Ph.D. THESIS SUMMARY

COPPER (II) COMPLEXES WITH AZOMETHINE LIGANDS DERIVED FROM PYRIDOXAL AND FROM 4-AMINOANTIPYRINE

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2018
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The Ph.D thesis „Copper (II) complexes with azomethine ligands derived from pyridoxal and from 4-aminoantipyrine” describes aspects from the coordinative chemistry of the Cu(II) complexes with condensation compounds of pyridoxal, respectively 4-aminoantipyrine as ligands. The selection of these compounds as key elements of the research strategy is due to the structural characteristics and specific biological properties.

The purpose of the thesis is the synthesis and characterization of complexes with azomethine ligands derived from vitamin B₆ (pyridoxal), respectively 4-aminoantipyrine.

The objectives are:
(i) synthesis and structural characterization of the ligands derived from the two biological-active compounds;
(ii) synthesis of complexes derived from these ligands;
(iii) structural and thermal characterization of complexes.

The Ph.D thesis targets three categories of compounds: Cu(II) complexes with pyridoxal-hydrazones, Cu(II) complexes with pyridoxal-thiosemicarbazones and Cu(II) complexes with Schiff bases derived from pyridoxal.

The thesis is structured in two parts. Chapter I and II belong to the first part and present a wide image of the current status of the thesis theme. The second part, Chapters III, IV, V and VI, bring original, valuable contributions in the thesis field. The thesis ends with General conclusions and Annexes.

Chapter I „Complexes with various azomethine ligands derived from vitamin B₆„, describes aspects related to the chemistry of interconvertible forms of vitamin B₆, specifically to the form pyridoxal. The main research directions in the field of chemistry and biochemistry of the pyridoxal refer to its involvement in the metabolism of the aminoacids [12, 14-17], the role of co-enzyme [22] and the antioxidant capacity [28, 29]. Many of the biological transformations which involve pyridoxal are possible due to its interaction with molecules with amine function, resulting the azomethine compounds. The compounds resulting from the interaction of azomethine compounds with metal ions are the first structural models of complexes with azomethine ligands derived from pyridoxal [37-39].

Complexes with some metal ions with hydrazones and thiosemicarbazones derived from pyridoxal are discussed. The main discussed aspects are the coordination mode, the tautomerism before and after coordination, the geometry and the biological properties of the complexes.

Pyridoxal-hydrazones coordinate in a bi-, tri- or polydentate manner. Hidrazones derived from hydrazines coordinate via at least two donor atoms: the azomethine nitrogen and
the hydroxyphenol oxygen of the pyridine ring in the pyridoxal moiety. In case of the pyridoxal-hydrazones derived from hydrazides the coordination sphere is supplemented with an oxygen atom. Pyridoxal-N-acyl-hydrazones participate to the keto-enol tautomer equilibrium, being able to coordinate to the metal ions in neutral, mononegative or dinegative form [47, 50-56].

In the majority of the cases the pyridoxal-thiosemicarbazones coordinate in a similar way, the only difference is that the hydrazonic oxygen is replaced by the sulfur atom and the tautomer equilibrium is a thiol-thione one [69-71].

The geometry of the complexes is influenced by both properties of the metallic ion and the ligand’s structure due to the number and type of donor atoms. We can observe a significant versatility among the complexes with pyridoxal-hydrazones and pyridoxal-thiosemicarbazones; square-planar, tetrahedral, octahedral or square-pyramidal complexes have been reported.

The ligands derived from pyridoxal and their complexes have antioxidant [85], antibacterial [102], antitumoral [78] effects and have an important role in the treatment of diabetes complications [95].

The second chapter „ Complexes with azomethine ligands derived from 4-aminoantipyrine „ describes aspects related to the chemistry of Schiff bases derived from 4-aminoantipyrine and their complexes. 4-aminoantipyrine is specific among the pyrazolones because the pyrazolonic fragment is completely substituted which imprint specific electronic and structural properties with an impact on the coordination manner.

Due to the amino group at the atom C4 4-aminoantipyrine has a remarkable potential of derivatization by condensation with carbonyl compounds. Mono Schiff bases derived from 4-aminoantipyrine [8, 13] as well as bis Schiff bases derived from 4-aminoantipyrine [16-18] were synthesized. Those ligands were further used for the synthesis of the complexes. The common coordination manner is ON [12, 20] in which case the ligand coordinates via the azomethine nitrogen and the exocyclic oxygen. Depending on the molecular structure of the carbonyl compound the coordination sphere can be extended resulting the tridentate ONO complexes [7]. In case of complexes with bis Schiff bases derived from 4-aminoantipyrine the specific coordination mode is OONN [16, 17]. Despite rarely reported, have been described also compounds with a special coordination mode, for example the metal ion does not interact with the exocyclic oxygen [8] or with the imine nitrogen [24, 2] or when the metal ion is pentacoordinated NNOOS [18].
Among the applications of Schiff bases derived from 4-aminoantipyrine and their complexes we can mention the antimicrobial [11], antifungal [16], antioxidant [8] properties, as well as their role in understanding the interaction mechanisms with the DNA [8, 11, 12].

The second part of the thesis is dedicated to the original contributions. The research strategy is focused on the rational development of a serie of ligands with varied structural properties. The gradual modification of some structural parameters (like the volume of the reagents, the steric positioning of some molecular fragments, the number and type of coordination sites) has a direct impact on the geometry of the complexes. By using different copper(II) salts the influence of the anion of the metal salt on the geometry of the complexes was evaluated.

Chapter III „Cu(II) complexes with hydrazones derived from pyridoxal„, describes four classes of complexes prepared by using the ligands L¹-L⁴ (fig. III.1).

The ligands pyridoxal-phenylhydrazone (L¹) and pyridoxal-2,4-dinitrophenylhydrazone (L²) are similar, consequently we can observe some similarities also among the structures of their complexes. The azomethine compounds were characterized by spectral analyses, like IR, ¹H-RMN, ¹³C-RMN spectroscopy and electrospray ionization-mass spectrometry (ESI-MS). The structure of the ligand was solved by single crystal X-ray diffraction. The crystalline molecular structure (fig. III.4) consists of a protonated ligand L¹ and a perchlorate anion. The perchlorate anion generates additional interactions in the crystal (fig. III.5). Each perchlorate ion interacts with 3 ligand molecules via hydrogen bonds Nₚrídina-H···O, Nₕidrazinic-H···O, O₂-H···O.
A bidimensional structure is formed due to the perchlorate ion and its interactions with the ligand L₁ (fig. III.6).

Using the ligands L₁ and L² I prepared 8 Cu(II) complexes. The synthesis was repeated and different metal salts were used: CuCl₂·2H₂O, Cu(OAc)₂·H₂O, Cu(NO₃)₂·3H₂O și CuSO₄·5H₂O.

The bidentate coordination mode of both ligands was confirmed by comparing the IR spectra of complexes and ligands. The ligands coordinate similarly via the azomethine nitrogen and the deprotonated hydroxyphenol group.

Because of the different metal salts used for the synthesis we can observe different geometries of the complexes C¹-C⁴ (fig. III.15). The complex C¹ has a distorted octahedral geometry [46]. Besides the two donor atoms of the ligand the coordination sphere is supplemented by a chloride ion and three water molecules. The complexes C² and C³ are similar in regards to the coordination number and the tetrahedral geometry. Complex C4 is tetrahedral as well. Still, it is different than the previous ones as it is dinuclear, the sulphate ion coordinating bidentate.
Among the complexes C\textsuperscript{5}-C\textsuperscript{8} derived from ligand L\textsuperscript{2} we can not observe a significant influence of the contra-anion of the metal salt on the geometry of the complexes. All the four complexes are mononuclear and the coordination number is 4. In regards to the coordination sphere the tetracoordination of the complexes C\textsuperscript{5} și C\textsuperscript{8} is ensured by two molecules of ligand per each Cu\textsuperscript{2+}, in a square-planar surrounding. In case of complex C\textsuperscript{7} the coordination sphere is supplemented by the two oxygen atoms of the nitrate ion coordinated bidentate [34]. For complex C\textsuperscript{6} the unidentate coordination mode of the acetate ion is emphasized by the specific bands in the IR spectra [34] while in the forth position a water molecule is present.

![Figure III.15. Structures of the Cu(II) complexes with ligands L\textsuperscript{1} și L\textsuperscript{2}](image)

The ligands pyridoxal-3-hydroxy-benzohydrazone (L\textsuperscript{3}) and pyridoxal-isonicotinoyl hidrazone (L\textsuperscript{4}) are different as an additional donor atom is introduced: then oxygen atom of the hydrazonic fragment. These ligands derive from the condensation of pyridoxal with hydrazides and they possess three coordination sites: the azomethine nitrogen, the oxygen atom of the hydroxyphenol group and the hydrazonic oxygen. Consequently, there are formed two chelate rings of five, respectively six atoms which imprint stability to the complex molecule. The hydrazonic fragment can participate to the \textit{keto-enol} tautomer equilibrium described in figures III.28 (L\textsuperscript{3}) and III.40 (L\textsuperscript{4}) [19b]. The IR, \textsuperscript{1}H-RMN și \textsuperscript{13}C-RMN spectra emphasize the \textit{keto} form in both solid state and in solution.

![Figure III.28. Tautomer equilibrium for ligand L\textsuperscript{3}](image)
The crystalline structure of the ligand pyridoxal-isonicotinoyl hydrazine consists of hydrochloride units H₄L⁴Cl and DMSO molecules, ratio 1:2 (fig. III.37). For each H₄L⁴Cl unit there are two additional DMSO molecules used as crystallization solvent. Multiple hydrogen bonds are formed: O-H···Cl, O-H···N, N-H···Cl, N-H···O și C-H···O.

The presence and the influence of the hydrochloride and DMSO molecules is very important in regards to the stabilized supramolecular structure in the crystal. The packing of the molecules describes a parallel distribution of the H₄L⁴Cl units generating layers interconnected via the hydrogen bonds. The crystal cohesion is supported by the π-π stacking interactions as well. The distance between the centroids Cg1 și Cg1’ of the centro-symmetric units formed by the aromatic rings C1/C2/C3/C4/N1/C5 of two parallel ligand molecules is 4.039 Å. The supramolecular motif in the H₄L⁴Cl crystal is supported by the parallel packing of the „column-type” architectures (fig. III.38) [67].

Using the ligand L³ the complexes C⁹-C¹² (fig. III.32) were prepared and characterized by IR, UV-Viz and EPR spectroscopy. The electronic spectra as well as the EPR spectra recorded on polycrystalline powder at room temperature for complexes C⁹ and C¹⁰ indicates an octahedral geometry [46]. The hexacoordination is ensured by the ligands’s donor atoms ONO, two water molecules and a chloride, respectively acetate anion. The complexes C¹¹ și C¹² are square-planar with the forth coordinative position occupied by monodentate nitrate ion, respectively a water molecule. The lack of the signal at half field (aproximative 1600 G) confirms that the complexes are mononuclear.
The complexes $C^{\text{13}}$-$C^{\text{17}}$ were prepared by coordination of the ligand $L^4$ to the $\text{Cu}^{2+}$ ion originating from various metal salts. The structures described in figure III.42 were proposed based on the holistic interpretation of the results provided by several techniques.

These complexes emphasize the influence of the anion from the metal salt on the geometry of the complexes. In order to be able to propose the geometry of the complexes we recorded the electronic and X-band EPR spectra (fig. III.47, III.48). The bands recorded in the electronic spectra, as well as the values of the parameter $g$, indicate the octahedral geometry of the complexes $C^{\text{13}}$ și $C^{\text{17}}$ [46, 76, 77, 83]. Moreover, the effective magnetic moments ($\mu_{\text{eff}} = 1.7 \text{ MB}$ for $C^{\text{13}}$ and $\mu_{\text{eff}} = 1.8 \text{ MB}$ for $C^{\text{17}}$) are similar to 1.73 MB which is specific to an unpaired spin in an octahedral surrounding [78]. Still, we can observe differences in regards to the coordination sphere. While for complex $C^{\text{13}}$ the coordination number six is ensured by the three ligand’s donor atoms, a chloride anion and two water molecules, in case of complex $C^{\text{17}}$ the metal ion is surrounded by two ligands. The complexes $C^{\text{14}}$ and $C^{\text{16}}$ are square-planar [58], the tetracoordination being ensured by the acetate and nitrate ions coordinated in a

Figure III.32. Structures of Cu(II) complexes with ligand $L^3$

Figure III.42. Structures of Cu(II) complexes with ligand $L^4$
monodentate manner. The UV-Viz and EPR spectral data indicates for complex C\textsuperscript{15} a tetrahedral geometry, characterized by a lower simetry [46].

![Figure III.47. EPR spectra recorded on microcrystalline powder for complexes C\textsuperscript{13}-C\textsuperscript{17}](image)

![Figure III.48. Simulated EPR spectra for complexes C\textsuperscript{13}-C\textsuperscript{17}](image)

The space group and crystal system, as well as the crystallographic parameters for complexes C\textsuperscript{13}-C\textsuperscript{17}, were identified by microcrystalline powder X-ray diffraction. Both complexes C\textsuperscript{13} and C\textsuperscript{17} share the triclinic system, space group P 1. The crystal system for complexes C\textsuperscript{14} and C\textsuperscript{16} is monoclinic. This time the compounds have different space groups: I 1 c 1 for C\textsuperscript{14} and P 1 21 1 for C\textsuperscript{16}. The crystallographic parameters for complex C\textsuperscript{15} are different compared with the previous ones; the crystal system is hexagonal and the space group is P 6\textsubscript{5}.

The thermal behavior of the complexes with pyridoxal-hydrazones L\textsuperscript{1}-L\textsuperscript{4} was evaluated as well. By heating the samples within a large temperature range (30-900 °C) we obtained a wide picture of the decomposition pattern and the eliminated fragments. At lower temperatures the thermogravimetric curves emphasize the elimination of the fragments outside the coordination sphere, afterwards the small, coordinated fragments are eliminated; at higher temperatures we can observe an advanced thermal degradation of the complex molecule.

The class of complexes derived from L\textsuperscript{4} was selected for the purpose of the antimicrobial studies. In order to obtain the antimicrobial spectrum the qualitative and quantitative action of each compound on four pathogenic strains was conducted: *Escherichia coli* W3110, *Pseudomonas aeruginosa* ATCC 9027, *Staphilococcus aureus* var. *Oxford* ATCC 6538 și *Bacillus cereus* ATCC 14579. The values of the minimum inhibitory concentration (MIC) emphasize the enhanced antimicrobial activity of the complexes compared to the ligand; namely 8 to 16 time higher (table III.17). In this way it is emphasized the importance of the coordination and the influence of the metal ion for the enhancement of the biologic effect. The antimicrobial effect follows the descending order: C\textsuperscript{13} = C\textsuperscript{14} = C\textsuperscript{16} (MIC=64 μg/mL...
against \textit{S. aureus}, \textit{B. cereus}, \textit{P. aeruginosa} and MIC=128 \(\mu\)g/mL against \textit{E. coli}) > C^{15} (MIC=64 \(\mu\)g/mL against \textit{S. aureus}, \textit{B. cereus} and MIC=128 \(\mu\)g/mL against \textit{E. coli}, \textit{P. aeruginosa}) > C^{17} (MIC=128 \(\mu\)g/mL against \textit{S. aureus}, \textit{B. cereus}, \textit{E. coli}, \textit{P. aeruginosa}). Comparing to the antibiotics used as standards an important effect is reported in case of C^{13}, C^{14} and C^{16}; these register a MIC value of 64 \(\mu\)g/mL against \textit{P. aeruginosa} and \textit{B. cereus}, 8 times lower than for ampicillin [67].

\textbf{Tabel III.17. MIC (\(\mu\)g/mL) for L^4, C^{13-17}, antibiotics used as standards and solvents}

<table>
<thead>
<tr>
<th>Compus</th>
<th>\textit{B. cereus} ATCC 14579</th>
<th>\textit{S. aureus var. Oxford} ATCC 6538</th>
<th>\textit{P. aeruginosa} ATCC 9027</th>
<th>\textit{E. coli} W3110</th>
</tr>
</thead>
<tbody>
<tr>
<td>L^4</td>
<td>1024</td>
<td>1024</td>
<td>1024</td>
<td>1024</td>
</tr>
<tr>
<td>C^{13}</td>
<td>64</td>
<td>64</td>
<td>64</td>
<td>128</td>
</tr>
<tr>
<td>C^{14}</td>
<td>64</td>
<td>64</td>
<td>64</td>
<td>128</td>
</tr>
<tr>
<td>C^{15}</td>
<td>64</td>
<td>64</td>
<td>128</td>
<td>128</td>
</tr>
<tr>
<td>C^{16}</td>
<td>64</td>
<td>64</td>
<td>128</td>
<td>128</td>
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<td>C^{17}</td>
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<td>128</td>
<td>128</td>
<td>128</td>
</tr>
<tr>
<td>Ampicillin</td>
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<td>resistant</td>
<td>2</td>
</tr>
<tr>
<td>Kanamycin</td>
<td>8</td>
<td>4</td>
<td>256</td>
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<tr>
<td>Streptomycin</td>
<td>64</td>
<td>32</td>
<td>256</td>
<td>1</td>
</tr>
<tr>
<td>Pyridine</td>
<td>1024</td>
<td>1024</td>
<td>1024</td>
<td>1024</td>
</tr>
<tr>
<td>DMSO</td>
<td>1024</td>
<td>1024</td>
<td>1024</td>
<td>1024</td>
</tr>
</tbody>
</table>

Chapter IV „\textit{Cu(II) complexes with thiosemicarbazones derived from pyridoxal}„, describes the compounds pyridoxal-4-phenyl-3-thiosemicarbazone (L^5) and pyridoxal-4-benzyl-3-thiosemicarbazone (L^6) and their nine complexes. The formation of the two thiosemicarbazones is confirmed by means of IR, \textit{\textsuperscript{1}H-RMN, \textit{\textsuperscript{13}C-RMN spectroscopy and ESI-MS.} Both L^5 and L^6 stabilize the thione tautomer [10].

By using the ligands L^5 and L^6 we prepared two classes of Cu(II) complexes: [CuL^5\textit{Cl}] (C^{18}), [CuL^5\textit{(OAc)(H_2O)}] (C^{19}), [CuL^5\textit{(ONO_2)}] (C^{20}), [CuL^5\textit{(H_2O)_2}SO_4] (C^{21}), [CuL^5\textit{(OAcac)}] (C^{22}), [Cu_2(HL^6)_2Cl_2] (C^{23}), [CuL^6\textit{(OAc)}] (C^{24}), [CuL^6\textit{(ONO_2)}] (C^{25}), [Cu(L^5)_2] (C^{26}). In regards to the coordinating fragment there is no difference between the two compounds. The difference is related to the increase of the thiosemicarbazide’s volume because of the methylene fragment -C^{17}H_2-. Although this is not probable to generate variations in regards to the coordination number and geometry of the complexes it is probable to induce steric hindrances. Moreover, this saturated, hydrophobic fragment can influence the physical properties of the complexes, their thermal behavior or their applications.

The structures of the complexes derived from ligands L^5 and L^6 as depicted in figure IV.15 were proposed based on the results provided by several analytical techniques (ESI-MS, IR, UV-Viz spectrometry and single crystal X-ray diffraction – for complexes C^{18} and C^{23}).
A modern method applied for the characterization of coordinative compounds which was used in case of complexes $C^{19}$-$C^{22}$ and $C^{24}$-$C^{26}$ is the mass spectrometry. It was useful to emphasize the formation of the chelates. The ESI-MS spectra for complexes $C^{19}$ (fig. IV.16), $C^{20}$, $C^{21}$ depict a signal corresponding to the molecular ion $[\text{CuL}_{5}]^+$, while the mass spectra for compounds $C^{24}$ (fig. IV.19), $C^{25}$, $C^{26}$ depict a signal at $m/z$ 392.3 which corresponds to the molecular ion $[\text{CuL}_{6}-\text{H}]^+$.

Despite the two ligands are structurally similar we can remark a high diversity among the complexes geometries. The complexes derived from ligand L$^5$ has square-pyramidal ($C^{19}$, $C^{21}$), square-planar ($C^{18}$, $C^{22}$) and tetrahedral ($C^{20}$) geometries [40, 41]. As the coordination mode is identical (ONS) the differences among the geometries are driven by the participation in the coordination sphere of the donor atoms of the anions from the metal salts and/or the water molecules. Thus, we can emphasize the influence of the metal salt on the geometry of the complexes.
The stereochimic variety is visible also among the complexes derived from thiosemicarbazone L\(^6\). They stabilize square-pyramidal (C\(^{23}\)), tetrahedral (C\(^{24}\), C\(^{25}\)) and octahedral (C\(^{26}\)) geometries. As a particularity, in case of C\(^{26}\) the hexacoordination of the Cu(II) is ensured by two ligand molecules per metal ion.

A very interesting aspect is the crystallographic analysis of complexes C\(^{18}\) and C\(^{23}\), obtained by coordination of L\(^5\), respectively L\(^6\) to the Cu\(^{2+}\) ion originating from the copper(II) chloride. The ligand coordination is similar via the same set of donor atoms (S1N3O1 – C\(^{18}\), S1N2O2 - C\(^{23}\)); still, the coordination manner is different.

![Molecular structure of complex C\(^{18}\)](image)

The Cu\(^{2+}\) ion in complex C\(^{18}\) has the coordination number 4 and is square-planar. The structure, as depicted in figure IV.22, consists of one molecule of ligand pyridoxal-4-phenyl-3-thiosemicarbazone and a chloride anion coordinated to the Cu\(^{2+}\) ion and a water molecule.

![Interactions between the complex molecules in the crystal of C\(^{18}\)](image)

The ligand L\(^5\) coordinates in a mononegative form resulted after the deprotonation of hydroxy group; the monopositive charge of the complex is compensated by a coordinated chloride (Cl1). The crystallographic data confirms the thione form of the thiosemicarbazone L\(^5\) post coordination. The bond C7=S1 is 1.735 Å. The interaction between the neighboring molecules of C\(^{18}\) is complex. Each molecule interacts with the neighboring one via three hydrogen bonds: O5-H⋯O1, N1-H⋯O1w, O1w-H⋯O5 (fig. IV.23). The packing in the crystal generates a „chain-type” structure (fig. IV.24).
Complex $C^{23}$ is dinuclear and has a square-pyramidal geometry as described in figure IV.25. The crystal system is monoclinic and the space group is $P2_1/c$.

![Figure IV.25. Molecular structure of dinuclear $[Cu_2(HL)_2Cl_2]^{2+}$ (the chloride ions outside the coordination sphere are not depicted)](image)

The dinuclear structure of $C^{23}$ is supported by the presence of coordinated chloride anions which act as „bridge” between the metal centers. Each chloride anion coordinates to a second $Cu^{2+}$ ion. The coordination number of $Cu^{2+}$ is five and its geometry is square-pyramidal. The ligand $L^6$ keeps its thione form after coordination. The asymmetric unit depicted in figure IV.26 describes a ligand molecule and a chloride anion, both coordinated, as well as a second chloride anion outside of the coordination sphere.

![Figure IV.26. Asymmetric unit in complex $C^{23}$](image)

Complex $C^{23}$ is very interesting in regards to the coordination mode of the ligand to the $Cu^{2+}$ ion. The ligands keeps the neutral form because the hydroxyphenyl group of the pyridine ring is not deprotonated, but participates to the coordination via a $O2 \rightarrow Cu$ bond. Other two coordination sites are occupied by the imine nitrogen $N2$ and the sulfur atom $S1$ which interacts with the metal center via the coordinative bonds $N2 \rightarrow Cu$ and $S1 \rightarrow Cu$. The forth coordination position is occupied by a chloride anion. The monopositive charge is compensated by the chloride anion outside the coordination sphere. The packing of the complex molecules generates a 2D structure (fig. IV.27).
Chapter V, named “Cu(II) complexes with Schiff bases derived from 4-aminoantipyrine” describes three azomethine ligands synthesized by condensation of 4-aminoantipyrine with the aldehydes 4-(dimethylamino)benzaldehyde (L₇), 3-benzyloxy-4-methoxybenzaldehyde (L₈) and 4-acetoxy-3-methoxybenzaldehyde (L₉). All the three imines were characterized by means of ESI-MS, IR spectroscopy, ¹H-RMN, ¹³C-RMN, UV-Viz spectrometry and single crystal X-ray diffraction. The crystallographic analysis emphasize the formation of the new azomethine bond and the spatial arrangement of the main fragments of the molecule (fig. V.5, V.7, V.8). We observe the pyrazolonic ring and the benzaldimine fragments are almost coplanar. On the other hand, the phenyl of the 4-aminoantipyrine moiety and the benzyloxy fragment are deviated outside the plan described by the pyrazolone ring and benzaldimine fragment. Also, in case of L₉ the acetate fragment is almost perpendicular to the aromatic ring from the aldehyde moiety.

The molecular packing in case of L₇ and L₉ is made via multiple hydrogen bonds and π-π stacking interactions (fig. V.6, V.9).
Nine complexes were prepared using the ligands $L^7$ and $L^8$ and various copper(II) salts: CuCl$_2$·2H$_2$O, CuBr$_2$, Cu(OAcac)$_2$, CuSO$_4$·5H$_2$O și Cu(ClO$_4$)$_2$·6H$_2$O. We obtain the complexes $C^{27}$-$C^{31}$ with ligand $L^7$ and complexes $C^{32}$-$C^{35}$ with ligand $L^8$ (fig. V.23). As a common characteristic all the complexes have been formed by coordination of two ligand molecules per each Cu$^{2+}$ ion. The coordination mode, identified based on IR spectral data, is neutral bidentate via the imine nitrogen and oxygen atom of the pyrazolone moiety. We obtained the square-planar complexes $C^{29}$, $C^{30}$ și $C^{34}$. The positive charge of the complexes is compensated by the acetylacetonate ($C^{29}$, $C^{34}$) and sulphate ($C^{30}$) ions. In case of the other complexes the coordination sphere is supplemented, generating complexes with different geometries. The complexes $C^{27}$, $C^{28}$, $C^{31}$ and $C^{32}$ are square-pyramidal due to the coordination of a water molecule in the axial position while the anions chloride, bromide and perchlorate are outside the coordination sphere. Complexes $C^{33}$ and $C^{35}$ are hexacoordinated in an octahedral geometry; the bromide anions ($C^{33}$), respectively the water molecules ($C^{35}$) are located in the axial positions. The presence of small fragments located inside or outside the coordination sphere is emphasized by means of thermogravimetric analysis.
As part of the class of complexes with Schiff bases derived from 4-aminoantipyrine it was prepared a complex in which structure the Cu$^{2+}$ ion originates from an organic salt: copper(II) salicylate. The complex C$^{36}$ obtained by coordination of the known ligand ASAAP [28] to the Cu$^{2+}$ ion originating from the copper(II) salicylate has a distorted octahedral geometry. The single crystal X-ray diffraction emphasizes a „chain-type” structure where the asymmetric units are connected via the salicylate fragment (fig. V.34). The hexacoordination is supported by the three ligand’s donor atoms ONO, two oxygen atoms of the carboxyl group in the organic salt and the oxygen atom of the hydroxy group belonging to the salicylate fragment of a neighboring molecule (fig. V.35).

**Figure V.23.** Proposed structures for complexes C$^{27}$-C$^{35}$

**Figure V.34.** The „chain-type” structure generated by interactions O5'-Cu1 in complex C$^{36}$

**Figure V.35.** Asymmetric unit in complex C$^{36}$
The polynuclear chains are connected via π-π stacking interactions between the pyrazolonic and phenyl fragments in the 4-aminoantipyrine moiety (fig. V.36) resulting a „stair-like” packing (fig. V.37). The „stair-like” units are assembled further via π-π interactions between the phenyl rings in the 4-aminoantipyrine moiety (fig. V.38).

![Figure V.36. π-π interactions in crystal C36](image1)

![Figure V.37. „Stair-like” packing in complex C36](image2)

![Figure V.38. Packing of the „stair-like” units in crystal C36](image3)

The last chapter „Comparative evaluation of the ligands stability and antioxidant effect of some complexes” is related to the properties and applications of the synthesized compounds. The ligands L₁-L₃ and L₅-L₉ were characterized in detail in regards to their thermal stability based on chemiluminescence studies, differential scanning calorimetry and thermogravimetry. The results show that the pyridoxal-hydrazone are less stable to high temperature, the pyridoxal-thiosemicarbazones have an intermediate stability while the Schiff bases derived from 4-aminoantipyrine are the most thermally stable. The thermal stability follows the decreasing order: L⁸ > L⁷ > L⁹ > L² > L¹ > L⁵ > L³ > L⁶. The crystallinity degree for ligands L⁷-L⁹ was evaluated based on the melting enthalpy. The decreasing order of the crystallinity is: L⁹ (ΔHₘ = 307 J/g) > L⁷ (ΔHₘ = 92 J/g) > L⁸ (ΔHₘ = 68 J/g).

The antioxidant effect of the complexes C², C⁶, C¹⁰ and C¹⁹ was determined by comparative evaluation of the stability of ethylen-propylen-terpolymer (EPDM) in the presence and absence of the complexes as protecting agents. The antioxidant effect was quantified with the help of the isotherm chemiluminescence (180 °C) and non-isotherm chemiluminescence studies at 3.7 °C/min, 5.0 °C/min, 10.0 °C/min, respectively 15.0 °C/min. The isotherm studies emphasize significant differences in regards to the antioxidant effect of
the four complexes; it decrease as follows: $C^6 > C^2 > C^{19} > C^{10}$. This is influenced by the ligand and by the electronic particularities of the compounds. The non-isotherm studies emphasize the influence of the heating rate over the evolution of the oxo-degradative process. We can remark that an increase of the heating rate results in a delay of the oxidation process with aproximative 25 °C.
Selective bibliography

Chapter I


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Chapter III


Chapter IV


Chapter V

List of published and presented scientific papers

List of articles in the Ph.D thesis field


List of papers presented at conferences
