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Thermoanalytical and spectral study of zinc(II) complexes containing theophylline

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Abstract

Treatment of theophylline (Tph) and zinc(II) acetate in various reaction media is studied in this paper. The synthesis, spectral and thermal properties of four theophyllinato complexes, namely $[Zn(NH_3)_2(Tph^-)_2]$ (Tph^-=theophyllinato monoanion), $[Zn(mea)_2(Tph^-)_2]$ (mea=ethanolamine), $[Zn(ipa)_2(Tph^-)_2]$ (ipa=isopropylamine) and $[Zn_2(OH)(CH_3COO)(Tph^-)_2]$ are reported. For successful reaction basic media (acetonitrile, methanol, liquid ammonia, ethanolamine, isopropylamine) were needed. No reaction was found in neutral or acidic water solutions. Differences in the thermal decompositions of the complexes containing one (NH_3, ipa) and two-donor-atom ligands (mea) were observed. Spectroscopic studies suggested that carboxylato and hydroxo bridges connect the zinc atoms in the complex $[Zn_2(OH)(CH_3COO)(Tph^-)_2]$. © 2000 Elsevier Science B.V. All rights reserved.

Keywords: Theophylline; Zinc(II) complex; Amines; Acetate; Thermal decomposition

1. Introduction

Metal complexes of theophylline have been the subject of numerous synthetic and characterization studies in recent years, because of the implications of interactions of metal ions and theophylline may serve as models for coordination of metals to nucleic acids [1,2]. Theophylline (Scheme 1) is not found in nucleic acids, but it is used as a model for guanosine [3].

It follows from the structural investigation of various theophylline complexes that there are three main ways of bonding to the theophylline molecule in the compounds. The first involves the theophylline bonding as a monoanion, with the coordination through deprotonated N(7) atom of the imidazole ring [4]. In complexes with neutral theophylline ligands coordination occurs via N(9) or N(7) nitrogen atom, involving a shift of the H atom on the N(9) [5]. The final way of the occurrence of the theophylline in the compounds is theophyllinium cation [6].

Besides structural studies the thermal properties of the theophylline compounds have been reported and Co(II), Ni(II) and Cu(II) complexes have been investigated from this point of view [4,7]. When heated in air or in an inert atmosphere these complexes undergo several decomposition steps resulting in Co_3O_4, NiO and CuO as the final decomposition products.

In this paper a thermal and spectroscopic study of four complexes containing theophylline have been made. These complexes were prepared as a part of

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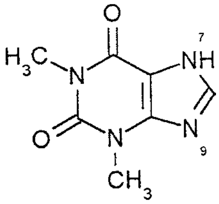


Scheme 1.

our study of the compounds arisen by reactions of zinc(II) carboxylates with N-donor organic ligands (nicotinamide, caffeine, papaverine, theophylline). Nicotinamide and caffeine compounds have been studied elsewhere [8–11].

2. Experimental

Theophylline (Tph), ethanolamine (mea), isopropylamine (ipa), liquid ammonia, methanol, zinc(II) carbonate, acetic acid were procured from Aldrich and used without further purification. Zinc(II) acetate was synthesized from zinc(II) carbonate and acetic acid.

2.1. Syntheses

2.1.1. $[Zn(NH_3)_2(Tph^-)_2]$

A solution of 0.509 g zinc(II) acetate (2.775 mmol) in 40 cm^3 water was added to a solution of 1 g (5.55 mmol) of theophylline in 40 cm^3 water/ammonia (1:1; v/v). The reaction mixture was stirred and after several minutes white powder precipitated. The powder was filtered off, washed with ethanol and dried over silicagel. The dried sample contained a physically adsorbed moisture (0.5 water molecule), which is evident from thermal and elemental analyses. Anal. calcd. for $C_{14}H_{21}N_{10}O_{4.5}Zn$: C, 36.02; H, 4.53; N, 30.00; Zn, 14.00 %. Found: C, 36.3; H, 4.6; N, 30.3; Zn, 14.1%.

2.1.2. $[Zn(mea)_2(Tph^-)_2]$

A batch of 1.0 g (5.55 mmol) of theophylline was dissolved in 40 cm^3 of water to which ethanolamine was added dropwise until pH 12 was reached. This solution was then slowly added to the 0.509 g (2.775 mmol) zinc(II) acetate dissloved in 40 cm^3 water. The white powder precipitated from the mixture after several minutes of stirring. The powder was filtered off, washed with ethanol and dried over silicagel. Anal. calcd. for $C_{18}H_{28}N_{10}O_6Zn$: C, 39.60; H, 5.17; N, 25.66; Zn, 11.97%. Found: C, 39.4; H, 5.02; N, 25.4; Zn, 11.8%.

2.1.3. $[Zn(ipa)_2(Tph^-)_2]$

A solution of 0.509 g zinc(II) acetate (2.775 mmol) in 40 cm^3 water was added to a solution of 1 g (5.55 mmol) of theophylline in 40 cm^3 water. The pH of the solution was adjusted by isopropylamine to 12. The reaction mixture was stirred and after several minutes white powder precipitated. The powder was filtered off, washed with ethanol and dried over silicagel. The dried sample contained a physically adsorbed moisture (0.5 water molecule), which is evident from thermal and elemental analyses. Anal. calcd. for $C_{20}H_{33}N_{10}O_{4.5}Zn$: C, 43.60; H, 6.03; N, 25.42; Zn, 11.86%. Found: C, 43.2; H, 6.3; N, 25.1; Zn, 11.9%.

2.1.4. $[Zn_2(OH)(CH_3COO)(Tph^-)_2]$

A solution of 0.509 g zinc(II) acetate (2.775 mmol) in 40 cm^3 acetonitrile/water (1:1; v/v) was added to a solution of 1 g (5.55 mmol) of theophylline in 40 cm^3 acetonitrile/water (1:1; v/v). The reaction mixture was stirred and after several minutes white powder precipitated. The powder was filtered off, washed with ethanol and dried over silicagel. There is also another way of preparation of $[Zn_2(OH)(CH_3COO)(Tph^-)_2]$. A suspension of $[Zn(NH_3)_2(Tph^-)_2]$ (1 g, 2.184 mmol) in methanol (150 cm^3) was heated to reflux. A methanolic solution of acetic acid (10:1; v/v) was then successivelly added to the suspension under continuous reflux till $[Zn(NH_3)_2(Tph^-)_2]$ dissolved. The reaction mixture was then still refluxed for several hours and white powder precipitated. This powder was filtered off, washed with methanol and air dried. Anal. calcd. for $C_{16}H_{18}N_8O_7Zn_2$: C, 34.00; H, 3.21; N, 19.83; Zn, 23.14%. Found: C, 34.1; H, 3.1; N, 19.9; Zn, 23.2%.

2.2. Instrumentation

IR spectra were recorded on a SPECORD M-80 spectrophotometer in the range 4000–400 cm^{-1} using KBr pellets.

TG/DTG and DTA measurements were carried out using Derivatograph (MOM OD-102) under dynamic conditions in air atmosphere, with heating rate 10°C min^{-1} and sample weight 100 mg.

Elemental analyses were performed using a Perkin–Elmer 2400 CHN analyser. Zinc content was determined complexometrically.

3. Results

3.1. IR spectra

In Table 1 relevant infrared absorption bands of the complexes are listed. It can be seen that the spectra of all the complexes are similar and differ only in several bands due to the presence of various amines. In the region of 3600–3400 cm^{-1} complexes [Zn(mea)$_2$-(Tph$^-$)$_2$] and [Zn$_2$(OH)(CH$_3$COO)(Tph$^-$)$_2$] exhibit strong absorption bands due to O–H stretching vibrations. This band is broad in the complex [Zn(mea)$_2$-(Tph$^-$)$_2$] but it is very sharp and situated at higher frequencies in [Zn$_2$(OH)(CH$_3$COO)(Tph$^-$)$_2$], indicative of μ-hydroxo bridge [12].

The N–H stretching vibrations of the ammino groups are visible in the region of 3300–3200 cm^{-1}. Weak absorption bands, typical of C–H stretching are in the region of 3200–2800 cm^{-1}. Strong absorption bands visible in the spectrum of each of the complexes in the region of 1710–1660 cm^{-1} has been assigned to ν(C=O) stretching vibrations of theophylline. In the region 1600–1500 cm^{-1} there are some intense absorptions due to the ring breathing mode. Bands at 1576 and 1456 cm^{-1} in the complex [Zn$_2$(OH)(CH$_3$COO)(Tph$^-$)$_2$] has been assigned to ν_{as}(COO) and ν_s(COO) vibrations.

3.2. Thermal analysis

3.2.1. [Zn(NH$_3$)$_2$(Tph$^-$)$_2$]

DTA, DTG and TG weight loss aganist temperature plots for the complex [Zn(NH$_3$)$_2$(Tph$^-$)$_2$] are shown in Fig. 1. It can be seen that, the air dried sample contains 0.5 molecule of physically adsorbed water, which is gradually evolved in the temperature range of 60–

Table 1
Characteristic absorption bands in the IR spectra of the prepared complexes

Assignment	Compound[a]			
	[Zn(NH$_3$)$_2$(Tph$^-$)$_2$]	[Zn(mea)$_2$(Tph$^-$)$_2$]	[Zn(ipa)$_2$(Tph$^-$)$_2$]	[Zn$_2$(OH)(CH$_3$COO)(Tph$^-$)$_2$]
ν(O–H)		3400s, broad		3608s, sharp
ν(N–H)	3368s, 3224m	3328s, 3196m	3196w	
ν(C–H)	2968w	2960w, 2880w	3064w 2992w	3136w, 2952w
ν(C=O)	1712s, 1696s, 1648s	1696s, 1652s	1712s, 1700, 1664s	1712s, 1672s, 1656s
δ(NH)	Overlapped	Overlapped	Overlapped	
ν(C=C)		1600m	1600w	1600m
ν(COO$^-$)				1576s
ν(C=C)	1536s	1536s	1548s	1552s, 1528s
ν(COO$^-$)				1456s
δ(C–H)	1420s, 1336m	1424m, 1328w	1448s, 1432s	1428s, 1328m
	1292m	1288w	1288w	1312m
	1260s	1260m	1260s	1264m
δ(C–H)	1224s	1220m	1232m	1232s
	1200m		1192s	1200m
ν(N–CH$_3$)	1108s	1112m	1104m	1108m
δ(C–H)	1064m	1064m	1060m	1064m
	1000m	1024w		1024w
	976s	976m	984m	988m
γ(C–H)	752s	748m	748s	752s
	716s		704m	

[a] Abbreviations: w — weak, m — medium, s — strong.

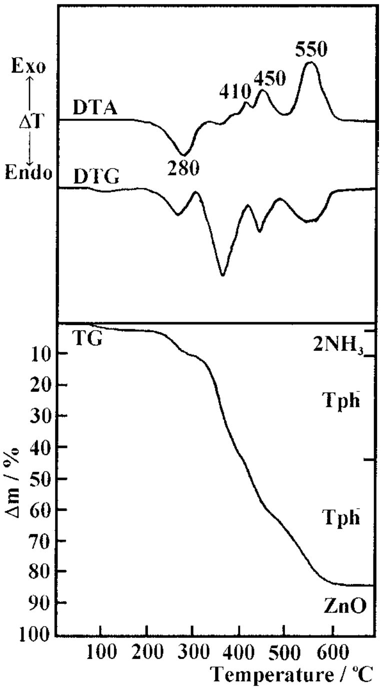


Fig. 1. Thermoanalytical curves of [Zn(NH_3)$_2$(Tph^-)$_2$].

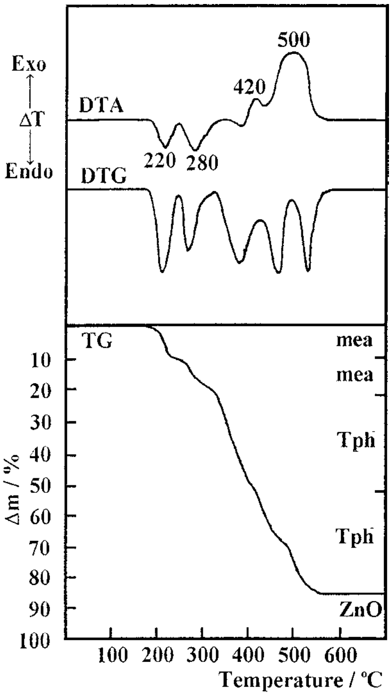


Fig. 2. Thermoanalytical curves of [Zn(mea)$_2$(Tph^-)$_2$].

100°C without any substantial change in the DTA curve.

Thermal decomposition begins at 190°C. Two molecules of ammonia are evolved above this temperature in the temperature range 190–300°C (exp. weight loss 7.0%; calcd. 7.29%) accompanied by endothermic effect with minimum at 280°C in the DTA response.

Further weight loss corresponds to the release and pyrolysis of two theophyllinato molecules. It can be seen from (DTG), that the first molecule of Tph^- is evolved in one step in temperature range of 300–410°C (experimental weight loss is 37%; calcd. 38.38%), while the pyrolysis of the second theophyllinato molecule (410–595°C) takes place in two steps (exp. weight loss is 37%). Release of the first theophylline molecule is accompanied on the DTA curve by exothermic process with maximum at 410°C and the second one with maxima at 450 and 550°C.

The final decomposition product, ZnO (exp. solid residue 17.0%; calcd. 17.4%), was analysed by X-ray powder diffraction (XRD) [13].

3.2.2. [Zn(mea)$_2$(Tph^-)$_2$]

Thermoanalytical responses of the complex [Zn(mea)$_2$(Tph^-)$_2$] are on Fig. 2. The compound is thermally stable up to 180°C.

Above this temperature two molecules of ethanolammine are evolved in two separate steps, the first in the temperature range of 180–250°C (exp. weight loss is 11%; calcd 11.2%) and the second one in 250–320°C (exp. weight loss is 10%; calcd 11.2%). These two steps are endothermic at 220 and 280°C.

The next step in the thermal decomposition is similar to that of [Zn(NH_3)$_2$(Tph^-)$_2$] with the release and pyrolysis of two theophyllinato molecules. It can be seen from the DTG, that the first molecule of Tph^- is evolved in the range of 320–420°C (experimental weight loss is 32%; calcd. 32.8%) and the second one in the temperature range of 420–540°C (exp. weight loss is 33%). The two decomposition steps are exothermic with maxima at 420 and 500°C and the final decomposition product as detected by X-ray powder diffraction, was ZnO (exp. solid residue 14%; calcd. 14.9%) [13].

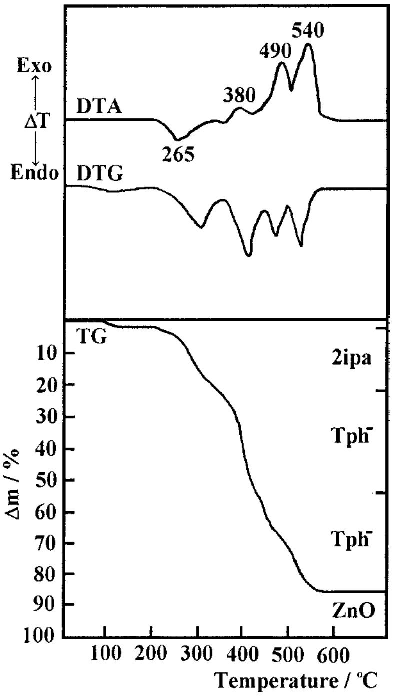


Fig. 3. Thermoanalytical curves of [Zn(ipa)$_2$(Tph$^-$)$_2$].

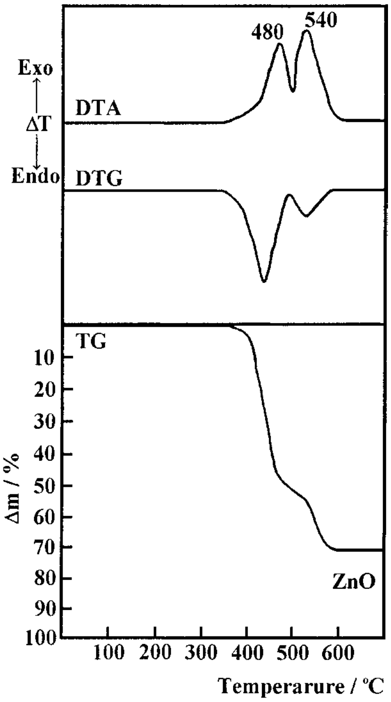


Fig. 4. Thermoanalytical curves of [Zn$_2$(OH)(CH$_3$COO)(Tph$^-$)$_2$].

3.2.3. [Zn(ipa)$_2$(Tph$^-$)$_2$]

Thermal decomposition as well as the thermoanalytical response of the complex [Zn(ipa)$_2$(Tph$^-$)$_2$] (Fig. 3) are similar to those of [Zn(NH$_3$)$_2$(Tph$^-$)$_2$]. As can be seen, the air dried sample contains 0.5 molecule of the physically adsorbed water, which is evolved in the temperature range 60–110°C without any substantial effect on the DTA curve.

The thermal decomposition began at 205°C. Two molecules of isopropylamine are evolved above this temperature in the range 205–330°C (exp. weight loss 21.0%; calcd. 21.45%) accompanied by endothermic effect with maximum at 265°C.

The next weight loss corresponded to the release and pyrolysis of two theophyllinato molecules. It can be seen for the (DTG), that the first molecule of Tph$^-$ is evolved in one step in the temperature range of 330–440°C (experimental weight loss is 32%; calcd. 32.51%) and the second one in the temperature range of 440–550°C (exp. weight loss is 37%). Release of the first theophylline molecule is accompanied on the DTA curve by exothermic process with maximum at 380°C and the second one with maxima at 490 and 540°C.

The final decomposition product ZnO (exp. solid residue 15.0%; calcd. 14.77%), is detected by X-ray powder diffraction [13].

3.2.4. [Zn$_2$(OH)(CH$_3$COO)(Tph$^-$)$_2$]

The thermoanalytical responses of the complex [Zn$_2$(OH)(CH$_3$COO)(Tph$^-$)$_2$] are shown in Fig. 4. Although this complex contained the largest organic component of all the complexes, it is more stable. Its thermal decompositions began at 360°C. The decomposition of the complex associated with the complete pyrolysis of the organic part of the compound starts above this temperature. The pyrolysis is very intense and it is hard to distinguish definite temperature range over which each of Tph$^-$ molecule was being released. All the complex decomposes in a relatively short temperature range from 360 to 580°C. The process of decomposition is accompanied on the DTA curve by two strong exothermic peaks at 480 and 540°C.

The final decomposition product, ZnO (exp. solid residue 29.0%; calcd. 28.80%), was detected by X-ray powder diffraction [13].

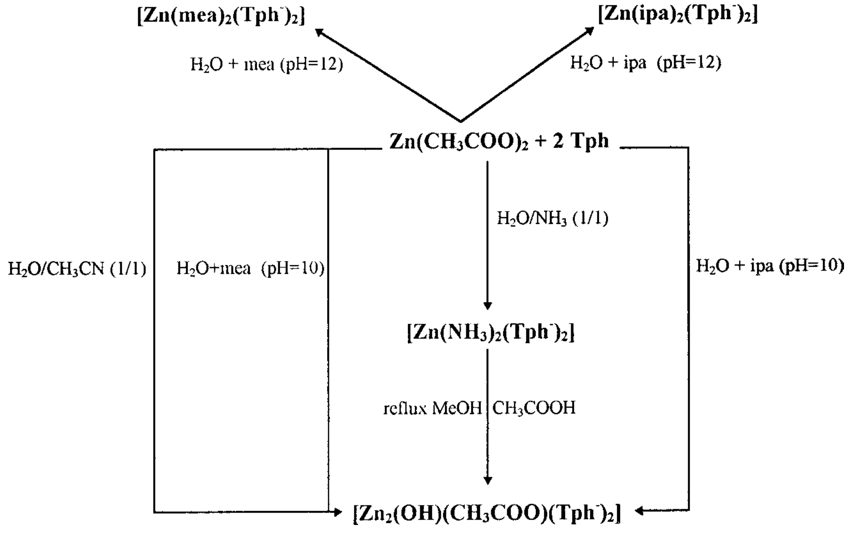
4. Discussion

Treatment of theophylline with the zinc(II) acetate results in various reaction products depending on the reaction media (Scheme 2). No reaction was observed in neutral or acidic water solutions and for successful reaction basic media were needed. These are necessary for the deprotonation of the N(7) theophylline atom and formation of theophyllinato anion, which is more reactive than the neutral theophylline [14].

To achieve the basic reaction media mixture acetonitrile/water (1:1; v/v) was used. Acetonitrile has a higher proton affinity than water and behaves as a base in the water solutions. This reaction media allow the deprotonation of the theophylline as well as ionization of water (OH^-) that leads to the formation of $[Zn_2(OH)(CH_3COO)(Tph^-)_2]$. We have obtained the same result using ethanolamine or isopropylamine. The pH was adjusted by mea or ipa to 10. This basic solution enables the deprotonation of theophylline and ionization of water similarly to the previous case leading to the formation of $[Zn_2(OH)(CH_3COO)(Tph^-)_2]$. Liquid ammonia is not suitable for this purpose because of the formation of solid $Zn(OH)_2$. Finaly, the complex $[Zn_2(OH)(CH_3COO)(Tph^-)_2]$ described above, can also be prepared from $[Zn(NH_3)_2(Tph^-)_2]$. This preparation requies MeOH as reaction media.

Increasing the pH to 12 and also increasing concentration of the base in the solution, carboxylate is completely displaced from the coordination sphere of the zinc and the complexes $[Zn(B)_2(Tph^-)_2]$ ($B{=}NH_3$, mea, ipa) are formed.

It can be seen from Table 1, that the IR spectra of the complexes $[Zn(B)_2(Tph^-)_2]$ ($B{=}NH_3$, mea, ipa) are very similar. Although they differ in positions and intensities of several bands as a consequence of the presence of various ligands B, the majority of the bands arising from the theophylline occur at similar frequencies in all the complexes. Some differences can be observed in the stretching vibrations of the C=O groups of theophylline. In the complex $[Zn(mea)_2(Tph^-)_2]$ these bands at 1696 and 1652 cm^{-1} are shifted by about 16 cm^{-1} lower wavelengths when compared to the free theophylline (1712 and 1668 cm^{-1}). This may be a consequence of the deprotonation of the theophylline molecule during coordination. In the complexes $[Zn(NH_3)_2(Tph^-)_2]$ and $[Zn(ipa)_2(Tph^-)_2]$ there are three C=O absorption bands 1712, 1696, 1648 cm^{-1} and 1712, 1700,



Scheme 2.

$1664\,cm^{-1}$. So there is difference between $[Zn(B)_2(Tph^-)_2]$ (B=NH_3, ipa) on the one side and $[Zn(mea)_2(Tph^-)_2]$ on the other side in number of C=O bands. This difference is also visible during thermal decomposition of the complexes (see below) and may be attributed to various coordination possibilities of NH_3, ipa and mea molecules.

For the complex $[Zn_2(OH)(CH_3COO)(Tph^-)_2]$ there are two main noteworthy features. A sharp absorption maximum at $3608\,cm^{-1}$ is indicative of μ-hydroxo bridges [12]. The $\nu_{as}(COO)$ and $\nu_s(COO)$ stretching frequencies of the carboxylate group are at 1576 and $1456\,cm^{-1}$, respectively. The value of separation $\Delta=\nu_{as}(COO)-\nu_s(COO)=1576-1456=120\,cm^{-1}$ indicates bidentate mode of carboxylate coordination. These results suggest hydroxo and carboxylato bridges between two zinc atoms in $[Zn_2(OH)(CH_3COO)(Tph^-)_2]$. Similar results were observed in the complex $[Zn_2(OH)(CH_3COO)_2(L)_2](ClO_4)\cdot H_2O$ (L=1,4,7-trimethyl-1,4,7-triazacyclononane) where X-ray structure analysis confirmed presence the both types of bridges [12].

The thermal stabilities of the complexes increase in the following order:

$$\underset{180°C}{[Zn(mea)_2(Tph^-)]} < \underset{190°C}{[Zn(NH_3)_2(Tph^-)_2]} < \underset{205°C}{[Zn(ipa)_2(Tph^-)_2]} < \underset{360°C}{[Zn_2(OH)(CH_3COO)(Tph^-)_2]}$$

In the thermal behaviour several trends can be observed. Firstly, while in $[Zn(B)_2(Tph^-)_2]$ (B=NH_3, ipa) ammonia and isopropylamine are liberated in one step, in the complex $[Zn(mea)_2(Tph^-)_2]$ ethanolamine is liberated in two separate steps. This can be connected with different coordination possibilities of the NH_3, ipa and mea molecules. Ammonia and isopropylamine have only one atom suitable for coordination. Thus, both the coordinated molecules of NH_3 or isopropylamine are equivalent and they evolve in the same temperature range. In ethanolamine, there are two possible donor atoms — oxygen and nitrogen. Ethanolamine can posses both unidentate and bidentate coordination. It can be clearly seen in the similar complex $[Cu(mea)_2(Tph^-)_2]\cdot 2H_2O$ [4]. X-ray structural analysis of this complex showed, that one of mea molecule was unidentately bonded through nitrogen atom of amino group, while the other one bidentately through both nitrogen and oxygen atoms [4]. These different coordinations of both mea molecules can also be present in the studied $[Zn(mea)_2(Tph^-)_2]$. The consequence are two separate steps during liberation of ethanolamine.

Secondly, liberation of the first theophyllinato anion in the complexes $[Zn(B)_2(Tph^-)_2]$ (B=NH_3, mea, ipa) takes one step, while the second one evolves more complicately. This difference can be conected with the formation of ZnO as final solid decomposition residue. Exocyclic oxygen of the second Tph^- molecule can be used for formation of ZnO and so both theophyllinato molecules evolve in different temperature ranges and in different courses.

Thirdly, during decomposition of the complex $[Zn_2(OH)(CH_3COO)(Tph^-)_2]$ both theophylline molecules liberate in one step. This can be the consequence of acetato group present in the complex. It is known from thermal decomposition of zinc(II) acetate, that oxygen atom of acetato group is used for formation of final decomposition product ZnO [15]. So exocyclic oxygen of one theophylline molecule is not involved in the process of formation of ZnO and consequently both Tph molecules may evolve at the same time.

References

[1] S. Steinkopf, A. Garoufis, W. Nerdal, E. Sletten, Acta Chem. Scand. 49 (1995) 495.

[2] W. Birdsall, Inorg. Chim. Acta 99 (1985) 59.

[3] D.J. Hodgson, Progress in Inorganic Chemistry, Wiley, New York, 1977, p. 211.

[4] P. Bombicz, J. Madarász, E. Forizs, I. Foch, Polyhedron 16 (1997) 3601.

[5] K. Aoki, H. Yamazaki, J. Chem. Soc., Chem. Commun. (1980) 186.

[6] E.H. Griffith, E.L. Amma, J. Chem. Soc., Chem. Commun. (1979) 322.

[7] S. Gál, J. Madarász, E. Forizs, I. Labádi, V. Izvekov, J. Therm. Anal. 53 (1998) 343.

[8] V. Zeleňák, K. Györyová, J. Simon, J. Therm. Anal. 46 (1996) 573.

[9] V. Zeleňák, K. Györyová, I. Císařová, J. Loub, Acta Crystallogr. C52 (1996) 1917.

[10] V. Zeleňák, K. Györyová, Z. Vargová, Main Group. Met. Chem. 22 (1999) 179.

[11] K. Györyová, V. Balek, B. Behrens, A. Kettrup, J. Therm. Anal. 48 (1997) 1263.

[12] Ch. Chaudhuri, C. Stockheim, K. Wieghardt, W. Deck, R. Gregorzik, H. Vahrenkamp, B. Nuber, J. Weiss, Inorg. Chem. 31 (1992) 1451.

[13] Powder Diffraction File, 5–0664 ICPDS.

[14] L. Marzilli, L. Epps, T. Sorrell, T. Kistenmacher, J. Am. Chem. Soc. (1975) 3351.

[15] V. Panevcik, V.M. Gorjajev, Chim. I Chim. Technol. 22 (1979) 1303.