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Synthesis and Characterization of Neutral Ru(III) Complexes Containing Schiff Bases and *N*-donor Heterocyclic Ligands

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Abstract: Two new neutral complex compounds of Ru(III) with Schiff bases and *N*-donor heterocyclic ligands have been synthesized. Based on MALDI TOF/TOF mass spectra, CHN elemental analysis, infrared and electronic spectra the synthesized compounds were formulated as [RuCl(*N*-Ph-5-X-salim)$_2$B], where X = Cl for B = Py and X = Br for B = Pym. In the octahedral environment of Ru(III), bidentate Schiff bases acts as anionic ligand where coordination occurs *via* deprotonated phenolic oxygen and azomethine nitrogen atom. Coordination of monodentate *N*-donor heterocyclic ligands occurs through free electronic pair on the nitrogen atom.

INTRODUCTION

The interest in the synthesis and characterization of Ru(III) complexes containing a Schiff base is due to their many significant biological activities, especially anticancer (Ejidike *et al*, 2016) or antibacterial (Kahrovic, Bektas, *et al.*, 2014; Priya *et al*, 2009) activities. Schiff bases derived from the condensation of 5-X-salicyladehyde (where X = Cl or Br) and aniline represent an important class of chelating ligands. There are relatively small number of complexes containing these Schiff bases whose structures are stored in Cambridge Structural Database (Blagus *et al*, 2010). Ruthenium(III) complexes with Schiff bases derived from 5-substituted-salicylaldehyde are described as DNA intercalators (Ljubijankic *et al*, 2013; Kahrovic *et al.*, 2014; Begic-Hairlahovic *et al*, 2014) and electrochemical mediators (Turkusic and Kahrovic, 2012, Kahrovic *et al.*, 2012, Kahrovic and Turkusic, 2012). Pyridine, pyrimidine and their derivatives have been widely used in medicinal applications (Akalin and Akyuz, 2008; Quin and Tyrell, 2010). The pyridine and pyrimidine ring systems provides a potential binding site for metals. Complex compounds containing pyridine or pyrimidine ring systems possesses a broad range of biological activities and can be used as potentially active therapeutic compounds (Colluccia, Natile, 2007; Kostova, 2006).

In this study, we report the synthesis and spectral characterization of Ru(III) neutral complex compounds with *N*-phenyl-5-X-salicylideneimine (where X = Cl or Br) and *N*-donor heterocyclic ligands, pyridine (py) or pyrimidine (pym). The present work is a continuation of our previously reported study on the synthesis, characterization and interaction with CT DNA of Ru(III) complexes with indazole and Schiff base derived from 5-Chlorosalicylaldehyde (Begic-Hairlahovic *et al*, 2014). The Schiff base and *N*-donor heterocyclic ligands used in this study are shown in (Fig. 1).

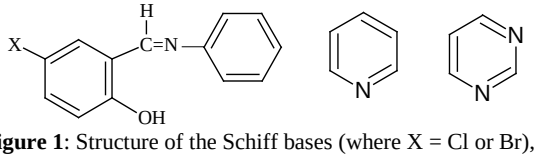

Figure 1: Structure of the Schiff bases (where X = Cl or Br), pyridine and pyrimidine.

EXPERIMENTAL

Materials

All chemicals were of analytical grade and were used as received without any purification with exception of aniline which is purified by distillation.

Starting materials

Schiff bases, *N*-phenyl-5-X-salicylideneimine (where X = Cl or Br) were synthesized according to the literature procedures (Dholakiya and Patel, 2002) and freshly prepared solutions were used for the synthesis of starting materials.
Sodium dichloro-bis-[*N*-phenyl-5-X-salicylideneiminato-*N,O*]ruthenate(III), hereinafter Na[$RuCl_2$(*N*-Ph-5-X-salim)$_2$] where X = Cl or Br were prepared using the reported procedures (Ljubijankic *et al.*, 2013) and were used without any purification as starting Ru(III) compounds in the synthesis of new neutral complexes. The purity of starting Ru(III) compounds were checked by infrared spectroscopy.

Synthesis of Complex 1

The preparation of Chloro(pyridine)bis[*N*-phenyl-5-chlorosalicylideneiminato-*O,N*]ruthenium(III), [RuCl(*N*-Ph-5-Cl-salim)$_2$py], hereinafter **Complex 1** was carried out by refluxing an ethanolic solutions of Na[$RuCl_2$(*N*-Ph-5-Cl-salim)$_2$] and an excess of pyridine. Absolute ethanol was added to 60 ml of ethanolic solution of Na[$RuCl_2$(*N*-Ph-5-Cl-salim)$_2$] (41.04 mg; 0.062 mmol) and pyridine (10 μL; 0.124 mmol). The mixture was refluxed for 10.5 hours at temperature 75 °C whereby the solution changed color from dark green to violet blue. The resulting solution was filtered off and kept in an ice-salt bath for seven days. The dark blue product was washed with water and diethyl ether to remove sodium chloride and excess of pyridine. The synthesized complex was dried under vacuum in a desiccator.
Yield: 68 %.
Complex 1: Anal. calcd for $C_{31}H_{23}Cl_3N_3O_2Ru$: C 55.00, H 3.42, N 6.21. Found: C 53.68, H 3.79, N 6.37. MALDI TOF/TOF MS (*m*/*z*) calcd for [$C_{31}H_{23}Cl_3N_3O_2Ru$], 676.9883; found, 676.9889; IR (KBr, cm^{-1}) 1589 s [ν(ring mode)], 1004 m [(ring breathing mode)], 669 vw [ν(Ru–N), 438 wv [ν(Ru–O)]; UV-Vis (CH_2Cl_2, λ/nm) 245, 260, 350, 607.

Synthesis of Complex 2

The compound, Chloro(pyrimidine)bis[*N*-phenyl-5-bromosalicylideneiminato-*O,N*]ruthenium(III), [RuCl(*N*-Ph-5-Br-salim)$_2$Pym], hereinafter **Complex 2** was prepared by stirring an ethanolic solutions of Na[$RuCl_2$(*N*-Ph-5-Br-salim)$_2$] and an excess of pyrimidine. The solution of pyrimidine (5 μL; 0.06 mmol) in 2 mL absolute ethanol was added to the solution of Na[$RuCl_2$(*N*-Ph-5-Br-salim)$_2$] (25.1 mg; 0.034 mmol) in absolute ethanol (40 mL). The mixture was stirred at room temperature for 29 hours until a light green solution was obtained. The resulting solution was evaporated to dryness and residue washed several times with diethylether and water to remove excess of pyrimidine and sodium chloride. The green product was dried in a vacuum desiccator.
Yield: 50 %.

Complex 2: Anal. calcd for $C_{30}H_{22}Br_2ClN_4O_2Ru$: C 46.99, H 2.89, N 7.31. Found: C 45.04, H 2.94, N 7.02. MALDI TOF/TOF MS (*m*/*z*) calcd for $C_{30}H_{22}Br_2ClN_4O_2Ru$, 766.8823; found, 766.8804. IR (KBr, cm^{-1}) 1589 s [ν(ring mode)], 1002 m [(ring breathing mode)], 663 wv [ν(Ru–N), 434wv [ν(Ru–O)]. UV-Vis (CH_2Cl_2, λ/nm) 245, 260, 350, 607.

Instrumentation – Physical measurements

Synthesized compounds were characterized by MALDI TOF/TOF mass spectrometry, CHN analysis, cyclic voltammetry, IR and UV/Vis spectrometry.
The mass spectra were recorded on a MALDI TOF/TOF (matrix-assisted laser desorption / ionization-time-of-flight) Analyzer model 4800 Plus (Applied Biosystems Inc., Foster City, CA, USA). Small amount of sample was mixed with 10 μL of MALDI matrix (DHAP (2,6-dihydroxyacetophenone); 5 mg/mL) and 1 μL was spotted on MALDI plate. The mass spectra were acquired in m/z range from 10 to 1000 Da (focus mass 500 Da, delay time 300 ns). Thiamine mononitrate, azithromycin and angiotensin were used as internal standards to calibrate the instrument.
The analysis of carbon, hydrogen and nitrogen was carried out by a Perkin Elmer 2400 Series CHNS/O Analyzer.
Infrared spectra (4000 – 400 cm^{-1}) were collected on a BX FTIR Perkin Elmer Spectrum System with samples prepared as KBr pellets.
The electronic spectra were obtained on a Perkin Elmer UV/Vis spectrometer model Lambda 35.
The characterization of Ru(III) complexes by cyclic voltammetry (CV) was investigated using a potentiostat/galvanostat Autolab PGSTAT 12 Analyzer equipped with glassy carbon (GC), Ag/AgCl and Pt wire as working, reference and auxiliary electrode, respectively. The cyclic voltammograms of the complexes were recorded in acetonitrile (MeCN) at scan rate 0.2 V s^{-1} where tetraethylammonium bromide (Et_4NBr) was used as supporting electrolyte.

RESULTS AND DISCUSSION

The starting Ru(III) compounds, Na[$RuCl_2$(*N*-Ph-5-X-salim)$_2$] (where X = Cl or Br) were synthesized by reacting $RuCl_3$ with freshly prepared Schiff bases, 5-X-salicylideneimine (Dholakiya and Patel, 2002) in 1 : 2 molar ratio in absolute ethanol. The freshly prepared Na[$RuCl_2$(*N*-Ph-5-X-salim)$_2$] compounds were used for the synthesis of new complex compounds.
Neutral ruthenium(III) complex compounds of general formula [RuCl(*N*-Ph-5-X-salim)$_2$B] (where X = Cl for B = py or X = Br for B = pym) were prepared by reacting Na[$RuCl_2$(*N*-Ph-5-X-salim)$_2$]with an excess of py or pym in absolute ethanol as shown in (Fig. 2). The synthesis of

the complexes was carried out in relative mild conditions by replacement of easily outgoing chloride ion in $Na[RuCl_2(N\text{-Ph-5-X-salim})_2]$ with py or pym. The products are stable in air, insoluble in water, soluble in dimethyl sulfoxide (DMSO), dichloromethane, acetonitrile (MeCN), dimethylformamide (DMF), tetrahydrofuran (THF).

Based on mass spectra, CHN elemental analysis, infrared and electronic spectra the synthesized compounds were formulated as $[RuCl(N\text{-Ph-5-X-salim})_2B]$, where X = Cl for B = py and X = Br for B = pym.

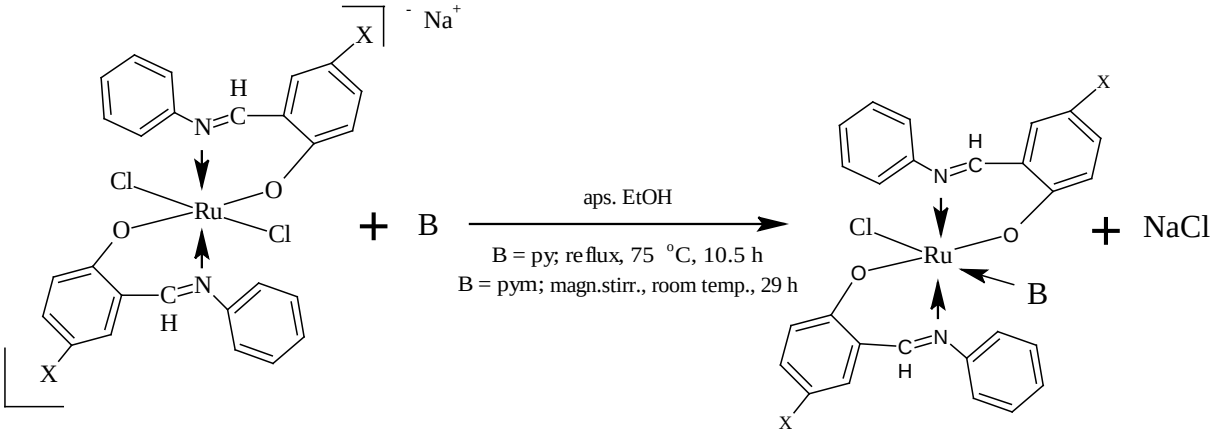

Figure 2: Formation of new Ru(III) complexes. (Where X = Cl for B = py and X = Br for B = pym).

MALDI-TOF/TOF mass spectrometry results confirmed existence of neutral molecules with general formula $[RuCl(N\text{-Ph-5-X-salim})_2B]$ (Table 1).

Table 1: MALDI TOF/TOF results of synthesized compounds

Compound	Empirical formula	Calc. mass m/z (100 %)	Measured mass m/z (100 %)	Mass error / ppm
Complex 1	$C_{31}H_{23}Cl_3N_3O_2Ru$	676.9883	676.9889	0.88
Complex 2	$C_{30}H_{22}Br_2ClN_4O_2Ru$	766.8823	766.8804	2.48

The compounds were characterized by IR spectroscopy in the solid state (KBr pellets). The main characteristic vibrations are given in Table 2. In studying coordination effects of metal complexes with pyridine or pyrimidine, ring breathing mode can be used as a guide which shifts to higher wavenumbers upon coordination (Bayari *et al*, 2003). Also when pyridine or pyrimidine ring nitrogen is involved in complex formation certain vibrational modes increase in value due to both coupling with M-N (pyridine or pyrimidine) vibration and alterations of the force field (Akalin, Akyuz, 2008; Bayari *et al*, 2003). The strong bands at 992 and 991 cm^{-1} could be attributed to the ring breathing mode of free pyridine or pyrimidine molecule, respectively. After coordination this bands were shifted for 12 or 11 cm^{-1} to higher wavenumbers.

Coordination of pyridine or pyrimidine to Ru(III) *via* electronic pair on the atom nitrogen affects ring stretching vibrations. This frequencies were shifted towards higher wavenumber, which is indicative of coordination of pyridine or pyrimidine through nitrogen atom to the Ru(III). The new weak bands in Complex 1 at 669 and 438 cm^{-1} could be assigned to Ru-N and Ru-O, respectively. This bands in Complex 2 appears at 663 and 434 cm^{-1}. Characteristic IR vibrations of starting Ru(III) compounds are azomethine C=N, C-O phenolic, Ru-N and Ru-O. After coordination of *N*-heterocyclic donor ligands this bands are not affected. Infrared spectra of synthesized complexes demonstrate that Schiff bases acts as anionic bidentate ligands while *N*-heterocycle as monodentate ligand.

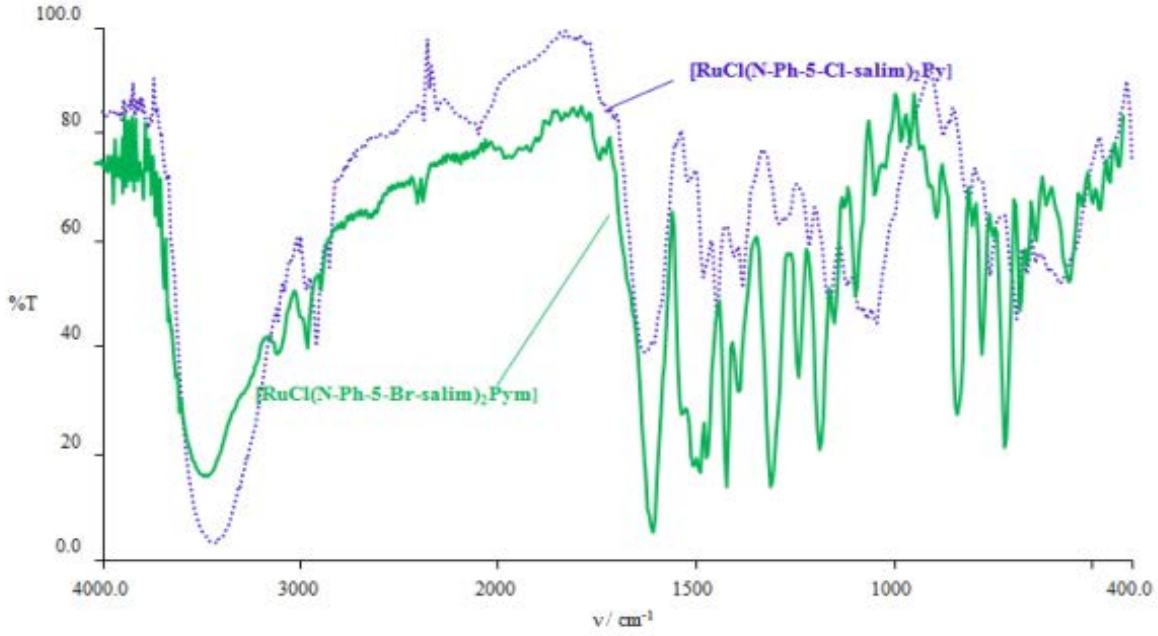

Figure 3: FT- IR spectra of Complex 1and Complex 2

Table 2: Characteristic vibrations (cm^{-1}) in FT-IR spectra of starting Ru(III) compounds, neutral complexes, free pyridine and pyrimidine

	Complex 1	Complex 2	Py	Pym
ν(ring) $_{py, pym}$	1589	1589	1580	1570
ring breathing $_{py, pym}$	1004	1002	992	991
$\nu(C=N)_{SB}$	1603	1600	-	-
	(1602)	(1601)		
$\nu(C=O_{Ph})_{SB}$	1295	1291	-	-
	(1295)	(1289)		
ν(Ru–N)	669	663	-	-
	(668)	(663)		
ν(Ru–O)	438	434	-	-
	(436)	(433)		

$_{SB}$ – assigned vibrations in Schiff base; $_{Py, Pym}$ – assigned vibrations in pyridine or pyrimidine; values in parentheses refer to starting Ru(III) compound

UV/Vis spectra of starting Ru(III) compounds, synthesized compounds and *N*-donor ligands were recorded in dichloromethane. Electronic spectra exhibit a few characteristic absorptions which are presented in Table 3. UV/Vis spectra of pyridine has one absorption band which could be attributed to π→π* transition, while pyrimidine showed two bands attributed to π→π* and n→π* transitions. In the electronic spectra of starting Ru(III) compounds weak broad absorptions bands centered at 609 nm for X = Cl or 625 nm for X = Br can be attributed to $^2T_{2g}\rightarrow{}^2A_{2g}$. In the spectra of neutral complexes this transitions moves towards lower value of wavelength (565 nm for B = py and 609 nm for B = pym). *N*-donor ligands in the synthesized complexes splits stronger crystal field than chloride ion in the starting material results in higher separation energies of d-atomic orbitals and moves d-d transitions to higher energies.

Since the synthesized complexes are insoluble in water, cyclicvoltammograms were recorded in non-aqueous solvent. The complete scan in the range -1.0 – 0.0 V of Complex 1 and Complex 2 in MeCN/Et_4NBr system showed one cathodic wave (-0.981 V and -0.931 V, respectively) and one anodic wave (-0.740 V and -0.738 V, respectively) (Fig. 4). This quasi-reversible waves can be assigned to the couple Ru(III)/Ru(II).

Table 3: Characteristic absorptions in electronic spectra of $Na[RuCl_2(N\text{-Ph-5-X-salim})_2]$, Complex 1, Complex 2 and nitrogenous bases in dichloromethane

Compound	π→π*	n→π*	IL (SB)	d-d
$Na[RuCl_2(N\text{-Ph-5-Cl-salim})_2]$	244	sh	348	613
Py	253	-	-	-
Complex 1	244	sh	348	565
$Na[RuCl_2(N\text{-Ph-5-Br-salim})_2]$	244	sh	351	625
Complex 2	244	sh	350	611
Pym	243	287	-	-

π→π* - electronic transition of delocalized electrons of the aromatic system; n→π* - electronic transitions of the atoms of azomethine group or free electron pair on the N atom of pyridine or pyrimidine with aromatic π electrons; IL (SB) – intraligand transition of whole molecule of Schiff base; d-d – transition of low spin complex; sh-shoulder.

In Table 4 are given characteristic half-wave potentials and peak-to-peak separation values of Complex 1 and Complex 2.

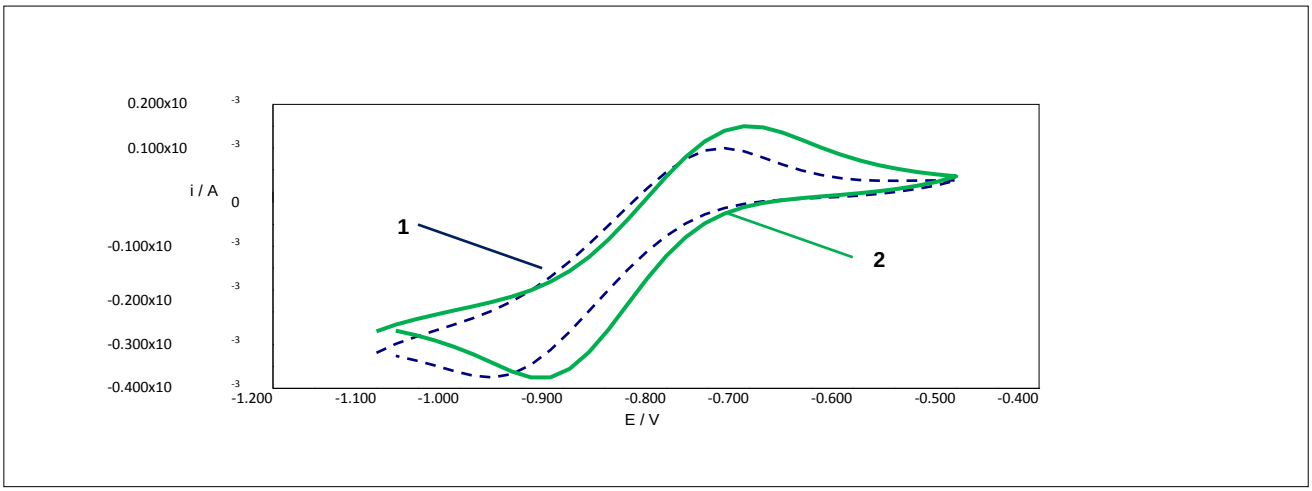

Figure 4: Cyclic voltammograms of Complex 1 (1) andComplex 2 (2) in MeCN; supporting electrolyte: Et_4NBr; potential range: -1.1 – -0.5 V; scan rate 0.2 V/s

Table 4: Characteristic potentials of Complex 1 and Complex 2 from cyclic voltammetric measurements in MeCN / Et_4NBr system

	Complex 1	Complex 2
E_{pc}/ V	-0.981	-0.931
E_{pa}/ V	-0.740	-0.738
$E_{1/2}$ / V	-0.861	-0.835
ΔE / V	0.241	0.193

All data are given vs Ag/AgCl reference electrode

CONCLUSION

New neutral complex compounds of Ru(III) with *N*-phenyl-5-X-salicylideneimine (where X = Cl or Br) and *N*-donor heterocyclic ligands (pyridine or pyrimidine) were synthesized. On the basis of mass spectra, CHN analysis, infrared and electronic spectra, the complexes were formulated as [RuCl(*N*-Ph-5-X-salim)$_2$B] where X = Cl for B= py and X = Br for B = pym. In the octahedral environment coordination of the Ru(III) to the imine nitrogen and phenolic oxygen atoms of the Schiff bases and nitrogen atom of py or pym occurred. MALDI TOF/TOF mass spectrometry confirmed existence of the neutral molecules. Redox property of complexes has been determined using cyclic voltammetry.

REFRENCES

Akalin, E., Akyuz, S. (2008). Vibrational study on Zn(Pyrimidine)$_2$Cl$_2$, Pyrimidine-Al(OH)$_3$ and Pyrimidine-(Al(OH)$_3$)$_2$ complexes. *Vibrational spectroscopy*, *48*,233-237.

Bayari, S., Ataç, A., Yurdakul, Ş. (2003). Coordination behaviour of nicotinamide: an infrared spectroscopic study. *Journal of Molecular Structure*, *655*, 163-170.

Begic-Hairlahovic, S., Kahrovic, E., Turkusic, E. (2014). Synthesis, characterization and interaction with CT DNA of novel cationic complex Ru(III) with indazole and Schiff base derived from 5-chlorosalicylaldehyde. *Bulletin of the Chemists and Technologists of Bosnia and Herzegovina*, 43, 15-20.

Blagus, A., Cincic, D., Friscic, T., Kaitner, B., Stilinovic, V. (2010). Schiff base derived from hydroxyarylaldehydes: molecular and crystal structure, tautomerism, quinoid effect, coordination compounds. *Maced. J. Chem. Chem. Eng.,29 (2)*, 117-138.

Coluccia, M., Natile, G. (2007). *Trans*-Platinum Complexes in Cancer Therapy. *Anti-Cancer Agents in Medicinal Chemistry*, 111-123.

Dholakiya, P. P., Patel M. N. (2002). Synthesis, spectroscopic studies, and antimicrobial activity of Mn(II), Co(II), Ni(II), Cu(II), and Cg(II) complexes with bidentate Schiff bases and 2,2′- bipyridilamine. *Synthesis and Reactivity in Inorganic and Metal-Organic Chemistry*, *32(4)*, 753-762.

EjidikeI. P., Ajibade p. A. (2016). Synthesis, Characterization, Anticancer, and Antioxidant Studies of Ru(III) Complexes of Monobasic Tridentate Schiff Bases. *Bioinorganic Chemistry and Applications, vol. 2016*, 11 pages.

Kahrovic , E. (2014). Ruthenium Compounds with Schiff Bases: Design and Promising Applications of Salicylideneimine Complexes. In Keeler, G. P. (Ed.), *Ruthenium: Synthesis, Physicochemical Properties and Applications.*,(p.p. 269-283).NOVA Publishers.

Kahrovic, E., Bektas, S., Turkusic, E., Zahirovic A. (2014). Evidence on antimicrobial activity of Sodium dichloro-bis[N-phenyl-5-chlorosalicylideneiminato-N,O]ruthenate(III) against gram positive bacteria. *SYLWAN*, *158(5)*, 482-493

Kahrovic, E., Dehari, S., Dehari, D., Begic, S. and Ljubijankic, N. (2010). Synthesis and characterization of new Ru (III) complexes with monobasic (NO) and dibasic (ONO) Schiff bases derived from salicylaldehydes. *Technics Technologies Education Management 5/4*, 799-803.

Kahrovic, E., Turkusic, E. (2012). New Ruthenium Complexes with Schiff Bases as Mediators for the Low Potential Amperometric Determination of Ascorbic Acid, Part II: Voltametric and Amperometric evidence of mediation with Bromo-derivative of Tetraethylamonium dichloro-bis[N-

phenyl-5-halogeno-salicylideniminato N,O]ruthenat(III).*HealthMED, 6/3,* 1046-1049.

Kahrovic, E., Turkusic, E., Zahirovic, A. (2014). Calf Thymus DNA Intercalation by Anionic Ru(III) Complexes Containing Tridentate Schiff Bases Derived from 5-X-Substituted Salicyladehyde and 2-Aminophenol. *Journal of Chemistry and Chemical Engeenering, 8,* 335-343.

Kahrovic, E.,Turkusic, E., Ljubijankic, N., Dehari, S., Dehari, D., Bajsman, A. (2012). New Ruthenium Complexes with Schiff Bases as Mediators for the Low Potential Amperometric Determination of Ascorbic Acid, Part I: Voltametric and Amperometric evidence of mediation with Tetraethylamonium dichloro-bis[N-phenyl-5-chloro-salicylideniminato-N,O]ruthenat(III). *HealthMED*, 6/2, 699-702.

Keppler, B. K., Henn,M., Juhl, U. M., Berger, M. R., Niebl, R., Wagner, F. E. (1989).New ruthenium complexes for the treatment of cancer. In *Ruthenium and Other Non-Platinum Metal Complexes in Cancer Chemotherapy* (p.p. 41-69). Springer Berlin Heidelberg.

Ljubijankic, N., Zahirovic, A., Turkusic, E., Kahrovic, E. (2013). DNA Binding Properties of Two Ruthenium (III) Complexes Containing Schiff Bases Derived from Salicylaldehyde: Spectroscopic and Electrochemical Evidence of CT DNA Intercalation. *Croatica Chemica Acta, 86(2),* 215-222.

Turkusic, E., Kahrovic, E. (2012). Development of new low potential amperometric sensor for L-cysteine based on carbon ink modification by Tetraethylamonium dichloro-bis[N-phenyl-5-bromosalicylideniminato-N,O]ruthenat(III). *Technics Technologies Education Management, 7/3,* 1300-1303.

Quin, L. D., Tyrell, J. A., *Fundametals of Heterocyclic Chemistry, Importance in Nature and in the Synthesis of Pharmaceuticals*, John Wiley & Sons, 2010.

Summary / Sažetak

Sintetizirana su dva nova neutralna kompleksna spoja Ru(III) sa Schiff-ovim bazama i *N*-donorskim heterocikličnim ligandima. Na bazi MALDI TOF/TOF masenih spektara, CHN elementarne analize, infracrvenih i elektronskih spektara sintetizirani spojevi su formulirani kao [RuCl(*N*-Ph-5-X-salim)$_2$B], gdje je X = Cl za B = Py i X = Br za B = Pym. U oktaedarskom okruženju Ru(III) bidentatna Schiff-ova baza djeluje kao anionski ligand gdje se koordinacija ostvaruje preko deprotoniranog fenolnog atoma kisika i azometinskog atoma azota. Koordinacija monodentatnih *N*-donorskih heterocikličnih liganada se odvija preko slobodnog elektronskog para na atomu azota.