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THERMAL STUDIES ON PURINE COMPLEXES. VIII. THERMAL BEHAVIOUR OF 8-ETHYLXANTHINE, 8-ETHYL-3-METHYLXANTHINE AND SOME OF THEIR METAL COMPLEXES

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ABSTRACT

Thermal decomposition processes for 8-ethylxanthine (8EH), 8-ethyl-3-methylxanthine (3MEH) and the complexes formed by these purine bases with Cu(II), Ag(I), Au(III) and Pd(II) ions have been studied using TG and DSC techniques. Infrared spectroscopy and X-ray diffraction have been used for the characterization of final products of the pyrolysis. Dehydration, deammination and dehalogenation energies have been calculated from DSC curves.

INTRODUCTION

Studies of purine–metal ion interactions have become one of the main topics in the research of bioinorganic chemistry, as described by several recent reviews [1–6]. Among the purine bases, xanthine occurs as a minor constituent in *t*-RNA and the methyl-substituted derivatives of this base have been utilized as model compounds for nucleosides [7,8].

A number of metal complexes of xanthine derivatives have been studied in detail, especially those in which theophylline acts as a ligand [9–18]; however, studies on the interactions between metal ions with xanthines substituted in the 8 position are scanty [19,20].

We have been involved for some time in the study of the thermal behaviour of metal–xanthine and metal–methylated xanthine derivative complexes [16,17,20–24]. In this line, this paper reports the thermal behaviour of two 8-alkylated xanthine derivatives (8-ethylxanthine (8EH) and 8-ethyl-3-methylxanthine (3MEH)) and their Cu(II), Ag(I), Au(III) and Pd(II) metal complexes.

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EXPERIMENTAL

8-Ethylxanthine and 8-ethyl-3-methylxanthine were prepared using a previously described method [25]. Preparative methods for the isolated metal complexes of these purine bases have been indicated in a previous paper [26].

Thermal studies have been carried out on a Mettler TA-3000 system provided with a Mettler TG 50 thermobalance and a Mettler DSC 20 differential scanning calorimeter. Thermogravimetric curves were registered in dynamic conditions (a flow rate of 100 ml min^{-1} of pure air was used), using sample weights between 4.793 and 19.323 mg and a heating rate of 10°C min^{-1}. DSC curves were obtained in static air atmosphere at a heating rate of 5°C min^{-1}. The temperature ranges investigated were 35–700°C (TG) and 35–550°C (DSC).

RESULTS AND DISCUSSION

TG and DSC diagrams for 8-ethylxanthine (8EH) and 8-ethyl-3-methylxanthine (3MEH) are shown in Fig. 1. The TG curve of anhydrous 3MEH shows a single and strong weight loss effect in the 340–410°C temperature range, in which 3MEH is practically removed from the reaction crucible (96% weight loss). On the other hand, the DSC of 3MEH exhibits one endothermic effect at 341°C and two exothermic effects at 390 and > 500°C. The endothermic effect corresponds to fusion of the sample. The value found for the melting point (341.1°C) is in good agreement with the literature data. The fusion enthalpy calculated from the area of the corresponding endothermic effect is 39.3 kJ mol^{-1}, which is similar to those found by Cammenga and co-workers [27,28] for the fusion enthalpy of other purine bases analogous to 3MEH. Once 3MEH has melted, it experiences a rapid decomposition process, responsible for the two exothermic effects cited above.

The TG diagram for 8EH is different to that of 3MEH. In this case, the decomposition process is completed for temperatures greater than those found for 3MEH (~ 850°C), showing a strong weight loss effect centered at 420°C in the DTG curve, in which 65.60% of the sample is eliminated. The DSC curve of 8EH shows an intense and sharp endothermic effect at 393°C which corresponds to the fusion of the 8-ethylxanthine, and the beginning of an exothermic effect, which has not been resolved. The calculated fusion enthalpy for 8EH is 92.9 kJ mol^{-1}, which is very large and suggests strong interactions between the molecules of 8EH.

In aqueous solution 8EH and 3MEH can be considered as weak dibasic acids. The acid dissociation constants of both purine bases were calculated by potentiometric methods. The values of the acidity constants obtained in the 20–50°C temperature range are comprised for K_1 between 1.8×10^{-9} and 4.5×10^{-9} mol l^{-1} (3MEH), and 2.0×10^{-8} and 5.9×10^{-8} mol l^{-1}

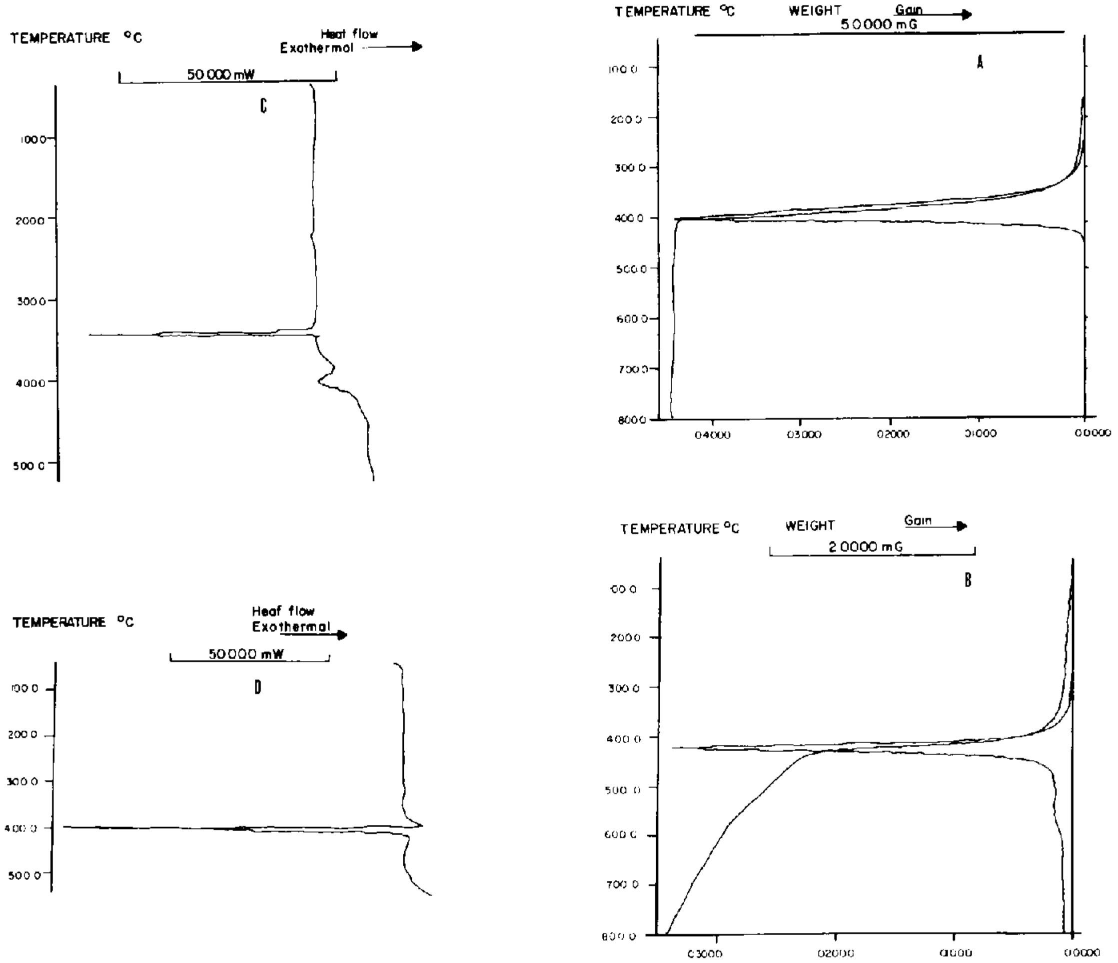

Fig. 1. TG diagram for 8EH (A) and 3MEH (B), and DSC curves for 8EH (C) and 3MEH (D).

(8EH) and for K_2, between 1.1×10^{-10} and 4.2×10^{-10} mol l^{-1} (3MEH) and 0.9×10^{-10} and 2.4×10^{-10} mol l^{-1} (8EH).

In aqueous media with pH controlled, 8EH and 3MEH react with the metal ions Cu(II), Pd(II), Ag(I) and Au(III) to give seven new compounds of compositions: $Cu(C_7H_7N_4O_2)_2(NH_3)_2 \cdot 2H_2O$ (**I**); $Cu(C_8H_9N_4O_2)(NH_3)_2 \cdot 4H_2O$ (**II**); $Pd(C_7H_8N_4O_2)_2Cl_2 \cdot H_2O$ (**III**); $Pd(C_8H_{10}N_4O_2)_2Cl_2 \cdot 2H_2O$ (**IV**); $Ag(C_7H_7N_4O_2) \cdot 2H_2O$ (**V**); $Ag(C_8H_9N_4O_2)$ (**VI**); and $(C_8H_{11}N_4O_2)(AuCl_4) \cdot H_2O$ (**VII**), whose preparative methods and spectroscopic characterizations have been described in a recent work [26]. These complexes show the following thermal behaviour.

Copper complexes

TG curves for compounds **I** and **II** are shown in Figs. 2A and 2B, respectively. Both diagrams are very similar, showing four weight loss effects centered in the DTG curves at 85, 195, 380 and 425°C (**I**) and 80, 175, 330 and 405°C (**II**). Experimental values for weight loss percentages in the effects centered at 85 and 80°C (**I** = 7.64%; **II** = 12.66%) are in good agreement with those calculated for the total dehydration of these complexes (**I** = 7.32%; **II** = 12.96%). These dehydration processes are responsible for the endothermic effects centered at 91 (**I**) and 86°C (**II**) in the DSC curves of these complexes (Figs. 3A and 3B). The values of the dehydration enthalpies were 23.8 kJ mol^{-1} H_2O (**I**) and 24.7 kJ mol^{-1}; analogous to that found in the dehydration process of silver(I) theophyllinato monohydrate [17].

The second step of the decomposition of **I** and **II** is a deammination process. The complexes become deamminated in the temperature ranges 150–220 (**I**) and 140–200°C (**II**). In these temperature ranges the observed weight losses (accumulated) were 14.34 (**I**) and 18.79% (**II**), which are in perfect accord with the calculated values (**I** = 14.32% and **II** = 19.08%). The expected endothermic behaviour for the deammination process associated with these compounds is supported by the DSC curves (Figs. 3A and 3B) in almost the same temperature ranges (endothermic effects at 189 (**I**) and 184°C (**II**)). From the areas of these effects the deammination enthalpy values were calculated: 43.8 kJ mol^{-1} (**I**) and 60.1 kJ mol^{-1} (**II**), which are similar to those found by us for bis(theophyllinato)diammine zinc(II) and bis(theophyllinato)diammine copper(II) [17].

Once dehydrated and deamminated, **I** and **II** decompose pyrolytically in the temperature ranges 300–510 (**I**) and 290–490°C (**II**), showing one strong exothermic effect in the DSC curves. In both cases, the pyrolysis process gave CuO. The residue weights were: 17.83 (**I**) and 15.94% (**II**) (theoretical values 16.78 (**I**) and 14.31% (**II**)).

Palladium complexes

Two pale yellow complexes (**III** and **IV**) are obtained when $PdCl_2$ reacts with 8EH and 3MEH in an aqueous medium [26].

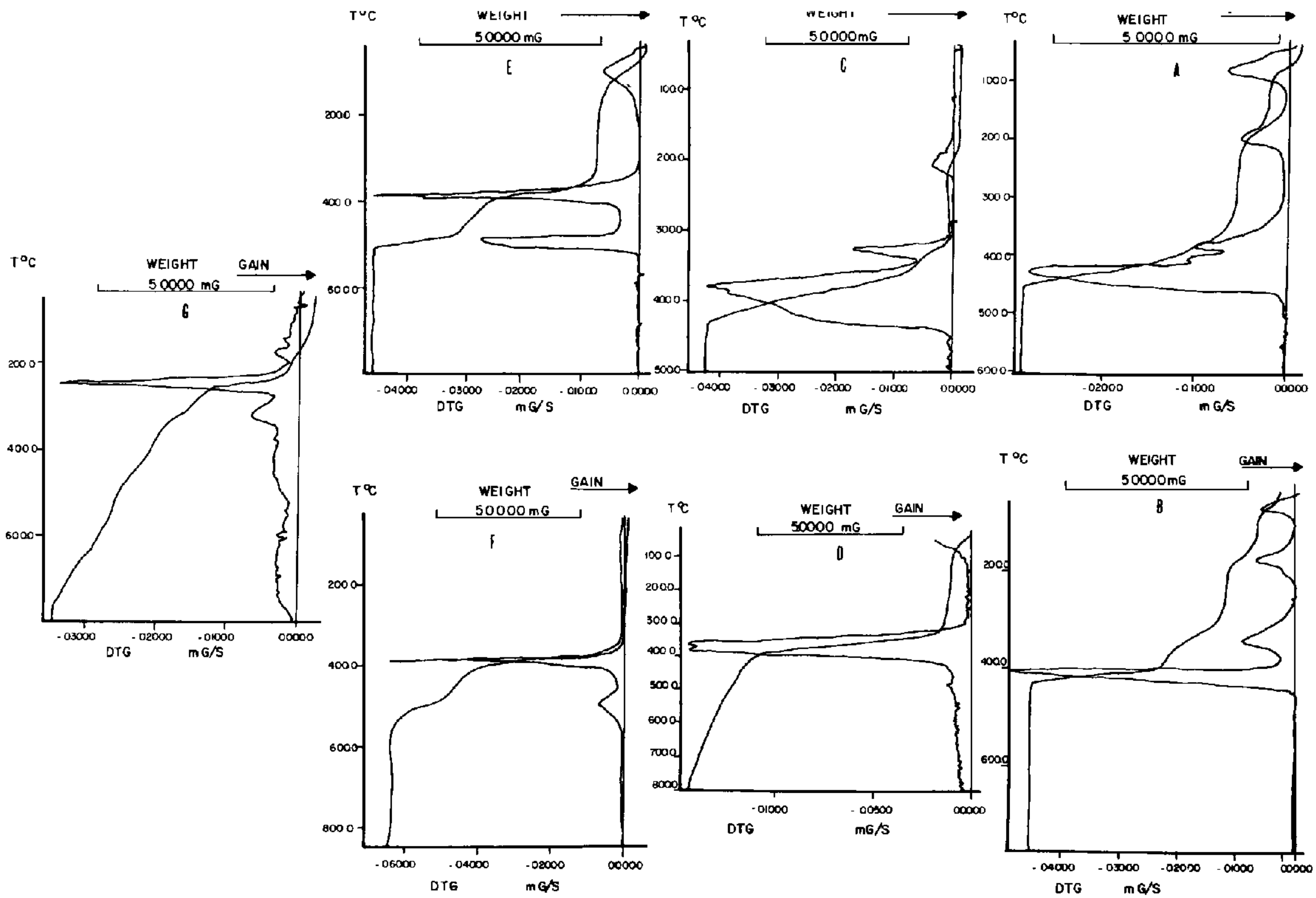

Fig. 2. TG diagrams for $Cu(8E)_2(NH_3)_2 \cdot 2H_2O$ (A); $Cu(3ME)_2(NH_3)_2 \cdot 4H_2O$ (B); $Pd(8EH)_2Cl_2 \cdot H_2O$ (C); $Pd(3MEH)_2Cl_2 \cdot 2H_2O$ (D); $Ag(8E) \cdot 2H_2O$ (E); $Ag(3ME)$ (F) and $(3MEH_2)^+(AuCl_4)^- \cdot H_2O$ (G).

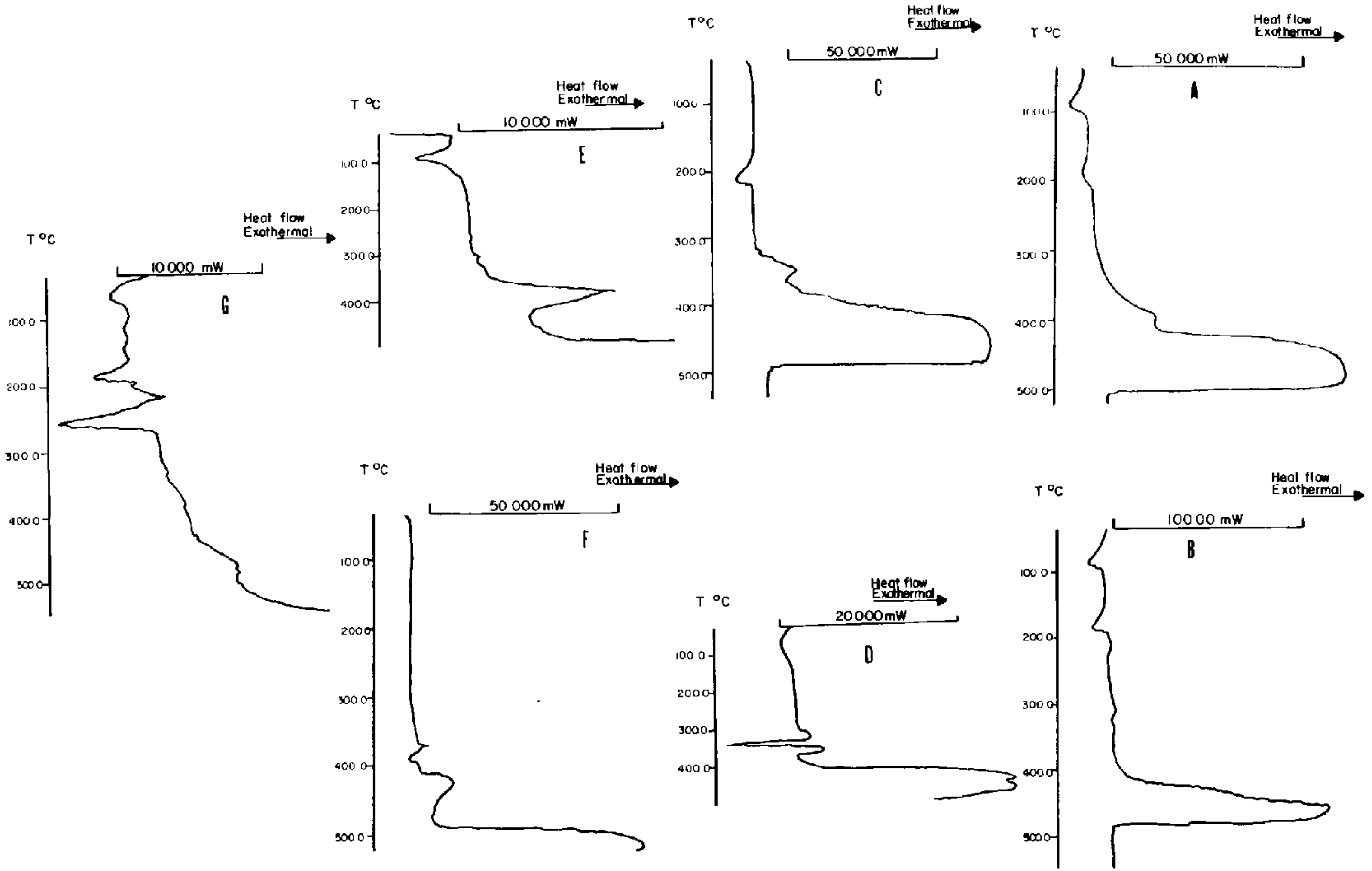

Fig. 3. DSC diagrams for $Cu(8E)_2(NH_3)_2 \cdot 2H_2O$ (A); $Cu(3ME)_2(NH_3)_2 \cdot 4H_2O$ (B); $Pd(8EH)_2Cl_2 \cdot H_2O$ (C); $Pd(3MEH)_2Cl_2 \cdot 2H_2O$ (D); $Ag(8E) \cdot 2H_2O$ (E); Ag(3ME) (F) and $(3MEH_2)^+(AuCl_4)^- \cdot H_2O$ (G).

The thermal behaviour of these complexes is composed of three steps: (i) dehydration, (ii) dehalogenation and (iii) pyrolytic decomposition.

The dehydration processes for **III** and **IV** are very different, thus, **III** became completely dehydrated in the 170–230°C temperature range. This process is responsible for the endothermic effect centered at 214°C in Fig. 3. The experimental weight loss in the above temperature range (3.02%), is in agreement with the calculated value (3.24%). On the other hand, the high value of dehydration enthalpy ($\Delta H = 89.6$ kJ mol^{-1}) indicates that the molecules of water are strongly linked by hydrogen bonds to chlorine atoms or to the molecules of the purine base. However, the dehydration process of **IV** starts at 40 and finishes at 110°C. In this temperature range two molecules of water per mole of complex are removed (experimental weight loss, 5.85%; calculated weight loss, 5.98%). These molecules of water are weakly linked to chlorine atoms or molecules of 3MEH and can be removed by placing the complex into a desiccator with H_2SO_4, which did not occur for complex **III**.

Once dehydrated, **III** and **IV** experience a dehalogenation process in one step; these processes have been observed in the 300–340 (**III**) and 310–350°C (**IV**) temperature ranges. The DTG curve for **III** (Fig. 3C) shows a weight loss effect centered at 325°C in which the experimental accumulated weight loss is 15.11% (calcd., 15.94%). The expected endothermic effect for this process has not been observed in the corresponding DSC curve due to overlapping with the beginning of the pyrolysis of **III**. Nevertheless, in the DSC curve of **IV**, an endothermic effect centered at 340°C can be observed. This effect corresponds to the total dehalogenation of **IV**, and from its area a value of 166 kJ mol^{-1} for dehalogenation enthalpy has been calculated. This value is slightly higher than that found for the dehalogenation processes of $PdCl_2L_2$ complexes (where L = theobromine and 1,3,8-trimethylxanthine) [29].

The dehalogenated compounds are not stable and rapidly start to decompose. These decompositions appear in the DSC curves as exothermic effects at 345 and 450°C (**III**) and 430 and 460°C (**IV**). In both cases PdO is obtained as the final product of the pyrolysis. The residue weights correspond to 20.20 (**III**) and 21.22% (**IV**) of the initial weight of the samples (calculated values: 20.35 (**III**) and 22.13% (**IV**)).

Silver complexes

When $AgNO_3$ reacts with 8EH and 3MEH in aqueous medium, the white compounds **V** and **VI** are isolated.

The thermal behaviour of these compounds is very similar, as may be seen from their corresponding TG and DSC curves (Figs. 2 and 3). Both compounds decompose in the 350–550°C temperature range to give Ag(0) as residue. The weight losses at 550°C (65.96 (**V**) and 64.26% (**VI**)) are in agreement with the calculated values. The decomposition processes occur in two steps causing exothermic effects centered at 415 and 525°C (**V**) and 385 and > 525°C in the DSC curve (**VI**).

On the other hand, the TG and DSC curves of **V** show that in the 50–120°C temperature range, the total dehydration of the compound takes place. This process occurs in one step, in which 11.12% of the sample is eliminated. This value is practically coincident with that calculated (11.15%). The expected endothermic behaviour for this dehydration process may be seen in the corresponding DSC curve (Fig. 3). From the area of the endothermic effect centered at 91°C a value of 29.7 kJ mol^{-1} H_2O was calculated for the dehydration enthalpy.

Gold complexes

In acid medium (HCl), 3MEH reacts with tetrachloroauric acid to give a solid constituted by yellow needle-like crystals (**VII**).

Spectroscopic and magnetic studies have permitted us to propose for this compound a structure in which the negative charge of the $(AuCl_4)$ square-planar ion is neutralized by a protonated molecule of 3MEH. The protonation occurs in the N-9 atom of the purine ring [26].

From the TG and DSC curves of **VII** the following scheme of thermal decomposition has been proposed

$$\begin{aligned}(C_8H_{11}N_4O_2)(AuCl_4)\cdot H_2O &\xrightarrow[77^\circ C]{\text{endo}} (C_8H_{11}N_4O_2)(AuCl_4)\\ &\xrightarrow[186^\circ C]{\text{endo}} (C_8H_{10}N_4O_2)(AuCl_3) + HCl\\ &\xrightarrow[256^\circ C]{\text{endo}} (C_8H_{10}N_4O_2) + 3/2\ Cl_2\\ &\xrightarrow[470^\circ C]{\text{exo}} \xrightarrow[>550^\circ C]{\text{exo}} \text{Au(0)} + \text{pyrolysis products}\end{aligned}$$

This same behaviour has also been observed in the thermal decomposition of the tetrachloroaurate of theophylline [16].

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