (5-فنيل -4,3,1-اوكساديازول-2-ثايون)في محلول الايثانول . درس وشخص (Z) بالطرق الفيزيائية المناسبة وهي طيف الاشعة تحت الحمراء والتحليل الدقيق للعناصر باستخدام تقنية C.H.N.S . تم تحضير عدد من المعقدات الجديدة من مفاعلة (Z) مع بعض ايونات العناصر الانتقالية حيث شخصت المعقدات الجديدة المحضرة بالحالة الصلبة باستخدام تقنية قياسات اطياف الاشعة تحت الحمراء وفوق البنفسجية – المرئية ، فضلا عن التحليل الدقيق للعناصر بتقنية (C.H.N.S) والامتصاص الذري اللهبي كذلك تم قياس درجات الانصهار . تم تقويم الفعالية المضادة للبكتريا وقد اختير نوعان من البكتريا Pseudomonas aeruginosa (سالبة الصبغة) و Bacillus Subtilis (موجبة الصبغة) لهذا الغرض .

Abstract

Anew mannich base (2-diphenyl amino methyl-2- thion -5-phenyl-1,3,4-oxadiazole) (Z) have been prepared in an attempt to introduce the amino methyl moiety in the structure of mercabto oxadiazole ring which is known to posses a number of therapeutically applications and to investigate the coordination behavior of the new compound (Z) toward some transition metal ions.

The compound (Z) was prepared by condensation of formaldehyde and appropriate amine (diphenyl amine) respectively with (-5-phenyl-2- thion -1,3,4-oxadiazole) derivative in ethanol solution , the product were isolated ,studied and characterization by appropriate physical measurement , i.e., FT-IR spectroscopy and elemental analysis (C.H.N.S) .

The new compound (Z) have been used as a ligand to prepare a number of new complexes with the selected metal ions . All the new prepared metals complexes have been isolated characterized and studied in solid state by studying their physicochemical and analytical properties such as FT-IR UV-Vis. Spectra , In addition The stereochemistry around the metal ion has been suggested using flame atomic absorption and elemental analysis (C.H.N.S) , also the characterization of melting points .The anti bacterial activity for ligand and its complexes were studied against two selected micro organisms , gram negative Pseudomonas aeruginosa and gram positive Bacillus Subtilis .

Introduction

Oxadiazole derivatives of 2-thion-1,3,4-oxadiazoles,were reported to have different interesting biological activities[1-3].A class of these derivatives of special interest are 3-substituted amino methyl-5-substituted-1,3,4-oxadiazole -2-thions,which have been reported to be biologically active[4 , 5].In continuation of previous work , the synthesis and characterization of the Mannich bases derived from 2-thion-1,3,4-oxadiazole and different aromatic amines were described along with a number of their transition metal complexes[6-11]. The present paper describes the preparation of a new Mannich base ,in an attempt to introduce the methyl amino moiety in the structure of mercapto oxadiazole ring which is known to possess a therapeutical applications. The coordination behavior of the prepared new ligand compound toward some transition metal ions , have also been investigated .

Experimental

A-Physical measurement and analysis

Elemental analysis (C.H.N.S) were obtained using EA- 034.mth.for only ligand. Melting points were recorded on Stuart Scientific Co.LTD Melting Point SMP1 apparatus. FT-IR spectra were recorded using Shemadzu FTIR 8000 Series in the range of (4000-200) cm^{-1}. Samples were measured as (CsI disc).Electronic spectra were obtained using Shemadzu UV-Visible Recorder Spectro Photometer UV-160 at room temperature. The measurement were recorded using a concentration of 10^{-3}M of the complex in chloroform. The metal content was estimated Spectrophotometrically using Flame Atomic absorp., Shimadzu \ 670 AA .

B-Materials and methods

All chemical were of highest purity and were used are received.

1 – Preparation of the Mannich base (Z)

(Z) was prepared as described in previous work[12,13],starting from methyl benzoate to prepare the(2-thione-5-phenyl-1,3,4-oxadiazole)which was then reacted with di phenyl amine in the presence of formalin to get the final product .i.e.(Z) . The physical properties of (Z)are shown in table (1).It was identified by elemental analysis(C.H.N.S)and (FT-IR),the results are shown in Table(1) and (3) respectively.

2 - Preparation of the metal complexes (J_1-J_4)

Ethanolic solutin of each of the following metal ion salts (0.25mmol) [$CuCl_2.2H_2O$,$RuCl_3.6H_2O$,$PdCl_2(phCN)_2$,$H_2PtCl_6.6H_2O$] was added to an ethanolic solution (1.15mmol) of (Z) with stirring .The mixture was heated under reflux for one hour. During this time a precipitate was formed. Stirring was continued for one hour to ensure a complete reaction. The product in each case was filtered off, washed with hot ethanol, followed by cold water and then dried under vacuum[12,13]. All complexes were identified by FT-IR, UV-Vis, spectrophotometers , The results obtained are shown in Table (2,3 and 4) respectively.

3 – Study of biological activity for Mannich base and its complexes

The biological activity of the prepared Mannich base and their respective complexes were studied against two selected types of bacteria which are Pseudomonase aeruginosa as (Gram negative) and Bacillus subtilis as (Gram positive).The two types were cultivated in Nutrient agar medium. In vitro test were proceeded for studying activity against the two strains, using disc technique . DMF was used as a solvent and as a control, for this technique. The construction of (Z) and its complexes (1-4) in this solvent were 5mM and 10mM .The plates were incubated for 24hr.at 37 ^{0}C, the zone of inhibition of bacterial growth around the disc was observed[12,13,16].

Results and Discution

The interaction of Mannich base (Z) with the metal ions under study in ethanol gave a crystalline products with different colors depending on the metal ion, Table(1). All complexes were readily soluble in ($CHCl_3$, DMF and DMSO) and were found to be stable toward air and moisture. The physical analytical data of (Z) and it's metal complexes given in Table (1).

Table (1) : Physical data for (Z) and it's metal complexes

mp.No.	Color	ting point C^0	eild %	Metal analysis					Suggested formula for isolated precipitate
				C%	H %	N %	S %	M%	
(Z)	white	58-60	5 %	65.18 5.75)cal	0.53 .58)cal	12.69 .50)cal	9.15 .76)cal	—	$C_{21}H_{35}N_3OS$
J_1	green	189	.1%	51.32 (50.59)	8.42 (7.51)	7.21 (7.69)	5.51 (5.86)	2.62 1.64)	$[Cu(Z)Cl_2].C_2H_5OH$
J_2	Dark brown	120	.2%	29.64 (28.06)	6.52 (4.16)	4.61 (4.27)	4.21 (3.25)	1.73 0.27)	$u(Z)_2Cl_2]\ Cl.2C_2H_5OH$
J_3	Brown	173	.4%	43.35 (42.82)	7.42 (6.60)	8.21 (7.49)	6.16 (5.71)	9.69 8.98)	$[Pd(Z)\ Cl_2].\ H_2O$
J_4	Red rownish	228	.8%	22.72 (22.11)	5.10 (3.40)	4.43 (3.87)	5.37 (3.00)	3.66 7.97)	$[Pt(Z)_2Cl_2]\ Cl_2.H_2O$

Infrared Spectroscopic Study

The FT-IR spectra of the free ligand showed bands due to $\upsilon_{(C=S)}$,$\upsilon_{(N-C=S)}$ and $\upsilon_{(CH_2N)}$ which were observed at (1270), (1070,1023)and (2960,2923)cm^{-1} respectively[13,17] .The (Z) exhibit different types of coordination patterns as shown by their FT-IR spectral changes. The observation were further indicated by the appearance of $\upsilon_{(M-S)}$, $\upsilon_{(M-N)}$ and $\upsilon_{(M-X)}$ respectively[13,17], Table (2). Abroad band was observed around (3456) cm^{-1} in the spectra of complexes, assigned as $\upsilon_{(OH)}$ suggested the presence of water or ethanol molecules in the complexes[13].

Table (2) : Characteristic vibrational frequencies (cm^{-1}) located in the FT-IR of

omp.NO.	$\upsilon_{(C=S)}$	$\upsilon_{(N-C=S)}$	$\upsilon_{(CH_2N)}$	$\upsilon_{(M-N)}$	$\upsilon_{(M-S)}$	$\upsilon_{(M-Cl)}$	Others
(Z)	1270	070,1023	923,2960	–	–	–	–
J_1	1172	1084	900,2842	525	468	425	$\upsilon_{(O-H)}$ 3450
J_2	1180	010,1080	947,2850	520	475	410	$\upsilon_{(O-H)}$ 3481
J_3	1211	006,1010	920,2845	532	455	420	$\upsilon_{(O-H)}$ 3452
J_4	1250	012,1080	852,2924	528	460	416	$\upsilon_{(O-H)}$ 3465

. UV-Vis. Spetroscopic study

The electronic spectra of the metal complexes were recorded their solution in chloroform in the range of 200-1100 nm .The U.V spectrum of (Z) mostly showed two intense maxima bands at 47620cm^{-1} and 30030 cm^{-1} which belong to $\pi \longrightarrow \pi^*$ and $n \longrightarrow \pi^*$ respectively[14,15].

[J_1] :- The solution spectrum of the green complex , exhibits intense bands at (10928 , 14662 , 20040 and 23529)cm^{-1} . The position of theses band is in agreement with that reported for a highly distorted octahedral geometry[12,18,19] . which agree well with square planar geometry around Cu (II) complex[12,13,19,20] , Table (3) .

[J_2] :- The UV-Vis. Spectrum of the dark brown complex show two shoulders at (21052 and 27624)cm^{-1}, which indicate an octahedral geometry[13,21,22]. . Table (3) .

[J_3] :- The brown palladium complex show two absorption bands which were observed at (22222 and 31250)cm^{-1} . The spectrum was a typical of square planar Pd (II) complexes [13,15,18,22]. Table (3).

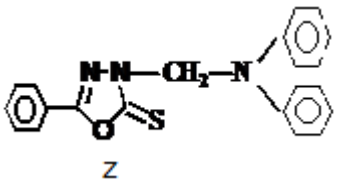
[J_4] :- The prepared red – brown Pt (IV) complex showed three bands at (19920 , 25125 and 30303)cm^{-1} , which indicate an octahedral geometry[13,18,22] . Table(3).

Table (3) : Electronic spectra ($CHCl_3$) for metal complexes

Comp.No	Bands cm^{-1}	Assignment	Suggested Structure
J_1	υ_1 (10928) υ_2 (14662) υ_3 (20040) υ_4 (23529)	$^2B_1g \longrightarrow {}^2Eg$ $^2B_1g \longrightarrow {}^2B_2g$ $^2B_1g \longrightarrow {}^2A_1g$ C . T	Square planar
J_2	(12726) cal υ_1 (21052) υ_2 (27624) υ_3	$^2T_2g \longrightarrow {}^4T_1g$ $^2T_2g \longrightarrow {}^4T_2g$ $^2T_2g \longrightarrow {}^2A_2g, {}^2T_1g$	Octahedral
J_3	υ_1 (22222) υ_2 (31250)	$^1A_1g \longrightarrow {}^1B_1g$ C . T	Square planar
J_4	υ_1 (199203) υ_2(25125) (30303) υ_3	$^1A_1g \longrightarrow {}^3T_1g$ $^1A_1g \longrightarrow {}^3T_2g$ C.T	Octahedral

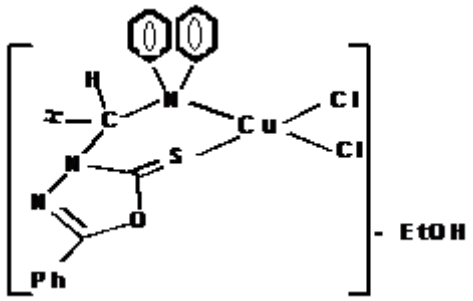
Suggested stereo chemical structures

According to the results obtained from the metal analysis and spectral analysis the structures of the above mention complexes can be illustrated as follows :-

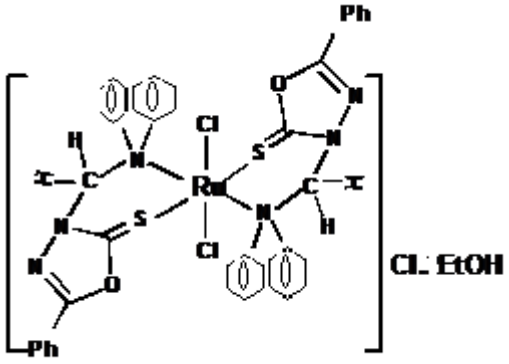


Z

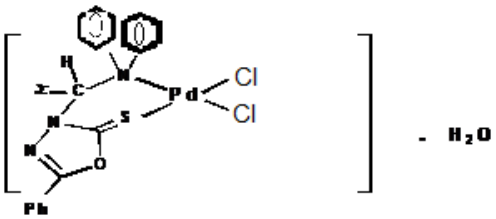
2-diphinyl aminomethyl-2-thion-5-phenyl- 1,3,4-oxadiazole
(Z)



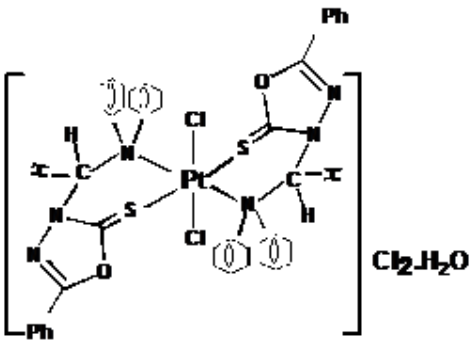
dichloro(2-diphynil aminomethyl-2-thion- 5-phenyl-1,3,4- oxadiazole). copper(II).ethanol
(J_1)



dicloro bis(2-diphynil aminomethyl-2-thion-5-phenyl-1,3,4- oxadiazole) . ruthinum(III)chloride.ethanol
(J_2)



dichloro (2-diphinyl aminomethyl-2-thion-5-phenyl-1,3,4- oxadiazole). palladium(II)water
(J_3)

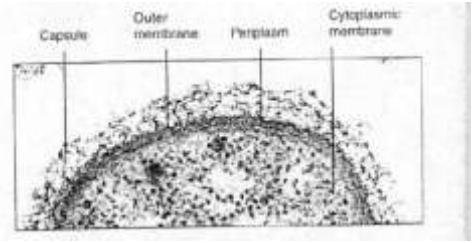


dichloro bis(2-diphynil aminomethyl-2-thion-5-phenyl-1,3,4-oxadiazole)platinum(IV) dichloride.water
(J_4)

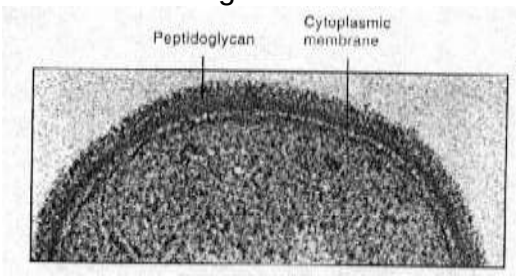
Bacteri cidal activity :-

The anti bacteri al activitie s of the (Z) and it's comple xes (J_1-J_4) was carried out against growth culture s of (Pseud omona s aerugin osa) and (Bacillu s Subtilis) respect ively . The all comple xes showe d a wider spectru m of activity against both type of bactera [13,23] ,

The metal ions Pd(II) , Ru(III) and Pt(IV) are considered to be soft metal ions , which render their complexes to be more lipophilic ,this will facilitate the penetration through the cell wall and effect the constituents of the cell [13,24] .

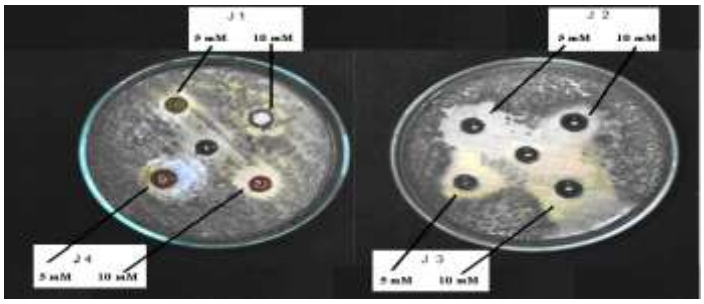


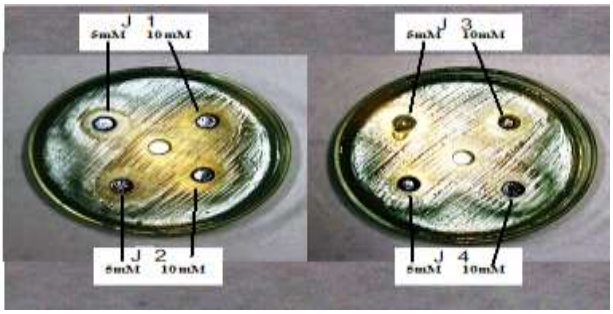
Gram negative cell wall



Gram positive cell wall

Common bacterial burn infection by *Pseudomonas aeruginosa*





Anti bacterial activity for the complexes at (5mM) and (10mM)

Table (5) : Anti bacterial activity for (DI) and their complexes at (5mM) and (10mM)

Comp.	Bacillus Subtilis		eudomonas aeruginosa	
Conc.	5mM	10mM	5mM	10mM
J_1	2	3	2	3
J_2	3	4	2	3
J_3	3	5	1	2
J_4	3	4	1	2

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