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THERMAL, SPECTRAL AND ANTIMICROBIAL PROPERTIES OF NEW ZINC(II) ISOBUTYRATE COMPOUNDS
Part I. Papaverine, phenazone

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Abstract

Zinc carboxylate complexes with N-donor ligands exhibit antimicrobial and antifungal effects. The preparation and thermal properties of complex compounds $Zn(isobut)_2$ and $Zn(isobut)_2L$ (*isobut*=$(CH_3)_2CHCOO^-$, *L*=papaverine – pap, phenazone – phen) are described in this paper. The newly synthesized compounds were characterized by elemental analysis, IR spectroscopy and TG/DTG, DTA methods.

During the thermal treatment it was found that the release of organic ligands (pap, phen) was followed by pyrolysis of zinc(II) isobutyrate. $(C_3H_7)_2CO$ and CO_2 were found as gaseous products and zinc oxide as the final product of thermal decomposition. Gaseous and solid products of thermal decomposition were confirmed by chemical analysis, IR spectra and X-ray powder diffraction.

Keywords: complex compounds, isobutyrate, papaverine, phenazone, thermal properties, zinc

Introduction

Biometals, which zinc is one of the most significant form, are a part of various metalloenzymes and participate in regulatory, metabolic and redox reactions in organisms [1]. They are very important from the aspect of environment and medicine. Zinc complexes with bioactive ligands catalyse many enzymatic processes in biological systems [2] and they are considered to have pharmaceutical effects against bacteria, fungi and viruses [3]. Most of zinc compounds inhibit the growth of microorganisms and support metabolic processes in cells [4].

In recent years we have studied synthesis, spectral, thermal, structural, chromatographic behaviour and biological properties of several zinc(II) carboxylates and halogenocarboxylates [5–9].

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The aim of this paper concerns with the preparation and the study of some physicochemical properties and thermal behaviour of zinc(II) isobutyrates.

Experimental

Synthesis of the compounds

The following A.R. grade chemicals were used in the synthesis of the compounds: $ZnCO_3$ (Lachema Neratovice), $(CH_3)_2CHCOOH$ 99%, papaverine, phenazone (Aldrich).

The preparation of the complexes can be expressed by the following equation:

$$2(CH_3)_2CHCOOH+ZnCO_3 \rightarrow Zn[(CH_3)_2CHCOO]_2+H_2O+CO_2$$

$$Zn[(CH_3)_2CHCOO]_2+L \rightarrow Zn[(CH_3)_2CHCOO]_2L$$

*Preparation of Zn(isobut)$_2$ **(I)***

Zinc(II) isobutyrate was prepared by the reaction of 1.05 g $ZnCO_3$ (0.0085 mol) suspended in 15 cm^3 of water and 20 cm^3 of water solution of 1.4 cm^3 99% isobutyric acid. The reaction mixture was stirred during 30 min. Then it was filtered off, evaporated and left to stand. White products precipitated within several days. The formed product is soluble in water, methanol and insoluble in diethylether, carbon tetrachloride. The yield of the reaction was 56%.

*Preparation of Zn(isobut)$_2$pap **(II)***

Under continual stirring 20 cm^3 of water solution of 1.42 g papaverine (0.0042 mol) was added to 15 cm^3 of water solution of 1 g zinc(II) isobutyrate (0.0042 mol). The solution was filtered off, evaporated and left to stand. A white product crystallized after a few days. The product is soluble in water, methanol and insoluble in diethylether, carbon tetrachloride. The yield of the reaction was 48%.

*Preparation of Zn(isobut)$_2$phen **(III)***

15 cm^3 of water solution of 1 g zinc(II) isobutyrate (0.0042 mol) was mixed with 20 cm^3 of water solution of 0.55 g phenazone (0.0029 mol) under continual stirring. The reaction mixture was filtered off, evaporated and left to stand. Within several days a white product precipitated. The product is soluble in water, methanol and insoluble in diethylether, carbon tetrachloride. The yield of the reaction was 45%.

Instrumentation and antimicrobial activity determination

Contents of carbon, hydrogen and nitrogen were determined by means of the CHN analyser Perkin Elmer 2400. Zinc content was determined complexometrically using Complexone III as an agent, Eriochrome black T as an indicator. IR spectra of solids

and gaseous products were measured by means of Specord IR M – 80 in the range 4000–200 cm^{-1} (KBr pellets, gas cuvette). TG/DTG and DTA measurements were carried out using derivatograph MOM OD-102 under dynamic conditions in air atmosphere and Pt crucibles (heating rate 9°C min^{-1}, 100 mg sample) and on Perkin Elmer DSC 7/TGA 7 instrument.

The compounds were screened for their antimicrobial activity against *Staphylococcus aureus*, *Escherichia coli* and *Candida albicans*. The tested compounds were diluted in culture media (nutrient broth for bacteria, Sabouraud's medium for fungi). After 24 h cultivation (bacteria 37°C, fungi 25°C) minimum inhibitory concentration (MIC) [μg mL^{-1}] was determined for each compound as the lowest concentration which was able to stop the microbial growth.

Results and discussion

Chemical and antimicrobial properties of the synthesized compounds

The prepared complex compounds are white in colour, stable at light, air and room temperature. The results of elemental analysis are in good accordance with calculated values. The solubilities of the prepared compounds in various solvents are given in Table 1.

The compounds $Zn(isobut)_2$ (**I**) and $Zn(isobut)_2phen$ (**III**) were tested against two bacterial species *Staphylococcus aureus*, *Escherichia coli* and a specie of fungi *Candida albicans*. It was shown that the compound $Zn(isobut)_2$ (**I**) has a bactericidal effect against *Staphylococcus aureus* and its MIC values (minimum inhibitory concentration) was found to be 312 μg mL^{-1}. The bactericidal activity of $Zn(isobut)_2phen$ (**III**) against *Staphylococcus aureus* is low and its value of MIC is 2500 μg mL^{-1}. The activity of the compounds $Zn(isobut)_2phen$ (**III**) and the compound $Zn(isobut)_2$ (**I**) against *Escherichia coli* and *Candida albicans* is low and the values of MIC are 5000 μg mL^{-1}.

For evaluation of the biological activity the compounds with MIC in the range of 0–100 μg mL^{-1} are considered as very good, compounds with MIC in the range 100–1000 μg mL^{-1} are considered to possess good biological activity, compounds with MIC in the range 1000–5000 weak and if MIC is above 5000 μg mL^{-1} the compounds are biologically inactive.

IR characteristic

The presence of individual functional groups was confirmed by IR spectra. The stretching vibration ν(C–H) of the methyl group is at 2980 cm^{-1} for the compounds (**I**), (**II**), (**III**) and the stretching vibration ν(C–H) of the phenyl ring is at 3080, 3070 cm^{-1} for the compounds (**II**), (**III**) (Table 2). The position of absorption band of stretching vibration ν(C–H) for isopropyl group is in the range from 1185 to 1160 cm^{-1}. Bending vibrations δ(C–H) of isopropyl group are found in the region 1375–1360 and 965–950 cm^{-1}, respectively.

Table 1 Solubilities of the prepared compounds in various solvents

Compound	Solvent[a]							
	H_2O	CH_3OH	C_2H_5OH	CCl_4	$(C_2H_5)_2O$	C_6H_6	DMSO	DMFA
$Zn(isobut)_2$ (**I**)	sol	sol	sol	insol	insol	insol	w sol	w sol
$Zn(isobut)_2$pap (**II**)	sol	sol	sol	insol	insol	insol	w sol	w sol
$Zn(isobut)_2$phen (**III**)	sol	sol	sol	insol	insol	insol	w sol	w sol

[a]Abbreviations: sol – soluble, insol – insoluble, w sol – weakly soluble, DMSO – dimethylsulphoxide, DMFA – dimethylformamide

Table 2 Characteristic absorption bands (ν/cm^{-1}) in IR spectra

Assignment	(**I**)	(**II**)	(**III**)
$\nu(C–H)_{ph}$	–	3080	3070
$\nu(C–H)_{CH_3–}$	2980	2980	2980
$\nu(C=O)$	–	–	1680
$\nu_{as}(COO^-)$	1560	1650	1650
$\nu(C=O)_{ph}$	–	1610–1480	–
$\nu_s(COO^-)$	1460–1420	1460–1400	1440–1400
$\nu(C–N)_{py}$	–	1440–1400	–
$\delta(C–H)_{ph}$	–	1430–1000	1420–1000
$\delta(C–H)_{(CH_3)_2CH–}$	1370–1365 960–950	1370–1360 965–950	1375–1360 960–955
$\nu(C–H)_{(CH_3)_2CH–}$	1175–1160 840–790	1185–1160 850–790	1180–1165 845–780
$\gamma(C–H)_{ph}$	–	800–580	820–580

ph – phenyl, py – pyridine; (**I**) – $Zn(isobut)_2$, (**II**) – $Zn(isobut)_2pap$; (**III**) – $Zn(isobut)_2phen$

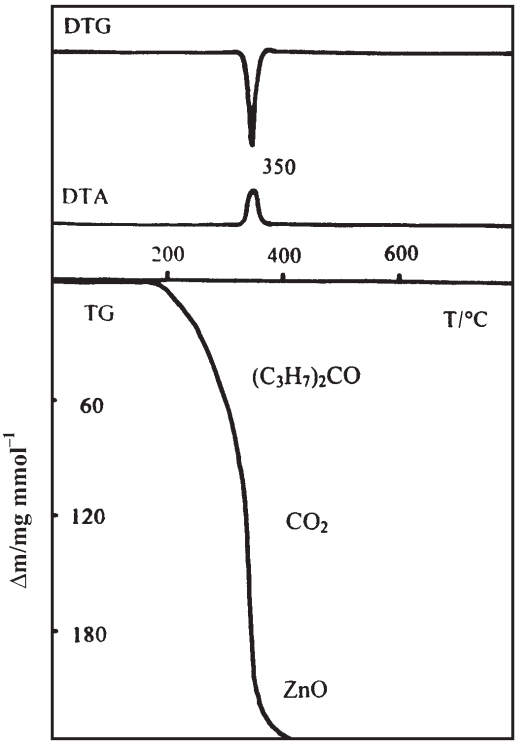

Fig. 1 TG/DTG and DTA curves of $Zn(isobut)_2$

The asymmetric vibration $\nu_{as}(COO^-)$ is at 1560 cm^{-1} for the compound (**I**). This vibration with the shift of about 90 cm^{-1} towards higher wavelengths for the compounds (**II**), (**III**) is caused by organic ligand binding [10]. The symmetric vibration $\nu_s(COO^-)$ is in the region 1460–1400 cm^{-1} for the compounds (**I**), (**II**), (**III**). The other observed values of characteristic vibrations are in good accordance with literature data [11].

Thermal behaviour

Thermal decomposition of the compound (**I**) starts at 180°C with the release of dipropylketone and carbon dioxide in one step as it is observed from the DTA curve with maximum at 350°C (Fig. 1). The final product of thermal decomposition up to 900°C is zinc oxide.

Thermal decomposition of the compounds (**II**), (**III**) can be characterized as several-step reaction (Figs 2, 3). The first step of thermal decomposition is the release of organic ligand (papaverine, phenazone) at 260 and 240°C (Table 2). In the second step of thermal decomposition one molecule of dipropylketone and carbon dioxide is released. The release is accompanied by exothermic effect on the DTA curve at 410,

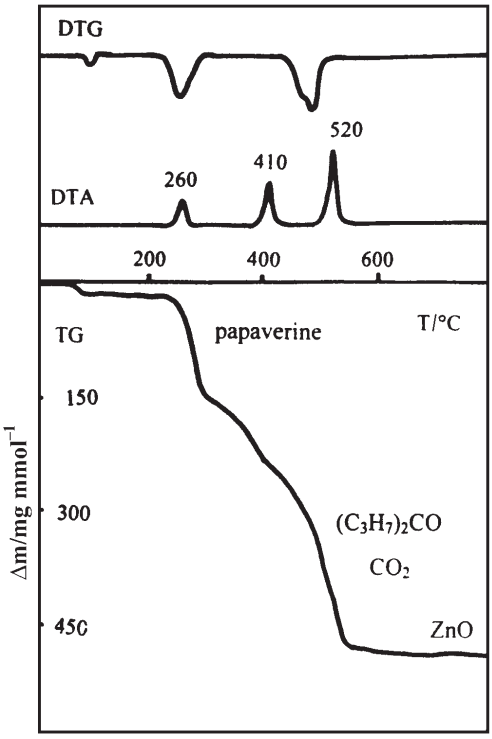

Fig. 2 TG/DTG and DTA curves of $Zn(isobut)_2pap$

520 and at 310, 490°C (Table 3). The final product of thermal decomposition is zinc oxide for both compounds (**II**), (**III**).

The following reaction scheme is proposed for the decomposition process:

$$Zn(isobut)_2L \rightarrow L+(C_3H_7)_2CO+CO_2+ZnO$$

The presence of organic ligands influenced thermal behaviour of zinc(II) isobutyrates.Thermal stability of newly synthetized compounds increases in the order:

$$Zn(isobut)_2phen < Zn(isobut)_2pap < Zn(isobut)_2$$
$$\text{DTA peak:} \quad 240°C < 260°C < 350°C$$

Comparison of thermal behaviour of newly synthetized zinc(II) isobutyrates with analogous zinc(II) butyrate compounds prepared earlier showed that the compound $Zn(isobut)_2$ (**I**) starts to decompose at higher temperature (350°C) than $Zn(but)_2$ which starts to decompose at 150°C [7, 12]. Thermal stability of these earlier studied zinc(II) butyrate complexes increases in the order [7]:

$$Zn(but)_22u < Zn(but)_22tu < Zn(but)_2tu < Zn(but)_2$$
$$\text{DTA peak:} \quad 120°C < 130°C < 140°C < 150°C$$

where *but*=$CH_3CH_2CH_2COO^-$, *u*=urea, *tu*=thiourea.

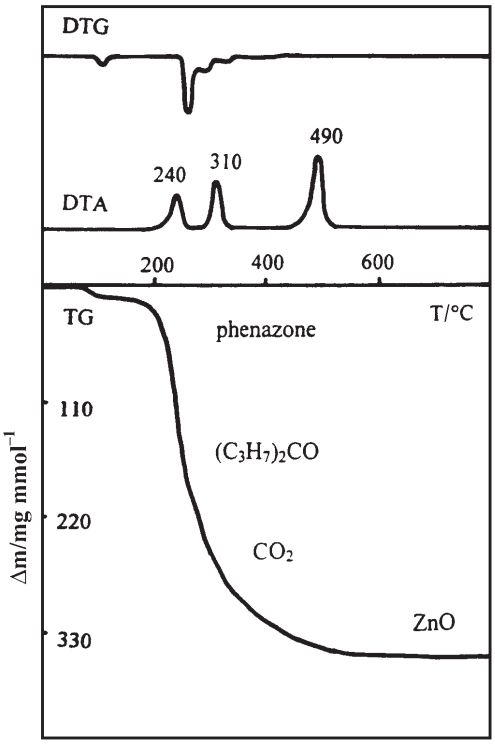

Fig. 3 TG/DTG and DTA curves of $Zn(isobut)_2phen$

Table 3 Thermal decomposition of the prepared compounds

Compound	Temperature of thermal decomposition/°C	Products of thermal decomposition	Mass loss/mg mmol^{-1}		DTA curve
			theor.	exp.	
Zn(isobut)$_2$ (**I**)	350	$(C_3H_7)_2CO$, CO_2	239.58	241.63	s – exo
	900	ZnO	81.38*	79.10*	
Zn(isobut)$_2$pap (**II**)	260	papaverine,	497.60	500.00	m – exo
	410, 520	$(C_3H_7)_2CO$, CO_2			m – exo, vs –exo
	900	ZnO	81.38*	78.03*	
Zn(isobut)$_2$phen (**III**)	240	phenazone	188.23	188.03	w –exo
	310, 490	$(C_3H_7)_2CO$, CO_2	158.20	160.25	m – exo, s – exo
	900	ZnO	81.38*	79.25*	

vs – very strong, s – strong, m – medium, w – weak, exo – exothermic effect, *solid residue

The coordinated organic molecules are released at the first step of thermal decomposition in zinc(II) isobutyrate as well as in zinc(II) butyrate complex compounds. It corresponds with data published for zinc formate, acetate and propionate complex compounds [5, 6]. If the carboxylate compounds contain organic molecules, the temperature of their thermal decomposition is lower than in respective aliphatic zinc carboxylates. The organic ligands (papaverine and phenazone) are released from the compound without their thermal decomposition. When the complex compounds contain thiourea and urea, then molecules of HNCS, HNCO and NH_3 are formed [7]. After releasing organic ligands, carboxylate anion (isobutyrate, butyrate) is decomposed and gaseous products $(C_3H_7)_2CO$ and CO_2 are formed. The final product of thermal decomposition was ZnO, which was confirmed by X-ray diffraction patterns and IR spectra.

Conclusions

We have found out that all the isobutyrate complexes start to decompose with releasing the organic ligand in the temperature range 240–350°C. By comparing analogous zinc(II) butyrate and zinc(II) isobutyrate compounds, the isobutyrate complexes show higher thermal stability than earlier prepared complexes. In gaseous products of both types of the compounds we have found dipropylketone and carbon dioxide. Zinc oxide was found as final product of thermal decomposition.

It was proved by bactericidal tests that the compound $Zn(isobut)_2$ (**I**) was the most active against gram-positive bacterial specie *Staphylococcus aureus*. This antimicrobial activity is similar to the antimicrobial activity of zinc(II) formate, zinc(II) acetate and zinc(II) butyrate [13].

* * *

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