MANNICH BASE DERIVED FROM 1,3,4-THIADIAZOLE AS CHELATING LIGAND FOR SOME TRANSITION METAL COMPLEXES

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Abstract

The compound(5-phenyl-1,3,4- thiadiazole-3-one) react with dibenzylamine and formaline to form new mannich base {N(2-(5-phenyl-1,3,4-thiadiazole-3-one)methyl) dibenzylamine} (DB).The product was characterized by (FT-IR) Spectroscopy and thermal analysis(TG-DTG). (DB) act as a ligand coordinating with some transiton metal ions{Co(II), Ni(II), Cu(II), Pd(II), Cr(III), Fe(III), Ru(III), Rh(III), Au(III), and Pt(IV)} through the oxygen of carbonyle group and the nitrogen of the amino methyl group.The steroochemistry around the metal ion has been suggested using flame atomic absorption, (FT-IR) and (UV-Vis) Spectroscopy, in addition to magnetic susceptibility , conductivity measurement and thermal analysis(TG-DTG). The study of the nature of the complexes formed in (ethanolic solution) following the mole ratio method, gave results which were compared successfully with those obtained from solid state studies. The apparent stability constant of the complexes have been studied with the time and their color were stable for more than (6) hours, as well as the molar absorptivities have been calculated.The antibacterial activity for the ligand and their metal complexes were studied against four selected microorganisms [(*Pseudo monase aeruginos*) and (*Klesbiella pneumonia*) as gram negative] and [(*Streptococcus faecalis)* and(*Bacillus subtlus*) as gram positive]. The minimal inhibitory concentration (MIC) have been also studied to determined the low concentration for inhibition. Further more the antifungl activity against two micro-organism (*Candida albicans* and *Aspergillus flavus*) were studied for the ligand and their metal complexes.

Introduction

The thiadiazole ring associated with antifungal, hypoglycemic, analgesic and antimycrobacterial properties (1-3). The 2-substituted amino methyl-5-substituted-1,3,4-thiadiazole-3-one,possess central nervous system depressant activity(4-6).The presence of nitrogen of aminomethyl and oxygen of carbonyl group provide more than one donor atom for complexation with metal ions,this may lead synergistic effect in biological activities as well as synthetic models in studying the effect of metal ion on some srructurally related enzyme activities (7,8) . The present work is repporting for first time, the synthesis of a new maanich base (DB) in an attempt to introduce the aminomethyl moiety in the structure of thiadiazole ring to investigate the coordination behaviour of the new ligand toward some hevy transition metal ions {Co(II), Ni(II), Cu(II), Pd(II), Cr(III) , Fe(III), Ru(III), Rh(III), Au(III), and Pt(IV)}, which have been choosen to react with (DB) and to determine 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 Mannich base (DB)

(DB) was prepared as described in our previous work(9-11), starting from {ethyl(5-phenyl-1,3,4-thiadiazole-2-yl-thio)acetate} to prepare the [5-phenyl-1,3,4- thiadiazole -3-(2H)-one] (5,6) ,which was then reacted with dibenzyl amine in the presence of formaline to get the final product(DB); i-e. The physical properties of (DB) are shown in Table (1), it was identified by (FT-IR) and thermal analysis (TG-DTG), the results are shown in Table (2) and (4) respectively.

B-Preparation of the metal complexes (R_1-R_{10})

Ethananolic solution of each of the following metal ion salts (0.75 mmol) [$CoCl_2.6H_2O$, $NiCl_2.6H_2O$, $CuCl_2.2H_2O$, $PdCl_2(PhCN)_2$, $CrCl_3.6H_2O$, $FeCl_3.9H_2O$,

$RuCl_3.XH_2O$, $RhCl_3.XH_2O$, $HAuCl_3$. H_2O and $H_2PtCl_6.6H_2O$] was added to an ethanolic solution (1.25 mmol) of (DB) with stirring . The mixture was heated under reflux for one hour during this time a precipitate was formed of the complexes. The product was filtered off, washed with hot ethanol, followed by cold water and then dried under vacuum.

C-__Study of complex formation in solution__

Complexes of (DB) with metal ions were studied in solution using ethanol as a solvent, in order to determined [M : (DB)] ratio in the complex following Molar ratio method (12). A series of solutions were prepared having a constant concentration [10^{-3}M] of the metal ion and (DB). The [M/(DB)] ratio was determined from the relationship between the absorption of the absorbed light and the mole ratio of [M: (DB)]. The results of complexes formation in solution were listed in Table (1).

__D- Stability constant of mannich base coplexes__

The conditional or apparent(12) stability constant of the (1:1) or (1:2) [Metal: Ligand] complex were evaluated as fallows:

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 in to a three series of 10 ml volumetric flasks. The solutions of the coloured complexes were diluted to the mark with ethanol. The second set were formulated to contain five fold excess (5 ml) of (10^{-3}M) ligand, by placing in to 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. The absorbance (As and Am) of the solutions, were measured at λmax of maximum absorption. The stability constant (K), and the molar absorptivity (εmax) have been calculated , were listed in Table (5).

__E- Study of biological activity for mannich base and its complex__

The biological activity of the prepared mannich base and their respective complexes were studied against selected types of bacteria which include [(*Pseudo monase aeruginos*) and (*Klesbiella pneumonia*) as gram negative] and [(*Streptococcus faecalis)* and (*Bacillus subtlus*)as gram positive], were cultivated in Nutrient agar medium.

Two *in vitro* techniques were procceded 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(13,14), this method involves the exposure of the zone of inhibition toward the diffusion of micro-organism on agar plate. The plates were incubated for 24 hr. 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 a chieved by using Tube Dilution Method(13,14). 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 45 hr.

In order to complete this study, the new ligand and their metal complexes 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, for both techniques, the constructions of the compounds in this solvent were 10^{-3}M. The inhibition of fugal growth, expressed in percentage terms, were determined on the growth in test plates compared to the respective control plates, as given by the Vincent equation(14) Table (6).

Physical measurements and analysis

Melting points were recorded on GallenKamp melting point apparatus and were uncorrected. FT-IR spectra were recorded using FT-IR.8300 Shimadzu in the range of (4000-200) cm^{-1}. Samples were measured as (CsI disc). Electronic spectra were obtained using UV-1650 PC Shimadzu Spectrophotometer at room temperature. The measurements were recorded using a concentration of 10^{-3}M of the complex in chloroform solvent. The metal content was estimated Spectrophotometrically using Atomic absorption Shimadzu AA 670 Spectrophotometer. Conductivity measurements were obtained using Corning conductivity meter 220. These measurements were obtained in DMF solvent using concentration of 10^{-3}M at 25C°. Magnetic susceptibility measurements were obtained at 25C° on the solid state applying Faraday's method using Bruker BM6 instrument.

Thermal analysis were performed using TG-DTG A6200-Thermo Haake.

Results and Discussion

(A)-Elemental Analysis :

The physical analytical data of (DB) and its metal complexes are given in Table (1), which are in a satisfactory agreement with the calculated values. The suggested molecular formulas also supported by subsequent spectral and molar ratio, as well as magnetic moment and thermal analysis.

Table (1)
Physical data for (DB) and its metal complexes.

Comp. No.	Color	Melting Point *a** C°	Yield %	Metal analysis		M:L Ratio **b*	Suggested Formula for isolated precipitate
				Found %	Calc. %		
(DB)	Off-white	170-167	95	-	-	-	$C_{23}H_{21}N_3SO$
[R_1]	Deep Blue	182	84	11.40	12.29	1:1	$[Co\ (DB)Cl_2]$
[R_2]	Brown	197	75	6.37	5.88	1:2	$[Ni\ (DB)_2Cl_2]\ .\ H_2O$
[R_3]	Green	186	80	11.78	11.62	1:1	$[Cu\ (DB)Cl_2]\ .\ H_2O$
[R_4]	Brown	193	72	18.85	18.09	1:1	$[Pd\ (DB)Cl_2]$
[R_5]	Deep Green	200	70	5.27	5.34	1:2	$[Cr\ (DB)_2Cl_2].Cl.3H_2O$
[R_6]	Brown	198	75	5.74	6.29	1:2	$[Fe(DB)_2Cl_2].Cl.2H_2O$
[R_7]	Deep Orang	202	83	10.28	9.77	1:1	$[Rh\ (DB)_2].Cl_3.\ H_2O$
[R_8]	Bright Yellow	209	70	17.05	16.89	1:2	$[Au(DB)_2].Cl_3.\ EtOH$
[R_9]	Dull Grey	<214	66	7.39	7.11	1:2	$[Ru(DB)_2\ Cl_2].Cl$
[R_{10}]	Brownish-red	212	80	15.95	16.22	1:2	$[Pt\ (DB)_2\ Cl_2].Cl_2.\ EtOH$

(a*) = All complexes were decomposed.
(b*) = Measured in EtOH solvent.

(B)-Infrared Spectra:

The characteristic stretching vibrational modes concerning (DB) and their metal complexes are described in Table (2) .(DB) exhibited a strong high intensity bands appeared at (1680) and (2868, 2972) cm^{-1}, and were assigned to the stretching mode of [ν C=O and ν CH_2N] respectively .In the all complexes (R_1-R_{10}) the ligand behave as a a bidentate coordinating to the metal throw the oxygen of carbonyl and nitrogen of the methylene groups, therefore the bands due to (ν C=O and ν CH_2N) were shifted to lower by (8-10) and (6-9,6-12) cm^{-1} respectively(15), Table(2). These observation were further indicated by the appearance of (ν M-O, ν M-N and ν M-Cl) respectively(16) , Table (2). A broad band was observed around (3456-3518) cm^{-1} in the spectra of [R_2, R_3, R_5-R_8 and R_{10}] complexes , assigned to a ν O-H and suggested the presence of a water or ethanol molecules in the complexe (15,16).

Table (2)
Characteristic Stretching Vibrational Frequencies (cm^{-1}) located in the FT-IR of (DB) and their Metal Complexes.

Comp. No.	νC=O	$νCH_2$ N	νM-O	νM-N	νM-Cl	νO-H
(DP)	$1680_{(S)}$	2868 $2972_{(S)}$	-	-	-	-
$[R_1]$	$1671_{(m)}$	2859 $2966_{(m)}$	$508_{(w)}$	$480_{(vw)}$	$399_{(vw)}$	-
$[R_2]$	$1670_{(m)}$	2860 $2963_{(m)}$	$510_{(w)}$	$488_{(vw)}$	$384_{(vw)}$	$3435_{(b)}$
$[R_3]$	$1669_{(m)}$	2859 $2966_{(m)}$	$506_{(w)}$	$483_{(w)}$	$402_{(vw)}$	$3447_{(b)}$
$[R_4]$	$1672_{(m)}$	2860 $2963_{(m)}$	$508_{(w)}$	$485_{(w)}$	$400_{(vw)}$	-
$[R_5]$	$1672_{(m)}$	2859 $2966_{(m)}$	$512_{(w)}$	$480_{(w)}$	$396_{(vw)}$	$3444_{(b)}$
[R6]	$1672_{(m)}$	2859 2966	$505_{(w)}$	$483_{(w)}$	$399_{(vw)}$	$3450_{(b)}$
$[R_7]$	$1670_{(m)}$	2860 $2963_{(m)}$	$504_{(w)}$	$488_{(w)}$	-	$3445_{(b)}$
$[R_8]$	$1670_{(m)}$	2859 $2966_{(m)}$	$511_{(w)}$	$481_{(w)}$	-	$3525_{(vb)}$
$[R_9]$	$1669_{(m)}$	2859 $2966_{(m)}$	$512_{(w)}$	$488_{(w)}$	$396_{(vw)}$	-
$[R_{10}]$	$1671_{(m)}$	2862 $2960_{(m)}$	$512_{(w)}$	$486_{(w)}$	$400_{(vw)}$	$3518_{(vb)}$

(C)- UV-Vis Spectroscopic study:

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

The blue cobalt $[R_1]$ complex existin in a divalent state with symmetrical tetrahedral geometry(10,17-21). This hypothesis is supported by the number of maxima observed in the UV-Vis spectra of the complex.The three maxima bands, Table (3) have been assigned to the transition $^4A_2 \rightarrow {}^4T_{1\ (p)}$ (10,17). The values of racah parameters (Dq, B^-, β, and $ν_2$) have been calculated to be (374.4), (722.8), (0.5) and (6770.9) respectively. The value of β(0.5) signifies a fair amount of covalent character in metal to nitrogen and oxygen bonds while the value of (Dq) to be (374.5) cm^{-1}, one should expect a band due the transition :- $^4A_2 \rightarrow {}^4T_{2\ (f)}$ in the infrared region at (3745) cm^{-1}, which could not be observed in the spectrum of the Co(II) complex(10,19).As well as the value of spin-orbit coupling constant($λ^-$) has been calculated to be (-161.03) ,this constant has been calculated using the followingequation :-

$$μo.b = μs.o - 15.49\ λ^- /10Dq$$

Where : –μo.b =The observed effective magnetic moment .

μs.o =The electronic spin only magnetic moment.

The measured magnetic moment was (4.58B.M) this show the cobalt ion in it's blue complex to be paramagnetic with d^7 configuration in a distorted tetrahedral environment(22,23) . Conductivity measurement showed that the complex was non ionc.

The magnetic moment of Ni(II) complex (2.79B.M) indicated octahedral sterochemistry (17,24-26) . Electronic spectra of this complex showed(d-d) bands in the (23529,16667 and 10642) cm^{-1},these are asigned to $^3A_2g \rightarrow {}^3T_1g_{(P)}$, $^3A_2g \rightarrow {}^3T_1g_{(F)}$ and $^3A_1g \rightarrow {}^3T_2g_{(F)}$ respectively for octahedral Ni(II) complex (24,27). Various spectral parameters (Dq, B^- and β) have been calculated to be (106.42), (551.7) and (0.53) respectively . Furthermore the ratio (ν_2/ν_1) come to (1.6),showing octahedral coordination in this complex(21,24,27). Conductivity measurement showed that the complex was non ionc, Table (3).

The solution spactrum of the green [R_3] complex, exhibits intense bands at (11055,14725,19908 and 22747) cm^{-1}. The position of these band is in agreement with that reported for a highly distorted octahedral geometry(27,28-30). The effective magnetic moment at room temperature was found to be (2.08B.M), which agree well with square planar geometry around Cu (II) complex (24,28), conductivity measurement showed that the complex was non ionc,Table (3).

The solution spectrum of the brown palladium [R_4] complex show three absorption bands which were observed at (22286,24667 and 30098) cm^{-1}.The spectrum was a typical of square planer Pd(II) complexes(30,31-33). The measured magnetic moment (0.72B.M) showed that the complex to be low spin. Conductivity measurements in DMF showed that the complex was non-conducting behavior, Table (3). Electronic spectrum of the deep green [R_5] complex in chloroform solution, showed three absorption bands, the first at 12376 cm^{-1}, a second band at 16501 cm^{-1} and the last absorption band at 30000 cm^{-1}, which came in accordance with the published data for octahedral Cr(III) complexes(27,29,31),as well as the ratio (ν_2/ν_1) (1.337) lies close to that required for octahedral geometry(30,34). The measured magnetic moment (3.91B.M). Conductivity measurement in DMF showed that the complex was to be ionic, Table (3).

The solution spectrum of the brown [R_6] complex shows three absorption bands at (14800, 17800 and 28640) cm^{-1} , which are assigned to the transitons:- $^6A_1g \rightarrow {}^4T_1g$, $^6A_1g \rightarrow {}^4T_2g$ and (DB) → Fe $_{(C.T)}$ (28,30,35). The values of (10Dq, B and β) come out to (6776,616 and 0.47) respectively.The magnetic moment of the present complex is (5.95B.M) with five unpaired electrons and an octahedral configuration. Conductivity measurement in DMF showed that the complex was to be ionic, Table (3). [R_7] Electronic spectrum of the deep orange complex in chloroform solution, showed two shoulders at 23492 and 26610 cm^{-1}. The octahedral geometry was excluded because the spectrum show no band below 20000 cm^{-1}, this suggest a square planer configuration(32,33,36). The distinction between ligand field and charge transfer bands can't be made sharply due to mixing of the ligand orbital with the metal orbital, therefore the ligand field bands can't be identified easily in the spectra of spin-paired square planer complexes. Never the less, and from the reference to the available data for low spin d^6 ions, i.e., Co(III), Rh(III) and Ir(III), published in the literature(31,33,36),the band at 23492cm^{-1} can be assigned to the transition of $^1A_1g \rightarrow {}^1B_1g$ which can be taken as the 10Dq value . Magnetic moment of solid complex, Table (3), showed a higher orbital contribution,and the conductivity measurement in DMF showed that the complex was conducting, Table (3), therefore the (Cl) atoms was not considered to be coordinated with metal ion and is located out side the coordination zone.

The spectrum of this complex [R_8] gave four absorption bands appeared at 16666 cm^{-1}, 23809,30770 and 36000 cm^{-1}, which indicat a square planar geometry(31,37,38) and were assigned to the transitions :-
$A_1g \rightarrow {}^3B_1g$, $^1A_1g \rightarrow {}^1B_1g$, $^1A_1g \rightarrow {}^1Eg$ and (DB) Au $_{(C.T)}$ transitions respectively (29,31). The complex was diamagnetic and conductivity measurement in DMF showed that the complex was to be ionic, Table (3) .

Four absorption bands of [R_9] complex were observed in the spectrum of this complex in chloroform solution at 15012,18731,29103 and 34055 cm^{-1}tentatively assigned to the transitions $^2T_2g \rightarrow {}^4T_1g$, $^2T_2g \rightarrow {}^4T_2g$, $^2T_2g \rightarrow {}^2Eg$ and $^2T_2g \rightarrow {}^2A_1$ grespectively,which agree with the published data for octahedral geometry Ru(III) complexes(33,39,40). The magnetic moment of the present complex is (1.84B.M) which agree well for low-spin trivalent ruthenium in octahedral coordination(33,37,39). Conductivity measurement in DMF showed that the complex was to be ionic, Table (3).

The prepared brownishred Pt (IV) complex [R_{10}]observed high magnetic value (2.49 B.M) of the present platinum (IV) complex (d^6) configuration agree with octahedral geometry around Pt (IV), this result indicates a higher orbital contribution around metal ion(20,28,30,31).The electronic spectrum of the [R_3] complex showed three bands at (19016 (ν_1), 23898 (ν_2) and 29210 (ν_3) cm^{-1}, and were assigned to $^1A_1g \rightarrow {}^3T_1g$, $^1A_1g \rightarrow {}^3T_2g$ and (DB) Pt $_{(C.T)}$ transitions respectively(30,31,41). The conductivity measurement, Table (3) showed that the complex to be ionic.

Table (3)

Electronic Spectra ($CHCl_3$), Conductance (in DMF), and Magnetic moment (B.M) for Metal Complexes.

Comp. No.	Bands cm^{-1}	Assignment	10Dq cm^{-1}	Molar cond. μ S.cm^{-1}	μ eff. B.M	Suggested Structure
[R_1]	37440 6770 (cal) 15774(av.)	$^4A_2 \rightarrow {}^4T_{2\ (F)}$ $^4A_2 \rightarrow {}^4T_{1\ (F)}$ $^4A_2 \rightarrow {}^4T_{1\ (P)}$	3744	10.9	4.61	Tetrahedral
[R_2]	10642 16667 23529	$^1A_1g \rightarrow {}^3T_1g$ $^1A_1g \rightarrow {}^3T_2g$ $^1A_1g \rightarrow {}^1T_1g$	10642	22.08	2.79	Octahedral
[R_3]	11055 14725 19908 22747	$^2B_1g \rightarrow {}^2Eg$ $^2B_1g \rightarrow {}^2B_2g$ $^2B_1g \rightarrow {}^2A_1g$ (DB) $\rightarrow$ Cu (C.T)	11055	18.2	2.08	Square planar
[R_4]	22286 24667 30098	$^1A_1g \rightarrow {}^1B_1g$ $^1A_1g \rightarrow {}^1Eg$ (DB) $\rightarrow$ Pd (C.T)	22286	10.68	0.72	Square planar
[R_5]	12376 16501 30000	$^3A_2g \rightarrow {}^3T_2g$ $^3A_2g \rightarrow {}^3T_1g$ $^3A_2g \rightarrow {}^3T_1g_{(P)}$	-	55.90	3.91	Octahedral
[R_6]	14800 17800 28640	$^6A_1g \rightarrow {}^4T_1g$ $^6A_1g \rightarrow {}^4T_2g$ (DB) $\rightarrow$ Fe(C.T)	6776	68.13	5.95	Octahedral
[R_7]	23492 26610	$^1A_1g \rightarrow {}^1B_1g$ (DB) $\rightarrow$ Rh(C.T)	23492	245.03	2.44	Square planar
[R_8]	16666 23809 30770 36000	$^1A_1g \rightarrow {}^3B_1g$ $^1A_1g \rightarrow {}^1B_1g$ $^1A_1g \rightarrow {}^1Eg$ (DB) $\rightarrow$ Au (C.T)	-	238.22	0.98	Square planar
[R_9]	15012 18731 29103 34055	$^2T_2g \rightarrow {}^4T_1g$ $^2T_2g \rightarrow {}^4T_2g$ $^2T_2g \rightarrow {}^2Eg$ $^2T_2g \rightarrow {}^2A_1g$	18731	62.98	1.84	Octahedral
[R_{10}]	19016 23898 29210	$^1A_1g \rightarrow {}^3T_1g$ $^1A_1g \rightarrow {}^1T_2g$ (DB) $\rightarrow$ Pt (C.T)	23898	176.12	2.49	Octahedral

(D)-Thermal analysis:

Thermogravimetric(TG) and differentiial thermogravimetric (DTG) analysis for (DB) and its metal complexes [R_1-R_{10}] were carried out in the range 25-700 C^o with a heating rate of 20 C^o/min in nitrogen atmosphere. Table (4) showed the following features:

1-The thermogram of [R_2, R_3, R_5-R_8,andR_{10}]complexes at low temperature started with the loss of solvent molecule in outer crystal lattice.

2- There was an agreement in weight loss between results obtained from the thermal decomposition and calculated values, which supports the results of elemental analysis and confirms the suggested formulae.

3- The ligand (DB) and all the studied complexes showed a common general behavior, in which the first pyrolysis step was the loss of dibenzyl amine moiety followed by the other part of the ligand except donor atoms which were left with the metal atom depending on the type of the metal ion.

4- The final step of the thermolysis reactions of the complexes were found to give the metal chlorid [$R_3$and R_4] or oxcid [R_5 - R_9] or metal only [R_2], which indicates the stability of such residues (42). While [$R_1$and R_{10}] complexes showed incomplete decompo-sition within temperature range of the experiment, therefore it was not possible to achieve their final product of the thermoly.

Table (4)
Thermal analysis by (TG)and(DTG) for(DB) and it's metal complexes.

Stable Phase	Temp.range of decomposition C^o	%Weight loss Found (Calc.)
(DH) $C_{23}H_{21}N_3SO$		
↓ $-C_{14}H_{14}N$	138-297	50.24 (50.65)
↓ $-C_6H_5$	297-343	18.99(19.89)
↓ $-C_2H_2N_2S$	343-486	22.86 (22.22)
↓ -CO	486-522	7.90 (7.24)
Nothing		
[R_1] [$C_{23}H_{21}N_3SOCoCl_2$]		
↓ $-C_{14}H_{14}N$	35-291	37.33 (37.92)
$-C_6H_5$ ↓ -2Cl	291-402	29.08 (28.62)
↓ $-C_2\ H_2N_2S$	402-528	16.92(16.64)
CoCO	528-700	16.65 (16.82)
[R_2] [$C_{46}H_{42}S_2N_6NiCl_2$]. H_2O		
↓ $-H_2O$	30-112	1.91 (1.95)
↓ $-C_{28}H_{28}N_2$	112-322	43.16 (42.53)
$-C_{16}H_{14}\ N_4$ ↓ -2Cl	322-486	35.52(36.13)

↓ $-C_2S_2O_2$	486-599	13.77 (13.02)
Ni	599-700	6.03 (6.37)
[R$_3$] $[C_{23}H_{21}N_3SOCuCl_2].\ H_2O$		
↓ $-H_2O$	30-116	3.43 (3.34)
↓ $-C_{14}H_{14}N$	116-339	37.08 (36.32)
↓ $-C_9H_7N_2SO$	339-575	35.14(35.40)
$CuCl_2$	575-700	24.31 (24.94)
[R$_4$] $[C_{23}H_{21}N_3SOPdCl_2]$		
↓ $-C_{14}H_{14}N$	122-311	34.84 (34.73)
↓ $-C_6H_5$	311-402	12.98 (13.65)
↓ $-C_3H_2N_2\ SO$	402-558	20.39 (20.19)
$PdCl_2$	558-700	31.77 (31.43)
[R$_5$] $[C_{46}H_{42}N_6S_2O_2CrCl_2].Cl.3H_2O$		
↓ $-3H_2O$	30-138	5.59 (5.47)
↓ $-Cl$ $-2C_{14}H_{14}\ N_2$	138-402	42.88 (43.34)
↓ $-2Cl$ $-2C_6H_5$	402-486	23.38 (22.81)
↓ $-C_6H_4N_4\ S_2$	486-592	19.11 (19.87)
CrO_2	558-700	31.77 (31.43)
[R$_6$] $[C_{46}H_{42}N_6S_2O_2FeCl_2].Cl.2H_2O$		
↓ $-2H_2O$	30-123	3.12 (3.70)
↓ $-C_{30}H_{32}\ N_2$ $-Cl$	123-368	46.36 (46.85)
↓ $-\ C_{16}H_{10}\ N_4S_2$ $-2Cl$	368-492	41.08 (40.42)
FeO_2	558-700	9.41 (9.03)
[R$_7$] $[C_{46}H_{42}N_6S_2O_2Rh].Cl_3.\ H_2O$		
↓ $-H_2O$	30-110	1.86 (1.80)
↓ $-2C_{14}H_{14}\ N$	110-416	39.21 (39.15)
↓ $-\ C_{28}H_{24}\ N_4$ $-Cl$	416-509	28.89 (29.71)

RhO_2	648-700	13.96 (13.47)
[R_8] [$C_{46}H_{42}N_6S_2O_2Au$].Cl_3. C_2H_6O		
↓ -C_2H_5OH	33-120	4.10 (4.09)
↓ -$C_{28}H_{28}N_2$ -3Cl	120-386	45.02 (44.37)
↓ - $C_{18}H_{14}N_4S_2$	386-593	30.83 (31.16)
AuO_2	593-700	20.04 (20.38)
[R_9] [$C_{69}H_{63}N_9S_3O_3Ru\ Cl_2$].Cl		
↓ -3Cl -$C_{42}H_{42}N_3$	112-324	50.48 (50.74)
↓ -$C_{24}H_{21}N_6$	324-459	29.33 (28.72)
↓ - C_3S_3	459-506	8.95 (9.65)
RuO_3	506-700	11.22 (10.89)
[R_{10}] [$C_{46}H_{42}N_6S_2O_2PtCl_2$].$Cl_2$.$C_2H_6O$		
↓ -C_2H_5OH	35-180	3.05 (3.98)
↓ -$C_{28}H_{28}N_2$ -2Cl	180-388	40.17 (40.01)
↓ - $C_{12}H_{10}$ -2Cl	388-506	20.11 (19.45)
↓ - $C_4H_4N_4$	506-610	8.61 (9.33)
$PtO_2C_2S_2$	610-700	28.02 (27.23)

Solution study

(1)- Molar ratio and Continuous variation methods

The Molar ratio and Continues variation methods were followed to determine the M:L ratio. The results of complexes in ethanol (solvents), suggest that the metal to ligand ratio was (1:1) for [R_1,R_3 and R_4], while (1:2) for [R_2, R_5-R_{10}], which were comparable to those obtained from solid state study Table (1).

(2)- Stability constant of the mannich base complexes

The apparent stability constant of the (1:1) and (1: 2) [Metal: Ligand] complexes ,were evaluated $^{(12)}$, Table (5).

The (As = Average of three measurements of the absorption of solution containing a stoichiometric amount of ligand and metal ions, and Am = Average of three measurements of the absorption of solution containing the same amount of metal and five fold excess of ligand) of the solutions, were measured at λmax of maximum absorption,. furthermore the the degree of dissociation (α) and molar absorptivity (εmax) for all complexes were calculated $^{(12)}$, Table (5).

The results indicate that mole ratio of (1:2) for [R_2 , R_5 -R_{10}] complexes , yielded rather high stability constants in contrast to the other values obtained with (1:1) for [R_1, R_3 and R_4] complexes,Table (5).

Furthermore the molar absorptivity (εmax) of all complexes is rather high, this probably due to the presence of a bulk group [dibenzyl] on the nitrogen atom of aminomethyl moiety in the structure of 3-one-5-phenyl-1,3,4-thiadiazole.

As well as the developed color become stable after one hour, up to six hours.

Table (5)

Stability constant and molar absorptivities of mannich base complexes at room temperature.

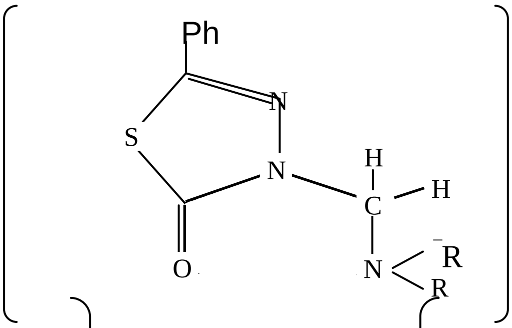
Complex	A_S	A_m	α	K L. mol^{-1}	εmax L.mol^{-1} cm^{-1}	λmax nm
[R_1]	0.255	0.299	0.150	3.95 *10^5	3862	563
[R_2]	0.495	0.551	0.101	2.18 *10^{10}	5511	509
[R_3]	0.369	0.441	0.169	5.13 *10^5	4332	668
[R_4]	0.380	0.459	0.128	6.00 *10^5	4532	415
[R_5]	0.410	0.458	0.104	1.99 *10^{10}	4588	663
[R_6]	0.495	0.551	0.101	2.18 *10^{10}	5511	561
[R_7]	0.294	0.336	0.125	4.48 *10^{10}	3363	438
[R_8]	0.259	0.309	0.161	5.03 *10^9	3090	430
[R_9]	0.481	0.499	0.157	6.22 *10^{10}	6682	442
[R_{10}]	0.489	0.502	0.160	6.53 *10^{10}	5720	521

Stereo chemistry structure of (DB) and thier Complexes:

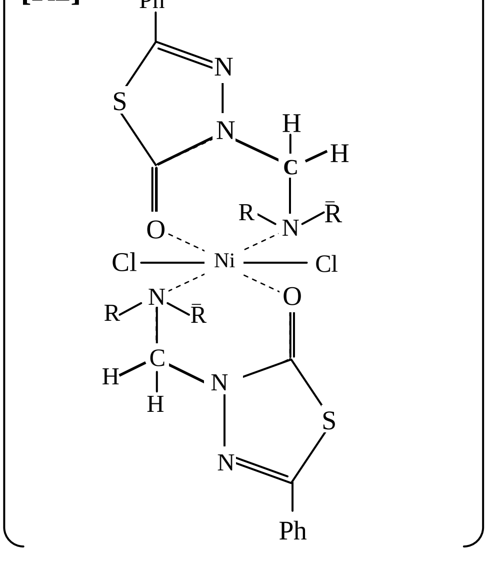
According to the results obtained, the structure of the above mentioned (DB) and thier complexes[R_1-R_{10}] can be illustrated as follow:

(DB)

$R = \bar{R} = (-CH_2C_6H_5)$

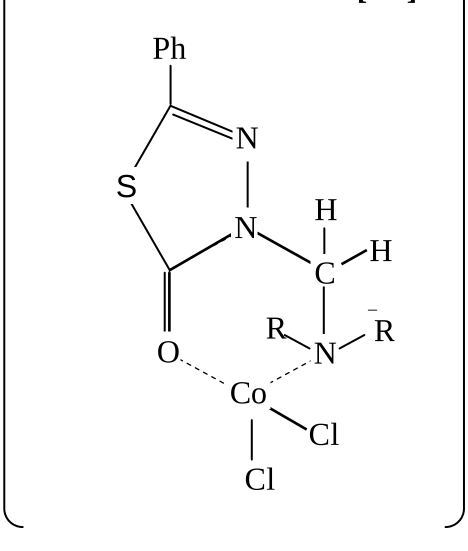


[R2]

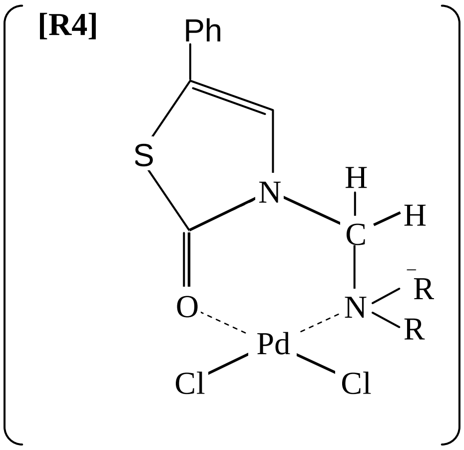


. H_2O

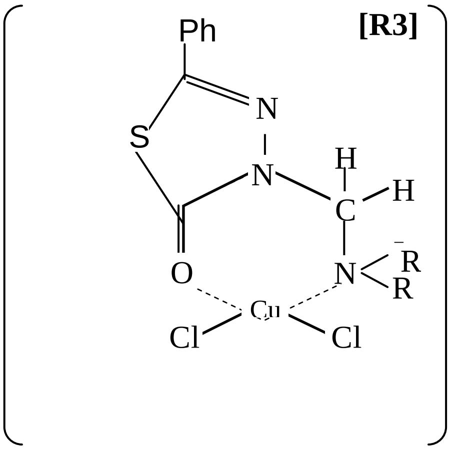
[R1]



[R4]

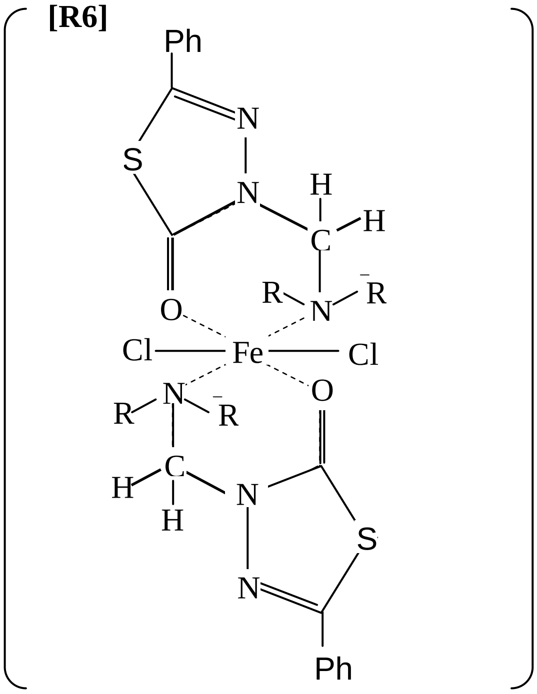


[R3]



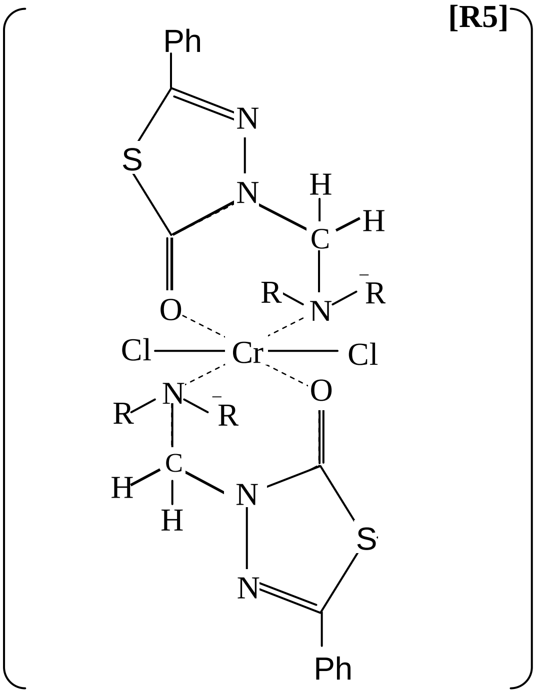
H_2O

[R6]



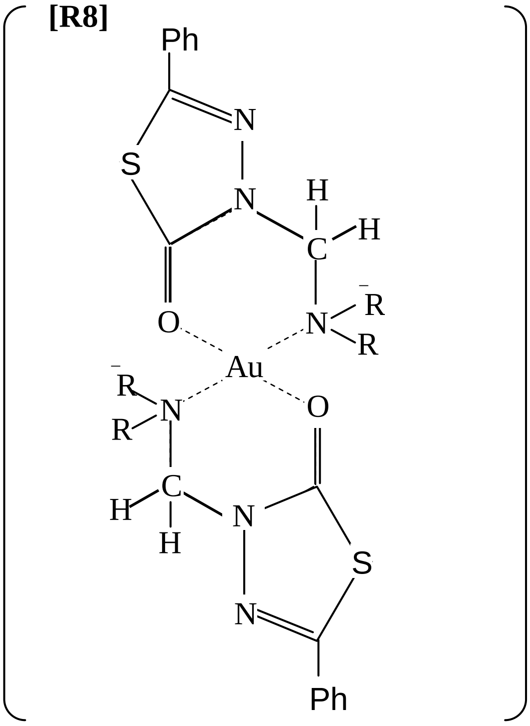
$. Cl.2H_2O$

[R5]



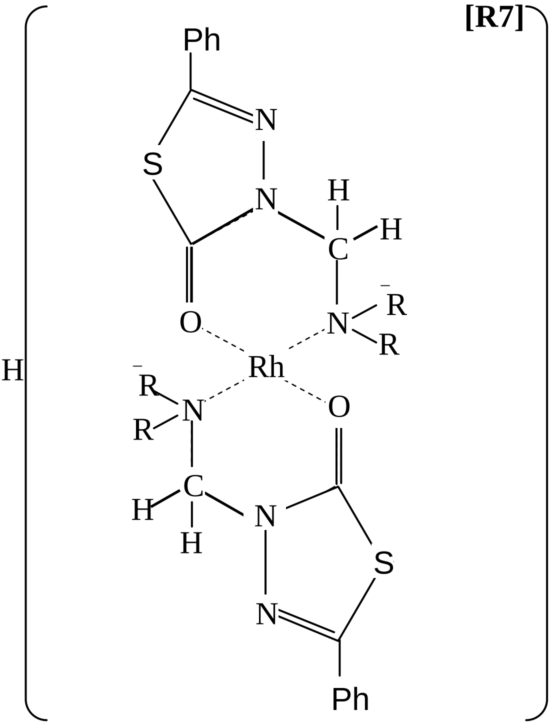
$. Cl.3H_2O$

[R8]



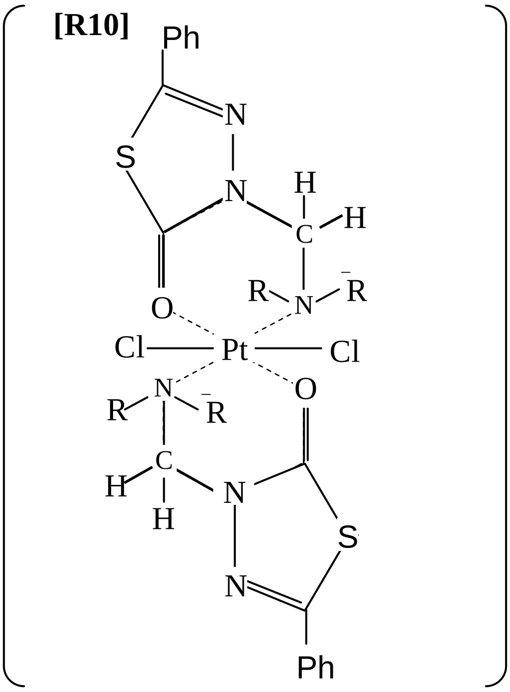
$. Cl_3. C_2H_5OH$

[R7]

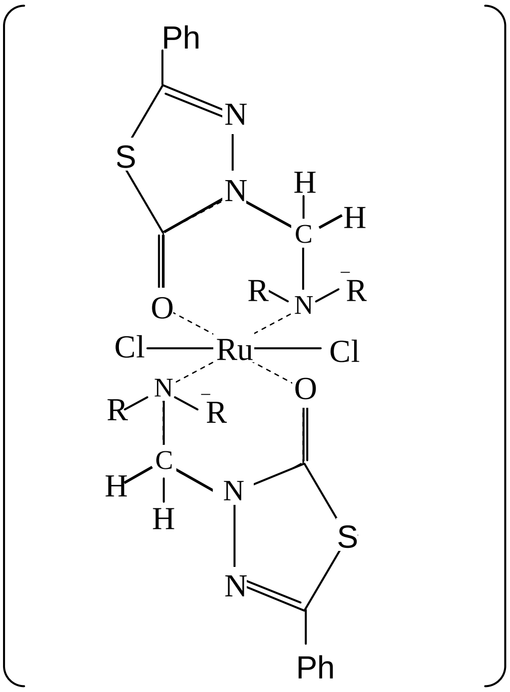


$. Cl_3. H_2O$

[R10]



. Cl. C_2H_5OH



. Cl

Antimicrobial activity

The biological activity of the prepared ligand (DB) and their respective metal complexes R_1-R_{10}] were studied against selected types of bacteria,which include (*Klesbiella pneumonia* and *Pseudo monase aeruginos* as Gram negative], and (*Streptococcus faecalis* and *Bacillus subtlus*) s [Gram positive], also the study was done against (*Candida albicans* and *Aspergillus flavus*) fungus .As a result frome this studies the following points wereconcluded :

(1). (DB) was highly active against *Klesbiella pneumonia* and *Pseudo monase aeruginos,* Tble (6).

(2). The[R_1-R_3 and R_5] complexes showed a moderate activities ,while [R_4 , R_6-R_{10}] complexes exhibited a great enhancement of activity against types of bacteria, Table (6), this difference in synergistic effect between the metal ion and the ligand molecule may be attributed to many factors, of these in that [R_1-R_3 and R_5] complexes are considered to be a hard metal ions making their complexes to be less lipophilic, this will relatively retard their permeation through the lipid part of the cell membrane. On the other hand the [R_4 , R_6-R_{10}] 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 affect the constituents of the cell.

(3). The results of the (MIC) study for the ligand and their metal complexes are shown in Table (7). The (DB, R_1-R_3 and R_5) showed high activity at (0.075) μ gm.ml^{-1} against *Klesbiella pneumonia* and *Pseudo* bacteria, while [R_4 , R_6-R_{10}] were active against at (0.05) and (0.075) μ gm.ml^{-1} against all types of bacteria , 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.

(4). Study of the antibacterial and antifungal activities revealed that the mannich bases derived from (5-phenyl-1,3,4- thiadiazole -3-one) and their metal complexes, exhibited a greater activity against all the studied micro-organisms compared to that of (5-phenyl-1,3,4- thiadiazole -3-one) it self (6). This indicate that introductions of the aminomethyl group on the triazole derivative ring were raise the killing zone.

(5). Results of the antifungal activity of the new compounds, Table (6) showed that the metal ion chelates were more toxic compared with their parent ligand 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 the metal ion on the normal cell process. These activities may be explained by Tweedy's Chelation theory(43), 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 favours permeation of the complexes through the lipid layer of cell membrane(7).

Table (6)

Antibacterial and antifungal activities for mannich bases and their metal complexes (10^{-3} mgm.ml^{-1}).

Compo.	Klesbiella pneumonia	Pseudo. monase aeruginos	Streptococcus faecalis	Bacillus subtlus	Aspergillus flavus	Candida albicans
Control (DMSO)	-	-			-	-
(DB)	8	8	-	4	28	36
$[R_1]$	-	-	-	-	14	21
$[R_2]$	-	-	8	4	23	27
$[R_3]$	6	6	6	-	24	30
$[R_4]$	8	10	10	10	20	14
$[R_5]$	6	6	6	6	21	20
$[R_6]$	15	10	15	15	11	21
$[R_7]$	10	8	10	10	10	26
$[R_8]$	20	24	15	18	10	17
$[R_9]$	8	10	8	8	13	11
$[R_{10}]$	20	25	18	20	11	10
Where:[6-8: (+),8-10: (++), >10: (+++)]					*30-40: (+++),20-30 :(++++)* *10-20: (+++++)*	

Table (7)

Minimal inhibitory concentration (MIC) for mannich bases and their metal complexes (μgm. ml^{-1}).

Compound	Klesbiella pneumonia				Pseudo. monase aeruginos				Streptococcus faecalis				Bacillus subtlus			
	0.05	0.075	0.1	2	0.05	0.075	0.1	2	0.05	0.075	0.1	2	0.05	0.075	0.1	2
(DB)	+	MIC	-	-	+	MIC	-	-	+	+	MIC	-	+	+	MIC	-
$[R_1]$	+	MIC	-	-	+	MIC	-	-	+	+	MIC	-	+	+	MIC	-
$[R_2]$	+	MIC	-	-	+	+	MIC	-	+	MIC	-	-	+	+	MIC	-
$[R_3]$	+	+	MIC	-	+	+	MIC	-	+	+	MIC	-	+	MIC	-	-
$[R_4]$	MIC	-	-	-	+	+	MIC	-	+	MIC	-	-	+	MIC	-	-
$[R_5]$	+	+	MIC	-	+	+	MIC	-	+	+	MIC	-	+	MIC	-	-
$[R_6]$	+	MIC	-	-	MIC	-	-	-	+	MIC	-	-	+	MIC	-	-
$[R_7]$	+	+	MIC	-	MIC	-	-	-	+	MIC	-	-	+	MIC	-	-
$[R_8]$	MIC	-	-	-	MIC	-	-	-	MIC	-	-	-	+	MIC	-	-
$[R_9]$	+	MIC	-	-	MIC	-	-	-	+	+	MIC	-	+	+	MIC	-
$[R_{10}]$	MIC	-	-	-	+	MIC	-	-	+	MIC	-	-	MIC	-	-	-

Where:[(+): Growth , (MIC): 99% , (-): No growt]

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