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Synthesis and Characterization of Cu(II), Ni(II), Co(II), Mn(II), Zn(II), Cd(II) Complexes of Isonicotinoylhydrazone-1-methyl-2-aldehydepyrrole

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A series of complexes of Cu(II), Ni(II), Co(II), Mn(II), Zn(II), Cd(II) with Isonicotinoylhydrazone-1-methyl-2-aldehydepyrrole (INHMAP) formed by condensation of isonicotinoylhydrazine with 1-methyl-2-aldehydepyrrole has been reported. All the complexes have been characterized by analytical data, IR, UV-VIS, NMR, magnetic susceptibility, thermal analysis and for Cu(II) complex by the ESR spectrum. For all complexes the antimicrobial activity have been tested as for the bacterias *Staphylococcus aureus*, *Escherichia coli* and *Proteus vulgaris*. Experimental data suggest the stoichiometry of 1:2 (metal:ligand) for the complexes of Cu(II), Co(II) and of 1:1 for the complexes of Ni(II), Mn(II), Zn(II), Cd(II). Electronic spectra and magnetic moments suggest octahedral stereochemistry for Cu(II), Co(II), tetrahedral configuration for the complexes of Mn(II), Zn(II), Cd(II) and square-planar geometry to the Ni(II) complex. From IR spectra results, it is concluded that the INHMAP ligand is coordinated at the metalic ions by oxygen amide (C=O) and the azomethine nitrogen.

Key Words: Template synthesis, Isonicotinoylhydrazone, Metal complexes, Azomethine group.

INTRODUCTION

The heterocyclic chemistry offers the results of the researches show a lot of bioactive substances. The parametres of the chemical structure, the physical and electronical characteristics of the molecule are determined factors in the manifestation of the bioactivity. A large number of complexes of the transition metals with the aroylhydrazone ligands present biological and pharmaceutical activities the antibacterial, antitumor, fungicide, antioxidative activities[1-3]. Complex formation of Ni(II) and Mn(II) with the isonicotinoylhydrazone-α-pyridinealdehyde manifest an antitubercular activity[4]. Mitu *et al.*[5] reported the preparation and characterization of the complexes of some transitional metals with the isonicotinoylhydrazone-2-aldehydepyrrole ligand. As regard the biological importance of the complex formations with ligands from the isonicotinoylhydrazone class, in this paper it is presented the synthesis and the study of the complexes of Cu(II), Ni(II), Co(II), Mn(II), Zn(II), Cd(II) with the isonicotinoylhydrazone-1-methyl-2-aldehydepyrrole.

EXPERIMENTAL

All reagents and solvents used are of AR grade and were used without further purification. The metal content and chlorine was obtained by the literature methods[6] and carbon, hydrogen and nitrogen were determined with an analyzer CHN-Hewlett Packard-185. The IR spectra were recorded between 4000-400 cm^{-1} on a BIORAD-FT-IR 135 FTS spectrophotometer in a disc of anhydrous KBr. The electronic spectra in reflection (300-1100 nm) were obtained on a VSU-2P Zeiss-Jena spectrophotometer using MgO as a standard. The ESR spectrum for the Cu(II) complex were registered at room temperature (293 K) on a microcrystalline powder with an ART-5 spectrophotometer. The magnetic moments were determined by the Faraday method at the room temperature. ^1H and ^{13}C NMR spectra were recorded on a device Varian Gemini 300 BB in DMSO-d_6. The molar conductivity for the complexes of Mn(II) and Zn(II) were measured with a HACH-sens ion 5-conductivity meter to the solutions in 10^{-3} M DMF. The thermal analysis was done on MOM-Q-1500 D derivatograph in air with a heating rate of 5ºC/min. The biological activity of the complexes was studied by the diffusion technique in agar plates using DMF as solvent at the concentration of 200 µg/mL.

Synthesis of hydrazone ligand: The INHMAP (HL) ligand was synthesized in the laboratory by the following method. To the methanolic solution of isoniazide (0.002 mol INH in 30 mL MeOH) was added, a methanolic solution of 1-methyl-2-aldehydepyrrole (0.002 mol MAP in 30 mL MeOH). The resulting solution was refluxed for 5 h on a waterbath after which it was concentrated to less than half of its initial volume. The precipitated hydrazone was filtered under vacuum, it was washed with methyl alcohol and then with ether and dried in vacuum on anhydrous $CaCl_2$ (Fig. 1).

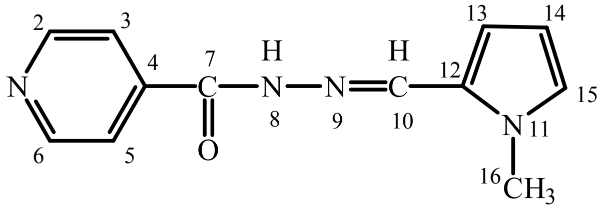

Fig. 1. Isonicotinoylhydrazone-1-methyl-2-aldehydepyrrole ($C_{12}H_{12}N_4O$) (INHMAP = HL)

% Analysis, Calculated for $C_{12}H_{12}N_4O$: C, 63.15; H, 5.26; N, 24.56. Found: C, 62.90; H, 5.02; N, 24.34. The colour of ligand is light-yellow. Melting point is 213-215ºC.

Synthesis of the metal complexes: A methanolic solution of the corresponding metal chloride (0.004 mol in 25 mL MeOH) was added to a mixture of isonicotinoyl-hydrazine (0.004 mol INH in 40 mL MeOH) and 1-methyl-2-aldehydepyrrole (0.004 mol MAP in 40 mL MeOH). The reaction mixture was refluxed on a water-bath for 3 h, after which a part of the solvent was removed by distillation. The precipitated complexes were filtered, washed with methyl alcohol and then with ether and finally dried in vacuum on anhydrous $CaCl_2$.

% Analysis, Calculated for $[Cu(HL)_2Cl_2]$: Cu, 10.75; C, 48.76; H, 4.06; N, 18.96; Cl, 12.02; Found: Cu, 10.54; C, 48.54; H, 3.83; N, 18.74; Cl, 11.79. Calculated for $[Ni(HL)Cl_2]\cdot 0.5H_2O$: Ni, 16.00; C, 39.27; H, 3.54; N, 15.27; Cl, 19.36; Found : Ni, 15.79; C, 39.04; H, 3.32; N, 15.06; Cl, 19.13. Calculated for $[Co(HL)_2Cl_2]\cdot H_2O$: Co, 9.75; C, 47.68; H, 4.30; N, 18.54; Cl, 11.75; Found : Co, 9.54; C, 47.46; H, 4.09; N, 18.34; Cl, 11.54. Calculated for $[Mn(HL)Cl_2]\cdot H_2O$: Mn, 14.76; C, 38.71; H, 3.76; N, 15.05; Cl, 19.08; Found: Mn, 14.57; C, 38.50; H, 3.55; N, 14.86; Cl, 18.89. Calculated for $[Zn(HL)Cl_2]$: Zn, 17.94; C, 39.51; H, 3.29; N, 15.36; Cl, 19.48; Found: Zn, 17.73; C, 39.32; H, 3.08; N, 15.17; Cl, 19.27. Calculated for $[Cd(HL)Cl_2]$: Cd, 27.32;C, 35.00; H, 2.91;N, 13.61;Cl, 17.25; Found: Cd, 27.13; C, 34.79; H, 2.72; N, 13.42; Cl, 17.04.

RESULTS AND DISCUSSION

All the sytnthesized metal complexes are microcrystalline powders by different colours, stable for a long time with high melting points. The complexes are insoluble in methyl alcohol, ethyl alcohol, chloroform and acetone. The complexes of Mn(II) and Zn(II) are solubles in DMF and others complexes are partly solubles in this solvent.

The analytical data indicate a stoichiometry 1:2 (metal:ligand) for the complexes of Cu(II), Co(II) and of 1:1 for the complexes of Ni(II), Mn(II), Zn(II), Cd(II) (Table-1). In the case of the complexes of Mn(II) and Zn(II) the molar conductivity present low values and this fact suggests an non-electrolytic nature of these complexes.

IR spectral bands are presented in the Table-2. In the ligand, spectrum ν(NH) vibration from the amide group is located at 3195 cm^{-1}. The amide band I is situated at 1673 cm^{-1} and the band at 1617 cm^{-1} is assigned to the vibration corresponding to the azomethine group[7]. The amide band II δ (NH) is present at 1572 cm^{-1}. For ligand the weak absorption at 604 cm^{-1} is associated to the deformation vibration in plane, β'' for the pyridinic ring. IR spectra of the complexes of Ni(II), Co(II), Mn(II) contain a broad band

TABLE-1
ANALYTICAL AND PHYSICAL DATA OF THE COMPLEXES*

Compounds	m.p. (ºC)	Colour	μ_{eff} (BM)	Λm† (Ω^{-1} cm^2 mol^{-1})
[Cu(HL)$_2$Cl$_2$]	235	Dark green	1.84	–
[Ni(HL)Cl$_2$]·½H$_2$O	> 350	Orange	Diamagnetic	–
[Co(HL)$_2$Cl$_2$]·H$_2$O	242	Brown	4.98	–
[Mn(HL)Cl$_2$]·H$_2$O	318	Yellow	5.89	10.61
[Zn(HL)Cl$_2$]	292	Yellow	–	11.83
[Cd(HL)Cl$_2$]	> 350	Light yellow	–	–

*All complexes provide satisfactory metal, as well as C, H, N, Cl analyses.
†10^{-3} M solution in DMF.

TABLE-2
CHARACTERISTIC IR (cm^{-1}) BANDS OF METAL COMPLEXES

Compounds	ν(OH) water	ν(NH) INH	ν(C=O) Amide I	ν(C=N)	δ(NH) Amide II	β ring Py in plane	ν(M-N)
INHMAP (HL)	–	3195	1673	1617	1572	604	–
[Cu(HL)$_2$Cl$_2$]	–	3097	1600	1572	1518	601	446
[Ni(HL)Cl$_2$].1/2H$_2$O	3407	3094	1603	1573	1519	600	450
[Co(HL)$_2$Cl$_2$].H$_2$O	3426	3101	1602	1570	1523	605	453
[Mn(HL)Cl$_2$].H$_2$O	3415	3091	1615	1542	1492	596	437
[Zn(HL)Cl$_2$]	–	3069	1603	1541	1491	604	425
[Cd(HL)Cl$_2$]	–	3055	1654	1607	1542	602	424

situated in the range 3426-3407 cm^{-1}; this band is associated to the lattice water from the composition of these complexes[8]. The imido ν(NH) frequency appears in the region 3101-3055 cm^{-1} and as cosequence the amide group does not changed its structure during the coordination. The amide I vibration shift towards lower values and as a result the hydrazone ligand is coordinated to the metal ions by mean of the amide oxygen (O=C). The azomethine frequency band ν(C=N) is found to the lower values suggests the azomethine nitrogen coordination in all the complexes. The amide band II δ(NH) presents a negative variation. The deformation in plane for the pyridinic ring is found at close values from that of free ligand and thus suggests that the nitrogen from the pyridinic ring is not involved in the coordination[9]. The fact that the ligand is coordinated to the metal ions by the azomethine nitrogen is confirmed by ν(M-N) vibrations which are present in the range 453-424 cm^{-1} and are not present in the spectrum of the free ligand.

The INHMAP ligand formation is confirmed by the singlet from δ 8.39 ppm assigned to the azomethine proton (-N=CH-) in ^{1}H NMR spectrum but also by the peak from δ 142.16 ppm associated to the azomethine carbon in the ^{13}C NMR spectrum. Beside these values in the ^{1}H NMR spectrum of the ligand show signal to δ 11.30; δ 8.78; δ 6.12; δ 3.87 ppm assigned to the protons amide (-NH-)[8], H-2,6 pyridine, H-15 pyrrole, 3H-16 methylpyrrole and also peaks in the ^{13}C NMR spectrum to δ 155.31; δ 149.801; δ 128.48; δ 115.12 ppm corresponding to the following atoms of carbon:amide-7; C-2,6 pyridine, C-12 pyrrole, C-15 pyrrole. In ^{1}H NMR spectra of the complexes of Zn(II), Cd(II) the signals of the protons (-NH-)[8] amide and azomethine shift with 0.51; 0.50 ppm and respectively 0.35; 0.34 ppm result which sustain the coordination of the ligand by the amide oxygen O=C and the azomethine nitrogen. The signals of the atoms of carbon C-7 and C-10 in the ^{13}C NMR spectra present shifts of 5.29; 9.14 ppm, respectively 5.82; 5.16 ppm and pointed clearly the involvement of the atoms of amide oxygen and azomethine nitrogen in coordination. The atoms of carbon C-2,6 have signals in the same region of the spectrum and the shift is very small Δ = 0.283; 0.482 ppm and in this way is confirmed that the pyridinic nitrogen is not involved in the coordination. For the pyrrole ring the positions C-12,15 give insignificant variations Δ = 0.08; 0.09 ppm, respectively Δ = 0.05; 0.06 ppm result demonstrates that the nitrogen of the pyrrole ring is not coordinated to the metal ions.

The electronic spectra and the magnetic moments (Table-3) support the stereochemistry of the complexes. The INHMAP ligand present in the electronic spectrum an absorption band at 27027 cm^{-1} (370 nm) assigned to the transition $n \rightarrow \pi^*$. This transition is found again in the spectra of the complexes but shifted towards lower frequencies which confirm the coordination of the ligand to the metal ions.

The Cu(II) complex presents a broad band at 14705 cm^{-1} (680 nm) which correspounds to the transition $^2E_g \rightarrow {}^2T_{2g}$ and from the results an octahedral configuration for this complex[10]. The transition is located towards lower frequencies proposed an octahedral structure. The experimental data present a magnetic moment of 1.84 BM and this value sustain a monomeric octahedral geometry.

For the Ni(II) complex, two absorption bands appeared at 16949 cm^{-1} (590 nm) and 21739 cm^{-1} (460 nm). These bands could be assigned to the transitions $^1A_{1g} \rightarrow {}^1A_{2g}$ and $^1A_{1g} \rightarrow {}^1B_{1g}$ which characterize the Ni(II) ion in the square-planar stereochemistry. The diamagnetism of the complex confirms this symmetry.

In the spectrum of Co(II) complex, the bands at 10101 cm^{-1} (990 nm) and 19607 cm^{-1} (510 nm) are associated to the transitions $^4T_{1g} \rightarrow {}^4T_{2g}(F)$ (ν_1), respectively $^4T_{1g} \rightarrow {}^4T_{1g}(P)$ (ν_2). These transitions are specified to the Co(II) ion in the field of octahedral symmetry and the magnetic moment of 4.98 BM corresponds to this geometry.

TABLE-3
REFLECTION SPECTRA FOR THE LIGAND AND COMPLEXES

Compounds	Frequencies (cm^{-1})	Assigning
INHMAP (HL)	27027	$n \rightarrow \pi^*$
$[Cu(HL)_2Cl_2]$	23809 14705	$n \rightarrow \pi^*$ $^2E_g \rightarrow {}^2T_{2g}$
$[Ni(HL)Cl_2] \cdot ½H_2O$	24390 21739 16949	$n \rightarrow \pi^*$ $^1A_{1g} \rightarrow {}^1B_{1g}$ $^1A_{1g} \rightarrow {}^1A_{2g}$
$[Co(HL)_2Cl_2] \cdot H_2O$	24096 19607 10101	$n \rightarrow \pi^*$ $^4T_{1g} \rightarrow {}^4T_{1g}(P)$ $^4T_{1g} \rightarrow {}^4T_{2g}(F)$
$[Mn(HL)Cl_2] \cdot H_2O$	25641 22727	$n \rightarrow \pi^*$ CT
$[Zn(HL)Cl_2]$	25641 24271	$n \rightarrow \pi^*$ CT
$[Cd(HL)Cl_2]$	25974 24691	$n \rightarrow \pi^*$ CT

The magnetic moment value of Mn(II) complex is of 5.89 BM suggesting a tetrahedral structure for this complex.

From the electronic spectra of the Zn(II) and Cd(II) complexes, one can not propose the exact geometry of the metal ions but because in the tetra coordination complex the Zn(II), Cd(II) ions present a tetrahedral configuration is supposed that Zn(II),Cd(II) complexes are tetrahedral.

The Cu(II) complex presents an ESR signal relatively broad and isotropic and the, 'g' parameter have only one value ($g_{isotropic} = 2.1147$). These characteristics are in the favour of a nondeformed octahedral stereochemistry.

Thermal analysis data of the complexes are presented in the Table-4. The Cu(II) complex in the interval from 55-70ºC loss the physically absorbed solvent during the synthesis. For the complexes of Ni(II), Co(II), Mn(II) the lattice water is eliminated in the domain 80-230ºC. All the complexes start to decompose to high temperatures (> 255ºC) and the ligand is lost by steps resulting as stable products the oxides CuO, NiO, Co_3O_4, Mn_2O_3, ZnO, CdO.

On the basis of the obtained results, the Cu(II), Co(II) complexes an octahedral geometry, for the Mn(II), Zn(II), Cd(II) complexes a tetrahedral geometry and for the Ni(II) complex, a square-planar geometry are suggested. The complexes formulations are presented in the Figs. 2-4.

TABLE-4
THERMAL ANALYSIS FOR THE COMPLEX COMBINATIONS

Complex	Total mass losses		Temp. (°C)	Loss (%)
	Theoretical (%)	Experimental (%)		
$[Cu(HL)_2Cl_2]$	77.21	77.58	55-70 70-430 430-615 615-700	3.43 33.27 44.31 13.73 exp./res 13.46 calc./res
$[Ni(HL)Cl_2]\cdot½H_2O$	83.98	84.36	80-150 150-570 570-700	2.64 81.72 20.57 exp./res 20.36 calc./res
$[Co(HL)_2Cl_2]\cdot H_2O$	78.49	79.09	80-230 230-425 425-680 680-700	3.19 42.13 33.77 13.50 exp./res 13.29 calc./res
$[Mn(HL)Cl_2]\cdot H_2O$	75.72	76.28	80-230 230-420 420-625 625-700	5.01 30.92 40.35 21.40 exp./res 21.22 calc./res
$[Zn(HL)Cl_2]$	82.04	82.41	270-460 460-680 680-700	25.18 57.23 22.49 exp./res 22.33 calc./res
$[Cd(HL)Cl_2]$	72.66	73.12	275-405 405-675 675-700	22.38 50.74 31.44 exp./res 31.21 calc./res

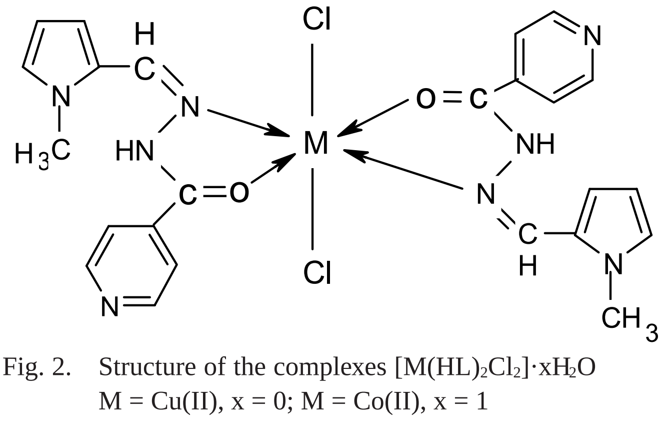

Fig. 2. Structure of the complexes $[M(HL)_2Cl_2]\cdot xH_2O$
M = Cu(II), x = 0; M = Co(II), x = 1

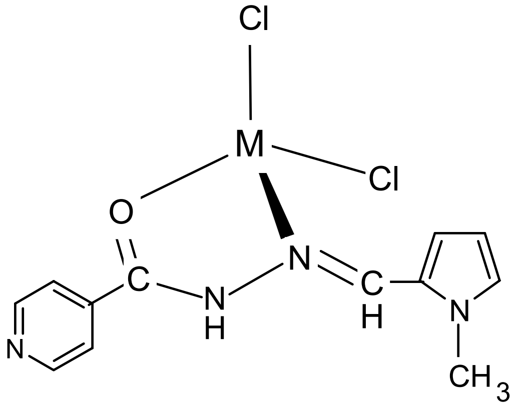

Fig. 3. Structure of the complexes $[M(HL)Cl_2]\cdot xH_2O$
$M = Mn(II)$, $x = 1$; $M = Zn(II)$, $Cd(II)$, $x = 0$

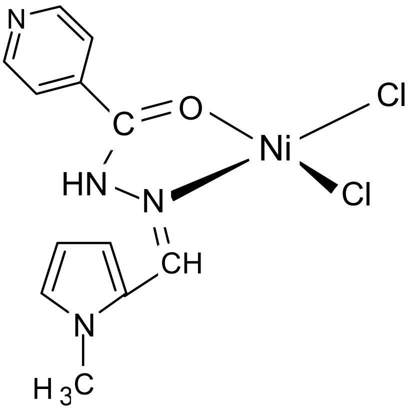

Fig. 4. Structure of the complex $[Ni(HL)Cl_2]\cdot 0.5H_2O$

In Table-5, the biological properties of ligand and its metal complexes are presented. For testing the antimicrobial activity both of the complex combinations and of INHMAP ligand was used the same amount of substance (200 µg/mL) and the reading of the diameter of the inhibition zone was realized after 18 h from incubation. It is clear that the synthesized complexes have high antimicrobial activity than the INHMAP ligand. This can be explained by the fact that the donors atoms which are not involved in the coordination become more actives. The Cu(II), Ni(II) complexes do not present an activity regarding *E. coli* and the Mn(II) complex is inactive in a rapport with the *S. aureus*. The Cd(II) complex is the most active concerning the agents *S. aureus* and *E. coli* while for *P. vulgaris* the best activity is manifested by the Co(II) complex.

TABLE-5
ANTIMICROBIAL ACTIVITY OF INHMAP AND ITS METAL COMPLEXES

Compounds	*S. aureus* Gram (+)	*E. coli* Gram (-)	*P. vulgaris* Gram (-)
INHMAP (HL)	5	6	5
$[Cu(HL)_2Cl_2]$	20	–	10
$[Ni(HL)Cl_2]\cdot½H_2O$	10	–	5
$[Co(HL)_2Cl_2]\cdot H_2O$	19	18	16
$[Mn(HL)Cl_2]\cdot H_2O$	–	17	9
$[Zn(HL)Cl_2]$	14	13	11
$[Cd(HL)Cl_2]$	23	20	12

–: No activity, inhibition zone (mm).

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