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Interactions of d^{10} metal ions with hippuric acid and cytosine. X-ray structure of the first cadmium (II)–amino acid derivative–nucleobase ternary compound

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Abstract

The interactions of Zn(II), Cd(II) and Hg(II) with hippuric acid (hipH) were studied and several novel compounds were synthesized and studied by NMR. Some new metal–hippuric–cytosine ternary compounds were formed and the structure of the $[Cd(hip)_2(cyt)(H_2O)]_2$ ternary complex resolved. Each cadmium (II) atom has a distorted trigonal bipyramid coordination which is linked to a water molecule, a cytosine via N(3), a carboxylic oxygen atom of a hippurate moiety and two bridging dicoordinated hippurates bound through the carboxylic oxygen atoms. To these five main bonds, two longer ancillary interactions can be observed: the second oxygen of the monocoordinated hippurate group and the carboxylic oxygen of the cytosine ligand. The compound is stabilized by an intramolecular stacking between the benzene and cytosine rings and by the hydrogen bonds between the coordinated water molecules and the ligands. This is, to our knowledge, the first structure of a cadmium–amino acid derivative–natural nucleobase compound described so far.

Keywords: Cadmium complex; Ternary complexes; Hippuric acid; Cytosine

1. Introduction

The study of ternary complexes of the metal–amino acid (or peptide)–nucleoside (or related base) type is a topic of increasing interest due to their presence in biological systems. As an example, in the active center of enzymes such as kinases, there is a metallic ion, e.g. Mg(II) or Ca(II), bound to a nucleotide, e.g. NMP or NTP (usually N=A, an adenosine derivative), which interacts noncovalently with the peptide pocket cavity of the active center. The ternary complex is formed only through stacking or hydrogen interactions [1]. Moreover, some metal–peptide or metal–nucleoside complexes could be used as a model of recognition for nucleic acids or peptides, respectively [2], or a model for the antineoplastic activity of the platinum–histone–DNA interaction [3]. Zinc finger, *mer* and *fur* proteins are also examples of ternary complex systems without direct covalent bonds [4].

The presence of such complexes cannot be disregarded in RNA or DNA synthesis or in the ribosomal synthesis of proteins [5]. There are very few reviews on this subject [6–8]. Furthermore, a small number of X-ray studies have been cited in the literature [9–20]. Generally, the ternary complexes isolated in the solid state have been obtained with inert cations, such as Pt(II) and Pd(II), or with Cu(II) (with very favorable equilibrium constants).

Lippert classified these ternary complexes into three different types depending on the direct bonding between the metal ion and the nucleotide or peptide [9]. In the first type, (a), there is direct metal-mediated interaction between nucleoside and protein. The second possibility is type (b), where the metal promotes indirect interactions (as in platinum cross-linking between histones and DNA) in which the metal ion is bound to a peptide (as in zinc fingers). And, finally, type (c), where the metal ion promotes indirect interactions in which the metal ion is bound to the nucleotide or nucleic acid sequence, and this

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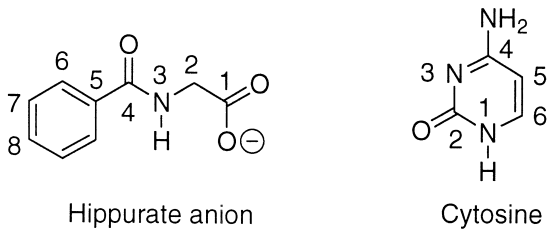

Fig. 1. Formulae and numeration of hippurate anion and cytosine.

complex recognizes a protein (as in, for example, the kinase or phosphorylase allosteric enzymes, or in *cis*-platin damage recognition proteins).

As a follow-up to our previous work on ternary complexes [6,18], the interactions of Zn(II), Cd(II), and Hg(II) with hippuric acid and cytosine were studied. Cadmium toxicity is a topic of major interest [21,22] and hippuric acid is synthesized in the liver as a derivative of glycine (as a metabolite of benzoic acid urinary excretion) [23].

To our knowledge, there is no cadmium ternary compound with nucleobases described in the literature except for the related dimeric $[Cd_2(imidazole)_2(glycylglycinato)_2]Cl_2$ compound [24]. In addition, very few X-ray structures with metal hippuric complexes have been reported, and, of these, there are none with cadmium metal. The most relevant structures are polymeric units with Fe(II), Co(II), and Ni(II) [25,26], monomer units with Zn(II) [27] and Au(I), with anticancer and antirheumatoid arthritis activity [28], and bis(hippurato)bisimidazolecopper(II) [29]. In this report, the interactions of d^{10} metal ions with hippuric acid and cytosine are described (Fig. 1).

2. Experimental

2.1. Analysis and physical measurements

Elemental microanalyses for carbon, hydrogen, and nitrogen were carried out using a Carlo Erba model 1106 microanalyser. The infrared spectra in the solid state (KBr pellets) were recorded on a PE 683 with a PE 1600 IR data station and the electronic spectra were registered on a PE 552 spectrophotometer. The ^{1}H NMR spectra were recorded on a Brucker AMX 300 spectrophotometer at room temperature. Proton chemical shifts in DMSO-d_6 were referenced to DMSO-d_6 [δ(DMSO): 2.60 ppm].

Reagents were used as received from Sigma, Merck (hippuric acid and cytosine), or Aldrich (metallic salts).

2.2. Crystallographic studies

X-ray analysis was performed on a suitable crystal of the $[Cd(hip)_2(cyt)(H_2O)]_2$ complex (**6**) (size 0.10×0.25×0.42 mm). All parameters were determined by a least squares refinement of 25 reflections on an Enraf-Nonius CAD4 diffractometer with Mo Kα radiation ($\lambda = 0.71069$ Å). Unscaled structural factors were determined after Lorentz-polarization and absorption corrections using the MolEN package [30]. A summary of the crystal and structure refinement is shown in Table 1. The structure was resolved by direct methods with the SHELXS86 program [31]. Refinement was carried out using the SHELXL93 least squares program [32]. Non-H atoms were refined anisotropically, and H atoms were situated in calculated positions and refined with a global isotropic temperature factor. Selected bond lengths and angles are given in Table 2. Fig. 2 shows a perspective view of the $[Cd(hip)_2(cyt)(H_2O)]_2$ complex **6** with the atom numbering as depicted using ORTEPII.

2.3. Preparation of the complexes

2.3.1. Preparation of binary compounds

2.3.1.1. $Zn(hip)_2 \cdot 6.5H_2O$ (*1*) and $Cd(hip)_2 \cdot 5H_2O$ (*2*)

A mixture of hippuric acid (10 mmol) and sodium hydroxide (10 mmol) in 55 ml of water–ethanol (10:1) was heated to solution. A metal solution of 5 mmol in 5 ml water of the corresponding metal acetate was added to the former solution, the mixture was heated to 60°C and stirred for 2 h. The reaction solution was left to stand and after 2 days white plates were formed. The crystals were filtered out and recrystallized from methanol. The yields obtained were 78% for the Zn(II) derivative and 79% for the Cd(II) derivative.

Complex **1**. *Anal.* Found: C, 39.80; H, 5.19; N, 5.06. Calc. for $C_{18}H_{29}N_2O_{12.5}Zn$: C, 40.12; H, 5.38; N, 5.20. Selected IR bands (cm^{-1}): 558w, 613m, 691s, 712m, 756m, 1005m, 1298s, 1398s, 1431m, 1490m, 1574vs, 1604vs, 1636vs, 1650vs, 3280bs, 3353bs. UV: $\lambda_{max} = 258$ nm (free hippuric acid 258 nm). ^{1}H NMR (DMSO-d_6): δ

Table 1
Selected crystallographic data for $[Cd(hip)_2(cyt)(H_2O)]_2$ (**6**)

Empirical formula	$C_{22}\ H_{23}Cd\ N_5\ O_8$
Crystal size (mm)	0.10×0.25×0.42
Crystal system	Monoclinic
Space group	P21/n
Molecular weight	597.85
a (Å)	7.047(2)
b (Å)	29.852(7)
c (Å)	11.412(4)
β (deg)	99.87(3)
Volume (Å^3)	2365.2(12)
Z	4
Density (calc.) (mg m^{-3})	1.679
Absorption coefficient (cm^{-1})	9.82
θ range (deg)	3.01–30.42
Reflections collected	7451
Independent reflections	7146 ($R_{int} = 0.1059$)
Final R indices ($I > 2\sigma(I)$)	0.1198, 0.3025
R indices (all data)	0.2540, 0.3023
Largest diff. peak and hole/e (Å^{-3})	2.471 and −4.592

Table 2
Selected bond lengths (Å) and angles (deg) for complex **7**[a]

Cd(1)–O(9)#1	2.222(8)
Cd(1)–N(5)	2.240(8)
Cd(1)–O(10)	2.305(8)
Cd(1)–O(1OA)	2.355(10)
Cd(1)–O(22)	2.372(9)
Cd(1)–O(9A)	2.573(10)
O(9)–Cd(1)#1	2.222(8)
O(9)–C(11)	1.267(13)
O(10)–C(11)	1.251(14)
O(9A)–C(11A)	1.263(14)
O(10A)–C(11A)	1.254(14)
O(9)#1–Cd(1)–N(5)	140.6(3)
O(9)#1–Cd(1)–O(10)	129.8(3)
N(5)–Cd(1)–O(10)	89.1(3)
O(9)#1–Cd(1)–O(10A)	83.1(3)
N(5)–Cd(1)–O(10A)	113.7(3)
O(10)–Cd(1)–O(10A)	80.9(3)
O(9)#1–Cd(1)–O(22)	86.1 (3)
N(5)–Cd(1)–O(22)	95.7(3)
O(10)–Cd(1)–O(22)	80.4(3)
O(10A)–Cd(1)–O(22)	144.7(3)
O(9)#1–Cd(1)–O(9A)	78.7(3)
N(5)–Cd(1)–O(9A)	84.3(3)
O(10)–Cd(1)–O(9A)	124.2(3)
O(10A)–Cd(1)–O(9A)	52.7(3)
O(22)–Cd(1)–O(9A)	155.4(3)
C(4)–N(5)–Cd(1)	137.1(7)
C(6)–N(5)–Cd(1)	103.0(6)
C(11)–O(9)–Cd(1)#1	122.3(7)
C(11)–O(10)–Cd(1)	150.1(7)
O(10)–C(11)–O(9)	126.3(11)
C(11A)–O(9A)–Cd(1)	87.1(7)
C(11A)–O(10A)–Cd(1)	97.4(7)
O(10A)–C(11A)–O(9A)	121.3(12)

[a] Symmetry transformations used to generate equivalent atoms: #1 $-x, -y, -z$.

8.66 [t, 1H, H(3), $J = 5.8$ Hz], 7.95 [dd, 2H, H(6), $J = 6.8$ and 1.5 Hz], 7.58 [m, 3H, H(7,8)], 3.92 [d, 2H, H(2), $J = 5.8$ Hz].

Complex **2**. *Anal*. Found: C, 38.45; H, 4.66; N, 5.04. Calc. for $C_{18}H_{26}CdN_2O_{11}$: C, 38.68; H, 4.66; N, 5.01. Selected IR bands (cm^{-1}): 550m, 576m, 727m, 1310s, 1394s, 1434m, 1490m, 1539s, 1577s, 1596vs, 1642s, 3297br. UV: $\lambda_{max} = 257$ nm. ^{1}H NMR (DMSO-d_6): δ 8.61 [t, 1H, H(3), $J = 5.9$ Hz], 7.95 [dd, 2H, H(6), $J = 6.8$ and 1.6 Hz], 7.60 [m, 3H, H(7,8)], 3.94 [d, 2H, H(2), $J = 5.9$ Hz].

*2.3.1.2. Hg(hip)$_2$ (**3**)*

Mercury (II) acetate in methanol (3 mmol in 20 ml) was added drop by drop to a stirred solution of hippuric acid (6 mmol in 5 ml of methanol). After a few minutes a precipitate was obtained. After 30 min it was filtered and dried in air (yield 72%). *Anal*. Found: C, 38.51; H, 2.90; N, 5.03. Calc. for $C_{18}H_{16}HgN_2O_6$: C, 38.80; H, 2.87; N, 5.03. Selected IR bands (cm^{-1}): 563m, 601m, 685m, 711m, 1406s, 1446m, 1488s, 1525s, 1576s, 1600s, 1625vs, 1635vs, 3393m. UV: $\lambda_{max} = 258$ nm. ^{1}H NMR (DMSO-d_6): δ 8.95 [t, 1H, H(3), $J = 5.9$ Hz], 7.95 [dd, 2H, H(6), $J = 6.8$ and 1.6 Hz], 7.60 [m, 3H, H(7,8)], 4.06 [d, 2H, H(2), $J = 5.9$ Hz].

2.3.2. Preparation of ternary compounds

*2.3.2.1. [Zn(hip)$_2$(cyt)$_2$]·3H$_2$O (**4**) and [Cd(hip)$_2$(cyt)$_2$]·4H$_2$O (**5**)*

These compounds were formed from 1 mmol of the corresponding binary derivative **1** or **2** dissolved in 10 ml of hot water (80°C). When the solution was completely clear, 2 mmol of cytosine in 15 ml water at 80°C were added. The mixture was heated to reflux for 2 h. The resulting precipitate was filtered out and dried over silica gel in a desiccator.

Complex **4**. *Anal*. Found: C, 44.99; H, 4.30; N, 15.67. Calc. for $C_{26}H_{32}N_8O_{11}Zn$: C, 44.73; H, 4.59; N, 16.06. Selected IR bands (cm^{-1}): 443vw, 552w, 603w, 691m, 710m, 794m, 931vw, 998m, 1030vw, 1079w, 1114w, 1162w, 1233m, 1289m, 1374m, 1396s, 1440w, 1490m, 1537s, 1576m, 1630vs, 1647s, 1693s, 1713m, 3200bs, 3494bs. UV: $\lambda_{max} = 257$ nm. ^{1}H NMR (DMSO-d_6): δ 10.60 [bs, 1H, NH(1) (cyt)], 8.66 [t, 1H, H(3), $J = 5.9$ Hz (hip)], 7.96 [dd, 2H, H(6), $J = 6.8$ and 1.5 Hz (hip)], 7.60 [m, 3H, H(7,8) (hip)], 7.44 [d, 1H, H(5), $J = 6.9$ Hz (cyt)], 7.21 [bs, 2H, NH_2 (cyt)], 5.71 [d, 1H, H(6), $J = 6.9$ Hz (cyt)], 3.92 [d, 2H, H(2), $J = 5.9$ Hz (hip)] (where 'hip' and 'cyt' indicate hippurate anion and cytosine, respectively).

Complex **5**. *Anal*. Found: C, 40.93; H, 4.46; N, 14.59. Calc. for $C_{26}H_{34}CdN_8O_{12}$: C, 40.92; H, 4.37; N, 14.69. Selected IR bands (cm^{-1}): 321vw, 406m, 548m, 566m, 603m, 693m, 715m, 793m, 932w, 1005w, 1031vw, 1079vw, 1103vw, 1162vw, 1230m, 1300m, 1397s, 1440w, 1466m, 1490m, 1531s, 1577s, 1635vs, 1645s, 1661s, 2930sh s, 3202bs, 3381bs. UV: $\lambda_{max} = 258$ nm. ^{1}H NMR (DMSO-d_6): δ 10.70 [bs, 1H, NH(1) (cyt)], 8.67 [t, 1H, H(3), $J = 5.8$ Hz (hip)], 7.96 [dd, 2H, H(6), $J = 6.7$ and 1.5 Hz (hip)], 7.58 [m, 3H, H(7,8) (hip)], 7.50 [d, 1H, H(5), $J = 6.9$ Hz (cyt)], 7.44 [bs, 2H, NH_2 (cyt)], 5.76 [d 1H, H(6), $J = 6.9$ Hz (cyt)], 3.96 [d, 2H, H(2) (hip), $J = 5.8$ Hz].

*2.3.2.2. [Cd(hip)$_2$(cyt)(H$_2$O)] (**6**)*

The complex was synthesized similarly to the former cadmium (II) derivative but using a molar 1:1 cadmium hippurate complex/cytosine ratio. A white precipitate of **6** appeared and was filtered off and the solution was left to stand for some days. Two days later, a few white monoclinic crystals of $[Cd(hip)_2(cyt)(H_2O)]_2$ (**6**) appeared in the solution, some of them being suitable for X-ray study.

Complex **6**. *Anal*. Found: C, 43.86; H, 3.66; N, 12.18. Calc. for $C_{22}H_{23}CdN_5O_8$: C, 44.20; H, 3.85; N, 11.72. Selected IR bands (cm^{-1}): 323w, 400w, 435w, 548sh,

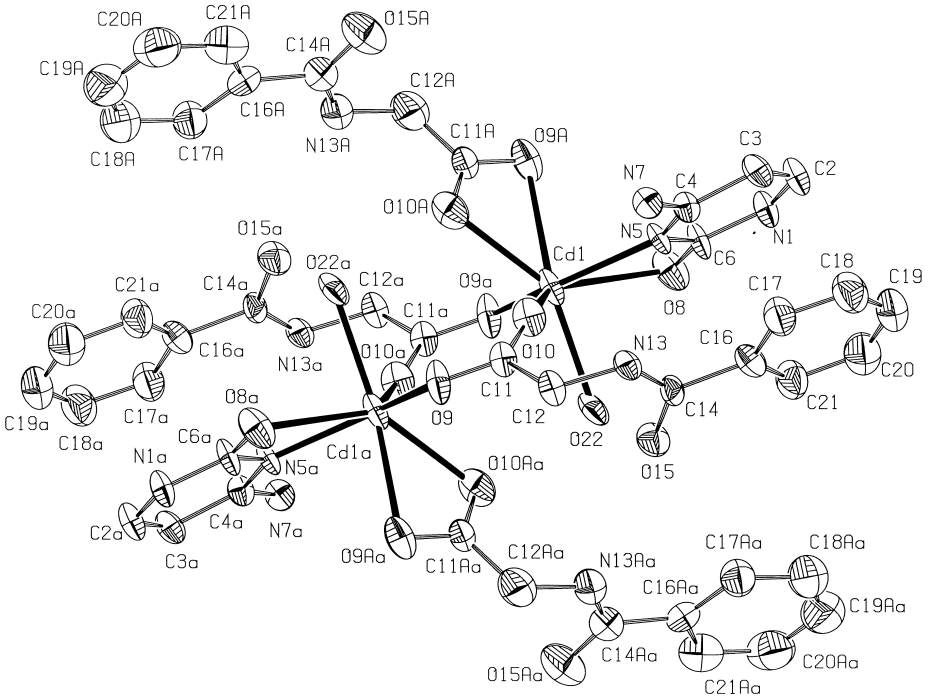

Fig. 2. ORTEP diagram and atom numbering scheme for the $[Cd(Hip)_2(Cyt)(H_2O)]_2$ (**6**) ternary compound.

562m, 585m, 618w, 669w, 690w, 724s, 796m, 818m, 850m, 929w, 1003m, 1031vw, 1078vw, 1106vw, 1147vw, 1165w, 1192vw, 1230m, 1290m, 1301m, 1315m, 1341vw, 1398m, 1432m, 1469m, 1490s, 1533s, 1573s, 1613vs, 1632vs, 1662s, 2832m, 2918m, 3223bs, 3328bs, 3384bs. UV: $\lambda_{max} = 258$ nm. ^{1}H NMR (DMSO-d_6): δ 10.75 [bs, 1H, NH(1) (cyt)], 8.66 [t, 2H, H(3) $J = 5.8$ Hz (hip)], 7.96 [dd, 4H, H(6), $J = 6.8$ and 1.5 Hz (hip)], 7.58 [m, 6H, H(7,8) (hip)], 7.50 [bd, 1H, H(5), $J = 6.9$ Hz (cyt)], 7.44 [bs, 2H, NH_2 (cyt)], 5.76 [d, 1H, H(6), $J = 7.0$ Hz (cyt)], 3.95 [d, 4H, H(2), $J = 5.8$ Hz (hip)].

3. Results and discussion

3.1. Hippuric derivatives

The infrared data for hippuric derivatives were assigned according to the literature [33–35]. The absence of the broad water bands in Hg[hip]$_2$ (**3**) in the 3500–3300 cm^{-1} zone confirms the absence of any water molecule in this complex, however a sharp band of the NH group from hippuric acid appears at 3393 cm^{-1}. The absence of the υ(COOH) band at 1761 cm^{-1} in all complexes indicates that the hippurate is the coordination ligand. The stretching asymmetric carboxylate bands between 1590 and 1577 cm^{-1} and the symmetric stretching between 1410 and 1398 cm^{-1} confirm these hypotheses. The coordination of a metal ion via O carboxylate is confirmed by the υ(M–O) bands at 558 (Zn), 550 (Cd), and 563 (Hg) cm^{-1}. The δ(N–H) bands appear at 1604–1596 cm^{-1} in all complexes. Furthermore, the NMR data are in agreement with coordination through the carboxylic group [disappearance of the H(1) signal] in a symmetrical geometry (only single peaks appear). Moreover, the δ values of H(3) and H(2) in complexes **1**–**3** show deshielded signals related to hippurate anion (^{1}H NMR data of hippurate anion (DMSO-d_6): δ 8.09 [bs, 1H, H(3)], 7.92 [dd, 2H, H(6), $J = 5.8$ and 1.5 Hz], 7.58 [m, 3H, H(7,8)], 3.71 [d, 2H, H(2), $J = 5.8$ Hz]). In **1** and **2**, H(3) and H(2) shift 0.50 and 0.20 ppm, respectively, which could derive from the coordination of the ligand to metal ions and from the formation of a hydrogen bond between the amide group and water coordinated to the Zn(II) and Cd(II) ions likely as it is presented in complex **6**. This suggestion may be supported by the similar chemical shifts of the H(3) and H(2) protons in the complexes **1**, **2** and **6**. On the other hand, the corresponding Hg(II) complex (**3**) does not present water molecules and its NMR behavior would be similar to that of hippuric acid (^{1}H NMR data of hippuric acid (DMSO-d_6): δ 12.70 [bs, 1H, COOH], 8.94 [t, 1H, H(3), $J = 5.9$ Hz], 7.97 [dd, 2H, H(6), $J = 6.9$ and 1.5 Hz], 7.62 [m, 3H, H(7,8)], 4.01 [d, 2H, H(2), $J = 5.9$ Hz]). The aromatic signals H(6), H(7), and H(8) do not shift significantly, thus showing that the magnetic environment of the aromatic ring has not changed significantly with coordination.

3.2. Hippuric–cytosine ternary derivatives

The infrared data for the ternary derivatives present bands belonging to both hippuric and cytosine modes. The spectra present a great number of medium bands and the frequencies of the two ligands overlap. It is possible to

assign, tentatively, bands clearly belonging to one of the two ligands. Typical cytosine υ(C=N) bands appear at 1531–1537 cm^{-1} (1539 cm^{-1} in free cytosine) [36], υ_r at 1230 cm^{-1} and γ(NH) at 800 cm^{-1} in the three derivatives. Moreover, characteristic hippurate bands appear at 1395 cm^{-1}, which correspond to the symmetric stretching of the carboxylic group, and at 710–720 cm^{-1}. In addition, the υ(M–O) band remains, which is indicative of the metal–hippurato interaction. The ^{1}H NMR data for the ternary complex **4** are practically the sum of those corresponding to both the binary complex **1** and cytosine (^{1}H NMR data for cytosine (DMSO-d_6): δ 10.59 [bs, 1H, NH], 7.44 [d, 1H, H(5), $J = 7.0$ Hz], 7.19 [bs, 2H, NH_2], 5.69 [d, 1H, H(6), $J = 7.0$ Hz]). Moreover, complexes **5** and **6** show a slight downfield shift of the signals for NH (0.16 ppm), NH_2 (0.25 ppm) and H(5) (0.06 ppm) of the cytosine moiety, which is in accordance with coordination via N(3). These very small changes are in agreement with other cytosine complexes (e.g., $[Cd(cyt)_2Cl_2]$, where cytosine NH shifts only 0.26 ppm) [37]. On the other hand, no signal was observed between the hippurate and cytosine moieties in 2D NMR (ROESY), and it is possible to conclude that, presumably during the time of the ROESY experiment, the ternary complex decomposes in solution.

*3.3. X-ray structure of $[Cd(Hip)_2(Cyt)(H_2O)]_2$ (**6**)*

The dimeric structure of $[Cd(Hip)_2(Cyt)(H_2O)]_2$ (**6**) is shown in Fig. 2. Each cadmium (II) atom has a distorted trigonal bipyramid coordination which is linked to a water molecule [Cd–O(22) = 2.372(9) Å], a cytosine [Cd–N(5) = 2.240(8) Å], a carboxylic oxygen atom of a hippurate moiety [Cd–O(10A) = 2.355(10) Å] and two bridging di-coordinated hippurates bound through the carboxylic oxygen atoms [Cd–O(10) = 2.305(8) Å and Cd–O(9a) = 2.355(10) Å]. To these five main bonds, two longer ancillary interactions can be observed: the second oxygen of the monocoordinated hippurate group [Cd–O(9A) = 2.573(10) Å] and the O(8) of the cytosine ligand [Cd–O(8) = ~2.69 Å]. An important distortion in the trigonal bipyramid environment of Cd(II) is indicated by the observed bond angles, which vary from 89.1 to 140.6°. Both distances and angles are shown in Table 2. Intramolecular stacking between the benzene and cytosine rings stabilizes the structure. Ring planes are not strictly parallel, with a tilting angle of approximately 10°; the closest distance between the rings is 3.36 Å and the average distance is 3.6 Å. Two types of hydrogen bonds are present. The first hydrogen bond takes place between the water molecule and the carboxamide group of the bridging hippurate [(C=O···H–OH) = 1.99 Å] and the second between the water molecule and the carboxylic oxygen of the monocoordinated hippurate [(CO–O···H–OH) = 2.12 Å]. Figures included in the supplementary data show these interactions.

To our knowledge, this is the first structure of a Cd(II)–amino acid derivative–cytosine ternary complex published so far.

4. Conclusions

This study of the ternary compound **6** revealed some relevant features.

(i) Cadmium (II) bonds to cytosine through N(3) [N(5) in Fig. 2] with an ancillary longer interaction with O(8), as in the previously described structure of $[Cd(cyt)_3Cl][Cd(cyt)Cl_3]$ [38]. The values for the Cd–N distances of between 2.253 and 2.289 Å for the latter structure are slightly higher than those for **6** [Cd–N(5) = 2.240 Å], however a similar Cd–O(8) interaction is present in both complexes [Cd–O(8) = 2.69 Å for **6** and 2.68 Å for the anion $[Cd(cyt)Cl_3]^-$ [38].
(ii) Cadmium (II) is coordinated to a large number of oxygen donors. Martin et al. have recently reported [39] that the softness of cadmium is not clearly correlated to the equilibrium constants with oxygen donors. In this sense, a far better correlation between acetate equilibrium constants ($\log K = 1.56$) and the electronic affinity of Cd (16.91 eV), which is similar to that of Mn (II), was established. This correlation is in agreement with the bridging hippurates and the coordinated carboxylic hippurate ligand in our structure. The ternary cadmium structure showing oxygen donor coordination offers ample reasons for the high toxicity of cadmium, and not only that which is confined to sulfur or other soft biological donors.
(iii) In this unique structure, three structural features which have been clearly established in metal–amino acid–nucleobase ternary complexes [6] are present. (A) An intramolecular stacking between the two ligands such as that in [Pd(gly-L-tyr)(cytidine)] [15] and other crystallographic and solution model systems such as [Cu(bpy)(L-tyr-gly] [40,41], where the tilting angle between the aromatic rings is 22.3° [41]. (B) A hydrogen bond between a coordinated water and a ligand, such as that in Marzilli's complex [Cu(glygly)(9-methylade)(H_2O)] [13]. And, finally, (C) the cytosine presents a longer ancillary bond, such as that, for example, in the [Cu(glygly)(cytidine)] complex [12]. These three structural features allow isolation of the ternary compound from equilibria of the binary compounds for a non-inert metal ion.

5. Supplementary data

Additional crystallographic data and geometrical details are available from the corresponding author on request.

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