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

II. Thermal behaviour of Cd(II) complexes of 6-amino-5-nitroso-uracil derivatives

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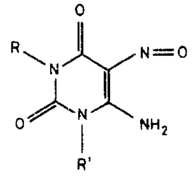
The following cadmium(II) complexes of deprotonated 6-amino-5-nitroso-uracil (AH), deprotonated 6-amino-3-methyl-5-nitroso-uracil (BH) and neutral 6-amino-1-methyl-5-nitroso-uracil (CH) have been prepared and their thermal behaviour studied by TG and DSC techniques: $CdA_2 \cdot 3\,H_2O$, $CdB_2 \cdot 2\,H_2O$, CdB_2 and $CdCl_2(CH)_2 \cdot 2\,H_2O$.

Dehydration processes of these complexes take place in only one step and the enthalpy values associated with them are comprised in the 42.7–80.5 kJ · $mole^{-1}$ H_2O range. The pyrolytic reactions finish in the 630–900 °C temperature range, remaining as final residue in the case of $CdA_2 \cdot 3\,H_2O$, $CdB_2 \cdot 2\,H_2O$ and CdB_2 complexes, cadmium oxide. The pyrolytic decomposition of $CdCl_2(CH)_2 \cdot 2\,H_2O$ complex does not yield any residue, due to the elimination of cadmium chloride.

The study of metal-pyrimidine derivatives complexes has received increasing attention in the last few years, both from the inorganic and biological points of view [1–11].

It is well known that some of these complexes play a dominant role in many biochemical systems and the interest that they have aroused is due, fundamentally, to their chemotherapeutic effects as anticancer agents [8–11]. For these reasons, many studies have aimed, primarily, to elucidate the mechanism of physiological actions of these compounds. The first step in these researches has been the determination of binding sites of the corresponding pyrimidine derivative to metal ion by spectral methods, such as IR, uv-visible and NMR [1–5], and X-ray diffraction methods. Thus, Cartwright et al. have reported the crystal structure of the bis(1,3-dimethyluracil) dichlorocopper(II) in which the metal is bonded strongly to the C(4)=O(4) group of the base, being the first uracil derivative for which a powerful metal-oxygen interaction has been demonstrated [12]. Recently, Lumme et al. have described the crystal structures of triaquabis(uracilato) cadmium(II) [13], diamminediaquabis(uracilato) nickel(II) [14] and some copper(II) and nickel(II) 2-aminopyrimidine mixed complexes [15].

In order to amplify the chemical information concerning these complexes, we are developing in our laboratory some studies about their thermal stability [16–18]. As a part of these researches we have described in this paper the thermal behaviour of Cd(II) complexes with 6-amino-5-nitroso-uracil (AH), 6-amino-3-methyl-5-nitroso-uracil (BH) and 6-amino-1-methyl-5-nitroso-uracil (CH).



R = R' = H ⟶ AH
R = CH_3 ; R' = H ⟶ BH
R = H ; R' = CH_3 ⟶ CH

Experimental

The pyrimidine derivatives were prepared by methods previously reported [19]. All the chemicals used in this work were analytical reagent grade.

Preparation of the complexes

The synthesis of cadmium complexes was carried out as follows: 10 ml of an aqueous solution of $CdCl_2 \cdot 2\frac{1}{2}H_2O$ (8 mmole) were added, slowly with stirring, to a hot aqueous solution (200 ml) of the corresponding ligand (2 mmole). After stirring for a half hour, the resulting solutions were allowed to stand at room temperature. In these conditions we obtained the following compounds:

a) Cd(II)/AH system: After standing one hour, we isolated the complex as a pink powder.

b) Cd(II)/BH system: By evaporation at room temperature during several days, an orange powder was obtained. From the filtrate solution, red crystals were isolated.

c) Cd(II)/CH system: When this solution was allowed to stand 24 hours, we obtained an orange powder.

All the compounds were filtered by suction, washed with water and ethanol and dried with diethylether. Their chemical analyses (%) were:

$Cd(C_4H_3N_4O_3)_2 \cdot 3H_2O$ (pink),
calcd., C = 20.15, H = 2.52, N = 23.51, Cd = 23.59,
found, C = 20.02, H = 2.39, N = 23.31, Cd = 22.60.

$Cd(C_5H_5N_4O_3)_2 \cdot 2H_2O)$ (orange)
calcd., C = 24.67, H = 2.88, N = 23.03, Cd = 23.11,
found, C = 24.53, H = 2.84, N = 22.86, Cd = 22.13.

$Cd(C_5H_5N_4O_3)_2$ (red)
calcd., $C = 26.64, H = 2.22, N = 24.86, Cd = 24.96,$
found, $C = 26.65, H = 2.10, N = 25.16, Cd = 24.80.$

$CdCl_2(C_5H_6N_4O_3)_2 \cdot 2\,H_2O$ (orange)
calcd., $C = 21.45, H = 2.86, N = 20.02, Cd = 20.09,$
found, $C = 21.51, H = 2.75, N = 19.83, Cd = 19{,}84.$

Apparatus

Chemical analyses of C, H and N were performed in the microanalysis laboratory of the Bioorganic Department of C. S. I. C. (Barcelona). Determination of the cadmium content of the samples was carried out in a Perkin–Elmer (mod. 290) atomic absorption spectrometer.

Thermogravimetric analyses were made in air atmosphere with a Mettler TG-50 thermobalance at a heating rate of 10 deg. min^{-1}. DSC runs were carried out on a Mettler differential scanning calorimeter model DSC–20, in the 35–550° temperature range, using a heating rate of 5 deg. min^{-1}. Thermolytic reactions were obtained with samples varying in weight from 3.40 to 6.21 mg.

Results and discussion

Recent studies by spectral methods (IR and ^1H–NMR) (20) have shown that the 6-amino-5-nitroso-uracil and its methylated derivatives as well as their deprotonated forms can behave as either mono- or bidentate ligands. In this work we have some examples of both coordination types. In $CdA_2 \cdot 3\,H_2O$, $CdB_2 \cdot 2\,H_2O$ and CdB_2 complexes, we observed that the coordination of the corresponding pyrimidine derivative to Cd(II) ion takes place as bidentate ligand, in deprotonated nitroso-phenolic form, being the binding sites the nitrogen and oxygen atoms of 5-nitroso and 6-oxide groups, respectively. From IR data [20], we have proposed for each $CdA_2 \cdot 3\,H_2O$ and CdB_2 complexes a distorted tetrahedral structure, while for $CdB_2 \cdot 2\,H_2O$ complex the IR data do not permit discern between a tetrahedral and an octahedral structure, since the IR spectrum of the ligand [5] shows several bands in the region where bands corresponding to vibrational modes of coordinated water molecules appear. On the other hand, IR data suggest for $CdCl_2(CH)_2 \cdot 2\,H_2O$ complex, an octahedral polymeric structure with chlorine bridging, in which the 6-amino-1-methyl-5-nitroso-uracil (CH) acts as a monodentate ligand through the nitrogen atom of 5-nitroso group, probably. In $CdA_2 \cdot 3\,H_2O$ and $CdCl_2(CH)_2 \cdot 2\,H_2O$ compounds, water molecules seem to be linked by hydrogen bonds to suitable atoms of the ligands.

Thermogravimetric analysis curves and DSC plots for the isolated complexes are given in Figs 1 and 2, respectively.

In all isolated complexes, two processes can occur: dehydration and pyrolytic decomposition.

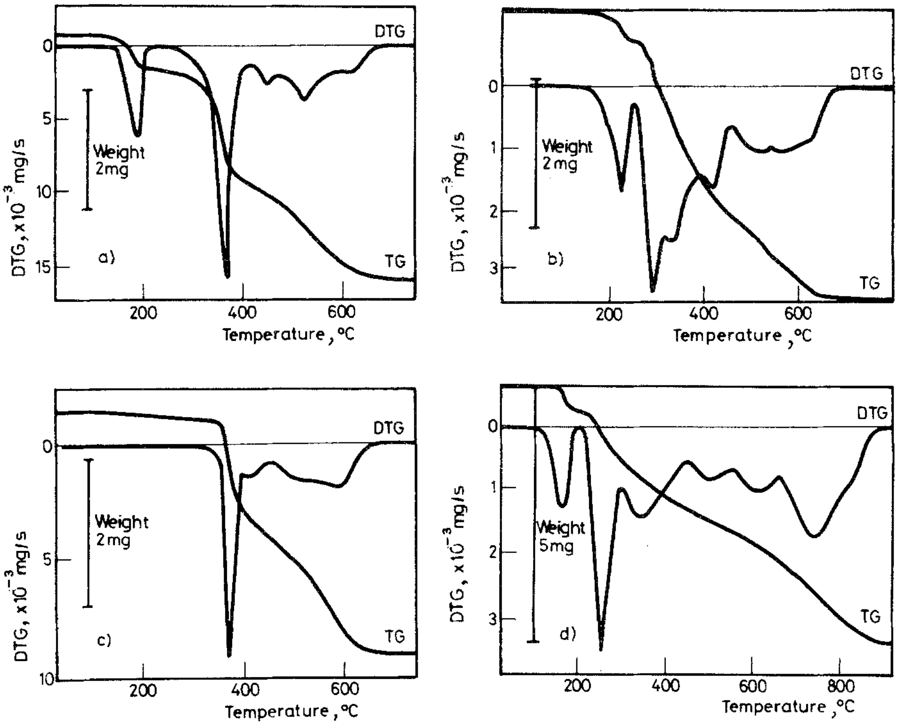


Fig. 1 TG plots for isolated complexes: A — $CdA_2 \cdot 3H_2O$, B — $CdB_2 \cdot 2H_2O$, C — CdB_2, D — $CdCl_2(CH)_2 \cdot 2H_2O$

Dehydration processes

The first step that takes place in the thermal decomposition of the complexes is the elimination of water molecules. Data for calculated and observed weight losses, DSC peaks temperatures and corresponding dehydration energy values are tabulated in Table 1.

In Fig. 1, we can observe that all dehydration processes take place in only one step, which suggests that the water molecules are equivalent in every case. Dehydration enthalpy values, calculated from the area of the corresponding endothermic peaks, indicate a great difference between the bond of water molecules in $CdB_2 \cdot 2H_2O$ complex and in the others two complexes. The observed value of dehydration enthalpy for $CdA_2 \cdot 3H_2O$ and $CdCl_2(CH)_2 \cdot 2H_2O$ is according to the ones found by IR spectral methods (water molecules linked to the ligands by hydrogen bonds).

The high value of dehydration energy for $CdB_2 \cdot 2H_2O$ complex suggests that water molecules are directly bonded to Cd(II) ion. On account of this fact it is reasonable to propose for this compound an octahedral structure, in which the equatorial positions are occupied by the ligands and the two water molecules are in the apical positions. This structure is analogous to the one found for the complex formed by

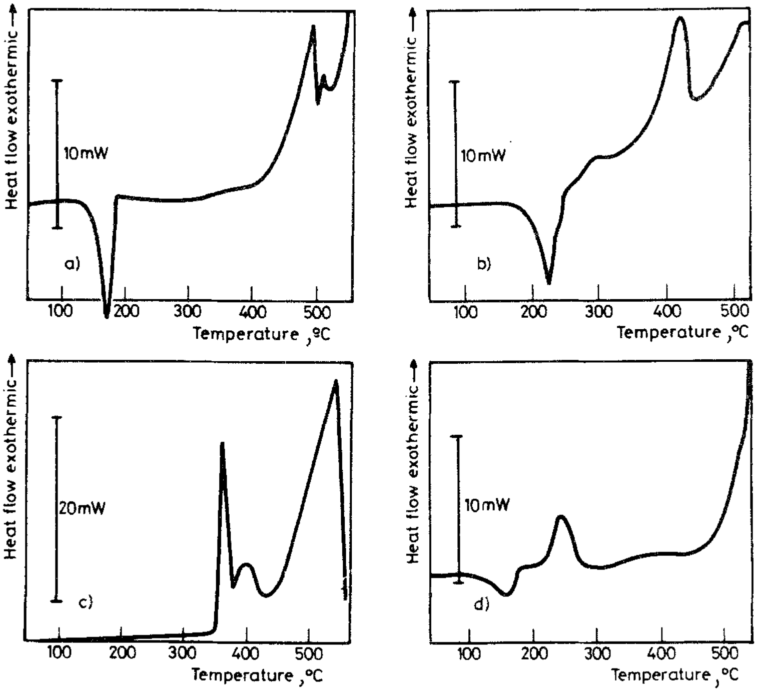


Fig. 2 DSC plots: A – $CdA_2 \cdot 3 H_2O$, B – $CdB_2 \cdot 2 H_2O$, C – CdB_2 D – $CdCl_2(CH)_2 \cdot 2 H_2O$

Table 1 Thermoanalytical data for dehydration processes

Process*	Weight loss, %		DSC peak temperature °C	Dehydration enthalpy, kJ · mol^{-1} water
	Calcd.	Found		
$CdA_2 \cdot 3 H_2O \rightarrow CdA_2 + 3 H_2O$	11.33	12.0	172	46.5
$CdB_2 \cdot 2 H_2O \rightarrow CdB_2 + 2 H_2O$	7.40	7.5	224	80.5
$CdCl_2(CH)_2 \cdot 2 H_2O \rightarrow CdCl_2(CH)_2 + 2 H_2O$	6.43	6.8	162	42.7

* A^- = deprotonated 6-amino-5-nitroso-uracil, B^- = deprotonated 6-amino-3-methyl-5-nitroso-uracil, CH = neutral 6-amino-1-methyl-5-nitroso-uracil.

Zn(II) ion and the 6-amino-5-nitroso-uracil [17, 20], in which calculated dehydration enthalpy was 76.5 kJ · $mole^{-1}$ H_2O [17].

Pyrolytic processes

Thermogravimetric and DSC data for the pyrolytic processes are given in Table 2. The dehydrated compounds decompose in the 225–900° temperature range. In the DSC plots (Fig. 2), it can be observed that every complex shows the same

Table 2 TG and DSC data for pyrolytic processes

Reaction	Weight loss (%) Calcd.	Found	Final temperature, TG (°C)	DSC peaks temperature (°C) Endo		Exo	
CdA_2 ---- CdO	73.05	72.5	650	–	490	510	> 550
CdB_2 ---- CdO	73.60	73.6	650	–	290	420	> 550
CdB_2 ---- CdO	71.49	72.9	630	–	365	400	540
$CdCl_2(CH)_2$ ---- (a)	(a)	97.0	900	–	245	420	> 550

(a) See text.

number of exothermic effect than the corresponding free ligand [20]. These effects must be attributed to the combustion of the organic matter. Likewise, it is interesting to observe the differences between the Figs 2B and 2C, which are in accordance with the two different structures that we have proposed for $CdB_2 \cdot 2\ H_2O$ and CdB_2 complexes, since if the structure of $CdB_2 \cdot 2\ H_2O$ was tetrahedral, after dehydration process its DSC plot (Fig. 2B) should be similar to the one corresponding for CdB_2 (Fig. 2C).

In Table 2, we have indicated that in three first compounds, the final residue is CdO, as revealed by IR and X-ray diffraction methods (d = 2.712 Å) [21], while the pyrolysis of $CdCl_2(CH)_2 \cdot 2\ H_2O$ complex does not yield practically any residue (3.0%). This fact is in agreement with those found in other analogous complexes of Cd(II) [22], since the cadmium chloride, at temperatures higher than 725°, is eliminated.

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Zusammenfassung — Folgende Cadmium(II)-Komplexe von deprotoniertem 6-Amino-5-nitroso-uracil (AH), deprotoniertem 6-Amino-3-methyl-5-nitroso-uracil (BH) und neutralem 6-Amino-1-methyl-5-nitroso-uracil (CH) wurden hergestellt: $CdA_2 \cdot 3\,H_2O$, $CdB_2 \cdot 2\,H_2O$, CdB_2 und $CdCl_2(CH)_2 \cdot 2\,H_2O$. Das thermische Verhalten dieser Komplexe wurde mittels TG und DSC untersucht. Die Dehydratisierung der Komplexe verläuft in nur einem Schritt. Die Enthalpiewerte für diese Prozesse liegen im Bereich von 42.7–80.5 $kJ \cdot mol^{-1}\ H_2O$. Die pyrolytischen Reaktionen verlaufen im Temperaturbereich von 630–900 °C zu Ende, wobei im Falle der Komplexe $CdA_2 \cdot 3\,H_2O$, $CdB_2 \cdot 2\,H_2O$ und CdB_2 Cadmiumoxid als Rückstand zurückbleibt. Die pyrolytische Zersetzung von $CdCl_2(CH)_2 \cdot 2\,H_2O$ verläuft wegen der Flüchtigkeit von $CdCl_2$ rückstandslos.

Резюме — Получены и исследованы методом ТГ и ДСК комплексы кадмия общего состава $CdA_2 \cdot 3\,H_2O$, $CdB_2 \cdot 2\,H_2O$, CdB_2 и $CdCl_2(CH)_2 \cdot 2\,H_2O$, где А — депротонированный 6-амино-5-нитрозоурацил, В — депротонированный 6-амино-3-метил-5-нитрозоурацил и СН — нейтральный 6-амино-1-метил-5-нитрозоурацил. Процессы дегидратации комплексов протекают в одну стадию. Значения энтальпий реакций дегидратации находятся в области значений 42.7–80.5 кдж • моль$^{-1}$. Реакции пиролиза заканчиваются в области температур 630–900°, давая в случае первых трех комплексов окись кадмия в качестве конечного продукта реакции. Разложение комплекса $CdCl_2(CH)_2 \cdot 2\,H_2O$ происходит без образования какого-либо остатка, сто обусловлено испарением хлорида кадмия.