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Thermal behaviour of some new complexes with bismacrocyclic ligands as potential biological active species

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Abstract Novel complexes of type $[M_2LCl_4]\cdot nH_2O$ ((**1**) M:Ni, $n = 5$; (**2**) M:Cu, $n = 0$ and (**3**) M:Zn, $n = 2$; L: ligand resulted from 1,2-phenylenediamine, 3,6-diazaoctane-1,8-diamine and formaldehyde template condensation) were synthesised and characterised. The features of complexes have been assigned from microanalytical, IR and UV–Vis data. The thermal analyses have evidenced the thermal intervals of stability and also the thermodynamic effects that accompany them. Processes as water or hydrochloric acid elimination as well as oxidative degradation of the organic ligand were observed. Complexes display a different thermal behaviour as result of dissimilar chemical interaction of metal ions with chloride anions. The final product of decomposition was metal(II) oxide as powder X-ray diffraction indicated.

Keywords Complexes · Bismacrocycle · One pot condensation · 1,2-Phenylenediamine · Thermal behaviour

Introduction

Although many complexes showed a good antimicrobial or antiviral activity so far only a few are used as metalloantibiotics (antiseptics and antimicrobial) or metalloantiviral drugs [1]. Having in view the increasing incidence of germs resistance the process of development new drugs becomes important.

Nowadays, complexes with bismacrocyclic ligands have drawn special attention since was evidenced that bicyclams are a class of highly potent and selective HIV inhibitors, which interact with the receptor CXCR4, the main co-receptor used by T cell tropic strains of HIV [2]. As a result, a large number of synthetic bismacrocyclic compounds as well as their complexes has been prepared and investigated concerning antiviral activity [3–5].

The importance of the complexes with bicyclams derived from the fact that they are active against both HIV-1 and HIV-2 [6]. Among these, the zinc and nickel complexes with the some bicyclams are slightly more active by comparison with ligand itself, whereas other bicyclam complexes containing Cu(II), Co(III) and Pd(II), are less active [7, 8].

Furthermore, some bismacrocycles or their complexes have anti-proliferative activities [9] or behaves as agents which can bind and cleave the DNA [10].

The complexes with mono- or bismacrocyclic fully saturated ligands can be easily synthesised by one pot condensation starting from suitable intermediates and closing the chelate rings by formaldehyde [11–14]. By using this method, we succeeded in obtaining new complexes with bismacrocyclic ligands. In order to evaluate the thermal stability of these species, we report here the synthesis and characterisation of Ni(II), Cu(II) and Zn(II) complexes with the ligand obtained by one pot condensation of 1,2-phenylenediamine, 3,6-diazaoctane-1,8-diamine and formaldehyde. The complexes have been characterised by different analytical and spectral methods.

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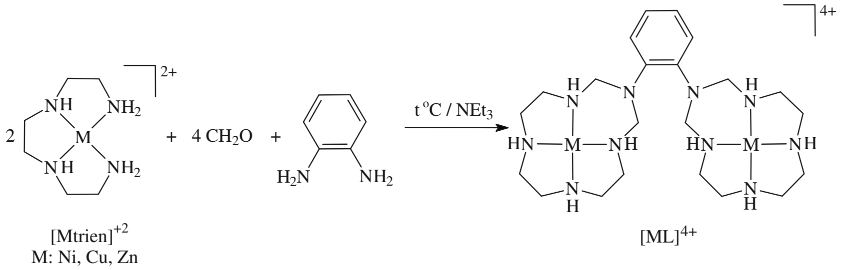
Scheme 1 Synthesis of complexes



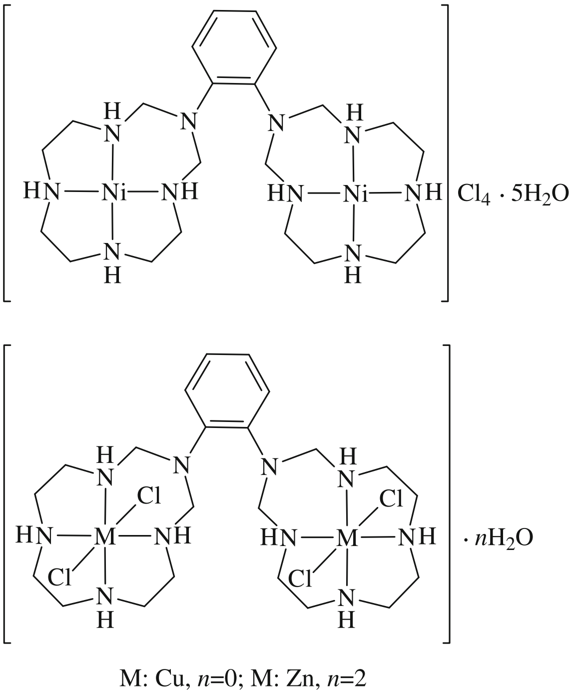


Fig. 1 The proposed coordination for complexes

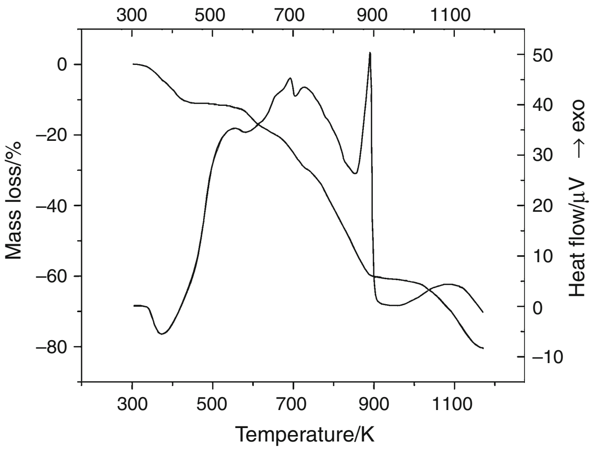


Fig. 2 TG and DTA curves for $[Ni_2L]Cl_4{\cdot}5H_2O$ (**1**)

The thermal behaviour of these derivatives was investigated in synthetic air by thermal analysis (TG, DTA). So far, our research group reported the thermal behaviour of other complexes with macrocyclic ligands that display an interesting thermal behaviour [15, 16] and some display also a good antimicrobial activity [16].

The thermal behaviour of these derivatives was investigated by thermal analysis (TG, DTA) in order to evidence the modification that appear at heating in synthetic air and also the thermodynamic effects that accompany them.

Experimental

All reagents were of commercial analytical quality and have been used without further purification. Chemical analysis of carbon, nitrogen and hydrogen has been performed using a Perkin Elmer PE 2400 analyzer.

IR spectra were recorded in KBr pellets with a Bruker Tensor 37 spectrometer in the range 400–4000 cm^{-1}.

Electronic spectra by diffuse reflectance technique, with Spectralon as standard, were recorded in the range 200–1500 nm, on a Jasco V670 spectrophotometer.

The heating curves (T, TG and DTA) were recorded using a Labsys 1200 SETARAM instrument, with a sample mass of 6–17 mg over the temperature range of 293–1173 K, using a heating rate of 10 K/min. The measurements were carried out in synthetic air atmosphere (flow rate 16.66 cm^3/min) by using alumina crucibles.

The X-ray powder diffraction patterns were collected on a DRON-3 diffractometer with a nickel filtered Cu K_α radiation ($\lambda = 1.5418$ Å) in 2θ range of 5°–70°, a step width of 0.05° and an acquisition time of 2 s per step.

Synthesis and spectral data of complexes

Synthesis of complexes

To a suspension that contain 3,6-diazaoctane-1,8-diamine (10 mmol), hydrated metal(II) chloride (10 mmol), 1 mL triethylamine and 2 mL formaldehyde (37%) in 100 mL methanol was added drop wise a solution of 1,2-phenylenediamine (5 mmol) in 50 mL methanol. The reaction mixture was refluxed 48 h until a sparingly soluble brown coloured compound was formed. The microcrystalline product were filtered off, washed with EtOH, Et_2O and air-dried.

Table 1 Thermal behaviour data (in synthetic air atmosphere) for complexes

Compound	Step	Thermal effect	Temperature range/K	$\Delta m_{exp}/\%$	$\Delta m_{calc}/\%$
$[Ni_2L]Cl_4 \cdot 5H_2O$ (**1**)	1.	Endothermic	338–443	11.0	11.3
	2.	Exothermic	533–913	49.8	49.7
	3.	Exothermic	983–1173	20.2	20.3
	(Residue NiO)			19.0	18.7
$[Cu_2LCl_4]$ (**2**)	1.	Exothermic	503–598	20.2	20.3
	2.	Exothermic	598–773	57.5	57.5
	(Residue CuO)			22.3	22.2
$[Zn_2LCl_4] \cdot 2H_2O$ (**3**)	1.	Endothermic	360–448	4.5	4.7
	2.	Exothermic	448–623	19.2	19.3
	3.	Exothermic	623–1173	54.6	54.5
	(Residue ZnO)			21.7	21.5

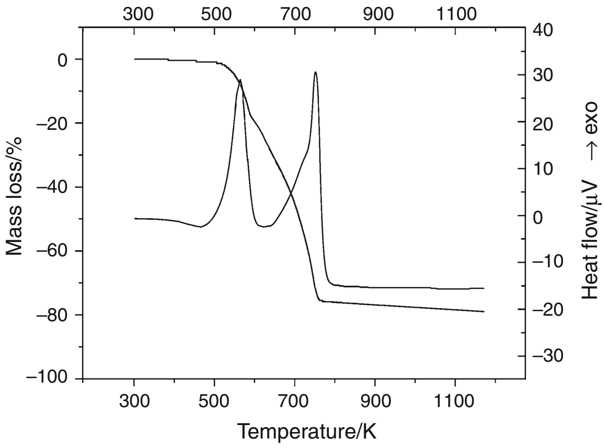


Fig. 3 TG and DTA curves for $[Cu_2LCl_4]$ (**2**)

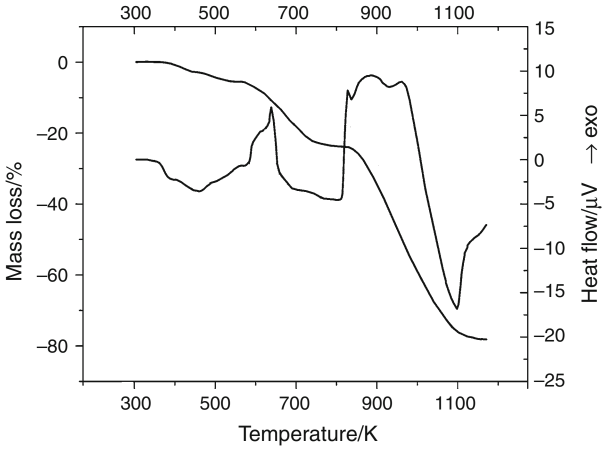


Fig. 4 TG and DTA curves for $[Zn_2LCl_4] \cdot 2H_2O$ (**3**)

IR (KBr pellet), cm^{-1}: $[Ni_2L]Cl_4 \cdot 5H_2O$: ν(OH), 3420vs; ν(NH), 3281m, sh.; $\nu_{as}(CH_2)$, 2926 m; $\nu_s(CH_2)$, 2810w; ν(C=C), 1457vs; $[Cu_2LCl_4]$: ν(NH), 3250s; $\nu_{as}(CH_2)$, 2944m; $\nu_s(CH_2)$, 2800m; ν(C=C), 1457s; $[Zn_2LCl_4] \cdot 2H_2O$: ν(OH), 3503m; ν(NH), 3263m; $\nu_{as}(CH_2)$, 2918m; $\nu_s(CH_2)$, 2849m; ν(C=C), 1467vs.

Results and discussions

Synthesis and physico-chemical characterisation of complexes

The one-pot reactions of excess formaldehyde with 2:2:1 molar mixture of nickel(II), copper(II) or zinc (II) chloride, 3,6-diazaoctane-1,8-diamine and 1,2- phenylenediamine in an alkaline medium produced the species $[M_2LCl_4] \cdot nH_2O$ ((**1**) M:Ni, $n = 5$; (**2**) M:Cu, $n = 0$ and (**3**) M:Zn, $n = 2$; L: bismacrocyclic ligand resulted in condensation). The chemical analyses are in accord with formulas proposed for complexes (Scheme 1).

The major goal of this paper was to evidence the thermal behaviour of these complexes that also present in vitro antimicrobial activity and ability to inhibit biofilm formation. The biological results will be published elsewhere.

The IR spectra of complexes presented in experimental part indicate the presence of bands that can be assigned to some fragments provided both by 3,6-diazaoctane-1,8-diamine and 1,2-phenylenediamine such is that associated with the CH_2 and C=C groups. The IR spectra showed also a single sharp absorption around 3300 cm^{-1} which arise from secondary amine stretching vibration. This band is shifted by 40–80 cm^{-1} to lower wavenumbers in comparison with metal-free ligand indicating that the secondary amine nitrogen atoms are involved in coordination [17].

In the characteristic ranges for water a broad band in the range 3400–3500 cm^{-1} can be assigned to ν(OH) stretching vibrations, except for complex (**2**) [18].

The electronic spectrum of compound (**1**) displays a band with maximum at 20830 cm^{-1}, pattern characteristic for the square-planar stereochemistry. The broad band with maximum 17860 cm^{-1} indicates for complex (**2**) rather an octahedral distorted stereochemistry [19]. It was assumed that the Zn(II) complex adopts the same stereochemistry.

The coordination proposed for the new complexes based on these data are presented in Fig. 1.

Thermal behaviour of complexes

The TG and DTA curves corresponding to the complex (**1**) heated in the 293–1173 K temperature range indicate that decomposition follows three steps (Fig. 2).

The first step of compound thermal transformation consists in an endothermic elimination of water molecules up to 443 K (Table 1). The second step, exothermic, is not a single one being an overlapping of at least four processes according to both TG and DTA curves profile. According to the mass lost the intermediate formed after this step is a paracyanide specie of type $NiCl_2(CN)$. The IR spectrum of this intermediate display indeed the characteristic bands of the paracyanide species at 1634 and 1510 (ν(C=N)), 1400 (ν(C=C)) and 775 cm^{-1} (ν(C–C)) as was observed for other species also [20]. This species is stable over a 343 K temperature range. Next step, exothermic also, corresponds to oxidative degradation of paracyanide together with the chloride elimination leading finally to the non-stoichiometric nickel(II) oxide (found/calcd. overall mass loss: 81.0/81.3). The nature of final product was confirmed by IR and powder X-ray diffraction data (ASTM 78-0423).

Complex (**2**) is anhydrous specie and as result their thermal degradation starts at 503 K and the decomposition pattern is different from that of compound (**1**) (Fig. 3). First step is exothermic one and according to the mass loss corresponds to chloride anions elimination as hydrochloric acid. It is to be pointed the negative reaction for the chloride anions with silver nitrate for the residue isolated at 603 K. Such behaviour was observed for other chloride complexes as well [21]. This behaviour could be generated by the fact that chloride anion is coordinated leading thus to a complex with a high degree of covalency. Next step, exothermic also, corresponds to organic part oxidative and consists in at least two processes (according to DTA curve profile). The final product is CuO as powder X-ray diffraction indicates (ASTM 5-661) (found/calcd. overall mass loss: 77.7/77.8).

The first step in the thermogram of compound (**3**) (Fig. 4) occurred in the temperature range 360–448 K, when the water molecules are lost in a well definite, endothermic step; the temperature range corresponding to the lost indicates their nature as crystallisation water [22, 23]. The next step, exothermic one, corresponds to hydrochloric acid elimination from the anhydrous complex. The third step, an exothermic and complex one being an overlap of at least three processes (as DTA curve profile indicates), corresponds to the organic residue pyrolise and zinc(II) oxide generation (ASTM 36-1451) (found/calcd. overall mass loss: 78.3/78.5).

Conclusions

The nickel(II), copper(II) and zinc(II) complexes with bismacrocyclic ligands resulted in one-pot condensation of 3,6-diazaoctane-1,8-diamine, formaldehyde and 1,2-phenylenediamine have been synthesised.

The ligand nature and stereochemistry were characterised by means of IR and electronic spectroscopy. Electronic spectrum of Ni(II) complex is characteristic for square planar stereochemistry while that of Cu(II) complex display the pattern of octahedral stereochemistry. The modifications in the IR spectra of complexes are in accord with the condensation process and secondary amine coordination.

Thermal decomposition of complexes allowed us to establish the number and nature of water molecule, the composition of complexes and also the intervals of thermal stability. The thermal degradation occurs in three steps for the hydrated complexes and in two for the anhydrous one. The Ni(II) complexes has a different behaviour and loss the chloride anion at the end of the thermal decomposition probably as result of the electrostatic interaction between the complex species and these anions. After water elimination up to 440 K, the complexes decompose in two steps leading to metal(II) oxides as final products. One intermediate was isolated and identified as a paracyanide type. The results are in good concordance with the complexes composition.

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