New Transition Metal Complexes of γ-L-glutamyl-5-(2-methoxy-*p*-nitroanilide): Synthesis, Spectroscopic, Magnetic and Thermal Investigations.

Leontin David, Cora Crăciun, Crăiţa Bălan, Onuc Cozar
Babes-Bolyai Univ., Dept. of Physics, 1 Kogalniceanu, 3400 Cluj-Napoca, Romania

Letiţia Ghizdavu, Carmen Bâtiu
Babes-Bolyai Univ., Dept. of Chemistry, 10 Arany-Janos, 3400 Cluj-Napoca, Romania

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Abstract

The $CuL_2·5H_2O$, $CoL_2·4H_2O$, $MnL_2·2H_2O$ and $FeL_3·7H_2O$ complexes for HL = γ–L–glutamyl–5–(2-methoxy–*p*–nitroanilide) were synthesized and their spectral, magnetic and thermal properties were investigated. The thermal stability of the synthesized complexes was discussed in the 20–500 °C temperature range. In all the studied complexes γ–L–glutamyl–5–(2-methoxy–*p*–nitroanilide) acts as a bidentate ligand with coordination involving the carboxylate oxygen and the nitrogen atom belonging to the amino group of the γ–L–glutamyl fragment. The local structure around the Cu(II) ion is pseudotetrahedral. In the Co(II), Mn(II) and Fe(III) complexes the metal ions are in the high-spin form, with an octahedral stereochemistry.

Introduction

Besides glutamic acid, its organic and inorganic derivatives also present a particular biological and pharmaceutical importance.

The inorganic compounds of the glutamine and glutamic acid with metal ions have antitumoral activity.[1-3]

In some previously synthesized metal complexes, the glutamic acid acts as a bidentate ligand and some of these complexes present cis-trans isomers.[1] The metal complexes of the glutation were proved to be chemically very stable[4] and to have a

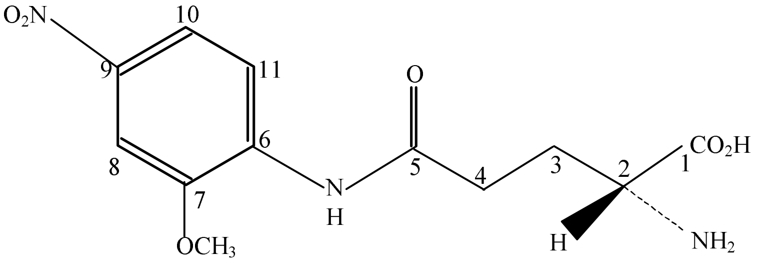

Figure 1. The ligand γ–L–glutamyl–5–(2-methoxy–nitroanilide), HL

considerable antifungal activity.[5]

We have also tested γ-L-glutamyl-5-(2-methoxy-*p*-nitroanilide) as a biochemical reagent for determination of γ-glutamyl transferaza (γ-GT) in the sanguine serum.[5]

Taking into account the important biochemical applications of γ-L-glutamyl-5-(2-methoxy-*p*-nitroanilide) (Figure 1), we report the synthesis and some physico-chemical properties of its coordinative complexes with the transition metals Cu(II), Co(II), Mn(II) and Fe(III).

Results and discussion

Thermal data

The thermal behavior of the ligand and of the synthesized complexes is described in Table 1.

Table 1. Thermal data of γ–L–glutamyl–5–(2-methoxy–*p*–nitroanilide) and its metal complexes

	Temperature range [^{o}C]	**DTA peak (^{o}C)**		**TG weight loss (%)**	
		Endo	**Exo**	**Calc.**	**Exp.**
HL·2H$_2$O	20 – 220	115	–	10.81	10.30
		191	–	–	–
		–	202	13.80	13.62
	220 – 400	–	260	36.31	35.844
	400 – 500	–	470	39.04	38.16
CuL$_2$·5H$_2$O	20 – 220	108	–	12.06	12.18
		195	–	–	–
		–	207	12.33	12.10
	220 – 400	–	243	28.79	28.48
	400 – 500	–	450	39.87	41.23
CoL$_2$·4H$_2$O	20 – 200	105	–	2.79	2.76
		130	–	5.58	5.53
		195	–	–	–
		–	205	14.25	14.12
	200 – 400	–	260	28.23	27.54
		–	430	39.06	38.54
MnL$_2$·2H$_2$O	20 – 200	160	–	5.58	6.31
	200 – 400	202	–	–	–
		–	206	14.77	14.52
		–	248	29.91	30.28
	400–500	–	438	40.44	38.94
FeL$_3$·7H$_2$O	20 – 200	110	–	4.04	4.21
		198	–	–	–
	200 – 400	–	202	15.44	15.10
		–	285	30.59	30.89
	400 – 500	–	460	41.89	41.05

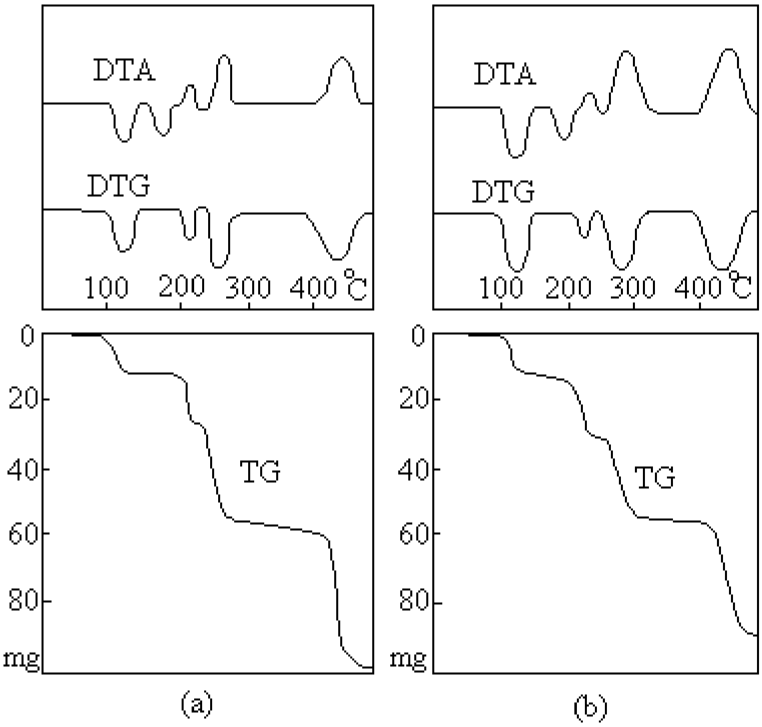

Figure 2. The derivatograms for L·2H_2O (a) and CuL_2·5H_2O (b) compounds

The DTA, TG and DTG curves have almost the same shape for all the investigated compounds, therefore Figure 2 presents the derivatograms recorded for the ligand and for its Cu(II) complex.

The endo peak at 115 °C on the ligands derivatograme indicates the loss of two crystal water molecules. The anhydrous compound is stable up to 191 °C, where an endo peak marks its melting.[6] The decomposing starts with the shoulder at ~200 °C, which was assigned to the losing of one -NO_2 group[6,7] and it continues at 260 °C where the aniline rest is lost. The theoretic weight loss (50.11%) and the experimental one (50.54%) agree with the loss of 2-methoxy-p-nitroanilide residue. The slow weight loss process presenting an endo peak at 470°C indicates the pyrolysis of the remaining L-glutamic acid ($C_5H_7O_3N$).

The derivatograms recorded on CuL_2·5H_2O and FeL_3·7H_2O compounds present each two endo peaks at 105 °C and 108 °C, which were assigned to the loss of the hydrating water. In the case of CoL_2·4H_2O compound, a stepped dehydration reaction is observed, the two endo peaks at 98 °C and 150 °C corresponding to the loss of two moles of hydrating water and two moles of coordination water, respectively.

The dehydration of $MnL_2{\cdot}2H_2O$ compound is marked by an endo peak at 130 ^oC, corresponding to the loss of two coordination water molecules.[8]

The melting points for the coordinative compounds (in the 195–198 ^oC temperature range) are higher then the ligands (191 ^oC), confirming an increased thermal stability as complexation effect and the metal-nitrogen and metal–oxygen bondings formation.

In the 200–400 ^oC temperature range, the stepped splitting of 2-methoxy-p-nitroanilide organic radical produces: the loss of nitro– and methoxy– groups takes place at ~200 ^oC[9,10] and the remaining aniline loss is marked by the exo peak between 265–280 ^oC. The pyrolysis of the remaining glutamic acid is marked by an exo peak in the temperature range 420–490 ^oC.

The thermal data of the studied compounds agree well with the chemical analysis, confirming the metal:ligand:water combination ratio in the complexes.

IR Spectra

Table 2 presents some selected vibration bands for the ligand and for the synthesized compounds. A comparative study of these spectral data revealed the lowering of the ligand ν(C=O) group frequency with 18÷45 cm^{-1}, due to the –COO–metal bonding which is formed.[11,12]

Table 2. Some IR absorption bands (cm^{-1}) for the ligand and its metal complexes derivatives

	$HL{\cdot}2H_2O$	$CuL_2{\cdot}5H_2O$	$CoL_2{\cdot}4H_2O$	$MnL_2{\cdot}2H_2O$	$FeL_3{\cdot}7H_2O$
ν(O–H); ν(O–H–O)	3385	3502	3428	3425	3410
$\nu(NH_2)$	3192	3144	3075	3108	3132
ν(C=O)	1650	1632	1614	1605	1610
ν(C–O)	1378	1364	1350	1372	1366
$\nu(NO_2)$	1628	1620	1618	1622	1623
$\rho_t(NH_2)$	1246	1220	1225	1231	1226
$\rho_w(NH_2)$	1026	1055	1028	1036	1030
$\nu(M{-}OH_2)$	–	–	764	762	–
δ(C=O)	748	726	738	736	732
π(C=O)	624	612	594	598	606
ν(M–N)	–	456	448	437	435

The shift of ν(N–H) absorption band with 48÷84 cm^{-1} in the metal complexes indicates the involvement of the nitrogen atom of the second amino group at the metal coordination.

The ν(M–N) stretchings are shifted to higher frequencies and the ν(C=O) and ν(NH_2) stretchings are shifted to lower frequencies as the metal is changed in the order Fe(III) < Mn(II) < Co(II) < Cu(II). The IR data are in good agreement with Irving–Williams stability series of the studied divalent ion complexes.[13,14]

The broad bands over 3300 cm^{-1} appearing both in ligand and in the coordinative compounds suggest the presence of hydrogen bonds. This wide band is slightly shifted towards higher frequency values for complex salts, in connection with the increasing energy values of the hydrogen bonds.

In the case of $CoL_2·4H_2O$ and $MnL_2·2H_2O$ compounds there is an additional band appearing at 764 and 762 cm^{-1}, respectively, due to the coordinative H_2O–metal bondings.[15]

ESR and magnetic susceptibility measurements

The powder ESR spectra of $CuL_2{}^{·}5H_2O$ at room temperature (Figure 3) are typical for pseudotetrahedral monomeric species. The $g_{||} = 2.417$ and $g_{\perp} = 2.065$ values correspond to a CuN_2O_2 cromophore.[16]

The powder ESR spectrum of $MnL_2·2H_2O$ is characterized by a quasi-isotropic **g** tensor with principal values (g = 2.0018) close to the spin-only value.

The ESR spectrum of $FeL_3·7H_2O$ is almost isotropic (g = 2.002). The presence of a weak signal at $g \approx 4$ suggests a small distortion of the octahedral symmetry around the metal ion.

The magnetic susceptibility measurements indicate a Curie–Weiss behavior (Figure 4), with values of magnetic moments specific for monomeric species.

The values of the magnetic moments were calculated considering also the temperature independent contribution. In the case of Cu(II) complexes the magnetic moment ($\mu_{eff} = 1.92$ μ_B) is in the normally observed range for pseudotetrahedral species, while those corresponding to high–spin ions Co(II), Mn(II) and Fe(III) ($\mu_{eff} = 5.2$ μ_B,

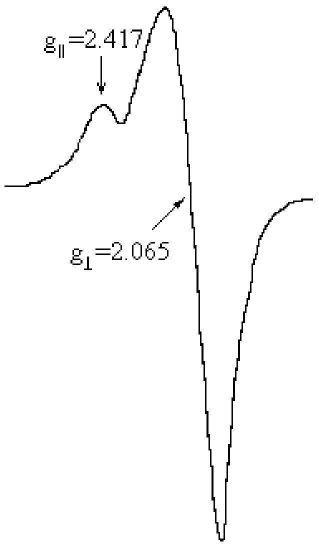

Figure 3. Powder spectrum of $CuL_2 \cdot 5H_2O$ at room temperature

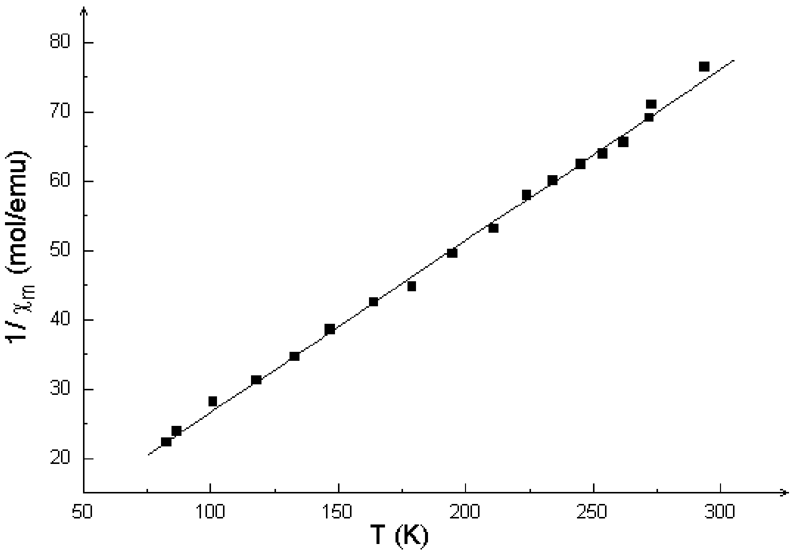

Figure 4. Temperature dependence of $1/\chi_m$ for $CoL_2 \cdot 4H_2O$

5.87 μ_B and 5.25 μ_B, respectively) indicate local octahedral environments. The paramagnetic Curie temperatures (θ = -10.76 K, -10.05 K, and 35.97 K for Cu(II), Co(II) and Mn(II) complexes, respectively) indicate the presence of some exchange interactions between the metal ions, due to the formation of intermolecular hydrogen bonds.[17]

Conclusions

Thermal and spectroscopic behavior of the synthesized metal complexes indicates that their stability range ($CuL_2 \cdot 2H_2O$ > $CoL_2 \cdot 4H_2O$ > $MnL_2 \cdot 4H_2O$) obeys the Irving – Williams series.

The IR spectra show γ–L–glutamyl–5–(2-methoxy–*p*–nitroanilide) acting as a bidentate ligand with coordination involving the carboxylate oxygen and the nitrogen atom of the amino group belonging to the γ–L–glutamyl molecular fragment. In the case of intermediate class Lewis acids Co(II) and Mn(II), two H_2O molecules are involved in the metal ion coordination, resulting in an octahedral local structure. Three bidentate ligand molecules coordinate the *a* class Lewis acid Fe(III). The ESR spectra and magnetic data confirm the pseudotetrahedral (for Cu(II) ion) and octahedral (for Co(II), Mn(II), Fe(III) ions) local symmetries.

The obtained structural data allow us to propose the following molecular formulas for the studied metal complexes:

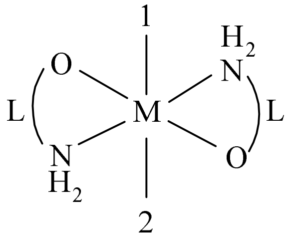

Figure 5. Partial structures for the studied complexes. For the Cu(II)-complex, the positions 1 and 2 are occupied by oxygen atoms, for Co(II) and Mn(II) complexes these positions are ocupied by H_2O molecules and for the Fe(III) compound, an oxygen atom is in position 1 and a nitrogen atom in position 2.

Experimental

The ligand γ-L-glutamyl-5-(2-methoxy-*p*-nitroanilide) was prepared by reported procedure.[5]

The metal complexes were prepared by solvating 0.05 mole of the corresponding metal salts ($CuSO_4·5H_2O$, $CoSO_4·7H_2O$, $MnSO_4·7H_2O$ and $Fe(NH_4)(SO_4)_2·12H_2O$) in distilled water (3.5 ml) at high temperature. An aqueous solution (7 ml) was prepared from 0.05 mole L-glutamyl-5-(2-methoxy-*p*-nitroanilide) solvated in NaOH (pH = 9.0) in excess (0.03 g) (molar ratio: 1:2 and 1:3, respectively) at room temperature. The precipitate formed by mixing the ligand solution with metal salts solutions was filtered off, washed in NaOH solution (pH = 9.0), then in cold water, dried in air (24–48h) and kept in dark bottles.

Table 3. Some physical and elemental analytical data of the synthesized metal compounds

		$CuL_2·5H_2O$	**$CoL_2·4H_2O$**	**$MnL_2·2H_2O$**	**$FeL_3·7H_2O$**
Colour		pale–blue	Pink-yellow	white-yellow	orange
Melting point (^{o}C)		195	197	198	199
Elemental analysis: found (calculated) (%)	**Metal (%)**	8.93 (8.51)	7.70 (8.14)	7.62 (8.04)	5.30 (5.48)
	C(%)	38.85 (38.63)	39.55 (39.84)	42.60 (42.17)	40.51 (40.27)
	H(%)	3.52 (3.78)	3.71 (3.90)	4.02 (4.13)	3.75 (3.94)
	N(%)	11.20 (11.26)	11.39 (11.61)	12.01 (12.29)	11.55 (11.74)

Table 3 presents some physico–chemical and elemental analysis data of the synthesized metal complexes. The compounds are slightly soluble in water and insoluble in organic solvents as benzene, toluene, acetone, ether, chloroform and CCl_4; they decompose in boiling DMF and DMSO.

Thermal studies were performed on an OD-103 type Paulik-Erdely Derivatograph, in air atmosphere, in the temperature range of 20-500^{o}C, at a rate of heating of 10^{o}C/min, using α-Al_2O_3 as reference compound. IR spectra were recorded with a Karl Zeiss Jena UR-20 Spectrophotometer, in KBr pellets, in a range of 400-4000cm^{-1}. EPR spectra were recorded at 9.4 GHz (X band), using a standard JEOL–JES–3B equipment. Magnetic susceptibility measurements were made on powered samples using a Faraday type balance.

References and Notes

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Povzetek

Pripravili smo komplekse $CuL_2 \cdot 5H_2O$, $CoL_2 \cdot 4H_2O$, $MnL_2 \cdot 2H_2O$ in $FeL_3 \cdot 7H_2O$, kjer je L = γ–L–glutamil–5–(2-metoksi–*p*–nitroanilid) in raziskali njihove spektralne, magnetne in termične lastnosti. V vseh raziskovanih kompleksih je ligand koordiniran s karboksilatnim kisikom in dušikom aminske skupine v γ–L–glutamilnem fragmentu. Razporeditev ligandov okoli Cu(II) je psevdotetraederska, okoli Co(II), Mn(II) in Fe(III) pa oktaederska.