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Thermal behaviour of new biological active cadmium mixed ligands complexes

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Abstract This paper reports the investigation on the thermal stability of new complexes with mixed ligands of the type $[Cd(NN)(C_3H_3O_2)_2(H_2O)_m]\cdot nH_2O$ [(**1**) NN: 1, 10-phenantroline, m = 1, n = 0; (**2**) NN: 2,2′-bipyridine, m = 0, n = 1.5 and ($C_3H_3O_2$): acrylate anion]. The IR data indicate a bidentate coordination mode for both heterocyclic amine and acrylate. The in vitro qualitative and quantitative antimicrobial activity assays showed that the complexes exhibited variable antimicrobial activity against planktonic as well as biofilm embedded Gram-negative (*Escherichia coli*, *Klebsiella* sp., *Proteus* sp., *Salmonella* sp., *Shigella* sp., *Acinetobacter boumani*, *Pseudomonas aeruginosa*), Gram-positive (*Bacillus subtilis*, *Staphylococcus aureus*) and fungal (*Candida* albicans) strains, reference and isolated ones from the hospital environment. The thermal behaviour steps were investigated in synthetic air flow. The thermal transformations are complex processes according to TG and DTA curves including dehydration, amine as well as acrylate thermolysis. The final products of decomposition are the most stable metal oxides.

Keywords Acrylate · Complexes · Carbonate · 1,10-Phenantroline · 2, 2′-Bipyridine · Thermal stability

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Introduction

The coordination compounds having as mixed ligands an amine and an organic derivative, which possesses a vinyl group, potentially polymerizable (as acrylate ion) are important due to the possibility of their inclusion in polymeric matrix. If the complex compounds are biologic active, the polymeric biocompatible material can assure the target delivery and the controlled release of the active compound [1–4]. Our research group have been synthesized and characterised some complexes of this type using beside acrylate, 1,10-phenantroline [5], 2,2′-bipyridine [6], 4,4′-bipyridine [7], ethylenediamine [8] and 3-amino-4H-1,2,4-triazole [9], respectively. Thermal analysis evidenced for all these complexes an interesting behaviour. Recently, it were reported the synthesis and X-ray characterisation of a cadmium complex, $[Cd(C_3H_3O_2)Cl(C_{12}H_8N_2)_2]$ with 1,10-phenantroline and acrylate [10].

In order to extend the series of compounds, new complexes of the type $Cd(NN)(C_3H_3O_2)_2(H_2O)_x$ [where (NN) is a bidentate heterocyclic amine and $C_3H_3O_2$ is acrylate anion] have been synthesized and characterized using IR spectroscopy and single crystal X-ray diffraction.

This study was initiated and developed as a consequence that so far, for cadmium complexes it was evidenced antifungal [11, 12] and antibacterial activities [13–15] and

we are interested to develop coordination compounds which such biological properties.

The in vitro qualitative and quantitative antimicrobial activity assays showed that the complexes exhibited variable antimicrobial activity against planktonic as well as biofilm embedded Gram-negative (*Escherichia coli*, *Klebsiella* sp., *Proteus* sp., *Salmonella* sp., *Shigella* sp., *Acinetobacter boumani*, *Pseudomonas aeruginosa*), Gram-positive (*Bacillus subtilis*, *Staphylococcus aureus*) and fungal (*Candida* albicans) strains, reference and isolated ones from the hospital environment.

The thermogravimetric analysis was performed in order to reveal the range of stability for these complexes. The thermal behavior of these compounds elucidated the composition and also the number and nature of the water molecules. It was also evidenced the existence of an intermediate step corresponding to the formation of cadmium carbonate for compound (**2**).

In all the cases, the final residue is cadmium oxide, as indicate the powder X-ray diffraction method.

Experimental

All reagents were purchased from Aldrich and Merck, reagent grade and were used without further purification.

The chemical analysis and IR spectral data were used in order to confirm the nature of complexes. Chemical analysis of carbon and nitrogen has been performed using Perkin Elmer PE 2400 analyzer. Cadmium was determined gravimetrically in the laboratories of Inorganic Chemistry Department.

IR spectra were recorded in KBr pellets with a BIO-RAD FTIR 135 spectrometer in the range 400–4000 cm^{-1}.

The qualitative screening of the susceptibility spectra of different microbial strains to the complexes was performed by adapted diffusion techniques, while the quantitative assay of minimal inhibitory concentration (MIC, $\mu g/cm^3$) value was based on liquid medium serial microdilutions [16]. The compounds were solubilised in DMF to a final concentration of 1 mg/mL. The in vitro biological screening effects were tested against a microbial inoculum of $\sim 1.5 \times 10^8$ UFC cm^{-3}, corresponding to 0.5 McFarland density, represented by *Enterobacteriaceae* (*E. coli*, *Salmonella* sp., *Shigella* sp., *Proteus* sp., *Klebsiella pneumoniae*) *Pseudomonadaceae* (*Pseudomonas aeruginosa*, *Acinetobacter boumani*), *Micrococcaceae* (*Staphylococcus aureus*), *Bacillaceae* (Bacillus sp.) and *Candida* strains reference ones and recently isolated from clinical samples, respectively.

The heating curves (TG and DTA) were recorded using a Labsys 1200 SETARAM instrument, with a sample mass of 11–15 mg over the temperature range of 20–1000 °C, using a heating rate of 10 K min^{-1}. The measurements were carried out in synthetic air atmosphere (flow rate 16.66 cm^{-3} min^{-1}) by using alumina crucibles.

Synthesis of the complexes

Complex $[Cd(phen)(C_3H_3O_2)_2(H_2O)]$ (**1**): An aqueous mixture formed from 1.15 g cadmium carbonate and 1.82 mL acrylic acid was stirred at room temperature for 3 h and then it was left to stand at room temperature for 2 days. Then, it was added an ethanolic solution that contained 0.66 g 1,10-phenantroline monohydrate and the mixture was stirred at room temperature for 2 h. The pale pink solution was filtered off. After 3 days, the colourless crystals suitable for X-ray analysis were filtered off, washed with ethylic alcohol and air dried.

Analysis, found: Cd, 24.78; C, 47.92; H, 3.48; N, 6.22%; calculated for $CdC_{18}H_{16}N_2O_5$: Cd, 24.83; C, 47.75; H, 3.56; N, 6.19%; IR (KBr pellet), cm^{-1}: $\nu(H_2O)$, 3400m; ν(C=C), 1636 m; ν_{as}(COO), 1559 vs; ν(C=N), 1426s; ν_s(COO), 1357m; δ(COO), 657m.

Complex $[Cd(dipy)(C_3H_3O_2)_2]\cdot 1.5H_2O$ (**2**): An aqueous mixture formed from 1.15 g cadmium carbonate and 1.82 mL acrylic acid was stirred at room temperature for 3 h and then it was left to stand at room temperature for 2 days. Then, it was added an ethanolic solution that contained 0.52 g 2,2′-bipyridine and the mixture was stirred at room temperature for 2 h. The pale pink solution was filtered off. After 1 week, the needle shaped colourless crystals were filtered off, washed with ethylic alcohol and air dried.

Analysis, found: Cd, 25.54; C, 44.08; H, 3.81; N, 6.48%; calculated for $CdC_{16}H_{17}N_2O_{5.5}$: Cd, 25.68; C, 43.90; H, 3.91; N, 6.40%; IR (KBr pellet), cm^{-1}: $\nu(H_2O)$, 3410m; ν(C=C), 1640m; ν_{as}(COO), 1540vs; ν(C=N), 1435s; ν_s(COO), 1368m; δ(COO), 665m.

Results and discussion

A series of complexes with mixed ligands (heterocyclic amine and acrylate) were obtained from the reaction of corresponding cadmium carbonate and amine. The purpose of this paper was to evidence the thermal behaviour, in synthetic air flow, of these complexes that could be considered metal containing monomers. The complexes have been formulated on the basis of chemical analysis and IR spectra as it follows:

$$\left[Cd(C_{12}H_8N_2)(C_3H_3O_2)_2(H_2O)\right] \quad (1)$$

$$\left[Cd(C_{10}H_8N_2)(C_3H_3O_2)_2\right]\cdot 1.5H_2O \quad (2)$$

These compounds were obtained in two steps. First, cadmium acrylate from the reaction of the cadmium carbonate

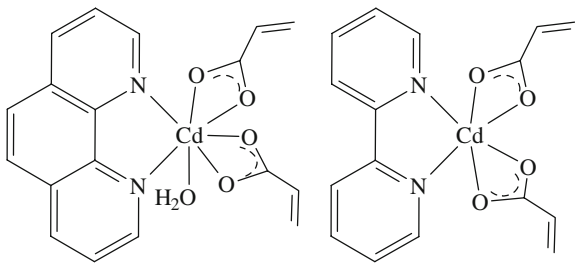
with acrylic acid in aqueous solution was obtained. Based on the low reactivity of metallic salt, an excess of acrylic acid were used (1:4 molar ratio). The second step consists in 1,10-phenatroline/2,2′-bipyridine reaction with cadmium acrylate.

These complexes are different as chemical formulae and IR spectra. According to IR spectra both the heterocyclic amine and acrylate act as chelate in complexes. The IR spectra exhibit the characteristic patterns of the amine (experimental part) that generate two strong bands about 1640 and 1435 cm^{-1} assigned to ν(C=C) and ν(C=N) vibrations. The acrylate fragment can be identified due ν_{as}(COO) and ν_s(COO) bands.

According to the literature data [17], the Δ criterion [$\Delta = \nu_{as}(COO) - \nu_s(COO)$] is used to establish the coordination mode of carboxylate ion. The Δ values of 202 cm^{-1} in the case of compound (**1**) and 172 cm^{-1} for complex (**2**) indicate a bidentate coordination.

The presence of water molecule in complexes could be responsible for the appearance of a large band at about 3400 cm^{-1} assigned to ν(OH) stretching vibrations [18].

On the basis of the above data the proposed coordination for the complexes is as it follows.



Biological activity

The antimicrobial activity of the tested compounds was performed against 15 microbial strains, the majority of them being recently isolated from different clinical samples and exhibiting different resistance patterns, i.e. *Enterobacteriaceae* (*E. coli*—enteropathogenic EPEC strains, as well as strains producing extended spectrum beta-lactamases—ESBL rendering them resistant to all beta-lactams, *Salmonella* sp., *Shigella flexneri* and *Shigella* sp., *Proteus* sp., *Klebsiella pneumoniae*) *Pseudomonadaceae* (*Pseudomonas aeruginosa*, *Acinetobacter boumani*—both microorganisms being known for their high natural resistance to antibiotics), *Micrococcaceae* (*Staphylococcus aureus—methicillin resistant—MRSA*), *Bacillaceae* (*Bacillus* sp.) and *Candida albicans* strains. The tested compound exhibit different levels of antimicrobial activity (ranging from low MIC of 64 to high values of 512 μg cm^{-3}) (Fig. 1).

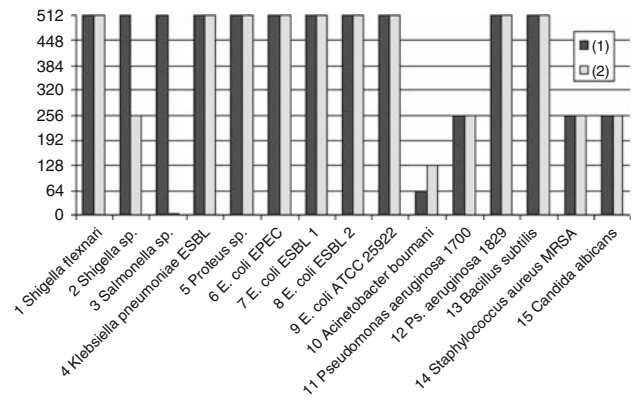


Fig. 1 The representation of the antimicrobial activity (MIC values) of the tested compounds

Both compounds inhibited preferentially the growth of *Pseudomonadaceae*, *Staphylococus aureus* and *Candida albicans* strains, being not active on Gram-negative, enterobacterial strains.

The complex (**2**) exhibit superior antimicrobial activity comparatively to (**1**), with lower MIC values against enterobacterial strains (i.e. *Shigella* sp. and *Salmonella* sp.).

The MIC values for the complexes are lower in comparison to other Cd(II) complexes with amino acids derivatives [19] or uracyl derivatives [20]. The tested strains isolated from clinical samples are multidrug resistant so the new complexes have promising antifungal activity in order to overcome this resistance.

Concerning the influence of the tested compounds on the ability of microbial strains to colonize the inert substratum, thus to interfere with this dual microbial strategy used for survival in the external environment and to initiate infections associated to prosthetic devices, our results show different efficiencies depending on the microbial tested strains.

Thermal decomposition of $[Cd(C_{12}H_8N_2)(C_3H_3O_2)_2(H_2O)]$

The results concerning the thermal decomposition of new complexes in synthetic air atmosphere are presented as follows.

The TG and DTA curves corresponding to the complex (**1**) heated in the 20–900 °C temperature range are presented in Fig. 2.

The thermal decomposition occurs in three, well-defined steps (Table 1). The first step, which is endothermic, corresponds to water molecules loss. The resulted anhydrous compound is stable over a range larger than 150 °C. The second step corresponds to acrylate into formate transformation, process accompanied by a very strong exothermic effect. The formate anion and phenanthroline oxidative

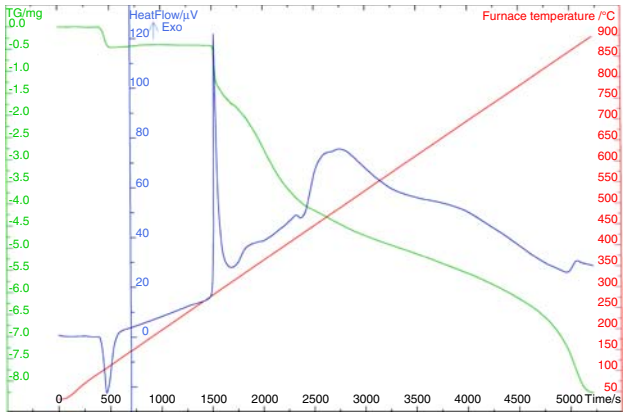


Fig. 2 TG and DTA curves of $[Cd(C_{12}H_8N_2)(C_3H_3O_2)_2(H_2O)]$ (**1**)

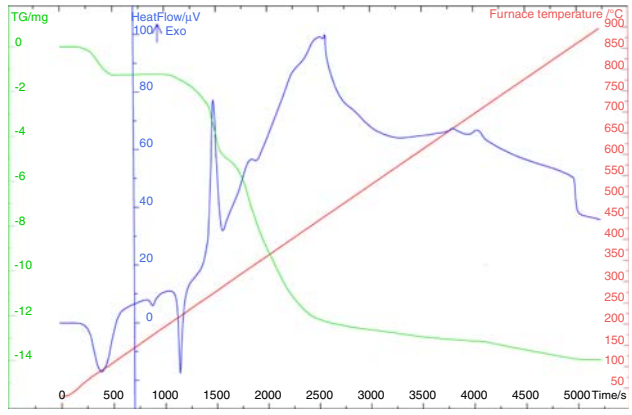


Fig. 3 TG and DTA curves of $[Cd(C_{10}H_8N_2)(C_3H_3O_2)_2]\cdot 1.5H_2O$ (**2**)

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

Complex	Step	Thermal effect	Temperature range/°C	Δm_{exp}/ %	Δm_{calc}/ %
$[Cd(C_{12}H_8N_2)(C_3H_3O_2)_2(H_2O)]$	1	Endothermic	89–110	4.0	4.0
	2	Strong exothermic	270–316	11.5	11.5
	3	Exothermic	316–900	56.5	56.2
	Residue (CdO)			28.0	28.3
$[Cd(C_{10}H_8N_2)(C_3H_3O_2)_2]\cdot 1.5H_2O$	1	Endothermic	50–120	6.1	6.2
	2	Endothermic	162*	0	0
	3	Endothermic	202**	0	0
	4	Exothermic	202–300	18.9	18.8
	5	Exothermic	300–465	35.7	35.7
	6	Exothermic	465–860	10.0	10.0
	Residue (CdO)			29.3	29.3

* Phase transformation, ** melting point

degradation follows as a third step, exothermic one. At least three processes occur as both TG and DTA curves indicate. The result of these processes is cadmium (II) oxide (found/calcd overall mass loss: 72.00/71.64).

Thermal decomposition of $[Cd(C_{10}H_8N_2)(C_3H_3O_2)_2]\cdot 1.5H_2O$

The decomposition of (**2**) starts with water elimination up to 100 °C, the resulted compound being very stable (100–200 °C) (Fig. 3). The anhydrous compound suffers a phase transition at 162 °C accompanied by a weak endothermic effect. This behavior could be associated with crystal lattice reorganization. After melting at 202 °C, the oxidative degradation starts immediately. The first single step consists in acrylate into carbonate conversion being accompanied by a strong exothermic effect. The thermal degradation of 2,2′-bipyridine occurs in at least three successive processes as DTA indicates. The formed intermediate is cadmium carbonate. The carbonate decomposition happens up to 860 °C, leading in two stages at cadmium oxide, as final product (found/calcd overall mass loss: 70.64/70.66).

Conclusions

The new complex compounds of Cd(II) with mixed ligands (1,10-phenantroline/2,2′-bipyridine and acrylate) belong to a class of coordination compounds of current interest having into its composition a ligand which allows inclusion of the metallic ions into a polymeric matrix.

The antimicrobial testing assay revealed that the compounds exhibited different levels of antimicrobial activity (ranging from 64 to 512 µg/cm^3), specially inhibiting the growth of *Pseudomonadaceae*, *Staphylococus aureus* and *Candida albicans* strains, being less active on Gram-negative, enterobacterial strains.

Thermal analysis (TG, DTA) of these complexes elucidated the composition and also the number and nature of the water molecules. It was also evidenced for (**2**) the existence of an intermediate step corresponding to the formation of cadmium carbonate.

In all the cases, the final residue is cadmium oxide.

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