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Preparation, thermal behaviour and spectroscopic properties of several mononuclear copper(II) complexes of uridine and cytidine

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Abstract

By reacting different copper(II) salts with uridine and cytidine in ethyl acetate, several mononuclear copper(II) complexes have been obtained. The complexes are pale in colour and exhibit hygroscopic behaviour. Both nucleosides coordinate in molecular form through a carbonyl group and through the nitrogen atom of the pyrimidine ring for uridine and cytidine, respectively, resulting in a weak ligand field. The spectroscopic data of the complexes and their thermal study using TG and DSC techniques are reported.

INTRODUCTION

Many examples of metal complexes formed by the interaction of nucleosides with a wide variety of metal salts have been reported since nucleosides were first described by Levene and Jacobs [1]. Studies on nucleosides and their metal complexes are of interest owing to their use as model compounds and their potential anti-neoplastic activity. Much of the studies concerning metal complexes of pyrimidine nucleosides have been devoted to the characterization of these systems in solution [2–5]. Those performed in the solid state, however, deal mainly with the palladium and platinum complexes formed with uridine, thymidine and cytidine [6–10]. However, to the best of our knowledge, references to the thermal behaviour of metal complexes of the *N*-nucleosides of pyrimidine are scanty. Therefore, we report here the thermal behaviour of several copper(II) complexes with uridine and cytidine (Scheme 1) as ligands.

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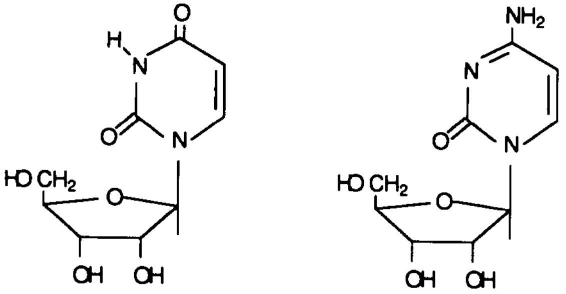


Scheme 1. Uridine (left) and cytidine (right).

EXPERIMENTAL

Apparatus

The microanalyses of carbon, hydrogen and nitrogen were carried out using a Perkin-Elmer model 240-C. Infrared spectra were recorded on a Perkin-Elmer 983-G spectrophotometer. Thermogravimetric (TG) and differential scanning calorimetry (DSC) curves were measured on a Mettler DSC-20 differential scanning calorimeter. TG diagrams were recorded in a dynamic atmosphere of pure air (100 ml min^{-1}), using samples varying in weight from 8.07 to 12.13 mg. DSC curves were obtained in a static atmosphere of air with samples varying in weight from 2.04 to 3.01 mg, at the same heating rate as for the TG plots.

EPR spectra were obtained with a Bruker 200 TT spectrometer operating at 9.4–9.5 GHz (X band). Electronic spectra were recorded on a Shimadzu MPC-3100 spectrometer.

Preparation of the complexes

All complexes were prepared by adding, as solids, the corresponding pyrimidine nucleoside and copper(II) salt in a 1:1 ratio to 50 ml of ethyl acetate. The suspension was then refluxed with vigorous stirring for three hours. The microcrystalline complexes were filtered off, washed with hot ethyl acetate and dried under nitrogen atmosphere. Analytical data are listed in Table 1.

RESULTS AND DISCUSSION

All the eight copper(II) complexes are pale in colour, being insoluble in non-polar solvents and decomposed by polar solvents. Moreover, all are hygroscopic with a variable degree of hydration. Interestingly, even though the complexes were synthesized using a ligand/metal ratio of 1:1, those involving chloride ions were obtained with a ligand/metal ratio of 2:1, suggesting that this latter ratio is favoured over the former.

TABLE 1

Analytical, diffuse reflectance and EPR data

Compound	C (%)		H (%)		N (%)		Cu (%)[a]		d→d (kK)	EPR		
	Found	Calc.	Found	Calc.	Found	Calc.	Found	Calc.		$g_\perp$	$g_\parallel$	g_{av}
$[Cu(CN)_2(Urd)(H_2O)]$	34.9	34.60	3.7	3.67	14.8	14.68	21.0	20.84	15.75	2.07	2.28	2.14
$[Cu(SO_4)(Urd)(H_2O)] \cdot H_2O$	22.7	23.61	4.0	3.93	6.2	6.12	[b]		13.33	2.08	2.27	2.14
$[Cu(Cl)_2(Urd)_2] \cdot 4H_2O$	29.9	31.10	4.4	4.61	8.0	8.06	11.5	11.45	11.90			2.10
$[Cu(Br)_2(Urd)(H_2O)]$	22.3	22.25	2.9	2.88	5.7	5.77	16.1	16.38	11.63	2.14	2.31	2.20
$[Cu(CN)_2(Cyt)(H_2O)]$	34.6	34.69	3.9	3.94	18.3	18.40	20.9	20.89	15.87	2.06	2.26	2.13
$[Cu(SO_4)(Cyt)(H_2O)_2]$	24.6	24.63	4.0	3.88	9.6	9.58	[b]		13.16	2.08	2.27	2.14
$[Cu(Cl)_2(Cyt)_2] \cdot H_2O$	33.7	33.83	2.9	2.82	13.1	13.16	12.4	12.45	12.66			2.10
$[Cu(Br)_2(Cyt)(H_2O)] \cdot H_2O$	21.4	21.50	3.3	3.38	8.2	8.36	15.9	15.83	11.83	2.08	2.35	2.17

[a] Calculated as CuO. [b] The residue was a mixture of CuO and $CuSO_4$.

The solid-state infrared spectra data of the complexes are presented in Table 2. The spectra display features characteristic of the expected molecular coordination mode of the nucleosides, in agreement with the analytical data. Moreover, owing to the strong hygroscopic behaviour shown by these complexes, the resolution decreases with the number of water molecules present in the complex. As a consequence of the molecular coordination form of the nucleosides to the copper ion, in all the complexes the charge is neutralized by the anions belonging to the copper(II) salt used in the synthesis. Thus, new bands observed in the spectra of the complexes, which are not present in the spectra of the free ligands, have been assigned to these coordinated anions.

However, one of the C=O stretching bands of uridine, occurring at 1694 cm^{-1}, is shifted to lower wavenumbers by approx. 14 cm^{-1}, indicating that coordination could take place through one of the C=O groups of the pyrimidine ring. This small displacement would be indicative of a weak ligand field, in agreement with the data previously reported for similar complexes [11–14].

The diffuse reflectance spectra consist of three bands in the 300–900 nm range. Two bands of medium intensity centred at about 320 and 400 nm are attributable to ligand transitions and/or change-transfer absorptions. The remaining broad band, which is listed in Table 1, is less intense and may be attributed to d→d transitions, the values being consistent with the existence of a weak ligand field [15].

The EPR spectra of the powdered samples present the resonances listed in Table 1. The signals are devoid of any hyperfine structure. From these

TABLE 2

Infrared data (cm^{-1})

Compound	ν(OH)	ν(NH)	ν(C=O)	δ(NH_2)	ν(ring)	ν(CN) + ν(ring)	ν(C–O) + ν(sugar)	ν(anion)
Uridine								
[Cu(CN)$_2$(Urd)(H_2O)]	3345	3111	1694, 1676	–	1468, 1421	1271	1174, 1137, 1096, 1053	
[Cu(SO_4)(Urd)(H_2O)$_2$] ·	3350	3112	1680 br	–	1462, 1426	1273	1171, 1093, 1053	2113
H_2O	3250 br	[a]	1681 br	–	1465, 1423	1269	1172, 1099 [b], 1047	1099, 980, 605
[Cu(Cl)$_2$(Urd)$_2$] · 4H_2O								
[Cu(Br)$_2$(Urd)(H_2O)]	3270 br	[a]	1679 br	–	1450 br	1270	1176, 1094, 1050 vw	
Cytidine	3341	3113	1684, 1676	–	1468, 1427	1274	1173, 1138 sh, 1092, 1051	
[Cu(CN)$_2$(Cyt)(H_2O)]	3445, 3347	3231, 3086	1644	1602	1496, 1430	1250	1135, 1102, 1054, 1035	
[Cu(SO_4)(Cyt)(H_2O)$_2$]	3440, 3343	3235, 3091	1645	1607	1483, 1428	1247	1108, 1059, 1031 sh	2115
[Cu(Cl)$_2$(Cyt)$_2$] · H_2O	3349 br	3233, 3085	1643 br	1598	1482, 1431	1248	1101, 1053 [b], 1029 sh	1053, 982, 619
[Cu(Br)$_2$(Cyt)(H_2O)] ·	3451, 3350	3238, 3092	1647 br	1599	1484, 1429	1251	1107, 1047, 1036 sh	
H_2O	3400 br	3190 br	1644 br	1607	1481, 1432	1245	1103, 1050, 1032 sh	

[a] Overlapping with the ν(OH) band. [b] Overlapping with the ν(SO) band.

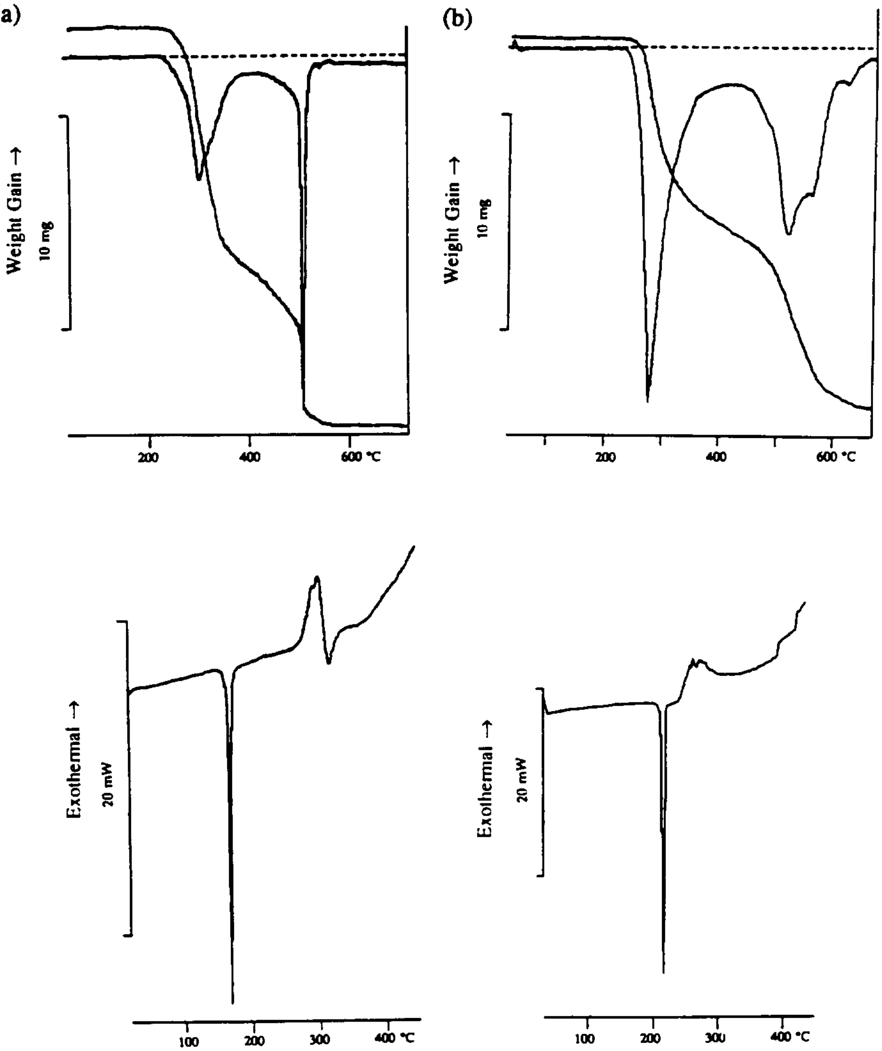


Fig. 1. TG and DSC curves of (a) uridine and (b) cytidine.

data, none of the five-coordinated copper(II) complexes is expected to have trigonal bipyramidal geometry [16].

The TG and DSC curves of the ligands as well as those of their corresponding complexes are shown in Figs. 1-3. Two different processes can be observed in the curves of uridine and cytidine (Fig. 1): fusion and pyrolysis. Thus, the DSC curves show an endothermic effect centred at 166 and 215°C, for uridine and cytidine, respectively, just before pyrolytic decomposition. The fusion enthalpy calculated from the peak area is approx. 4 kJ mol^{-1} for both nucleosides. The difference between the fusion temperatures, $\Delta\theta = 49°\mathrm{C}$, can be explained on the basis of the number of

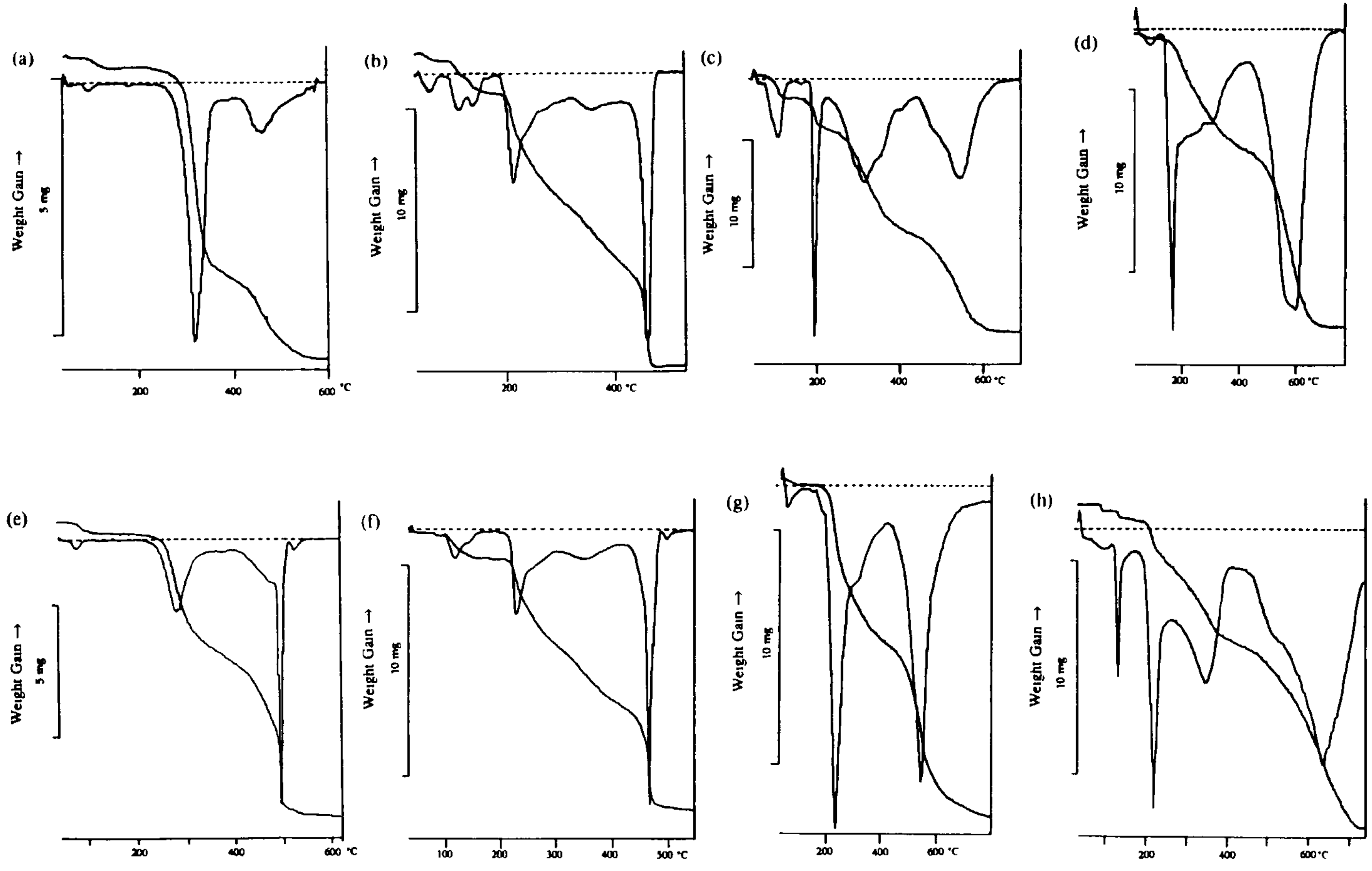


Fig. 2. Thermogravimetric curves of (a) $[Cu(CN)_2(Urd)(H_2O)]$, (b) $[Cu(SO_4)(Urd)(H_2O)_2]\cdot H_2O$, (c) $[Cu(Cl)_2(Urd)_2]\cdot 4H_2O$, (d) $[Cu(Br)_2(Urd)(H_2O)]$, (e) $[Cu(CN)_2(Cyt)(H_2O)]$,(f) $[Cu(SO_4)(Cyt)(H_2O)_2]$, (g) $[Cu(Cl)_2(Cyt)_2]\cdot H_2O$ and (h) $[Cu(Br)_2(Cyt)(H_2O)]\cdot H_2O$.

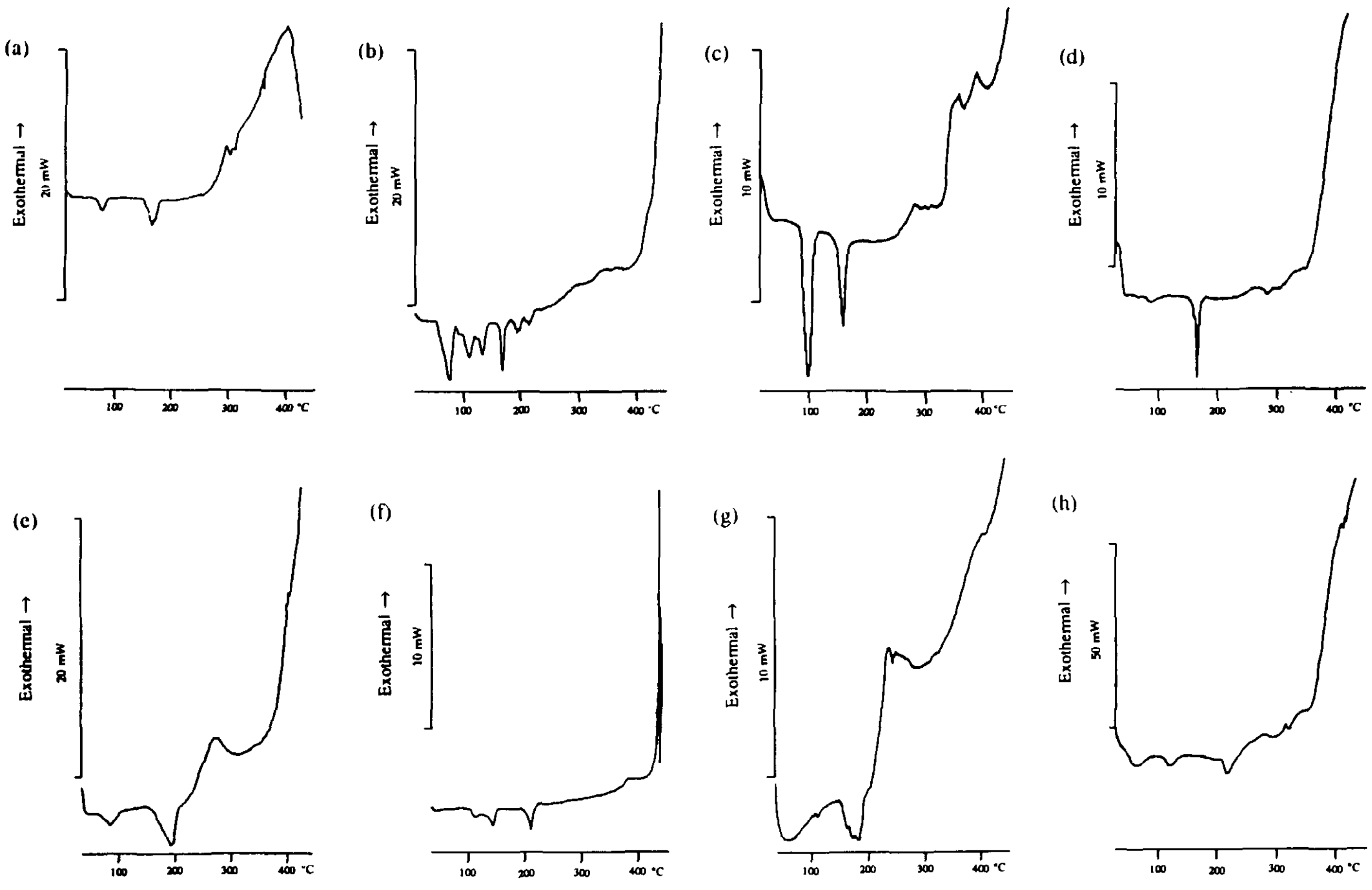


Fig. 3. Differential scanning calorimetric curves of (a) [Cu(CN)$_2$(Urd)(H$_2$O)], (b) [Cu(SO$_4$)(Urd)(H$_2$O)$_2$] · H$_2$O, (c) [Cu(Cl)$_2$(Urd)$_2$] · 4H$_2$O, (d) [Cu(Br)$_2$(Urd)(H$_2$O)], (e) [Cu(CN)$_2$(Cyt)(H$_2$O)], (f) [Cu(SO$_4$)(Cyt)(H$_2$O)$_2$], (g) [Cu(Cl)$_2$(Cyt)$_2$] · H$_2$O and (h) [Cu(Br)$_2$(Cyt)(H$_2$O)] · H$_2$O.

hydrogen bonds present in their crystal structures [17–19]. The pyrolytic process takes place in two steps. The first one, which starts at around 230°C and ends at around 340°C, corresponds to the partial pyrolysis of the sugar ring. This step has also been observed in several other nucleosides [20]. The latter step, which overlaps with the former, corresponds with the combustion of the organic matter.

Three different processes can be observed in the curves of the complexes: dehydration, dehalogenation and pyrolysis.

Dehydration processes

The first thermal decomposition step for all the complexes is the elimination of the water molecules. The corresponding data for these processes are given in Table 3. Dehydration of these compounds occurs over a variable temperature range, ranging from 70 to 135°C. The weight losses observed in the TG curves are in agreement with those calculated from the proposed formulae. The expected endothermic behaviour for the dehydration processes is observed in the corresponding DSC curves. Some of the dehydration enthalpy values, which are fairly high, would suggest a very strong interaction between the water molecules and either the sugar moiety or the copper ion.

Dehalogenation processes

Data corresponding to the dehalogenation of halogenated compounds are shown in Table 4. The elimination of the chloride and bromide ions overlaps with the pyrolysis of the sugar moiety, with the exception of the

TABLE 3

Thermoanalytical data for the dehydration processes

Process	θ (°C)	ΔH (kJ mol^{-1})	Weight loss	
			Found	Calc.
$Cu(CN)_2(Urd)(H_2O) \rightarrow Cu(CN)_2(Urd)$	90	11.6	4.6	4.78
$Cu(SO_4)(Urd)(H_2O)_3 \rightarrow Cu(SO_4)(Urd)(H_2O)_2$	74	92.0	3.9	3.93
$Cu(SO_4)(Urd)(H_2O)_2 \rightarrow Cu(SO_4)(Urd)$	109–135		7.9	7.87
$Cu(Cl)_2(Urd)_2(H_2O_4) \rightarrow Cu(Cl)_2(Urd)_2$	99	37.7	10.1	10.37
$Cu(Br)_2(Urd)(H_2O) \rightarrow Cu(Br)_2(Urd)$	85–95		3.7	3.71
$Cu(CN)_2(Cyt)(H_2O) \rightarrow Cu(CN)_2(Cyt)$	88	10.5	5.0	4.79
$Cu(SO_4)(Cyt)(H_2O)_2 \rightarrow Cu(SO_4)(Cyt)$	135	52.2	8.1	8.21
$Cu(Cl)_2(Cyt)_2(H_2O) \rightarrow Cu(Cl)_2(Cyt)_2$	60–80		3.1	2.82
$Cu(Br)_2(Cyt)(H_2O)_2 \rightarrow Cu(Br)_2(Cyt)(H_2O)$	70	5.8	6.4	6.57
$Cu(Br)_2(Cyt)(H_2O) \rightarrow Cu(Br)_2(Cyt)$	115	31.2		

TABLE 4

Thermoanalytical data for the dehalogenation processes

Process	θ (°C)	ΔH (kJ mol^{-1})	Weight loss	
			Found	Calc.
$[Cu(Cl)_2(Urd)_2] \rightarrow [Cu(Urd)_2]$	158	30.9	10.2	10.22
$[Cu(Br)_2(Urd)] \rightarrow [Cu(Urd)]$	166			
$[Cu(Cl)_2(Cyt)_2] \rightarrow [Cu(Cyt)_2]$	185	51.9		
$[Cu(Br)_2(Cyt)] \rightarrow [Cu(Cyt)]$	213			

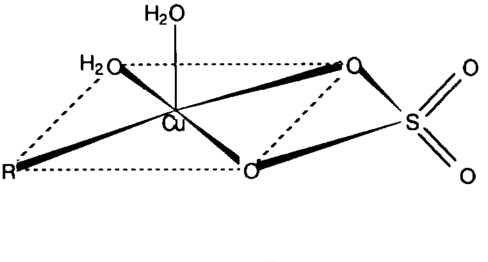
$Cu(Cl)_2(Urd)_2 \cdot 4H_2O$ complex, for which the observed weight loss observed in the TG curve is in agreement with that calculated from the proposed formula. Nevertheless, the temperatures of the dehalogenation processes obtained from the DSC curves are lower than those previously reported by us [21, 22] for halogenated complexes.

Pyrolytic processes

Once the dehydration and dehalogenation processes have taken place, all the compounds undergo pyrolytic processes. The pyrolytic processes of all the complexes follow a two-step pattern, similar to those observed for the respective nucleosides.

It must be pointed out that for the $[Cu(CN)_2(Urd)(H_2O)]$ and $[Cu(CN)_2(Urd)(H_2O)]$ complexes, before the pyrolytic process takes place and overlapping with it, the elimination of the cyanide group occurs. Both processes appear as endothermic effects in the DSC curves at 170 and 194°C respectively.

In conclusion, the spectroscopic data would suggest a weak ligand field for these complexes. The coordination seems to occur through one of the carbonyl groups of the pyrimidine ring for the uridine and through the nitrogen atom for the cytidine. However, an additional auxiliary coordination of the hydroxyl groups of the sugar cannot be rejected. For the



Scheme 2.

complexes obtained from the copper(II) sulphate, a square-pyramidal geometry is proposed (Scheme 2), whilst for the rest a tetrahedral geometry, probably distorted to some extent to square-planar, is assumed.

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