

## Cadmium(II) Complexes of Cytosine

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**Summary.** Complexes of cadmium(II) with cytosine obtained from aqueous or physiological solutions at room temperature are reported. The complexes were characterized by spectroscopic, conductometric,  $^1\text{H-NMR}$ , and  $^{13}\text{C-NMR}$  measurements and also by thermogravimetry.

**Keywords.** Cytosine; Complexes; Coordination sites; Cadmium(II).

### Cadmium(II)-Komplexe von Cytosin

**Zusammenfassung.** Es wird über Komplexe von Cadmium(II) mit Cytosin berichtet, die aus wäßrigen oder physiologischen Lösungen erhalten wurden. Die Komplexe wurden mittels spektroskopischer Methoden, Konduktometrie,  $^1\text{H-}$  und  $^{13}\text{C-NMR}$ -Messungen und mittels Thermogravimetrie charakterisiert.

### Introduction

In a previous communication [1] we have reported the interaction of adenine with cadmium(II) salts. We found that this ligand exhibits different coordination modes with different cadmium salts, showing a preferential tendency to give chloride-complexes in presence of this ion. The main objective of the present study has been to prepare some cadmium(II)-cytosine complexes in order to see if also this ligand behaves differently towards different cadmium salts.

Up to date one cadmium-cytosine complex [2] and some complexes between cadmium(II) ions and cytosine derivatives as 1-methyl-cytosine [3] and cytidine-5'-monophosphate [4–6] have been obtained and investigated.

### Experimental

All the chemical products used were reagent grade and were used without purification. The complexes were obtained at room temperature (25–37°C) by mixing unsaturated solutions of cytosine (Cyt) (in order to avoid its precipitation) and of cadmium(II) chloride or sulfate or nitrate, being 1 : 2 the metal-ligand ratio. As solvent it was used water or 0.9% aqueous NaCl solution, as medium simulating physiological conditions. The complex formation is rather slow and solid compounds were obtained after storing the solutions in closed Erlenmeyer flasks (to avoid the solvent evaporation) for several days or weeks. The precipitates were filtered in vacuum, washed repeatedly with water, air dried by suction and stored in vacuo over silica gel. Because their slow precipitation or also decomposition the compounds were recrystallized only sometimes from aqueous solutions (for example the compound obtained in

physiological solution from sulfate, after recrystallization contains more cytosine: found C 24.95; H 3.42; N 21.32).

All of them were characterized by elemental analysis, IR spectra, thermogravimetry (TG), conductivity measurements and  $^1\text{H-NMR}$ ,  $^{13}\text{C-NMR}$  and electronic spectra.

Elemental analyses of C, H and N were carried out at the Organic Chemistry Institute of Milan University, while chlorine was determined by potentiometric titration following the destruction of the organic moiety by the oxygen flask method.

IR spectra were recorded on a Perkin-Elmer 983 G spectrophotometer in the wavenumber range  $4000\text{--}200\text{ cm}^{-1}$ , using CsI cells, in nujol or hexachlorobutadiene mulls.

TG measurements were carried out with a Mettler TA3000 System in pure nitrogen atmosphere.

The molar conductivities were measured on a Crison conductimeter 522 at  $25 \pm 0.1^\circ\text{C}$ . Conductivity grade water and doubly distilled dimethylsulfoxide (*DMSO*) were used as solvents.

$^1\text{H-NMR}$  and  $^{13}\text{C-NMR}$  spectra were run on a Bruker WP 80 spectrometer, deuterated *DMSO* being used as solvent and  $(\text{CH}_3)_4\text{Si}$  as internal standard.

Electronic absorbance spectra were recorded on a Beckmann DU 7 spectrophotometer, in the wavelength range  $350\text{--}200\text{ nm}$ , using aqueous solutions and quartz cells of 1.000, 2.000 and 10.000 cm.

## Results and Discussion

All cadmium(II) salts used give after reaction with cytosine in 0.9% aqueous NaCl solution the differently hydrated complexes  $\text{Cd}(\text{C}_4\text{H}_5\text{N}_3\text{O})_2\text{Cl}_2$  ( $\text{CdCyt}_2\text{Cl}_2$ ) being only weakly soluble both in water and in *DMSO*. When the reaction was carried out in absence of NaCl the compounds obtained with cadmium chloride, sulfate, or nitrate were  $\text{CdCyt}_2\text{Cl}_2 \cdot 2\text{H}_2\text{O}$ ,  $\text{CdCyt}_2\text{SO}_4 \cdot 1.5\text{H}_2\text{O}$  and  $\text{CdCyt}_4(\text{NO}_3)_2 \cdot \text{H}_2\text{O}$ , respectively. After recrystallization in aqueous medium,  $\text{CdCyt}_2\text{Cl}_2 \cdot 2\text{H}_2\text{O}$  gives  $\text{CdCyt}_2\text{Cl}_2$  or  $\text{CdCyt}_2\text{Cl}_2 \cdot 1.5\text{H}_2\text{O}$ . All the complexes are white and have good crystalline forms [except  $(\text{CdCyt}_2\text{SO}_4 \cdot 1.5\text{H}_2\text{O})$ ], so X-rays measurements on them are in progress. Because the different metal-ligand ratio obtained in the nitrate-complex we prepared again this compound in the 2 : 1 metal-ligand ratio obtaining a compound corresponding to  $\text{CdCyt}_2(\text{NO}_3)_2 \cdot 0.5\text{H}_2\text{O}$ . Analytical data are reported in Table 1.

The IR spectra of all complexes are rather similar (Table 2). Bands attributable to stretching vibrations of water molecules are overlapping very probably with the rather broad ones of  $\text{NH}_2$  and  $\text{N}_1\text{—H}$  groups [7–8]. The  $\text{NH}_2$  stretching band out-of-phase at  $3370\text{ cm}^{-1}$  in the spectrum of free cytosine (probably a composite one) splits, increases in frequency and sharpens in the spectra of the most complexes, being almost unperturbed in the spectra of  $\text{CdCyt}_2\text{SO}_4 \cdot 1.5\text{H}_2\text{O}$  and  $\text{CdCyt}_4(\text{NO}_3)_2 \cdot \text{H}_2\text{O}$ ; so the spectra of the complexes show two or more of these bands, one of them being very probably due to  $\text{N}_1\text{—H}$  stretching vibration. The broad band  $\nu_{\text{sym}}\text{NH}_2$  at  $3165\text{ cm}^{-1}$ , superimposed on the C—H stretching modes, is resolved in two or more bands, showing less strongly hydrogen-bonded  $\text{NH}_2$  and  $\text{N}_1\text{—H}$  groups in the complexes.

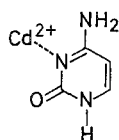
In the  $1700\text{--}1600\text{ cm}^{-1}$  range only a very broad composite band with several shoulders can be seen in the cytosine spectrum. The spectra of the complexes show also one or two rather broad composite bands falling in a position depending on the relative intensities of overlapping bands. Furthermore a new band, a bending vibration of  $\text{H}_2\text{O}$ , overlapping the others, must be present in this range in all but one spectra of the complexes, making it impossible to identify all the expected modes.

**Table 1.** Analytical data of cadmium-cytosine compounds

Compound	C% found (calcd.)	H% found (calcd.)	N% found (calcd.)	Cl% found (calcd.)	H <sub>2</sub> O% found (calcd.)
CdCyt <sub>2</sub> Cl <sub>2</sub>	23.06 (23.69)	2.42 (2.48)	20.28 (20.72)	17.73 (17.48)	0.00 (0.00)
CdCyt <sub>2</sub> Cl <sub>2</sub> · 0.5 H <sub>2</sub> O	22.76 (23.18)	2.72 (2.67)	19.86 (20.27)	18.00 (17.11)	0.00 (2.17)
CdCyt <sub>2</sub> Cl <sub>2</sub> · H <sub>2</sub> O	22.48 (22.69)	2.91 (2.86)	19.74 (19.84)	15.96 (16.74)	6.83 (4.49)
CdCyt <sub>2</sub> Cl <sub>2</sub> · 1.5 H <sub>2</sub> O	22.01 (22.22)	2.98 (3.03)	19.28 (19.43)	16.29 (16.39)	3.81 (6.25)
CdCyt <sub>2</sub> Cl <sub>2</sub> · 2 H <sub>2</sub> O <sup>a</sup>	22.14	3.27	19.47	15.67	7.53
CdCyt <sub>2</sub> Cl <sub>2</sub> · 2 H <sub>2</sub> O <sup>a</sup>	21.68	3.16	18.80	16.62	6.52
CdCyt <sub>2</sub> Cl <sub>2</sub> · 2 H <sub>2</sub> O <sup>a</sup>	21.85	3.19	19.18	16.26	7.56
CdCyt <sub>2</sub> Cl <sub>2</sub> · 2 H <sub>2</sub> O <sup>a</sup>	21.87	3.22	18.88	15.55	7.66
CdCyt <sub>2</sub> Cl <sub>2</sub> · 2 H <sub>2</sub> O <sup>a</sup>	22.18	3.01	19.37	16.19	8.02
CdCyt <sub>2</sub> Cl <sub>2</sub> · 2 H <sub>2</sub> O <sup>a</sup>	21.88 (21.76)	3.25 (3.30)	19.04 (19.03)	15.35 (16.06)	8.01 (8.16)
CdCyt <sub>2</sub> SO <sub>4</sub> · 1.5 H <sub>2</sub> O	20.81 (20.99)	2.87 (2.86)	18.21 (18.26)		5.29 (6.27)
CdCyt <sub>2</sub> (NO <sub>3</sub> ) <sub>2</sub> · 0.5 H <sub>2</sub> O	20.27 (20.55)	2.39 (2.37)	23.63 (23.96)		0.00 (1.93)
CdCyt <sub>4</sub> (NO <sub>3</sub> ) <sub>2</sub> · H <sub>2</sub> O	27.34 (27.50)	3.03 (3.17)	28.46 (28.06)		2.70 (2.58)

<sup>a</sup> Repeated preparations of the same compounds, eventually starting from different cadmium salts, gave consistent analytical results

Nevertheless, one can see generally a shift of the bands attributable to C=O and C<sub>5</sub>=C<sub>6</sub> stretching modes at lower and higher wavenumbers, respectively. Drastic variations of the bands assigned to mixed vibrations involving both N<sub>1</sub>—H in plane deformation and ring stretching modes, to C—H bending and out-of-phase deformation, and to the C—NH<sub>2</sub> stretching vibration [7–10] and of bands in the 1250–440 cm<sup>-1</sup> range, due to ring stretching or bending modes can be seen in the complexes spectra below 1600 cm<sup>-1</sup>. This suggests a ring involvement in the complex-formation, very probably through N(3), which is the most basic site [11]. The shift at higher frequency of the C—NH<sub>2</sub> vibration might be due to a greater participation of the nitrogen electron pair to the resonance structures of the ligand ring according to the structures suggested for the zinc complex [12].



The IR spectra of the complexes give little other information. A band attributable to  $\nu(\text{Cd—Cl})$  is observed at 215 cm<sup>-1</sup> only in the spectrum of

**Table 2.** Some meaningful infrared absorption frequencies ( $\text{cm}^{-1}$ ) of cytosine and its cadmium-complexes<sup>a</sup>

Cyt	$\text{CdCyt}_2\text{Cl}_2$	$\text{CdCyt}_2\text{Cl}_2 \cdot 0.5 \text{H}_2\text{O}$	$\text{CdCyt}_2\text{Cl}_2\text{H}_2\text{O}$	$\text{CdCyt}_2\text{Cl}_2 \cdot 1.5 \text{H}_2\text{O}$
1 700 sh, m	1 720 sh, s			
1 660 vs, b	1 668 sh, s	1 680 vs		
1 635 sh, vs } 1 615 sh, s }	1 620 vs, vb	1 650 sh, vs 1 620 vs	1 644 vs, b 1 611 vs, b	1 620 vs, vb
1 540 s	1 525 sh, ms	1 565 w } 1 502 vs }	1 501 m, b	1 525 sh, ms } 1 504 s }
1 504 s	1 505 ms			
1 465 vs, b	{ 1 453 m 1 442 m	1 473 m 1 445 m	1 443 ms	1 444 s
1 362 vs	{ 1 378 m, b 1 360 mw	1 364 m	1 369 ms	1 370 ms
1 275 s	{ 1 303 mw 1 285 mw	1 288 mw	{ 1 304 m 1 280 w	1 305 m 1 288 mw
1 232 s, b	{ 1 245 mw 1 216 ms	1 243 m 1 221 s	1 233 ms	{ 1 246 sh, mw 1 232 ms 1 217 s
1 012 mw		1 008 w		
965 m	976 mw, b	979 m	973 m, b	976 mw
820 ms, b	850 w	873 m, b	852 m, b	853 m, b
792 s	{ 811 sh, m 800 sh, m 793 ms	819 vs } 795 s }	806 ms	803 m, b
600 s	608 s	611 s	600 ms	{ 609 ms 601 ms
570 mw	578 m	564 ms	570 m	578 m
548 s	560 ms	548 ms	556 m	{ 560 m 553 m
440 s	438 m	438 ms	438 vw	435 mw

<sup>a</sup> s, strong; m, medium; w, weak; b, broad; sh, shoulder;  $\nu$  stretching mode;  $\delta$  bending mode;  $\gamma$  out-of-plane bending; sk, skeletal

<sup>b</sup> Band assignments as in Refs. [7–8, 15–16, 19–20]

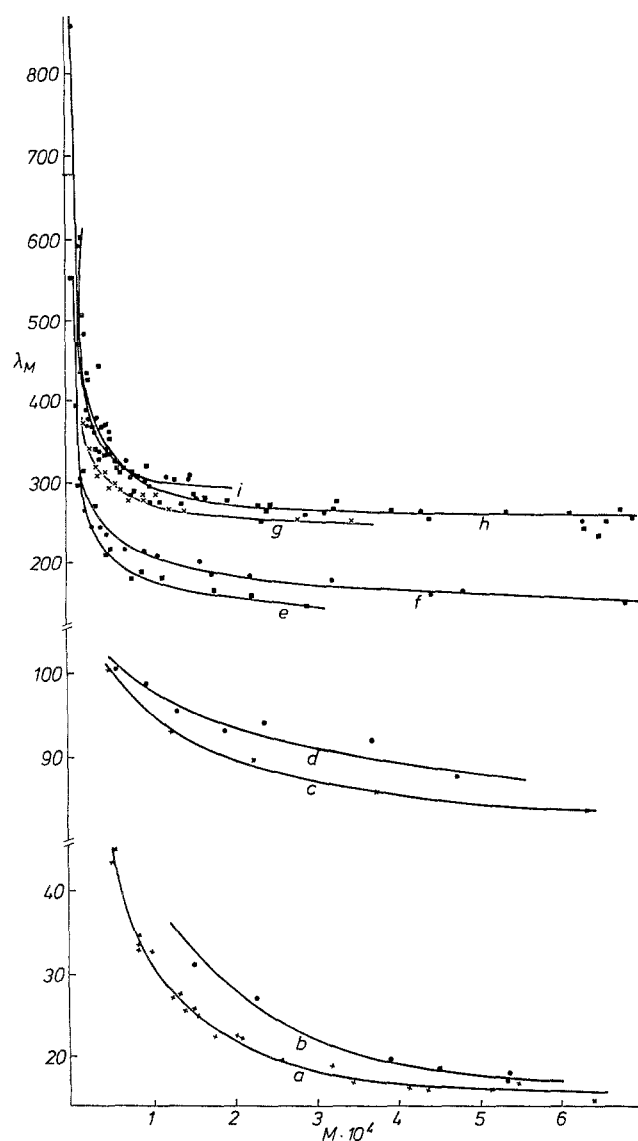
$\text{CdCyt}_2\text{Cl}_2 \cdot 2\text{H}_2\text{O}$	$\text{CdCyt}_2\text{SO}_4 \cdot 1.5\text{H}_2\text{O}$	$\text{CdCyt}_2(\text{NO}_3)_2 \cdot 0.5\text{H}_2\text{O}$	$\text{CdCyt}_4(\text{NO}_3)_2 \cdot \text{H}_2\text{O}$	Band assignment <sup>b</sup>
				$\nu \text{C}=\text{O}$
1 670 sh, s, b	1 679 sh, s, b	1 669 vs, b	1 665 vs, b	$\nu \text{C}_5=\text{C}_6$
1 646 vs		1 645 sh, s, b	1 641 vs	
1 612 vs, b	1 621 vs, b	1 612 vs, b	1 600 sh, ms	$\delta \text{NH}_2$
1 501 s, b				$\delta \text{N}-\text{H} + \nu \text{ ring}$
				$\nu \text{ ring} + \delta \text{N}-\text{H}$
1 444 s	{ 1 459 s 1 445 sh, s	1 453 vs 1 414 s, vb	1 453 vs	$\delta \text{C}-\text{H} + \nu \text{C}-\text{N}$
				$\delta \text{C}-\text{H} + \nu \text{C}-\text{N}$
1 370 ms	1 374 ms	1 376 s, b	{ 1 372 s 1 368 sh, s 1 328 s, b	$\nu \text{C}-\text{N} + \delta \text{C}-\text{H}$
				$\nu \text{NO}_3?$
1 304 m	{ 1 300 m 1 283 m	1 309 sh, ms 1 288 s	1 291 ms	Kekulé
1 233 s	1 234 vs	1 229 ms		$\nu \text{ ring}$
	{ 1 172 vs 1 087 vs 1 048 vs }			$\nu_3\text{SO}_4$
		1 042 mw		$\nu \text{NO}_3$
974 mw	1 015 sh, w	1 033 m	1 008 vw	$\nu \text{ ring}$
852 m	972 s	975 mw, b	977 mw	$\nu \text{ ring} + \nu_1\text{SO}_4$
	835 sh, m			$\gamma \text{N}-\text{H}$
	820 sh, m			
806 s	806 s	818 m	814 ms	$\nu, \delta \text{ ring (breath)}$
		682 mw, b		$\nu \text{NO}_3$
	678 ms, b			
		665 sh, w, b	661 s, b	$\nu \text{NO}_3$
	631 ms			$\nu_4\text{SO}_4$
600 s	605 s	605 m	600 s	$\delta \text{ ring}$
571 ms	562 m	567 ms, b	570 w	sk
553 m	545 sh, mw	550 ms	551 m	$\delta \text{ ring}$
	472 mw			$\nu_2\text{SO}_4$
436 w	438 m, b	432 m, b	432 mw	sk

$\text{CdCyt}_2\text{Cl}_2 \cdot 2 \text{H}_2\text{O}$ . A band at about  $260 \text{ cm}^{-1}$  appearing in almost all the complexes cannot be attributed to a  $\nu(\text{Cd}-\text{Cl})$  stretching vibration. So very probably the chloro-complexes have distorted octahedral structures with the chlorine atoms in bridging positions [13–14]. In the spectrum of the sulfate-complex strong bands  $\nu_1$ ,  $\nu_2$ ,  $\nu_3$ , and  $\nu_4$  due to the sulfate group are observed, the  $\nu_1$  vibration overlapping with one of the ligands [15–16]. The appearance of these bands supports a lowering of the sulfate symmetry probably due to interactions both with water molecules and cadmium ions. The band at  $678 \text{ cm}^{-1}$  could be probably a  $\text{Cd}-\text{OH}$  vibration [16–17], and that at  $820 \text{ cm}^{-1}$  a wagging vibration mode of coordinated water [18]. It was possible to identify only one band surely due to the nitrate group in  $\text{CdCyt}_4(\text{NO}_3)_2 \cdot \text{H}_2\text{O}$ , while a number of these band can be seen in the spectrum of  $\text{CdCyt}_2(\text{NO}_3)_2 \cdot 0.5 \text{H}_2\text{O}$  [19–20] (see Table 2).

TG measurements on  $\text{CdCyt}_2\text{Cl}_2 \cdot 2 \text{H}_2\text{O}$  obtained from different cadmium salts (and repeated several times) show a water loss between  $110$  and  $160^\circ\text{C}$ , of two or less than two water moles per mole of complex (1.6–2.0 moles, being 1.9 the mean value).  $\text{CdCyt}_2\text{Cl}_2 \cdot 0.5 \text{H}_2\text{O}$  and  $\text{CdCyt}_2(\text{NO}_3)_2 \cdot 0.5 \text{H}_2\text{O}$  show no water loss,  $\text{CdCyt}_2\text{Cl}_2 \cdot \text{H}_2\text{O}$  loses more than one water mole (1.6), probably because of absorbed water.  $\text{CdCyt}_2\text{Cl}_2 \cdot 1.5 \text{H}_2\text{O}$  and  $\text{CdCyt}_4(\text{NO}_3)_2 \cdot \text{H}_2\text{O}$  lose about one mole of water per complex (0.91 and 1.05 moles respectively), the two chloro-complexes between  $113$ – $150^\circ\text{C}$  (similarly to the temperature range in which the  $\text{CdCyt}_2\text{Cl}_2 \cdot 2 \text{H}_2\text{O}$  is losing water), the nitrate-complex below  $100^\circ\text{C}$  ( $55$ – $95^\circ\text{C}$ ), so that probably in these complexes the water does not coordinate to metal ion. In  $\text{CdCyt}_2\text{SO}_4 \cdot 1.5 \text{H}_2\text{O}$  it must be more strongly bonded and probably coordinated to cadmium ion, which is indicated by a loss of 1.34 water moles between  $188$ – $271^\circ\text{C}$ . TG measurements performed up to  $410^\circ\text{C}$  on the chloro-complexes show that they all decompose between  $276$ – $390^\circ\text{C}$  losing about one cytosine mole per mole complex (1.00–1.17, being 1.05 the mean value). The residual product at  $410^\circ\text{C}$  could be partially decomposed  $\text{CdCytCl}_2$  (% calcd. 72.60, 71.02, 69.91, 68.07, and 66.68, respectively; found 67.34, 69.61, 65.25, 65.19, and 63.40). The sulfate-complex decomposes between  $272$ – $572^\circ\text{C}$  losing about two cytosine moles per complex mole (% calcd. 48.55, found 44.29). The residual product at  $600^\circ\text{C}$  seems to be  $\text{CdSO}_4$  (% calcd. 45.55; found 46.56). Also  $\text{CdCyt}_2(\text{NO}_3)_2 \cdot 0.5 \text{H}_2\text{O}$  loses about two cytosine molecules in the temperature range  $229$ – $247^\circ\text{C}$ , the found and the calculated percentual losses being 45.87 and 47.52, respectively. The residual compound at  $400^\circ\text{C}$  could be partially decomposed cadmium nitrate (% calcd. 50.56, found 47.59).  $\text{CdCyt}_4(\text{NO}_3)_2 \cdot \text{H}_2\text{O}$  decomposes by losing more than two cytosine moles per complex mole between  $244$ – $373^\circ\text{C}$ , the TG measurement being performed until  $400^\circ\text{C}$ . A comparison of the temperature ranges where the cytosine molecules are lost shows that they are less strongly bonded in  $\text{CdCyt}_2(\text{NO}_3)_2 \cdot 0.5 \text{H}_2\text{O}$ .

In aqueous solution the chloride-complexes dissociate totally: UV measurements show only a band in the same position as the free ligand, the absorption index being about twice of that of cytosine [ $(13.0 \pm 0.1) \cdot 10^3$  and  $(6.3 \pm 0.1) \cdot 10^3 \text{ M}^{-1} \text{ cm}^{-1}$  respectively] and conductivity measurements give values which, plotted versus the molar concentrations of  $\text{CdCl}_2 \cdot 2.5 \text{H}_2\text{O}$  and of the chloride-complexes, fall on a single curve (Fig. 1); the conductivity of cytosine is very low and can be disregarded. The dissociation of  $\text{CdCyt}_2\text{SO}_4 \cdot 1.5 \text{H}_2\text{O}$  in aqueous

solution seems to be not total and it increases with dilution because the  $\lambda_M$  values are only for dilute solutions the same like those of  $\text{CdSO}_4$  (less than  $4 \cdot 10^{-5} M$ ) but they decrease for higher concentrations with respect to the  $\text{CdSO}_4$   $\lambda_M$  values (Fig. 1). Moreover, the UV spectra of this complex show a band at 266.5 nm with an absorption index of  $(12.0 \pm 0.1) \cdot 10^3 M^{-1} \text{cm}^{-1}$ , less than twice that of cytosine. Also, the UV spectra of aqueous solutions of  $\text{CdCyt}_4(\text{NO}_3)_2 \cdot \text{H}_2\text{O}$  and  $\text{CdCyt}_2(\text{NO}_3)_2 \cdot 0.5 \text{H}_2\text{O}$  show absorption indices less than four and two times to that of free ligand [ $(23.6 \pm 0.1) \cdot 10^3 M^{-1} \text{cm}^{-1}$  and  $(11.3 \pm 0.5) \cdot 10^3 M^{-1} \text{cm}^{-1}$ , respectively] the complexes being probably partially dissociated in this solvent. The partial dissociation of these complexes is confirmed by conductivity measurements in water. We cannot compare their molar conductivities with that of cadmium nitrate, which is so hygroscopic that it was impossible to obtain standard solutions of it. However, we can observe very high  $\lambda_M$  values falling on two little different



**Fig. 1.** Molar conductivities,  $\lambda_M$ , vs. concentration measured in *DMSO* (*a-d*) or water (*e-i*); curve *a*: cadmium chloride complexes of cytosine; curve *b*:  $\text{CdCl}_2 \cdot 2.5 \text{H}_2\text{O}$ ; curve *c*:  $\text{CdCyt}_2(\text{NO}_3)_2 \cdot 0.5 \text{H}_2\text{O}$ ; curve *d*:  $\text{CdCyt}_4(\text{NO}_3)_2 \cdot \text{H}_2\text{O}$ ; curve *e*:  $\text{CdCyt}_2\text{SO}_4 \cdot 1.5 \text{H}_2\text{O}$ ; curve *f*:  $3 \text{CdSO}_4 \cdot 8 \text{H}_2\text{O}$ ; curve *g*:  $\text{CdCyt}_2(\text{NO}_3)_2 \cdot 0.5 \text{H}_2\text{O}$ ; curve *h*:  $\text{CdCl}_2 \cdot 2.5 \text{H}_2\text{O}$  and cadmium chloride complexes of cytosine; curve *i*:  $\text{CdCyt}_4(\text{NO}_3)_2 \cdot \text{H}_2\text{O}$

curves for both complexes (conductivity values of  $\text{CdCyt}_4^{++}$  and  $\text{CdCyt}_2^{++}$  must be enough different, in spite of a different solvation grade of the two ions).

The conductivities of  $\text{CdCyt}_2\text{SO}_4 \cdot 1.5 \text{H}_2\text{O}$  and of cadmium sulfate could not be measured in *DMSO* because of their very low solubility. Conductivity measurements on  $\text{CdCl}_2 \cdot 2.5 \text{H}_2\text{O}$  and on the chloro-complexes in this solvent show  $\lambda_M$  values falling on two different curves and only at concentration values higher than  $8 \cdot 10^{-4} \text{M}$  the two curves overlap each other, suggesting a partial dissociation involving only the Cd—Cl bond rupture in both cases. Due to the different conductivity of  $\text{Cd}^{++}$  and  $\text{CdCyt}_2^{++}$  ions, the separation between the two curves increases with dilution as the amount of ions increases in the solutions.  $\text{CdCyt}_4(\text{NO}_3)_2 \cdot \text{H}_2\text{O}$  and  $\text{CdCyt}_2(\text{NO}_3)_2 \cdot 0.5 \text{H}_2\text{O}$  show high conductivity values in *DMSO* solutions, the first complex being more dissociated than the second (Fig. 1). Therefore it follows that in *DMSO* very probably the Cd—Cyt bonds persist. Also different values of chemical shifts are found in NMR measurements for cytosine and its cadmium complexes. Only one set of base peaks can be seen in all  $^1\text{H}$ -NMR and  $^{13}\text{C}$ -NMR spectra confirming that no break of the cytosine-cadmium ion bonds takes place. Because of its very poor solubility the  $^1\text{H}$ -NMR spectra of  $\text{CdCyt}_2\text{SO}_4 \cdot 1.5 \text{H}_2\text{O}$  were performed on saturated solutions and  $^{13}\text{C}$ -NMR spectra could not be measured. Chemical shift values are reported in Table 3. We performed measurements on solutions of cytosine at different concentrations and found a linear correlation between chemical shifts of protons and concentration values:  $\delta = 5.515 + 0.276 \cdot m$ ,  $\delta = 7.247 + 0.322 \cdot m$ ,  $\delta = 6.922 + 1.447 \cdot m$ , and  $\delta = 10.268 - 0.964 \cdot m$  for  $\text{C}_5\text{—H}$ ,  $\text{C}_6\text{—H}$ ,  $\text{NH}_2$  and  $\text{N}_1\text{—H}$  respectively ( $\delta$  values of  $\text{C}_5\text{—H}$  and  $\text{C}_6\text{—H}$  concern the first peak of two signals). Similar linear relations can

**Table 3.**  $^1\text{H}$ -NMR spectra of cytosine and its cadmium complexes in *DMSO* solution ( $\delta$  is in ppm downfield from internal *TMS*)

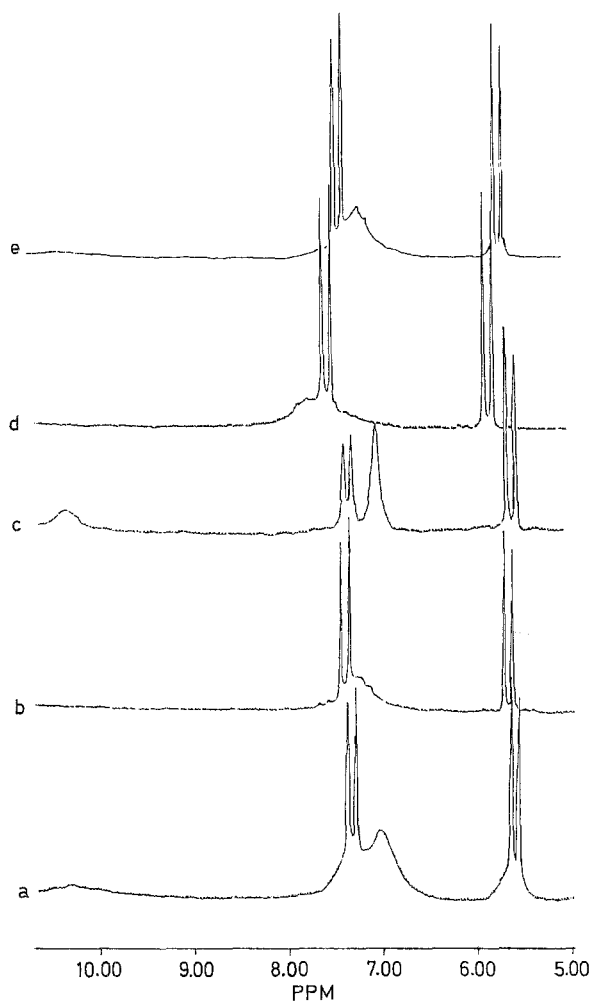
Compound	m	$\delta\text{C}_5\text{-H}$	$\delta\text{NH}_2$	$\delta\text{C}_6\text{-H}$	$\delta\text{N}_1\text{-H}$	$J_{5-6}$	$J_{6-5}$
Cytosine	0.0270	5.524 5.612	6.962	7.257 7.344	10.23	0.088	0.087
$\text{CdCyt}_2\text{Cl}_2$	0.0116	5.578 5.665	7.15 <sup>a</sup>	7.314 7.402	10.49	0.087	0.088
$\text{CdCyt}_2\text{Cl}_2 \cdot 0.5 \text{H}_2\text{O}$	0.0198	5.614 5.702	7.30 <sup>a</sup>	7.349 7.437	10.58	0.088	0.088
$\text{CdCyt}_2\text{Cl}_2 \cdot \text{H}_2\text{O}$	0.0124	5.661 5.749	7.20 <sup>a</sup>	7.316 7.404	10.5 <sup>b</sup>	0.088	0.088
$\text{CdCyt}_2\text{Cl}_2 \cdot 2 \text{H}_2\text{O}$	0.0259	5.628 5.716		7.364 7.452	10.64	0.088	0.088
$\text{CdCyt}_2(\text{NO}_3)_2 \cdot 0.5 \text{H}_2\text{O}$	0.0307	5.778 5.866	7.72 <sup>a</sup>	7.494 7.582	10.86	0.088	0.088
$\text{CdCyt}_4(\text{NO}_3)_2 \cdot \text{H}_2\text{O}$	0.0141	5.573 5.660	7.06	7.302 7.389	10.45	0.087	0.087
$\text{CdCyt}_2\text{SO}_4 \cdot 1.5 \text{H}_2\text{O}$	<0.005	5.534 5.622	7.014	7.268 7.353	10.31	0.088	0.085

<sup>a</sup> Shoulder not well-defined

<sup>b</sup> Very broadened peak



be found also for C<sub>5</sub>—H and C<sub>6</sub>—H protons of chloro-complexes:  $\delta = 5.524 + 4.309 \cdot m$  and  $\delta = 7.270 + 3.703 \cdot m$ , respectively. As can be seen, these chemical shift values are much more concentration-dependent. The NH<sub>2</sub> signal, falling under that of C<sub>6</sub>—H in the spectra of chlorocomplexes, is often not visible at all or it shows up as an unresolved shoulder. The more pronounced downfield positions must be due to more important base-base interactions in the cytosine molecules which are cadmium-bonded in the complexes. The values of NH<sub>2</sub> chemical shifts could be measured only for solutions less than 0.02 *m* and are very much concentration-dependent:  $\delta = 6.940 + 17.078 \cdot m$ . The similar shifts of C<sub>5</sub>—H and C<sub>6</sub>—H signals and the constant values of the proton coupling constant *J* for both free ligand and chloro-complexes show that the metal ion must be bound equally apart from 5- and 6-positions, supporting N<sub>3</sub> as coordination site in these complexes. The spectrum of a saturated solution of CdCyt<sub>2</sub>SO<sub>4</sub> · 1.5 H<sub>2</sub>O in *DMSO* shows little downfield shifts more pronounced for nitrogen-bonded protons, but more meaningful differences in the spectrum shape, the NH<sub>2</sub> peak being well-defined and the C<sub>6</sub>—H signals less sharp (Fig. 2). <sup>1</sup>H-NMR spectra of nitrate complexes show a different coordination mode: remarkable downfield shifts are observed for CdCyt<sub>2</sub>(NO<sub>3</sub>)<sub>2</sub> · 0.5 H<sub>2</sub>O, the NH<sub>2</sub> signal being downfield from the C<sub>6</sub>—H signal and little differences being



**Fig. 2.** Proton chemical shifts of cytosine (a), CdCyt<sub>2</sub>Cl<sub>2</sub> · H<sub>2</sub>O (b), CdCyt<sub>2</sub>SO<sub>4</sub> · 1.5 H<sub>2</sub>O (c), CdCyt<sub>2</sub>(NO<sub>3</sub>)<sub>2</sub> · 0.5 H<sub>2</sub>O (d) and CdCyt<sub>4</sub>(NO<sub>3</sub>)<sub>2</sub> · H<sub>2</sub>O (e)

observed for  $\text{CdCyt}_4(\text{NO}_3)_2 \cdot \text{H}_2\text{O}$ . The  $^{13}\text{C}$ -NMR spectra of cytosine are little dependent from concentration. In the  $^{13}\text{C}$ -NMR spectra of the complexes the signals show small shifts from those of the ligand [21], the  $\text{C}_2$  and  $\text{C}_4$  signals being shifted upfield,  $\text{C}_5$  and  $\text{C}_6$  downfield and more pronouncedly shifted, especially in the nitrate-complexes. Any way, it is possible to reject the oxygen as coordination site being the shifts rather small. The different chemical shifts confirm the assumption of a different coordination mode in the two nitrate-complexes, probably the nitrate ion being cadmium-bonded in  $\text{CdCyt}_2(\text{NO}_3)_2 \cdot 0.5 \text{H}_2\text{O}$ , which is not the case in  $\text{CdCyt}_4(\text{NO}_3)_2 \cdot \text{H}_2\text{O}$ .

In conclusion, taking into consideration all presented data, it is possible to suppose an octahedral coordination in the chloro-complexes through two cytosine molecules and four bridging-chloride ions, the water molecules being only hydrogen-bonded. While the cadmium ion in  $\text{CdCyt}_2\text{SO}_4 \cdot 1.5 \text{H}_2\text{O}$  and in  $\text{CdCyt}_2(\text{NO}_3)_2 \cdot 0.5 \text{H}_2\text{O}$  binds two cytosine molecules through  $\text{N}_3$  and also oxygens of the water molecules and of the sulfate group in the first and of nitrate ion in the second complex, both having probably polymeric structures. At last, in  $\text{CdCyt}_4(\text{NO}_3)_2 \cdot \text{H}_2\text{O}$  the four cytosine molecules are cadmium-bonded and probably prevent any other interaction. We feel that in this case the cadmium ion must exhibit a tetracoordination.

Because the cytosine moieties in *DNA* or *RNA* molecules are bonded through  $\text{N}_1$ , eventually present cadmium ions can still bind these ligands. Actually, cadmium ions were found *DNA*-bonded in most cellular extracts.

## References

- [1] Fontana A., Maggio F., Pizzino T. (1987) *J. Inorg. Biochem.* **29**: 165
- [2] Sakaguchi T., Fujita T. (1977) *Yakugaku Zasshi* **97**: 65
- [3] Gagnon C., Beauchamp A. (1979) *Can. J. Chem.* **57**: 1372
- [4] Clark G. R., Orbell J. D. (1975) *J. C. S. Chem. Comm.*: 697
- [5] Clark G. R., Orbell J. D. (1978) *Acta Cryst.* **B34**: 1815
- [6] Shiba J. K., Bau R. (1978) *Inorg. Chem.* **17**: 3484
- [7] Susi H., Ard J. S., Purcell J. M. (1973) *Spectrochim. Acta* **29A**: 725
- [8] Nishimura Y., Tsuboi M. (1985) *Chem. Phys.* **98**: 71
- [9] Angell C. L. (1961) *J. Chem. Soc.*: 504
- [10] Tsuboi M., Kyogoku Y., Shimanouchi T. (1962) *Biochim. Biophys. Acta* **55**: 1
- [11] Pullmann A., Pullmann B. (1980) *J. Quantum Chem.: Quantum Biol. Symp.* **7**: 245
- [12] Wang S. M., Li N. C. (1968) *J. Am. Chem. Soc.* **90**: 5069
- [13] Coates G. E., Ridley D. (1964) *J. Chem. Soc.*: 166
- [14] Goggin P. L., Goodfellow R. J., Kessler K. (1977) *J. Chem. Soc. Dalton*: 1914
- [15] Nakamoto K., Fujita J., Tanaka S., Kobayashi M. (1957) *J. Am. Chem. Soc.* **79**: 4904
- [16] Ferraro J. R., Walker A. (1965) *J. Chem. Phys.* **42**: 1278
- [17] Nakagawa I., Shimanouchi T. (1964) *Spectrochim. Acta* **20**: 429
- [18] Nakamoto K. (1963) *Inorganic Compounds, Part II. In: Infrared Spectra of Inorganic and Coordination Compounds.* Wiley, New York, sect. II-3, p. 418
- [19] Gatehouse B. M., Livingstone S. E., Nyholm R. S. (1957) *J. Chem. Soc.*: 4222
- [20] Addison C. C., Sutton D. (1967) *Prog. Inorg. Chem.* **8**: 195
- [21] Matczak-Jon E., Jezowska-Trzebiatowska B., Kozłowski H. (1980) *J. Inorg. Biochem.* **12**: 143