Inorganica Chimica Acta 373 (2011) 62–67

Contents lists available at ScienceDirect

Inorganica Chimica Acta

journal homepage: www.elsevier.com/locate/ica

Synthesis and chemical characterization of Cu^{II}, Ni^{II} and Zn^{II} complexes of 3,5-bis(2′-pyridyl)-1,2,4-oxadiazole and 3-(2′-pyridyl)5-(phenyl)-1,2,4-oxadiazole ligands

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ARTICLE INFO

Article history:
Received 10 December 2010
Received in revised form 16 February 2011
Accepted 18 March 2011
Available online 31 March 2011

Keywords:
Copper(II) complexes
Crystal structure
Nickel(II) complexes
1,2,4-Oxadiazoles
Zinc(II) complexes

ABSTRACT

The synthesis and structural characterization of Ni^{II}, Cu^{II} and Zn^{II} complexes of two chelating 1,2,4-oxadiazole ligands, namely 3,5-bis(2′-pyridyl)-1,2,4-oxadiazole (bipyOXA) and 3-(2′-pyridyl)5-(phenyl)-1,2,4-oxadiazole (pyOXA), is here reported. The formed hexacoordinated metal complexes are $[M(bipyOXA)_2(H_2O)_2](ClO_4)_2$ and $[M(pyOXA)_2(ClO_4)_2]$, respectively (M = Ni, Cu, Zn). X-ray crystallography, ^1H and ^{13}C NMR spectroscopy and C, N, H elemental analysis data concord in attributing them an octahedral coordination geometry. The two coordinated pyOXA ligands assume a *trans* coplanar disposition, while the two bipyOXA ligands are not. The latter result is a possible consequence of the formation of H-bonds between the coordinated water molecules and the nitrogen atom of the pyridine in position 5 of the oxadiazole ring. The expected splitting of the d metal orbitals in an octahedral ligand field explains the observed paramagnetism of the d^8 and d^9 electron configuration of the nickel(II) and copper(II) complexes, respectively, as determined by the broadening of their NMR spectra.

1. Introduction

Oxadiazole-based ligands have been recently used for complexation of metals such as platinum, silver, palladium and copper [1–3]. Recently, a series of Pt^{II} complexes of substituted 1,2,4-oxadiazole derivatives have shown cytotoxic activity towards human ovarian cancer cell lines, as well as in colon and testicular cancer cell lines and the results have been correlated to their DNA-binding properties [4]. These heterocyclic systems are easily accessible and the modulation of their properties is achievable through the introduction of appropriate substituents on the central heterocycle. In particular, 1,2,4-oxadiazole ligands can be designed so as to chelate metal ions by the heteroatoms of the ring and of the side chain substituents in the ring positions 3 and 5.

Based on the considerations above, we have started a research project on the synthesis and characterization of novel 1,2,4-oxadiazole complexes of Ni^{II}, Cu^{II} and Zn^{II}, with the aim to obtain metal compounds with potential antitumor properties. The three metal ions are present as essential elements in the biological intracellular environment of living organisms [5–8]. Moreover, their complexes with planar heterocyclic ligands are efficient DNA-binders and have a stronger affinity toward DNA than the corresponding isolated ligands [9–11].

Recently, the first study of the biological activity of a copper(II) complex of 1,2,4-oxadiazole ligands was reported [12]. In this respect, biological assays showed that, despite the free ligand is not being effective, its Cu^{II} complex reduces the vitality of human hepatoblastoma and colorectal carcinoma cells in a dose- and time-dependent manner [12]. Interestingly, the results of the biological assays receive a positive feedback in the DNA binding studies performed for the same complex [12].

The structure of $[Cu(3,5\text{-bis}(2'\text{-pyridyl})\text{-}1,2,4\text{-oxadiazole})_2(H_2O)_2](ClO_4)_2$ was characterized in the solid state by X-ray crystallography [12]. Its structure consists of a discrete $[Cu(3,5\text{-bis}(2'\text{-pyridyl})\text{-}1,2,4\text{-oxadiazole})_2(H_2O)_2]^{2+}$ cation and two ClO_4^- anions. The Cu^{II} ion lies in a distorted octahedral environment, where each 3,5-bis(2′-pyridyl)-1,2,4-oxadiazole behaves as bidentate ligand and the two ligands are not coplanar. Two coordinated water molecules occupy the *cis* positions in the equatorial plane. The 1,2,4-oxadiazole ligand only uses two of its five potential donor atoms, acting as a typical chelator and forming a five-membered Cu–N–C–C–N cyclic moiety. The two non-coordinating

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doi:10.1016/j.ica.2011.03.057

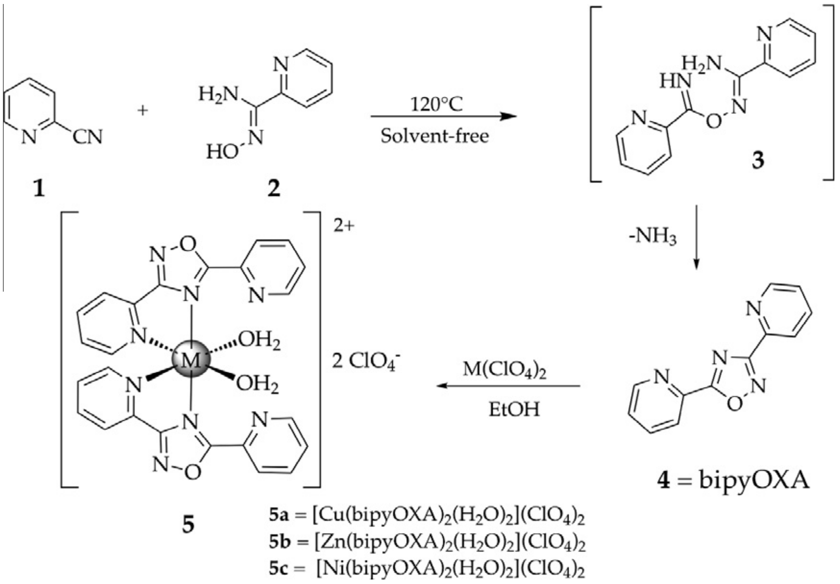

Fig. 1. Synthesis of bipyOXA and of its Ni^{II}, Cu^{II} and Zn^{II} complexes.

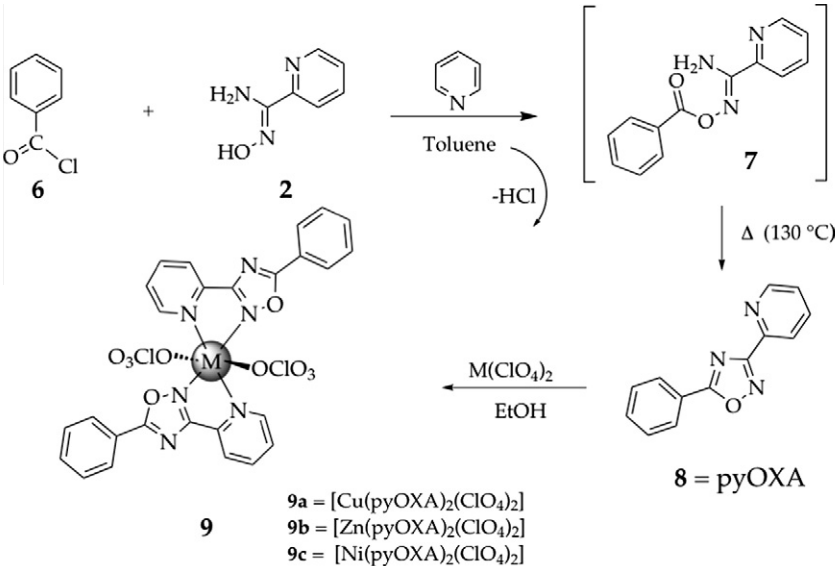

Fig. 2. Synthesis of pyOXA and of its Ni^{II}, Cu^{II} and Zn^{II} complexes.

ClO_4^- counter anions are involved in hydrogen bonds with the coordinated water molecules. The water molecules are also involved in intramolecular hydrogen bonding interactions with the uncoordinated nitrogen of one pyridine moiety. The two pyridine rings of 3,5-bis(2′-pyridyl)-1,2,4-oxadiazole are not coplanar with the oxadiazole ring and their orientation is forced by the coordination to Cu^{II} [12]. Only few Cu^{II} complexes of oxadiazole ligands, but the 1,3,4 isomers, have been synthesised up to now [13–15].

The synthesis and characterization of the Ni^{II} and Zn^{II} complexes of 3,5-bis(2′-pyridyl)-1,2,4-oxadiazole (here called bipyOXA), and of the Ni^{II}, Cu^{II} and Zn^{II} complexes of 3-(2′-pyridyl)5-(phenyl)-1,2,4-oxadiazole (called pyOXA), is reported in the present paper. The two ligands differ in the substituent in position 5 of the oxadiazole ring (see Figs. 1 and 2), being a pyridine and a phenyl in bipyOXA and pyOXA, respectively.

2. Experimental

2.1. Materials and methods

All chemicals and solvents were purchased from Sigma–Aldrich, Fisher or Alfa Aesar and used as received, without further purification.

^1H NMR and ^{13}C NMR spectra were recorded on a Bruker AC300 spectrometer, solvent residual peaks were used as reference. Flash chromatography was performed by using silica gel (Merck, 0.040-0.063 mm) and mixtures of ethyl acetate and petroleum ether (fraction boiling in the range of 40–60 °C) in various ratios.

Mass spectrometry (MS) and MS/MS measurements of the complexes have been carried out by using electrospray ionization (ESI) with a LCQ-DECA ion trap (Thermo, Bremen, Germany). Operating conditions of the ESI source were as follows: spray voltage 4.5 kV; capillary temperature 200 °C; sheath gas (nitrogen) flow rate ca. 0.75 L min^{-1}. Ultra-pure helium was the collision gas. CID collision energy: 0.5÷1.0 eV (laboratory frame). A methanol solution of the complex (1×10^{-4} M) was introduced into the mass spectrometer using a syringe pump at a flow rate of 5 μL min^{-1}.

Melting points were determined on a Reichart-Thermovar hot stage apparatus and are uncorrected. IR spectra were registered with a Shimadzu FTIR-8300 instrument.

2.2. X-ray crystallography

A Oxford-Diffraction Xcalibur Sapphire 3 diffractometer with a graphite monochromated Mo Kα radiation (λ = 0.71073 Å) was used for data collection at 293(2) K. The [Cu(pyOXA)$_2$(ClO$_4$)$_2$] complex crystallizes in the triclinic crystal system, $P\bar{1}$ space group. The structure was solved by direct methods implemented in the SHELXS-97 program [16]. The refinement was carried out by full-matrix anisotropic least-squares on F^2 for all reflections for non-H atoms by using the SHELXL-97 program [17].

2.3. Synthesis and characterization

2.3.1. BipyOXA ligand and its Cu^{II}, Zn^{II} and Ni^{II} complexes

*2.3.1.1. 3,5-Bis(2′-pyridyl)-1,2,4-oxadiazole (bipyOXA). 1.00 g of 2-cyanopyridine (**1**) (8.14 mmol) and 0.56 g of 2-picolinamidoxime (**2**) [18] (4.07 mmol) were mixed in a sealed tube and heated at 120 °C for 8 h. The residue was chromatographed yielding 0.59 g of 3,5-bis(2′-pyridyl)-1,2,4-oxadiazole (65%): mp 173–176 °C (from EtOH) (lit. 173–175 °C) [19]; ^{1}H NMR (300 MHz, CDCl$_3$) δ (ppm): 7.44–7.58 (m, 2H); 7.87–7.98 (m, 2H); 8.28–8.31 (d, 1H); 8.42–8.44 (d, 1H); 8.84–8.89 (m, 2H).*

^{1}H NMR (300 MHz, CD$_3$CN) δ (ppm): 8.96–8.70 (m, 2H), 8.34 (dt, J = 7.9, 1.0 Hz, 1H), 8.21 (dt, J = 7.9, 1.1 Hz, 1H), 8.13–7.91 (dtd, J = 17.3, 7.8, 1.8 Hz, 2H), 7.64 (ddd, J = 7.7, 4.8, 1.2 Hz, 1H), 7.56 (ddd, J = 7.7, 4.8, 1.2 Hz, 1H). ^{13}C NMR (75 MHz, CD3CN) δ (ppm): 176.1 (C), 170.0 (C), 151.5 (CH), 151.3 (CH), 147.3 (C), 144.5 (C), 138.7 (CH), 138.4 (CH), 128.1 (CH), 126.9 (CH), 125.3 (CH), 124.4 (CH). UV(MeOH): ε = 1.7×10^4 (λ = 274 nm); ε = 1.5×10^4 (λ = 231 nm)cm^{-1} M^{-1}. UV (Tris–HCl, pH 7.5): 1.5×10^4 (λ = 275 nm); ε = 1.7×10^4 (λ = 231 nm) cm^{-1} M^{-1}.

*2.3.1.2. [Zn(bipyOXA)$_2$(H$_2$O)$_2$](ClO$_4$)$_2$, **5b**.* A solution of Zn(ClO$_4$)$_2$·6H$_2$O (0.14 g, 0.4 mmol) in absolute ethanol was added drop wise and under constant stirring to a colorless solution of 3,5-bis(2′-pyridyl)-1,2,4-oxadiazole (0.179 g, 0.8 mmol) in absolute ethanol and at room temperature. The mixture was left under stirring for 12 h in the dark, the white precipitate filtered, washed by cold absolute ethanol and dried under vacuum (0.215 g; 72%). The solid was recrystallized from acetonitrile.

MS-ESI (m/z): 610.9 ({[Zn(bipyOXA)$_2$]ClO$_4$}$^+$); 386.9 ({[Zn(bipyOXA)]ClO$_4$}$^+$). Elemental *Anal.* Calc. for C$_{24}$H$_{20}$Cl$_2$N$_8$O$_{12}$Zn : C, 38.50; H, 2.69; N, 14.97. Found: C, 38.31; H, 2.63; N, 15.06%. UV(-Tris–HCl, 1 mM, pH 7.5): ε = 3.9×10^4 (λ = 273 nm); ε = 4.2×10^4 (λ = 231 nm) cm^{-1} M^{-1}.

^{1}H NMR (300 MHz, CD$_3$CN) δ (ppm): 8.69–8.37 (m, 4H), 8.31 (t, J = 7.8 Hz, 1H), 8.18 (t, J = 7.8 Hz, 1H), 7.89–7.68 (m, 2H). ^{13}C NMR (75 MHz, CD$_3$CN) δ (ppm): 176.3 (C), 166.5 (C), 150.9 (CH), 150.0 (CH), 142.5 (CH), 142.1 (C), 140.8 (C), 140.6 (CH), 130.3 (CH), 130.0 (CH), 127.2 (CH), 125.1 (CH).

*2.3.1.3. [Ni(bipyOXA)$_2$(H$_2$O)$_2$](ClO$_4$)$_2$, **5c**.* A light green solution of Ni(ClO$_4$)$_2$·6H$_2$O (0.15 g, 0.4 mmol) in absolute ethanol was added drop wise and under constant stirring to a colorless solution of 3,5-bis(2′-pyridyl)-1,2,4-oxadiazole (0.179 g, 0.80 mmol) in absolute ethanol and at room temperature. The mixture was left under stirring for 12 h in the dark, the precipitate filtered, washed by cold absolute ethanol and dried under vacuum (0.244 g; 83%). The solid was recrystallized from acetonitrile.

MS-ESI (m/z): 604.9 ({[Ni(bipyOXA)$_2$]ClO$_4$}$^+$); 380.9 ({[Ni(bipyOXA)]ClO$_4$}$^+$). Elemental *Anal.* Calc. for C$_{24}$H$_{20}$Cl$_2$N$_8$O$_{12}$Ni: C, 38.85; H, 2.72; N, 15.10. Found: C, 38.67; H, 2.68; N, 15.07%. UV(-Tris–HCl 1 mM, pH 7.5): ε = 1.0×10^3 (λ = 340 nm) ; ε = 3.9×10^4 (λ = 275 nm); ε = 4.4×10^4 (λ = 231 nm) cm^{-1} M^{-1}.

2.3.2. PyOXA ligand and its Cu^{II}, Zn^{II} and Ni^{II} complexes

2.3.2.1. 3-(2′-Pyridyl)5-(phenyl)-1,2,4-oxadiazole (pyOXA). 1 g of 2-picolinamidoxime (**2**) (7.3 mmol) and 1.12 g of benzoyl chloride (**6**, 8.03 mmol, d = 1.2 g/mL) were mixed in 120 mL of toluene. 0.64 mL of pyridine (0.63 g, 8.03 mmol, d = 0.98 g/mL) was added and the mixture was left refluxing for 12 h. The residue was chromatographed yielding 0.60 g of 3-(2′-pyridyl)5-(phenyl)-1,2,4-oxadiazole (70%) [20].

^{1}H NMR (300 MHz, CD$_3$CN) δ (ppm): 8.77 (dd, J = 11.8, 7.8 Hz, 1H), 8.30–8.15 (m, 3H), 8.04–7.91 (m, 1H), 7.76–7.59 (m, 3H), 7.59–7.49 (m, 1H). ^{13}C NMR (75 MHz, CD$_3$CN) δ (ppm): 177.1 (C), 169.8 (C), 151.3 (CH), 147.4 (C), 138.3 (CH), 134.1 (CH), 130.4 (CH), 128.9 (CH), 126.8 (CH), 125.1 (C), 124.3 (CH). UV(CH$_3$CN): ε = 2.1×10^4 (λ = 259 nm); ε = 1.8×10^4 (λ = 234 nm) cm^{-1} M^{-1}.

*2.3.2.2. [Cu(pyOXA)$_2$(ClO$_4$)$_2$], **9a**.* A light blue solution of Cu(ClO$_4$)$_2$·6H$_2$O (0.15 g, 0.4 mmol) in absolute ethanol was added drop wise and under constant stirring to a colorless solution of pyOXA (0.178 g, 0.8 mmol) in absolute ethanol and at room temperature. The mixture was left under stirring for 12 h, the precipitate filtered, washed by cold absolute ethanol and dried under vacuum (0.230 g; 81%). The solid was recrystallized from acetonitrile. After 1 week at 4 °C, blue crystals of Cu(pyOXA)$_2$(ClO$_4$)$_2$ suitable for X-ray crystallographic analysis, were obtained.

MS-ESI (m/z): 607.8 ([Cu(pyOXA)$_2$ClO$_4$]$^+$); 385.1 ([Cu(pyOXA)ClO$_4$]$^+$). Elemental *Anal.* Calc. for C$_{26}$H$_{18}$Cl$_2$N$_6$O$_{10}$Cu: C, 44.05; H, 2.56; N, 11.85. Found: C, 44.19; H, 2.35; N, 11.83%. UV(CH$_3$CN): ε = 4.0×10^4 (λ = 259 nm); ε = 4.2×10^4 (234 nm) cm^{-1} M^{-1}.

*2.3.2.3. [Zn(pyOXA)$_2$(ClO$_4$)$_2$], **9b**.* A solution of Zn(ClO$_4$)$_2$·6H$_2$O (0.149 g, 0.4 mmol) in absolute ethanol was added drop wise and under constant stirring to a colorless solution of pyOXA (0.179 g, 0.8 mmol) in absolute ethanol and at room temperature. The mixture was let under stirring for 12 h in the dark but no precipitate was observed. The solution was let for 6 h at −18 °C the precipitate was filtered, washed by cold absolute ethanol and dried under vacuum (0.20 g; 70%). The solid was recrystallized from acetonitrile.

MS-ESI (m/z): 608.9 ([Zn(pyOXA)$_2$ClO$_4$]$^+$); 386.1 ([Zn(pyOXA)ClO$_4$]$^+$). Elemental *Anal.* Calc. for C$_{26}$H$_{18}$Cl$_2$N$_6$O$_{10}$Zn: C, 43.94; H, 2.55; N, 11.82. Found: C, 42.48; H, 2.32; N, 11.37%. UV(CH$_3$CN): ε = 4.4×10^4 (λ = 259 nm); ε = 3.9×10^4 (λ = 236 nm) cm^{-1} M^{-1}.

^{1}H NMR (300 MHz, CD$_3$CN) δ (ppm): 9.02 (d, J = 5.23 Hz, 1H), 8.47–8.25 (dd, J = 4.46, 8.32 Hz, 2H), 8.14–7.93 (dd, J = 4.91, 9.41 Hz, 1H), 7.88–7.60 (m, 3H), 7.49 (t, J = 7.80, 7.80 Hz, 2H). ^{13}C NMR (75 MHz, CD$_3$CN) δ (ppm): 178.7 (C), 165.3 (C), 150.2 (CH), 143.3 (CH), 141.6 (C), 135.1 (CH), 130.3 (CH), 130.1 (CH), 129.5 (CH), 124.8 (CH), 121.2 (C).

2.3.2.4. [Ni(pyOXA)$_2$(ClO$_4$)$_2$], 9c. A light green solution of Ni(ClO$_4$)$_2$ · 6H$_2$O (0.15 g, 0.4 mmol) in absolute ethanol was added drop wise and under constant stirring to a colorless solution of pyOXA (0.179 g, 0.80 mmol) in absolute ethanol and at room temperature. The mixture was left under stirring for 12 h in the dark but no precipitate was observed. The solution was let for 6 h at -18 °C the precipitate was filtered, washed by cold absolute ethanol and dried

Table 1
Crystallographic data for [Cu(pyOXA)$_2$(ClO$_4$)$_2$].

Formula	$C_{26}H_{18}Cl_2N_6O_{10}Cu$
Formula weight	708.90
Crystal color, habit	Light blue, prism
Crystal dimensions (mm)	0.5 × 0.3 × 0.3
Crystal system	triclinic
Space group	$P\bar{1}$
a (Å)	8.103(5)
b (Å)	8.647(5)
c (Å)	10.033(5)
α (°)	86.736(5)
β (°)	86.273(5)
γ (°)	78.892(5)
V	687.6(7)
Z	1
T (K)	293(2)
D_{calc} (g cm^{-3})	1.71
F (0 0 0)	359
μ (mm^{-1})	3.125
Number of observations (all reflections)	4748
Final R (all data)	$R_1 = 0.087$, $wR_2 = 0.115$

Table 2
Selected bond lengths (Å) and angles (°) for [Cu(pyOXA)$_2$(ClO$_4$)$_2$].

Bond lengths	(Å)
Cu–N2	2.007(3)
Cu–N4	2.023(3)
Cu–O4	2.354(3)
Bond angles	(°)
N2A–Cu–N4*	100.03(12)
N2A–Cu–N4	79.97(12)
N2A–Cu–O4	89.34(10)
N2A–Cu–O4*	90.66(10)
N4–Cu–O4	87.45(10)
N4–Cu–O4*	92.55(10)
C5–N4–Cu	113.5(2)
O3–N4–Cu	139.3(2)
Cl1–O4–Cu	130.05(15)

* Symmetry transformations used to generate equivalent atoms: −x,−y,−z + 1.

under vacuum (0.210 g; 75%). The solid was recrystallized from acetonitrile.

MS-ESI (m/z): 602.9 ([Ni(pyOXA)$_2$ClO$_4$]$^+$); 379.9 ([Ni(pyOXA)ClO$_4$]$^+$). Elemental analysis calcd (%) for $C_{26}H_{18}Cl_2N_6O_{10}Ni$: C, 44.35, H, 2.58, N, 11.94; found: C, 44.05, H, 2.74, N, 11.22. UV(CH$_3$CN): $\varepsilon = 4.3 \times 10^4$ ($\lambda = 259$ nm); $\varepsilon = 4.0 \times 10^4$ ($\lambda = 236$ nm) cm^{-1}M^{-1}.

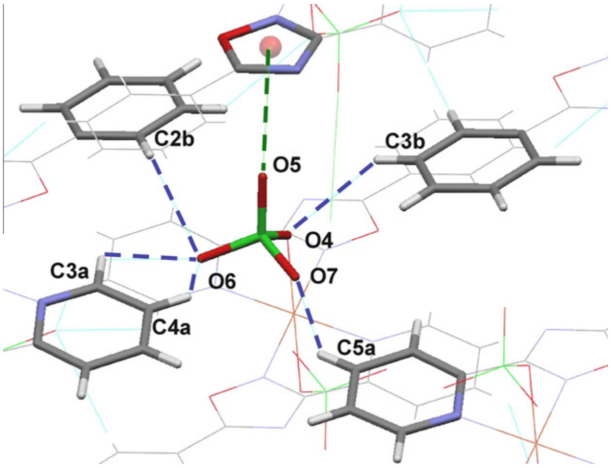

Fig. 4. Anion–π and O···H(–C) interaction motif in [Cu(pyOXA)$_2$(ClO$_4$)$_2$] (**9a**).

3. Results and discussion

3.1. Synthesis and structural characterization

The ligand bipyOXA was synthesised through a solvent-free reaction between amidoxime **2** (Fig. 1) and 2-cyanopyridine (**1**). The same amidoxime, together with benzoyl chloride (**6**, Fig. 2) was used to synthesize the ligand pyOXA. The reaction was conducted in toluene at 130 °C (see Fig. 2). BipyOXA and pyOXA were characterized by elemental analysis, ESI mass spectrometry experiments and NMR (see also Supplementary Information).

All the metal complexes have been synthesised in absolute ethanol by mixing the hydrate metal perchlorate salt and the ligand in a 1:2 molar ratio (see Figs. 1 and 2 and Section 2).

Due to their paramagnetism, it was not possible to acquire noiseless NMR spectra for the copper(II) and the nickel(II) complexes, both presenting an octahedral coordination geometry leading to open shell electron configurations. Suitable crystals for X-ray diffraction analysis were obtained only for the two copper complexes. The crystal structure of the copper(II)–bipyOXA complex

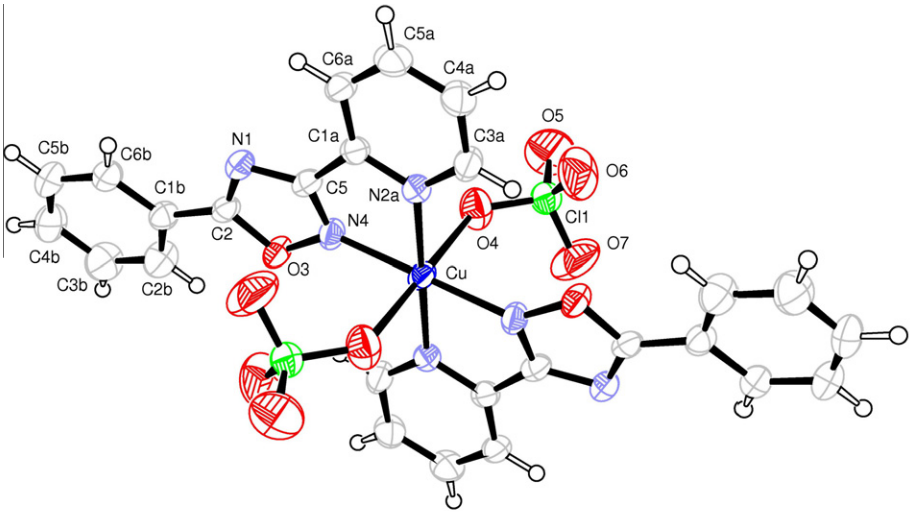

Fig. 3. Crystal structure of the [Cu(pyOXA)$_2$(ClO$_4$)$_2$] (**9a**) complex. Unlabeled atoms are generated by symmetry (−x,−y,−z + 1).

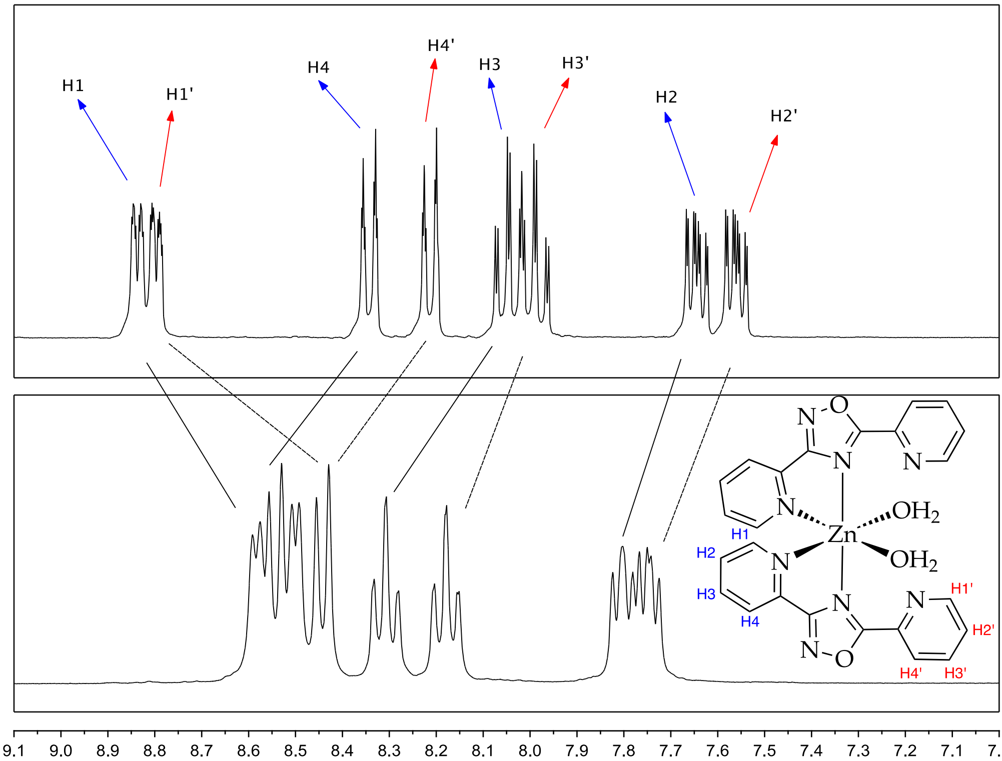

Fig. 5. Partial 1H NMR (CD_3CN, 300 MHz) of bipyOXA (**4**) (upper) and of its Zn^{II} (**5b**) complex.

was recently reported [12], while that of the copper(II)–pyOXA complex is described in the next paragraph. Nevertheless, elemental analysis data confirm that the three metal complexes of bipyOXA contain two hydration water molecules, presumably coordinated as in the structure of the copper(II)–bipyOXA complex.

3.2. X-ray crystallography

Single crystals of $[Cu(pyOXA)_2(ClO_4)_2]$ (**9a**) were obtained by crystallization from acetonitrile. Crystallographic data and selected geometrical parameters are reported in Tables 1 and 2, respectively. Differently than the complex with the ligand bipyOXA **4** [12], in $[Cu(pyOXA)_2(ClO_4)_2]$ copper has no coordinated water molecules (Fig. 3). The metal ion lies at an inversion center and PyOXA acts as a bidentate ligand. Copper is coordinated to two symmetry-related ligands that are in *trans* disposition and to two perchlorate molecules occupying the two axial positions of the octahedral structure. This results in a neutral complex with a consistently lower water solubility compared to $[Cu(bipyOXA)_2(H_2O)_2](ClO_4)_2$. The ligand forms a five-membered Cu–N–C–C–N cyclic moiety with a N–Cu–N angle equal to 79.97(12)°. The Cu–N(pyridine) bond distances are equal to 2.007(3) Å, while Cu–N(oxadiazole) and Cu–O(perchlorate) bond lengths are 2.023(3) and 2.354(3) Å, respectively.

A non-conventional intramolecular hydrogen bond occurs between the endocyclic oxygen of the 1,2,4-oxadiazole moiety and H–C(3a) of the pyridine ring (d $O(3)(x,y,z)\cdots H(3a)(2-x,-y,1-z) = 2.46$ Å), thus forming a six-membered chelate ring.

The crystal packing reveals interesting features (Fig. 4). The oxadiazole ring is involved in an anion–π interaction with the perchlorate, thus suggesting a π-acidic character of this heterocyclic ring. The distance $O(5)\cdots$ring centroid (CpOxa) is 2.985(4) Å and the angle $Cl–O(5)\cdots$CpOxa is 174.8(3)°. The crystal packing also includes intermolecular hydrogen bonding interactions involving the perchlorate anion and different C–H groups: O(4) interacts with H–C(3b) of the phenyl ring (d $O(4)(x,y,z)\cdots H(3b)(1-x,1-y,1-z) = 2.61$ Å), O(6) with the pyridyl H–C(4a) (d $O(6)(x,y,z)\cdots H(4a)(2-x,-1-y,1-z) = 2.66$ Å) and H–C(3a) (d $O(6)(x,y,z)\cdots H(3a)(2-x,-1-y,1-z) = 2.63$ Å), and with H–C(2b) of the phenyl ring (d $O(6)(x,y,z)\cdots H(2b)(x,-1+y,z) = 2.67$ Å), while O(7) interacts with H–C(5a) of the pyridine ring (d $O(7)(x,y,z)\cdots H(5a)(x,y,1+z) = 2.55$ Å).

3.3. NMR spectroscopy

Fig. 5 shows the comparison between the ^1H NMR spectra of the ligand bipyOXA and of its Zn^{II} complex. The complexation of the ligand with the metal center can be argued by the upfield shift of the protons H1 and H1′ and by the downfield shift of the remaining protons.

Analogously, the comparison between the ^1H NMR spectra of the ligand pyOXA, **8**, and its Zn^{II} complex **9b** is shown in Fig. 6. It can be noticed that all the pyridine protons (H1–H4, Fig. 6) are shifted in the left part of the spectrum (downfield shift) while the phenyl protons are slightly shifted in the right part of the spectrum (upfield shift) or remain essentially in the same position. Taking into account that, according to the crystal structure of its Cu^{II} complex (see Fig. 3), the coordinated pyOXA ligands are coplanar, the change in the chemical shift of the pyridine protons to lower fields can be attributed only to zinc coordination. In fact, a low field shift indicates that the electron density around the pyridine protons decreases. The observed chemical shift values of $[Zn(bipyOXA)_2(H_2O)_2]^{2+}$, **5b**, compared to those of the isolated ligand, are more difficult to rationalize, because the two coordinated bipyOXA ligands are not coplanar, in analogy with the structure of $[Cu(bipyOXA)_2(H_2O)_2]^{2+}$, **5a** (see Figs. 1 and 5). In this case, non-bonding (or through space) interactions could indeed contribute to determine the observed shifts. As a matter of fact, concentration dependent ^1H NMR spectra of **5b** in acetonitrile showed an effect on the chemical shift values (see Fig. S2) that suggest the occurrence of displacement of coordinated water by solvent molecules.

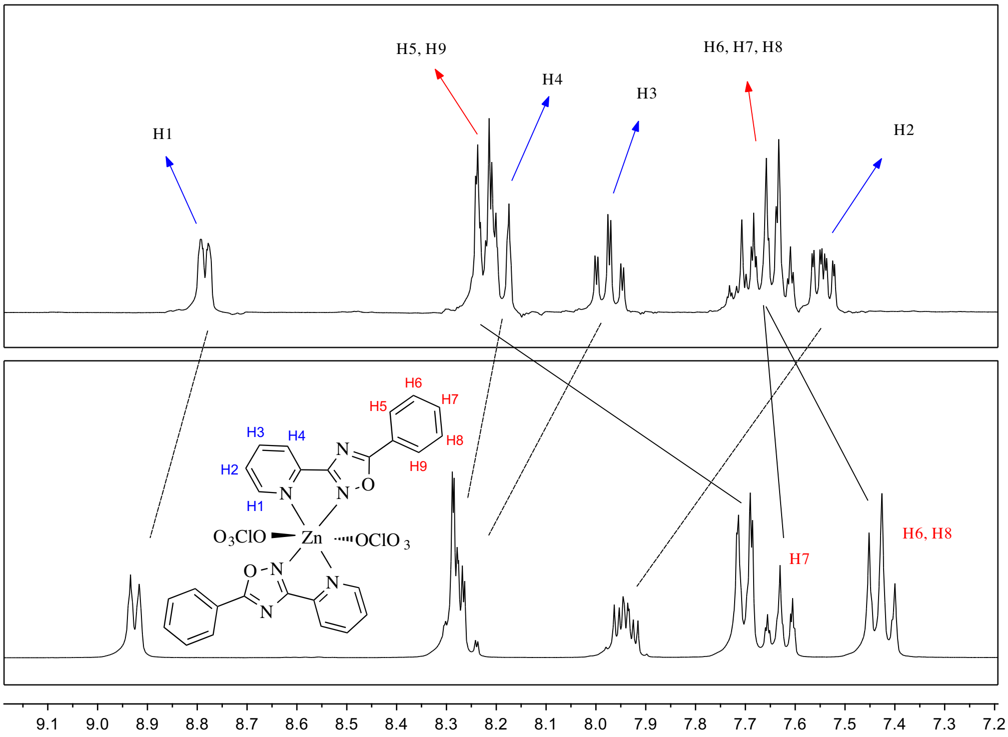

Fig. 6. Partial 1H NMR (CD_3CN, 300 MHz) of bipyOXA (**8**) (upper) and of its Zn^{II} (**9b**) complex.

3.4. ESI mass spectrometry

The ESI(+) mass spectrum of a methanolic solution of $[M(bipyOXA)_2(H_2O)_2](ClO_4)_2$ shows the presence of different ions attributed to $\{[M(bipyOXA)_2](ClO_4)\}^+$, $\{[M(bipyOXA)_2]Cl\}^+$, $[M^I(bipyOXA)_2]^+$ and $\{[M(bipyOXA)](ClO_4)\}^+$, respectively and confirmed by the analysis of their isotopic clusters and by tandem mass spectrometry experiments. Methanolic solutions of $[M(pyOXA)_2(ClO_4)_2]$ show ions due to $[M(pyOXA)_2(ClO_4)]^+$ and to $[M(pyOXA)(ClO_4)]^+$, together with some adducts containing methanol. These data suggest that (i) the species formed in the gas phase are mainly singly positively charged ions while multiply charged species are not detectable; (ii) the two coordinated water molecules of the copper(II)–bipyOXA complex are easily lost; (iii) the copper ion(II) can undergo a reduction process with the formation of Cu^I.

4. Conclusions

The novel complexes $[M(bipyOXA)_2(H_2O)_2](ClO_4)_2$ (M = Ni^{II}, and Zn^{II}) and $[M(pyOXA)_2(ClO_4)_2]$ (M = Ni^{II}, Cu^{II}, and Zn^{II}), were synthesised and structurally characterized in the solid state and in solution.

The pyOXA ligand and its Ni^{II}, Cu^{II} and Zn^{II} complexes are consistently less soluble in water solution than the same metal complexes of bipyOXA.

The agreement among X-ray crystallography, NMR spectroscopy and elemental analysis measurements allow to assign an octahedral coordination geometry to all the investigated metal complexes. However, the two coordinated pyOXA ligands assume a *trans*-coplanar disposition, while the two bipyOXA ligands are in an almost orthogonal arrangement.

Considerations based on the splitting of the d metal orbitals in an octahedral ligand field allow to explain the observed paramagnetism of the d^8 electron configuration of the nickel(II) complexes of both bipyOXA and pyOXA ligands, as determined by the broadening of their NMR spectra.

Appendix A. Supplementary material

CCDC 804195 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via http://www.ccdc.cam.ac.uk/data_request/cif. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.ica.2011.03.057.

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