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# THERMAL STUDIES ON METAL COMPLEXES OF 5-NITROSO-PYRIMIDINE DERIVATIVES

## I. Thermal behaviour of Zn(II) complexes of 6-amino-5-nitrosouracil derivatives

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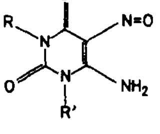
The following Zn(II)complexes of deprotonated 6-amino-5-nitrosouracil (AH), 6-amino-3-methyl-5-nitrosouracil (BH) and 6-amino-1-methyl-5-nitrosouracil (CH) have been prepared and their thermal behaviour studied by TG and DSC techniques: $ZnA_2(H_2O)_2$, $ZnB_2 \cdot 4H_2O$, $ZnC_2 \cdot 4H_2O$ and $ZnC_2(H_2O)_2 \cdot H_2O$. The values of the dehydration enthalpy of the complexes are in the 31.3–76.5 kJ $mol^{-1}$ $H_2O$ range and, except in the first complex, the dehydration processes take place in several steps. The pyrolysis of the complexes finishes between 540 and 725° C ZnO remaining as residue.

In recent years, the study of interactions between transition metal ions and some biological molecules, such as pyrimidine and purine derivatives, enjoys growing interest due to the chemotherapeutic effects shown by some of these complexes [1–4].

It has recently been disclosed that the Zn(II) ion stimulates the adenine nucleotides diffusion across lipide cellular membranes [5] and inhibits the replication of some viruses [6]. However, an understanding of Zn(II) ion function in the nucleotides has been hindered by lack of definite information concerning its binding sites.

Many studies [7–14] of metal-pyrimidine derivative complexes have aimed primarily at elucidated the structure and coordination positions in these complexes. However, there is no information in the literature about the thermal behaviour of these compounds. In a previous work [15], we have described the results obtained in the thermal study of Ag(I) complexes with 6-amino-5-nitrosouracil derivatives. As a part of these researches we report in this paper the thermal behaviour of Zn(II) complexes of 6-amino-5-nitrosouracil (AH), 6-amino-3-methyl-5-nitrosouracil (BH) and 6-amino-1-methyl-5 nitrosouracil (CH).

$R = R' = H \rightarrow AH$; $R = CH_3$, $R' = H \rightarrow BH$; $R = H$, $R' = CH_3 \rightarrow CH$



## Experimental

The uracil derivatives were prepared by methods previously reported [16]. All the chemicals used in this work were of analytical reagent grade.

### *Preparation of the complexes*

10 ml of an aqueous solution of zinc acetate (4 mmole) was added, slowly with stirring, to a hot aqueous solution (200 ml) of the corresponding ligand (2 mmole):

- Zn(II)/AH system: A yellow powder precipitates immediately.
- Zn(II)/BH system: After a few days, red crystals were isolated.
- Zn(II)/CH system: After a few days, a yellow powder was obtained and, from the filtrate, a red powder can be isolated.

The isolated complexes were washed with water and ethanol and dried with diethyl ether. Their chemical analysis were:

**Table 1** Chemical analysis of the complexes

| Compound | Colour | C, % |  | H, % |  | N, % |  | Zn, % |  |
|---|---|---|---|---|---|---|---|---|---|
|  |  | calcd. | found | calcd. | found | calcd. | found | calcd. | found |
| $Zn(C_4H_3N_4O_3)_2(H_2O)_2$ | yellow | 23.33 | 23.24 | 2.43 | 2.54 | 27.22 | 26.42 | 15.89 | 15.35 |
| $Zn(C_5H_5N_4O_3)_2 \cdot 4\,H_2O$ | red | 25.24 | 25.96 | 3.79 | 3.61 | 23.56 | 23.51 | 13.76 | 13.68 |
| $Zn(C_5H_5N_4O_3)_2 \cdot 4\,H_2O$ | yellow | 25.24 | 25.53 | 3.79 | 3.63 | 23.56 | 22.77 | 13.76 | 13.27 |
| $Zn(C_5H_5N_4O_3)_2(H_2O)_2 \cdot H_2O$ | red | 26.23 | 26.30 | 3.50 | 3.16 | 24.49 | 24.81 | 14.29 | 13.56 |

### *Apparatus*

Microanalytical methods were used for the quantitative determination of C, H and N in the samples in the Bioinorganic Department of C. S. I. C. (Barcelona). The determination of Zn was carried out in a Perkin–Elmer (mod. 290) atomic absorption spectrometer.

TG curves were obtained under static air atmosphere in a Mettler TG-50 thermobalance at a heating rate of 10 deg $min^{-1}$. The DSC curves were recorded in a Mettler differential scanning calorimeter model DSC-20, in the 35–550° temperature range, using a heating rate of 5 deg $min^{-1}$. The weight of samples was comprised between 3.33 and 11.26 mg.

## Results and discussion

Recent works [17] carried out by spectral methods (IR and $^1H$-NMR) on the compounds studied in the present paper have shown that the coordination of the corresponding pyrimidine derivative to Zn(II) ion takes place in anionic nitroso-phenolic form with the binding sites being the nitrogen and oxygen atoms of 5-nitroso and 6-oxide groups, respectively.

On the other hand, the IR studies suggest for $ZnA_2(H_2O)_2$ and $ZnC_2(H_2O)_2 \cdot H_2O$ complexes an octahedral structure in which two water molecules are bound to Zn(II) ion. For $ZnB_2 \cdot 4H_2O$ and $ZnC_2 \cdot 4H_2O$ complexes we have proposed a tetrahedral structure in which the water molecules are linked by hydrogen bonds to suitable atoms of the ligands.

Thermogravimetric analysis curves for the isolated complexes are given in Fig. 1 and differential scanning calorimetry curves are given in Fig. 2.

In the isolated pyrimidine derivative complexes, two processes can occur: dehydration and pyrolytic decomposition.

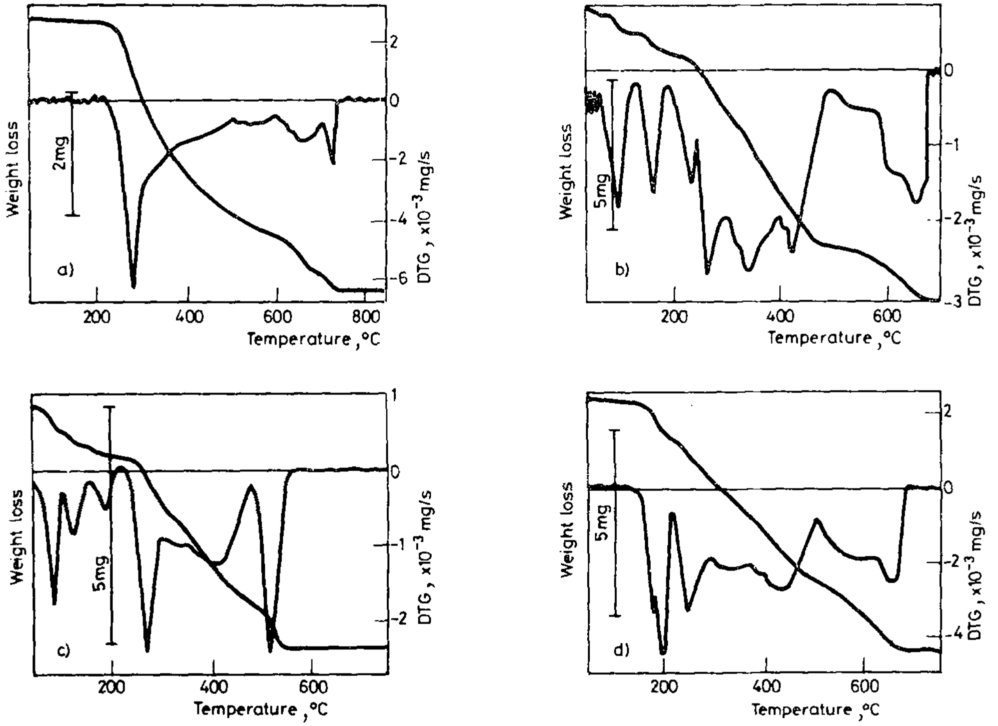


**Fig. 1** TG and DTG curves of Zn(II) complexes. A: $ZnA_2(H_2O)_2$, B: $ZnB_2 \cdot 4H_2O$, C: $ZnC_2 \cdot 4H_2O$ and D: $ZnC_2(H_2O)_2 \cdot H_2O$

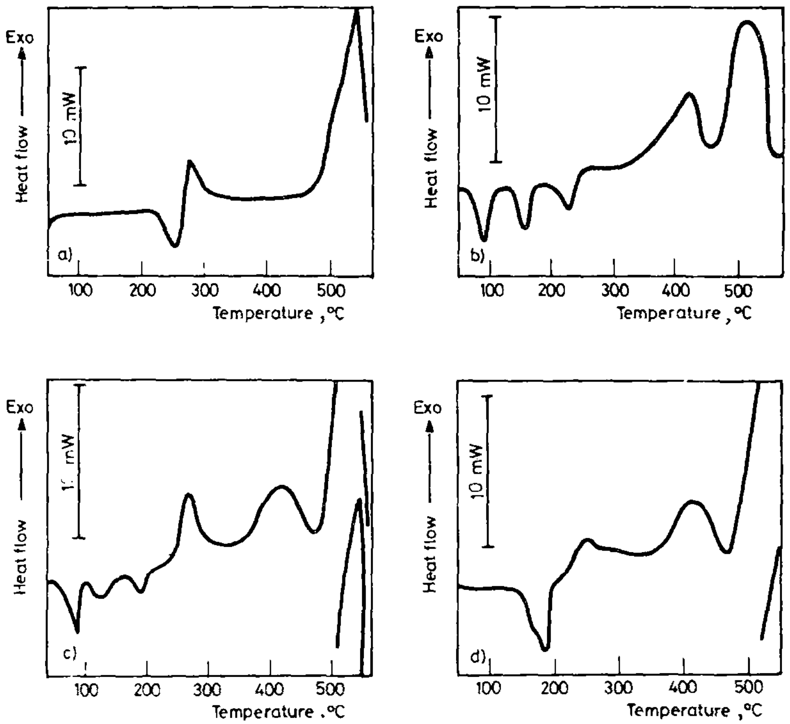


Fig. 2 DSC curves of Zn(II) complexes. A: $ZnA_2(H_2O)_2$, B: $ZnB_2 \cdot 4H_2O$, C: $ZnC_2 \cdot 4H_2O$ and D: $ZnC_2(H_2O)_2 \cdot H_2O$

### *Dehydration processes*

The first step that takes place in the thermal decomposition of the complexes is the elimination of water molecules. The data for calculated and observed weight losses, the DSC peak temperatures and the corresponding dehydration enthalpy values are given in Table 2.

The high value of dehydration enthalpy for the $ZnA_2(H_2O)_2$ complex suggests that the two water molecules are coordinated to Zn(II) ion, which is consistent with the IR data [17]. In Figs 1a and 2a it can be observed that the anhydrous compound ($ZnA_2$) is not stable. This fact hampers the experimental calculation from TG plot of the weight loss due to the dehydration process. However, the expected endothermic behaviour for this reaction has been observed from DSC curve in the same temperature range (Fig. 2a).

The dehydration processes of $ZnB_2 \cdot 4H_2O$ and $ZnC_2 \cdot 4H_2O$ are very similar. Both complexes become completely dehydrated in three consecutive steps. At the first step, the observed weight loss indicates the elimination of two molecules of water. The observed weight losses at the second and the third steps correspond to the loss of one molecule of water each. In the same temperature ranges, the DSC curves show three endothermic peaks. From the area of these peaks we have calculated the corre-

**Table 2** Thermoanalytic data for dehydration processes of isolated compounds

| Process[a] | Weight loss, % calcd. | Weight loss, % obsd. | Peak temperature, DSC, °C | Dehydration enthalpy, kJ $mol^{-1}$ $H_2O$ |
|---|---|---|---|---|
| $ZnA_2(H_2O)_2 \rightarrow ZnA_2 + 2\,H_2O$ | 8.75 | b | 260 | 76.5 |
| $ZnB_2 \cdot 4\,H_2O \rightarrow ZnB_2 \cdot 2\,H_2O + 2\,H_2O$ | 7.57 | 7.6 | 93 | 49.8 |
| $ZnB_2 \cdot 2\,H_2O \rightarrow ZnB_2 \cdot H_2O + H_2O$ | 3.78 | 3.7 | 157 | 71.4 |
| $ZnB_2 \cdot H_2O \rightarrow ZnB_2 + H_2O$ | 3.78 | 3.8 | 232 | 55.8 |
| $ZnC_2 \cdot 4\,H_2O \rightarrow ZnC_2 \cdot 2\,H_2O + 2\,H_2O$ | 7.57 | 8.4 | 86 | 35.6 |
| $ZnC_2 \cdot 2\,H_2O \rightarrow ZnC_2 \cdot H_2O + H_2O$ | 3.78 | 3.7 | 126 | 41.3 |
| $ZnC_2 \cdot H_2O \rightarrow ZnC_2 + H_2O$ | 3.78 | 3.6 | 192 | 31.3 |
| $ZnC_2(H_2O)_2 \cdot H_2O \rightarrow ZnC_2 + 3\,H_2O$ | 11.81 | 11.9 | 185 | 58.2 |

a) $A^-$ = Deprotonated 6-amino-5-nitrosouracil; $B^-$ = Deprotonated 6-amino-3-methyl-5-nitrosouracil; $C^-$ = Deprotonated 6-amino-1-methyl-5-nitrosouracil. b) See text.

sponding enthalpies of dehydration (Table 2). For $ZnB_2 \cdot 4\,H_2O$ the dehydration enthalpy values are higher than the corresponding ones for $ZnC_2 \cdot 4\,H_2O$ which indicates that in the first complex the water molecules are more strongly linked than in the second. Likewise, the forms of DSC curves for these two complexes are very similar, which suggests that probably both have the same structure. On the other hand, the existence of three different types of water molecules can be explained either by the different binding sites of each molecule of water in the initial structure or by the consecutive structural changes that can take place during the heating process.

The DTG curve of the complex $ZnC_2(H_2O)_2 \cdot H_2O$ (Fig. 1d) shows that the three water molecules are not equivalent. However, although the TG and DSC curves were repeated at lower heating rates, it was impossible to separate these two processes. The DSC curve (Fig. 2d) shows an asymmetric endothermic effect assignable to total dehydration of the complex. The asymmetry of this peak is consistent with the existence of two different types of water molecules. The average enthalpy for the elimination of these water molecules indicates that they are less strongly linked than in the $ZnA_2(H_2O)_2$ complex.

### *Pyrolytic processes*

The dehydrated compounds decompose in the 220–725° temperature range, showing the same number of exothermic effects in the corresponding DSC curve than the free ligands [17]. These effects must be attributed to the combustion of the organic matter. They appear at lower temperature values than in the DSC curve of the corresponding free ligand. This fact can be due to a decrease of the thermal stability of the pyrimidine derivative in the complexation process. In all cases, the final residue is ZnO, as revealed by X-ray diffraction methods ($d = 2.476$ Å) [18] and IR spectroscopy. The thermogravimetric and DSC data for the pyrolytic processes are given in Table 3.

**Table 3** Thermogravimetric and DSC data for the pyrolytic processes

| Reaction | Weight loss, % calcd. | Weight loss, % obsd. | Final temperature, TG, °C | DSC peak temperature, °C endo | | exo | |
|---|---|---|---|---|---|---|---|
| $ZnA_2 \rightarrow ZnO$ | 79.73 | 77.2 | 725 | – | 275 | 540 | |
| $ZnB_2 \rightarrow ZnO$ | 82.88 | 85.0 | 670 | – | 265 | 429 | 516 |
| $ZnC_2 \rightarrow ZnO$ | 82.88 | 79.8 | 540 | – | 267 | 420 | 548 |
| $ZnC_2 \rightarrow ZnO$ | 82.22 | 81.5 | 670 | – | 241 | 416 | > 550 |

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**Zusammenfassung** — Die folgenden Zn(II)-Komplexe von deprotoniertem 6-Amino-5-nitrosouracil (AH), 6-Amino-3-methyl-5-nitrosouracil (BH) und 6-Amino-1-methyl-5-nitrosouracil(CH) wurden dargestellt und hinsichtlich ihres thermischen Verhaltens durch TG und DSC untersucht: $ZnA_2(H_2O)_2$, $ZnB_2 \cdot 4\,H_2O$, $ZnC_2 \cdot 4\,H_2O$ und $ZnC_2(H_2O)_2$. Die Werte der Dehydratisierungsenthalpien dieser Komplexe liegen im Bereich von 31.3 bis 76.5 kJ per mol $H_2O$. Die Dehydratisierung verläuft, außer beim ersten Komplex, in mehreren Stufen. Die Pyrolyse der Komplexe ist bei 540 bis 725° C beendet und ergibt als Rückstand ZnO.

**Резюме** — Методом ТГ и ДСК изучено термическое поведение комплексов депротонированных 6-амино-5-нитрозоурацила (АН), 6-амино-3-метил-5-нитрозоурацила (БН) и 6-амино-1-метил-5-нитрозоурацила (СН) с цинком со следующим стехиометрическим составом: $ZnA_2(H_2O)_2$, $ZnB_2 \cdot 4\,H_2O$, $ZnC_2 \cdot 4\,H_2O$ и $ZnC_2(H_2O)_2$. Значения энтальпии дегидратации комплексов расположены в области 31,3–76,5 кдж/моль. За исключением первого комплекса, процесс дегидратации протекает в несколько стадий. Пиролиз комплексов заканчивается в области температур 540–725 °С с образованием окисла цинка.