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Dedicated to the memory of
Professor Maria Brezeanu (1924–2005)

SYNTHESIS AND STRUCTURAL CHARACTERIZATION OF A NEW CADMIUM COMPLEX WITH CYTOSINE

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A new cytosine cadmium(II) bromide compound was prepared and characterized by electrical conductivity measurements, UV and FT-IR spectra and X-ray structural analysis. The compound is monoclinic, space group *C*2/*c*, $a = 7.355(1)$, $b = 15.051(1)$, $c = 24.266(1)$ Å, $\beta = 90.89(1)°$, $V = 2685.9(4)$ Å^3, Z = 4, $D_c = 2.177$ g/cm^3. The crystal structure is rather unusual and it is formed by two crystallographic independent cytosine cations, $[CytH]^+$ and one $[CdBr_4]^-$ anion. The cations of cytosine are hydrogen bounded to Br anions in an arrangement allowing both inter-base stacking interactions and base pairing *via* hydrogen bonds.

INTRODUCTION

Cadmium is classified in the extremely toxic group of elements influencing plants metabolism as well as animals and human. The high toxicity of heavy metals including Cd is caused by their ability to bind to the SH groups of enzymes and proteins leading to their conformation changes and producing reactive oxygen species. Both effects inhibit the activity of the enzymes involved in the photosynthetic Calvin cycle, nitrogen and sulphate metabolism and glycolysis, interfere with membrane structure (peroxidation of lipids), and induce DNA injury.[1]

The Cd toxic effect is surprisingly specific. There are many mutation avoidance systems that correct damaged DNA, including direct damage reversal, base excision repair, nucleotide excision repair, double-strand-break repair and mismatch repair. The interaction of the cadmium ions with the nucleic acids and their constituents (nucleotide, nucleosides and free bases) is a topic of increasing interest due to their presence in the biological systems.

An analysis of Cambridge Crystallographic Data Center[2] has shown that cytosine, with a monohydrate structure determined in studies[3-6] forms with cadmium halides different types of structures. In the structure of the complex compound $[CdBr_2(Cyt)_2]$[7] cadmium(II) lies in a distorted tetrahedral environment and it is coordinated by two neutral cytosine molecules through the N6, N6' atoms of the cytosine rings and two bromide ions. In the structure of the complex compound $[CdCl_2(H_2O)_2]\cdot 2Cyt$[8] cytosine molecules are not linked to the Cd(II), metallic cation having a distorted octahedral coordination with four equatorial chlorine atoms and two axial water molecules; the two cytosine molecules are hydrogen bonded to the water molecules by the exocyclic oxygen atoms of the bases. In another complex compound $[CdCyt_3Cl][CdCytCl_3]$[8] cadmium is coordinated to the neutral cytosine molecules like in $[CdBr_2(Cyt)_2]$.

As a part of our studies concerning complexes of carcinogenic ions with nucleic acid components, the synthesis, electrical conductivity measurements, UV and FT-IR spectra and the crystal and molecular structure of a new $[CytH]_2[CdBr_4]$ compound are reported.

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RESULTS AND DISCUSSION

The infrared spectral data for cytosine and compound synthesized together with the band assignments are reported in Table 1.

Table 1

Some relevant infrared bands (cm^{-1}) of cytosine and its compound

$[CytH]_2[CdBr_4]$	Cyt	Band assignments
	3400-3450	ν_{OH}, ∂_{HOH}
3370 m	3370 m	ν_{as} (H_2N)
3150 m	3165 m	ν_s (H_2N)
3030 m		ν_{as} (CH)
3000 m	3000 m	ν_s (CH)
1700 m	1700 m	ν (H_2N)
1660 i	1660 i	ν (CO)
1630 i	1630 i	ν ring
1610 i	1610 i	ν (C=C), ν (CO)
1595 i	1595 i	δ (HN)
1560 i	1570 i	ρ (HN)
1550 i	1550 i	ν (C=N)
1510 i	1510 i	ν ring
1500 i	1480 i	δ (CH)
1380 s	1362 s	δ (HN)
1300 i	1290 i	δ (CH)
1240 i	1240 i	ν ring
	1165 m	δ ring
1120 s	1110 s	γ ring
	1020 s	δ ring
1000 s	1000 s	δ ring
970 s	980 s	ρ (HN)
795 i	795 i	γ (HN)
610 i	605 i	δ ring
565 i	565 i	δ (CO)
552 i	552 i	δ ring
510 m	510 m	γ (HN)
440 m	440 m	δ (CO)

The spectra of both cytosine and compound show in the 3600-3000 cm^{-1} region one set of bands assigned to the NH_2 and NH vibrations.

All the characteristic bands of cytosine (ν_{C4N3} (1550 cm^{-1}), $\nu_{C2=O2}$ of carbonyl group (1610 and 1660 cm^{-1}), bend C2=O2 (565 cm^{-1}) and δ_{N1C6H} (795 cm^{-1}) have the same frequencies in the infrared spectrum of compound.

Below 1600 cm^{-1} the bands in the cytosine spectrum are mainly due to ring stretching and bending modes, but also to CH and NH bending modes and to C-NH_2 stretching and bending modes. There are some changes in the frequency and intensity of these bands with respect to cytosine and these variations may be ascribed to the cytosine-bromide interactions *via* hydrogen bonding and to the stacking interactions between bases.

Table 2

Measurements of molar conductivity and data of electronic spectra

Complex	Conductivity* (S) (Type of electrolyte)	Electronic spectra*, λ (nm) (Assignments)
$[CytH]_2[CdBr_4]$	120,5 (1:2 electrolyte)	290 (Cyt)

* DMF solution, 10^{-3}M, t = 25^0C

Description of the structure

Fig. 1 presents the independent part of the crystal structure with the atom numbering scheme. The compound consists of two different ionic moieties: one positively charged formed by two crystallographic independent cytosine cations and the other, negatively charged, formed by the $[CdBr_4]^-$ anion. One cytosine cation (named A) is protonated at the exocyclic atom N55, while the other (named B) is protonated at the endocyclic atom N6. Probably such favorable hydrogen atoms distribution in cytosine cations is determined by molecule self-

organization during the dimerization process and it can be represented according to [13] by formulation R_2^2 (8) (N55A-H...O11B-C1B-N6B-H...N6A-C5A-) and R_2^2 (8) (N55B-H...O11A-C1A-N6A...H-N6B-C5B-). Hydrogen bonds parameters are: N55A-H...O11B - N55A...O11B 2.792 Å H...O11B 2.12 Å bond angle NHO 132°, N6B-H...N6A - N6B N6A 2.878 Å H...N6A 2.03 bond angle NHN 171°, N55B-H...O11A – N55B O11A 2.296 Å H...O11A 2.08 Å bond angle NHO 170°. The dimer units are linked along axis [-110] by hydrogen bonds N2A-H...O11B(x+1/2, y+1/2, z) – N2A...O11B 2.797 Å H...O11B 2.95 Å bond angle NHO 170°, N2B-H...O11A(x-1/2, y-1/2, z) – N2B O11A 2.801 Å H...O11A 1.94 Å bond angle NHO 176° (Fig. 2).

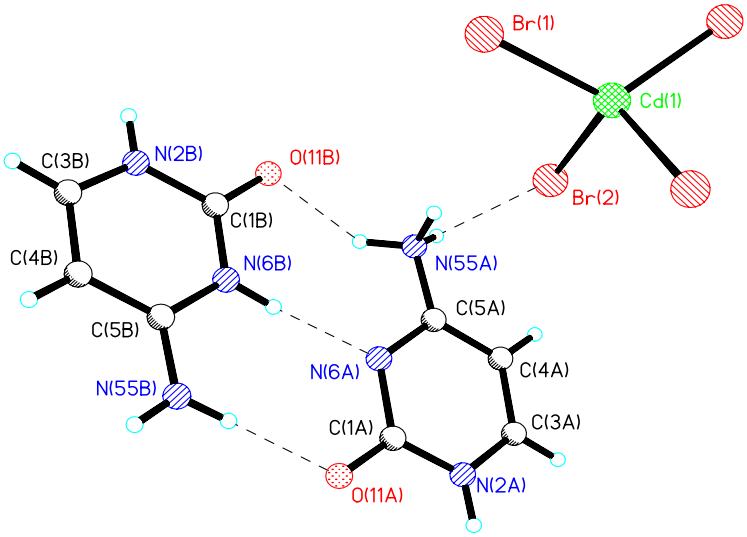

Fig. 1 – View of the $[CytH]_2[CdBr_4]$ crystal structure with the atom numbering scheme.

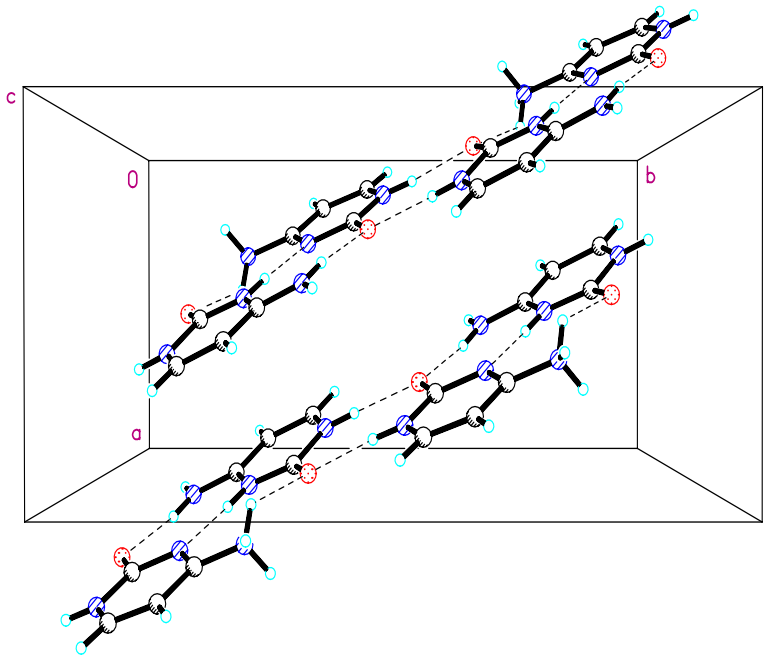

Fig. 2 – Organic chains along axis [-110].

The tridimensional crystal structure is governed by a number of hydrogen bonds N-H…Br which link the organic chains to the inorganic $[CdBr_4]^{2-}$ anion. Hydrogen bonds parameters are: N55A-H...Br1 – N55A...Br1 3.847 Å H... Br1 3.11 Å angle NHBr 142°, N55B-H...Br1A(-x-1/2, -y+1/2, -z) – N55B Br1

3.654 Å H...Br1 2.91 angle NHBr 146°, N55A-H...Br2 - N55A...Br2 3.339 Å H... Br2 2.56 Å angle NHBr 147°, N55A-H...Br2(-x-1, y, -z+1/2) – N55A Br2 3.291 Å H...Br2 2.83 Å angle NHBr 114° (Fig. 3).

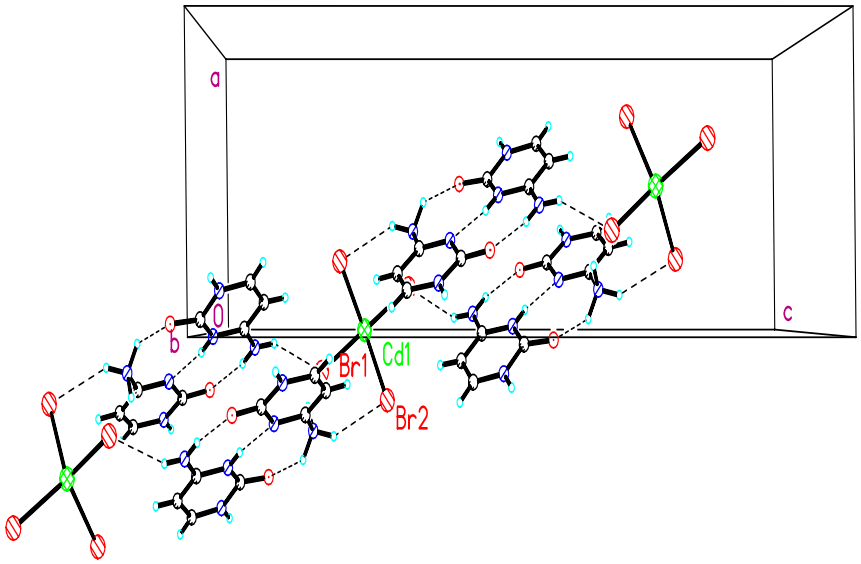

Fig. 3 – A view of the packing diagram of compound $[CytH]_2[CdBr_4]$ showing chaining and pairing.

Such interligand hydrogen bonding confers additional stability and plays an important role in the metal-nucleic acid recognition.

The interatomic distances in the cytosine molecule for our compound are presented in Table 3. For comparison, the interatomic distances for other some cytosine complexes are also presented in the table. The differences between the bond lengths of the two cations are probably because of the different hydrogen atoms distribution. According to Cambridge Crystallographic Data Center, cytosine presents an essential electronic density delocalization and can act as uncoordinated,[4] coordinated,[7] as neutral molecule in the outer sphere of coordination[8] or as cation in different tautomeric forms.[14,15]

Cadmium has a tetrahedral geometry in the $[CdBr_4]^{2-}$ anion and the medium values of the bond lengths Cd-Br and interbond angles Br-Cd-Br (2.556 Å, respectively 109°43') do not differ significantly from those reported in the compound $[CdBr_2(Cyt)_2]$[7] or in the anionic part $[CdBr_4]^{2-}$ of the complex compound N-methyl-1,3-propandiammonium tetrabromo-cadmiu(II).[16]

Table 3

Selected bond lenghts for some cytosine complexes

Bond	d, Å (*)		d, Å (**) [4]	d, Å (***) [7]	d, Å (****) [15]		d, Å (*****) [16]	
	Cation A	Cation B			Cation A	Cation B	Cation A	Cation B
C(1)-N(2)	1.35(1)	1.38(1)	1.371	1.370	1.356	1.382	1.358	1.328
C(1)-O(11)	1.24(1)	1.27(1)	1.261	1.274	1.215	1.207	1.245	1.226
N(2)-C(3)	1.37(1)	1.32(1)	1.361	1.355	1.351	1.347	1.354	1.343
C(3)-C(4)	1.35(1)	1.39(1)	1.353	1.343	1.344	1.347	1.338	1.356
C(4)-C(5)	1.37(1)	1.38(1)	1.431	1.440	1.422	1.418	1.411	1416
C(5)-N(55)	1.34(1)	1.30(1)	1.339	1.320	1.329	1.302	1.276	1.329
C(5)-N(6)	1.37(1)	1.37(1)	1.346	1.349	1.355	1.345	1.345	1.335
N(6)-C(1)	1.38(1)	1.31(1)	1.351	1.332	1.389	1.371	1.374	1.395

* cytosine cation protonated at the exocyclic nitrogen atom for cytosine A or endocyclic nitrogen atom for cytosine B
** monohydrate neutral cytosine molecule
*** coordinated neutral cytosine molecule
**** cytosine cation protonated at the exocyclic nitrogen atom for both cations
***** cytosine cation protonated at the endocyclic nitrogen atom for both cations

EXPERIMENTAL

Synthesis of $[CytH]_2[CdBr_4]$

All the products were grade reagents used as received.

The compound was prepared by mixing a solution of 1 mmol $CdBr_2$ in 5 mL of water and a solution 1 mmol of cytosine in 5 mL of hot water. The reaction solution was left to stand at normal temperature for 4-5 days. The obtained crystals were washed first with a water-ethanol (10:1) solution, then with ethylic ether and dried over P_4O_{10} in a dessicator.

(Found: Cd, 17.36; C, 14.58; H, 1.79; N, 12.74; Br, 48.83. Calc.: Cd, 17.07; C, 14.63; H, 1.83; N, 12.80; Br 48.78).

Physical Data

Elemental chemical analyses were performed in the INCCF Laboratory-Bucharest.

Molar electrical conductivities were recorded in DMF solutions at 250C, with a OK 102/1 Radelkis Conductometer with a 0.1 S – 0.5 S measuring rang.

FT-IR spectra were recorded with a Perkin-Elmer spectrophotometer using KBr pellets as reference, in the wave number range 4000-400 cm^{-1}.

Crystallography

Diffraction data were collected on a Nonius Kappa CCD diffractometer with graphite monochromated Mo-K_α radiation using ω rotations with sample to detector distance of 25 mm. Preliminary orientation matrices and unit cell parameters were obtained from the peaks of the first 10 frames, respectively, and refined using the whole data set. The frames were integrated and corrected for Lorentz and polarization effects using DENZO.[9] The scaling as well as the global refinement of crystal parameters were performed by SCALEPACK.[9] Reflections, which were partly measured on the previous and following frames, were used to scale these frames on each other. The absorption correction was introduced by the semi-empirical method from symmetry equivalent reflections.[10] All the structures were solved by the standard direct method using SHELXS-97 and refined by full-matrix least squares based on F^2 using SHELXL97.[11] ORTEP[12] was used for the molecular drawings.

Crystal data for $[CytH]_2[CdBr_4]$: $C_{16}H_{24}Br_2CdN_{12}O_4$, M = 880.51, crystal dimensions 0.25 × 0.15 × 0.10 mm, monoclinic, space group $C2/c$, a = 7.355(1), b = 15.051(1), c = 24.266(1) Å, β = 90.89(1)°, V = 2685.9(4) $Å^3$, Z = 4, D_c = 2.177 g/cm^3, μ(Mo-K_α) = 6.812 mm^{-1}, T = 100(2) K, θ range 2.71 to 27.44°, number of all reflections 8901, number of unique reflections 3033, number of parameters 169, R_1 = 0.0705, wR_2 = 0.1958 ($I>2\sigma(I)$), R_1 = 0.1162, wR_2 = 0.2165 (all data).

Crystallographic data for $[CytH]_2[CdBr_4]$ were deposited with the Cambridge Crystallographic Data Center, CCDC 297842. Copies of this information may be obtained from The Director, CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK(fax: +44-1233-336033; e-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk).

CONCLUSION

The crystal structure of compound $[CytH]_2[CdBr_4]$ shows a particular way of cytosine cation stabilization in the crystallization process with formation of two different tautomeric forms.

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