

PREPARATION, STRUCTURAL AND ANTIMICROBIAL STUDIES OF A NEW BIMETALLIC COMPLEXES INVOLVING A NEW SCHIFF AND MANNICH BASES

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Abstract

The present work includes the synthesis of mannich and Schiff bases [dichloro(N{3-(5-furfuralidene)-1,3,4-thiadiazole-2-thione} methylpyrazole)] cadmium(II)[A₃], by reacting (5-amino-2-thione-1,3,4-thiadiazole) with furfuraldehyde and pyrazol to form new mannich base [3-pyrazole amino methyl-2-thione-5-amino-1,3,4-thiadiazole][A₁]. Reaction of this derivative with cadmium chloride to give complex with tetrahedral geometry [dichloro(N{3-(5-amino-2-thione-1,3,4-thiadiazole)} methyl pyrazole)]Cadmium(II)[A₂], this [A₂] complex on further reaction with furfuraldehyde to give new Schiff base compound [A₃]. The products [A₁, A₂ and A₃] were characterized by FT-IR and elemental analysis (C.H.N). [A₃] act as ligand coordinating with various valent metal ions {Mn(II), Pd(II), Fe(III), Au(III), V(IV) and Pt(IV)}. The prepared complexes were identified and their structural geometries were suggested by using elemental analysis (C.H.N), Flame atomic absorption technique, FT-IR and UV—Vis Spectroscopy, in addition to magnetic susceptibility and conductivity measurements. The study of the nature of the complexes formed in mixture of chloroform-ethanol solution, following the mole ratio method, gave results which were compared successfully with those obtained from solid state studied. The apparent stability constant of the complexes have been studied with the time and their color were stable for more than (4) hours, as well as the molar absorptivities have been calculated. The antibacterial activity for the ligand (A₃) and their metal complexes (R₁-R₆) were studied against two selected micro-organisms (*Shigella flexneri*, as gram negative) and (*Staphylococcus aureus*, as gram positive), also the minimal inhibitory concentration (MIC) have been studied to determined the low concentration for inhibition. Further more the antifungi activity against two micro-organism (*Candida albicans* and *Aspergillus flavus*) were studied for the ligand and their metal complexes.

Introduction

Thiadiazole derivatives, especially those of 2-thio-1,3,4-thiadiazole-5-substituted, were reported to have different interesting biological activities⁽¹⁻³⁾. In continuation of previous work⁽⁴⁾, the synthesis and characterization of the mannich base derived from 5-phenyl-2-thione-1,3,4-thiadiazole and diphenyl amine was described along with a number of its transition metal complexes and were found that a synergic effect in the bioactivity took place upon complexation and different structural behavior was reported depending on the type of the metal besides the ligand structure. These results promote us to continue our work, and we here synthesis a new mannich base derivative of this hetrocyclic ring with involving imino group, to be used as a ligand to form a new type of bimetallic complexes toward some transition metal ions {V(IV), Mn(II), Fe(III), Pd(II), Au(III) and Pt(IV)} to investigate the

introduction the imino moiety in the structure of mannich base derivative of mercaptothiadiazole ring and coordination behaviour, then compare the biological activity of the ligand and their complexes with the main ring structure.

Experimental :

All chemicals were of highest purity and were used as received.

(A)-Preparation of the ligand

(1)-Preparation [N{3-(5-amino-2-thione-1, 3, 4-thiadiazole) methyl pyriazole}] (A₁)

(A₁) was prepared as described in our previous work⁽⁴⁻⁷⁾, starting from thio semicarbazid to prepare the -2-thione-5-amino-1,3,4-thiadiazole, which was then reacted with pyrazol in the presence of formaline to get the final product [A₁].

(2)-Preparation [dichloro (N{3-(5-amino-2-thione-1,3,4-thiadiazole)methyl pyrazole}] cadimium (II) (A2).

Ethanol solution of cadimium chloride (0.52 mmol) was added to ethanolic solution of (A₁) (1.15 mmol) with stirring. The white precipitate was formed immediately upon stirring at room temperature. Stirring was continued for one hour to ensure a completion of reaction. The product was filtered off, washed with hot ethanol, followed by cold water and then dried under vacuum.

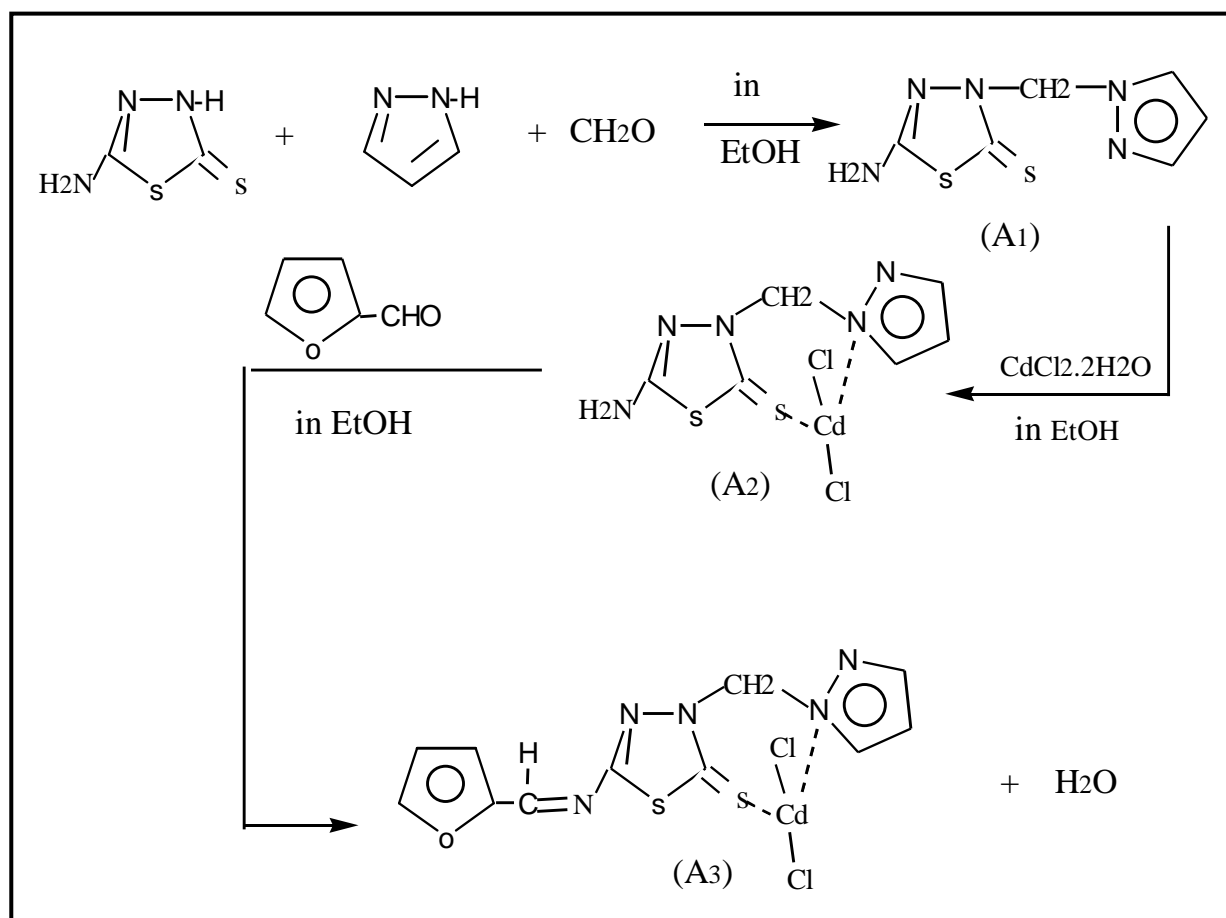
(3) Preparation of [dichloro (N{3-(5-furfuralidene)-2thione-1,3,4-thiadiazole} methyl pyrazole] Cadimium (II) (A3).

To a hot ethanolic solution of (A₂) (0.01mole), a solution of furfuraldehyde (0.01 mole) in (25 ml) ethanol was added with catalytic amount of glacial acetic acid, the reaction mixture was refluxed for (3)hours on cooling the separated solid was filtered and recrystallized form ethanol.

The physical properties of (A₁),(A₂) and (A₃) are shown in Table (1) and were identified by elemental analysis (C.H.N)and FT-IR.

(B)- Preparation of metal complexes[R₁-R₆]

Ethanol solution of each of the following metal ion salts (0.82 mmol) [VoSO₄.xH₂O, MnCl₂.2H₂O, FeCl₃.9H₂O, PdCl₂ (PhCN)₂, H₂AuCl₄.H₂O and H₂PtCL₆.6H₂O] was added to ethanolic solution (1.21mmol) of (A₃)with stirring . The mixture was heated under reflux for one hour during this time a precipitate was formed. The product of complex was filtered off, washed with hot ethanol, followed by cold water and then dried under vacuum.



Scheme (1) :The following scheme illustrate the structures of (A₁),(A₂) and (A₃).

(C)- Study of complex formation in solution

Complexes of (A_3) with metal ions were studied in solution using mix (chloroform-ethanol) as a solvent, in order to determined $[M:(A_3)]$ ratio in the complex following molar ratio method^(8,9). A series of solutions were prepared having a constant concentration (10^{-3} M) of the metal ion and (A_3). The $[M/(A_3)]$ ratio was determined from the relationship between the absorption of the absorbed light and the mole ratio of $[M:(A_3)]$. The results of complexes formation in solution were listed in Table (1).

(D)- Stability constant of complexes (R_1 - R_6)

The conditional or apparent⁽⁹⁾ stability constant of the (1:1) (metal : ligand) complex were evaluated as follows:

Two sets of solutions were prepared, the first set of solutions were formulated to contain stoichiometric amount (1 ml) of (10^{-3} M) ligand to (1 ml) of (10^{-3} M) of metal ion by placing into a three series of (10 ml) volumetric flask. The solution of the colored complexes were diluted to the mark with (ethanol-chloroform). The second set were formulated to contain five fold excess (5 ml) of (10^{-3} M) ligand, by placing into a three series of (10 ml) volumetric flasks followed by addition of (1 ml) of (10^{-3} M) of metal ion solution, the volumes were then completed to the mark with (ethanol-chloroform) mixture. The absorbance (A_s and A_m) of the solution were measured at (λ_{max}) of maximum absorption. The stability constant (K), and the molar absorptivity (ϵ_{max}) have been calculated, were listed in Table (4).

(E)- Study of biological activity for Mannich-Schiff bases and its complexes (R_1 - R_6)

The biological activity of the prepared compounds (A_1, A_2 and A_3) and their respective complexes (R_1, R_6) were studied against selected types of bacteria which include (*Shigella flexneri*) and (*Staphylococcus aureus*) were cultivated in nutrient agar medium.

Two *in vitro* techniques were proceeded for studying antibacterial activity against the two strains, DMSO was used as a solvent and as a control, for both techniques the constructions of the compounds in this solvent

were (10^{-3} M). The first technique was the Disc Sensitivity Test⁽¹⁰⁾, 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 37 C° , the zone of inhibition of bacterial growth around the disc was observed.

The second technique was to get the sensitivity of each micro-organism toward the new compounds by determining the minimal inhibitory concentration (MIC) which was achieved by using Tube Dilution Method⁽¹⁰⁾. The (MIC) of the new compounds for each micro-organism was measured at the lowest concentration of the compound required to inhibit the growth of this micro-organism, these tubes containing different concentrations of the new compounds were incubated at 37 C° for 45hr. Furthermore, the compounds (A_1, A_2 and A_3) and metal complexes [R_1, R_6] were tested for their *in vitro* growth inhibitory activity against a pathogenic fungi, i.e. *Candida albicans* and *Aspergillus flavus* on potato dextrose agar medium and incubated at 30 C° for 72 hr., DMSO was used as a solvent and as a control, the concentration of the compounds in this solvent were (10^{-3} M).

Physical measurements and analysis

Melting points were recorded on Gallen kamp melting point apparatus and were uncorrected. FT-IR spectra were recorded using FT-IR.8300 Shimadzu in the range of ($4000-200$) cm^{-1} and samples were measured as (CsI) disc. Electronic spectra were obtained using UV-1650 PC Shimadzu Spectrophotometer at room temperature. The measurements were recorded using concentration of (10^{-3} M) of the complex in chloroform. The metal content was estimated spectrophotometrically using atomic absorption Shimadzu AA670 Spectrophotometer. The elemental analysis (C.H.N.S) were obtained using EA-034.mth . Conductivity measurements were obtained using Corning conductivity meter 220, these measurements were obtained in DMF solvent using concentration of (10^{-3} M) at 25 C° . Magnetic susceptibility measurements were obtained at 25 C° on the solid state applying Faraday's method using Bruker BM6 instrument.

Results and Discussion

The interaction of [A₃] with the metal ions under study in (ethanol-chloroform) gave a crystalline products with different colours depending on the metal ion, Table (1). All complexes were readily soluble in CHCl₃, DMF and DMSO, and were found to be stable toward air and moisture, as well as they were decomposed before melting. The metal to ligand ratio were followed molar ratio method.

Table (1)
Physical data for [A₁, A₂ and A₃] and complexes [R₁-R₆].

COMP. No.	Color	Melting point C	Yield %	(Metal analysis) Found (calc.)					M:L Ratio	Suggested formula
				C%	H%	N%	S%	M%		
(A ₁)	Off white	162-165	85	33.61	3.34	33.06	30.11	-	-	C ₆ H ₇ N ₅ S ₂
(A ₂)	White	185-188	90	33.80	3.29	32.86	30.04			
				18.21	1.69	18.37	15.94	28.09	1:1	[C ₆ H ₇ N ₅ S ₂ CdCl ₂]
(A ₃)	Light yellow	200-203	80	18.16	1.77	17.66	16.15	28.36		
				27.92	1.66	15.48	13.27	23.86	1:1	[C ₁₁ H ₈ N ₅ S ₂ CdCl ₂]
[R ₁]	Dark green	215	82	28.86	1.75	15.30	13.99	24.57		
[R ₂]	Light brown	219	75	20.88	1.27	10.65	15.18	9.03	1:1	[Vo(A ₃)SO ₄]
				21.31	1.29	11.28	15.48	8.21		
[R ₃]	Red-brown	225	70	21..08	1.85	12.97	9.63	8.15	1:1	[Mn(A ₃)Cl ₂ (H ₂ O)].H ₂ O
				21.31	1.94	11.30	10.33	8.87		
[R ₄]	Brown	212	86	17.83	2.61	10.43	9.36	8.65	1:1	[Fe(A ₃)Cl ₂ (H ₂ O)]Cl.4H ₂ O
				18.59	2.54	9.86	9.02	7.87		
[R ₅]	Light brown	220	75	22.34	1.99	10.03	8.86	15.58	1:1	[Pd(A ₃)Cl ₂].Et
				22.91	2.06	10.28	9.40	15.63		
[R ₆]	Red	228	78	17.76	1.43	8.84	8.10	25.26	1:1	[Au(A ₃)Cl ₂].Cl
				17.35	1.05	9.20	8.41	25.89		
				16.08	1.14	9.79	6.93	24.19	1:1	[Pt(A ₃)Cl ₃].H ₂ O.Cl
				16.25	1.23	8.62	7.88	24.01		

Infrared spectroscopic study

The FT-IR.spectra of (A₁) was characterized by bands at (1120), (1068,1089), (2864,2952), (3500),(950) and (660)cm⁻¹, these can be assigned to (ν_{C=S}), (ν_{N-C=S}), (ν_{CH₂N}), (ν_{NH₂}), (ν_{N-N}) and (ν_{C-S-C}) respectively^(11,12). In the (A₂) complex a negative shift with reduced intensity were observed for (C=S), (N-C=S) and (CH₂N) stretching bands, while no significant change in the position of ν_{NH₂}, ν_{N-N} and ν_{C-S-C}, these clearly indicate that the (A₁) act as a bidentate

chelating agent by coordinating to the cadmium ion through sulphur atom of the thione and nitrogen of the amino methyl group to form tetrahedral geometry around Cd (II) complex^(7,13). An analysis the spectrum of (A₃) ligand of their respective (A₂) complex, show absence of the absorption band at (3500)cm⁻¹ for ν_{NH₂}, the appearance of the (C=N) stretching mode of azomethine group at (1650) cm⁻¹, are utilized to confirm the structure of (A₃), furthermore a new band

appearance at $(1295)\text{cm}^{-1}$ is ascribed to $[\text{C-O-C}]$ of [furan ring] stretching vibration^(11,12,14). When comparison of the spectra of (A_3) ligand and those of its complexes suggests that the (A_3) ligand coordinates to metal ions $[\text{Vo(IV)}, \text{Mn(II)}, \text{Fe(III)}, \text{Pd(II)}, \text{Au(III)}]$ and Pt(IV) in four different ways:

- (1)- In the case of $[\text{R}_1]$ the (A_3) ligand behave as bidentate coordinating with the vanadium oxide through both nitrogen of the azomethine and oxygen of furan ring, where the bands due to $(\nu_{\text{N-N}})$ and $(\nu_{\text{C-S-C}})$ vibration were still unchanged, Table (2).
- (2)- In the case of $[\text{R}_2]$ and $[\text{R}_3]$ complexes the bands due to $(\nu_{\text{N-N}})$, $(\nu_{\text{C=N}})$ and $(\nu_{\text{C-O-C}})$ were shifted to lower frequencies, Table (2), while the band related to $(\nu_{\text{C-S-C}})$ vibration was still unchanged, this suggests the involvement of nitrogen of azomethine, nitrogen of thiadiazole ring and oxygen of furan ring in the coordination.
- (3)- In the case of $[\text{R}_4]$ and $[\text{R}_5]$ the ligand of (A_3) behaves as bidentate chelating agent, and the coordinating sites are nitrogen of azomethine group and sulphur atom of the thiadiazole ring. Both bands of $(\nu_{\text{C=N}})$ and

$(\nu_{\text{C-S-C}})$ shifted and reduced intensity, Table (2), but the bands related to $(\nu_{\text{N-N}})$ and $(\nu_{\text{C-S-C}})$ remains in the same region in complexation, Table (2).

- (4)- In the case of $[\text{R}_6]$ complex the bands due to $(\nu_{\text{C-S-C}})$, $(\nu_{\text{C=N}})$ and $(\nu_{\text{C-O-C}})$ were shifted to lower frequencies side on complexation, where the band related to $(\nu_{\text{N-N}})$ remain unaltered in the spectra of the complex, indicating that the nitrogen atom of thiadiazole moiety don't take part in coordination, Table (2).

The behavior of (A_3) was further indicated by appearance of (M-N), (M-S), (M-O) and (M-Cl) bands stretching frequencies respectively⁽¹⁵⁾, Table (2). As well as a strong band was observed at 992 cm^{-1} due to (V=O) stretching mode in $[\text{R}_1]$ complex⁽¹⁵⁾, while band related to sulfate anion in the same complex was observed at 1502 cm^{-1} , indicated a bidentate behavior⁽¹⁵⁾. A broad band was observed around $(3435-3504)\text{ cm}^{-1}$ in the spectra of $[\text{R}_2-\text{R}_4]$ and $[\text{R}_6]$ complexes, assigned as (ν_{OH}) suggested the presence of water or ethanol molecule, while a weak band observed at 1610 cm^{-1} in the spectra of $[\text{R}_2]$ and $[\text{R}_3]$ complexes suggests the presence of coordinated water⁽¹⁵⁾.

Table (2)
Characteristic stretching vibrational frequencies (cm^{-1}) located in the FT-IR of $[\text{A}_1, \text{A}_2]$ and $[\text{A}_3]$ and complexes $[\text{R}_1-\text{R}_6]$.

Comp	ν C-S	ν N-C-S	ν CH2-N	ν C=N	ν N-H	ν C-O-C	ν C-S-C	ν M-O	ν M-N	ν M-Cl	ν O-H
(A_1)	1120 (s)	1068, 1089(ms)	2864, 2952 (s)	-	950 (s)	-	660 (s)	-	-	-	-
(A_2)	1109 (m)	1060, 1077(m)	2855, 2945 (vm)	-	949 (s)	-	660 (s)	-	481 (m)	389 (w)	-
(A_3)	1110 (m)	1060, 1078(m)	2855,2945 (vm)	-	950 (s)	1295 (ms)	659 (s)	-	481 (m)	389 (w)	-
$[\text{R}_1]$	1110 (m)	1059, 1077(m)	2855,2946 (vm)	1650 (s)	949 (s)	1286 (m)	660 (s)	515 (m)	484 (m)	388 (w)	-
$[\text{R}_2]$	1109 (m)	1060, 1077(m)	2854,2946 (vm)	1643 (m)	942 (ms)	1283 (m)	660 (s)	520 (m)	484 (m)	389 (w)	3435
$[\text{R}_3]$	1110 (m)	1061, 1077(m)	2855,2945 (vm)	1641 (m)	941 (ms)	1285 (m)	659 (s)	522 (m)	488	385	3450
$[\text{R}_4]$	1108 (m)	1060, 1078(m)	2854,2945 (vm)	1641 (m)	949 (s)	1293 (ms)	652 (m)	-	490	388	3504
$[\text{R}_5]$	1109 (m)	1059, 1078(m)	2854,2944 (vm)	1642 (m)	948 (s)	1295 (ms)	650 (m)	-	489	389	-
$[\text{R}_6]$	1109 (m)	1060, 1077(m)	2855,2945 (vm)	1640 (m)	948 (s)	1283 (m)	650 (m)	518	490	392	3441

Electronic spectra, Magnetic susceptibility and Conductivity measurements

As further structural tools, electronic spectral, magnetic and conductivity studied have been used to confirm the geometry of the complexes.

The electronic spectra of the [R₁-R₆] metal complexes were recorded for their solution in chloroform in the range (200-1100) nm.

[R₁] : The dark green spectrum of vanadyl (IV) complex show two main absorption bands, Table (3) , which are assigned to the transition ${}^2B_2 \rightarrow {}^2E_g$ and ${}^2B_2 \rightarrow {}^2B_1$ respectively in a square pyramidal geometry⁽¹⁶⁻¹⁸⁾. The magnetic moment (2.04 B.M) is higher than spin value of the vanadium metal only, this result indicates a higher orbital contribution^(16,19-21). Conductivity measurement in (DMF) showed that the complex was nonionic, Table (3).

[R₂] : This complex showed a series of very weak and some were narrow bands have been observed in Mn(II) spectra, this is expected because the only sextet term of the (d⁵) configuration in octahedral stereochemistry is the ${}^6A_{1g}$, consequently, there can be no spin-allowed transitions^(16,22), and were assigned to ${}^6A_{1g} \rightarrow {}^4T_{2g}(G)$, ${}^6A_{1g} \rightarrow {}^4T_{1g}(G)$ and ${}^6A_{1g} \rightarrow {}^4T_{1g}(4E)$ respectively⁽¹⁶⁾. The values of racah parameters (10 Dq , B' and β) have been calculated to be (10058,810 and 0.89) respectively, the value of β (0.89) signifies a fair amount of ionic character⁽²³⁾. Magnetic moment of the solid complex (5.89 B.M) showed a high spin Mn (II) complex^(20,22). Conductivity measurement showed the complex was noionic, Table (3).

[R₃] : Three absorption bands of the brown complex were observed at (15021,17890 and 30112) cm⁻¹, which are assigned to the transitions: ${}^6A_{1g} \rightarrow {}^4T_{1g}(G)$, ${}^6A_{1g} \rightarrow {}^4T_{2g}(G)$ and ligand→Fe(C.T)⁽²³⁻²⁵⁾. The values of (10 Dq, B' and β) came out to (6811,620 and 0.48) respectively. The magnetic moment is (5.92 B.M) with five unpaired electrons and an octahedral configuration. Conductivity measurement in DMF showed that the complex was to be ionic, Table (3).

[R₄] : The prepared brown Pd(II) complex showed strong charge transfer band at 39630 cm⁻¹, which was extended to the visible region, as well as two ligand field bands at 22580 and 26334 cm⁻¹ which may be assigned to the transitions : ${}^1A_{1g} \rightarrow {}^1B_{1g}$ and ${}^1A_{1g} \rightarrow {}^1E_g$ ^(24,26,27), respectively. The magnetic moment value was (0.68) B.M. conductivity in DMF showed that the complex was non ionic, Table (3).

[R₅] : The spectrum of this complex gave four absorption bands appeared at (16588, 23799, 31004 and 36016) cm⁻¹, which indicate a square planer geometry^(17,24,28,29), and were assigned to ${}^1A_{1g} \rightarrow {}^3B_{1g}$, ${}^1A_{1g} \rightarrow {}^1B_{1g}$, ${}^1A_{1g} \rightarrow {}^1E_g$ and ligand→Au (C.T) transition respectively. The complex was diamagnetic and conductivity measurements in DMF showed that the complex was ionic, Table (3).

[R₆] : The observed magnetic value (2.46 B.M) of the present platinum (IV) complex (d⁶) configuration agree with octahedral geometry around Pt(IV) ,this result indicates higher orbital contribution^(7,16,28). The prepared red Pt(IV) complex showed three bands at (19112,23896 and 29083)cm⁻¹, and were assigned to ${}^1A_{1g} \rightarrow {}^3T_{1g}$, ${}^1A_{1g} \rightarrow {}^3T_{1g}$ and ligand→Pt(C.T) transition respectively^(17,28). The conductivity measurement showed that the complex to be ionic, Table (3).

Table (3)
Electronic spectra (CHCl₃), magnetic moment (B-M) and conductance (in DMF) for metal complexes [R₁-R₆].

Comp. No.	Bands cm ⁻¹	Assignment	10 dq cm ⁻¹	Molar Cond. MS.cm ⁻¹	Meff. B.M	Suggested structure
[R ₁]	11784 17222	² B ₂ → ² E _g ² B ₂ → ² B ₁	-	20.33	2.04	Square pyramidal
[R ₂]	17998 23034 25760	⁶ A _{1g} → ⁴ T _{1g} (G) ⁶ A _{1g} → ⁴ T _{2g} (G) ⁶ A _{1g} → ⁴ T _{1g} (4E)	10058	15.86	5.89	Octahedral
[R ₃]	15021 17890 30112	⁶ A _{1g} → ⁴ T _{1g} ⁶ A _{1g} → ⁴ T _{2g} [A ₃] → Fe(C.T)	6811	64.29	5.92	Octahedral
[R ₄]	22580 26334 39630	¹ A _{1g} → ¹ B _{1g} ¹ A _{1g} → ¹ E _g [A ₃] → Pd(C.T)	22580	18.61	0.68	Square planar
[R ₅]	16588 23799 31004 36016	¹ A _{1g} → ³ B _{1g} ¹ A _{1g} → ¹ B _{1g} ¹ A _{1g} → ¹ E _g [A ₃] → Au(C.T)	23799	72.89	0.73	Square planar
[R ₆]	19112 23896 29083	¹ A _{1g} → ³ T _{1g} ¹ A _{1g} → ³ T _{2g} [A ₃] → Pt(C.T)	-	69.43	2.46	Octahedral

Solution study

1) Molar ratio method

The molar ratio method were followed to determine the M:L ratio. The results of complexes in (ethanol-chloroform) as (solvents) suggested that the metal to ligand ratio was (1:1) for [R₁-R₆] complexes, which were comparable to those obtained from solid state study, Table (1).

2) Stability constant of the mannich-schiff bases complexes

The apparent stability constant (K) of the [1:1] [Metal : Ligand] were evaluated using the following equation:

$$K = \frac{(1-\alpha)}{\alpha^2 C}$$

Where (α) is the degree of dissociation, were evaluated using the following equation:

$$\alpha = \frac{A_m - A_s}{A_m}$$

Where (A_m = average of three measurements of the absorption of solution containing the same amount of metal and five fold excess of ligand) while (A_s = average of three

measurements of the absorption of solution containing a stoichiometric amount of ligand and metal ions). Furthermore the molar absorptivity (ϵ_{max}) for all complexes were measured at λ_{max} of maximum absorption and were calculated from the following equation: $A_m = \epsilon_{max} b c$.

The results shown in Table (4), indicate that [R₁-R₃ and R₆] complexes yield rather high stability constant as well as high molar absorptivity contrast to the [R₄ and R₅], this probably due to the different coordination behavior of the new ligand toward metal ions. As well as the developed color become stable after (one hour) up to (4 hours).

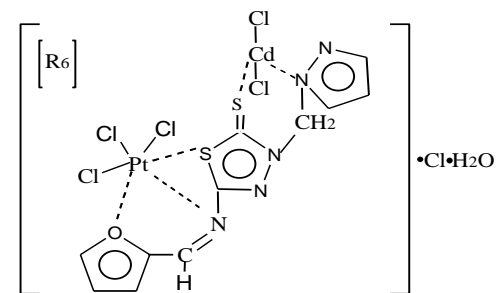
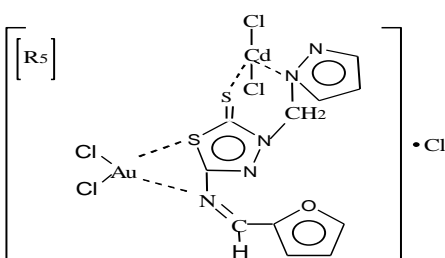
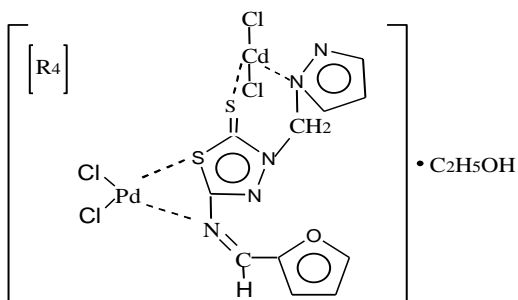
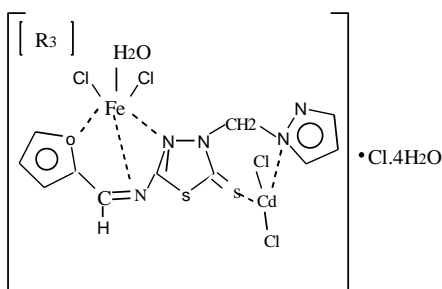
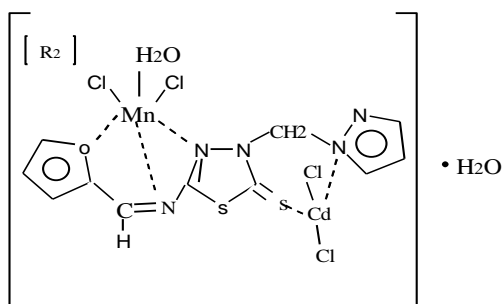
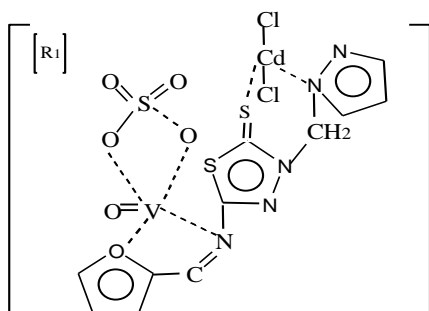
Table (4)
Stability constant and molar absorptivities of mannich Schiff bases complexes at room temperature.

Complexes	As	Am	α	K L.mol ⁻¹	ϵ_{\max} L.mol ⁻¹ .cm ⁻¹	λ_{\max} nm
[R ₁]	0.374	0.430	0.131	4.25×10 ⁵	3785	756
[R ₂]	0.293	0.316	0.073	1.74×10 ⁶	3166	498
[R ₃]	0.398	0.453	0.121	6.00×10 ⁵	4532	506
[R ₄]	0.259	0.309	0.161	3.95×10 ⁵	2862	438
[R ₅]	0.324	0.378	0.142	4.25×10 ⁵	3785	430
[R ₆]	0.336	0.399	0.157	5.84×10 ⁵	3991	515

Stereochemistry structure of [R₁-R₆] complexes

According to the results obtained from the elemental analysis (C.H.N), atomic absorption and spectral analyses the structure

of the above mentioned complexes [R₁-R₆] can be illustrated as follow:



Biological activity

As a result from the study of antimicrobial for (A_1), (A_2), (A_3) and [R_1 - R_6] complexes, the following points were concluded :

- 1- (A_1) Showed a moderate activity against the studied bacteria and the fungus, while its metal complex (A_2) showed a wider spectrum of activity toward all types of the microorganisms. This difference in synergistic effect⁽³⁰⁾ between the cadmium ion and the (A_1) molecule, Table (5).
- 2- It was of interest to investigate the effect of introducing the pharmacologically important Schiff base moiety in the structure of the prepared (A_2) complex and their antibacterial with antifungal activities. For this purpose six complexes were prepared and the results in Table (5) show large increase in the activity of all complexes, which indicate the importance of the Schiff base moiety (imin groups) in enhancement of biological activity of the studied complexes.
- 3- The presence of a second metal center in one structure, exhibited a greater activity against all the studied microorganism compared to that of (A_3) it self, this indicates that dinuclear nature are more important than mononuclear analogues.
- 4- The results reflect the different effects of introducing the metal ion on the (A_3) ligand structure, where some metal ion enhanced activity, while others retarded it, this phenomena is known as synergistic effect⁽³⁰⁾. The difference in synergistic effect between the metal ion and the ligand molecule may be attributed to many factors, of these in that [$Vo(IV)$, $Mn(II)$

and $Fe(III)$] are considered to be a hard metal ion making its complexes to be less lipophilic, this will relatively retard its permeation through the lipid part of the cell membrane .On the other hand the [$Pd(II)$, $Au(III)$ and $Pt (IV)$]are all 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⁽³⁰⁾.

- 5- The results of the (MIC) study for the [A_1 , A_2 and A_3] and the [R_1 - R_6]complexes are shown in Table (6). These results indicate that some of the new compounds exhibited antibacterial activity against the studied bacteria at lower concentration, while they don't show such activity at higher concentration.
- 6- Results of the anti fungal activity of the new compounds, Table (5)showed that the metal ion chelates were more toxic compared with their parent ligaund (A_3) toward the same micro-organism and under the identical experimental conditions. The increase in the antifungal activity of metal chelates may be due to the effect of metal ion on the normal cell process .These activities may be explained by Tweedy's Chelation Theory⁽³¹⁾, according to which chelation reduces the polarity of the metal atom mainly ,because of the partial sharing of its positive charge with the donor groups of the ligand which favors permeation of the complexes through the lipid layer of cell membrane⁽³²⁾.

Table (5)

Antibacterial and antifungal activities for [A_1 , A_2 , A_3] and [R_1 - R_6] complexes (10^{-3} mgm.ml⁻¹).

Comp.	Staphylococcus aureus	Shigella flexneri	Aspergillus flavus	Candida albicans
(A_1)	6	-	30	26
(A_2)	10	10	18	21
(A_3)	15	10	14	12
[R_1]	10	6	12	14
[R_2]	6	10	20	17
[R_3]	15	20	12	14
[R_4]	15	15	10	12
[R_5]	25	15	12	14
[R_6]	20	25	10	10

Where [6-8 (+) , 8-10 (++) ,
> 10 (+++)]

[30-40 (+++) , 20-30 (++++) ,
10-20 (++++)]

Table (6)
Minimal inhibitory concentration (MIC) for [A₁, A₂, A₃] and [R₁-R₆] complexes (μgm.l⁻¹).

Comp.	Staphylococcus aureus					Shigella flexneri				
	0.02	0.075	0.5	2.5	5	0.025	0.075	0.5	2.5	5
(A ₁)	+	+	MIC	-	-	+	+	+	MIC	-
(A ₂)	+	MIC	-	-	-	+	+	MIC	-	-
(A ₃)	MIC	-	-	-	-	+	MIC	-	-	-
[R ₁]	-	MIC	-	-	-	+	MIC	-	-	-
[R ₂]	+	+	MIC	-	-	+	+	MIC	-	-
[R ₃]	+	MIC	-	-	-	+	MIC	-	-	-
[R ₄]	MIC	-	-	-	-	+	MIC	-	-	-
[R ₅]	+	MIC	-	-	-	+	+	MIC	-	-
[R ₆]	MIC	-	-	-	-	+	MIC	-	-	-

Where : (+) Growth , (MIC) 99% , (-) no growth

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الخلاصة

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يتضمن هذا البحث تحضير قاعدتي مانخ و شف الجديدتين **dichloro[N{3-(5-furfuralidene)-1,3,4-thiadiazole-2-thione}methylpyrazole].cadimium (II) (A₃)** من مفاعلة (5-amino-2-thione-1,3,4-thiadiazle) مع كل من الفورمالين و البايروزول للحصول على قاعدة مانخ الجديدة (3-pyrazole amino methyl-2-thione- (A₁) (5-amino-1,3,4-thiadiazole) ومن مفاعلة (A₁) مع ملح كلوريد الكادميوم المائي للحصول على معقد رباعي السطوح dichloro (3-pyrazole amino methyl-2-thione-5-amino-1,3,4-thiadiazole). Cadimium (II). (A₂). ومن ثم مفاعلة (A₂) مع الفورفرلديهايد للحصول على قاعدة شف الجديدة (A₃). جرى تشخيص المركبات المحضرة (A₁ و A₂ و A₃) بطرق طيف الأشعة تحت الحمراء و التحليل الدقيق للعناصر . تم استخدام (A₃) كالكاند لتحضير عدد من المعقدات الجديدة مع بعض ايونات العناصر الأنتقالية الثنائي (المنغنيز و البلاديوم) و الثلاثية التكافؤ (الحديد و الذهب) و الرباعية التكافؤ (الفناديوم و البلاتين) . تم اقتراح الشكل الهندسي للمعقدات المحضرة باستخدام التحليل الدقيق للعناصر (C.H.N) وتقنية الامتصاص الذري للهيبي للعناصر و طيف الأشعة تحت الحمراء و طيف الأشعة فوق البنفسجية المرئية فضلاً عن قياسات الحساسية المغناطيسية و التوصيلية الكهربائية . تم كذلك دراسة طبيعة المعقد المتكون في مزيج من الايثانول - كلوروفورم باتباع طريقة النسبة المولية ، وقد اعطت هذه الدراسة نتائجاً مطابقة مع تلك التي تم الحصول عليها في الحالة الصلبة ، كما درست ثوابت الاستقرار للمعقدات المتكونة مع الزمن و كانت مدة ثبات اللون اكثر من (4) ساعات ، فضلاً عن ذلك تم حساب قيمة الممتصية المولارية للمعقدات . تم تقويم الفعالية المضادة للبكتريا لليكاند (A₃) و معقداته (R_6-R_1) و اختير نوعان من البكتريا *Shigella flexneri* سالبة الصبغة و *Staphylococcus aureus* موجبة الصبغة لهذا الغرض ، كما تم دراسة اقل تركيز يحدث عنده التثبيط (MIC) بالاضافة الى ذلك تم اجراء التقويم الحيوي لليكاند و معقداته ضد نوعين من الفطريات (*Candida albicans*) و (*Aspergillus fla*).