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Three new modes of adenine-copper(II) coordination: interligand interactions controlling the selective N3-, N7- and bridging μ-N3,N7–metal-bonding of adenine to different N-substituted iminodiacetato-copper(II) chelates

E. Bugella-Altamirano [a], D. Choquesillo-Lazarte [a], J.M. González-Pérez [a], M.J. Sánchez-Moreno [a], R. Marín-Sánchez [a], J.D. Martín-Ramos [b], B. Covelo [c], R. Carballo [c], A. Castiñeiras [d], J. Niclós-Gutiérrez [a,*]

[a] Department of Inorganic Chemistry, Faculty of Pharmacy, University of Granada, Campus de Cartuja, s/n, E-18071 Granada, Spain
[b] Department of Mineralogy and Petrology, Faculty of Sciences, University of Granada, E-18071 Granada, Spain
[c] Department of Inorganic Chemistry, Faculty of Sciences, University of Vigo, E-36200 Vigo, Spain
[d] Department of Inorganic Chemistry, Faculty of Pharmacy, University of Santiago de Compostela, E-15706 Santiago de Compostela, Spain

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Dedicated to Professor Helmut Sigel

Abstract

The reaction of $Cu_2CO_3(OH)_2$, various N-substituted-iminodiacetic acids $[R–N(CH_2CO_2H)_2]$ and adenine (AdeH) in water yields crystalline samples of mixed-ligand copper(II) complexes of formulas $[Cu(A)(N7–AdeH)(H_2O)]\cdot H_2O$ (A = *N*-methyl- or *N*-ethyl-iminodiacetato(2−); compounds **1** and **2**, respectively), $[Cu(B)(N3–AdeH)(H_2O)]\cdot H_2O$ (B = *N*-benzyl- or *N*-(*p*-methylbenzyl)-iminodiacetato(2−); compounds **3** and **4**, respectively) as well as $[Cu_4(pheida)_4(\mu\text{-}N3,N7–AdeH)_2(H_2O)_4]\cdot 2H_2O$ (pheida = *N*-phenethyl-iminodiacetato(2−)). Crystal structures of the acid H_2pheida and compounds **1**–**5** are reported. H_2pheida acid exhibits a typical zwitterionic structure. Copper(II) compounds were also studied by TG analysis (with FT-IR study of the evolved gasses), IR, electronic and ESR spectra and magnetic susceptibility data. The *N*-alkyl- or *N*-benzyl-like-iminodiacetato(2−) ligands (A or B) give complexes with Cu(II)/(A or B)/AdeH equimolar ratio, whereas pheida yields an unexpected tetranuclear compound with a 2:2:1 Cu(II)/pheida/AdeH molar ratio. In **1** and **2** AdeH binds to the metal by N7, whereas in **3** and **4** the N3 atom is used. An unexpected bridging μ-N3,N7–AdeH–dicopper(II) binding mode is found in the tetra-nuclear compound **5** (without interligand π,π-stacking interactions). These AdeH–Cu(II) binding modes have not been referred in the literature before. The difference in AdeH–Cu(II) binding modes in compounds **1** or **2** and **3** or **4** is rationalised on the basis of the absence or presence of a flexible *N*-benzyl-like substituent in the iminodiacetato(2−) ligand skeleton, which prevents or permits the interligand π,π-stacking interactions.

Keywords: Crystal structures; Adenine; N-substituted iminodiacetate; Copper(II); π,π-Stacking; Molecular recognition

1. Introduction

The interaction of nucleic acids or their constituents with metal ions has been a matter of extensive studies for the past decades because of their chemical and biological interest. A critical and actualised review accounts for the multiplicity of the metal ion binding patterns to nucleobases, mainly concerning the metal coordination chemistry of nucleic acid and their constituents, has recently appeared [1]. Indeed there is important research in this field about structural, thermodynamics, kinetic and biological aspects, and appro-

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

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

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priate reviews are made from time to time [2]. In this broad context certain recent studies are devoted to find metal complexes that can specifically recognise one among various nucleobases. We are interested in the structure of mixed-ligand copper(II) complexes with iminodiacetato(2−) (IDA) or a closely related compound and N-heterocyclic bases. In this sense, we have considered the use of adenine (AdeH) as an auxiliary ligand because this N-rich nucleobase has proved to be a rather versatile metal-binding biomolecule [1]. Surprisingly, only a few copper(II) structures with this non-substituted nucleobase have been reported, including anionic adeninato (Ade^-) [2–5], neutral AdeH [6–8] or cationic adeninium(1+) ($AdeH_2^+$) [9–11]. These are mono-nuclear [2,4,5,8,10,11], binuclear [3,6,7] or tri-nuclear [9] complexes, which present copper(II) atom in different coordination polyhedrons (type 4, 4+1 or 4+2). In these compounds the nucleobase species (Ade^-, AdeH or $AdeH_2^+$) links the copper(II) atom by the N(9) donor (as mono-dentate) [2,4,5,8,10,11] or in a bridging mode μ-N(3),N(9) (poly-nuclear) [3,6,7,9]. Such coordination modes in non-substituted AdeH species can be understood on the basis that the N(9) donor atom is the most basic among their five nitrogen atoms [10], followed by N(1), N(7) and N(3) [1]. In one case [2], it has been argued that an interligand intra-molecular hydrogen bond associated with the steric factors around the metal participates in the base-selectivity. However, some questions seem to remain unclear. For example, the reaction of $[Cu(H_2EDTA)(H_2O)]$ with AdeH affords the salt $(AdeH_2)[Cu(HEDTA)(H_2O)]\cdot 2H_2O$ [12] but not a ternary complex (H_4EDTA = ethylenediaminetetraacetic acid). The structure of this salt [12] proves that the $AdeH_2^+$ ion recognises the counter-anion complex out-spherically (by means of two inter-ionic hydrogen bonds) and the resulting ion pair recognises itself by π,π-stacking interaction between both $AdeH_2^+$ cations to form di-copper(II) aggregates. Such di-copper(II) entities act as building blocks of the crystal (with the corresponding water molecules). In this case, it has been suggested that the overcrowding of donors from the penta-dentate chelating $HEDTA^{3-}$ ligand precludes the substitution of water by $AdeH_2^+$ ion around the copper(II) atom [12]. On the other hand, single metal–N3 or –N7(AdeH) coordinations are very unusual. The single N3(AdeH) metal coordination only seems supported by the structures of [Ni(AdeH)(tren)Cl]Cl [13] and $[Pd(thiacyclophane)(AdeH)]BF_4$ [14]. The mono-nuclear metal–N7 coordination for N9-non-substituted AdeH is known in $AdeH_2^+$ derivatives of Ni(II) [15] and Zn(II) [16]. In this context and as a part of our present research project, we are interested in the structure and properties of mixed-ligand Cu(II) complexes having a *N*-carboxymethyl-glycinato(2−) or IDA ligand or a IDA-like derivative as a chelating agent and a variety of N-heterocycles (including AdeH) as an auxiliary ligand [17]. Some of these essays were proposed to students of *Inorganic Aspects of Biological Processes* [12,18]. As Sigel [19] pointed out some years ago, the best way to prove the formation of a mixed-ligand complex is to carry out its crystal structure determination, which, besides, is an excellent source of chemical information. Attempts to obtain crystals of a ternary AdeH–IDA–Cu(II) complex suitable for X-ray diffraction studies have not been successful yet, but this paper reports the synthesis, structure and properties of five new ternary copper(II) complexes with AdeH and N-substituted-IDA derivatives. IDA-like ligands were chosen concerning whether the N-substituent could or could not be involved in aromatic π,π-stacking interactions, so important for molecular recognition phenomena in biological systems [20].

2. Experimental

2.1. Ligands and other reagents

Samples of *N*-methyl- and *N*-ethyl-iminodiacetic acid (H_2MIDA and H_2EIDA, respectively) were supplied by Mederos and co-workers for previous work [21]. *N*-Benzyl-, *N*-(*p*-methylbenzyl)- and *N*-phenethyl-iminodiacetic acids (H_2BzIDA, $H_2MEBIDA$ and $H_2pheida$, respectively) were prepared in our laboratories by reaction of potassium chloroacetate with the appropriate amine (benzylamine, 4-methylbenzylamine or phenethylamine, respectively, purchased from Aldrich) in alkaline aq. solution (pH ~10–11) at 70–90 °C, during approximately 2 h. Then the reaction mixture was cooled to room temperature (r.t.) and acidified with HCl 6 N (pH ~3.0–2.5) until the desired white acid precipitated. New additions of HCl 6 N gave successive fractions of these ligands in their acid forms, which were collected by filtration, washed with water and re-crystallised in water by reaction with $NaHCO_3$ (until complete solution) followed by addition of the equivalent amount of HCl 6 N. Re-crystallised *N*-(aryl-alkyl)-iminodiacetic acids were washed with water and C_3H_6O or EtOH, and air dried. H_2MIDA and H_2BzIDA are also commercially available. Crystals of $H_2pheida$ were grown by re-crystallisation in a 30:70 water/ethanol mixture. This and other similar procedures failed to grow suitable crystals of H_2BzIDA and $H_2MEBIDA$, which produced extremely long filaments. For H_2BzIDA, starting from 1 mol of benzylamine, the yield was 195.5 g, 87.6%. *Anal*. Calc. for $C_{11}H_{13}NO_4$: C, 59.19; H, 5.87; N, 6.27. Found: C, 59.07; H, 5.89; N, 6.22%. FT-IR relevant frequencies (cm^{-1}): 3064, 3024, 2999 and 2974 for ν(C–H) modes; peaks at 2700–2300, including one at 2522 of $\nu(N^+–H)$; ~3420 m (broad), 1729 or 1719, ~1250 and 704 for ν(O–H), ν(C=O), δ(O–H) and π(O–H) of –COOH; 1619 and 1385 for ν_{as} and ν_s of $–COO^-$. For H_2ME-

BIDA, starting from 0.5 mol of 4-methylbenzylamine, the yield was 82.8 g, 69.8%. *Anal*. Calc. for $C_{12}H_{15}NO_4$: C, 60.75; H, 6.37; N, 5.90. Found: C, 60.32; H, 6.64; N, 6.01%. FT-IR relevant frequencies (cm^{-1}): 3018, 2966 and 2917 for ν(C–H) modes; peaks at 2700–2300, including one at 2572 of $\nu(N^+–H)$; ~3450 m (broad), 1719, 1250 and 704 for ν(O–H), ν(C=O), δ(O–H) and π(O–H) for –COOH; 1619 and 1385 for ν_{as} and ν_s of –COO^-. ^1H NMR (300 MHz, D_2O+NaOD; δ, ppm): 2.17 (s, 3H) from CH_3–, 2.97 (s, 4H) from –CH_2–COO moieties, 3.55 (s, 2H) from ϕ-CH_2–N, and 7.08 (d, 2H, $J = 8.1$ H-2,6 arom.), 7.12 (d, 2H, $J = 8.1$ H-3,5 arom.). ^{13}C NMR (75 MHz, D_2O+NaOD; δ, ppm): 19.68 from CH_3–, 56.45 from –CH_2–N, 57.05 from CH_2–(COO), 128.43 from C-2,6 arom., 129.69 from C-3,5 arom., 133.37 from C-1 arom., 137.00 from C-4, 178.92 from –COO. For H_2pheida, starting from 0.5 mol (123.44 g) of phenethylamine, the yield was 199.9 g, 80.2%. *Anal*. Calc. for $C_{12}H_{15}NO_4$: C, 62.64; H, 6.07; N, 5.62. Found: C, 60.19; H, 6.00; N, 6.90%. FT-IR relevant frequencies (cm^{-1}): 3030, 2993 and 2969 for ν(C–H) modes; peaks at 2700–2300, including one at 2521 for $\nu(N^+–H)$; ~3500 m (broad), 1713, 1195 and 726 for ν(O–H), ν(C=O), δ(O–H) and π(O–H) of –COOH; 1607 and 1383 for ν_{as} and ν_s of –COO^-. ^1H NMR (300 MHz, d_6-DMSO; δ, ppm): 2.69 (m, 2H) and 2.85 (m, 2H) from –CH_2–CH_2– moiety, 3.45 (s, 4H) from N–CH_2–COO^-, and 7.22 (m, 5H) from C_6H_5-ring. ^{13}C NMR (75 MHz, d_6-DMSO; δ, ppm): 33.66, 54.46, 55.66, from CH_2 groups, 125.78, 128.13, 128.50 and 139.83, from the aromatic C–H groups, and 172.37 from the COO– carboxyl groups). All other chemicals are commercially available products of reagent grade and were purchased from Aldrich, and used without further purification.

2.2. Synthesis of copper(II) complexes

A general procedure to obtain the studied mixed-ligand copper(II) complexes can be described as follows: $Cu_2CO_3(OH)_2$ (221 mg, 0.5 mmol, Aldrich) and the appropriate N-substituted iminodiacetic acid (H_2L, 1 mmol, Aldrich) reacted in water (150 ml) in a Kitasato flask, by heating (15 min, $t < 50$ °C) and stirring under reduced pressure (to remove the CO_2, by-product). The resulting slurry or solution was left to cool and AdeH (135.1 mg, 1 mmol) was added. The reacting mixture was stirred half an hour and then filtered without vacuum (to remove a variable amount of the desired product, as could be confirmed by elemental analysis and IR spectroscopy, and a very small amount of CuO) directly on a crystallisation device. By evaporation of clear blue solutions, abundance of crystals was obtained, and they were removed by filtration without vacuum on another crystallisation device. The products were washed with cool water and air-dried. Yields were variable, depending on the amount of initial precipitation of the products, but usually over 50%. When the reaction between $CuCO_3(OH)_2$ and H_2L did not precipitate, before adding the required amount of AdeH, the solution should be slowly filtered (without vacuum) on a Erlenmeyer and left to cool, and after that stirred until the base was dissolved completely. The resulting blue solution would be filtered without vacuum on crystallisation device. This procedure rose considerably the yield up to 85–90%. The use of largest amounts of solvent could avoid such precipitation, but would increase the time required for crystallisation and, therefore, the risk of microbiological contamination. The formation of filamentous colonies was frequent. When it happened, we proceeded to add ethanol, cover the crystallisation device with a plastic film and filtrate the preparation after several days. However, this undesired contamination phenomenon did not impede the formation of many and good crystals, of which we have photographic evidences available upon request. The re-crystallisation of the products in water usually required heat and it did not always give good results. However, a re-crystallisation experience with the Cu(II)–pheida–AdeH derivative afforded little amount of crystal which have enabled the structural results referred below. This compound was surprisingly a molar ratio Cu/pheida/AdeH 2/2/1. Indeed the general procedure represents the use of 100% of AdeH in excess. The compound was also obtained when a stoichiometric ratio of reactants (Cu/pheida/AdeH 2/2/1) was employed in the synthesis. The use of large volume of solvent to preclude some initial precipitation yields crystalline samples, but not single-crystals of this compound. *Anal*. Calc. for [Cu(MIDA)-(AdeH)(H_2O)]·H_2O ($C_{10}H_{16}CuN_6O_6$, compound **1**): C, 31.62; H, 4.25; N, 22.13. Found: C, 31.70; H, 4.51; N, 22.47%. *Anal*. Calc. for [Cu(EIDA)(AdeH)(H_2O)]·H_2O ($C_{11}H_{18}CuN_6O_6$, compound **2**): C, 33.55; H, 4.61; N, 21.34. Found: C, 33.50; H, 4.95; N, 21.67%. *Anal*. Calc. for [Cu(NBzIDA)(AdeH)(H_2O)]·H_2O ($C_{16}H_{20}CuN_6O_6$, compound **3**): C, 42.15; H, 4.42; N, 18.34. Found: C, 42.06; H, 4.63; N, 18.60%. *Anal*. Calc. for [Cu(MEBIDA)(AdeH)(H_2O)]·H_2O ($C_{17}H_{22}CuN_6O_6$, compound **4**): C, 43.44; H, 4.72; N, 17.88. Found: C, 43.19; H, 4.72; N, 17.68%. *Anal*. Calc. for [Cu_4(pheida)$_4$(AdeH)$_2$-(H_2O)$_4$]·2H_2O ($C_{58}H_{70}Cu_4N_{14}O_{22}$, compound **5**): C, 44.27; H, 4.74; N, 12.46. Found: C, 43.93; H, 5.18; N, 12.63%.

2.3. Crystal structure determination

A prismatic crystal of each studied compound was mounted on a glass fibre and used for data collection. Only twinned crystals were available for compounds **4** and **5**. Crystal data were collected at 237 (H_2pheida) or 291(2) K (Cu derivatives) using a Bruker SMART CCD 1000 diffractometer. Graphite monochromated Mo Kα radiation ($\lambda = 0.71073$ Å) was used throughout. The

Table 1
Crystal data and structure refinement for copper(II) compounds **1**–**5**

Cu(II) compound	**1**	**2**	**3**	**4**	**5**
Empirical formula	$C_{10}H_{16}CuN_6O_6$	$C_{11}H_{18}CuN_6O_6$	$C_{16}H_{20}CuN_6O_6$	$C_{17}H_{22}CuN_6O_6$	$C_{58}H_{70}Cu_4N_{14}O_{22}$
Formula weight	379.83	393.85	455.92	469.95	1569.44
Temperature (K)	293(2)	293(2)	293(2)	293(2)	293(2)
Wavelength (Å)	0.71073	0.71073	0.71073	0.71073	0.71073
Crystal system	monoclinic	monoclinic	orthorhombic	orthorhombic	triclinic
Space group	$P2_1/n$	$P2_1/c$	$Pbca$	$Pca2_1$	$P\bar{1}$
Unit cell dimensions					
a (Å)	7.546(1)	14.371(1)	8.376(1)	8.361(3)	10.534(3)
b (Å)	24.618(3)	7.861(1)	13.411(2)	17.824(7)	10.534(3)
c (Å)	7.931(1)	13.301(1)	34.106(5)	13.214(5)	31.036(9)
α (°)	90	90	90	90	90.819(6)
β (°)	101.369(3)	90.352(2)	90	90	90.819(6)
γ (°)	90	90	90	90	108.429(4)
V (Å^3)	1444.4(3)	1502.6(3)	3831.0(9)	1969.2(2)	3266.3(2)
Z	4	4	8	4	2
D_{calc} (Mg m^{-3})	1.747	1.741	1.581	1.585	1.596
Absorption coefficient (mm^{-1})	1.556	1.499	1.188	1.158	1.373
F(000)	780	812	1880	972	1616
Crystal size (mm)	0.2 × 0.07 × 0.05	0.17 × 0.14 × 0.07	0.22 × 0.21 × 0.02	0.32 × 0.21 × 0.15	0.39 × 0.22 × 0.06
θ Range data collection (°)	1.65–28.04	1.42–28.08	2.39–28.08	2.24–28.07	0.66–27.45
Index ranges	$-9 \leq h \leq 8$, $-32 \leq k \leq 32$, $-10 \leq l \leq 9$	$-15 \leq h \leq 18$, $-9 \leq k \leq 10$, $-13 \leq l \leq 17$	$-11 \leq h \leq 8$, $-17 \leq k \leq 17$, $-45 \leq l \leq 34$	$-10 \leq h \leq 10$, $-23 \leq k \leq 23$, $-13 \leq l \leq 17$	$-13 \leq h \leq 13$, $-13 \leq k \leq 13$, $0 \leq l \leq 40$
Reflections collected/unique	8183/3231 [$R_{int} = 0.0757$]	8848/3454 [$R_{int} = 0.0680$]	19 891/4573 [$R_{int} = 0.0944$]	9822/3832 [$R_{int} = 0.1896$]	14 910/14 910 [$R_{int} = 0.0000$]
Completeness to θ	28.02°/92.6%	28.02°/94.6%	28.02°/98.2%	28.02°/96.8%	27.45°/100%
Absorption correction	SADABS	SADABS	SADABS	empirical	SADABS
Max./min. transmission	1.000/0.785	1.000/0.826	1.000/0.826	0.8454/0.7082	0.9222/0.6166
Refinement method	FMLS [a] on F^2	FMLS [a] on F^2	FMLS [a] on F^2	FMLS [a] on F^2	FMLS [a] on F^2
Data/restraints/parameters	3231/0/272	3454/0/224	4573/0/277	3832/7/277	14 910/0/835
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.047$, $wR_2 = 0.064$	$R_1 = 0.046$, $wR_2 = 0.107$	$R_1 = 0.051$, $wR_2 = 0.060$	$R_1 = 0.0817$, $wR_2 = 0.1701$	$R_1 = 0.082$, $wR_2 = 0.198$
R indices (all data)	$R_1 = 0.130$, $wR_2 = 0.078$	$R_1 = 0.100$, $wR_2 = 0.120$	$R_1 = 0.170$, $wR_2 = 0.079$	$R_1 = 0.2452$, $wR_2 = 0.2428$	$R_1 = 0.084$, $wR_2 = 0.200$
Goodness-of-fit on F^2	0.813	0.903	0.887	0.757	1.003
Largest difference peak and hole (e Å^{-3})	0.613/−0.411	0.397/−0.324	0.362/−0.310	0.570/−0.756	4.419/−1.682
Type of crystal	single crystal	single crystal	single crystal	twinned crystals	twinned crystals

[a] FMLS, full-matrix least-square.

data were processed with SAINT [22] and corrected for absorption using SADABS [23]. The structures were solved by direct methods using the program SHELXS-97 [24] and refined by full-matrix least-square techniques (FMLS below and in Table 1) on F^2 using SHELXL-97 [25]. Positional and anisotropic atomic displacement parameters were refined for all non-hydrogen atoms. Because of the twinned crystal used, some atoms of the compound **4** did not present defined maximal on the anisotropic refinement and were refined isotropically. For compound **1**, hydrogen atoms were located from difference Fourier maps and refined isotropically. For compounds **2**–**5**, hydrogen atoms were placed geometrically and positional parameters were refined using a riding model. Water hydrogen atoms in compound **3** were unambiguously located from difference Fourier maps. Isotropic displacement parameters for hydrogen atoms were constrained to be 1.2 (1.5 for methyl groups). Atomic scattering factors were obtained from the 'International Tables for X-ray Crystallography' [26]. Molecular graphics have been obtained from SHELXTL [27]. Crystal data for H$_2$pheida ($C_{12}H_{15}NO_4$, FW 237.25, T 293(2) K): orthorhombic system, space group $Pca2_1$, $a = 8.425(1)$, $b = 13.307(1)$, $c = 9.851(1)$ Å, $\alpha = \beta = \gamma = 90°$, $V = 1104.3(1)$ Å^3, $Z = 4$, $D = 1.427$ Mg m^{-3}, $\mu = 0.108$ mm^{-1}, $F(000) = 504$, crystal size 0.26 × 0.28 × 0.91 mm, θ from 2.86 to 28.00°, $-11 \leq h \leq 7$, $-17 \leq k \leq 17$, $-12 \leq l \leq 12$, collected/independent reflections 6614/2503, completeness to $2\theta = 98.7\%$, data/restraints/parameters 2503/1/159, Goodness-of-fit (on F^2) = 0.993, final $R_1 = 0.043$, $wR_2 = 0.103$ [$I > 2\sigma(I)$], $R_1 = 0.048$ and $wR_2 = 0.106$ (all data), largest difference peak and hole 0.184 and −0.213 e A^{-3}. A summary of the crystal data, experimental details and refinement results for copper(II) complexes **1**–**5** are listed in Table 1.

2.4. Physical measurements

Elemental analyses were performed on a Fisons–Carlo Erba EA 1108 micro-analyser. NMR spectra were recorded in Bruker AMX300 or ARX400 spectrometers. IR spectra were obtained by the KBr disc technique on a Nicolet FT-IR 20SXB or Jasco FT-IR 410 instrument. TG analysis (pyrolysis) of the studied compounds (295–875 K) in air flow (100 ml min^{-1}) and corresponding IR spectra of evolved gasses were recorded using a Shimazu Thermobalance TGA-DTG-50H coupled with an IR-FT Nicolet Magna 550. Electronic (reflectance) spectra (175–3300 nm) were obtained in a Varian Cary-5E spectrophotometer. ESR spectra of polycrystalline samples were recorded without magnetic dilution in a spectrophotometer Bruker ESP 300E (X band) at r.t. Magnetic susceptibilities were measured in the temperature range 80–300 K (excepting those of compound **4**, measured at r.t.) with a Manics DM magnetometer. The susceptometer was calibrated with mercury tetrakis(thiocyanato)cobaltato(II). Corrections for the diamagnetism were estimated from Pascal's constants [28a]. Experimental susceptibilities were also corrected for the metal temperature-independent paramagnetism (60×10^{-6} cm^3 mol^{-1}) [28b].

3. Results and discussion

3.1. Structure of H_2pheida acid

Tables about this amino-diacid may be obtained from the corresponding deposited files. Its structure is shown in Fig. 1, which also gives the numbering schema adopted for the atoms. H_2pheida acid exists as zwitterions stabilised by an intra-molecular hydrogen bond (N(1)–H(1)···O(1), 2.615(2) Å, 108(2)°). These dipolar ions link to each other (translation) by an intermolecular hydrogen bond (O(4)–H(4)···O(1)^{ii}; 2.486(2), 157°; symmetry code ii = $x+1$, y, z) forming chains along a-axis (Fig. 1(a)). Two anti-parallel chains form a double chain by a multi-π,π-stacking interaction. The structural parameters for this π,π-stacking (as depicted in the diagram 1) were obtained with the program PLATON [29]. Significant results are: centroid–centroid distance for stacked rings d(C_I–C_J) = 4.29 Å; dihedral angles between the planes I and J of the stacked rings, $\alpha = 2.1°$; d($\perp C_I$–C_J) = 3.39 Å; $\beta = 37.1°$; d($\perp C_J$–C_I) = 3.42 Å; $\gamma = 37.8°$. These data represent an appropriate stacking distance of 3.40(2) Å. A remarkable parallelism between stacked rings ($\alpha \sim 2°$) but a large slipping between rings (β and $\gamma \sim 37.5°$), suggest that there is a significant σ,π-contribution to the π,π-stacking [20]. In each double chain, the multiplicity of such interaction is obtained connecting each phenethyl aromatic ring with other two from the anti-parallel strand. In addition, these double chains supply up and down, and to each other sides, N(1)–H(1) 'onium' groups which form N(1)–H(1)···O(2)^{i} hydrogen bonds (2.833(2) Å, 150(2)°, symmetry code i = $-x+3/2$, y, $z+1/2$). Such links generate a 2D framework with IDA moieties towards the external surfaces and multi-stacked aromatic phenethyl rings inside it. 2D frameworks are laid out in the crystal parallel to plane ac and connected by van der Waals contacts (Fig. 1(b)).

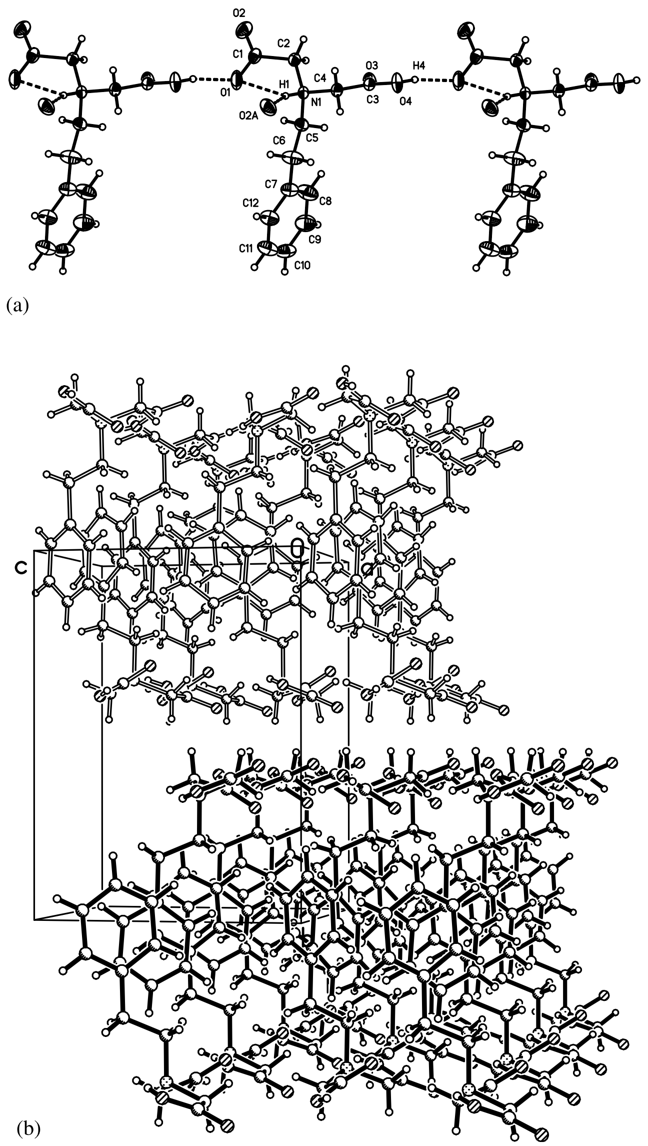

Fig. 1. (a) Three hydrogen bonded H_2pheida$^{\pm}$ zwitterions in a chain along a-axis. (b) Fragments of two 2D framework in the crystal of H_2pheida acid extending parallel to plane ac.

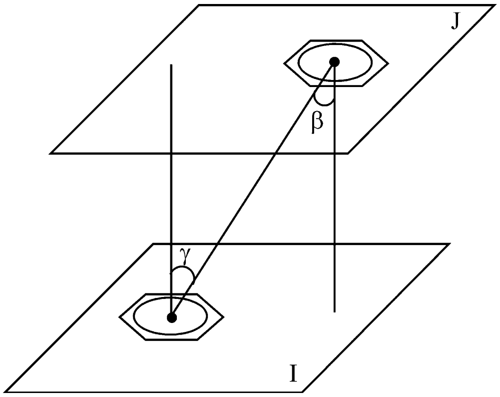

Diagram 1.

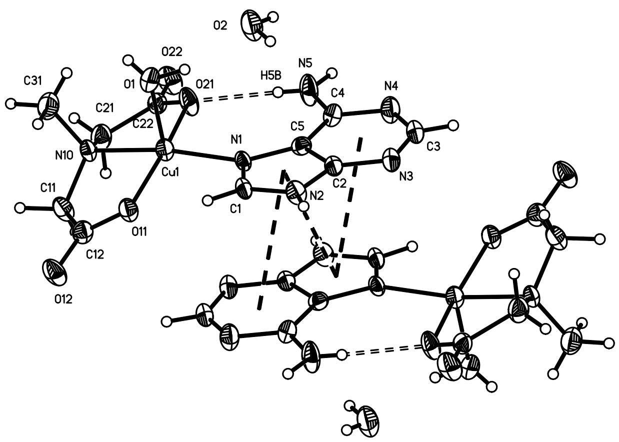

Fig. 2. Pair of asymmetric units of [Cu(MIDA)(AdeH)(H_2O)]·H_2O (**1**) showing the *intra*-molecular interligand hydrogen bond in both molecules (open dashed lines) and the *inter*-molecular π,π-stacking interaction between five- and six-membered rings of AdeH ligands (black dashed lines).

3.2. Copper(II) coordination in mixed-ligand complexes

Table 2 shows data of metal–ligand bond distances in the studied compounds **1**–**5**. The numbering schema adopted in each compound is shown in appropriate figures. Data for Cu(1) and Cu(2) atoms in compound **5** are averaged values from appropriate pairs of very similar metal atoms. Non-centro-symmetry of the tetra-nuclear complex unit is due to the space group used for the solution of the structure (because only few twinned crystals were obtained). Additional information about bond distances and angles for these copper(II) compounds could be obtained from appropriate files of Section 5 or directly from the authors upon request. Mono-nuclear compounds **1**–**4** exhibit a roughly elongated square-base pyramidal coordination type 4+1 (see Figs. 2–5). One N and two O donors from tri-dentate IDA derivative and the N7 or N3 donor atom from AdeH (in compounds **1** and **2** or in **3** and **4**, respectively) define the basal coordination plane. An aqua ligand supplies the apical O donor atom at approximately 2.30–2.35(2) Å. The tetra-nuclear compound **5** exhibits two different Cu(II) coordination polyhedrons. Two atoms (Cu1 and Cu1A in Fig. 6) have the same type 4+1 of coordination above referred for mononuclear complexes **1**–**4**, with O(11) and O(10A) water atoms as apical donors (Fig. 6) and the N7 donor from AdeH in *trans* to the Cu–N bond of the Cu–pheida chelate, at the basal coordination plane. The other two metal atoms (Cu2 and Cu2A) also have roughly 4+1 coordination. This is built up by one N and two O donors from tri-dentate pheida and one N3 donor from AdeH, plus one apical O donor from a bridging carboxylate group of pheida (O12 or O12A in Fig. 6). However, these Cu atoms interact very weakly with an O from water (referred as O20 and O20A in Fig. 6) at approximately 3 Å. The coordination around these Cu(II) atoms could be referred as a very unsymmetrical elongated octahedron, of type 4+1+1* (the asterisk emphasises the very weak Cu–O interaction). These copper(II) coordination polyhedrons are very common in mixed-ligand complexes which have an equimolar ratio Cu(II)/IDA or IDA-like/N-heterocyclic (imidazole (Him) or Him derivative) [17]. In these complexes, the Him or Him-like binds the copper(II) in *trans* to the Cu–N(IDA or IDA-like) bond, and the chelating IDA or derivative adopts *mer*-configuration, as rules in the structures reported here. The Cu(II) binding to one mono-functional AdeH in compounds **1**–**4** or a half of bridging-bidentate μ-AdeH in **5**, makes AdeH display a

Table 2
Coordination bond distances in compounds **1**–**5** and parameters of the polyhedron distortion

	1	**2**	**3**	**4**	**5**(Cu1)	**5**(Cu2)
Cu–N(amine)	2.030(3)	2.013(3)	2.012(3)	1.98(2)	1.876(4)	1.884(5)
Cu–O(carboxyl)	1.930(3)	1.935(3)	1.937(2)	1.96(1)	1.948(4)	2.045(5)
Cu–O(carboxyl)	1.945(3)	1.962(3)	1.943(2)	1.99(1)	2.002(4)	1.991(5)
Cu–N(AdeH)	2.017(3)	1.977(3)	1.981(3)	1.88(1)	2.022(4)	2.037(5)
Cu–O(water)	2.299(4)	2.351(3)	2.303(3)	2.27(1)	2.277(4)	2.380(5)
τ (%)	11.93	5.93	17.35	14.67	3.27	0.49 [a]
T	0.86	0.84	0.86	0.86	0.86	0.73

[a] τ is obtained assuming an ‘effective’ coordination type 4+1, because of the weakness of the ‘additional’ Cu–Ow interaction at 3.02(1) Å (averaged).

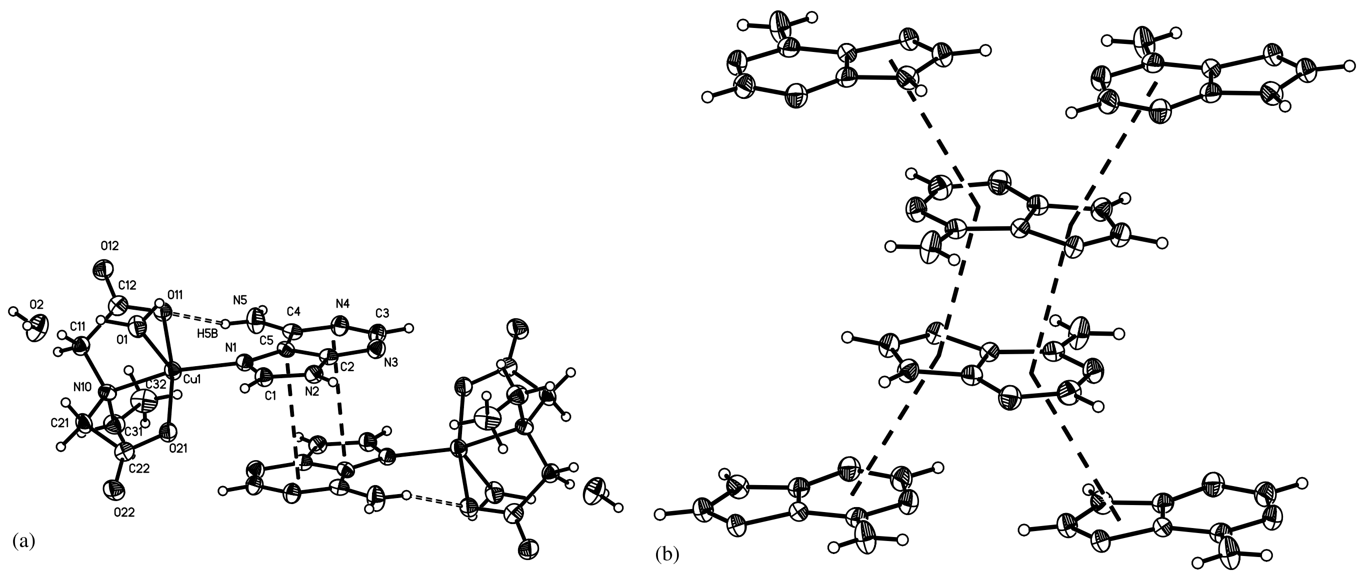

Fig. 3. (a) Pair of molecules [Cu(EIDA)(AdeH)(H_2O)]·H_2O (**2**) showing the *intra*-molecular interligand hydrogen bond (open dashed lines) and the *inter*-molecular π,π-stacking interactions between five- and six-membered rings of AdeH ligands (black dashed lines). (b) π,π-Stacking interactions (black dashed lines) between anti-parallel AdeH ligands of a pair of complex units and other stacking connecting them with AdeH ligands from four adjacent pairs in the crystal of compound **2** (metal, EIDA and water molecules have been omitted for clarity).

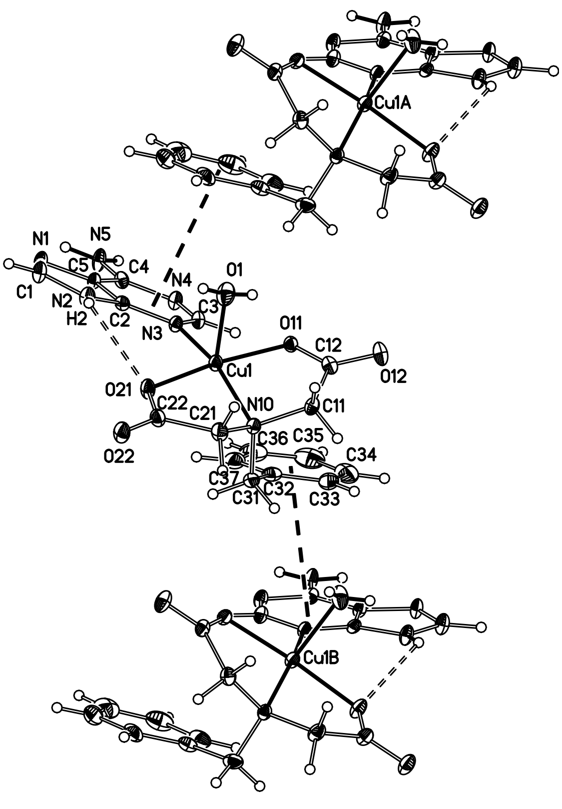

Fig. 4. Three complex units of [Cu(NBzIDA)(AdeH)(H_2O)]·H_2O (**3**) in a stacked 'chain' showing the *intra*-molecular interligand hydrogen bond (open dashed lines) and the *inter*-molecular π,π-stacking interaction (black dashed lines) between six-membered aromatic rings from NBzIDA and AdeH ligands (non-coordinated water omitted for clarity).

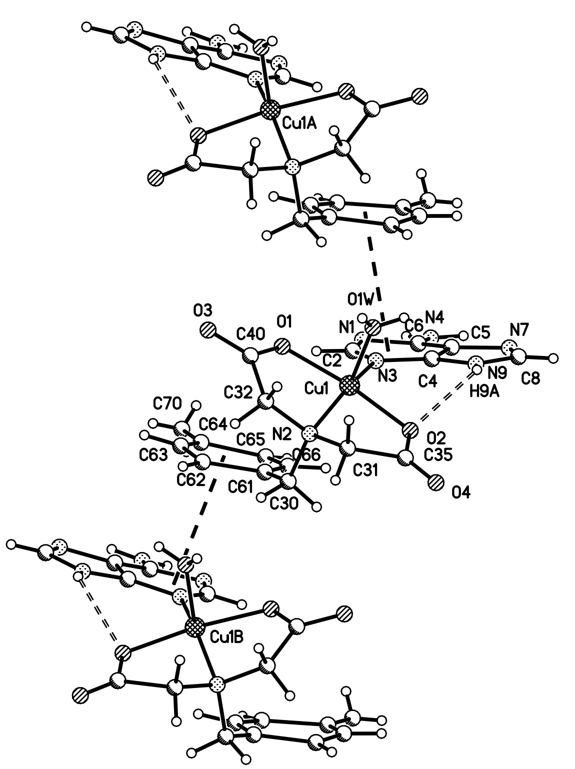

Fig. 5. Three complex units of [Cu(MEBIDA)(AdeH)(H_2O)]·H_2O (**4**) in a multi-stacked chain, showing the *intra*-molecular interligand hydrogen bond (open dashed lines) and the *inter*-molecular π,π-stacking interaction (black dashed lines) between six-membered aromatic ring of MEBIDA and AdeH ligands (non-coordinated water omitted).

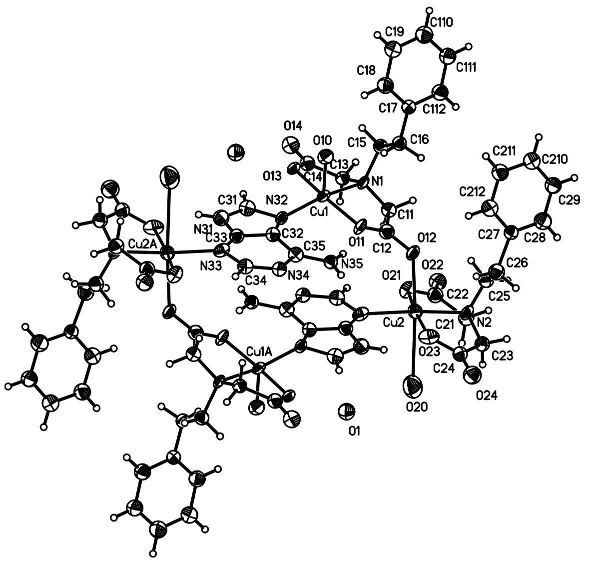

Fig. 6. Asymmetric unit of $[Cu_4(pheida)_4(AdeH)_2(H_2O)_4]\cdot 2H_2O$ (**5**) where the μ-N3,N7-bridging role of AdeH ligands can be observed.

similar role that Him or Him-like in such mixed-ligand complexes. All these cases are in contrast with the *fac*-configuration of IDA or IDA-like in $[Cu(IDA)(H_2O)_2]_n$ [17] or in mixed-ligand complexes with a 1/1/2 Cu/IDA/(N-heterocyclic donor) molar ratio (as in $[Cu(IDA)(2,2'\text{-bipy})]\cdot 6H_2O$ and closely related compounds (see appropriate references in [17]) as well as a 1/1/(1+1) Cu/IDA-like/(N-heterocyclic+N-aliphatic) donors ratio (for example, $[Cu(NBzIDA)(histamine)]\cdot 2H_2O$ [30] and related cases [31]).

3.3. Interligand interactions in N-alkyl-, N-benzyl-like or N-phenethyl–IDA–copper(II) chelates with AdeH as secondary ligand and molecular recognition significance

In the compounds studied, the most remarkable feature is that AdeH binds the copper(II) by N7, N3 or μ-N3,N7 when the chelating ligand is a *N*-alkyl-, *N*-benzyl-like or *N*-phenethyl–IDA. These are three new and selective modes for the copper(II)–AdeH binding which could reflect in some way the influence of the N-substitution in the IDA skeleton on molecular recognition processes. In attempts to rationalise these finding we have focused our attention on the hydrogen bonds and the possibilities of displaying π,π-stacking interactions between ligands. Table 3 and Figs. 2–5 show intramolecular interligand hydrogen bonds in compounds **1**–**4**. These data reveal that (*N*-alkyl–IDA)–Cu(II) chelates form a rather opened hydrogen bond (angles 171 and 157°, in Table 3) between an N–H bond of the exocyclic primary amino group from AdeH and one O carboxylate atom from the *N*-alkyl–IDA derivative (Table 3). In contrast, compounds **3** and **4** form a rather closed hydrogen bond (angles of 115 and 118°, in Table 3) between the N9–H heterocyclic group from AdeH and one O carboxyl atom from the *N*-(benzyl-like)–IDA chelating ligand. In order to discern if such intramolecular interligand hydrogen bonds are imposed by the formation of a Cu–N7(AdeH) or a Cu–N3(AdeH) bond or such coordination modes are selectively promoted by molecular recognition phenomena, we have proceeded to an analysis of the different possibilities of displaying π,π-stacking interactions between ligands. Calculations were carried out using the program PLATON [29] estimating short ring interactions which have a centroid–centroid vector < 6 Å and β angle $< 60°$ (see diagram 1). Tables 4 and 5 show significant data of parameters used to describe such π,π-stacking interaction (see diagram 1).

In compound **1** (Fig. 2) there is an anti-parallel π,π-stacking of AdeH to give pairs of complex units (related by the symmetry code $i = 2-x, -y, -z$). In this way the five-membered ring (A5) of each AdeH is stacked to the five- (A5) and six-membered ring (A6) of the adjacent AdeH ligand, as it is referred in Table 4 for the interactions A5/A5 and A5/A6. Note the very low value of $\alpha < 1°$ (indicating the AdeH–AdeH parallelism) and β and γ angles of approximately 18° revealing a moderate slipping of the stacked rings. In this compound the averaged stacking distance is 3.41 ± 0.01 Å. These interactions indicate that compound **1** recognises itself by forming pairs of complex units by AdeH/AdeH π,π-stacking. Then, such pairs and water molecules form a hydrogen-bonding network to build the crystal.

Compound **2** also displays an anti-parallel π,π-stacking involving the five- and six-membered rings (A5 and A6, respectively in Table 4) of each AdeH, at a mean distance of 3.42 Å, and giving pairs of complex units (symmetry related by $i = 1-x, 2-y, 1-z$) (Fig. 3(a)).

Table 3
Intra-molecular interligand hydrogen bonds in compounds $[Cu(A\ or\ B)(AdeH)(H_2O)]\cdot H_2O$

Compound	D–H···A	d(D–H)	d(H···A)	d(D···A)	<(DHA)
1	N(5) [a]–H(5B)···O(21)	0.72(4)	2.06(4)	2.78(1)	171(5)
2	N(5) [a]–H(5B)···O(11)	0.86	2.06	2.88(1)	157
3	N(2) [b]–H(2)···O(21)	0.71(3)	2.54(4)	2.91(1)	115(4)
4	N(9)–H(9)···O(2)	0.86	2.46(1)	2.96(1)	118

[a] Exocyclic N6 atom in AdeH conventional notation.

[b] Heterocyclic N9 atom in AdeH conventional notation.

Table 4
Parameters for inter-molecular interligand π,π-stacking interactions between five- (A5) and six-membered (A6) rings of anti-parallel AdeH in compounds $[Cu(A)(AdeH)(H_2O)]\cdot H_2O$ of *N*-alkyl-iminodiacetato ligands (A) with *N*-methyl- (**1**) or *N*-ethyl- (**2**) groups

	1 (pairs)	**1** (pairs)	**2** (pairs)	**2** (between pairs)
Ring I/ring J	A5/A5	A5/A6	A5/A6	A5/A6
$d(C_I-C_J)$ (Å)/α^0	3.60/0.02	3.59/0.4	3.52/2.2	3.74/9.1
$d(\perp C_I-C_J)$ (Å)/β^0	3.41/18.5	3.42/41.9	3.46/9.1	3.11/24.8
$d(\perp C_I-C_J)$ (Å)/γ^0	3.41/18.5	3.42/41.4	3.48/11.2	3.40/33.8
Stacking	anti-parallel	anti-parallel	anti-parallel	~ anti-parallel

Table 5
Parameters for the B/AdeH inter-molecular interligand π,π-stacking interactions in compounds $[Cu(B)(AdeH)(H_2O)]\cdot H_2O$ of *N*-(benzyl-like)–iminodiacetato ligand (B) between the aromatic benzyl ring (I or B6 ring) and the six-membered ring (A6 or J ring) of AdeH

	Compound **3**	Compound **4**
Ring I/ring J	B6/A6	B6/A6
$d(C_I-C_J)$ (Å)/α^0	3.53/6.24	3.65/3.41
$d(\perp C_I-C_J)$ (Å)/β^0	3.42/15.8	3.46/15.3
$d(\perp C_I-C_J)$ (Å)/γ^0	3.41/14.4	3.53/18.6

This π,π-stacking is something different from that referred for compound **1**. Each pair of stacked molecules of **2** connects with four adjacent pairs by additional π,π-stacking interactions at an averaged distance of approximately 3.3 Å (Fig. 3(b)). That represents four slightly tilted ($\alpha = 9.1°$) and clearly slipped ($\beta = 24.8°$ and $\gamma = 33.8°$) A5/A6-stacking interactions. Consequently, pairs of complex units recognise themselves by additional π,π-stacking links, which co-operate with hydrogen bonds to build the crystal. We can see how a small modification in the *N*-alkyl–IDA substituent modifies the molecular recognition in the crystals building of compounds **1** and **2**.

The aromaticity in the *N*-benzyl-like groups from NBzIDA or MEBIDA ligands in compound **3** and **4**, respectively, opens new possibilities of π,π-stacking interactions. Indeed, the crystal of compound **3** contains complex units connected in the chain along *b*-axis by a π,π-stacking interaction between the six-membered rings of the *N*-benzyl group (B6) and the adjacent AdeH (A6) (see Fig. 4 and Table 5). This stacked rings are laid out roughly parallel ($\alpha = 6.24°$) and moderately slipped (β and $\gamma \sim 15°$), at an averaged distance of 3.4 Å. No other π,π-stacking interactions could be considered in this compound. This means that compound **3** recognises itself by a multi-stacking interaction between NBzIDA and AdeH ligands. Chains are connected by hydrogen bonds in the crystal. A very similar π,π-stacking system and crystal building is observed in compound **4** (see Fig. 5 and Table 5), with a stacking distance of approximately 3.5 Å and the chains extending along *c*-axis of the crystal. Comparing with **3**, the influence of *p*-methyl group in *N*-(benzyl-like)–IDA for molecular recognition in **4** is not significant. Curiously, the electron-donating effect of the *p*-methyl group does not represent a shortening of the stacking distance. Finally, there are not aromatic ring–ring stacking interactions in the crystal of compound **5** (Fig. 5).

3.4. *Properties of copper(II) compounds*

A summary of some physical properties of the studied Cu(II) compounds is shown in Table 6. TG/DTG analyses of compound **1**–**5** are rather similar and present three or four steps. The first step is only due to the dehydration process (non-coordinated and apical coordinated water) but starting from an 'actual formula' with less water than calculated contents. That is due to the effect of air-dried flow during 20–30 min before each experiment. The other steps are due to the pyrolysis of organic ligand with production of various gasses. In all cases there is a production of ammonia (more or less evident, but easily identified by two peaks at 934.7 and 970.3 cm^{-1} in the FT-IR spectra), and NO and/or N_2O (at higher temperatures). Curiously the pyrolysis of MIDA or EIDA derivatives produces trimethylamine. At the end, all complexes give a residue of CuO at 425–475 °C (with calculated and experimental values in agreement within approximately 1%). The IR spectra show peaks and bands due to modes of water and/or aqua, AdeH and the N-substituted–IDA ligands (see Table 6).

Electronic spectra show an unsymmetrical d–d band with ν_{max} usually in the range of 14–15 kK in agreement with the elongated pyramidal chromophore CuN_2O_2+O. Powder ESR spectra at room temperature is of axial type for compounds **1**, **2** and **5** ($g_\parallel = 2.23–2.25 > g_\perp = 2.05$) and quasi-isotropic or near isotropic $g_{av} \sim 2.10$ for **3** and **4**. These spectra are in accordance with a $d_{x_2-y_2}$ Cu(II) ground state and grossly misaligned tetragonal axes in the crystal of magnetically diluted compounds [28]. A plot of χ data versus T (K) ($T = 80–300$ K) is linear ($1/\chi = (1/C)T-(\theta/C)$ with a statistical factor $r^2 > 0.998$) according to a Curie–Weiss behaviour, $\chi = C/(T-\theta)$ [32,33]. Curie constant is $C = 0.37–0.43$ K emu mol^{-1} and Weiss constant $\theta = 19.8–41.1$. Estimated values of μ_{eff} for Cu(II) atom are 1.73–1.85 BM, in

Table 6
Summary of thermal, spectral and magnetic properties of Cu(II) compounds **1**–**5**

	1	**2**	**3**	**4**	**5**
TG					
Steps	4	3	4	4	3
Δt (°C)	90–425	95–440	65–480	100–475	65–470
1st step loss	H_2O	H_2O	H_2O	H_2O	H_2O
2nd step loss	$N(CH_3)_3+X$ [a]	$N(CH_3)_3+X$ [a]	X [a]	X [a]	X [a]
Residue	CuO	CuO	CuO	CuO	CuO
IR spectrum (cm^{-1})					
H_2O					
ν_{as}	3456	3465	3450	3430	3440
δ	1630	1635	1617	1650	1630
AdeH					
$\nu_{as}(NH_2)$	3383	3381	3317	3250	3336
ν(N–H)	3191	3214	3117	3114	3200
Carboxylate					
ν_{as}	1592	1591	1602	1596	1610
ν_s	1382	1385	1385	1385	1389
Electronic spectrum					
ν_{max} (cm^{-1})	14.225	14.300	14.990	15.015	14.000
$\nu_{baricenter}$ (cm^{-1})	12.885	13.775	13.330	13.475	13.035
ESR					
Type	axial	axial	quasi-iso	quasi-iso	axial
$g_{\parallel}$	2.23	2-24			2.25
$g_{\perp}$	2.05	2.05			2.05
$g_{average}$			2.08	2.2	
Magnetic properties (80–300 K)					
Behaviour type	C–W [b]	C–W [b]	C–W [b]	C–W [b]	C–W [b]
μ (MB)	1.85	1.83	1.73	1.77	1.81
C (Curie constant)	0.43	0.42	0.37	0.39	0.41
θ (Weiss constant)	30.0	41.1	27.3	26.2	19.8

[a] Other gasses: H_2O, CO_2, CO and NH_3 (plus NO and /or N_2O in various cases).
[b] Curie–Weiss type.

accordance with the structures reported here and metal–metal separation ≥5.5(1) Å. In the studied compounds, the shortest Cu–Cu distance (5.23(1) Å) corresponds to metal atoms of compound **5** connected by the bridging carboxylato group of pheida ligand (Fig. 6).

4. Concluding remarks

In the complexes studied here, the copper(II) atom exhibits a typical metal ion coordination and a typical *mer*-chelating configuration in the Cu–(IDA-like) chelate moiety. Copper(II) complexes with *N*-alkyl–IDA ligands and AdeH recognise each other selectively by an interligand hydrogen bond N(6, exocyclic)–H···O(carboxyl) and a Cu–N7(AdeH) coordination bond. The resulting mixed-ligand complexes (**1** and **2**) recognise themselves by a π,π-stacking interaction between anti-parallel AdeH ligands, forming pairs of complex units. On the other hand, copper(II) compounds with *N*-(benzyl-like)–IDA ligands and AdeH recognise one another selectively by means of an interligand hydrogen bond N(9, heterocyclic)–H···O(carboxyl) and a Cu–N3(AdeH) coordination bond. The resulting complexes (**3** and **4**) recognise themselves through a multi-π,π-stacking interaction of alternating six-membered aromatic rings from *N*-(benzyl-like)–IDA and AdeH ligands, giving a 'stacked' complex chain. A surprising μ-N3,N7-bridging mode is observed for Cu(II)–AdeH coordination in the structure of the tetra-nuclear compound **5** where no π,π-stacking interaction is operative. Perhaps an excess of conformational free-down in the phenethyl arm of pheida ligand and other unclear reasons govern the tetra-nuclear formula.

5. Supplementary material

Crystallographic data for the structural analysis have been deposited with the Cambridge Crystallographic Data Centre, CCDC Nos. 172940 for H_2pheida acid, 172944 for $[Cu(MIDA)(AdeH)(H_2O)]\cdot H_2O$ (compound **1**), 172941 for $[Cu(EIDA)(AdeH)(H_2O)]\cdot H_2O$ (compound **2**), 172942 for $[Cu(NBzIDA)(AdeH)(H_2O)]\cdot H_2O$ (compound **3**), 172945 for [Cu(MEBIDA)(AdeH)-

$(H_2O)]\cdot H_2O$ (compound **4**) and 172943 for $[Cu_4(pheida)_4(AdeH)_2(H_2O)_4]\cdot 2H_2O$ (compound **5**). Copies of this information may be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (fax: +44-1223-336-033; e-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk).

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