



University of Bahrain
Journal of the Association of Arab Universities for
Basic and Applied Sciences

www.elsevier.com/locate/jaaubas
www.sciencedirect.com



تحضير، الخواص الفيزيائية والتقييم البيولوجي لمعقدات فلز (II) مع قاعدة شيف

محاسن الياس، هدى قاسم، كارولين شاكر

قسم الكيمياء، كلية العلوم للبنات، جامعة بغداد، بغداد، العراق

الملخص:

معقدات الفلزات (II) من النحاس، النيكل والكوبلت مع قاعدة شيف المشتقة من البوتاسيوم $2-N-4$ ثنائي مثيل امينوبنزايلدين) 4- ثلاثي ثيوكربونات 1,2,3- ثيادايازول تم تحضيرها وتشخيصها بواسطة الطرق الفيزيوكيميائية المعروفة والتي تشمل (الامتصاص الذري A.A، التحليل الكيميائي للعناصر C.H.N.S، طيف الأشعة تحت الحمراء FTIR وفوق البنفسجية UV، التحاليل الحرارية TGA، القابلية المغناطيسية وقياسات التوصيلية). وبناء على هذه الدراسات، تم اقتراح شكل تناسقي سداسي الابعاد لجميع المعقدات المحضرة. تم اختبار قاعدة شيف ومعقداتها كمضاد للبكتريا لتقييم قدرتها التثبيطية ضد نوعين من البكتريا *Pseudomonas aeruginosa* (كبتريا سالبة الصبغة و *Staphylococcus aureus*) كبتريا موجبة الصبغة وذلك باستخدام تركيزين مختلفين (5 ملي مول و 10 ملي مول). لقد أظهرت النتائج أن معقد النيكل (II) يمتلك أعلى نسبة تثبيط في فعاليته المضادة لنشاط البكتريا مقارنة بالمعقدات الأخرى وأربطتها عندما قورنت النتائج مع الامبسيلين كعقار قياسي.



University of Bahrain
**Journal of the Association of Arab Universities for
Basic and Applied Sciences**

www.elsevier.com/locate/jaaubas
www.sciencedirect.com



ORIGINAL ARTICLE

Synthesis, physical characterization and biological evaluation of Schiff base M(II) complexes



Mahasin Alias, Huda Kassum, Carolin Shakir *

Department of Chemistry, College of Science for Women, University of Baghdad, Baghdad, Iraq

Received 24 November 2012; revised 24 January 2013; accepted 3 March 2013

Available online 4 April 2013

KEYWORDS

Schiff base;
Trithiocarbonate;
1,3,4-Thiadiazole;
Physico-chemical;
Antibacterial

Abstract Metal (II) complexes of Cu, Ni, and Co with Schiff base derived from potassium 2-N (4-N,N-dimethylaminobenzylidene)- 4-trithiocarbonate 1,3,4-thiadiazole (L) were synthesized and characterized by standard physico-chemical procedures i.e. (metal analysis A.A, elemental chemical analysis C.H.N.S, FTIR, UV–vis, thermal analysis TGA, magnetic susceptibility and conductometric measurements). On the basis of these studies, a six coordinated octahedral geometry for all these complexes has been proposed. The Schiff base ligand and its complexes were also tested for their antibacterial activity to assess their inhibiting potential against *Pseudomonas aeruginosa* (as gram negative bacteria) and *Staphylococcus aureus* (as gram positive bacteria) using two different concentrations (5 and 10 mM). The results showed the Ni(II) complex have the higher rate in antibacterial activity than other complexes and ligand when compared them with ampicillin as standard drug.

© 2013 Production and hosting by Elsevier B.V. on behalf of University of Bahrain.

1. Introduction

Schiff bases and their bio-active complexes have been studied extensively over the past decade. Schiff bases provide potential sites for bio-chemically active compounds. Various transition and inner-transition metal complexes with bi, tri and tetradentate Schiff bases containing nitrogen and oxygen or sulfur

donor atoms play an important role in biological systems (Malik et al., 2011; Raman et al., 2007). The thiadiazole ring and its derivatives possess good coordination behavior, since they have sulfur atom and two nitrogen atoms in addition to the substituent having a donating group in the structure (March and Smith, 2007) therefore the study of its metallic complexes is of structural importance in addition to many important applications such as fungicidal and leishmanicides (ukaszuk et al., 2007; Foroumadi et al., 2005). Trithiocarbonate complexes have received attention because of the dual nature of metal-CS₃ moiety as electrophilic and nucleophilic reagents, which make them versatile intermediates for the synthesis of other oil thio species (Vicente et al., 1995). Although the main application is the treatment of a variety of rheumatic diseases, some of these compounds have shown to have antileishmanial activity *in vitro* inhibitory effect on HIV or activity of tumor cell (Vicente et al., 1995; Dehmel et al., 2007).

* Corresponding author. Address: Chemistry Dept., College of Science for Women, University of Baghdad, Jadiriyah, P.O. Box 47162, Baghdad, Iraq. Tel.: +964 7902789368.

E-mail address: carolin.sh86@yahoo.com (C. Shakir).

Peer review under responsibility of University of Bahrain.

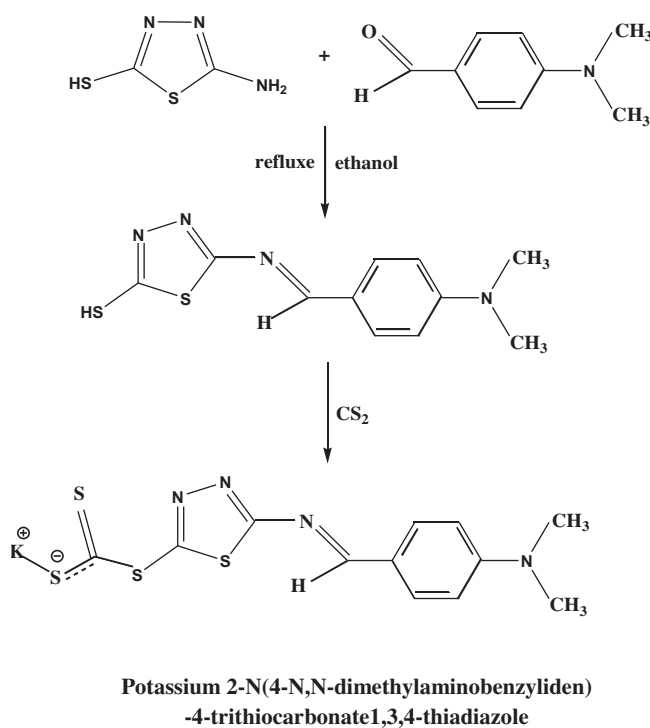


Production and hosting by Elsevier

Organotrithiocarbonates have found many applications in various fields such as analysis, organic synthesis, medicine, industry and agriculture, some of these applications are as flotation agents, vulcanization accelerators, pesticides, plant defoliant, rust inhibitor, lubricating oil additives, and some have recently reported to possess activity as anti-radiation drugs (Srivastava et al., 1990; Ali and Abbas, 2006). In this paper, we focused on a synthesized new derivative of trithiocarbonate in an attempt to introduce the azomethine moiety in the structure of the thiadiazole ring with the 4-trithiocarbonate group in the same structure and investigate the coordination behavior as well as study the antibacterial activity.

2. Experimental

All the chemicals used in this work were of analytical reagent grade. Metal salts used in this study are copper chloride dihydrate $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ from Fluka, nickel chloride hexahydrate $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ from BDH and cobalt chloride hexahydrate $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$ from Fluka. The metal analysis was performed by



Scheme 1 General steps for preparation of the new ligand (L).

a Perkin Elmer 5000 Atomic Absorption Spectrophotometer. Elemental Analysis (C.H.N.S) of compounds was carried out with EM-034.mth. The electronic spectra were recorded on a Shimadzu (UV-vis 1600 A) Ultra Violet Spectrophotometer using quartz cell at a wave length range of 200–1100 nm. FTIR spectra were recorded on a Shimadzu 8400 Fourier Transform Spectrophotometer by using CsI disk in the wave number range of 4000–200 cm^{-1} . Thermal analysis TGA was performed with 4000 Perkin–Elmer. Magnetic susceptibility measurements were determined using Magnetic Susceptibility Balance of Johnson matting catalytic system division, England at room temperature. The molar conductance was measured in DMSO as a solvent at room temperature using Coring Conductivity Meter 220. Melting point apparatus of Gallencamp M.F.B-600.01 was used.

2.1. Synthesis of Schiff base potassium 2-N(4-N,N-dimethylaminobenzylidene)-4-trithiocarbonate 1,3,4-thiadiazole (L)

A mixture of 2 g, 0.015 m mol of 2-amino-5-mercapto-1,3,4-thiadiazole and 3.07 g, 0.015 m mol of 4-N,N-dimethylaminobenzylidene in 10 ml of absolute ethanol and one drop of glacial acetic acid was continuously stirred and heated in a water bath at 60–70 °C then refluxed for 1 h, left to cool in ice-water bath until orange precipitate was obtained. 2 g, 0.0075 mol of the previous mixture i.e. 2-N(4,4-dimethylamin benzylidene)-5-mercapto-1,3,4-thiadiazole in 20 ml of absolute ethanol was added to 1.5 ml of carbon disulfide and 0.42 g, 0.0075 mol potassium hydroxide as alkali media. The mixture was refluxed for 3 h then the solvent was distilled off and the precipitate crystals were filtered and recrystallized from ethanol and distilled water to obtain orange precipitate (Scheme 1). The physical properties are shown in Table 1.

2.2. Synthesis of complexes

A general method has been used for the preparation of the new complexes by the reaction of the hydrate metal salts of copper, cobalt and nickel which dissolved in 5 ml of absolute ethanol and 0.378 g, 1 m mol of the Schiff base ligand at a metal to ligand molar ratio of 1:1, while 0.756 g, 2 m mol at a metal to ligand molar ratio of 1:2 which dissolved in 10 ml of absolute ethanol. The metal salts were added gradually drop by drop to a solution of ligand. The reaction mixture was allowed to stir magnetically for 1 h at room temperature. The reaction mixture was filtered, washed with ethanol and dried at 50 °C by using an oven for 1 h Table 1.

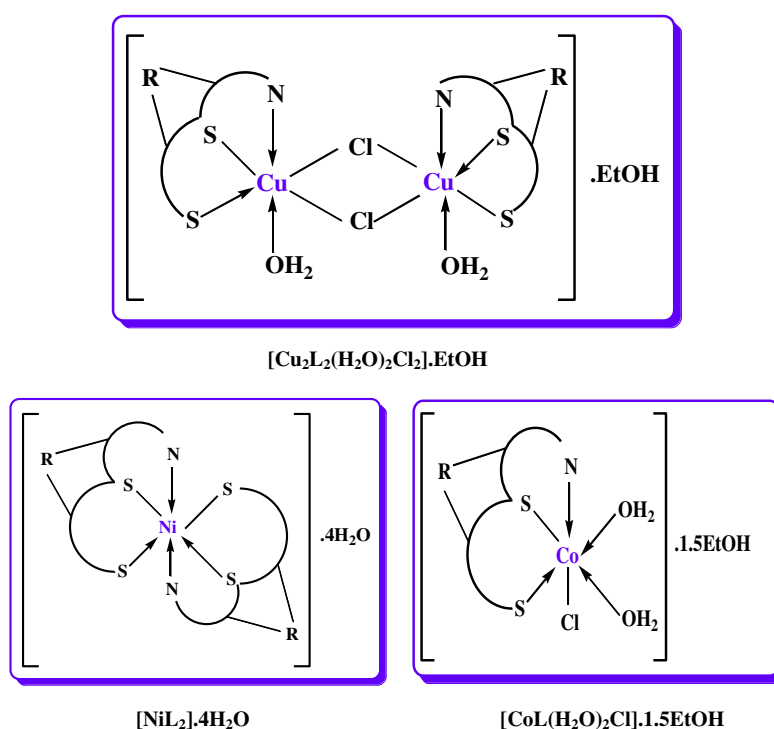
Table 1 Physical data of new ligand (L) and its metal complexes.

Comp.	Color	M.P. °C	Yield %	M. Wtg. mol^{-1}	Elemental analysis found(Calc.)				Metal percentage	
					C	H	N	S	found	Calc.
L	Darkorange	150	70.0	378.09	38.25(38.08)	2.98(2.91)	14.55(14.81)	33.53(33.85)	—	—
Cu_2L_2	Brown	240d	54.1	958.09	32.25(32.56)	3.25(3.34)	11.81 (11.69)	26.47(26.72)	13.50	13.26
NiL_2	Lightbrown	290d	55.5	808.69	35.27(35.61)	3.68(3.70)	13.35(13.84)	31.96(31.65)	7.15	7.25
CoL	Darkbrown	250d	52.3	538.43	33.92(33.43)	4.77(4.45)	10.12(10.40)	23.95(23.77)	11.00	10.94

d = decomposition degree

Table 4 Thermal analysis data for metal complexes.

Comp.	Dissociation stages	Temp range in TG °C	Weight loss Found (Calcd.)%	Decomposition assignment
Cu ₂ L ₂ (958.09)	Stage I	70–130	4.69 (4.80)	Outer sphere EtOH
	Stage II	130–250	3.35 (3.75)	Coordinated water molecules
	Stage III	250–340	6.57 (6.26)	2CH ₃
	Stage IV	340–810	51.61 (51.87)	2C ₁₀ H ₅ N ₄ S, Cl ₂ of ligand
	Stage V	810–900	33.20 (33.30)	2CuS ₃
NiL ₂ (808.69)	Stage I	35–180	8.95 (8.90)	Outer sphere water molecules
	Stage II	180–390	7.68 (7.41)	4CH ₃
	Stage III	390–820	52.71 (52.67)	2C ₁₀ H ₅ N ₄ S of ligand
	Stage IV	820–900	31.29 (30.99)	NiS ₆
CoL (538.43)	Stage I	55–145	12.88 (12.81)	Outer sphere EtOH
	Stage II	145–200	6.42 (6.68)	Coordinated water molecules
	Stage III	200–295	5.39 (5.57)	2CH ₃
	Stage IV	295–780	46.35 (46.15)	C ₁₀ H ₅ N ₄ S, Cl of ligand
	Stage V	780–865	29.67 (29.63)	CoS ₃

**Figure 1** Shows the suggested structures of prepared new complexes.

Cu(II) complex: Electronic spectrum of brown complex displayed bands in the range of 23.955–37.037 cm⁻¹ which can be assigned to charge transfer as well as the spectrum showed d–d electronic transition at 14.814 cm⁻¹ which was assigned to ²E_g → ²T_{2g} transition, the broadness of the band is due to the ligand field and the Jahn–Teller effect, these absorptions prefer the distorted octahedral geometry for the Cu(II) ion (Solomon and Lever 2006; Alhadi et al., 2012). Moreover, the magnetic moment for the Cu(II) complex is 1.2 B.M. suggesting a dimeric structure leading to spin–spin coupling (Greenwood and Ernschaw, 1998). Furthermore, the complex is non-electrolyte as the molar conductance was found to be 28 μscm⁻¹ in 10⁻³ M in DMSO as solvent Table 3.

Ni(II) complex: In the present work, light brown color of the new complex is postulated to be distorted octahedral with its respective values. The 10Dq (10.267 cm⁻¹) is equal to the

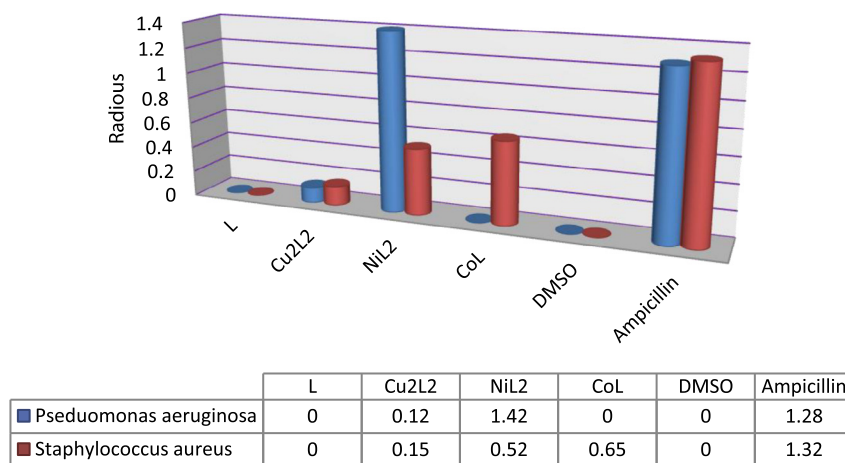
first transition ν_7 . The band at 13.947 cm⁻¹ is assigned to the spin-forbidden transition ³A_{2g} → ¹E_g (Pastorek et al., 2001) Table 3. More evidence for the suggested octahedral geometry of present complex is supported by the absence of band in the range of 20000 cm⁻¹ which is characteristic of square planar Ni(II) complexes (Greenwood and Ernschaw, 1998; Siddiqi et al., 2006). Magnetic moment 3.2 B.M. and the conductivity measurement show that the complex is non-ionic.

Co(II) complexes: In the spectrum of Co(II) complex, the bands at 10.040 cm⁻¹, 15.070 cm⁻¹ and 19.980 cm⁻¹ are associated to the transitions ⁴T_{1g} → ⁴T_{2g} (ν₁), ⁴T_{1g} → ⁴A_{2g} (ν₂) and ⁴T_{1g} → ⁴T_{1g(P)} (ν₃) respectively. These transitions are specified to the Co(II) ion in the field of octahedral symmetry and the magnetic moment of 4.9 B.M. shows the complex is paramagnetic and has three unpaired electrons corresponding to a high spin of this geometry (Rathore et al., 2010; Al-Najjar,

Table 5 Antibacterial screening data for the ligands and their complexes.

Comp.	Diameter of inhibition zone (mm); Concentration in mM			
	<i>Pseudomonas aeruginosa</i>		<i>Staphylococcus aureus</i>	
	5 mM	10 mM	5 mM	10 mM
L	–	–	–	–
Cu ₂ L ₂	–	–	–	–
NiL ₂	+++	++	+	+
CoL	–	–	+	++
DMSO	–	–	–	–
Ampicillin	++	+++	++	+++

(–) no inhibition; (+) inhibition in diameter (0.25–0.82)mm; (++) inhibition in diameter (0.83–1.37)mm; (+++) inhibition in diameter (1.38–1.93)mm.

**Figure 2** Shows the effect of ligand and its metal complexes toward *Pseudomonas aeruginosa* and *Staphylococcus aureus* at concentration 5 mM.

2009). The ligand field splitting energy (10 Dq), interelectronic repulsion parameter (B') and nephelauxetic ratio (β) for the Co(II) complex were calculated, and these correspond to the 10 Dq = 11.896 cm⁻¹, $B' = 661$ cm⁻¹, $\beta = 0.68$ values Table 3. The value of the β parameter indicates a covalent character for the metal–ligand bonds. The conductivity measurement recorded 29 μscm^{-1} and this refers that the complex is non-electrolyte.

3.4. Thermal analysis

The results of the solid complexes are listed in Table 4. The results show good agreement with the structures suggested from the analytical data Table 1. A general decomposition pattern was concluded, whereby the complexes decomposed in three stages for ligand this decomposition began from almost between 180 and 900 °C. Besides these three decomposition stages, those complexes which have coordinated water and/or ethanol exhibited additional decomposition steps, the structural formula assigned to the complexes are presented in Fig. 1.

3.5. Suggested structure of complexes

Fig. 1.

3.6. Antibacterial activities

The results obtained for biological activity for the prepared ligand and its metal complexes are given in Table 5. Diameter of inhibition zone (mm) including the disk diameter was measured for each treatment. The ligand showed no antimicrobial activity against both kinds of bacteria i.e. *P. aeruginosa* and *S. aureus*. The copper(II) complex shows a slight effect compared with ligand in both concentrations and organisms used, while nickel(II) complex exhibited the maximum antibacterial activity against all organisms used in this study and recorded high inhibition activity against *P. aeruginosa* comparable with standard drug. Moreover, cobalt complex showed moderate activity against *S. aureus* microorganism comparable with ligand and standard drug ampicillin, while against *P. aeruginosa* the results do not record any biological activity of this complex in both concentrations (Figs. 2 and 3). The higher inhibition zone of metal complexes than those of the ligand can be explained on the basis of Overtone's concept and Chelation theory. On chelation, the polarity of the metal ion will be reduced to a greater extent due to the overlap of the ligand orbital and partial sharing of the positive charge of the metal ion with donor groups. Further, it increases the delocalization of π -electrons over the whole chelating ring and enhances the penetration of the complexes into lipid membranes and

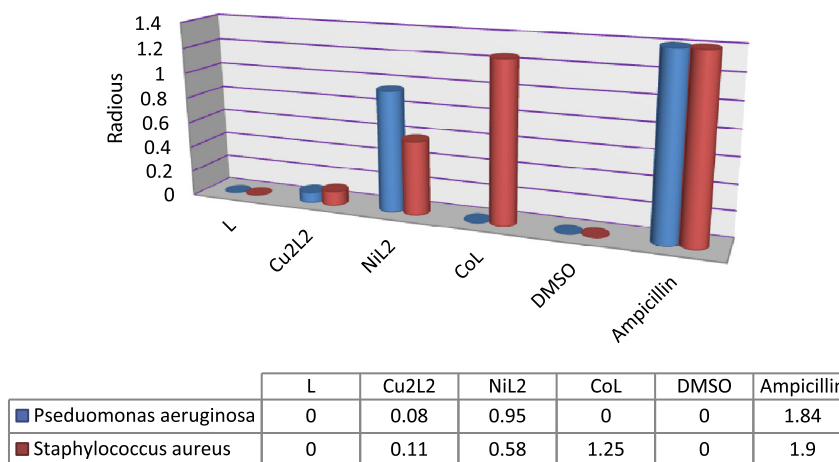


Figure 3 Shows the effect of ligands and their metal complexes toward *Pseudomonas aeruginosa* and *Staphylococcus aureus* at concentration 10 mM.

blocking of the metal binding sites in the enzymes of microorganisms. There are other factors which also increase the activity are solubility, conductivity and bond length between the metal and ligand (Chohan et al., 2001; Iqbal et al., 2006; Singh et al., 2008).

4. Conclusion

In the present research study, we synthesized new ligand of tri-thiocarbonate from 2-amino-5-mercapto-1,3,4-thiadiazole. This new compound was used to prepare some new complexes of Cu(II), Ni(II) and Co(II), these complexes are characterized by various physicochemical and spectral analyses. The results exhibit that the synthesized ligand binds with metal ions in tridentate through S,S donor sites of trithiocarbonate as well as N atom of the azomethine group. Thermogravimetric studies of the complexes also helped to characterize the complexes. The antibacterial data show that the metal complexes have biological activity compared to that of parent ligand.

References

- Alhadi, A.A., Shaker, S.A., Yehye, W.A., Ali, H.M., Abdullah, M.A., 2012. Synthesis, magnetic and spectroscopic studies of Ni(II), Cu(II), Zn(II) and Cd(II) complexes of a newly Schiff base derived from 5-bromo-2-hydroxybenzylidene-3,4,5-trihydroxybenzohydrazide. *Bull. Chem. Soc. Ethiop.* 26 (1), 95–101.
- Ali, M.F., Abbas, S., 2006. A review of methods for the demetallization of residual fuel oils. *Fuel Process. Technol.* 87 (7), 573–584.
- Al-Najjar, N., 2009. Preparation and identification of some PVA-metal complexes. *Iraqi J. Sci.* 50 (3), 271–278.
- Arora, S., Vijay, S., Kumar, D., 2011. Phytochemical and antimicrobial studies on the leaves of *Spilanthes acmella*. *J. Chem. Pharm. Res.* 3 (5), 145–150.
- Chohan, Z., Munawar, A., Supuran, C., 2001. Transition metal ion complexes of Schiff-base. Synthesis, characterization and antibacterial properties. *Met. Based Drugs* 8, 137–143.
- Dehmel, F., Ciossek, T., Maier, T., Weinbrenner, S., Schmidt, B., Zoche, M., Beckers, T., 2007. Trithiocarbonates: exploration of a new head group for HDAC inhibitors. *Bioorg. Med. Chem. Lett.* 17 (17), 4746–4752.
- Foroumadi, A., Pournourmohammadi, S., Soltani, F., Asgharian-Rezaee, M., Dabiri, S., Kharazmi, A., Shafiee, A., 2005. Synthesis and in vitro leishmanicidal activity of 2-(5-nitro-2-furyl) and 2-(5-nitro-2-thienyl)-5-substituted-1,3,4-thiadiazoles. *Bioorg. Med. Chem. Lett.* 15 (8), 1983–1985.
- Greenwood, N.N., Earnshaw, A., 1998. *Chemistry of Elements*, 2nd ed. Pergamon Press.
- Iqbal, J., Tirmizi, S.A., Wattoo, F.H., Imran, M., 2006. Biological properties of chloro-salicylidene aniline and its complexes with Co(II) and Cu(II). *Turk. J. Biol.* 30, 1–4.
- ukaszuk, C., Krajewska-Kuak, E., Niewiadomy, A., Stachowicz, J., Gaszcz, U., Oksiejczuk, E., 2007. In vitro antifungal activity of 2,5-disubstituted amino-oksometyloso-arylo-thiadiazole derivatives. *J. Adv. Med. Sci.* 52 (1), 26–29.
- Malik, S., Ghosh, S., Mitu, L., 2011. Complexes of some 3d-metals with a Schiff base derived from 5-acetamido-1,3,4-thiadiazole-2-sulphonamide and their biological activity. *J. Serb. Chem. Soc.* 76 (10), 1387–1394.
- March, J., Smith, M.B., 2007. *Advanced Organic Chemistry*, 6th Ed. John Wiley & Sons, Hoboken, New Jersey.
- Mitu, L., Iliş, M., Raman, N., Imran, M., Ravichandran, S., 2012. Transition metal complexes of isonicotinoyl-hydrazone-4-diphenylaminobenzaldehyde: synthesis, characterization and antimicrobial studies. *E. J. Chem.* 9 (1), 365–372.
- Nakamoto, N., 2009. *Infrared and Raman Spectra of Inorganic and Coordination Compounds*. 6th Ed. Springer, Berlin.
- Pastorek, R., Kamenicek, J., Husarek, J., Sindelar, Z., 2001. Nickel (II) dithiocarbamates with 1,4,8,11-tetraazacyclotetradecane in the coordination sphere. *J. Chem.* 40, 57–63.
- Raman, N., Raja, S., Joseph, J., Raja, J., 2007. Synthesis, spectral characterization and DNA cleavage study of heterocyclic Schiff base metal complexes. *J. Chil. Chem. Soc.* 52 (2), 1138–1141.
- Rathore, K., Rajiv, K.R., Singh, H.B., 2010. Structural, spectroscopic and biological aspects of O, N-donor Schiff base ligand and its Cr(III), Co(II), Ni(II) and Cu(II) complexes synthesized through green chemical approach. *Eur. J. Chem.*, S566–S572, 7(S1).
- Siddiqi, K.S., Nami, S.A., Lutfullaha, Chebude, Y., 2006. Template synthesis of symmetrical transition metals dithiocarbamates. *J. Braz. Chem. Soc.* 17 (1), 107–112.
- Singh, V.P., Katiyar, A., Singh, S., 2008. Synthesis, characterization of some transition metal(II) complexes of acetone p-amino acetophenone salicyloyl hydrazone and their anti microbial activity. *Biometals* 21 (4), 491–501.

- Soleimani, E., 2010. Synthesis and characterization of a novel benziloxime ligand and its iron(III) and nickel(II) complexes. *J. Chin. Chem. Soc.* 57 (3A), 332–337.
- Solomon, E.I., Lever, A.B.P., 2006. In: *Inorganic Electronic Structure and Spectroscopy: Applications and Case Studies*, vol. II. John Wiley and Sons, Inc, New York, Chester, Singapore, Toronto.
- Srivastava, A., Singh, S.K., Gupta, A., 1990. Determination of organotrithiocarbonates with O-diacetoxyiodobenzoate and N-chlorosuccinimide in aqueous and non-aqueous media. *Analyst* 115 (4), 421–423.
- Vicente, J., Chicote, M.T., González-Herrero, P., Jones, P.G., 1995. Synthesis of the first trithiocarbonatogold complex: $[\text{N}(\text{PPh}_3)_2]_2[\text{Au}_2(\mu^2-\eta^2-\text{CS}_3)_2]$. First crystal structure of a $\mu^2-\eta^2$ -bridging trithiocarbonato complex. *J. Chem. Soc Chem. Commun.* 7, 745–746.
- Vicente, J., Chicote, M.T., González-Herrero, P., Jones, P.G., 1997. Complexes with S-donor ligands. Synthesis of the first family of (trithiocarbonato) gold complexes. Crystal structure of $[(\text{PPh}_3)_2\text{N}][\text{AuCl}_2(\text{CS}_3)]$. *J. Inorg. Chem.* 36 (25), 5735–5739.