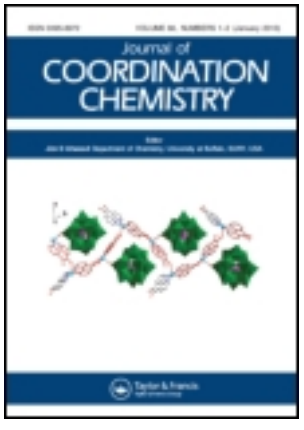

Journal of Coordination Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/gcoo20

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Published online: 10 Dec 2013.

To cite this article: Soraia Meghdadi, Mehdi Amirnasr, Zahra Azarkamanzad, Kurt Schenk Joß, Farzaneh Fadaee, Ahmad Amiri & Soheila Abbasi (2013) Benign synthesis of the unsymmetrical ligand N-(quinolin-8-yl)pyrazine-2-carboxamide. Preparation, electrochemistry, antibacterial activity, and crystal structures of Cu(II) and Zn(II) complexes, Journal of Coordination Chemistry, 66:24, 4330-4343, DOI: 10.1080/00958972.2013.867024

To link to this article: http://dx.doi.org/10.1080/00958972.2013.867024

Journal of Coordination Chemistry, 2013
Vol. 66, No. 24, 4330–4343, http://dx.doi.org/10.1080/00958972.2013.867024

Benign synthesis of the unsymmetrical ligand N-(quinolin-8-yl) pyrazine-2-carboxamide. Preparation, electrochemistry, antibacterial activity, and crystal structures of Cu(II) and Zn(II) complexes

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(*Received 11 May 2013; accepted 31 October 2013*)

Hqpzc has been synthesized by a highly efficient procedure using the ionic liquid TBAB as an environmentally benign reaction medium. $[Cu(qpzc)(OAc)]\cdot H_2O$ (**1**) and $[Zn(qpzc)(OAc)(H_2O)]$ (**2**), complexes of the deprotonated ligand, $qpzc^-$ [$qpzc^-$ = N-(quinolin-8-yl)pyrazine-2-carboxamide], have been synthesized and characterized by elemental analyses, spectroscopic methods, and X-ray crystallography. The coordination geometry around the metal ions in both complexes is distorted square pyramidal. The mono-anionic $qpzc^-$ is a tridentate unsymmetrical ligand furnishing an N3 set, occupying three of the four basal positions. Acetate is a bidentate ligand in **1** and unidentate in **2**. The apical position in **2** is occupied by water. Quite strong O-H…O hydrogen bonds create columns of complexes [rod group p21(11)] in the copper complex, but in conjunction with π-π interactions, a 3D edifice in the zinc complex. The electrochemical behavior of the ligand and its copper and zinc complexes shows that the quinoline ring reduces at more positive potentials in these complexes relative to the free ligand. The *in vitro* antibacterial activities of these complexes were tested against *Escherichia Coli* and *Staphylococcus Aureus*.

Keywords: Cu(II), Zn(II) carboxamide complexes; Crystal structure; Cyclic voltammetry; Antibacterial

1. Introduction

The carboxamide linkage, [–C(O)NH–], is an essential building unit in the primary structure of proteins, which has attracted much attention because it can provide models from the standpoint of bioinorganic chemistry [1]. Consequently, the behavior of carboxamide ligands, containing this linkage, towards biologically relevant metals has been widely investigated [2]. The pyrazine ring is present in a number of naturally occurring compounds in the form of pteridines and antibiotics. Pyrazine-2-carboxamide was recognized as the first-line antimycobacterial agent exhibiting a promising antibacterial and antifungal activity.

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Pyrazine-2-carboxamide may be used in the treatment of multidrug resistant tuberculosis, a major growing problem among HIV-infected patients [3]. A diverse range of pyridineamide ligands have been synthesized for investigation of their metal-binding properties as models for bioinorganic systems [4, 5], for dendrimer synthesis [1], preparation of metal complexes with antitumor properties [2], and for controlling the molecular architecture [3]. The classical method for the synthesis of carboxamide derivatives, used as ligands, is the reaction of the amines with the appropriate carboxylic acids in pyridine in the presence of an activator such as triphenyl phosphate [4]. Drawbacks of this method include modest yields as well as potential health hazards resulting from the pyridine solvent. One of the key areas of green chemistry is the replacement of hazardous solvents with environmentally benign ones or the elimination of solvents altogether [5]. Thus, preparation of differently functionalized carboxamide ligands under green conditions with shorter reaction time and better yield would be highly desirable for a range of applications [6]. ILs possess an excellent and tunable solvent power; thus the combination of these excellent properties allows for designing green processes based on ILs [7]. In this context, we have recently developed a benign and efficient method for the synthesis of these ligands using tetrabutylammonium bromide (TBAB) as the reaction medium, eliminating the necessity to use pyridine as solvent [8].

The design and synthesis of drugs based on essential metals such as copper and zinc have been the focus of intensive research [9, 10]. Copper among biologically relevant d-block metals is a suitable candidate for studying the behavior of pyridine carboxamides [11]. Carboxamido copper(II) complexes have demonstrated a wide range of physiological and pharmacological properties, such as antiviral [12], anticancer [13], and antibacterial activities [14]. Zinc plays a significant role in many biological systems. It is vital for numerous cell processes and is a major regulatory ion in the metabolism of cells [15]. Many zinc complexes with biological activity are reported in the literature, however only those with drugs used for the treatment of Alzheimer's disease [16], and other zinc complexes that have demonstrated antidiabetic [17], antimicrobial [18] and antiproliferative-antitumor [19] activity, are structurally characterized.

In continuation of our studies on carboxamido metal complexes [5, 20], we herein report the preparation of the Hqpzc ligand using a benign synthetic method and the synthesis and characterization of two new complexes $[Cu(qpzc)(OAc)]\cdot H_2O$ and $[Zn(qpzc)(OAc)(H_2O)]$. The X-ray crystal structures of the two complexes and the spectroscopic and electrochemical properties of these compounds are also reported and discussed. Preliminary antibacterial activity of these complexes is also presented.

2. Experimental

2.1. *Materials and physical measurements*

All solvents and chemicals were of commercial reagent grade and used as received from Aldrich and Merck. Elemental analyses were performed using a Perkin–Elmer 2400II CHNS-O elemental analyzer. UV–Vis spectra were recorded on a JASCO V-570 spectrophotometer. Infrared spectra (KBr pellets) were obtained on a FT-IR JASCO 680 plus spectrophotometer. The ^{1}H-NMR spectra were obtained on a Bruker AVANCE III 400 spectrometer. Proton chemical shifts are reported in ppm relative to an internal standard of Me_4Si. Cyclic voltammograms were recorded using a SAMA Research Analyzer M-500. Three electrodes were utilized in this system, a glassy carbon working electrode, a platinum

disk auxiliary electrode, and Ag wire as reference electrode. The glassy carbon working electrode (Metrohm 6.1204.110) with 2.0 ± 0.1 mm diameter was manually cleaned with 1 μm alumina polish prior to each scan. Tetrabutylammonium hexafluorophosphate (TBAH) was used as supporting electrolyte. The solutions were deoxygenated by purging with Ar for 5 min. All electrochemical potentials were calibrated *versus* internal $Fc^{+/0}$ (E^0 = 0.40 V *versus* SCE) couple under the same conditions [21].

2.2. *Synthesis*

2.2.1. ***Carboxamide ligand, Hqpzc.*** A mixture of 1.6 g (5 mM) triphenyl phosphate (TPP), 1.61 g (5 mM) tetrabutylammonium bromide (TBAB), 0.620 g (5 mM) pyrazine carboxylic acid and 0.721 g (5 mM) 8-aminoquinoline in a 25 mL round bottom flask was placed in an oil bath. The reaction mixture was heated until a homogeneous solution was formed. The solution was stirred for 20 min at 120 °C. The product was precipitated by adding 10 mL methanol and the resulting light yellow solid was filtered-off and washed with cold methanol. Yield 70%. Anal. Calcd for $C_{14}H_{10}N_4O$ (%): C, 67.19; H, 4.03; N, 22.39. Found (%): C, 66.92; H, 3.99; N, 22.17. FT-IR (KBr pellet, cm^{-1}): 3321 s (υ N–H), 1686 s (υ C=O), 1535 s (υ C=C), 1486 m (υ C-N). UV–Vis: λ_{max} (nm) (ε, M^{-1} L cm^{-1}) (chloroform): 336 (5750), 292 (33780). ^{1}H-NMR ($CDCl_3$, 400 MHz): δ = 7.50-9.59 (9H, ArH), 12.08 (s, 1H, NH).

2.2.2. ***[Cu(qpzc)(OAc)]·H_2O (1).*** To a stirring solution of Hqpzc (0.0250 g, 0.1 mM) in chloroform (15 mL) was slowly added a solution of $Cu(CH_3COO)_2·H_2O$ (0.020 g, 0.1 mM) in water/2-propanol (1: 10, V/V). The resulting green solution was stirred for 4 h and then toluene (0.4 mL) was added dropwise. Slow evaporation of this solution afforded green crystals suitable for X-ray crystallography. The crystals were filtered off and dried in vacuum. Yield 78%. Anal. Calcd for $C_{16}H_{14}N_4O_4Cu$ (%): C, 49.29; H, 3.62; N, 14.37. Found (%): C, 49.03; H, 3.42; N, 14.41. FT-IR (KBr pellet, cm^{-1}): 3471, 3387 m (υ O-H), 1644, 1581, 1392 s (υ C=O), 1501 s (υ C–N). UV–Vis: λ_{max} (nm) (ε, M^{-1} L cm^{-1}) (dichloromethane): 598 (98), 378 (8000), 293 (7500).

2.2.3. ***[Zn(qpzc)(OAc)(H_2O)] (2).*** To a stirring solution of Hqpzc (0.0500 g, 0.2 mM) in dichloromethane (15 mL) was added slowly a solution of $Zn(CH_3COO)_2·2H_2O$ (0.0440 g, 0.2 mM) in methanol (15 mL). The resulting yellow solution was stirred for 24 h. Slow evaporation of this solution at low temperature afforded yellow crystals suitable for X-ray crystallography. The crystals were filtered off and washed with cold diethyl ether, and dried in vacuum. Yield 67.3%. Anal. Calcd for $C_{16}H_{14}N_4O_4Zn$ (%): C, 49.06; H, 3.60; N, 14.30. Found (%): C, 48.86; H, 3.82; N, 13.92. FT-IR (KBr pellet, cm^{-1}): 3209 s (υ O-H), 1613, 1571, 1392 s (υ C=O), 1500 s (υ C–N). UV–Vis: UV–Vis: λ_{max} (nm) (ε, M^{-1} L cm^{-1}) (methanol): 369 (9150), 292 (5100). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.20-9.81 (9H, ArH), 1.85 (5H, CH_3 and H_2O).

2.3. *X-ray crystallography for 1 and 2*

Green crystals of **1** suitable for X-ray crystallography were obtained by slow evaporation of solution of the complex at room temperature. X-ray data of the complexes were

collected at $T = 292$ K on a Stoe IPDS II diffractometer with graphite monochromated Mo Kα ($\lambda = 0.71073$ Å) radiation. Cell refinement, data reduction and a numerical absorption correction were performed with the help of the program XRED32 (1.31) [22]. The structures were solved with direct methods using the program SIR2004 [23] and structure refinement on F^2 was carried out with the program SHELXL [24]. Details of crystallographic data and refinements of the complexes are summarized in table 1, while selected bond lengths and angles are presented in table 2. A list of hydrogen bonds in the complexes is given in tables 3 and 4. The molecular structures and stereoscopic views of crystal packing of the two complexes have been drawn by the ORTEPIII software and the CrystalMaker program, respectively [25, 26].

3. Results and discussion

3.1. *Synthesis of the ligand*

Since the recognition of ILs as new reaction media and catalysts, these compounds have been used for replacing hazardous solvents, reducing reaction time, and increasing yields of products compared to conventional methods [6, 27]. We have synthesized the carboxamide ligand, Hqpzc, by eliminating the toxic pyridine solvent and using TBAB as the reaction

Table 1. Crystal data and structure refinement parameters for **1** and **2**.

Compound	**1**	**2**
Chemical formula	$C_{16}H_{14}CuN_4O_4$	$C_{16}H_{14}ZnN_4O_4$
Formula weight	389.85	391.68
Temperature (K)	292 (2)	292 (2)
Crystal system	Triclinic	Monoclinic
Space group	$P\bar{1}$	$P2_1/c$
a (Å)	6.9263(14)	12.2132(8)
b (Å)	9.762(2)	10.2443(6)
c (Å)	12.716(3)	13.3422(9)
α (°)	69.78(3)	90.00
β (°)	90.07(3)	105.436(5)
γ (°)	82.43(3)	90.00
V (Å^3)	798.8(3)	1609.10(18)
Z	2	4
Calculated density (Mg m^{-3})	1.621	1.617
Crystal size (mm)	0.80 × 0.22 × 0.03	0.30 × 0.27 × 0.20
μ (mm^{-1})	1.397	1.56
F (000)	398	800
θ Ranges (°)	2.3–29.2	1.7–29.5
Index ranges	$-9 \le h \le 8$, $-13 \le k \le 13$, $-17 \le l \le 17$	$-16 \le h \le 16$, $-13 \le k \le 14$, $-18 \le l \le 17$
Absorption correction	Integration	Integration
Reflections collected	9508	25635
Independent reflections (R_{int})	4222 (0.071)	4315 (0.044)
Min. and max. transmission	0.496, 0.954	0.606, 0.789
Data/restraints/parameters	4222/0/234	4315/0/234
Goodness-of-fit on F^2	1.066	1.072
Final R indices [$I>2\sigma(I)$]	$R_1 = 0.0462$, $wR_2 = 0.0881$	$R_1 = 0.0290$, $wR_2 = 0.0670$
R indices (all data)	$R_1 = 0.0796$, $wR_2 = 0.1053$	$R_1 = 0.0440$, $wR_2 = 0.0742$
Max./min. $\Delta\rho$ (e Å^{-3})	0.53 and −0.52	0.29 and −0.37

Table 2. Selected bond lengths (Å) and angles (°) for **1** and **2**.

Compound	**1**	**2**
Bond lengths		
M–N1	1.986(3)	2.1071(15)
M–N2	1.927(3)	2.0395(16)
M–N3	2.019(3)	2.1744(17)
M–O2	1.950(3)	1.9933(14)
M–O3	2.625(3)	–
M–O1w	–	2.0382(17)
Bond angles		
N1–M–N2	83.34(12)	79.25(6)
N1–M–N3	165.01(12)	156.69(6)
N1–M–O2	98.65(10)	97.81(6)
N1–M–O3	102.84(11)	–
N2–M–N3	81.68(11)	77.85(6)
N2–M–O2	175.19(11)	149.39(6)
N2–M–O3	129.01(11)	–
N3–M–O2	96.24(11)	99.67(6)
N3–M–O3	87.28(10)	–
O2–M–O3	54.96(9)	–
N1–M–O1w	–	97.22(7)
N2–M–O1w	–	110.40(7)
N3–M–O1w	–	94.74(7)
O2–M–O1w	–	100.21(7)
O3–M–O1w	–	–

Table 3. Hydrogen bond lengths (Å) and angles (°) for **1**.

No.	D–H…A	D–H	H…A	D…A	D-H…A
1	O1W–H1O…O3	0.80	1.99	2.784	175
2	O1W–H2O…O2$^{(i)}$	0.79	2.07	2.852	169

Symmetry code: (i) 1 + x, y, z.

Table 4. Hydrogen bonds and C-H…π (C) interactions: lengths (Å) and angles (°) for **2**.

No.	D–H…A	D–H	H…A	D…A	D-H…A
1	O1W-H1O…O3$^{(i)}$	0.75	1.94	2.678	170
2	O1W-H2O…O1$^{(ii)}$	0.74	1.95	2.690	177
3	C21-H21A…centroid[a] $^{(iii)}$	0.96	2.678	3.614	165
4	C8-H8....O2$^{(iv)}$	0.93	2.56	3.460(2)	162

[a]The distance C-H…center of the aromatic ring {C10, C11, C12, C13, C14, N1}. Symmetry codes: (i) x, $3/2 - y$, $1/2 + z$; (ii) $2 - x$, $1/2 + y$, $1/2 - z$; (iii) x, $3/2 - y$, $-1/2 + z$; (iv) x, $-1 + y$, z.

media. The optimization of the reaction condition by varying the reaction temperature, period of heating, and amount of TBAB were examined to obtain the products in high yield. Interestingly, in the preparation of Hqpzc carried out by this method, a significant improvement was observed in the reaction time (20 min) and yield (70%) as compared to the conventional method reported for a closely related compound (1 h and 47%) [28].

3.2. *Spectral characterization*

The newly prepared metal complexes are all air-stable solids and have good elemental analyses. The FT-IR data of the complexes are listed in the Experimental section. Meaningful

information regarding the bonding sites of the ligand molecule can be obtained by comparing the IR spectra of two complexes with the free ligand. The IR spectrum of the Hqpzc ligand exhibits a band at 3321 cm^{-1} due to NH group. The absence of υ(N–H) in the IR spectra of the two complexes confirms that the ligand is coordinated in the deprotonated form [3]. A further indication of the formation of deprotonated complexes is the rather large decrease in the carbonyl stretching frequency exhibited by the ligand upon complex formation. The sharp C=O stretching vibration band at 1686 cm^{-1} for free Hqpzc is shifted to lower frequencies upon coordination of the deprotonated amide, which is in agreement with the data reported for the related complexes [25, 34]. The peaks at 1581 cm^{-1} for **1** and 1571 cm^{-1} for **2** are attributed to υ_{as}(COO), while those at 1392 cm^{-1} for both **1** and **2** are assigned to υ_{s}(COO). It is well known that comparison of the Δυ [υ_{as}(COO) – υ_{s}(COO)] value of the respective carboxylate complexes with that of the corresponding carboxylate salt can be used as a guideline in assigning the carboxylate coordination mode [35, 36].

The Δυ values of 189 and 179 cm^{-1} for **1** and **2** are close to that reported for sodium acetate (Δυ = 164 cm^{-1}), which indicate a bidentate coordination mode of the acetate ligand. The Δυ conform to the structure observed for **1** but not to that of **2**. Though a larger Δυ value is expected for the monodentate mode of coordination of acetate in **2**, the observed value of Δυ is presumably due to the existence of a very strong intermolecular O–H…O hydrogen bond between the uncoordinated acetate oxygen atom and the coordinated water of the neighboring molecule (see figure 1), giving what may be regarded as a "pseudo-bridging" arrangement. In addition, the υ(COO) frequencies of the zinc complex are sufficiently close to those of alkali metal acetates [36]. Though, there appears to be no unequivocal example of a unidentate acetate complex with Δυ < 200 cm^{-1}, this conclusion on the mono-coordinating acetate ligand in **2** is confirmed by X-ray crystallography (*vide infra*).

The observation of a sizable increase in the frequency of C–N stretching vibration of medium intensity for the coordinated $qpzc^{-}$ (1501 and 1500 cm^{-1}, respectively) relative to the free ligand (1486 cm^{-1}) gives additional support to the coordination of this amide in its deprotonated form. This is presumably due to the resonance enhancement in the

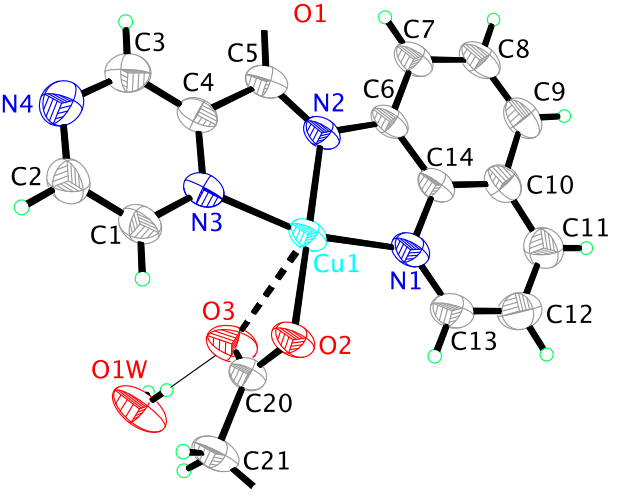

Figure 1. The molecular structure of **1** with its atom labeling scheme. Displacement ellipsoids are drawn at 50% probability.

deprotonated amide which in turn leads to the strengthening of C–N bond [3]. Two peaks at 3471 and 3387 cm^{-1} are assigned to strong intermolecular O–H…O hydrogen bonds in **1** with different bond lengths (1.99 and 2.07 Å) as shown in figure 2. The broad vibration band at 3209 cm^{-1} is attributed to the coordinated water molecule in **2** [38].

The UV–Vis data are presented in the Experimental section. The electronic spectrum of Hqpzc ligand in chloroform shows a shoulder at 336 nm (ε = 5750 M^{-1} L cm^{-1}), and the band in the higher energy region at 292 nm (ε = 33780 M^{-1} L cm^{-1}). The UV–Vis data of the complexes ([Cu(qpzc)(OAc)]·H_2O in dichloromethane and [Zn(qpzc)(OAc)(H_2O)] in methanol) are presented in the Experimental section. The new complexes, **1** and **2**, show two bands in the 290-380 nm region, assigned to the intraligand $\pi\rightarrow\pi^*$ (of aromatic rings) and $n\rightarrow\pi^*$ (of electron pairs of carboxamide-O atom) transitions. The low intensity band (ε = 98 M^{-1} L cm^{-1}) observed at 598 nm in the electronic spectrum of **1** is attributed to the ligand field transition of the copper(II) complex.

The ^{1}H NMR spectral measurements were performed in $CDCl_3$ for Hqpzc ligand and Zn (II) complex. The main ^{1}H NMR spectroscopic data of the carboxamide ligand Hqpzc and its zinc complex are given in the Experimental section. The ^{1}H NMR spectrum of the ligand features a singlet at 12.08 ppm for the amidic N–H proton and signals in the range of 7.50–9.59 ppm attributed to the nine aromatic protons, and is consistent with the structure of the ligand. There are two main features in the ^{1}H NMR spectrum of the complex: (i) The absence of the amidic (δ = 12.08 ppm) proton signal, which clearly indicates that the Hqpzc carboxamide ligand is coordinated in an anionic form [25]. (ii) The expansion, toward downfield chemical shifts, of the aromatic protons signal range. These signals in the spectrum of the free Hqpzc ligand are located between 7.50–9.59 ppm ($\Delta\delta$ = 2.09 ppm), while in the spectrum of the Zn complex these aromatic protons are located between 7.20–9.81 ppm ($\Delta\delta$ = 2.61 ppm).

3.3. *Crystal structure of [Cu(qpzc)(OAc)]·H_2O (1)*

The geometry and dynamics of **1** are shown in figure 1 and selected bond lengths and angles are summarized in table 2.

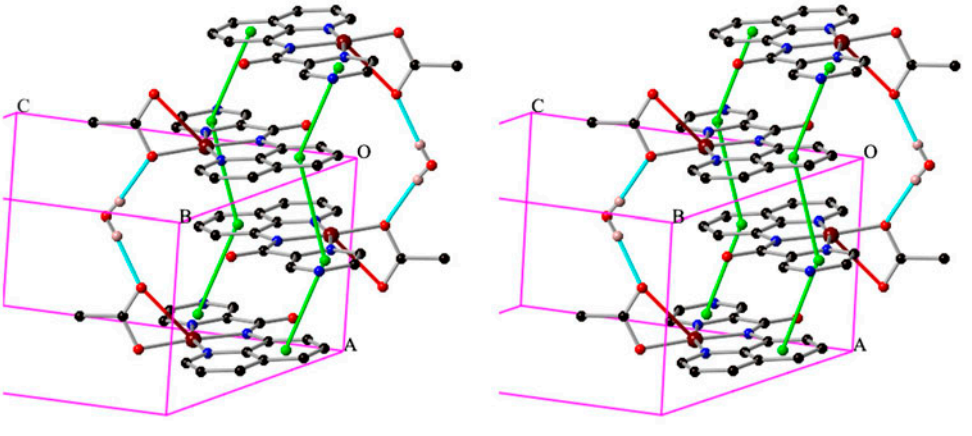

Figure 2. Stereoscopic view of the hydrogen bonds (turquoise tubes) and π-π stacking interactions (green tubes) in **1** along the *a* axis (see http://dx.doi.org/10.1080/00958972.2013.867024 for color version).

This complex crystallizes in the triclinic space group $P\bar{1}$, and the copper coordination is a distorted square-pyramid. As anticipated, the ligand qpzc$^-$ acts as a tridentate mono-anionic ligand and binds to the copper ion *via* quinoline-N, pyrazine-N and carboxamide-N atoms in a basal disposition. The acetate anion coordinates as a bidentate ligand through one of its oxygen atoms (O2) occupying one of the basal positions of the square pyramid. The apical site is occupied by the other oxygen atom (O3) of the acetate anion.

The Cu–N_{amido}, 1.927(3) Å, Cu–$N_{quinolyl}$, 1.986(3) Å, and Cu–$N_{pyrazyl}$, 2.019(3) Å, bond lengths are comparable to those observed in related Cu(II) complexes [39, 40]. The Cu–N_{amido} (1.927(3) Å) bond is shorter than that of Cu–$N_{pyrazyl}$ (2.019(3) Å) and compares well with the Cu–N_{amido} and Cu–$N_{pyrazyl}$ bond lengths {(1.9180(15) and 2.0429(15) Å, respectively} in the [Cu(pzpy)(CH_3CO_2)(OH_2)] complex [40]. The Cu1–O2(acetate), 1.950(3) Å, and Cu1–O3(acetate), 2.625(3) Å, bond distances are not identical due to the Jahn-Teller effect reflecting the ability of copper(II) to accommodate long, axial metal–ligand bonds [41]. The two chelate angles N1–Cu1–N2 83.34(12)° and N2–Cu1–N3 81.68(11)°, formed by the quinoline-N, pyrazine-N and carboxamide-N atoms are almost similar and are close to those reported for related complexes [38, 39]. The two *trans* angles, N1–Cu1–N3 165.01(12)° and N2–Cu1–O2 175.19(11)°, deviate significantly from the ideal value of 180° for a regular square pyramid structure.

The deviations of the four basal donor atoms from the mean basal plane N1, N2, N3, and O2 are −0.025(1), 0.028(1), –0.025(1) and 0.021(1) Å, respectively, and the Cu1 atom is −0.049(1) Å out of the plane towards O3. The trigonality–index (Addison Parameter [42]) τ = 0.17 [= (β–α)/60°, where α, β are the two largest L–M–L angles of the coordination sphere, with τ = 0 and 1 for perfect square pyramid and trigonal bipyramid geometries, respectively] confirms the square pyramidal environment for Cu1.

As shown in figure 2, the crystal edifice is stabilized by two types of intermolecular forces: (i) strong intermolecular O–H…O hydrogen bonds between hydrogen atoms of the free water molecule in the crystal packing and the adjacent acceptor oxygen atoms of

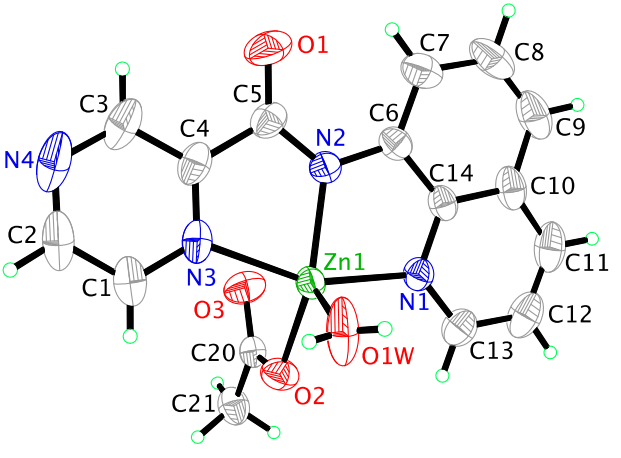

Figure 3. The molecular structure of **2** with its atom labeling scheme. Displacement ellipsoids are drawn at 50% probability.

coordinated acetate belonging to the two neighboring complexes (table 3); (ii) intermolecular π–π stacking interactions between pyrazine ring of one complex and phenyl ring in quinolyl moiety of the adjacent complex, the distance between adjacent planes is 3.42 Å, and the angle between the line joining the centroids and that from a centroid to its foot-point onto the adjacent plane is 26.51°. Thus, all interactions give birth to an interesting one-dimensional structure along [100].

3.4. *Crystal structure of [Zn(qpzc)(OAc)(H_2O)] (2)*

The geometry and dynamics of **2** are shown in figure 3 and table 2 gives the significant bond lengths and angles.

This complex crystallizes in monoclinic space group $P2_1/c$ and its metal ion is lodged in a distorted square-pyramidal environment containing the three N-atoms of the qpzc$^-$ ligand, one of the acetate oxygens O2 in the basal plane and a water molecule apically coordinated.

The Zn–N_{amido}, 2.0395(16) Å, the Zn–$N_{quinolyl}$, 2.1071(15) Å, and the Zn–$N_{pyrazyl}$, 2.1744(17) Å, bond distances compare well with the Zn–$N_{pyrazyl}$ bond lengths (2.086(4) Å) in the [$Zn(pzc)_2Br_2$] complex [43]. The Zn–$O_{acetato}$ (1.9933(14) Å) bond length is also in agreement with that of Zn–$O_{acetato}$ (2.0058(12) Å) in the [$Zn(OAc)(L\text{-}Arg)_2$] $OAc\cdot 3H_2O$ complex [44]. The aqua ligand in the apical position has a Zn–O1W bond distance of 2.0382(17) Å. The two chelate angles N1–Zn1–N2 79.25(6)° and N2–Zn1–N3 77.85(6)°, formed by the quinoline-N, pyrazine-N and carboxamide-N atoms are almost identical. The two *trans* angles, N1–Zn1–N3 156.69(6)° and N2–Zn1–O2 149.39(6)°, deviate considerably from the ideal value of 180° for a regular square pyramid structure.

The deviations of the four basal donor atoms from the mean basal plane N1, N2, N3, and O2 are 0.172(1), −0.201(1), 0.167(1) and −0.137(1) Å, respectively, and the Zn1 atom is −0.363(1) Å out of the plane towards O1W. The trigonality–index (Addison Parameter [42]) $\tau = 0.12$ confirms the square pyramidal environment for Zn1.

A comparison between the values of Addison's Parameter in **1** and **2** shows that the deviation from square-pyramidal geometry is larger in the copper complex relative to that of zinc.

The crystal edifice of **2** is stabilized by three types of intermolecular forces: (i) strong intermolecular O–H…O hydrogen bonds between hydrogen atoms of the aqua ligand and the adjacent free acceptor oxygen atoms ($O1_{amido}$ and $O3_{acetato}$) belonging to two neighboring complexes; (ii) intermolecular π–π stacking interactions more precisely between quinoline rings of two neighboring complexes and also between the pyrazine ring of one complex and a phenyl ring in the quinolyl moiety of an adjacent complex and the distance between the adjacent planes is 3.53 and 3.24 Å, respectively. Actually, there are two offset angles in this compound. Let us name the planes:

Π quinolone-plane
Σ pyrazine-plane

Then the angles are 28.24 and 37.24 between the Π and Π (centre of inversion) and the Π and Σ, respectively. (iii) intermolecular C-H…π (C) interactions between a quinoline ring of one complex and a hydrogen atom (of a methyl group of an acetate ligand) of the adjacent complex (figure 4 and table 4).

3.5. *Cyclic voltammetry*

The electrochemistry of the carboxamide ligand, Hqpzc, [Cu(qpzc)(OAc)]·H_2O (**1**) and [Zn(qpzc)(OAc)(H_2O)] (**2**) were recorded in DMF solutions with 0.1 M TBAH as the supporting electrolyte at a glassy carbon working electrode.

As expected and previously reported, the carboxamide ligands are electro-active in common organic solvents [5, 20]. As shown in the voltammogram of Hqpzc (figure 5), the three irreversible reduction waves of quinoline rings are observed at −1.7 V, -2.22 V and -2.43 V and are shifted to more positive values for the corresponding **1** and **2** complexes [25, 45].

The electrochemistry of [Cu(qpzc)(OAc)]·H_2O (**1**) in DMF (figure 6) shows an irreversible reduction process at −0.82 V and is attributed to the reduction of $Cu^{II/I}$ center in [CuL(OAc)]. This value is in agreement with those reported in the related Cu(II) carboxamide complexes [45]. The identification of the irreversible reduction waves observed in the potential range of −1 to −1.90 V is not quite clear to us and may be due to the solvated Cu(II) species. The irreversibility of redox processes can be attributed to the instability of the reduced species in DMF solvent.

The last three irreversible reduction processes observed in the potential range of −1.95 to −2.4 V are suggested to be mainly ligand centered due to the reduction of quinoline rings and are shifted to more positive potentials in Cu(II) complex relative to the free ligand [25, 45].

The electrochemistry of [Zn(qpzc)(OAc)(H_2O)] (**2**) shows two irreversible reduction processes at −1.37 V and −1.67 V (figure 7). These reductions are ligand centered and attributed to the reduction of quinoline rings. As expected, no metal centered redox process was observed in the cyclic voltammogram of **2** since Zn(II) is not electroactive in the studied potential range.

3.6. *Antibacterial activity*

Antibacterial activities of the complexes were tested by the well-known diffusion method using Sabouraud dextrose agar and Müller Hinton agar [46]. The zone of inhibition was

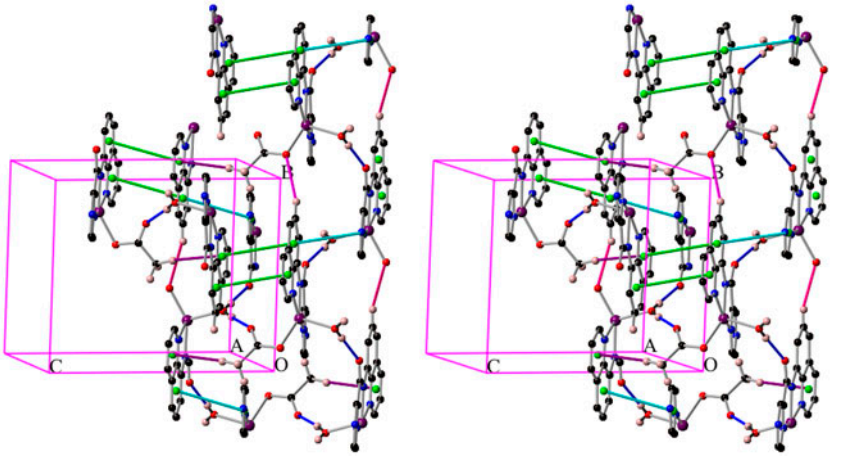

Figure 4. Stereoscopic view of the hydrogen bonds (blue tubes), C(H)…π (C) and π-π stacking interactions (green tubes) in **2** (see http://dx.doi.org/10.1080/00958972.2013.867024 for color version).

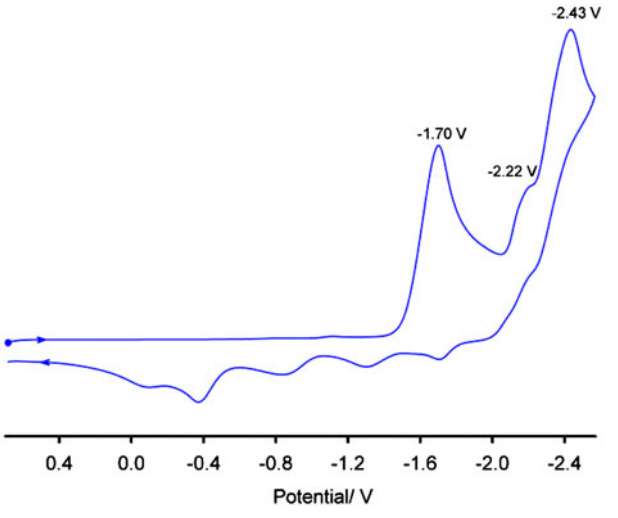

Figure 5. Cyclic voltammogram of Hqpzc in DMF at 298 K, c = 10^{-3} M, scan rate = 100 mVs^{-1}.

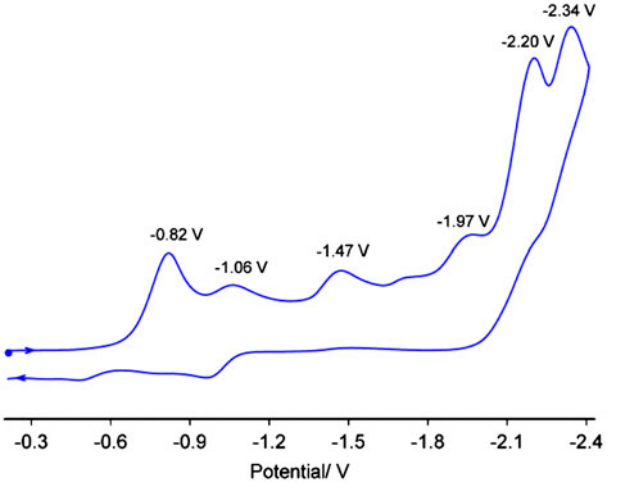

Figure 6. Cyclic voltammogram of $[Cu(qpzc)(OAc)]\cdot H_2O$ in DMF at 298 K, c = 10^{-4} M, scan rate = 100 mVs^{-1}.

recorded on the completion of the incubation and the mean diameter for each complex at 400 μg mL^{-1} was recorded (the MZI is shown in figures SIa and SIb (see online supplemental material at http://dx.doi.org/10.1080/00958972.2013.867024)) Stock solutions of **1** and **2** were prepared in dimethylsulfoxide. The diameters of the zone of inhibition produced by the compounds were compared with the standard disc having antibiotic Penicillin concentration of 10 units per disc.

The ligand and the two complexes were subjected to antibacterial activity against Gram-positive *Staphylococcus aureus* and Gram-negative *Escherichia coli*. The screening results are summarized in table 5. While the ligand and its zinc complex do not show any activity,

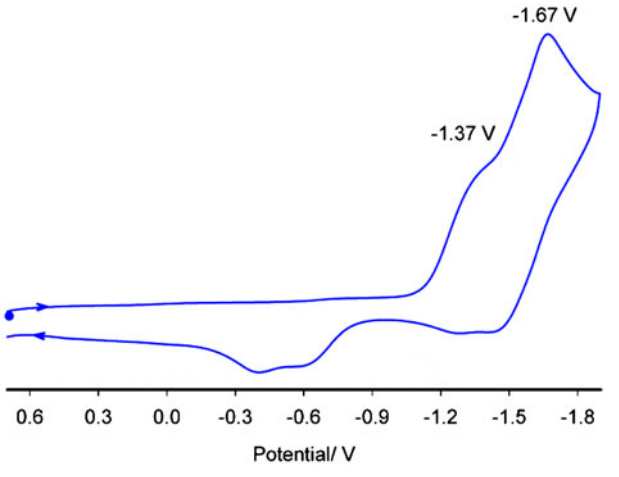

Figure 7. Cyclic voltammogram of [Zn(qpzc)(OAc)(H_2O)] in DMF at 298 K, c = 10^{-4} M, scan rate = 100 mVs^{-1}.

Table 5. MZI (mm) for the antimicrobial activity of Hqpzc and its complexes.

Compound	Bacteria	MZI
Hqpzc	*Escherichia coli*	None
	Staphylococcus aureus	None
[Zn(qpzc)(OAc)(H_2O)]	*Escherichia coli*	None
	Staphylococcus aureus	None
[Cu(qpzc)(OAc)]·H_2O	*Escherichia coli*	20
	Staphylococcus aureus	30
Penicillin	*Escherichia coli*	1.4
	Staphylococcus aureus	4.0

it is evident that the copper complex has a stronger antibacterial activity than that of the standard antibiotic Penicillin [47]. The strong antibacterial activity of the copper complex is in accord with many other related studies [48–51] and may stem from the stronger copper (II)-ligand bond as compared to the zinc(II) complex which is prone to dissociation and solvolysis in DMSO. The inertness of the metal-ligand linkage presumably increases its lipophilicity, cell permeability, and protection against enzymatic degradation [48]. However the exact mechanism is unrevealed and further biological studies are necessary to get a clear picture of this behavior.

4. Conclusion

The present work shows copper(II) and zinc(II) chemistry with a tridentate unsymmetrical carboxamide ligand $qpzc^-$. The crystallographic characterization of these complexes shows a square pyramidal geometry around the metal centers. The mono-anionic $qpzc^-$ furnishes an N3 set from one N of quinoline, one N from pyrazine, and one amido N occupying three basal positions of the square pyramidal structure. Acetate coordinates as a bidentate ligand

in **1** with O2 occupying a basal position and O3 the apical site of the square pyramid. Acetate is unidentate in **2** with O2 in the basal plane and a water coordinating at the apical position.

The absence of the amidic proton signal (free ligand, δ = 12.08 ppm) in the ^{1}H NMR spectra of Zn(II) complex clearly indicates that Hqpzc is coordinated in its anionic form. This is further corroborated by the shift in the positions of the ligand reduction peaks to more positive potentials in the cyclic voltammograms of the two complexes and X-ray crystal structures of **1** and **2**.

The copper complex has strong biological activity compared to the antibiotic Penicillin while the ligand and the zinc complex are not active. The present work will be further extended to the synthesis of carboxamide complexes using other biologically active metals and evaluation of their biological activities.

Supplementary material

^{1}H NMR, IR, and UV spectra for **1** and **2**; data on antibacterial activity studies. X-ray crystallographic data for **1** and **2** have been deposited with the Cambridge Crystallographic Data Center as supplementary publication, CCDC No. 905831 (for **1**) and No. 905832 (for **2**). Copies of the data can be obtained free of charge on request at www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Center (CCDC), 12 Union Road, Cambridge CB2 1EZ, UK; Fax: +44(0)1223 336033; E-mail: deposit@ccdc.cam.ac.uk).

Acknowledgements

Partial support of this work by the Isfahan University of Technology Research Council is gratefully acknowledged.

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