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THERMAL STUDIES ON PURINE COMPLEXES. X. HEXACHLOROPLATINATES(IV) OF SOME XANTHINE DERIVATIVES

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ABSTRACT

The thermal behaviour of hexachloroplatinates(IV) of monoprotonated xanthine, theobromine, theophylline, 1,3,8-trimethylxanthine, caffeine and 8-ethyl-theophylline has been studied by IR, TG and DSC techniques. The data obtained are in accordance with the non-equivalence of the chlorine atoms coordinated to the Pt(IV) ion and also show that dehalogenation processes take place with the loss of Cl and HCl.

The pyrolysis of these compounds ends between 420 and 520°C, with metallic platinum remaining as final residue.

INTRODUCTION

In the last few years the study of interactions between metal ions and purine derivatives has became a research line of great importance [1–5] due, fundamentally, to the important role that some of these complexes play in many biological processes [3,6].

Likewise, the investigation of hexachloroplatinates(IV) of important biological molecules has aroused increasing attention, since some of these compounds have shown antitumour properties [7,8]. 8-Dialkylaminoalkoxy-caffeine hexachloroplatinates(IV) are citostatically active against various tumour systems in animal, showing, at the same time, minimal toxicity [9,10].

For the above reasons, and following our studies on halometallates of xanthine derivatives [11–16], we report in this paper the study, by IR, TG

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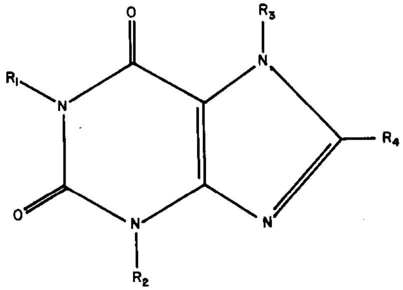
and DSC, of the thermal behaviour of hexachloroplatinates(IV) of xanthine (XH), theobromine (TBH), theophylline (TFH), 1,3,8-trimethylxanthine (TMH), caffeine (CF) and 8-ethyl-theophylline (ETH).

	R_1	R_2	R_3	R_4
XH	H	H	H	H
TBH	H	CH_3	CH_3	H
TFH	CH_3	CH_3	H	H
TMH	CH_3	CH_3	H	CH_3
CF	CH_3	CH_3	CH_3	H
ETH	CH_3	CH_3	H	CH_2CH_3



EXPERIMENTAL

The xanthine derivatives were synthesized according to methods previously reported [17,18]. $PtCl_4$ was purchased from Engelhard. All the inorganic products used in this work were of analytical reagent grade.

Microanalyses of C, H, N and Cl were performed in the Institute of Bio-organic Chemistry of CSIC. Platinum was determined gravimetrically.

IR spectra were recorded in KBr pellets (4000–200 cm^{-1}) and in polyethylene pellets (600–200 cm^{-1}) using a Beckman 4250 spectrophotometer.

TG studies were made in a dynamic atmosphere of air (100 ml min^{-1}), with a Mettler TG-50 thermobalance, using samples varying in weight from 5.56 to 9.75 mg and a heating rate of 10°C min^{-1}.

The DSC plots were recorded in air on a Mettler DSC-20 differential scanning calorimeter at a heating rate of 10°C min^{-1}, in the 35–550°C temperature range, with samples of 3.45–7.74 mg.

Preparation of the compounds

The synthesis of these products was carried out, in all cases, as follows: 2 mmol of each xanthine derivative were added, with stirring, to a hot aqueous solution (50 ml) of 0.5 M HCl containing 1 mmol of $PtCl_4$. After standing for a few days, crystals appeared in each of the six cases. These were filtered off, washed with ethanol and diethylether, and air dried. Their chemical analyses and colour are given in Table 1.

RESULTS AND DISCUSSION

Spectral studies carried out on these compounds [16] have shown that they are all salts containing the corresponding xanthine derivative in monoprotonated form as cation. In their IR spectra there are few bands in the

TABLE 1

Analytical data of isolated hexachloroplatinates

Compound	Colour	C (%)	H (%)	N (%)	Cl (%)	M (%)
$PtCl_6(XH_2)_2 \cdot 2Cl(XH_2) \cdot 8H_2O$	Yellow	20.17 (19.43)	2.69 (2.91)	18.85 (18.13)	23.53 (22.99)	14.91 (15.80)
$PtCl_6(TBH_2)_2 \cdot 2H_2O$	Orange	20.75 (20.84)	2.81 (2.73)	13.61 (13.89)	26.02 (26.42)	22.62 (24.20)
$PtCl_6(TFH_2)_2 \cdot 2H_2O$	Orange	21.30 (20.84)	2.50 (2.73)	14.16 (13.89)	25.56 (26.42)	23.46 (24.20)
$PtCl_6(TMH_2)_2 \cdot 2H_2O$	Orange	23.67 (23.02)	3.12 (3.12)	13.42 (13.45)	25.06 (25.54)	22.45 (23.39)
$PtCl_6(CFH)_2$	Orange	24.83 (24.06)	2.80 (2.76)	14.12 (14.03)	27.00 (26.69)	23.35 (24.44)
$PtCl_6(ETH_2)_2 \cdot 2H_2O$	Orange	25.45 (25.05)	3.50 (3.48)	12.95 (12.99)	24.39 (24.70)	21.80 (22.63)

TABLE 2

IR data (cm^{-1})

Compound	ν(O–H)	ν(N–H)	ν(C=O)	ν(C=C)+ν(C=N)	ν(Pt–Cl)
$PtCl_6(XH_2)_2 \cdot 2Cl(XH_2) \cdot 8H_2O$	3530 3430	3200–2700 [a]	1720 1690	1600	335 300
heated at 280°C	–	3200–2700 [a]	1715 1690	1600	340 325
$PtCl_6(TBH_2)_2 \cdot 2H_2O$	3570 3500	3200–2400 [a]	1700 [b]	1605,1570	320 300
heated at 360°C	–	3180	1690 [b]	1545,1525	–
$PtCl_6(TFH_2)_2 \cdot 2H_2O$	3470	3350–2300 [a]	1710 1665	[c], 1570	320 300
heated at 375°C	–	3120	1695 1650	1540 [b]	–
$PtCl_6(TMH_2)_2 \cdot 2H_2O$	3420 3300	3200–2400 [a]	1720 1680	1610,1565	325 315
heated at 295°C	–	3120	1700 1650	1555,1525	–
$PtCl_6(CFH)_2$	–	3300–2700 [a]	1725 1680	[c],1555	330 310
heated at 340°C	–	–	1700 1660	1550,1525	–
$PtCl_6(ETH_2)_2 \cdot 2H_2O$	3500–3300 [b]	3200–2400 [a]	1720 1680	1575	330 315
heated at 325°C	–	3160	1700 1665	1555,1520	–

[a] Few bands. [b] Broad band. [c] Overlapping with ν(C=O).

3200–2400 cm^{-1} range (Table 2) assignable to the $\nu(N^+\text{–}H)$ stretching vibration and, also, the bands corresponding to $\nu(C{=}C)$ and $\nu(C{=}N)$ vibrations are displaced to a higher wavenumber, with respect to their position in

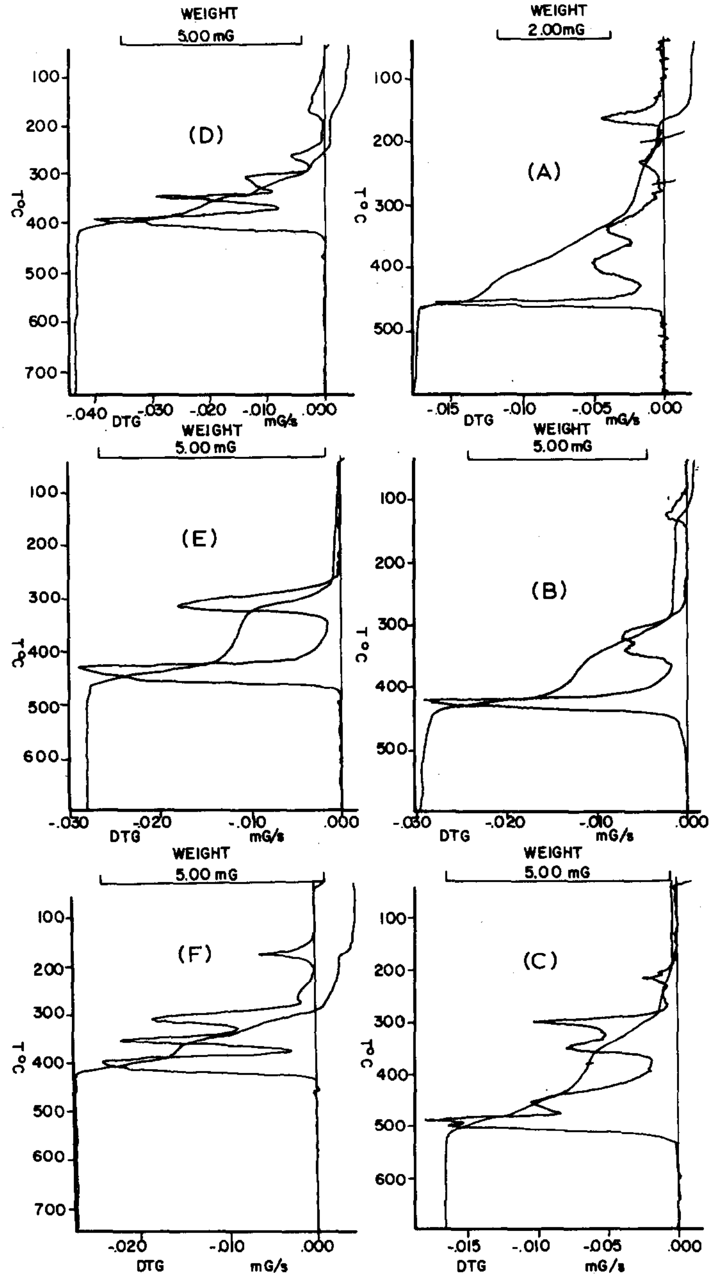


Fig. 1. TG plots: (A) $PtCl_6(XH_2)_2 \cdot 2Cl(XH_2) \cdot 8H_2O$; (B) $PtCl_6(TBH_2)_2 \cdot 2H_2O$; (C) $PtCl_6(TFH_2)_2 \cdot 2H_2O$; (D) $PtCl_6(TMH_2)_2 \cdot 2H_2O$; (E) $PtCl_6(CFH)_2$; (F) $PtCl_6(ETH_2)_2 \cdot 2H_2O$.

the IR spectra of free purine derivatives. This is in agreement with protonation in one of the imidazolic nitrogen atoms, since, consequently, there is an increased electronic density in the carbon atoms adjacent to these nitrogen atoms [19]. Likewise, the protonation on the imidazole ring has been confirmed by ^{1}H-NMR spectra [16], in which the signals corresponding to

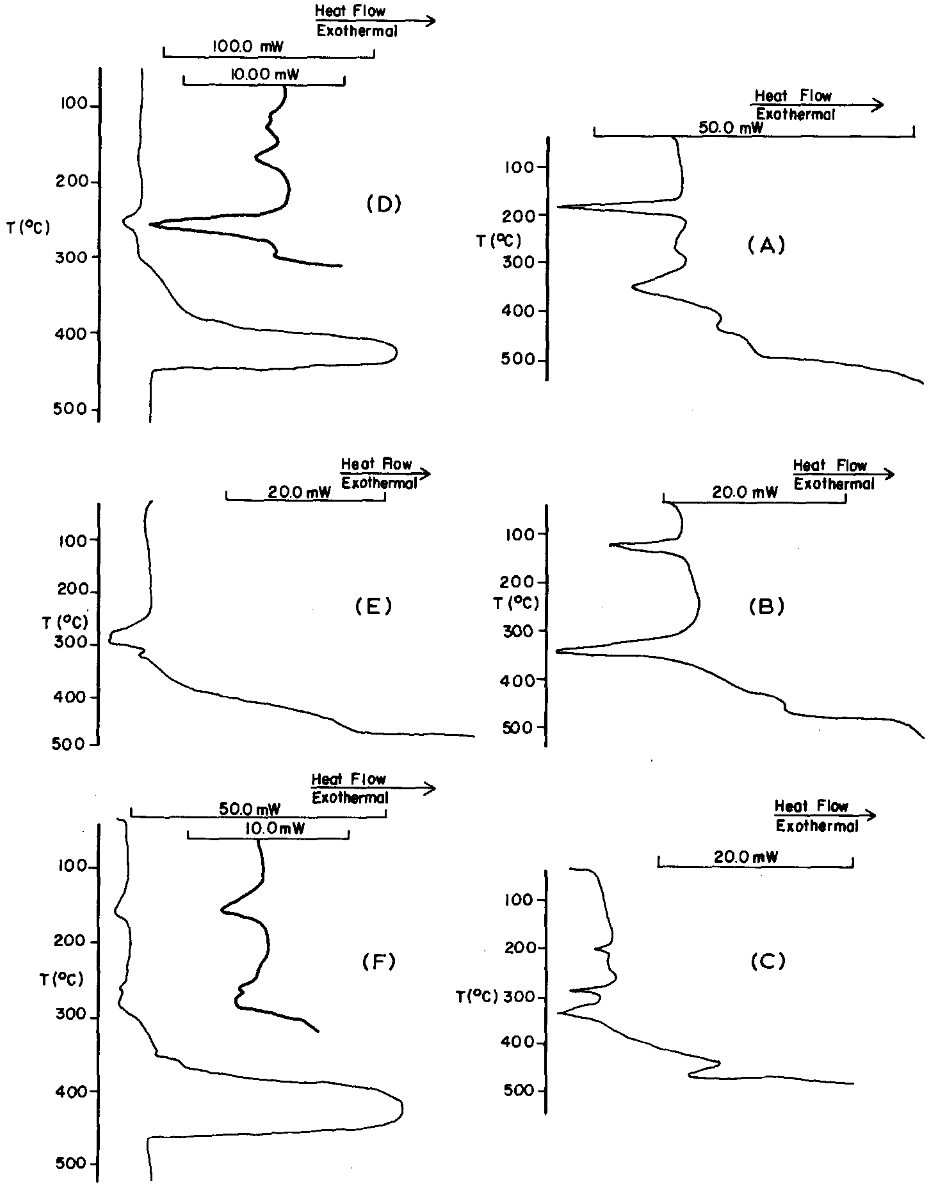


Fig. 2. DSC curves: (A) $PtCl_6(XH_2)_2 \cdot 2Cl(XH_2) \cdot 8H_2O$; (B) $PtCl_6(TBH_2)_2 \cdot 2H_2O$; (C) $PtCl_6(TFH_2)_2 \cdot 2H_2O$; (D) $PtCl_6(TMH_2)_2 \cdot 2H_2O$; (E) $PtCl_6(CFH)_2$; (F) $PtCl_6(ETH_2)_2 \cdot 2H_2O$.

hydrogen atoms bound to substituents in the 8-position are shifted downfield due to the positive character of this ring. On the other hand, the presence of the octahedral hexachloroplatinate(IV) anion has been made clear by the presence, in the IR spectra of these compounds (Table 2), of two bands corresponding to the ν(Pt–Cl) stretching vibration. The appearance of two bands for this vibrational mode indicates a distortion of the octahedral $PtCl_6^{2-}$ anion, probably by the involvement of the chlorine atoms in the formation of hydrogen bonds with either the xanthine derivatives or the water molecules.

On heating these compounds three processes can occur: dehydration, dehalogenation and pyrolytic decomposition. These have been discerned and studied from the corresponding TG and DSC curves, which are drawn in Figs. 1 and 2, respectively.

Dehydration processes

The dehydration temperatures, observed and calculated weight losses, as well as dehydration enthalpies calculated from DSC plots are tabulated in Table 3.

Hydrated compounds lose water molecules between 100 and 210°C in a one-step process (Fig. 1). From the DSC curves (Fig. 2) it can be observed that the endothermic effects associated with these eliminations appear in the same temperature range as they do in the TG plots. The existence of three endothermic peaks and an asymmetric peak for the dehydration of $PtCl_6(TMH_2)_2 \cdot 2H_2O$ and $PtCl_6(ETH_2)_2 \cdot 2H_2O$, respectively, suggests that, in both compounds, the water molecules are not equivalent.

In each case, from the area of the peaks, dehydration enthalpies have been calculated (Table 3), their values being in good agreement with the bonding of these water molecules by hydrogen bonds.

TABLE 3

Thermoanalytical data for dehydration processes

Compound	Wt. loss (%)		DSC peak temp. (°C)	ΔH (kJ mol^{-1} H_2O)
	Found	Calcd.		
$PtCl_6(XH_2)_2 \cdot 2Cl(XH_2) \cdot 8H_2O$	10.6	11.66	182	45
$PtCl_6(TBH_2)_2 \cdot 2H_2O$	4.8	4.47	121	43
$PtCl_6(TFH_2)_2 \cdot 2H_2O$	4.1	4.47	201	62
$PtCl_6(TMH_2)_2 \cdot 2H_2O$	4.3	4.32	110, 125, 164	25 [a]
$PtCl_6(CFH)_2$	–	–	–	–
$PtCl_6(ETH_2)_2 \cdot 2H_2O$	4.2	4.18	158	56

[a] Average value.

TABLE 4

TG and DSC data for dehalogenation processes

Compound	Process	Wt. loss (%)		DCS peak temp. (°C)	ΔH (kJ mol^{-1})
		Found	Calcd.		
$PtCl_6(XH_2)_2 \cdot 2Cl(XH_2) \cdot 8H_2O$	$-2HCl$	6.7	5.91	261	66
	$-6Cl$	19.4	17.24	351	528
$PtCl_6(TBH_2)_2 \cdot 2H_2O$	$-2HCl$–$4Cl$	26.0	26.67	342	243
$PtCl_6(TFH_2)_2 \cdot 2H_2O$	$-2HCl$	9.2	9.06	287	45
	$-4Cl$	16.4	17.62	334	114
$PtCl_6(TMH_2)_2 \cdot 2H_2O$	$-2HCl-2Cl$	17.3	17.26	252	145
	$-2Cl$	7.7	8.51	300	a
$PtCl_6(CFH)_2$	$-2HCl-4Cl$	27.0	26.93	293	305
$PtCl_6(ETH_2)_2 \cdot 2H_2O$	$-2HCl-4Cl$	25.2	24.93	283	249

[a] No calculated due to overlapping with the exothermic effects.

Dehalogenation processes

The simultaneous study of the TG and DSC curves indicates that dehalogenation processes occur in the 210–410°C temperature range, in which all DSC plots show endothermic effects assigned to chlorine eliminations. Thermoanalytical data for these reactions are given in Table 4.

As indicated in this table, dehalogenation processes take place with the loss of HCl and Cl, which has been confirmed by recording the IR spectra of samples heated to temperatures just above those corresponding to the end of the weight loss effects assigned to these processes, under the same conditions that the TG curves were carried out. The IR data obtained are also given in Table 2.

For the xanthine compound, it has not been possible to record the IR spectrum in the dehalogenated state, because the last loss of chlorine atoms (between 280 and 410°C in the TG plot and centered at 351°C in the DSC curve) yields an unstable product that decomposes very quickly. However, the IR spectrum of this compound heated at 280°C (a temperature just above the end of the endothermic effect centered at 261°C) has been recorded, which shows that some xanthinium cations are not deprotonated, since few bands assignable to the $\nu(N^+–H)$ stretching vibration remain in this IR spectrum. Moreover, the band assigned to the $\nu(C=C) + \nu(C=N)$ vibration appears in the same position as that in the IR spectrum of the initial product, which is compatible with the above conclusion, and the non-disappearance of $\nu(Pt–Cl)$ bands is in accordance with the existence of a $PtCl_6^{2-}$ anion in the heated product. All these data suggest that the first two hydrogen chloride molecules lost are those corresponding to both the xanthine hydrochloride molecules that are present in $PtCl_6(XH_2)_2 \cdot 2Cl(XH_2) \cdot 8H_2O$.

TABLE 5

TG and DSC data for pyrolytic processes

Compound	Weight loss (%)		Final temp. TG (°C)	DSC peak temp. (°C) (exo)
	Found	Calcd.		
$PtCl_6(XH_2)_2 \cdot 2Cl(XH_2) \cdot 8H_2O$	85.1	84.20	465	410, > 500
$PtCl_6(TBH_2)_2 \cdot 2H_2O$	76.8	75.80	480	450, > 500
$PtCl_6(TFH_2)_2 \cdot 2H_2O$	76.4	75.80	520	440, > 500
$PtCl_6(TMH_2)_2 \cdot 2H_2O$	77.6	76.61	420	420
$PtCl_6(CFH)_2$	76.6	75.56	460	430, > 500
$PtCl_6(ETH_2)_2 \cdot 2H_2O$	77.8	77.37	425	425

The IR spectra of the other heated compounds show that the dehalogenation processes take place with loss of Cl and HCl, since there is a total disappearance of $\nu(N^+-H)$ and $\nu(Pt-Cl)$ bands and, also, bands corresponding to $\nu(C=C) + \nu(C=N)$ vibrations are shifted to a lower wavenumber with respect to their positions in the IR spectra of the initial products, which indicates that there is not yet a positive charge on the imidazole ring.

On the other hand, the presence of several endothermic effects for dehalogenation processes of the $PtCl_6^{2-}$ anion in theophylline and 1,3,8-trimethylxanthine, and the asymmetric endothermic effect assigned to these reactions in the rest of the compounds confirms, in accordance with the IR data, that the $PtCl_6^{2-}$ octahedron is distorted.

Pyrolytic processes

Finally, dehydrated and dehalogenated compounds undergo a pyrolitic decomposition, which is reflected in the DSC curves by the presence of several exothermic effects. These may be attributed to the total combustion of organic matter. Pyrolytic processes finish in the 420–520°C temperature range, with metallic platinum remaining as final residue.

The thermogravimetric and DSC data for these processes are given in Table 5.

REFERENCES

1 G.L. Eichhorn, Inorganic Biochemistry, Vol. 2, Elsevier, New York, 1973.
2 L.G. Marzilli, Prog. Inorg. Chem., 23 (1977) 255.
3 D.J. Hodgson, Prog. Inorg. Chem., 23 (1977) 211.
4 H. Sigel, Metal Ions in Biological Systems, Dekker, New York, 1979.
5 T.G. Spiro, Nucleic Acid–Metal Ion Interactions, Wiley, New York, 1980.
6 E.B. Goodsell, H.H. Stein and J. Wenzke, J. Med. Chem., 14 (1971) 1202.
7 S.K. Klimenko, L.K. Kulikova, T.V. Stolbova and V.G. Klarchenko, Khim. Pharm. Zh., 17 (1983) 167.

8 S.K. Klimenko, L.K. Kulikova, T.I. Tyrina and V.G. Klarchenko, Khim. Pharm. Zh., 16 (1982) 1318.

9 H. Kroeger and J. Klosa, Naturwissenschaften, 68 (1981) 628.

10 J. Klosa, Eur. Pat. Appl. EP 54, 215 (CL C07D473/12) (1982).

11 E. Colacio-Rodríguez, J.M. Salas-Peregrin, R. López-Garzón and J.D. López-González, Thermochim. Acta, 71 (1983) 139.

12 E. Colacio-Rodríguez, J.M. Salas-Peregrin and J.D. López-González, An. Quim., 80B (1984) 223.

13 E. Colacio-Rodríguez, J.D. López-González and J.M. Salas-Peregrin, J. Therm. Anal., 28 (1983) 3.

14 E. Colacio-Rodríguez and J.M. Salas-Peregrin, Thermochim. Acta, 74 (1984) 45.

15 E. Colacio-Rodríguez, M.N. Moreno-Carretero and J.M. Salas-Peregrin, J. Therm. Anal., in press.

16 M.N. Moreno-Carretero, E. Colacio-Rodríguez, J.M. Salas-Peregrin and M.P. Sánchez-Sánchez, An. Quim., in press.

17 H. Bredereck, I. Henning, W. Pfleiderer and G. Weber, Chem. Ber., 86 (1953) 333.

18 J.H. Speer and A.L. Raymond, J. Am. Chem. Soc., 75 (1953) 114.

19 W. Adam, A. Grimison and G. Rodríguez, Tetrahedron, 23 (1967) 2513.