

# An aqua-adenine H-bonding interaction controlling the formation of the rare Zn(II)–N9(adenine) bond in crystal structure of diaqua(adenine)(iminodiacetato)zinc(II)

A.C. Morel<sup>a</sup>, D. Choquesillo-Lazarte<sup>a</sup>, C. Alarcón-Payer<sup>a</sup>, J.M. González-Pérez<sup>a</sup>,  
A. Castiñeiras<sup>b</sup>, J. Niclós-Gutiérrez<sup>a,\*</sup>

<sup>a</sup> Department of Inorganic Chemistry, Faculty of Pharmacy, University of Granada, Campus de Cartuja, s/n, Granada E-18071, Spain

<sup>b</sup> Department of Inorganic Chemistry, Faculty of Pharmacy, University of Santiago de Compostela, E-15706 Santiago de Compostela, Spain

Received 23 May 2003; accepted 30 June 2003

Published online: 23 September 2003

## Abstract

A novel mixed-ligand zinc(II) complex with iminodiacetato(2-) (IDA) and adenine (AdeH) ligands has been obtained. Its crystal consists of octahedral molecules  $[\text{Zn}(\text{IDA})(\text{AdeH})(\text{H}_2\text{O})_2]$  where the selective Zn–N9(AdeH) bond, involving the most basic N(AdeH) donor atom, occupies the *trans* position versus the Zn–N(IDA) bond. The Zn(II)–N9(AdeH) binding mode seems to be rare enough in comparison to those previously reported for Zn(II) and AdeH or a variety of related ligands. The chelate-nucleobase recognition process is further accomplished by an O–H(aqua) ··· N3(adenine) inter-ligand H-bonding interaction, without any intra-molecular IDA–nucleobase interaction. This finding is attributed to the polarizing effect of Zn(II) on the aqua ligand and the possibilities of AdeH acting as N-donor for the metal(II) atom and H-acceptor for an intra-molecular inter-ligand H-bonding interaction. There are no aromatic  $\pi$ ,  $\pi$ -stacking contributions in the 3D H-bonded network, where all polar N–H (IDA or AdeH) and O–H (aqua) bonds are involved as donors in H-bonding interactions, which include AdeH:AdeH and IDA:AdeH pairing by double inter-molecular bridges.

© 2003 Elsevier B.V. All rights reserved.

**Keywords:** Crystal structure; Adenine; Iminodiacetate; Zinc(II); Molecular recognition; H-bonding; Inter-ligand interactions

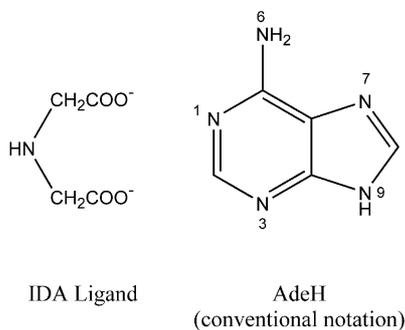
## 1. Introduction

A new look on mixed-ligand metal complexes considers the reaction of a metal chelate and a nucleobase as a source of valuable information of molecular recognition processes, which should be discussed also regarding inter-ligand interactions [1,2]. In this context, non-substituted adenine (AdeH) has proved to be a very versatile ligand. In a recent report we have proved that the AdeH–copper(II) coordination by N7, N3 or  $\mu$ -N3, N7 (as a bridge) to Cu-(N-substituted-iminodiacetato) chelates (N-*R*-IDA =  $R\text{-N}(\text{CH}_2\text{CO}_2^-)_2$ , where *R* is an alkyl, benzyl or phenethyl, respectively) is clearly influ-

enced by the nature of the non coordinating N-*R*-arm in the chelating ligand [1a,1b]. In addition, we have found that the N-benzyl-IDA-Cu(II) chelate is able to discriminate the nucleobase as free AdeH or as the complementary base pair adenine:thymine [1e]. Most of these ternary complexes have one intra-molecular inter-ligand H-bonding interaction reinforcing the appropriate Cu–N(AdeH) coordination bond. These researches require a large and deep work oriented to the development of metal chelates able to display a significant regio-specificity or selectivity for nucleic acids or its constituents, as metal-chelate targets [2]. Curiously, until now, all attempts to solve the structure of a ternary Cu-(non-substituted IDA)–AdeH complex have failed. Now we have succeeded in preparing a ternary complex of Zn(II), IDA and AdeH, which has been studied by thermal stability, FT–IR spectroscopy and X-ray crystallography.

\* Corresponding author. Tel.: +34-958-243-855; fax: +34-958-246-219.

E-mail address: [jniclos@ugr.es](mailto:jniclos@ugr.es) (J. Niclós-Gutiérrez).



Scheme 1.

These structural results are discussed in terms of possibilities of developing inter-ligand interactions in the molecular recognition process between the Zn(IDA) chelate and AdeH (see Scheme 1).

## 2. Results and discussion

The new compound was prepared by reaction of  $\text{Zn}_2\text{CO}_3(\text{OH})_2$ ,  $\text{H}_2\text{IDA}$  and AdeH, in water, using stoichiometric amounts (for 1 mmol of  $\text{H}_2\text{IDA}$  and 70 ml of water). The reaction between the metal salt and  $\text{H}_2\text{IDA}$  was initiated by heating ( $\sim 40^\circ\text{C}$ ), stirring and vacuum (1 h) followed by stirring and heating until obtaining a solution. After cooling, AdeH was added and the mixture was stirred for 4 h. The colourless solution obtained by filtration (without vacuum) was left to evaporate slowly and the collected product was twice re-crystallised from a water–ethanol mixture to obtain high quality crystals for X-ray diffraction purposes.

Crystal data for  $[\text{Zn}(\text{IDA})(\text{AdeH})(\text{H}_2\text{O})_2]$ :  $\text{C}_9\text{H}_{14}\text{N}_6\text{O}_6$  Zn, formula weight 367.63; triclinic system, space group P-1;  $a = 6.367(1)$  Å,  $b = 7.211(1)$  Å,  $c = 14.377(1)$  Å,  $\alpha = 80.17(1)^\circ$ ,  $\beta = 81.65(1)^\circ$ ,  $\gamma = 77.41(1)^\circ$ ,  $Z = 2$ ;  $T = 100(2)$  K, solved and refined by direct methods (on  $F^2$ ) from 2834 reflections for 223 parameters to final  $R1 [I > 2\sigma(I)] = 0.023$ ,  $wR2 = 0.055$  and  $\text{GOF} = 1.063$  agreement factors. Hydrogen atoms were included in geometrically idealized positions employing appropriate riding models with isotropic displacement parameters constrained to 1.2U(eq) of their carrier atoms.

The new compound exhibits a rather typical octahedral zinc(II) coordination, with a *fac*-tridentate IDA conformation, two *cis*-aqua ligands and the most basic N9(AdeH) donor in the *trans*-site to the Zn–N(IDA) bond (Fig. 1 and Table 1). Metal–N9(AdeH) bond formation is largely supported from a structural point of view, as could be found in a CSD search for nearly 30 compounds. That is in agreement of the relative basicity

Table 1  
Hydrogen bonding interaction involving, as donors, all O–H and N–H bonds in the 3D framework of  $[\text{Zn}(\text{IDA})(\text{AdeH})(\text{H}_2\text{O})_2]$

H-bonding interactions	$d(\text{D}\cdots\text{A})$ (Å)	$\angle(\text{D}-\text{H}\cdots\text{A})$ (°)
O(1W)–H(1WA)···O(14a)	2.761(2)	173(3)
N(7)–H(7)···O(19b)	2.841(2)	160(2)
O(2W)–H(2WA)···N(3)	2.756(2)	156(3)
O(2W)–H(2WB)···O(15c)	2.704(2)	164(3)
O(1W)–H(1WB)···O(19d)	2.791(2)	161(2)
N(11)–H(11)···O(15a)	2.996(2)	155(2)
N(6)–H(6B)···O(1We)	3.047(2)	163
N(6)–H(6A)···N(1f)	2.941(2)	172

Symmetry codes:  $a = x + 1, y, z$ ;  $b = -x + 1, -y, -z$ ;  $c = -x, -y, -z + 1$ ;  $d = x, y + 1, z$ ;  $e = -x + 1, -y + 1, -z$ ;  $f = -x, -y + 2, -z$ .

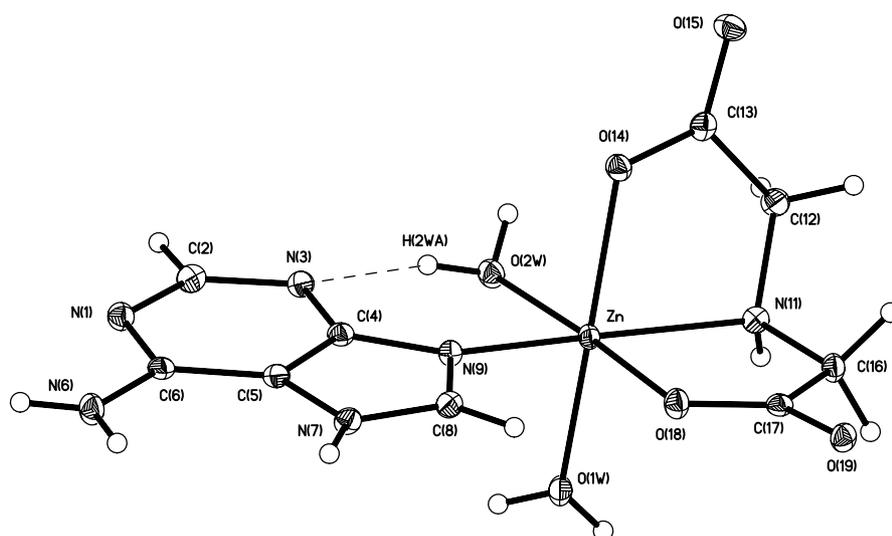


Fig. 1. Molecular structure of  $[\text{Zn}(\text{IDA})(\text{AdeH})(\text{H}_2\text{O})_2]$  showing the intra-molecular inter-ligand O(2W)–H(2WA)···N(3) interaction (dashed line) reinforcing the Zn–N(9)(AdeH) coordination. Ellipsoids are shown at 50% probability level. Bond lengths: Zn–N(9) 2.083(2), Zn–O(18) 2.112(2), Zn–O(14) 2.125(2), Zn–O(1W) 2.138(2), Zn–N(11) 2.167(2) and Zn–O(2W) 2.186(2) Å. Trans-angles: O(18)–Zn–O(2W) 176.9(1), N(9)–Zn–N(11) 164.5(1) and O(14)–Zn–O(1W) 163.4(1)°.

of the N-rich AdeH nucleobase ( $N9 > N1 > N7 > N3 > N6$ -exocyclic) [2].

However, the formation of the Zn–N9 bond seems to be rare enough and unexpected for two main reasons. First, the chelated IDA can only act as H-acceptor for a possible intra-molecular inter-ligand interaction of the type AdeH(donor)···O(carboxylate-IDA acceptor), as indeed was repeatedly observed for various Cu-(IDA-like)-AdeH derivatives (which also frequently have one apical aqua ligand) [1]. These later interactions could be achieved using N7 or N3 donors and, in addition, one N6–H or the N9–H bonds of AdeH to build up one intra-molecular N–H···O(IDA) bridging interaction. Second, in zinc(II) derivatives of non-substituted adeninium(1+) ligand ( $\text{Cl}_3\text{Zn}(\text{N7-AdeH}_2) \cdot \text{AdeH}_2\text{Cl} \cdot \text{H}_2\text{O}$  [3a] or two polymorphs of  $\text{Cl}_3\text{Zn}(\text{N7-AdeH}_2) \cdot \text{H}_2\text{O}$  [3b,3c]) the Zn(II)–(N7–AdeH<sub>2</sub>) bond is formed. Obviously, with 9-methyl-adenine (9MeAde), such as in  $[\text{Cl}_3\text{Zn}(\text{N7-9MeAdeH})] \cdot \text{H}_2\text{O}$  [3d], the polymer  $[\text{Cl}_2\text{Zn}(\mu\text{-N1, N7-9MeAde})]$  [3f], the salt  $(9\text{MeAdeH})[\text{Cl}_3\text{Zn}(\text{N1-9MeAde})] \cdot \text{H}_2\text{O}$  [3f] or closely related derivatives (as  $[\text{Cl}_3\text{Zn}(\text{N7-9RAdeH})] \cdot \text{H}_2\text{O}$ , with R = 2-chloro-6-fluorobenzyl [3b]), the N9-substituted-adenine uses N7 and/or N1 atoms to bind Zn(II). More recently, two interesting mono- or tri-nuclear Zn(II) derivatives with N9-(2-(ethylenediamino)ethyl)adenine were reported with the N9-tethered adenine moiety linked to the Zn(II) atom by N3 or N7 depending on the different metal(II) coordination mode developed for a Zn(II):(Ade-like) mole ratio 1:1 or 3:2, respectively [3g]. The only case of Zn(II)–N9(purine) bond is that of compound  $(7\text{MeAdeH})[\text{Cl}_3\text{Zn}(\text{N9-7MeAde})] \cdot \text{H}_2\text{O}$  [4] where the 7-methyl-adenine has the N7 atom unable for metal binding. In order to rationalize the noticeable formation of the Zn–N9(AdeH) bond in the novel compound, it seems instructive to keep in mind two relevant features.

On the one hand, IDA and AdeH ligands occupy only four of the six coordination sites of the environment of the zinc(II) atom, which completes the octahedron with two aqua ligands. From a bioinorganic point of view, we should expect a remarkable polarization effect of the Zn(II) ion on the O–H bonds of these aqua ligands. That would enhance their possibilities to act as H-donors in hydrogen-bonding interactions. On the other hand, we can hypothesize that the molecular recognition process between a metal(II)-iminodiacetate chelate and the AdeH should be displayed by two different ways. One way consists of the formation of a metal(II)–N(AdeH) bond which is further reinforced by one N–H···O(carboxylate) interaction, as it seems to be preferred in various Cu-(IDA-like)-AdeH ternary compounds (where the apical/distal aqua ligand would not be efficiently metal-polarized) [1]. The other way should also imply the formation of a metal(II)–N(AdeH) bond but in such a way that a D–H···N(AdeH) intra-molecular interaction would contribute to the metal chelate-nucleobase recognition mode (note that for steric reasons, IDA could not play the required intra-molecular role of D–H). This later case would be convincingly represented by the novel Zn-IDA-AdeH derivative, on the assumption that the D–H group is one O–H bond of the polarized O(2)-aqua ligand. It is noteworthy that the Zn–O(2W) bond has the longest coordination distance of the studied compound (see legend of Fig. 1). On the other hand, all polar O–H and N–H bonds of ligands in the reported structure act as donors in H-bonding interactions to build a 3D framework (see Table 1). Among such relevant ligand-ligand interactions, two pairs of symmetry related H-bonds should be remarked, of the type N(7)–H(7)···O(19b) or N(6)–H(6A)···N(1f), which build up IDA:AdeH pairs or AdeH:AdeH pairs, respectively (Fig. 2). The

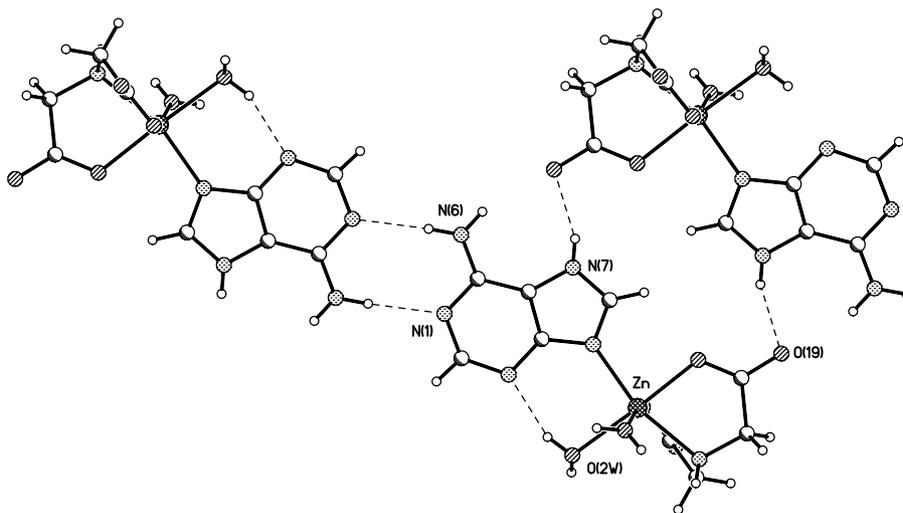


Fig. 2. A plot of some molecules  $[\text{Zn}(\text{IDA})(\text{AdeH})(\text{H}_2\text{O})_2]$  showing, in dashed lines, the intra-molecular aqua-AdeH H-bond and, the symmetry related inter-molecular interactions of the type N(7)–H(7)···O(19b) or N(6)–H(6A)···N(1f) which connect adjacent IDA:AdeH or AdeH:AdeH pairs, respectively. For symmetry codes, see footnote of Table 1.

compound loses coordinated water (175–215 °C) prior to the overlapped pyrolysis of organic ligands, in three additional steps (215–475 °C, producing CO<sub>2</sub>, H<sub>2</sub>O, CO, N<sub>2</sub>O, NO and NO<sub>2</sub>, but not NH<sub>3</sub>) to give ZnO. The FT-IR spectrum (KBr disk) shows the following relevant bands (cm<sup>-1</sup>) for aqua ( $\nu_{\text{as}}$  3449,  $\delta(\text{H}_2\text{O})$  1637), IDA ( $\nu_{\text{as}}(\text{COO})$  1600,  $\nu_{\text{s}}(\text{COO})$  1403,  $\delta(\text{N-H})$  1500) and AdeH ( $\nu_{\text{as}}(\text{NH}_2)$  3280,  $\nu(\text{N-H})$  3168),  $\delta(\text{NH}_2)$  1614,  $\delta(\text{N-H})$  1519,  $\delta(\text{C-H})$  720 and 668). Additional information on the properties of the reported compound or its molecular and crystal structure has been submitted as Supplementary material and it can be obtained from the authors or from the appropriate deposited structural files.

Crystallographic data for the structural analysis of compound [Zn(IDA)(AdeH)(H<sub>2</sub>O)<sub>2</sub>] has been deposited with the CCDC No. 210321 in the Cambridge Crystallographic Data Centre.

### Acknowledgements

Financial support from Research Projects PI021029 (MSC-FIS funds) and BQU2002-04523-C02-01/02 (ERDF+MCYT funds) are gratefully acknowledged. ACM and DChL also thank AEI-MAE for the International Cooperation Programme AL/E 2003 and Ph.D. grants, respectively.

### References

- [1] (a) E. Bugella-Altamirano, D. Choquesillo-Lazarte, J.M. González-Pérez, M.J. Sánchez-Moreno, R. Marín-Sánchez, J.D. Martín-Ramos, B. Covelo, R. Carballo, A. Castiñeiras, J. Niclós-Gutiérrez, *Inorg. Chim. Acta* 339 (2002) 160;  
(b) M.J. Sánchez-Moreno, D. Choquesillo-Lazarte, J.M. González-Pérez, R. Carballo, A. Castiñeiras, J. Niclós-Gutiérrez, *Inorg. Chem. Commun.* 5 (2002) 800;  
(c) Md. Abdus Salam, K. Aoki, *Inorg. Chim. Acta* 311 (2000) 15;  
(d) Md. Abdus Salam, K. Aoki, *Inorg. Chim. Acta* 314 (2001) 71;  
(e) P.X. Rojas-González, A. Castiñeiras, J.M. González-Pérez, D. Choquesillo-Lazarte, J. Niclós-Gutiérrez, *Inorg. Chem.* 41 (2002) 6190, and references therein.
- [2] B. Lippert, *Coord. Chem. Rev.* 487 (2000) 200.
- [3] (a) M.R. Taylor, J.A. Westphalen, *Acta Crystallogr. A* 37 (1981) C63;  
(b) P.T. Muthiah, S.K. Mazumdar, S. Chaudhuri, *J. Inorg. Biochem.* 19 (1983) 237;  
(c) M.R. Taylor, L.M. Wilkins, M.J. McCall, *Acta Crystallogr. B* 45 (1989) 1625;  
(d) J. Maixner, J. Zachova, *Acta Crystallogr. C* 49 (1993) 927;  
(e) M.J. McCall, M.R. Taylor, *Acta Crystallogr. B* 32 (1976) 1687;  
(f) M.J. McCall, M.R. Taylor, *Biochim. Biophys. Acta* 390 (1975) 137;  
(g) M.A. Shipman, C. Price, A.E. Gibson, M.R.J.G. Elsegood, W. Clegg, A. Houlton, *Chem.-Eur. J.* 6 (2000) 4371.
- [4] C.L. Price, M.R. Taylor, *Acta Crystallogr. C* 52 (1996) 2736.