UNIVERSITY OF BUCHAREST
FACULTY OF CHEMISTRY
DOCTORAL SCHOOL OF CHEMISTRY

DOCTORAL THESIS SUMMARY

COPPER (II), NICKEL (II) AND PALLADIUM (II) COMPLEXES WITH LIGANDS DERIVED FROM 4-PHENYLTHIOSEMICARBAZIDE AND THIOCARBOHYDRAZIDE

Ph.D. student:

Diana-Carolina ILIEȘ

Ph.D. adviser:

Prof. Dr. Tudor ROȘU

2015

CONTENTS[1]

PART I

Characterization of Cu(II), Ni(II) and Pd(II) complexes with thiosemicarbazone and thiocarbohydrazone type ligands

- literature data-

---

[1] Numbering of tables, figures and bibliographical references is the one from the doctoral thesis.

PART II

Characterization and properties of Cu(II), Ni(II) and Pd(II) complexes with ligands derived from 4-phenylthiosemicarbazide and thiocarbohydrazide

- original contributions -

Intoduction

The present thesis entitled "***Copper (II), nickel (II) and palladium (II) complexes with ligands derived from 4-phenylthiosemicarbazide and thiocarbohydrazide***" aims to bring original contributions to the field of divalent transition metal ions complexes with ligands having *NS*, *NSO*, *NNS* or *NNNS* donor atoms.

This paper is divided into two parts; relevant literature data (**Chapters 1** and **2**) followed by the original contributions (**Chapters 3** and **4**), conclusions (**Chapter 5**) and supplementary data (**Annexes**).

In **Chapter 1** ***"Cu(II), Ni(II) and Pd(II) complexes with thiosemicarbazone"*** are discussed structural aspects of the thiosemicarbazone ligands focusing on the coordinating possibilities at different metal ions. Also, this chapter describes the characterization of Cu(II), Ni(II) and Pd(II) complexes with thiosemicarbazone based on the metal ion stereochemistry and nuclearity of the complexes. Important aspects sought in this chapter refers to the ligand coordination mode, the conformation of the free and coordinated ligand, the metal ion geometry, the presence of the metal salt anion or a co-ligand in the coordination sphere, and the substituents nature on the carbon atom C^2 and nitrogen atom N^1.

Thiosemicarbazones and metal complexes show a considerable interest for the fields chemistry and biology. The structural characteristics of these compounds have enabled them to be used in a large number of analytical applications. The thiosemicarbazones ligands are used for metal ions analysis, for manufacturing colorimetric chemosensors for anions, in devices intended for communications, processing of optical calculations, storage and processing of information. The interest in thiosemicarbazones and metal complexes is revealed by the great variety of biological properties exhibited by these compounds, such as antibacterial activity, antifungal, antimicrobial, antioxidant, antituberculostatică, anti-HIV and anti-tumor [1-3].

Thiosemicarbazones are Schiff bases obtained by condensation reaction of an aldehyde or ketone with a thiosemicarbazide. They are classified as mono-thiosemicarbazones (Fig. 1.1), and bis-thiosemicarbazones. The basic skeleton of a mono-thiosemicarbazone has different R^1-R^4 substituents and, depending on their nature, are obtained various sub-classes of ligands.

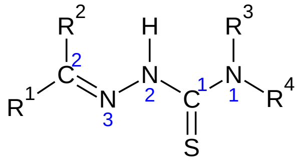


Figure 1.1. The general formula of mono-thiosemicarbazones, R^1, R^2, R^3, R^4 = H or organic radical.

Thiosemicarbazones, obtained from aldehydes, present as substituents on the C^2 carbon atom a hydrogen atom, and the second substituent may be an alkyl or aryl radical or a heterocycle. Similarly, the substituents on the N^1 nitrogen atom may be the same or different, hydrogen, alkyl or aryl radicals. Also, the N^1 nitrogen atom can be included in a heterocyclic ring [1]. If the condensation is carried out starting from a ketone, both substituents at the C^2 carbon atom may be the same or different alkyl or aryl radicals. Like the N^1 nitrogen atom and the C^2 carbon atom can be part of a ring.

Thiosemicarbazones may exist in two tautomeric forms and the thiol-thione tautomerism is manifested in solution (Fig. 1.5). The thiol form is generated by the shift of the hydrogen atom from the group -N^2H to the sulfur atom and following its loss from the -SH group the anionic form of the thiosemicarbazone is obtained. The thiosemicarbazones can coordinate to the metal centre in either a neutral or anionic form.

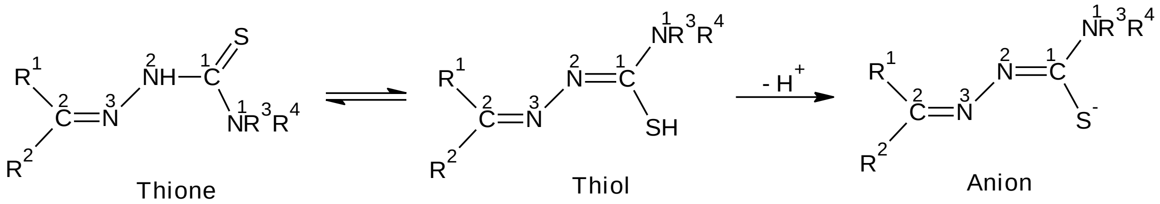


Figure 1.5. The thiol-thione tautomerism of thiosemicarbazones.

(i) Coordination modes of thiosemicarbazones in neutral form

In neutral form, the binding occurs via only S atom in η^1 – S (A); μ_2 – S (B); η^2 – N^3, S – chelation (C); η^3 – N^3, S – chelation and S – bridging (D) (Fig. 1.6). However, if the substituent at C^2 has a donor atom, and engages in bonding, the additional binding modes observed are η^3 – X, N^3, S – chelation (E); η^4 – X, N^3, S – chelation and S – bridging (F), η^4 – X; N^3, S – chelation and X – bridging (G) (X= O, N) [1,4-10] (Fig. 1.6).

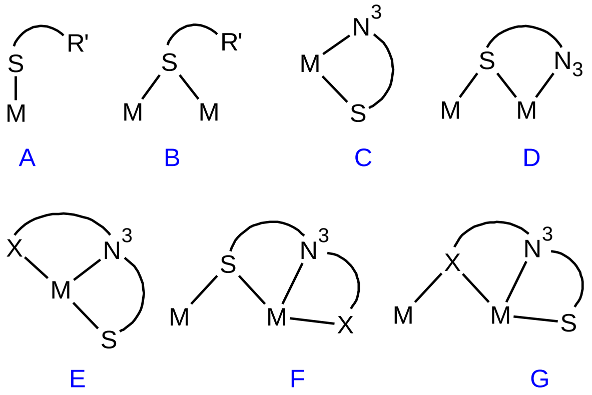


Figure 1.6. Coordination modes of thiosemicarbazones in neutral form [1].

(ii) Coordination modes of thiosemicarbazones in anionic form

The modes A – G shown by the neutral ligands are also exhibited by the anionic ligands [1,11,12]. In addition, η^2 – N^2, S (H) and N^2, S – bridging and S – bridging modes (I) (Fig. 1.7) are identified [13,14]. A rare example of pentacoordination (J, Fig. 1.7) by a thiosemicarbazone ligand has also been reported by Pal [15].

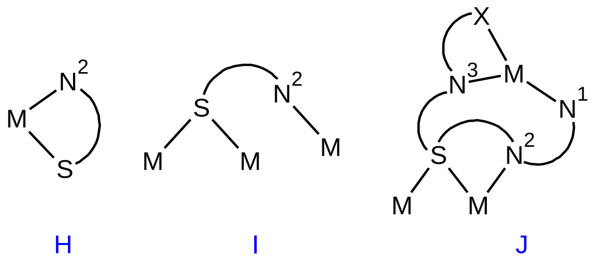


Figure 1.7. Coordination modes of thiosemicarbazones in anionic form [1].

Also, in the literature, it is stated that thiosemicarbazones assume *E* or *Z* form (Fig. 1.8). Thus, in neutral, they coordinate to the metal ion via sulfur donor atom by adopting the *E* form, in the case of deprotonation of the hydrazine group NH, thiosemicarbazones coordinate through the nitrogen and sulfur atoms, adopting the Z form [1,5,10,14,16 17].

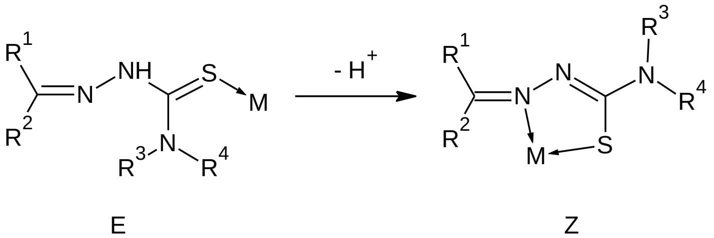


Figure 1.8. *E* and *Z* forms of thiosemicarbazones, R^1, R^2, R^3, R^4 = H or organic radical.

Due to the their excellent ability of complexing, thiosemicarbazones react with a large number of transition metal ions, and p block elements, forming complexes which have various physical and chemical properties, and therefore, applications.

Highly studied, copper is the most important metal ion for the complexation reactions with thiosemicarbazones. In terms of biological storage and transport, in order of decreasing abundance in living organisms, copper ranks third after iron and zinc [45]. Along with iron, copper participates in many biological reactions. For example, the copper in the enzyme cytochrome c oxidase catalyzes the four-electron transfer to molecular oxygen to form water during respiration.

The interest in Cu(II), Ni(II) and Pd(II) complexes with thiosemicarbazones are due to the structural features of these compounds, and their properties. The Cu(II) ion forms, in general, mononuclear, dinuclear, tetranuclear, hexanuclear, and polymeric complexes. Ni(II) and Pd(II) ions form mononuclear, dinuclear and trinuclear complexes. In addition, the Pd(II) ion forms tetranuclear complexes. For the copper complexes with thiosemicarbazones, the coordination number ranges from three to six, and among geometries encountered are distorted plan-trigonal, tetrahedral, square-planar, and octahedral. Geometries encountered for the nickel complexes are square-planar and octahedral, and for the palladium complexes is a square-planar geometry.

Chapter 2 *"**Cu(II) complexes with thiocarbohydrazones**"* presents structural characteristics of Cu(II) complexes with thiocarbohydrazone.

Thiocarbohydrazones are condensation products of thiocarbohydrazide with various carbonyl compounds. Because of the symmetry of the molecule, both hydrazine groups are highly reactive. The condensation reactions involving thiocarbohydrazide occupy an important place due to various classes of compounds that can be obtained: thiocarbohydrazones, thiosemicarbazides, pyrazoles, thiazoles, thiadiazines, thiazolidines, thiadiazoles, triazines etc. [2]. Thiocarbohydrazone are studied because they have a broad spectrum of chemical and biological properties, and applications in various fields.

Regarding the biological properties of thiocarbohydrazone, these compounds exhibited anti-tumor activity, which has been highlighted since 1956 [4], antituberculostatic, antibacterial, antihelmintic [3] and antiviral activity [5].

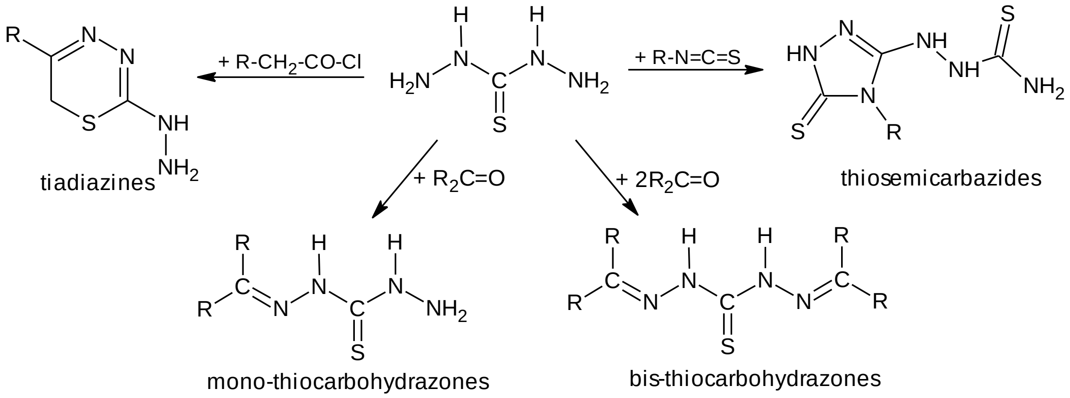


Figure 2.2. Examples of classes of compounds obtained from thiocarbohydrazide [3].

Thiocarbohydrazones are Schiff bases obtained by condensation reaction of tiocarbohydrazide with a carbonyl compound. Thiocarbohydrazide reacts easily in a molar ratio of 1: 2 with an aldehyde or a ketone to form 1,5-bisthiocarbohydrazones [1] (Fig. 2.3, a). At a molar ratio of 1: 1 are obtained mono-thiocarbohydrazones [1] (Fig. 2.3, b).

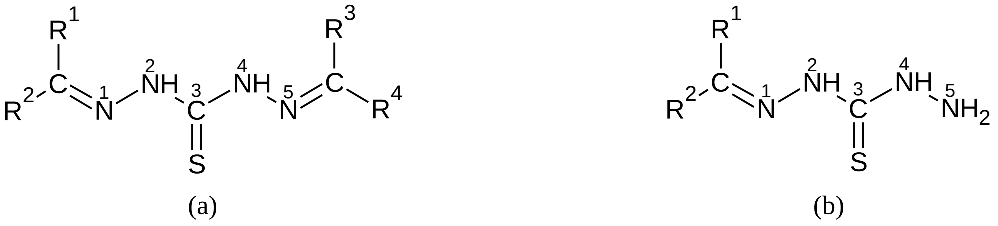


Figure 2.3. The general formulas for (a) bis- and (b) mono-thiocarbohydrazones, R^1, R^2, R^3, R^4 = H or organic radical.

Similar to thiosemicarbazones, thiocarbohydrazones may exist in two tautomeric forms, thio-enol and thio-ketone tautomers, manifested especially in solution (Fig. 2.4). The thio-enol form is generated by the shift of the hydrogen atom from one of the two NH groups to the sulfur atom, and the loss from the group -SH leads to the anionic form of the thiocarbohydrazone.

The thiocarbohydrazones can coordinate to the metal center in either a neutral or anionic form.

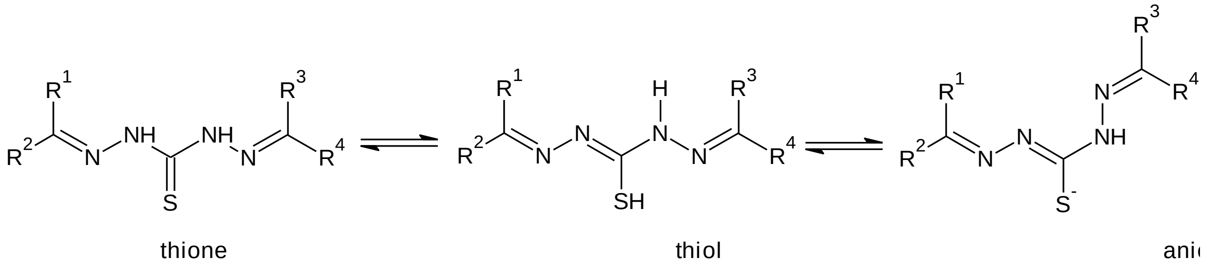
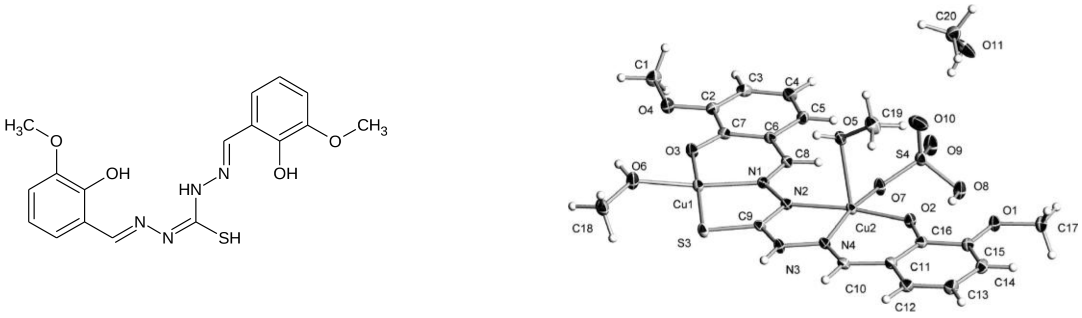


Figure 2.4. The thiol-thione tautomerism of thiocarbohydrazones, R^1, R^2, R^3, R^4 = H or organic radical.

Like any other compounds possessing sulfur and nitrogen donor atoms, thiocarbohydrazones can coordinate through these atoms, allowing the formation of complexes with different geometries from tetrahedral to octahedral or square-planar, thus presenting various structural particularities [6-8]. Due to the large number of nitrogen atoms in the structure of thiocarbohydrazones, complexes with one and two metal centers can be obtained, and depending on the nature of the thiocarbohydrazones substituents these ligands can coordinate in a mono-, bi-, or trideprotonated or in neutral form.

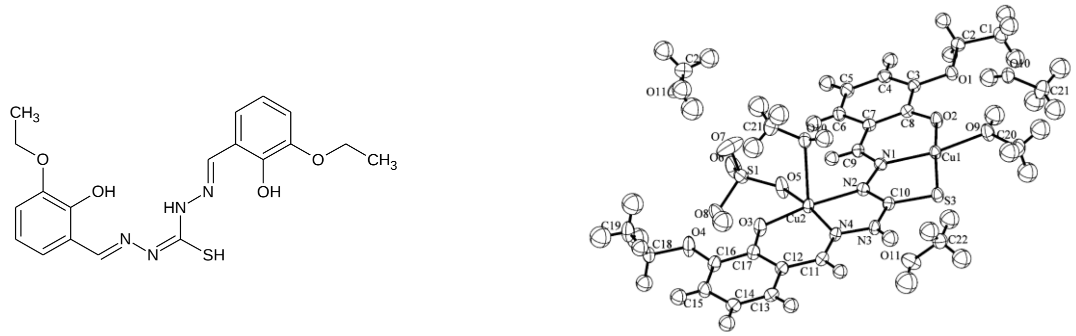
Two dinuclear complexes $[Cu_2(HL^{Me,Et})(HSO_4)(CH_3OH)_2] \cdot CH_3OH$ ($HL^{Me,Et}$ = bis(3-methoxysalicylaldehyde)thiocarbohydrazone, bis(3-ethoxysalicylaldehyde) thiocarbohydrazone) were obtained from the reaction of the ligand with copper sulphate (II) in a molar ratio of 1: 2 [29]. The HL^{Me} (Fig. 2.13) and HL^{Et} (Fig. 2.14) ligands coordinate in a deprotonated manner to the copper ion, both ligands providing two tridentate sites, one *NNO* and one *ONS*.



HL^{Me} $[Cu_2(HL^{Me})(HSO_4)(CH_3OH)_2] \cdot CH_3OH$

Figure 2.13. Structure of complex $[Cu_2(HL^{Me})(HSO_4)(CH_3OH)_2] \cdot CH_3OH$ [29].

The two hexadentate thiocarbohydrazones coordinate each to two copper ions to form dinuclear units of type $[Cu_2L]^+$. An interesting feature of the two complexes is that the copper (II) ions of the dimer show different geometries. Cu1 has a square-planar geometry made by the phenolic oxygen, azomethine nitrogen, hydroxyl oxygen, and sulfur atoms. The second metal center has a square pyramidal geometry in which the apical position is occupied by the oxygen atom from methanol. The basal plane is achieved by the imine nitrogen, phenolic oxygen, azomethine nitrogen, and sulphate oxygen atoms. Another unusual feature of these two complexes is the presence of the sulphate ion coordinated to the metal ion as a protonated ligand HSO4$^-$, the proton is stabilized by hydrogen bonding with oxygen atoms and methoxy groups derived from phenol [29].



HL^{Et} $[Cu_2(HL^{Et})(HSO_4)(CH_3OH)_2] \cdot CH_3OH$

Figure 2.14. Structure of $[Cu_2(HL^{Et})(HSO_4)(CH_3OH)_2] \cdot CH_3OH$ [29].

PART II - Original contributions

Chapter 3

Cu(II), Ni(II) and Pd(II) complexes with thiosemicarbazone derived from 4-phenylthiosemicarbazide

Chapter 3 describes the Cu(II), Ni(II) and Pd(II) complexes obtained with thiosemicarbazone ligands derived from 4-phenylthiosemicarbazide. By condensing, in a molar ratio of 1: 1, 4-phenylthiosemicarbazide with various aldehydes, six ligands were synthesized: 2-furaldehyde-*N*(4)-phenylthiosemicarbazone (**HL^1**), 5-methyl-2-furaldehyde-*N*(4)-phenylthiosemicarbazone (**HL^2**), 2-formylpyridine-*N*(4)-phenylthiosemicarbazone (**HL^3**), 4-formylpyridine-*N*(4)-phenylthiosemicarbazone (**HL^4**), 3-formyl-6-methylchromone-*N*(4)-phenylthiosemicarbazone (**HL^5**), 9-ethyl-9*H*-carbazol-3-carboxaldehyde-*N*(4)-phenylthiosemicarbazone (**HL^6**), and complexes with transition metal ions: Cu^{2+}, Ni^{2+}, Pd^{2+}.

The characterisation of the ligands was carried out by elemental analysis, FT-IR, UV-Vis, and ^{1}H-NMR, ^{13}C-NMR. The molecular structures of the ligands **HL^1**, **HL^2**, **HL^3**, **HL^4** and **HL^6**, were determined by X-ray diffraction. In order to characterize the metal complexes conventional and modern methods have been used. The electron paramagnetic resonance spectroscopy (EPR) was used to characterize the compounds in solid and solution state. The thermal analysis was used to determine the number and nature of the water molecules and the X-ray diffraction to establish the geometry of the metal complexes.

With the ligand **HL^1** six Cu(II) complexes, one Ni(II) complex, and one Pd(II) complex were synthesized. The analytical data indicated the following molecular formulas: **$[Cu(L^1)_2(H_2O)_2]$** (**1**), **$[Cu(L^1)(OAc)(H_2O)_2]$** (**2**), **$[Cu(L^1)_2]$** (3), **$[Cu_2(L^1)_2(Et_3N)_2(H_2O)_4]SO_4$** (**4**), **$[Cu_2(L^1)_2(Et_3N)_2(H_2O)_4](NO_3)_2$** (5), **$[Cu(L^1)(ClO_4)(H_2O)_2]$** (**6**), **$[Ni(L^1)_2]$** (7), **$[Pd(L^1)_2]$** (**8**). These complexes exhibit a square-planar (**3**, **7**, **8**) and an octahedral geometry (**1**, **2**, **4**, **5**, **6**). Complexes (**1**) - (**3**), (**6**) - (**8**) are mononuclear, and the dinuclear nature of complexes (**4**) and (**5**) was established by EPR. The ligand **HL^1** coordinates bidentate through the azomethine nitrogen and the sulfur atom.

For complexes (**4**) and (**5**), the EPR spectra recorded on powder at 298 K and 77 K (Fig. 3.20), on an extended magnetic field, show signals at the magnetic field value ~ 1600 G that indicate the existence of copper dimers. At 77 K, a change in the form of the EPR spectrum for complex (**4**) was observed. The spectral parameters are $g_{//} = 2.132$, $g_{\perp} = 2.036$ at 298 K and $g_{//} = 2.120$, $g_{\perp} = 2.010$ at 77 K; The equation $g_{//} > g_{\perp} > 2.0023$ indicates that the fundamental state is described by the $d_{x^2-y^2}$ orbital [33].

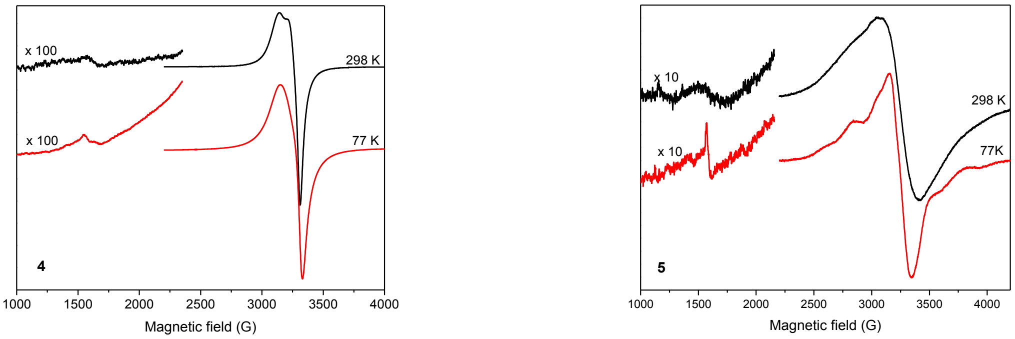


Figure 3.20. EPR spectra for complexes (**4**) and (**5**), recorded on powder at 298 K and 77 K.

Also, the shape of the EPR spectrum of the complex (**5**) has changed by cooling at 77 K. The signal narrowed from ~ 360 G at 298 K to 190 G at 77 K when it was observed the presence of inflections separated from each other by more than 200 G, which cannot be considered components of the hyperfine structure, but rather an overlap of signals for dinuclears with mononuclears. If the coupling of the two centers of copper (II) from the dimer is antiferromagnetic, the difference between the two signals is the EPR signal of the dimer (Fig. 3.21, DIF) [34], whose intensity decreased with the decrease of the temperature. This signal can be considered to be due to the fine structure transitions ($\Delta M_s = \pm 1$) between the levels of the triplet (S = 1) associated with the Cu^{2+} ion pairs and is characterized by the spectral parameters: $D_{//}$ = 1056 G, $g_{//}$ = 2.058, $D_{\perp}$ = 280 G, $g_{\perp}$ = 2.056. The fact that no hyperfine splitting structure associated with the two metal centers is observed could be due to intermolecular dipolar interactions, which can cause enlargement of the lines, the sample having high concentration of paramagnetic centers. From the spectral parameters of this signal is possible to estimate the distance between the two copper (II) atoms of the dimer using the expression $R\,[\text{Å}] = (0.650 \cdot g_{\perp}^2 / D_{\perp}\,[\text{cm}^{-1}])^{1/3}$ [34]. This distance has a value of 4.7 Å.

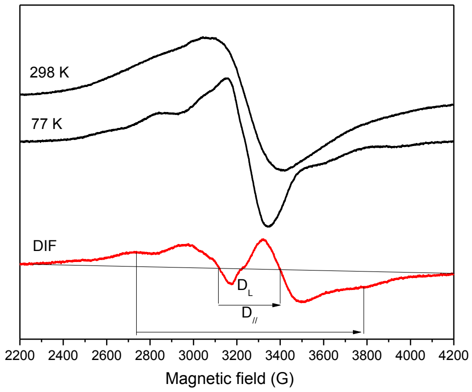


Figure 3.21. EPR spectrum of complex (**5**), recorded on powder at 298 K, 77 K and the difference (DIF).

Complexes (**3**), (**7**) and (**8**) are molecular species of Cu(II), Ni(II) or Pd(II) ions whose square-planar geometry was established by X-ray diffraction. The equatorial plane is defined by the *NS* donor atoms of two ligand molecules. Complex (7) in *cis*-form was obtained using $NiF_2 \cdot 4H_2O$, while the *trans*-form, as described in the literature, was obtained from $Ni(OAc)_2 \cdot 4H_2O$.

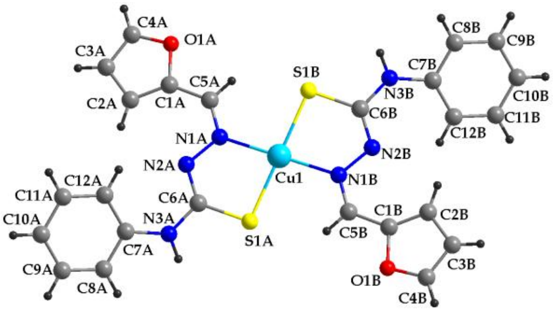


Figure 3.34. The molecular structure of the complex **$[Cu(L^1)_2]$** (**3**).

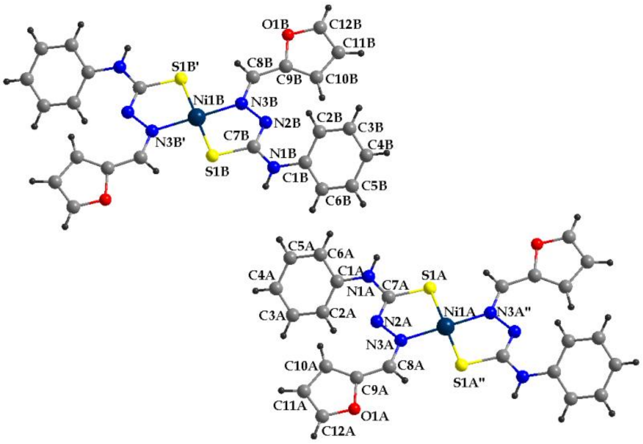


Figure 3.36. The asymmetric unit for the complex **$[Ni(L^1)_2]$** (**7**).

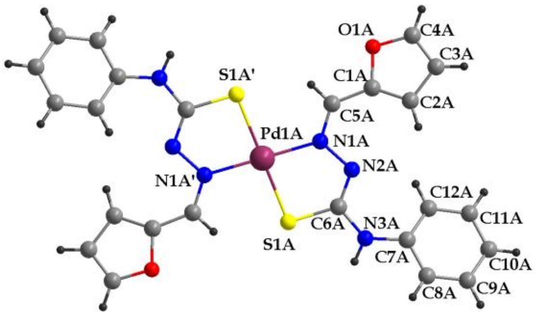


Figure 3.39. The molecular structure of the complex **$[Pd(L^1)_2]$** (**8**).

At supramolecular level, differences between these complexes consist in the types of interactions. The molecular packaging of complex (**3**) is influenced by C–H···Y (Y=N or S) intramolecular hydrogen bonds, π – π stacking interactions between the furan and the phenyl rings, CH–π and π–Cu supramolecular interactions [15].

In the crystal, the molecules of type A and B of complex (**7**) are associated in infinite chains along the crystallographic axis *a*. The chains are achieved through N1B–H···S1A' intermolecular hydrogen bonds. The other NH group of the complex is not involved in the formation of hydrogen bonds, the intermolecular separation between the atoms N1A' and S1B is 4.21 Å.

The molecular packaging of complex **$[Pd(L^1)_2]$** (**8**) is influenced by C–H···O intermolecular hydrogen bonds with the formation of 1D chains. The π – π stacking interactions between the furan rings, at a distance of 4.019 Å lead to a 3D supramolecular network.

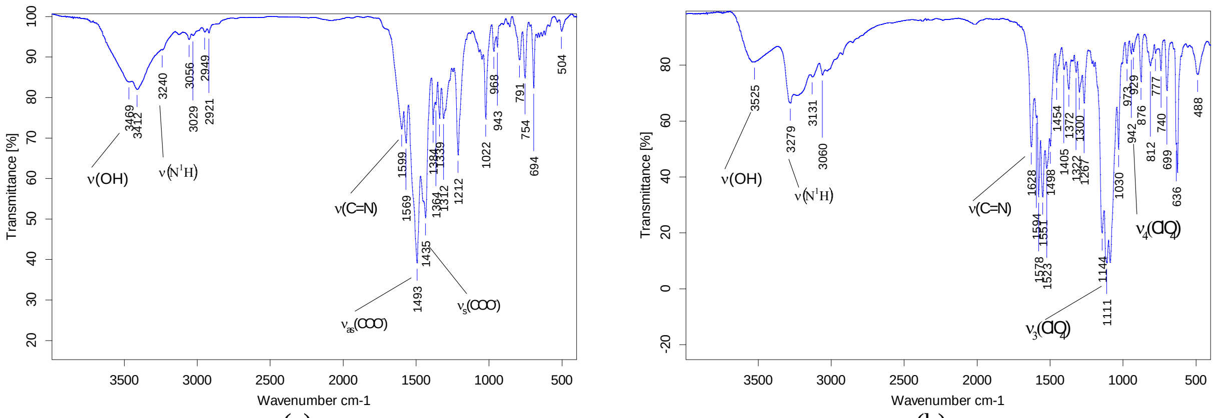
The ligand **HL^1** and the complexes (**3**), (**7**) și (**8**) were tested in terms of antioxidant activity and showed an increasing inhibitory effect with the metal ion nature in the sequence: $Pd^{2+} < Ni^{2+} < Cu^{2+}$.

Table 3.13. The antioxidant activity of **HL^1** and complexes (**3**), (**7**), (**8**) assessed by the DPPH method.

Compound	**Antioxidant activity (%)**						**IC$_{50}$ (µM)**
	Concentration (µM)						
	25	**50**	**75**	**100**	**125**	**250**	
HL^1	3,69 ± 0,85	8,22 ± 0,78	10,54 ± 0,21	12,87 ± 0,56	14,61 ± 0,40	22,98 ± 0,81	> 250
(3)	31,99 ± 1,00	50,31 ± 1,96	62,29 ± 1,10	62,89 ± 1,70	63,14 ± 0,18	66,86 ± 0,96	49,63
(7)	20,23 ± 0,10	20,62 ± 0,70	21,90 ± 0,76	22,95 ± 0,13	23,59 ± 0,77	25,63 ± 0,12	> 250
(8)	0,14 ± 1,05	4,71 ± 1,65	10,75 ± 1,55	12,58 ± 0,81	14,45 ± 1,04	20,61 ± 0,65	> 250
BHA	41,58 ± 0,59	63,81 ± 1,42	80,15 ± 0,89	85,12 ± 0,71	89,02 ± 1,22	91,97 ± 0,63	34,49
BHT	9,57 ± 1,39	11,48 ± 1,05	16,22 ± 1,09	18,30 ± 0,90	24,38 ± 0,46	47,86 ± 0,34	>250

With **HL^2** ligand six Cu(II) complexes and one Ni(II) complex were synthesized: **$[Cu(HL^2)(Cl)_2(H_2O)_2] \cdot H_2O$** (**9**), **$[Cu(HL^2)(Br)_2(H_2O)_2]$** (**10**), **$[Cu(L^2)(OAc)(H_2O)_2]$** (**11**), **$[Cu(HL^2)(SO_4)(H_2O)_2]$** (**12**), **$[Cu(L^2)_2(H_2O)_2]$** (**13**), **$[Cu(L^2)(ClO_4)(H_2O)_2]$** (**14**), **$[Ni(L^2)_2] \cdot 2CH_3CN$** (**15**). Complexes (**9**) - (**14**) exhibit an octahedral geometry, and the square-planar geometry of the complex (**15**) was determined by XRD. **HL^2** coordinates in the same manner as ligand **HL^1**.

The IR spectrum of the complex (**11**) exhibits two intense absorption bands at 1493 and 1435 cm^{-1}, which were attributed to $\nu_{as}(COO^-)$ and $\nu_s(COO^-)$ vibrations (Fig. 3.42). The difference between the two frequencies $\Delta = [\nu_{as}(COO^-) - \nu_s(COO^-)]$ is 58 cm^{-1} and indicates the bidentate coordination mode of the acetate ion [18,21,24]. The presence in the IR spectrum of the complex (**12**) of one absorption band splitted into three at 1182, 1158 and 1115 cm^{-1} suggests the presence of SO_4^{2-} anion coordinated bidentate to the metal center [16]. Also, the presence of an absorption bands splitted into three at 1144, 1111 and 1089 cm^{-1} and an absorption band at 942 cm^{-1} indicates for complex (**14**) the bidentate coordination mode of the perchlorate ion [21].



(a) (b)

Figure 3.42. IR spectra of complexes (a) (**11**), (b) (**14**).

The thermograms indicate the presence of two molecule of coordinated water for complexes (**9**) - (**13**), lost in the temperature range 110 - 180°C [30].

The square-planar geometry of the Ni^{2+} ion is provided by the *NS* donor atoms of two molecules of ligand. The C7–S1 bond length is 1.744 (3) Å, value specific to a simple C–S bonds, which indicates the presence of the thiosemicarbazone in its thiol form. The complex (**15**) crystallizes with two molecules of CH_3CN which allows the formation of intramolecular N1–H1···N4 hydrogen bonds. The Ni1–S1 and Ni1–N3 bond lengths are 2.1698(7) Å and 1.923(2) Å, respectively. These values are close to those obtained for complex (**7**) synthesized with ligand **HL^1**. The values of the angles S1—Ni1—N3^i and N3—Ni1—S1^i (94.93(6)°), N3—Ni1—S1 and N3^i—Ni1—S1^i (85.07(6)°), N3—Ni1—N3^i and S1—Ni1—S1^i (180°) indicate a square-planar geometry of the nickel complex.

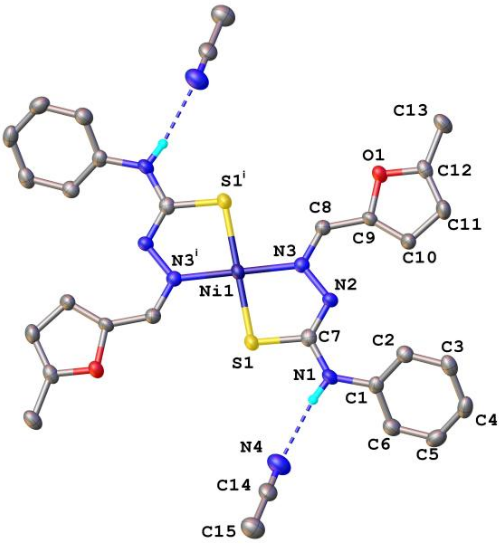


Figure 3.62. The molecular structure of complex **$[Ni(L^2)_2]\cdot 2CH_3CN$** (**15**).
The hydrogen atoms were omitted. Hydrogen bonds parameters: N1–H1···N4
[N1–H1 0.86 Å, H1···N4 2.22 Å, N1···N4 3.071(3) Å, N1–H1···N4 170.2°].

EPR studies carried out on DMSO solutions at 289 K show the influence, on the metal center geometry, of the anions metal salt nature, depending on their volume.

The **HL^2** ligand and complexes (**9**) - (**14**) were tested in terms of antimicrobial activity. The complexes (**10**) - (**12**) showed a low inhibitory effect against *Staphylococcus aureus*, *Enterococcus faecalis*, *Eescherichia coli*, *Salmonella enteritidis* and *Candida albicans strains*.

Table 3.19. MIC (μg/mL) and MBC (μg/mL) values for **HL^2** and complexes (**9**) - (**14**).

Compound	*S. aureus*		*E. faecalis*		*E. coli*		*S. Enteritidis*		*C. albicans*	
	MIC (μg/mL)	MBC (μg/mL)	MIC (μg/mL)	MBC (μg/mL)	MIC (μg/mL)	MBC (μg/mL)	MIC (μg/mL)	MBC (μg/mL)	MIC (μg/mL)	MBC (μg/mL)
HL^2	**512**	**512**	**512**	**512**	**512**	**512**	**512**	**512**	**512**	**512**
(9)	>1024	>1024	>1024	>1024	>1024	>1024	>1024	>1024	>1024	>1024
(10)	**512**	>1024	**512**	>1024	>1024	>1024	>1024	>1024	>1024	>1024
(11)	**512**	**512**	**512**	**512**	>1024	>1024	**512**	**512**	**512**	**512**
(12)	**512**	>1024	**512**	>1024	**512**	>1024	**512**	>1024	**512**	>1024
(13)	>1024	>1024	>1024	>1024	>1024	>1024	>1024	>1024	>1024	>1024
(14)	>1024	>1024	>1024	>1024	>1024	>1024	>1024	>1024	>1024	>1024
$CuCl_2 \cdot 2H_2O$	512	-	512	-	1024	-	512	-	-	-
$CuBr_2$	512	-	512	-	512	-	1024	-	-	-
$CuSO_4 \cdot 5H_2O$	512	-	512	-	512	-	1024	-	1024	-
$Cu(ClO_4)_2 \cdot 6H_2O$	1024	-	512	-	1024	-	1024	-	-	-
$Cu(NO_3)_2 \cdot 2H_2O$	1024	-	1024	-	1024	-	1024	-	-	-
$Cu(OAc)_2 \cdot H_2O$	1024	-	512	-	512	-	1024	-	-	-
Streptomycin	4	8	8	16	8	16	8	16	-	-
Fluconazole	-	-	-	-	-	-	-	-	2	8

In order to increase the number of potential donor atoms and for structural diversity was synthesized the **HL^3** ligand. With this ligand six copper (II) complexes and one nickel (II) complex were synthesized: **$[Cu(L^3)(Cl)]$** (**16**), **$[Cu(L^3)(Br)(H_2O)_2]$** (**17**), **$[Cu(L^3)(OAc)(H_2O)_2]$** (18), **$[Cu(HL^3)(H_2O)]SO_4$** (19), **$[Cu(L^3)(NO_3)(H_2O)_2]$** (**20**), **$[Cu(L^3)(ClO_4)(H_2O)_2]$** (21), **$[Ni(HL^3)_2]Cl_2 \cdot 2.5\ H_2O$** (22).

The complexes (**16**) and (**19**) have a square-planar geometry, and the complexes (**17**) - (**21**), (**22**) have an octahedral stereochemistry of the metal center. The **HL^3** ligand derived from 2-formylpyridine coordinates in a tridentate manner through the *NNS* donor atoms in anionic form in complexes (**16**) - (**21**), and in neutral form in complexes (**19**) and (**22**). The ligand crystallized as hydrochloride ($HL^3 \cdot HCl$), and the three N–H···Cl hydrogen bonds lead to the formation of "zig-zag" polymer chains oriented along the crystallographic axis *c*.

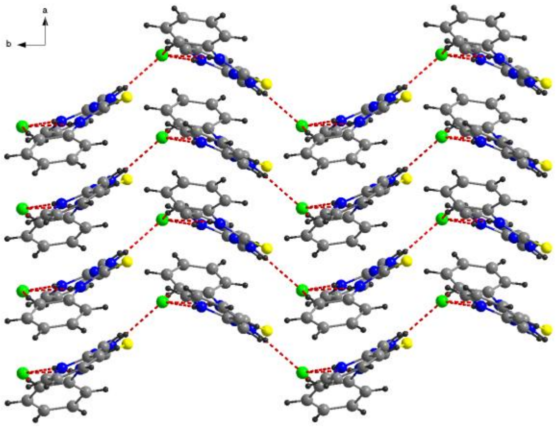


Figure 3.69. The "zig-zag" polymer chains oriented along the crystallographic axis *c*.

The mononuclear nature of the complexes is suggested by the EPR spectra, and the values of spectral parameters, $g_1 = 2.121$, $g_2 = 2.081$, $g_3 = 2.039$ for the complex (**16**) and $g_1 = 2.122$, $g_2 = 2.083$, $g_3 = 2.040$ for the complex (**19**) indicates a rhombic symmetry of the metal center, the square-planar geometry of complex (**16**) was confirmed by XRD.

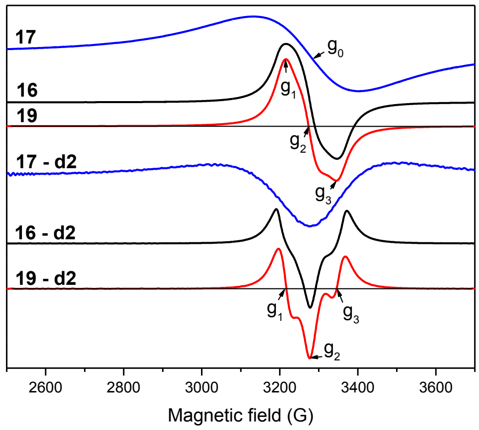


Figure 3.80. EPR spectra for complexes (**16**), (**17**) and (**19**), recorded on powder at 298 K and derived signals (d2).

The coordination sphere of the Cu^{2+} ion for complex (**16**) is formed by one molecule of tridentate ligand which coordinates monodeprotonated through the azomethine and the pyridine nitrogen atoms, the thiol sulfur atom and a chlorine atom. Two molecules of complex (**16**) are associated in a dimeric unit through an N–H···Cl hydrogen bond.

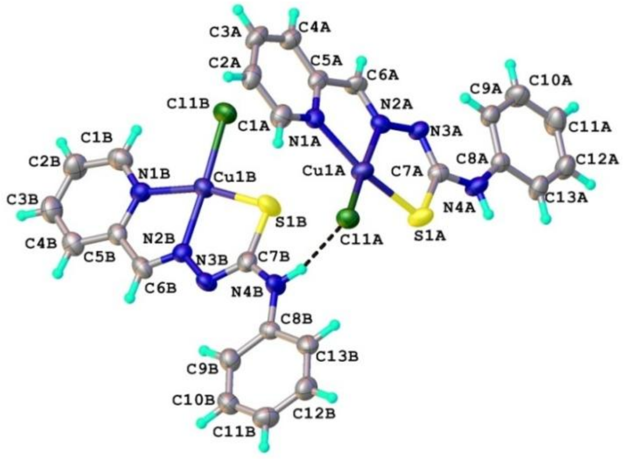


Figure 3.85. Asymmetric unit for complex **[Cu(L^3)Cl]** (**16**).

The complex (**22**) has an ionic crystalline structure formed by the complex cation $[Ni(HL^3)_2]^{2+}$ which has an octahedral geometry, Cl^- anions and water molecules in the ratio of 1: 2: 2.5.

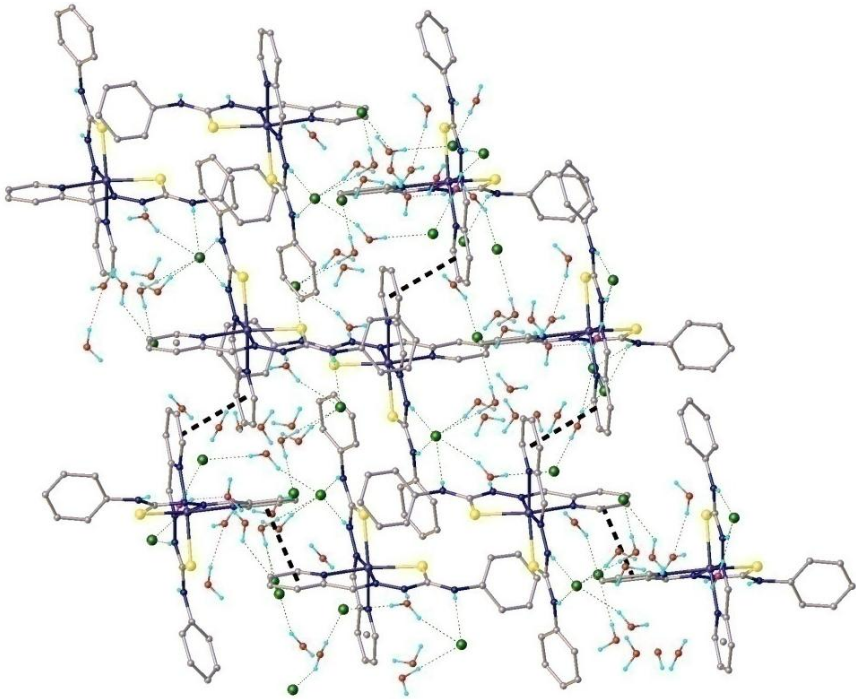


Figure 3.89. Perspective view of three-dimensional architecture demonstrating hydrogen bonding and π-π stacking interactions in complex **$[Ni(HL^3)_2]Cl_2 \cdot 2,5\ H_2O$ (22)**. Centoid-to-centroid distances are shown in black dashed lines.

Both **HL^3** ligand and complexes (**16**) - (**22**) were tested in terms of antioxidant activity by DPPH and ABTS methods. For complexes (**16**) - (**21**), the IC_{50} (μM) values were influenced by the metal ion salt, as follows: $ClO_4^- < SO_4^{2-} < NO_3^- < OAc^- < Cl^- < Br^-$.

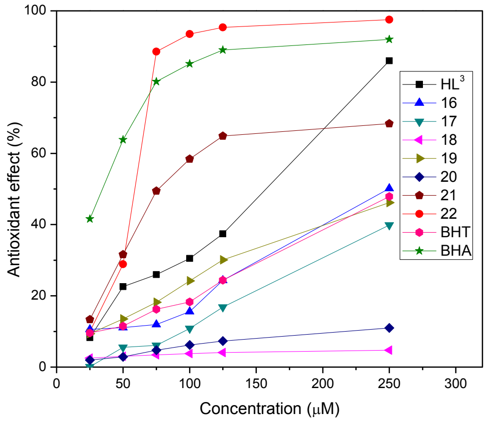


Figure 3.90. The antioxidant activity of **HL^3**, the complexes (**16**) - (**22**), BHT and BHA assessed by the DPPH method.

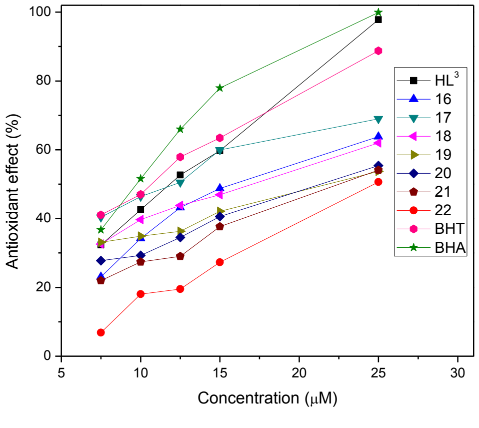


Figure 3.91. The antioxidant activity of **HL^3**, the complexes (**16**) - (**22**), BHT and BHA assessed by the ABTS method.

Six copper (II) complexes were synthesized with **HL^4** ligand. In the crystal structure of the ligand via NH2B–H···N4A intermolecular hydrogen bonds dimers are formed and via N–H···S intermolecular hydrogen bonds along with CH···π interactions between the phenyl-phenyl-pyridine rings lead to a 2D molecular packing.

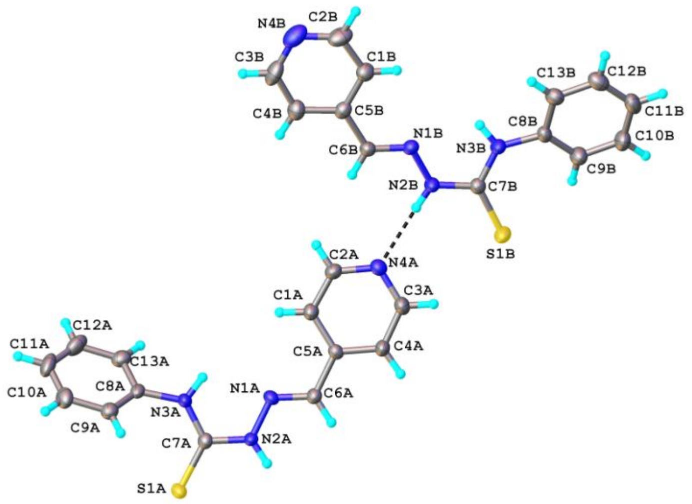
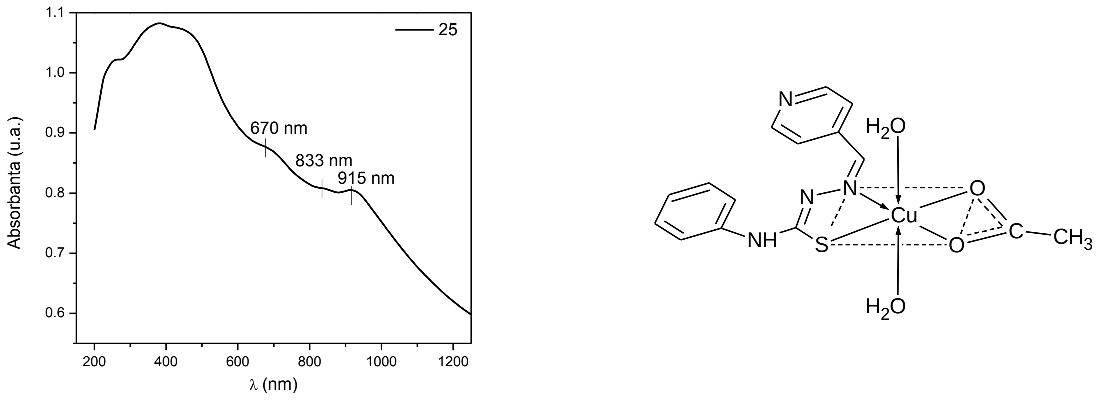


Figure 3.71. Dimer from the crystal structure of the ligand **HL^4**.

Electronic spectrum of the complex (**25**) (Fig. 3.95, a) shows absorption bands of medium intensity at 15 000, 12 000 and 10 900 cm^{-1}, which were attributed to d-d transitions: $^2B_{1g}\rightarrow{}^2A_{1g}$, $^2B_{1g}\rightarrow{}^2B_{2g}$ and $^2B_{1g}\rightarrow{}^2E_g$, respectively. These transitions are characteristic to a distorted octahedral stereochemistry for copper (II) complexes and for complex (**25**) such geometry was proposed (Fig. 3.95, b) in which the ligand coordinates mononegative bidentate to the metal center.



(a) (b)

Figure 3.95. (a) Electronic spectrum, and (b) proposed structure for complex (**25**).

For complexes (**23**) - (**28**), with octahedral geometry, the presence of coordinating water has been solved by means of thermal analysis, the weight losses occurs in the temperature range 110 - 280°C. EPR spectral parameters values, g_0 = 2.120 - 2.170 characterizes a metal center with an axial symmetry.

In order to obtain a thiosemicarbazone containing as potential donor atoms the *NSO* group ligand **HL^5** was synthesized. With this ligand six Cu(II) complexes were obtained. Analytical data indicated the following molecular formulas: **$[Cu(L^5)_2]$** (**29**), **$[Cu(HL^5)Br_2]$** (**30**), **$[Cu(L^5)(OAc)(H_2O)]$** (**31**), **$[Cu(L^5)SO_4Cu(L^5)][Cu(L^5)(H_2O)]_2(HSO_4)_2$ $10.5H_2O$** (**32**),

[Cu(L^5)(NO$_3$)(H$_2$O)$_2$] (**33**), **[Cu(L^5)(ClO$_4$)(H$_2$O)]** (**34**). The values of the molar conductivity of complexes (**29**) - (**31**), (**33**) and (**34**) (2 -53 Ω^{-1} cm^2 mol^{-1}) obtained for DMF solutions at a concentration of 10^{-3} M indicate the noneletrolite nature of these compounds. Except for complex (**32**), whose electrolyte behavior is evidenced by the value of the molar conductivity, 123 Ω^{-1} cm^2 mol^{-1} [20].

Electronic transitions values indicate an octahedral geometry for complexes (**29**), (**31**), (**33**) and (**34**), a square pyramidal geometry for complex (**30**) and a square-planar for complex (**32**). Magnetic moment values (1.43 to 2.08 MB) for complexes (**29**) - (**34**) suggests the presence of one unpaired electron. They also indicate the existence of monomer Cu(II) species The lower values of magnetic moment (1.46 - 1.63 MB) suggest antiferromagnetic coupling of the Cu(II) ion with S = 1/2 at room temperature [62,73,74].

The **HL^5** ligand coordinates tridentate through the *NSO* donor atoms in anionic form in complexes (**29**), (**31**) - (**34**), and neutral in complex (**30**). For complex (**30**), the coordination sphere is completed by two bromine atoms.

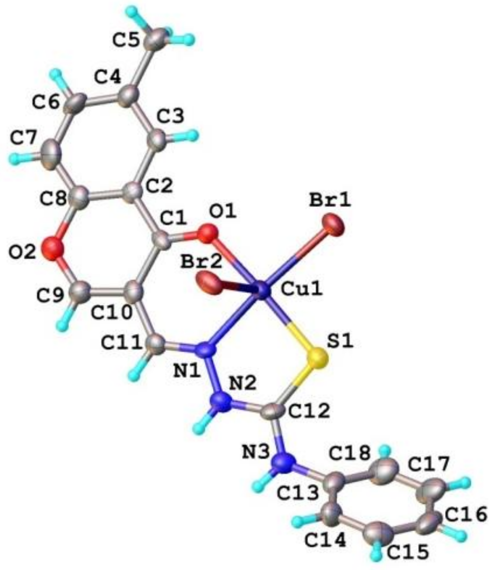
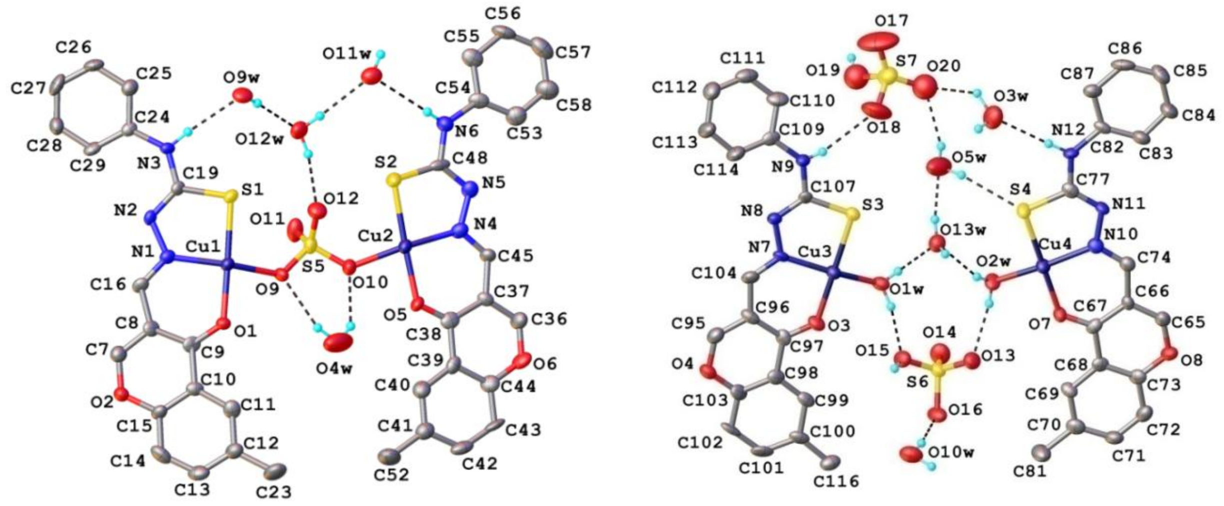


Figure 3.121. Molecular structure of complex **[Cu(HL^5)Br$_2$]** (**30**).

According to XRD studies, complex (**32**) has a crystal structure composed of the dication tetranuclear {[Cu(L^5)SO$_4$Cu(L^5)][Cu(L^5)(H$_2$O)]$_2$}$^{2+}$, HSO$_4^-$ anions and water molecules in a ratio of 1: 2: 10.5. Each copper atom has a square-planar geometry provided by **HL^5** tridentate ligand and an oxygen atom from SO$_4^{2-}$ anion, which is bridged between the Cu1 and Cu2 centers or an oxygen atom from a water molecule for Cu3 and Cu4 centers. Cu···S′ interactions exists in the apical position with the sulfur atom of the adjacent ligand molecule to indicate the possibility of characterizing this complex as a tetranuclear cluster {[Cu(L^5)SO$_4$Cu(L^5)][Cu(L^5)(H$_2$O)]$_2$}$^{2+}$.



(a) (b)

Figure 3.123. Structures of fragments containing atoms (a) Cu1 and Cu2, (b) Cu3 and Cu4.

The **HL**^{5} ligand and complexes (**29**) - (**34**) were tested for their antimicrobial activity. The best bactericidal activity has been demonstrated by complex (**30**) against strains of Gram-positive *Staphylococcus aureus* (MBC = 64 µg/mL) and *Enterococcus faecalis* (MBC = 64 µg/mL) and is most likely determined by the square pyramidal geometry of the copper atom. The antimicrobial activity of complex (**34**) against *Salmonella enteritidis* strains (MBC = 32 µg/mL) and *Candida albicans* (MIC = 16 µg/mL) may be due to the presence in the coordination sphere of the perchlorate anion.

Table 3.47. MIC (µg/mL) and MBC (µg/mL) values for **HL**^{5} and complexes (**29**) - (**34**).

Compound	***S. aureus***		***E. faecalis***		***E. coli***		***S. Enteritidis***		***C. albicans***	
	MIC (µg/mL)	MBC (µg/mL)	MIC (µg/mL)	MBC (µg/mL)	MIC (µg/mL)	MBC (µg/mL)	MIC (µg/mL)	MBC (µg/mL)	MIC (µg/mL)	MBC (µg/mL)
HL^5	>1024	>1024	>1024	>1024	>1024	>1024	>1024	>1024	>1024	>1024
(**29**)	>1024	>1024	512	>1024	>1024	>1024	>1024	>1024	512	>1024
(**30**)	**64**	**64**	**64**	**64**	512	512	512	512	>1024	>1024
(**31**)	512	>1024	512	>1024	512	>1024	512	>1024	>1024	>1024
(**32**)	512	>1024	>1024	>1024	>1024	>1024	>1024	>1024	512	>1024
(**33**)	128	256	128	128	>1024	>1024	>1024	>1024	512	>1024
(**34**)	**64**	>1024	**64**	>1024	**64**	**64**	**32**	**32**	**16**	>1024
$CuCl_2\cdot 2H_2O$	512	-	512	-	1024	-	512	-	-	-
$CuBr_2$	512	-	512	-	512	-	1024	-	-	-
$CuSO_4\cdot 5H_2O$	512	-	512	-	512	-	1024	-	1024	-
$Cu(ClO_4)_2\cdot 6H_2O$	1024	-	512	-	1024	-	1024	-	-	-
$Cu(NO_3)_2\cdot 2H_2O$	1024	-	1024	-	1024	-	1024	-	-	-
$Cu(OAc)_2\cdot H_2O$	1024	-	512	-	512	-	1024	-	-	-
Streptomycin	4	8	8	16	8	16	8	16	-	-
Fluconazole	-	-	-	-	-	-	-	-	2	8

The antioxidant activity of the complexes (**29**), (**30**) and (**32**) was highlighted by the stabilizing effect of ethylene-propylene-diene terpolymer (EPDM). This occurs after the polymer bond splitting when the hydrocarbon radicals oxidation is prevented.

A clearer picture of the stabilizing effect of the complexes was achieved by isothermal chemiluminescence measurements. As shown in Fig. 3.131, the unmodified and non-irradiated EPDM polymer is slowly oxidized at a temperature of 170°C, while the modified polymer remains stable over a long period of time, depending on the complex added, after its rapid oxidation occurs. The most stable was the EPDM-**29** system.

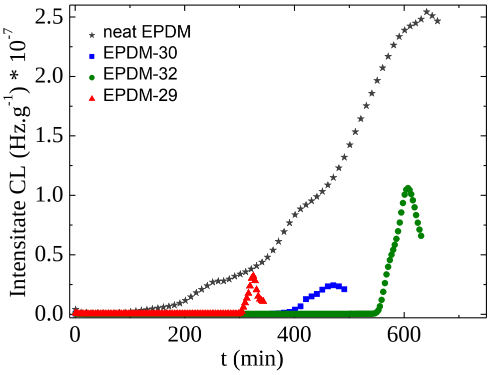


Figure 3.131. Isothermal CL spectra of irradiated samples of unmodified and modified EPDM, recorded at 170°C.

Four copper (II) complexes with ligand **HL^6** were synthesized. They exhibit an octahedral geometry and the ligand coordinates in a bidentate monodeprotonate manner. The structure of the ligand was determined by XRD and shows the existence of two-dimensional chains defined by intermolecular N3–H3···N1 hydrogen bonds and π – π stacking interactions that occurs between the carbazole rings. The intermolecular N2–H2···S1 hydrogen bonds interconnects the two-dimensional chains with the formation of a three-dimensional network.

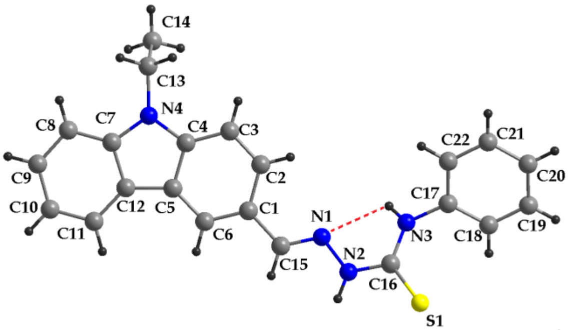


Figure 3.136. The molecular structure of ligand **HL^6**.

The monomeric nature of the complexes was determined by EPR. The EPR spectrum of the complex (**35**) recorded on powder at 298 K shows a signal characteristic to an orthorhombic symmetry. The g tensor values that characterize this signal are: $g_1 = 2.276$, $g_2 = 2.192$ and $g_3 = 2.069$. The EPR spectrum of the complex (**36**) is a complex one that allowed the characterization of only one signal characterized by parameters $g_o = 2.087$ and $A_o = 190$ G. EPR spectra of complexes (**37**) and (**38**) show similar signals, signals specific to a metal center with an axial symmetry and a slight rhombic distortion. The spectral parameters evaluated are: $g_{//} = 2.282$ and $g_{\perp} = 2.060$ for complex (**37**), $g_{//} = 2.262$ and $g_{\perp} = 2.007$ for complex (**38**). Given that $g_{//} > g_{\perp} > 2.0023$ the ground state term is defined by $d_{x^2-y^2}$ orbital [105].

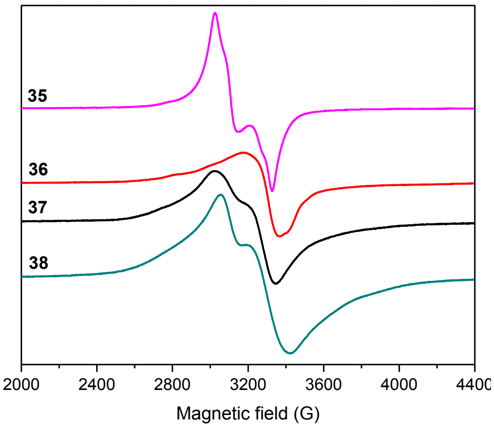


Figure 3.142. EPR spectra of complexes (**35**) - (**38**) recorded on powder at 298 K.

Chapter 4

Cu(II) complexes with ligands derived from thiocarbohydrazide

Chapter 4 describes the copper (II) complexes obtained with symmetrical thiocarbohydrazone. Thus, by condensing, in a molar ratio of 1: 2 various aldehydes with thiocarbohydrazide four ligands were synthesized: 1,5-bis(2-furaldehyde)thiocarbohydrazone (**HL^7**), 1,5-bis(5-methyl-2-furaldehyde)thiocarbohydrazone (**HL^8**), 1,5-bis(thiophene-2-aldehyde)thiocarbohydrazone (**HL^9**) and 1,5-bis(3-formyl-6-methylchromone) thiocarbohydrazone (**HL^{10}**).

Using the **HL^7** ligand five copper (II) complexes were synthesized: **$[Cu(L^7)(H_2O)_2]Cl$** (**39**), **$[Cu(L^7)_2]$** (**40**), **$[Cu(HL^7)_2](SO_4)$** (**41**), **$[Cu(HL^7)_2](NO_3)_2$** (**42**), **$[Cu_2(L^7)(ClO_4)_2](ClO_4)$** (**43**). XRD studies indicate the existence of dimers in the crystal structure of the **HL^7** ligand formed via intermolecular N–H···S hydrogen bonds, the conformation *EZ* is adopted by the ligand. Complexes (**39**) and (**43**) exhibit a tetrahedral geometry, and the square-planar geometry was outlined for complexes (**40**) - (**42**).

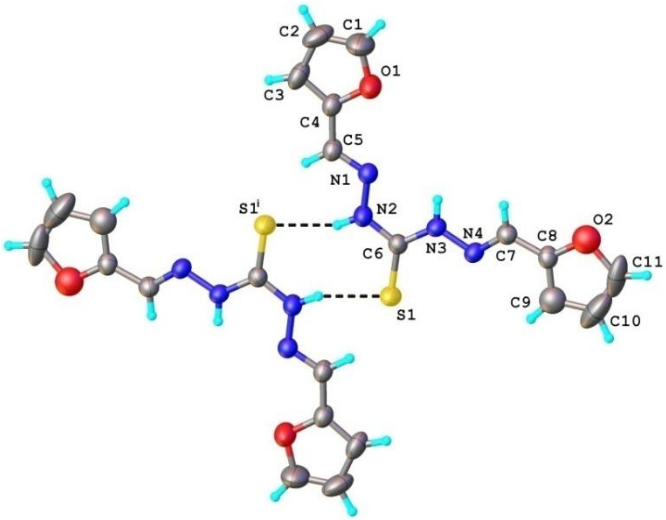


Figure 4.7. Dimers in the crystal structure of the ligand **HL**^{7}.

The electronic spectra of complexes (**39**) and (**43**) exhibit one absorption band at 12 800 and 14 900 cm^{-1}, respectively. These bands were assigned to d–d transitions: $^2B_2\rightarrow{}^2B_1$, $^2B_2\rightarrow{}^2A_1$ for a tetrahedral stereochemistry of the copper (II) ion [15]. The electronic spectra of the complexes (**40**) - (**42**) show absorption bands in regions 12 800 - 12 900 cm^{-1}, 16 100 - 16 200 cm^{-1} and 18 500 - 18 800 cm^{-1} that were assigned to d–d transitions: $^2B_{1g}\rightarrow{}^2B_{2g}$, $^2B_{1g}\rightarrow{}^2E_g$ și $^2B_{1g}\rightarrow{}^2A_{1g}$. These transitions are characteristic of copper (II) complexes with a square-planar geometry [16].

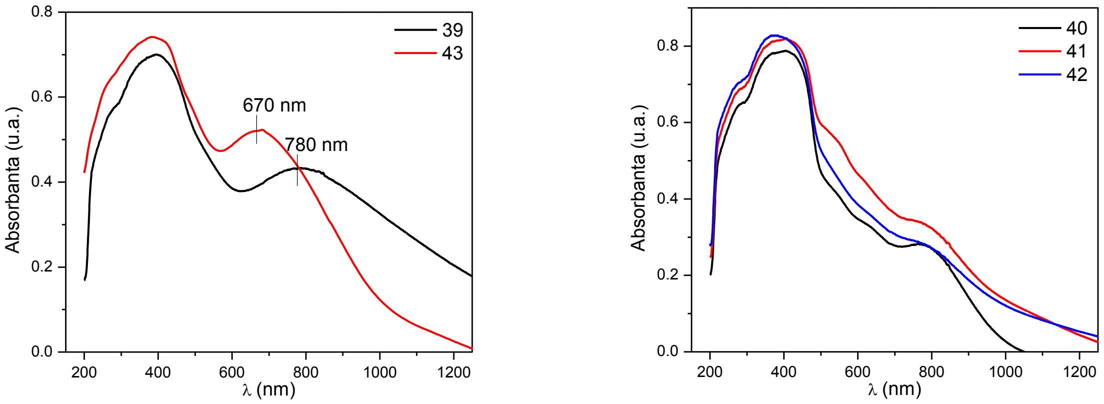


Figure 4.9. Electronic spectra of complexes (**39**) - (**43**).

Due to structural diversity of thiocarbohydrazone ligands and the heat labile nature of copper (II) perchlorate, to elucidate the structure of the complex (**43**) mass spectrometry was used (Annex I). Also, the structure complex (**40**) was confirmed by this technique. Thus, the peaks corresponding to the pseudomolecular ions were identified, as well as other species resulting from their fragmentation [19].

The m/z values of the fragments identified in the mass spectra led to the confirmation of their molecular weight and structure. Identified pseudomolecular ions for complexes (**40**) and (**43**) are: $[Cu(L^7)_2{+}Na{+}H^+]^+$ (m/z: 610,26), and $[Cu_2L^7(ClO_4)_2(ClO_4){-}2H^+]^+$ (m/z: 684,28).

Table 4.5. The m/z values for complexes (**40**) and (**43**).

Complex	**Fragments identified in ESI-MS (m/z calc./ m/z exp.)**
$[Cu(L^7)_2]$ (**40**)	$[Cu(L^7)_2 +Na+H^+]^+$ (610,26 / 610,10), $[L^7]^+$ (261,28 / 261,09).
$[Cu_2(L^7)(ClO_4)_2]ClO_4$ (**43**)	$[Cu_2L^7(ClO_4)_2(ClO_4)\text{-}2H^+]^+$ (684,72 / 684,28), $[Cu_2L^7(ClO_4)_2\text{-}2H^+]^{2+}$ (585,27 / 585,09), $[Cu_2L^7(ClO_4)_2)]^{3+}$ (487,82 / 487,05), $[L^7]^+$ (261,28 / 261,10).

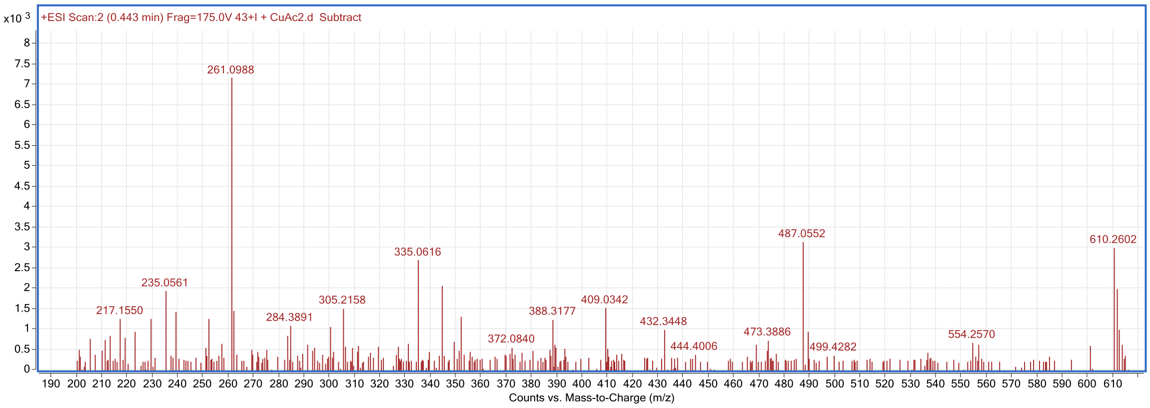
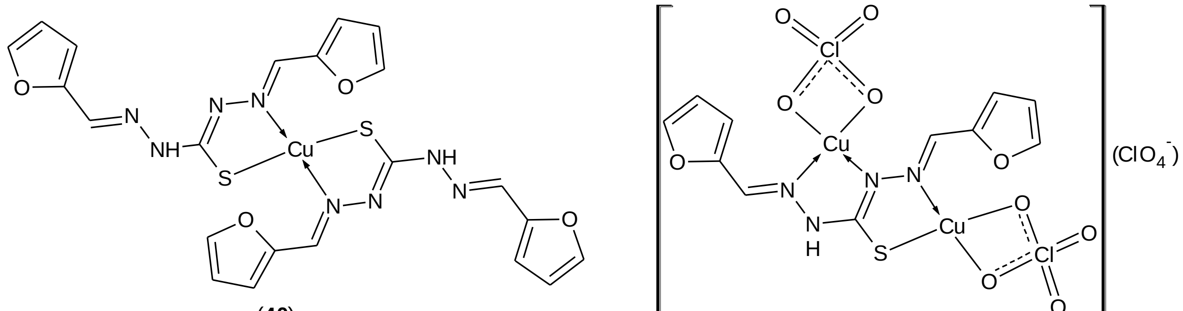


Figure 4.11. MS spectra of complex (**40**).



(**40**) (**43**)

Figure 4.12. The proposed structures for complexes (**40**) and (**43**).

In complex (**43**), the $\mathbf{HL^7}$ ligand is at the same time *NS* and *NN* donor. The EPR spectral parameters values $A_{//}$, $g_{//}$ and $g_{\perp}$ are characteristic to a Cu^{2+} ion with a square-planar stereochemistry for complexes (**40**) - (**42**) and respects the relationship $g_{//} > g_{\perp} > 2.0023$, the ground state being described by $d_{x^2-y^2}$ orbital.

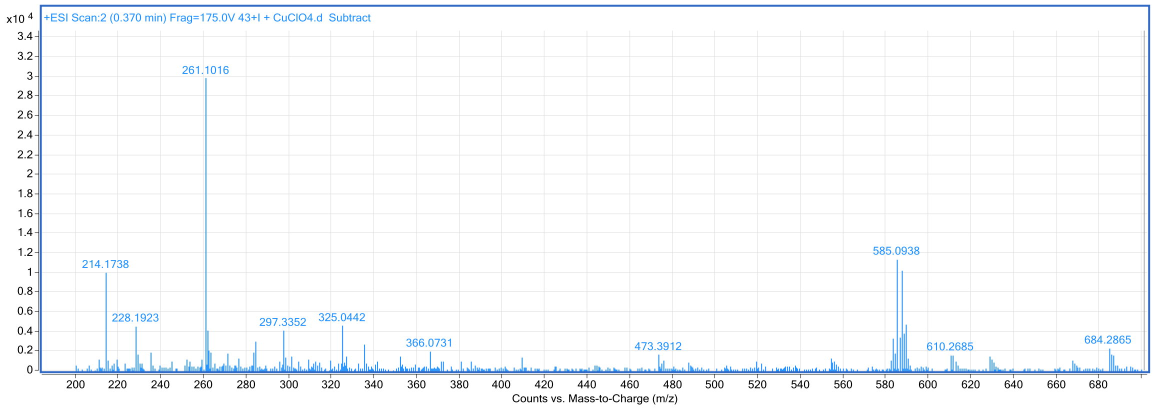


Figure 4.13. MS spectra of complex (**43**).

The complexes **[Cu(L^{8})$_2$]** (**44**), **[Cu(HL^{8})(SO$_4$)(H$_2$O)$_2$]** (**45**), **[Cu(L^{8})(NO$_3$)(H$_2$O)]** (**46**), and **[Cu(L^{8})(ClO$_4$)]** (**47**) were synthesized with **HL^{8}** ligand. A square-planar geometry was indicated by the experimental data for complexes (**44**), (**46**) and (**47**) and one octahedral for complex (**45**). As a result of qualitative screening, the complex (**47**) showed very good antimicrobial activity against one of the two tested microbial strains, *Escherichia coli*. As a result of the quantitative screening, all the complexes showed low antimicrobial activity against Gram-positive bacterial strains, except for complex (**46**) who presented a better activity (MIC = 256 μg/mL). The complex (**47**) exhibited the best antimicrobial activity against strains of *E. coli*. The MIC and MBC values are 128 and 256 μg/mL, respectively. The best antifungal agent was complex (**46**), MIC = 128 μg/mL and MBC = 256 μg/mL.

Using a template method two copper (II) complexes were synthesized with **HL^{9}** ligand: **[Cu(HL^{9})$_2$]Cl$_2$ · 3CH$_3$OH· 0.25H$_2$O** (**48**), **[Cu(HL^{9})$_2$]SO$_4$ · 2CH$_3$OH** (**49**).

For ligand **HL^{9}** by recrystallization from methanol single crystals suitable for XRD. The data indicate that the ligand crystallizes with one molecule of water in the monoclinic crystal system, space group *P2$_1$/c*.

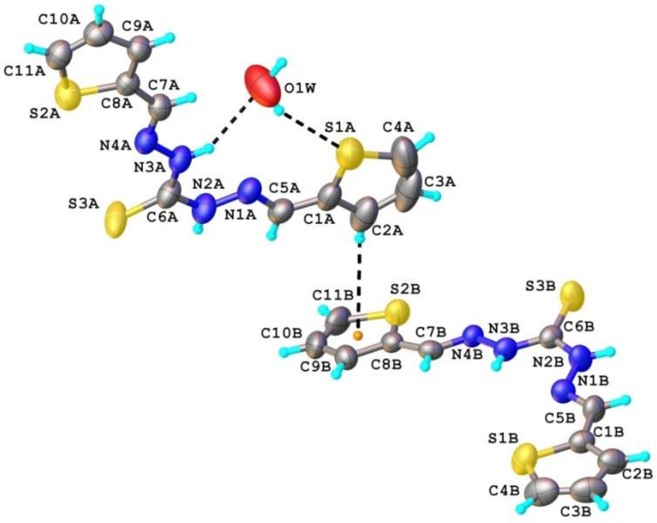


Figure 4.28. Asymmetric unit for ligand **HL^{9}**.

According to X-ray diffraction studies, the complex (**48**) has a crystal structure formed by the cation [Cu(HL^{9})$_2$]$^{2+}$, Cl^{-} anions, solvent and water molecules in a ratio of 1: 2: 3: 0.25. Also, complex (**49**) has a crystal structure formed by the cation [Cu(HL^{9})$_2$]$^{2+}$, SO$_4^{2-}$ anions and solvent molecules in a ratio of 1: 1: 2. The geometry of the two complexes is one tetrahedral wherein the ligand acts bidentate neutral coordinating through the *NS* donor atoms (azomethine nitrogen and thione sulfur atoms).

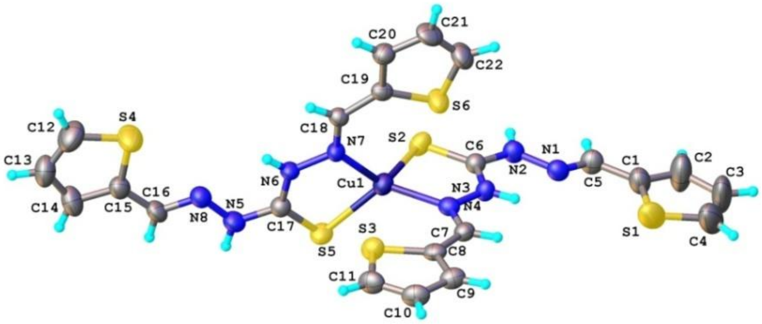


Figure 4.34. The molecular structure of the cation $[Cu(HL^9)_2]^{2+}$ from complex (**48**).

The molecular packaging for both complexes is governed by an extensive system of hydrogen bonds involving the NH group of the ligand, Cl^- and SO_4^{2-} ions, and solvent and water molecules.

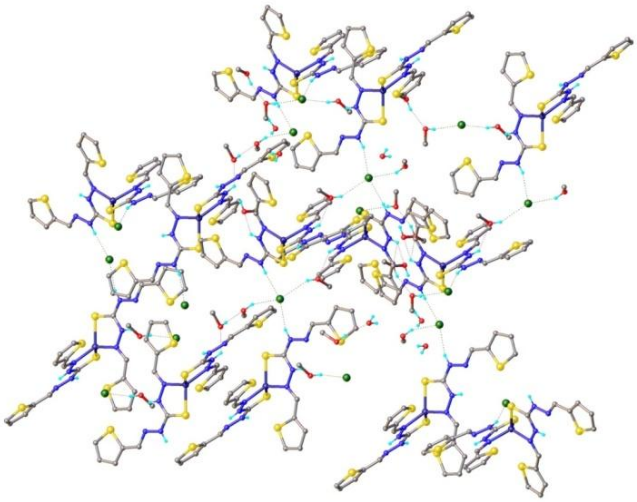


Figure 4.35. Molecular packing for complex (**48**).

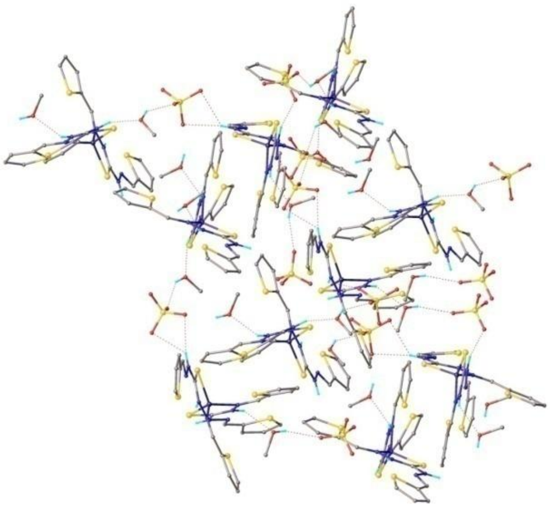


Figure 4.37. Molecular packing for complex (**49**).

With **HL^{10}** ligand five copper (II) complexes were synthesized: **$[Cu(L^{10})(Cl)(H_2O)_2]$** (**50**), **$[Cu(L^{10})(Br)(H_2O)_2]$** (**51**), **$[Cu(L^{10})(OAc)(H_2O)_2]$** (**52**), **$[Cu(HL^{10})(SO_4)(H_2O)]$** (**53**), **$[Cu(L^{10})(NO_3)(H_2O)_2]$** (**54**). The molar conductivity values (9 - 42 Ω^{-1} cm^2 mol^{-1}) obtained for DMF solution at a concentration of 10^{-3} M, at room temperature, demonstrates the nonelectrolite nature of these complexes [12].

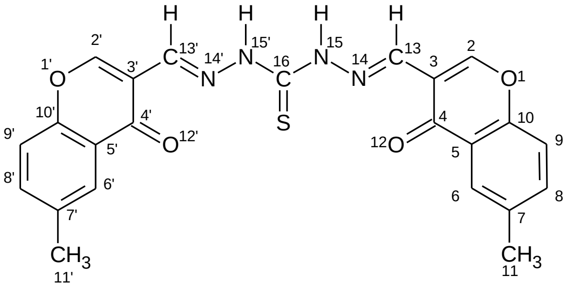


Figure 4.39. The structure of ligand **HL^{10}**.

^{1}H–NMR (DMSO-d_6, δ ppm, *J* Hz): 11.96 (s, 2H, H-15,15’); 9.28 (s, 2H, H-2,2’); 8.27 (s, 2H, H-13,13’); 7.92 (s, 2H, H-6,6’); 7.66 (dl, 8.5, 2H, H-8,8’); 7.65 (dl, 8.5, 2H, H-9,9’); 2.50 (s, 6H, H-11,11’).

^{13}C–NMR (DMSO-d_6, δ ppm): 175.95 (C-16); 174.79 (C-4,4’); 154.18 (C-2,2’); 152.78 (C-10,10’), 139.27 (C-3,3’); 135.88 (C-13,13’); 130.51 (C-5,5’); 124.48 (C-9,9’); 123.10 (C-6,6’); 118.61 (C-8,8’); 118.40 (C-7,7’); 20.60 (C-11,11’).

The ligand structure was confirmed using mass spectrometry. The peak corresponding to the molecular ion $[HL^{10}+H]^+$ was found at the value 447.10 m/z (m/z calc. = 447.48). The peak at 469.08 m/z corresponds to the pseudomolecular ion $[HL^{10}+Na]^+$ (m/z calc. = 469.47).

The presence of water molecules in these complexes is shown by the equivalent weight loss that takes place in the temperature range 110 - 250°C.

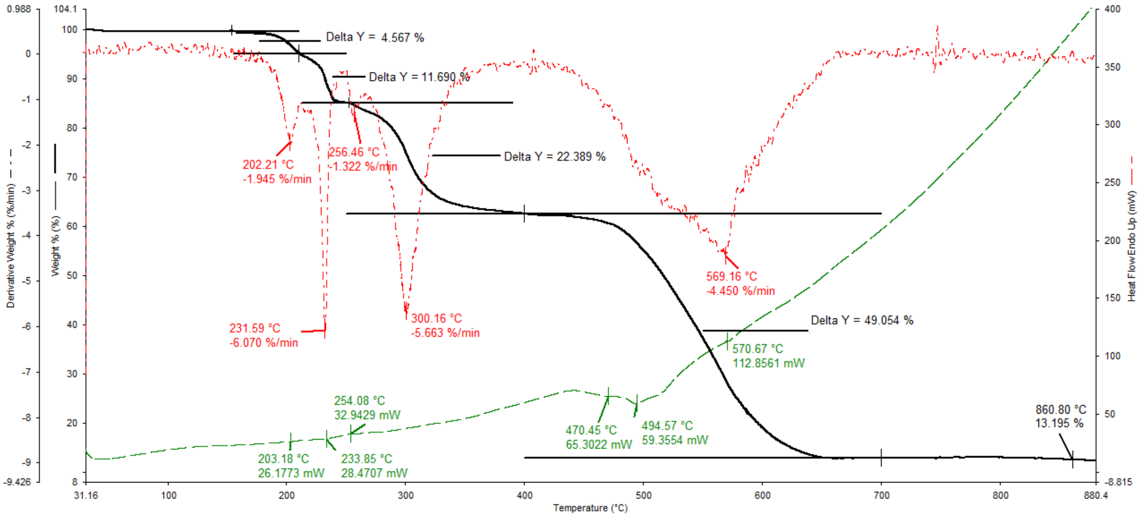


Figure A.V.35. Thermogram of complex $[Cu(L^{10})(Br)(H_2O)_2]$ (**51**).

These complexes showed an octahedral geometry. The antioxidant activity of the complexes (**50**), (**51**) and (**53**) has been highlighted by the effect of stabilizing of the EPDM terpolymer. The degradation of the polymer substrate from modified EPDM samples takes place at temperatures higher than 200°C. While the degradation state of polymer is advancing due to radiolysis, the complexes's efficiency becomes more relevant by stabilizing the EPDM polymer. The maximum intensity measured on the unmodified EPDM polymer is 3.5 times higher than that recorded for the most unstable system EPDM-**53**.

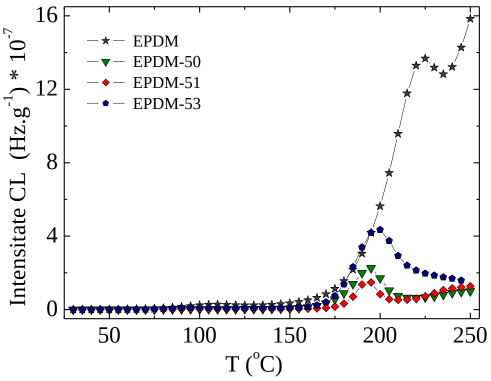


Figure 4.52. Non-isothermal CL spectra of unmodified and modified EPDM samples, irradiated with 100kGy.

At the end of Chapter 4 is presented the characterization of a mono-thiocarbohydrazone (**HL**^{11}) considered an intermediate for the synthesis of **HL**^{12} precursor that contains six nitrogen atoms in the molecule according to the sequence >C=N–NH–(C=S)–NH–NH–(C=S)–NH–N=C<.

The crystal structure of **HL**^{11} is stabilized by intramolecular N3–H···N1 hydrogen bonds that gives the *E* form to the compound and intermolecular N2–H···N4’ hydrogen bonds that lead to the formation of molecular chains (Fig. 4.60).

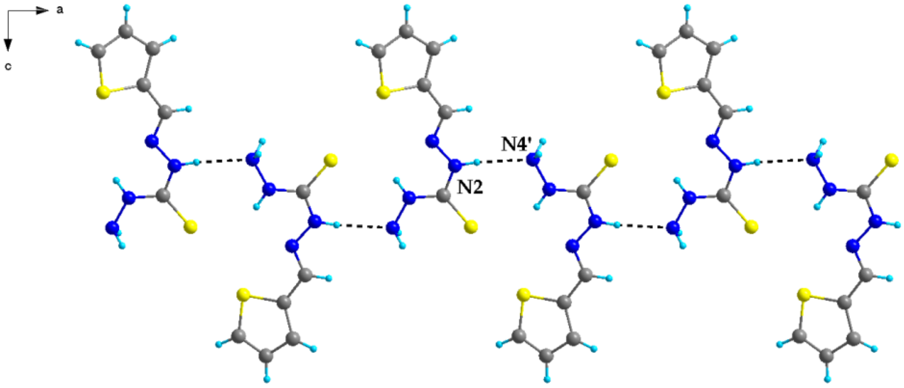


Figure 4.60. 1D chain from the crystal structure of the compound **HL**^{11}.

The compound **HL**^{12} was characterized by mass spectrometry, identifying the appropriate pseudomolecular ion peak $[HL^{12}+Na]^+$ at m/z = 391.29 (m/z calc. = 391.51). Also, the molecular structure of the compound **HL**^{12} was determined by X-ray diffraction. The molecular packing of compound **HL**^{12} is influenced by the formation of 1D supramolecular chains supported by intermolecular hydrogen bonds N–H···S.

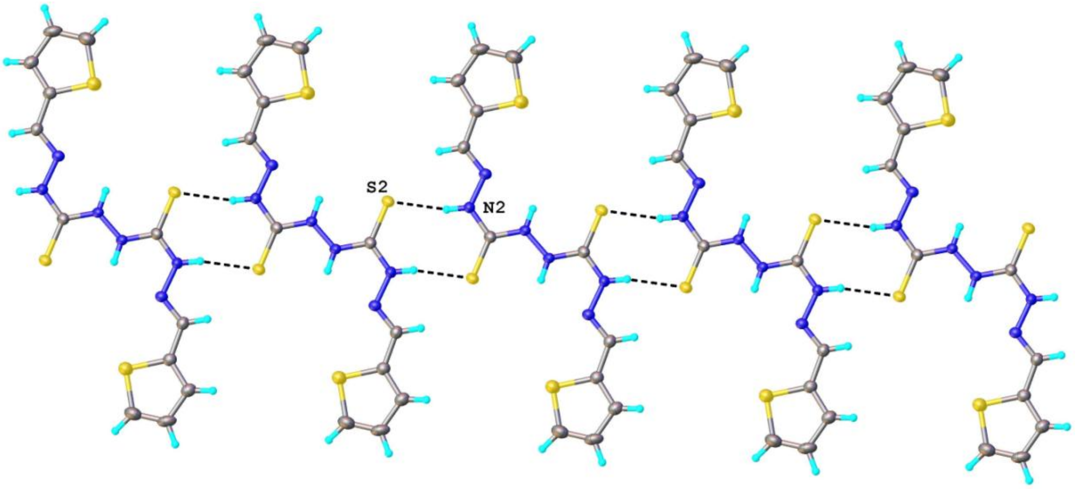


Figure 4.65. 1D chain for compound **HL^{12}**. Hydrogen bonds parameters: N2−H···S2 [N2−H 0.86 Å, H···S2 2.68 Å, N2···S2 3.358(2) Å, N2−H···S2 136.9°].

Selective Bibliography

- chapter 1

[1] a) Casas J.S., Garcia-Tasende M. S., Sordo J., Coord. Chem. Rev. 209 (2000) 197-261; b) Gómez Quiroga A., Navarro Ranninger C., Coord. Chem. Rev. 248 (2004) 119-133; c) Lobana T. S., Sharma R., Bawa G., Khanna S., Coord. Chem. Rev. 253 (2009) 977-1055; d) Medici S., Peana M., Nurchi V. M., Lachowicz J. I., Crisponi G., Zoroddu M. A., Coord. Chem. Rev. 284 (2015) 329-350;

[2] Wilson B. A., Venkatraman R., Whitaker C., Tillison Q., Int. J. Environ. Res. Pub. Health 2 (2005) 170-147;

[3] Keiko N. A., Mamashvili T. N., Pharm. Chem. J. 39 (2005) 82-83;

[4] Lobana T. S., Rekha R., Butcher R. J., Transition Met. Chem. 29 (2004) 291-295;

[5] Lobana T. S., Rekha R., Butcher R. J., Castineiras A., Bermejo E., Bharatam P. V., Inorg. Chem. 45 (2006) 1535-1542;

[6] Lobana T. S., Khanna S., Butcher R. J., Hunter A. D., Zeller M., Inorg. Chem. 46 (2007) 5826-5828;

[7] Lobana T. S., Khanna S., Butcher R. J., Z. Anorg. Allg. Chem. 633 (2007) 1820-1826;

[8] Lobana T. S., Kumari P., Butcher R. J., Inorg. Chem. Commun. 11 (2008) 11-14;

[9] Jouad E. M., Riou A., Allain M., Khan M. A., Bouet G. M., Polyhedron 20 (2001) 67-74;

[10] Lhuachan S., Siripaisarnpipat S., Chaichit N., Eur. J. Inorg. Chem. 2 (2003) 263-267;

[11] Lobana T. S., Bawa G., Castineiras A., Butcher R. J., Inorg. Chem. Comm. 10 (2007) 506-509;

[12] Halder S., Peng S. M., Lee G. H., Chatterjee T., Mukherjee A., Dutta S., Sanyal U., Bhattacharya S., New J. Chem. 32 (2008) 105-114;

[13] Lobana T. S., Bawa G., Butcher R. J., Liaw B.-J., Liu C. W., Polyhedron 25 (2006) 2897-2903;

[14] Ashfield L. J., Cowley A. R., Dilworth J. R., Donnelly P. S., Inorg. Chem. 43 (2004) 4121-4123;

[15] Pal I., Basuli F., Mak T. C. W., Bhattacharya S., Angew. Chem. Int. Ed. 40 (2001) 2923-2925;

[16] Belicchi-Ferrari M., Bisceglie F., Buluggiu E., Pelosi G., Tarasconi P., Polyhedron 28 (2009) 1160-1168;

[17] Lobana T. S., Khanna S., Butcher R. J., Hunter A. D., Zeller M., Polyhedron 25 (2006) 2755-2763;

[45] Bertini I., Gray H. B., Lippard S. J., Selverstone Valentine J., Bioinorganic Chemistry, University Science Books, Mill Valley, California, 1994.

- chapter 2

[2] Aly A., Brown A., El-Emary T., Mohamed Ewas A. M., Ramadan M., ARKIVOC (2009) 150-197;

[3] Metwally M. A., Khalifa M. E., Koketsu M., American Journal of Chemistry 2 (2012) 38-51;

[4] Brockman R. W., Thopson J. R., Bell M. J., Skipper H. E., Cancer Res 16 (1956) 167-170;

[5] Qing Han Li, Chin. Chem. Lett. 20 (2009) 793-796;

[6] Esmadia F., Khabour O. F., Albarqawi Ala' I., Ababneh M., Al-Talib M., Jordan J. Chem. 8 (1) (2013) 31-43;

[7] Zhang A., Hou Y., Zhang L., Xiong Y., Synth. Commun. 32 (2002) 3865-3869;

[8] Manoj E., Kurup M. R. P., Fun H.-K., Punnoose A., Polyhedron 26 (2007) 4451-4462;

[29] Dragancea D., Addison A. W., Zeller M., Thompson L. K., Hoole D., Revenco M. D., Hunter A. D., Eur. J. Inorg. Chem. (2008) 2530-2536;

- chapter 3

[15] Sun P. P., Jian F. F., Wang X., J. Chem. Crystallogr. 40 (2010) 4-9;
[16] Rajendran G., Amritha C. S., Anto R. J., Cheriyan V. T., J. Serb. Chem. Soc. 75 (2010) 749-761;
[17] Ilies D.-C., Pahontu E., Shova S., Gulea A., Rosu T., Polyhedron 51 (2013) 307-315;
[18] (a) Joseph M., Kuriakose M., Kurup M. R. P., Suresh E., Kishore A., Bhat S. G., Polyhedron 25 (2006) 61-70; (b) Belicchi-Ferrari M., Bisceglie F., Pelosi G., Tarasconi P., Polyhedron 27 (2008) 1361-1367;
[20] Geary W. J., Coord. Chem. Rev. 7 (1971) 81-122;
[21] (a) Nakamoto K., Infrared Spectra of Inorganic and Coordination Compounds, Wiley and Sons, New York, 1986; (b) Nakamoto K., Infrared and Raman Spectra of Inorganic and Coordination Compounds, fifth ed., Wiley-Interscience, New York, 1997;
[24] Belicchi-Ferrari M., Bisceglie F., Cavalieri C., Pelosi G., Tarasconi P., Polyhedron 26 (2007) 3774-3782;
[30] Jayakumar K., Sithambaresan M., Aiswarya N., Prathapachandra Kurup M. R., Spectrochimica Acta Part A 139 (2015) 28-36;
[33] Kneubuhl F. K., J. Chem. Phys, 33(4), 1074-1078 (1960) 244/70;
[34] Hochmuth D. H., Michel S. L. J., White A. J. P., Williams D. J., Barrett A. G. M., Hoffman B. M., Eur. J. Inorg. Chem. (2000) 593-596;
[62] Raman N., Selvan A., Manisankar P., Spectrochim. Acta Mol. Biomol. Spectrosc. 76 (2010) 161-173;
[73] Ballhausen C. J., An Introduction to Ligand Field Theory, New York, NY: McGraw Hill, 1962.
[74] Latheef L., Kurup M. R. P., Spectrochim. Acta Mol. Biomol. Spectrosc. 70 (2008) 86-93.
[105] Kozlevcar B., Segedin P., Croat. Chem. Acta 81 (2008) 369-379.

- chapter 4

[12] Geary W. J., Coord. Chem. Rev. 7 (1971) 81-122;
[15] Jouad E. M., Riou A., Allain M., Khan M. A., Bouet G.M., Polyhedron 20 (2001) 67-74;
[16] Abu-Melha K. S., El-Metwally N. M., Spectrochim. Acta Mol. Biomol. Spectrosc. 70 (2008) 277-283;
[19] (a) Grazul M., Kufelnicki A., Wozniczka M., Lorenz I. P., Mayer P., Jozwiak A., Czyz M., Budzisz E., Polyhedron 31 (2012) 150-158; (b) Dragancea D., Shova S., Enyedy E. A., Breza M., Rapta P., Carrella L. M., Rentschler E., Dobrov A., Arion V. B, Polyhedron 80 (2014) 180-192;

List of scientific papers

Papers published in the field of the Ph.D. thesis:

1. *Synthesis, characterization and crystal structures of nickel(II), palladium(II) and copper(II) complexes with 2-furaldehyde-4-phenylthiosemicarbazone*, **Diana-Carolina Ilieș**, Elena Pahonțu, Sergiu Shova, Aurelian Gulea, Tudor Roșu, *Polyhedron* 51 (**2013**) 307–315, (FI = 2,047);

2. *Synthesis, characterization, crystal structure and antimicrobial activity of copper(II) complexes with a thiosemicarbazone derived from 3-formyl-6-methylchromone*, **Diana-Carolina Ilieș**, Elena Pahonțu, Sergiu Shova, Rodica Georgescu, Nicolae Stanică, Rodica Olar, Aurelian Gulea, Tudor Roșu, *Polyhedron* 81 (**2014**) 123–131, (FI = 2,011);

3. *Synthesis, characterization, crystal structure and antioxidant activity of Ni(II) and Cu(II) complexes with 2-formilpyridine N(4)-phenylthiosemicarbazone*, **Diana-Carolina Ilieș**, Sergiu Shova, Valeria Rădulescu, Elena Pahonțu, Tudor Roșu, *Polyhedron* 97 (**2015**) 157–166, (FI = 2,011);

4. *Thermal and spectroscopic analysis of stabilization effect of copper complexes in EPDM*, Traian Zaharescu, Diana-Carolina Ilieș, Tudor Roșu, *J. Therm. Anal. Calorim*. (**2015**), DOI 10.1007/s10973-015-4893-5, (FI = 2,042);

Other published papers:

1. *Cu(II) complexes with nitrogen-oxygen donor ligands: synthesis and biological activity*, Mădălina Veronica Angelușiu, Gabriela Laura Almăjan, Diana-Carolina Ilieș, Tudor Roșu, Maria Negoiu, *Chem. Bull. "POLITEHNICA" Univ. (Timișoara)* 53(67) (1-2) (**2008**) 78-82;

2. *Analysis of volatile compounds from infusion and hydrodistillate obtained from the species Thymus pulegioides L. (Lamiaceae)*, Valeria Rădulescu, Mariana Pavel, Ana Teodor, Alexandra Tănase, Diana-Carolina Ilieș, *Farmacia* 57(3) (**2009**) 282-289, (FI = 0,144);

3. *GC-MS analysis of essential oil obtained from the species Thymus comosus Heuff. Ex Griseb. (Lamiaceae)*, Mariana Pavel, Valeria Rădulescu, Diana-Carolina Ilieș, *Farmacia* 57(4), (**2009**) 479-484, (FI = 0,144);

4. *Chemical composition of the volatile oil from different plant parts of Anethum graveolens L. (Lamiaceae) cultivated in Romania*, Valeria Rădulescu, Maria Lidia Popescu, Diana-Carolina Ilieş, *Farmacia* 58(5) (**2010**) 594-600, (FI = 0,850);

5. *Chemical composition and antimicrobial activity of essential oil from shoots spruce (Picea abies L)*, Valeria Rădulescu, Crina Saviuc, Carmen Chifiriuc, Eliza Oprea, Diana-Carolina Ilieş, Luminița Marutescu, Veronica Lazăr, *Rev. Chim.-Bucharest* 62(1) (**2011**) 69-74, (FI = 0,599);

6. *Chemical composition and cancer chemopreventive effect of volatile oil isolated from Thymus pulegioides L.*, Valeria Rădulescu, Maria Monica Nistoroiu, Marieta Elena Panait, Diana-Carolina Ilieş, Eugenia Tirifon, *Farmacia* 59(2) (**2011**) 228-238, (FI = 0,669);

7. C*hemical composition of the essential oil of Urtica dioica*, Diana-Carolina Ilieș, Ioana Tudor, Valeria Rădulescu, *Chem. Nat. Compd.* 48(3) (**2012**) 506-507, (FI = 0,599);

8. *Synthesis, structural and spectral studies of Cu(II) and V(IV) complexes of a novel Schiff base derived from pyridoxal. Antimicrobial activity*, Tudor Rosu, Elena Pahonțu, Mezey Reka-Ștefana, Diana-Carolina Ilieș, Rodica Georgescu, Sergiu Shova, Aurelian Gulea, *Polyhedron* 31(1) (**2012**) 352-360, (FI = 1,813);

9. *Synthesis and characterization of some new complexes of Cu(II), Ni(II) and V(IV) with Schiff base derived from indole-3-carboxaldehyde. Biological activity on prokaryotes and eukaryotes*, Tudor Roșu, Elena Pahonțu, Diana-Carolina Ilieș, Rodica Georgescu, Mihaela Mocanu, Mircea Leabu, Sergiu Shova, Aurelian Gulea, *Eur. J. Med. Chem.* 53 (**2012**) 380-389, (FI = 3,499);

10. *Contributions at phytochemical study of Thymus vulgaries L. species from Lebanon*, Lakis Zeinab, Cerasela Gârd, Valeria Rădulescu, Diana-Carolina Ilieș, Simona Ardelean, Denisa Mihele, *Studia Universitatis Vasile Goldis Seria Stiintele Vietii (Life)* 22(1) (**2012**) 79-82, (B^+);

11. *Preliminary research regarding the therapeutic uses of Urtica Dioica L. NOTE II. The dynamics of accumulation of total phenolic compounds and ascorbic acid,* Ioana Nencu, Viorica Istudor, Diana-Carolina Ilieș, Valeria Rădulescu, *Farmacia* 61(2) (**2013**) 276-283, (FI = 1,251);

12. *A comparative morphological and chemical study of the seeds from Trigonella foenum graecum (L.) and T. caerulea (L.) ser. species*, Mihaela Dinu, Robert Ancuceanu, Valeria Rădulescu, Diana-Carolina Ilieş, Cornel Munteanu, Corina Aramă, *Farmacia* 61(6) (**2013**)

1069-1081, (FI = 1,251);

13. *Determination of ascorbic acid in shoots from different coniferous species by HPLC,* Valeria Rădulescu, Diana-Carolina Ilieş, Ion Voiculescu, Iovu-Adrian Biriş, Adam Crăciunescu, *Farmacia* 61(6) (**2013**) 1158-1166, (FI = 1,251);

14. *Synthesis and antioxidant activity evaluation of new compounds from hydrazinecarbothioamide and 1,2,4-triazole class containing diarylsulfone and 2,4-difluorophenyl moieties,* Ștefania-Felicia Bărbuceanu, Diana-Carolina Ilieș, Gabriel Șaramet, Valentina Uivaroși, Constantin Drăghici, Valeria Rădulescu, *Int. J. Mol. Sci.* 15 (**2014**) 10908-10925, (FI = 2,862);

15. *Volatile constituents from the flowers of two species of honeysuckle (Lonicera japonica and Lonicera caprifolium),* Diana-Carolina Ilieş, Valeria Rădulescu, Ligia Duţu, *Farmacia* 62(1) (**2014**) 194-201, (FI = 1,005);

16. *Synthesis, characterization and antioxidant activity evaluation of some 1,3,4-thiadiazole and 1,3,4-oxadiazole compounds,* Ștefania-Felicia Bărbuceanu, Diana-Carolina Ilieș, Valeria Rădulescu, Laura-Ileana Socea, Constantin Drăghici, Gabriel Șaramet, *Rev. Chim.-Bucharest* 65(10) (**2014**) 1172-1175, (FI = 0,810);

17. S*ynthesis, characterization, crystal structure and antimicrobial activity of copper(II) complexes with the schiff base derived from 2-hydroxy-4-methoxybenzaldehyde*, Elena Pahonțu, Diana-Carolina Ilieș, Sergiu Shova, Codruța Paraschivescu, Mihaela Badea, Aurelian Gulea, Tudor Roșu, *Molecules* 20 (**2015**) 5771-5792, (FI = 2,416);

Papers presented at conferences:

1. *Synthése, caractérisation et étude de l΄activitébiologique de nouveaux complexes de Cu (II), Ni (II) et VO (II) avec des bases de Schiff dérivées de l'indole-3-carboxaldehida,* Tudor Roşu, Elena Pahonţu, Diana-Carolina Ilieş, Raluca Ioana Stefan-van Staden, Mirea Leabu, Aurelian Gulea; 1^er^Colloque Franco-Roumain de Chimie Medicinale, Iași, România, 7 - 8 Octombrie 2010, p.184, lucrare poster;

2. *Synthesis, characterization, crystal structures of Ni(II), Pd(II) and Cu(II) complexes with 2-furaldehyde 4-phenylthiosemicarbazone,* Tudor Roșu, Diana-Carolina Ilieș, Elena Pahonțu, Rodica Georgescu, Sergiu Shova, Sesiunea de comunicări științifice studențești - ediția a VII-a, Facultatea de Chimie, Universitatea din București, 20 mai 2011, prezentare orală;

3. *Complexes of Ni(II), Pd(II) and Cu(II) with 2-furaldehyde-N(4)-phenyl thiosemicarbazone.* Tudor Roșu, Elena Pahontu, Diana-Carolina Ilieş, Rodica Georgescu, Sergiu Shova, Prioritățile chimiei pentru o dezvoltare durabilă – Priochem ediția a VII-a, București, Romania, 27 - 28 octombrie 2011; prezentare orală;

4. *Synthesis, characterization and antioxidant activity of Co(II) and Cu(II) complexes with 3-formyl-6-methyl-chromone 4-phenylthiosemicarbazone,* Diana-Carolina Ilieş, Rodica Georgescu, Valeria Rădulescu, Sergiu Shova, Tudor Roșu, Sesiunea de comunicări științifice studențești - ediția a VIII-a, Facultatea de Chimie, Universitatea din București, 18 mai 2012, prezentare orală;

5. *Synthesis, structural and spectral studies of Cu(II) and V(IV) complexes of a novel Schiff base derived from pyridoxal. Antimicrobial activity*, Ștefana Mezey Reka, Elena Pahonțu, Diana Carolina Ilieş, Sergiu Shova, Aurelian Gulea, Tudor Roșu, XVIIth International Conference: Physical methods in coordination and supramolecular chemistry, Chișinău, Republica Moldova, 24 - 26 Octombrie 2012, p. 151, lucrare poster;

6. *Synthesis, characterization, crystal structures of Ni(II), Pd(II) and Cu(II) complexes with 2-furaldehyde-4-phenylthiosemicarbazone,* Diana-Carolina Ilieș, Elena Pahonțu, Ștefana Mezey Reka, Sergiu Shova, Aurelian Gulea, Tudor Roșu, XVIIth International Conference: Physical methods in coordination and supramolecular chemistry, Chișinău, Republica Moldova, 24 - 26 Octombrie 2012, p. 117, lucrare poster;

7. *Synthesis, crystal structures and antimicrobial activity of Cu(II), Ni(II) and Pd(II) complexes with Schiff bases derivates from 4-phenylthiosemicarbazide,* Diana-Carolina Ilieș, Elena Pahonțu, Irina Grecu, Sergiu Shova, Rodica Georgescu, Aurelian Gulea, Tudor Roșu, Congresul Universității de Medicină și Farmacie "Carol Davila" București - *Perspective interdisciplinare,* București, Romania, 30 mai - 1 iunie 2013, lucrare poster;

8. *Some new Cu(II) and Ni(II) complexes containing an ONS or NS donor thiosemicarbazone: Synthesis, crystal structures and biological activity,* Elena Pahonțu, Felicia Julea, Diana-Carolina Ilieș, Yurie Chumacov, Valeriu Fala, Doina Drăgănescu, Tudor Roșu, Aurelian Gulea, Congresul UMF „Carol Davila" - Perspective interdisciplinare, București, România, 30 Mai - 1 Iunie 2013, lucrare poster;

9. *Synthesis, characterization and crystal structure of copper (II) complexes with 1,5-bis(thiophenylidene)thiocarbohydrazone*, Diana-Carolina Ilieș, Sergiu Shova, Rodica Georgescu, Nicolae Stănică, Tudor Roșu, The 15th International Conference of Physical

Chemistry - ROMPHYSCHEM 15, București, România, 11 - 13 Septembrie 2013, lucrare poster;

10. *New compounds from hydrazinecarbothioamide and triazole class with potential antioxidant activity*, Ștefania-Felicia Bărbuceanu, Diana Carolina Ilieș, Ioana Șaramet, Valentina Uivaroși, Constantin Drăghici, Valeria Rădulescu, 5th BBBB International Conference, From drug discovery and formulation strategies to pharmacokinetics-pharmacodynamics, Athens, Greece, 26 - 28 Septembrie 2013, lucrare poster;

11. *New copper(II) complexes with 1,5-bis(thiophenylidene)thiocarbohydrazone. Synthesis, characterization and crystal structure,* Diana-Carolina Ilieș, Sergiu Shova, Elena Pahonțu, Aurelian Gulea, Tudor Roșu, The International Conference dedicated to the 55th anniversary from the foundation of the Institute of Chemistry of the Academy of Sciences of Moldova, Chișinău, Republica Moldova, 28 - 30 Mai 2014, lucrare poster;

12. *Copper(II), nickel(II) and palladium(II) complexes with thiosemicarbazone derivated from 4-phenylthiosemicarbazide,* Diana-Carolina Ilieș, Elena Pahonțu, Reka-Ștefana Mezey, Sergiu Shova, Rodica Georgescu, Tudor Roșu, Simpozionul Aniversar "Facultatea De Chimie - 150 de ani de tradiție", București, 14 Iunie 2014, prezentare orală.

13. *New copper(II) complexes with 1,5-bis(thiophenylidene)thiocarbohydrazone*, Diana-Carolina Ilieș, Sergiu Shova, Elena Pahonțu, Aurelian Gulea, Tudor Roșu, INFOINVENT - 2014, București, Romania, 15 - 18 Octombrie 2014;

14. *Synthesis, characterization, crystal structure of copper(II) complexes containing an ON donor Schiff base. Antimicrobial activity,* Elena Pahonțu, Diana-Carolina Ilieș, Sergiu Shova, Codruța Paraschivescu, Mihaela Badea, Aurelian Gulea, Tudor Roșu, 3rd French-Romanian Colloquium on Medicinal Chemistry, Iași, Romania, 30 - 31 Octombrie 2014, lucrare poster.