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THERMAL STUDIES ON PURINE COMPLEXES. V. THERMAL BEHAVIOUR OF TETRACHLOROPALLADATES OF THEOPHYLLINE AND THEOBROMINE AND THEOPHYLLINE COMPLEXES OF Cd(II) AND Hg(II)

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ABSTRACT

Palladium compounds $|LH_2^+|_2|PdCl_4|$ (where LH = theophylline or theobromine) and theophylline complexes $CdT_2(OH_2)_4$, $HgTCl \cdot H_2O$ and $Hg(TH)Cl_2$, have been prepared in acid and hydroethanolic medium, respectively, and studied by IR and ^1H-NMR spectroscopy. The thermal behaviour of these compounds has been studied using TG, DTG and DSC techniques. Dehydration and dehalogenation enthalpies have been calculated.

INTRODUCTION

The involvement of metal-containing species in genetic information transfer [1], nucleotide biochemistry and in mutagenesis [2] and carcinogenesis [3], has led to considerable recent efforts at understanding the structural nature of the interaction of metal compounds with nucleotides and nucleic acids [4–6]. A variety of purine bases has been employed in model system studies of the metal–nucleic acid constituents interactions [4–6]. For this reason and following the thermal studies on compounds containing metal ions and xanthine derivatives [7–9], we report in this work the synthesis, characterizations and thermal behaviour of two new Pd(II) salts of theophylline (TH) and theobromine (TBH). Likewise, we report the thermal behaviour of the three new complexes of theophilline.

EXPERIMENTAL

Theophylline (1,3-dimethylxanthine) and theobromine (3,7-dimethylxantine) were purchased from Carlo Erba. All the inorganic products were of analytical reagent grade.

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Microanalysis of C, H, N and Cl were performed in a Carlo Erba model 1106 microanalyzer. The determination of Pd(II) was carried out gravimetrically. The determination of Cd(II) was carried out in a Perkin–Elmer model 290 absorption spectrometer. Infrared spectra were recorded in the region 4000–200 cm^{-1} using a Beckman 4250 spectrophotometer, in KBr pellets. The 600–200 cm^{-1} region was also registered in polyethylene pellets.

The ^1H-NMR spectra were recorded on a Hitachi–Perkin–Elmer model R-600, FT-NMR spectrometer, using DMSO-d_6 as solvent and TMS as internal standard.

The TG studies were made in a static atmosphere of air (in the case of the mercury compound a pure air flow of 100 ml min^{-1} was used) on a Mettler TG-50 thermobalance, using samples varying in weight from 6.18 mg to 11.26 mg and a heating rate of 10°C min^{-1}. The DSC curves were recorded on a Mettler differential scanning calorimeter model DSC-20 at a heating rate of 5°C min^{-1}, in the temperature range 40–560°C (in the mercury compounds the temperature range was 40–325°C), using samples varying in weight from 2.52 mg to 3.56 mg.

PREPARATION OF THE COMPOUNDS

Palladium compounds

A solution of 0.85 mmol of $PdCl_2$ in 50 ml of 2.4 M HCl was added to 1.7 mmol of xanthine derivative in 50 ml of 2.4 M HCl. The mixture was heated at 80°C with continuous stirring for 30 min. The resulting clear solution was allowed to cool slowly to room temperature. After 10 days, brown precipitates appeared, which were filtered, washed consecutively with water and ethanol and dried with ether. Their chemical analyses were:

$|TH_2^+|_2|PdCl_4|$

Found: C, 27.68%; H, 2.98%; N, 18.53%; Cl, 23.12%; Pd, 16.82%.
Calcd.: C, 27.52%; H, 2.95%; N, 18.35%; Cl, 23.26%; Pd, 17.43%.

$|TBH_2^+|_2|PdCl_4|$

Found: C, 27.39%; H, 3.01%; N, 18.64%; Cl, 23,32%; Pd, 17.25%.
Calcd.: C, 27.52%; H, 2.95%; N, 18.35%; Cl, 23.26%; Pd, 17.43%.

Theophylline compounds

Theophylline complexes of Cd(II) and Hg(II) were obtained in hydroethanolic medium, by mixing solutions containing 5×10^{-3} mol of theophylline and 3×10^{-3} mol of metal chloride, respectively. The mixture was heated at 70°C with continuous stirring for about 1 h. The resulting clear solution was allowed to cool slowly to room temperature. After 10 days, colourless crystals appeared for the cadmium complex. In the case of the mercury compound, after 24 h a white precipitate was obtained, which was filtered. After 10 days, colourless crystals were obtained from the resulting filtrate solution. In all cases, the compounds were washed consecutively with water and ethanol and dried with ether.

Their chemical analyses and colour were:

$CdT_2(OH_2)_4$ (colourless)

Found: C, 31.59%; H, 4.01%; N, 20.65%; Cd, 19.45%.
Calcd.: C, 30.95%; H, 4.05%; N, 20.63%; Cd, 20.72%.

$Hg(TH)Cl_2$ (white)

Found: C, 18.94%; H, 1.68%; N, 12.41%.
Calcd.: C, 18.59%; H, 1.77%; N, 12.39%.

$HgTCl \cdot H_2O$ (colourless)

Found: C, 19.92%; H, 1.94%; N, 12.98%.
Calcd.: C, 19.39%; H, 1.85%; N, 12.92%.

RESULTS AND DISCUSSION

Palladium compounds

The most significant IR absorption bands, for theophylline, theobromine and their palladium compounds are given in Table 1.

In the palladium compounds isolated, theophylline and theobromine are protonated, since their IR spectra show new bands in the region 3200–2700 cm^{-1}, which correspond to $\nu(\overset{+}{N}-H)$ stretching vibrations. Likewise, the bands corresponding to $\nu(C=C)$ and $\nu(C=N)$ appear at higher wavenumbers with respect to the position of these bands in the free xanthine derivatives, which is due to the protonation [10].

In the region 600–200 cm^{-1} IR spectra show absorption bands at 330 cm^{-1} ($[TH_2^+]_2[PdCl_4]$) and 305 cm^{-1} ($[TBH_2^+]_2[PdCl_4]$), assigned to stretching vibrations $\nu(Pd-Cl)$. The positions of these bands is according to the bibliographic data for compounds containing the $[PdCl_4]^{2-}$ square-planar anion [11].

The square-planar nature of the $[PdCl_4]^{2-}$ anion was confirmed by magnetic measurements, because the Pd(II) isolated compounds are not paramagnetic.

The ^{1}H-NMR spectra of $[LH_2^+]_2[PdCl_4]^{2-}$ (Fig. 1) (where LH_2^+ is the protonated form of theophylline and theobromine) in DMSO-d_6 were compared to ^{1}H-NMR spectra of the free TH and TBH. The downfield shift of

TABLE 1

Infrared data of the isolated compounds (cm^{-1})

	ν(OH)	ν(N–H)	ν(C=O)	δ_{as}(OH)	ν(C=C)	ν(C=N)	ν(M–Cl)
Theophylline		3120	1715 1665		1605	1560	
Theobromine		3120	1700 1675		1600	1550	
$\vert TH_2^+\vert_2\vert PdCl_4\vert$		3200–2700 [a]	1725 1690		1625	1565	330
$\vert TBH_2^+\vert_2\vert PdCl_4\vert$		3200–2700 [a]	1700 [b]		1650	1570	305
$CdT_2(OH_2)_4$	3440 [b]		1680 1615	1655	1575	1525	
$HgTCl \cdot H_2O$	3490(as) 3410(sy)		1685 1630	1640	1550	1530	340
$Hg(TH)Cl_2$		3120	1680 [b]		[c]	1550	350

[a] Few bands.

[b] Broad band.

[c] Not observed due to the overlapping with the ν(C=O) band.

T = Theophyllinato anion.

the signals corresponding to the proton bonding to C(8) in the two isolated compounds is due to the protonation on a nitrogen atom of the imidazolic ring. The downfield shift was also observed in the ^{1}H-NMR spectra of the salts $|LH_2^+||AuCl_4|$ (where LH = xanthine derivative) and $(9EG)_2|PtCl_4| \cdot 2\ H_2O$ (where 9EG = 9-ethylguaninium) [12,13].

Likewise, the ^{1}H-NMR spectrum of the $|TH_2^+|_2|PdCl_4|$ presents a new signal over 10 PPM corresponding to two protons, which can be assigned to the protons of the imidazolic ring (N_7 and N_9). These protons are equivalents due to (A) and its resonance equivalent form (B), which places the positive charge on the N(9) atom (Fig. 2). The ^{1}H-NMR spectrum of the $|TBH_2^+|_2|PdCl_4|$ also shows a new signal over 11 PPM corresponding to one proton, which is due to the proton on the N_9 atom. These new signals are removed to add D_2O to the DMSO-d_6.

The above data suggest for these compounds a salt-like structure in which the charge of the anion $PdCl_4^{2-}$ is neutralized by two molecules of protonated theophylline or theobromine (Fig. 3). These salts are similar to those obtained for the reaction between cytosine and K_2PdCl_4 in acid medium [14].

Thermogravimetric analysis curves for theobromine, theophylline and their isolated palladium complexes are presented in Fig. 4 and differential scanning calorimeter curves are given in Fig. 5.

In the isolated palladium compounds two processes can occur: dehalogenation and pyrolitic decomposition. In $|TH_2^+|_2|PdCl_4|$, the dehalogenation take place in one step, in the 240–320°C temperature range. The

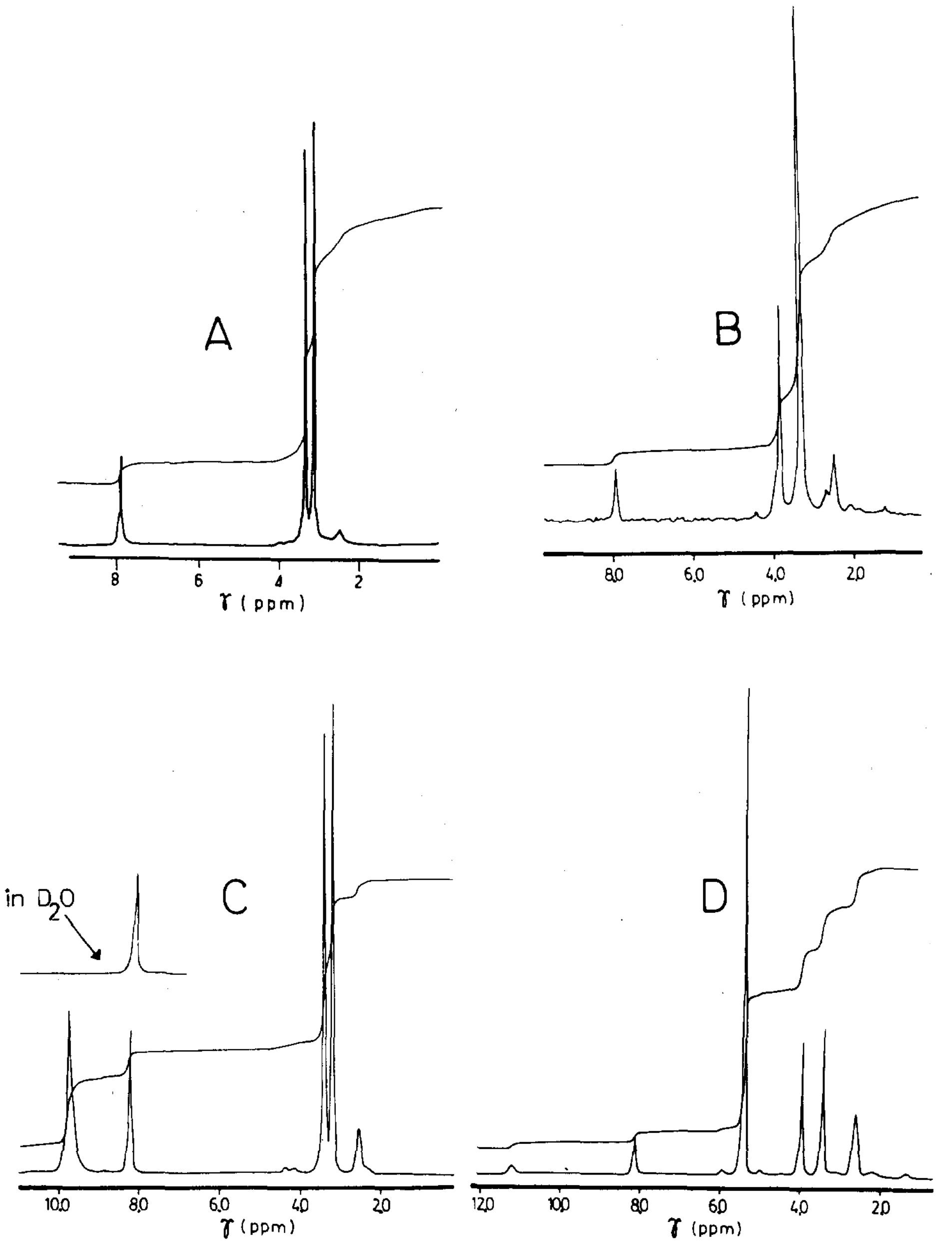

Fig. 1. ^{1}H-NMR of theophylline (A); theobromine (B); $|TH_2^+|_2|PdCl_4|$ (C); and $|TBH_2^+|_2|PdCl_4|$ (D).

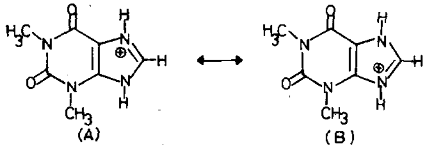

Fig. 2. Resonance forms for the protonation of theophylline in the imidazolic ring.

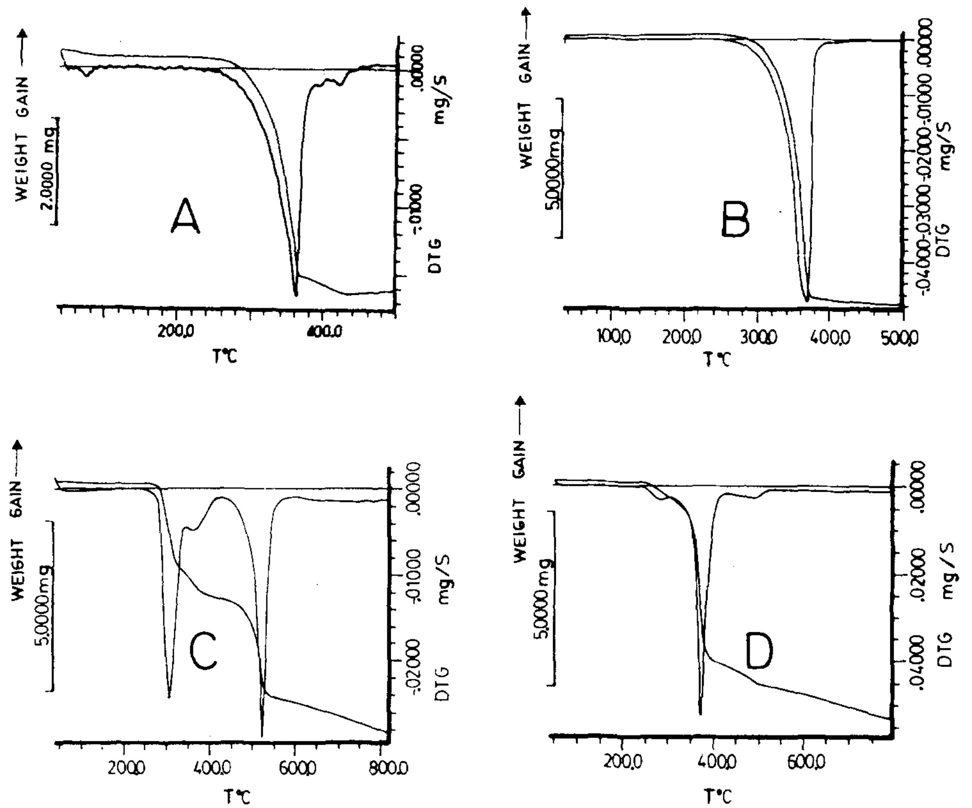

Fig. 3. TG curves of theophylline (A); theobromine (B); $[TH_2^+]_2[PdCl_4]$ (C); and $[TBH_2^+]_2[PdCl_4]$ (D).

observed weight loss was 24.46% (theoretical weight loss for the elimination of the four chlorine atoms 23.26%). The expected endothermic behaviour for the dehalogenation process has been observed from the DSC curve (endothermic effect centred at 293.5°C). The dehalogenation enthalpy was 194 kJ mol^{-1}.

The dehalogenated compound is not stable and rapidly starts its decomposition (strong weight loss effect in the 400–570°C temperature range). This decomposition appears in the DSC curve as an exothermic effect at 430°C.

In the theobromine compound dehalogenation takes place in two steps. In the TG curve the first step occurs between 235 and 340°C. The observed weight loss (5.9%) corresponds with the elimination of one HCl molecule (theoretical weight loss 5.98%). The DSC curve shows HCl elimination as an endothermic effect centred at 264°C. The dehalogenation enthalpy, calculated from the area of the endothermic effect, was 39 kJ mol^{-1}. The second step of dehalogenation starts in the TG curve at 340°C. At this temperature the compound is very unstable and a strong weight loss occurs which

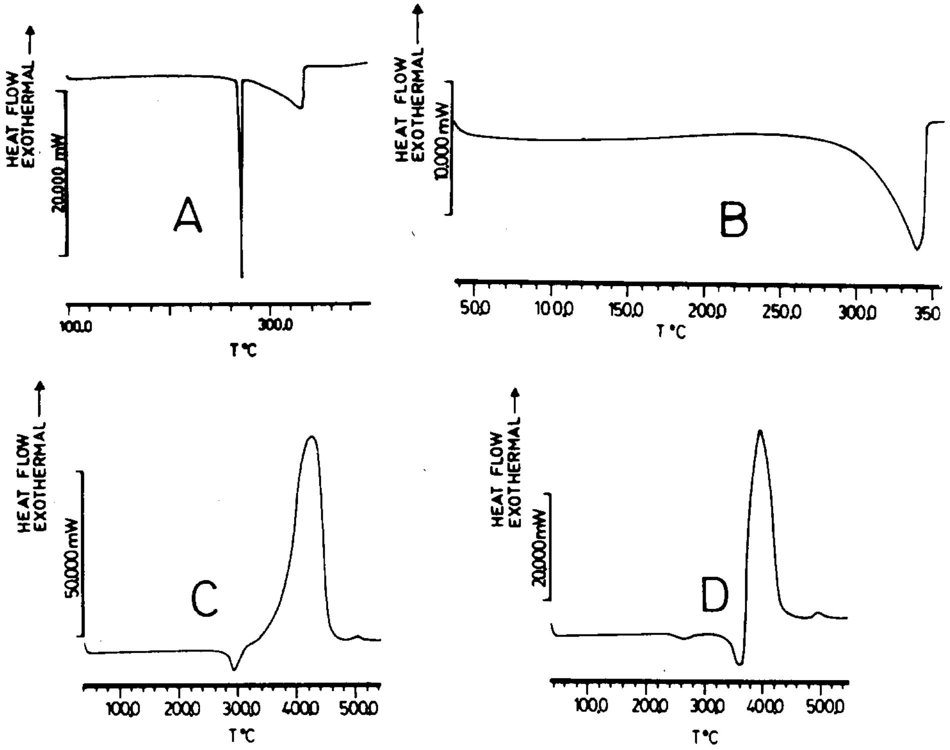

Fig. 4. DSC curves of theophylline (A); theobromine (B); $|TH_2^+|_2|PdCl_4|$ (C); and $|TBH_2^+|_2|PdCl_4|$ (D).

corresponds to the elimination of the three remaining chloride atoms and the pyrolysis of the organic matter. The DSC curve shows these processes as an endothermic effect at 362°C and an exothermic effect at 398°C, respectively. The enthalpy value associated with chlorine elimination was 237 kJ mol^{-1}.

Non-thermal equivalence between the four chlorine atoms would suggest, according to the bibliographic data [14,15], a little distortion in the planar structure of $|PdCl_4|^{2-}$ due to hydrogen bonding interactions with theobrominium cations. In both cases at the end of the pyrolysis the residues obtained were PdO, which has been proved by IR spectroscopy. The residues

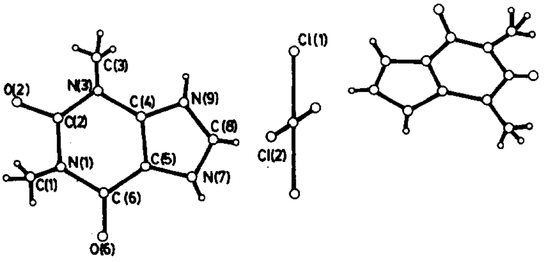

Fig. 5. Possible structure for the compounds $|LH_2^+|_2|PdCl_4|$.

were 19.4% in $|TH_2^+|_2|PdCl_4|$ and 19.7% in $|TBH_2^+|_2|PdCl_4|$ (theoretical residue for both compounds 20.05%).

Theophylline compounds

Table 1 also gives the most significant bands for the isolated theophylline compounds. These bands were assigned by comparison with the spectrum of free theophylline.

Complexes $CdT_2(OH_2)_4$ and $HgTCl \cdot H_2O$ did not present the band corresponding to $\nu(N_7{-}H)$, which appears in the IR spectrum of theophylline at 3120 cm^{-1}. This observation suggests an anionic coordination of theophylline through the N_7 atom to metal ion. This coordination site is also found in most of the theophyllinato complexes decribed in the literature [16–18].

The IR spectrum of the complex $Hg(TH)Cl_2$ shows the band corresponding to $\nu(N_7{-}H)$ at 3120 cm^{-1}, which suggests that the coordination of the theophylline to Hg(II) takes place in molecular form through the N_9 atom.

TG and DSC curves of theophylline compounds are given in Fig. 6. The thermal behaviour of $CdT_2(OH_2)_4$ consists of two major processes: dehydration and decomposition of the anhydrous complex to CdO. The dehydration occurs in the temperature range 105–210°C. The observed weight loss (13.8%) shows the tetrahydrate nature of this compound (calculated weight loss 13.27%). The endothermic effect associated with the elimination of the four molecules of water has been observed in the DSC curve at 148°C. This endothermic effect is symmetric, which indicates that these molecules of water are equivalent and the structure of the complex is probably octahedral. This process is analogous to that previously described for $X_2M(OH_2)_4$ complexes [where X = xanthinate ion and M = Co(II), Cu(II) or Cd(II) [7]]. The calculated dehydration enthalpy was 61 kJ $(mol\ H_2O)^{-1}$. This high value indicates a strong interaction between the Cd(II) ion and the molecules of water.

The anhydrous cadmium theophyllinato is stable from 210 to 360°C. The TG curve shows a decomposition in three steps in the temperature range 360–650°C. At this point the residual weight is 24.5% of the original weight, which corresponds to CdO (theoretical value 23.67%).

The exothermic effects corresponding to the pyrolysis of theophylline have been observed in the DSC curve at 435°C, 447°C and > 550°C.

The TG curve of $HgTCl \cdot H_2O$ shows that this compound becomes completely dehydrated in the temperature range 140–210°C. The theoretical weight loss (4.15%) for dehydration is in good agreement with the experimental value (3.6%). The DSC curve shows the endothermic effect corresponding to this process at 151°C. The dehydration enthalpy calculated from the DSC curve was in this case 61 kJ mol^{-1}.

The anhydrous compound HgTCl is stable between 210 and 280°C, after

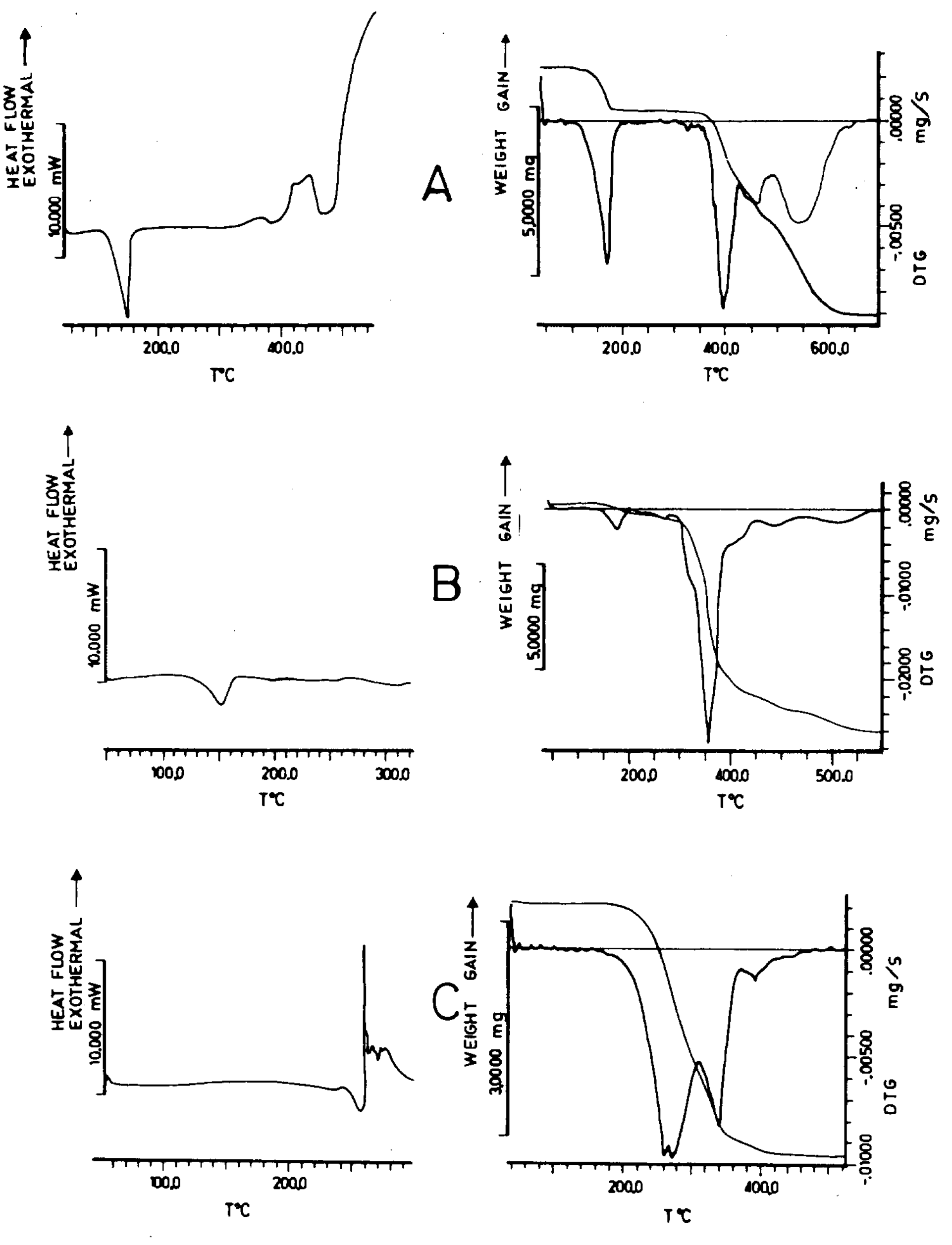

Fig. 6. TG and DSC curves of $CdT_2(OH_2)_4$ (A); $HgTCl \cdot H_2O$ (B); $Hg(TH)Cl_2$ (C).

which an intense weight loss effect starts, which finishes at 400°C, followed by a slower weight loss from 400°C to the end of the run at 700°C. These effects have been assigned to partial sublimation of Hg as $HgCl_2$ and pyrolysis of the theophylline, respectively, since the residue obtained at the end of the run (700°C) was 6% of the original weight.

The TG curve of Hg(TH)Cl_2 shows that this compound is stable until 180°C. At this temperature its decomposition starts which takes place in two steps which overlap. The first process has been assigned to the sublimation of $HgCl_2$ (the temperature range of $HgCl_2$ sublimation is 180–290°C [19] which is in good agreement with the temperature range obtained for the sublimation of $HgCl_2$ in the compound Hg(TH)Cl_2. The second process corresponds to the pyrolysis of the theophylline. At the end of the pyrolysis (500°C) no residue was obtained.

The DSC curve of Hg(TH)Cl_2 shows the process corresponding to the sublimation as an endothermic effect at 254°C, which overlaps with the exothermic effect, due to pyrolysis.

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