Synthesis, Characterization and Biological Activity of Some Novel Metal Complexes of Schiff Base Derived from *p*-phenyldiamine and 2-thiophene Carboxaldehyde

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Platinum(II), palladium(II), copper(II), rhodium(III), ruthenium(III) complexes of Schiff bases derived from from p-phenyldiamine and 2-thiophene carboxaldehyde were reported and characterizied based on elemental analysis, ESR, IR and UV-VIS spectroscopy, atomic absorbtion spectroscopy, molar conductibility, NMR techniques and cyclic voltammetric studies. Furthermore, their ability to inhibit proliferation of human stem mezechimale cell lines was tested and the results indicate that they exert different cytotoxic effects.

Keywords: Schiff base, UV-VIS, IR spectroscopy, cyclic voltammetry

A special interest for the coordinative chemistry is represented by heterocyclic ligands, which contain sulphur atoms, because of the coordination potential and their implications in biological activity [1].

Schiff Bases are considered a very important class of compounds from organic chemistry, having biological application [2].

These applications of Schiff Bases have been generated by the possibility of formation of some complex combinations with transition metals.

It is known that tetradentate Schiff Bases generate very stable complex combinations with different metallic ions [3-5].

Schiff bases continue to occupy an important position as ligands in metal coordination chemistry [3], even almost a century since their discovery. The study of the reactivity of various types of heteroaromatic containing Schiff bases linked to metal complexes has received a great deal of attention during the past decades [2].

In the present work, a new Schiff base derived from p-phenyldiamine and 2-thiophene carboxaldehyde (L) was prepared. The obtained Schiff base ligand is reacted in 1:2 mole ratio with the appropriate metal salt using ethanol solvent. The work is dedicated to the synthesis, structural characterization of a new Pd(II), Pt(II), Cu(II), Rh(III), Ru(III), complexes by using Schiff Base ligand.

Experimental part

Synthesis of the ligand (L)

The Schiff base, L was prepared by mixing hot solution (~70°C) of p-phenyldiamine with 2-thiophene-carboxaldehyde in alcoholic solution, at reflux. The mixture was refluxed for 2 h. The formed solid product was separated by filtration, purified by crystallization from ethanol, washed several times with diethyl ether and dried in vacuum over anhydrous calcium chloride; ligand as yellow crystals was obtained with a yield of 95%.

Synthesis of metal complexes

The hot ethanolic solution (20 mL) of corresponding metal salts (M:L = 2:1 for Cu(II), Pd(II), Pt(II) and M:L = 1:1 for Rh(III) and Ru(III)) was mixed with hot ethanolic solution of the respective ligand and refluxed for 2 h on a water bath. By cooling the contents, the colored complex separated out in each case. The same was filtered, washed with ethanol and dried in vacuum over $CaCl_2$.

Instruments

The elemental microanalyses of the prepared compounds for C, H, N and S were performed on COSTECH ECS 4010 CHNSO analyzer. Infrared spectra were recorded on an Escalibur FT-IR spectrometer, IR spectra of ligand and of the compounds have been achieved by reflexion on ATR with diamond crystal deposited onto KRS5, on the domain 4000-250cm^{-1}. ^{1}HNMR and ^{13}CNMR spectra were performed on Varian-Gemini 300 MHz spectrometer. The samples were dissolved in DMSO-d6 using tetramethyl silane as internal references. The UV-VIS spectra were recorded on a Jasco UV-VIS 540V spectrophotometer ranged from 200-900 nm. The molar conductance of solid complexes in DMSO was measured using Consort conductometer. The mass spectra were performed using Varian mass spectrometer. The magnetic susceptibilities of the solid complexes were recorded on Sherwood Scientific Magnetic Susceptibility Balance. The thermo gravimetric analyses (TGA were carried out in a dynamic He atmosphere (20 mL min^{-1}) with a heating rate of 10°C min^{-1}) using a TGA Q5006.7 Build 203. Metal contents were determined with the Atomic Absorption Varian spectrometer. The biological activity experiments was performed using DMSO as solvent. Cell viability was determined by absorbance measurements at 570 nm and correlated to the ability of reducing MTT to produce formazan.

Biological activity

The stem mezechimale cell strain was cultured at 37°C in a humidified atmosphere containing 5% CO_2. Cells were suspended (7000cells/well) in 150 uL of media w/phenol red (RPMI 1640+10%FCS); 15 uL of Alamar reagent were added/well, after A 24 h. incubation. Reading was performed at 570 nm on an ELISA plate reader. 2 mg of sample was disolved in 1 mL DMSO figure 4.

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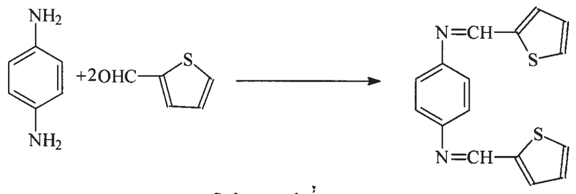
Table 1
DATA FOR ELEMENTAL ANALYSIS, MOLAR ELECTRICAL CONDUCTIBITY

Compound	%C	%H	%N	%S	%M	Colour	Λ_M^a $(\Omega^{-1}mol^{-1}cm^2)$
	Exp/calc	Exp/calc	Exp/calc	Exp/calc	Exp/calc		
L	64.50/ 64.86	4.3/ 4.05	9.14/ 9.46	20.87/ 21.62	-	yellow	2,6
$[Cu_2L(SO_4)_2(H_2O)_2]$	29.5/ 29.44	2.9/ 2.45	4.54/ 4.29	18.83/ 19.63	20,02/ 19,63	Brown	3,0
$[Pd_2LCl_4]$	29.10/ 29.53	2.5/ 1.85	5.0/ 4.30	10.3/ 9.85	31,87/ 32,61	Pale brown	15
$[Pt_2LCl_4]$	24.5/ 25.32	1.9/ 1.58	3.54/ 3.69	8.06/ 8.44	50,31/ 51,45	Pale brown	7
$[RhLCl_2]Clx2H_2O$	36.2/ 35.46	3.28/ 2.96	5.0/ 5.17	10.56/ 11.81	19,53/ 19,02	Brown-red	74
$[RuLCl_2]Cl$	38.45/ 38.13	2.81/ 2.38	5.63/ 5.56	13.01/ 12.71	20.67/ 20,05	Brown-red	67

[a] c 10^{-3}M DMSO

Results and discussion

L ligand is formed via the condensation of the p-phenyldiamine with 2-thiophene carboxaldehyde. It is characterized based on elemental analyses (C, H, N and S), (table 1). The results obtained are in good agreement with those calculated for the suggested formula (fig. 1). Schiff bases were obtained according to the scheme 1.



Scheme 1

^{1}H-NMR spectra of the Schiff base ligand HL revealed its formation by the presence of - CH = N [6] proton signal at (δ= 8.831ppm). This is further supported by the appearance of stretching vibration band ν (CH=N) azomethine at 1603 cm^{-1}. Also, the ^{1}H NMR of the ligand exhibits signals at, 7.2ppm (m, 1H, thiophene-H3), 7.7ppm (dd, *J*= 1.24 Hz, 1H, thiophene-H4), 7.8ppm (dt, *J*= 1,1 Hz, 1H, thiophene-H2), 7.3 ppm 4H, Ph).

The mass spectrum of ligand L showed molecular ion peak at (296, 100%) which corresponding to its molecular formula $C_{16}H_{12}N_2S_2$ (scheme 2), base peak at m/z (%)= 213 (80%), peak at 186 (71%), peak at 129 (25%), which confirms the suggested structure (fig. 1). Further insight concerning the structure of the ligand is obtained from IR, UV-Vis. IR and UV-Vis measurements, of L ligands will be discussed with its metal complexes.

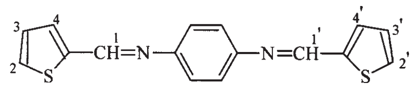
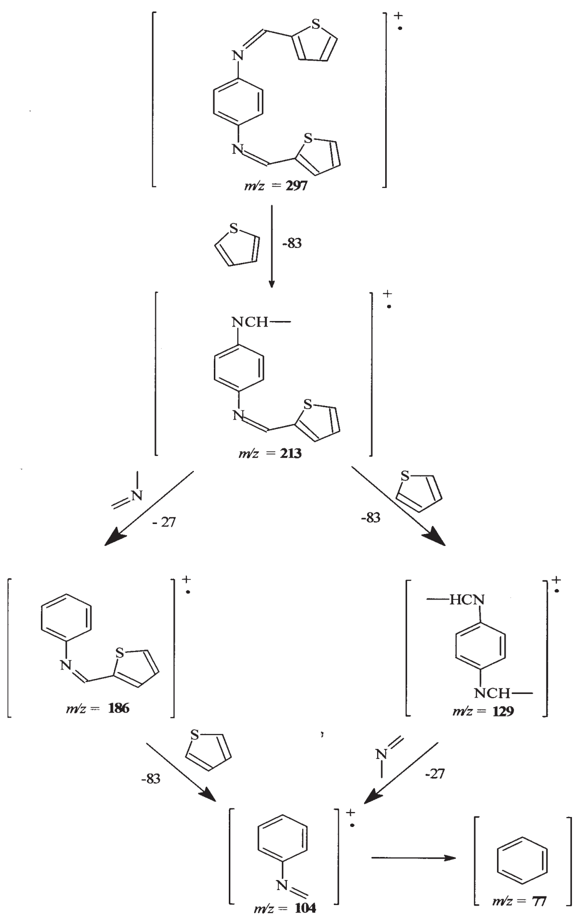


Fig. 1.

*IR Spectr*a

IR spectra for ligand and complexes were performed in domain 150-4000cm^{-1}. Main vibration frequencies from IR spectra of ligand and complex combinations and their assignements are presented in table 2.



Scheme 2. Suggested mass fragmentation of L ligand

By analyzing IR spectra of ligand and complexes there are observed the following aspects: a displacement of the vibration frequency assigned to azomethine group $\nu_{HC=N}$ in complex combinations with values beween Δν = 7-55 cm^{-1}, compared to ligand (1603cm^{-1}). This suggests that this group participate to coordination.

Vibration frequency characteristic to C-S group from thiophene ring which appears at 721cm^{-1} in ligand is displaced with frequency values of 6-35cm^{-1}, indicating

Compus	$\nu_{HC=N}$ (cm^{-1})	ν_{C-S} (cm^{-1})	$\nu_{C=C}$ (cm^{-1})	ν_{H-C} (cm^{-1})	ν_{M-S} (cm^{-1})	ν_{M-N} (cm^{-1})
L($C_{16}H_{12}N_2S_2$)	1603	721	1491	3060	-	-
[$Cu_2L(SO_4)_2(H_2O)_2$]	1592	714	1517	3145	355	405
[Pd_2LCl_4]	1585	756	1501	2803	360	400
[Pt_2LCl_4]	1658	737	1504	2830	390	410
[$RhLCl_2$]Clx2H_2O	1596	716	1508	3065	389	403
[$RuLCl_2$]Cl	1589	718	1504	3056	378	413

Table 2
ABSORPTION MAXIM VALUES IN IR(cm^{-1}) OF THE SYNTHESIZED COMPOUNDS

the implication of sulphur atom in coordination at metal ion.

In domain 500-250cm^{-1} there appear new vibration frequencies assigned to bonds metal -atom – donor [7].

ESR Measuremements

ESR spectra were performed at room temperature on crystaline powder, the values of g parameter are presented in table 3.

ESR spectrum of copper complex presents an anisotropic signal with $g_{//}$ = 2.26 and $g_{\perp}$ =2.12. Higher value of parameter $g_{//} > g_{\perp} > g_e$(2,.0023) indicates the existance on an impair electron in orbital $d_{x^2-y^2}$, characteristic to an axial symmetry [8]. Interraction of exchange coupling between two copper ions, G, was explained by Hathaway, where G is expressed by the relation: G = $(g_{II} – 2)/(g_{\perp} - 2)$ [8-9].

The value of G<4 G=2.16 suggest that exchange interraction between two copper ions is important. Information about nature of metal-ligand bond are obtained also from $g_{//}$ value. Kivelson and Neiman considered that values for $g_{//}$ >2.3 suggest a bond with ionic character and values less than 2.3 confirm a covalent bond. The value of $g_{//}$ = 2,26 for copper complex give information about covalent bond of metal-ligand bond [10,11].

RES spectrum for Ru complex explains the axial symmetry of the system by values $g_{//}$ = 2.040 and $g_{\perp}$= 1.98, characteristic to a distortion octahedric geometry. In case of Rh complex, the values of *g* parameters indicates an octahedric geometry [12].

Electronic spectra

In electronic spectra of copper complex combination there are observed two absorption bands at 23419 cm^{-1}, and 14265 assigned to transitions $^2B_{1g} \rightarrow {}^2B_{2g}$ and $^2B_{1g} \rightarrow {}^2A_{1g}$ table 4. Such transitions are characteristic to copper complex combinations with a tetrahedric geometry [13]. This aspect is sustained by the value of magnetic moment μ = 1.82MB.

No.	Complexes	g_{II}	$g_{\perp}$	$g_{iso/av}$	G
1	[$Cu_2L(SO_4)_2(H_2O)_2$]	2.26	2.12	2.16	2.16
2	[$RuLCl_2$]Cl	2.040	1.98	-	-
3	[$RhLCl_2$]Clx2H_2O	2.07	2.03	-	-

Table 3
EPR PARAMETERS FOR THE COMPLEXES

Compound	Absorption band (cm^{-1})	Assignements	Magnetic moment (MB)	Reference
L	49643 37174 34013 26737	$\pi\rightarrow\pi^*$ $\pi\rightarrow\pi^*$ $n\rightarrow\pi^*$ $n\rightarrow\pi^*$	-	[15,16]
[$Cu_2L(SO_4)_2(H_2O)_2$]	31055 23419 14265	$n\rightarrow\pi^*$ $^2B_{1g}\rightarrow{}^2B_{2g}$ $^2B_{1g}\rightarrow{}^2A_{1g}$	1.82	[13,14]
[Pd_2LCl_4]	29850 23474	MLCT $^1A_{1g}\rightarrow{}^1B_{1g}$	-	[16,21]
[Pt_2LCl_4]	27100 20920	$^1A_{1g}\rightarrow{}^1B_{1g}$ $^1A_{1g}\rightarrow{}^1A_{2g}$	-	[16,21]
[$RhLCl_2$]Clx2H_2O	29850 21186 15503	$n\rightarrow\pi^*$ MLCT $^1A_{1g}\rightarrow{}^1T_{1g}$	1.43	[17]
[$RuLCl_2$]Cl	26455 19342	MLCT $^2T_{2g}\rightarrow{}^2A_{2g}$	1.71	[12]

Table 4
ELECTRONIC SPECTRA AND MAGNETIC MOMENTS VALUES

Complexes	E_{pc}(V)	E_{pa}(V)	$E_{1/2}$(V)	ΔE(V)	K_{con}
Metal based reduction $[Cu_2L(SO_4)_2(H_2O)_2]$	-0.889	-0.608	-0.748	0.281	$5.49x10^4$
Metal based oxidation $[Cu_2L(SO_4)_2(H_2O)_2]$	0.247	0.161	0.204	-0.086	-

Supporting electrolyte: TBABF4, (0.1M); Complex: 0.001M; Solvent: DMSO; ΔEp= Epa - Epc
Where Epa and Epc are anodic and cathodic potentials respectively; E1/2 = 0.5(Epa + Epc); scan rate: 50mVs-1

Table 5
ELECTROCHEMICAL DATA FOR COPPER(II) COMPLEX

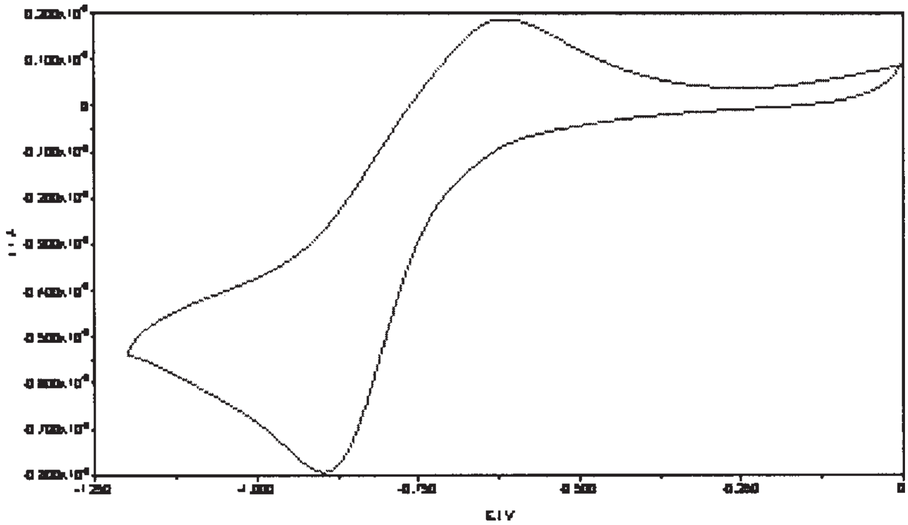


Fig. 2. Cyclic voltammogram of complex $[Cu_2L(SO_4)_2(H_2O)_2]$

In UV-VIS spectrum of paladium complex there are observed absorption bands characteristic to ligand slightly dispaced to higher frequencies suggesting ligand coordination at the metallic ion. The absorption band from 29850 cm^{-1} is assigned to charge transfer ligand → metal and the absorption band from 23474cm^{-1} corresponds to transition $^1A_{1g}\rightarrow{}^1B_{1g}$ specific to a plane square geometry.

The complex combination of platinum presents two absorption bands at 27100 $cm^{-1}$and 20920cm^{-1}, characteristic to transitions $^1A_{1g}\rightarrow{}^1B_{1g}$ and $^1A_{1g}\rightarrow{}^1A_{2g}$, specific to a plane square geometry.

Electronic spectra of Ru(III) and Rh(III) combinations present large absorption bands characteristic to charge transfer and bands from 19342cm^{-1} correspond to transition $^2T_{2g}\rightarrow{}^2A_{2g}$, and at 15503$cm^{-1}$ correspond to transition $^1A_{1g}\rightarrow{}^1T_{1g}$. From electronic spectra analysis there was observed that these two complex combinations presented an octahedric geometry.

Cyclic voltammetry studies

Redox properties of complex combinations were examined by cyclic voltammetry in DMSO in presence of TBABF4, the reference electrode is Ag/AgCl, working electrode is made of platinum with a diameter of 3 mm and as counter electrode there was used a platinum electrode, the scanning rate was of 50mV/s .

The cyclic voltammograms of the copper complex at negative potential were recorded in the potential range from 0 → -0.200V and the reduction potential were recorded in the potential range from 0 → 1.2V; the data are summarized in table 5. The cyclic voltammograms obtained for the complex $[Cu_2L(SO_4)_2(H_2O)_2]$ in the cathodic and anodic region are shown in figure 2.

The stability of the mixed-valence species Cu(II) and Cu(I) can be related to their conproportionation K_{con} constant [18]. The conproportionation constant for the

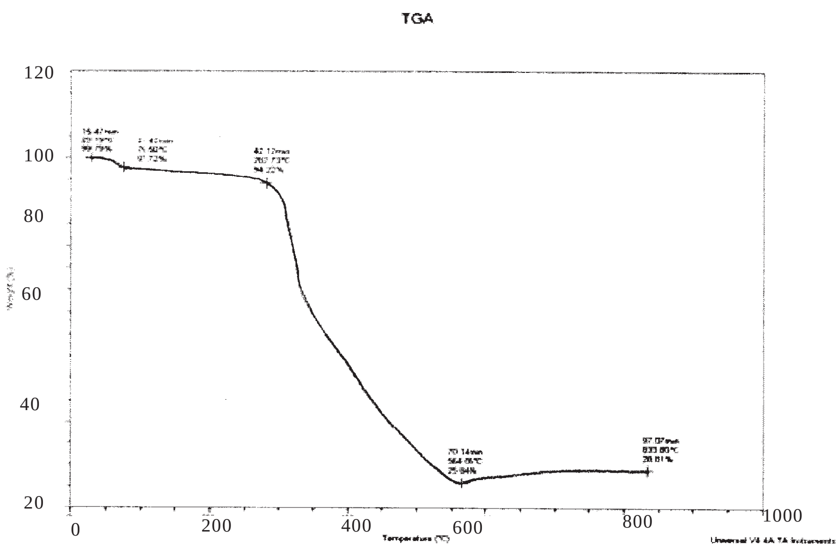


Fig. 3. Derivatogram of complex combination $[Cu_2L(SO_4)_2(H_2O)_2]$

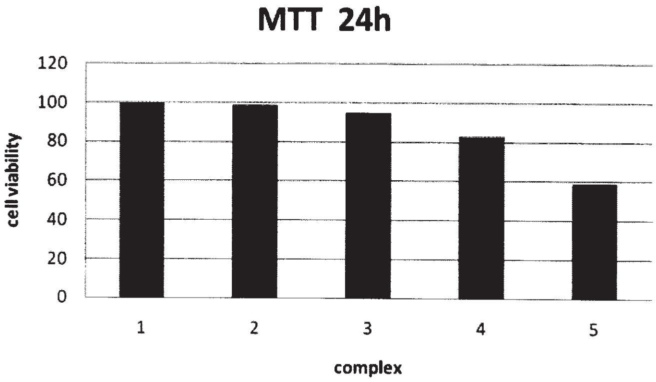


Fig. 4. Cell viability **1** - control; **2** - $C_{16}H_{12}N_2S_2$; **3** - $[RuLCl_2]Cl$; **4** - $[RhLCl_2]Clx2H_2O$; **5** - $[Pt_2LCl_4]$

equilibrium was calculated using the relationship $\log K_{con} = \Delta E/0.0591$. A higher K_{con} value indicates higher stability for the mixed-valence species or that the exchange interaction is higher with respect to the isovalent species[18-20].

Thermal analysis

Thermal analysis of copper complex was performed in domain 20-1000^{0}C figure 3 .

Experimental results correspond to those calculated. Thermal analysis was made in two steps:

- in the first step, for 50-282^0 C there were eliminated two water molecules which participate at coordination, exp (5,78%), calc(5,51%);

- in the second step, at 282-564^{0}C there were eliminated two sulphate molecules from ligand molecule. The obtained ressidue is CuO, the value determined experimentally (25.64%) correspond to calculated value. (25.11%).

From thermal analysis data there is confirmed that combination ratio metal:ligand is 2:1.

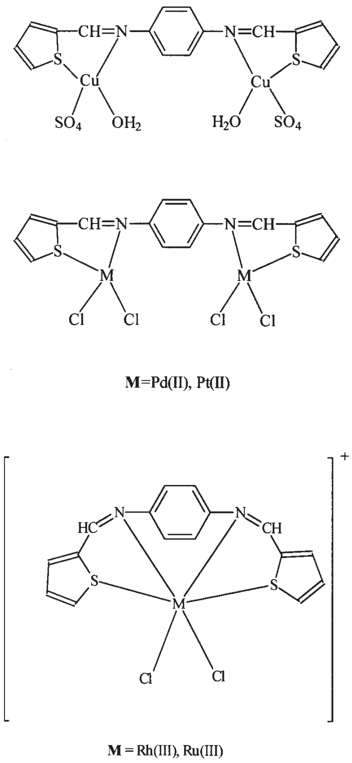


Fig. 5. Proposed structures of the complexes

From the experimental data analyses there have been proposed the following structures (fig. 5).

Conclusions

There have been prepared five new complex compounds of Pd(II), Pt(II), Cu(II), Rh(III), Ru(III) by using Schiff Base ligand.

IR spectra show that L is coordined to the metal ions in a tetradentate manner, through sulphur and azomethine-nitrogen hetero-five-member ring.

The low molar conductance values suggest the nonelectrolytic nature of these complexes.

The ability of these compounds to inhibit proliferation of human stem mezechimale cell lines was tested and the results indicate that they exert different cytotoxic effects.

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