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Synthesis, Crystal Structure and Antimicrobial Properties of an Anhydrous Copper(II) Complex of Pyridine-2-Carboxylic Acid

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Abstract

A copper(II) complex with picolinic acid as ligand has been synthesised and characterised by elemental analysis, magnetic susceptibility, Fourier transform infrared spectroscopy (FTIR) and ultraviolet-visible spectroscopic techniques. The crystal structure of the complex has been determined by single crystal X-ray diffraction technique and the ligand was found to coordinate through N- and O-atoms. The ligand and the complex were screened for their activity against resistant strains of fungi (*Candida albicans* ATCC P37039, *Candida albicans* 194 B, *Candida glabrata* 44B, *Cryptococcus neoformans*) and bacteria (*Staphylococcus aureus* CIP 7625, *Pseudomonas aeruginosa* CIP 76110, *Salmonella typhi* and *Escherichia coli* ATCC 25922) isolated from humans in Cameroon.

Keywords: Antimicrobial properties, copper(II), picolinic acid, pyridine-2-carboxylic acid, X-ray structure

1. Introduction

Pyridine-2-carboxylic acid (picolinic acid) which is a naturally occurring product of the degradation of tryptophan is a biologically important ligand found in some enzymes. It has metal ion-chelating activity and is an active agent in some drugs (Masui 2001, Beuerle & Pichersky 2002, Kalinowska *et al.* 2007, Kukovec *et al.* 2013). Picolinic acid and its metal complexes has been the subject of intense research activity recently due to their broad spectrum of physiological activity as well as for the design of new metallopharmaceuticals (Yasui *et al.* 2002, Chaudhary *et al.* 2005, Kalinowska *et al.* 2007, Mautner & Massoud 2007, Kukovec *et al.* 2013). It has been shown to bind different metal ions including alkali metals, transition metals and lanthanides (Goher *et al.* 1992, Goher *et al.* 1993, Goher & Mautner 1994, Goher & Mautner 1995, Goher *et al.* 1996, Mautner *et al.* 1997, Barandika *et al.* 1999, Chattopadhyay *et al.* 2003, Mautner & Massoud 2007, Casas *et al.* 2008, Siddiqui 2012, Wang *et al.* 2012). This may be due to the versatile bonding nature of the picolinate ligand. A literature survey of the reported crystal structures of picolinic acid with diverse metal ions indicates picolinic acid exhibits different bonding modes which include monodentate through oxygen atom of the carboxyl group or through its pyridine nitrogen atom and bidentate through nitrogen and oxygen atoms (Yasui *et al.* 2002, Kalinowska *et al.* 2007). The ligand can also form polynuclear complexes in which it acts as a bridge between metal ions (Wu *et al.* 2005, Girginova *et al.* 2007). The N, O-chelating bonding mode and H-bonding between the carboxylate moiety and water molecules are predominant (Kalinowska *et al.* 2007, Kukovec *et al.* 2013).

The crystal structures, chemical properties and biological activities of picolinic acid and some of its metal complexes, have been reported (Goher *et al.* 1992, Goher *et al.* 1993, Goher *et al.* 1993, Goher & Mautner 1994, Goher & Mautner 1995, Goher *et al.* 1996, Mautner *et al.* 1997, Barandika *et al.* 1999, Chattopadhyay *et al.* 2003, Mautner & Massoud 2007, Casas *et al.* 2008, Siddiqui 2012, Wang *et al.* 2012). The crystal structures of polymorphic forms of $Cu(pic)_2$ have also been reported (Zurowska *et al.* 2004, Zurowska *et al.* 2007, Dutta *et al.* 2008). The hydrated copper picolinate, $Cu(Pic)_2.H_2O$ has been synthesised and the x-ray structure of the complex reveals a distorted octahedral shape (Dutta *et al.* 2008, Wang *et al.* 2012). It has in its structure, H-bonded zig-zag chains of intercalated H_2O molecules forming H-bonds between a carbonyl O-atom and a H_2O molecule (Zurowska *et al.* 2007, Dutta *et al.* 2008, Wang *et al.* 2012). The polymorphs of $Cu(pic)_2$ have both a

square planar shape (Zurowska *et al.* 2004) and a distorted octahedral shape (Zurowska *et al.* 2007). The oxidation state, coordination number and structure of the metal-picolinate complexes do affect their physico-chemical and biological properties (Kalinowska *et al.* 2007). For example, picolinic acid complexes of lanthanides (e.g. Sm^{3+} and Tb^{3+}) show interesting photoluminescent behaviour (Girginova *et al.* 2007). Iron, manganese, cobalt, nickel, zinc and copper picolinates do exhibit antimicrobial properties against some pathogens (Kalinowska *et al.* 2007, Oladipo *et al.* 2013). Silver picolinate has been shown to have strong antimicrobial activity against *E. coli*, *B.subtilis* and *S. cerevisiae* (Kalinowska *et al.* 2007). Zn picolinate and $Cr(pic)_3$ have been used as nutritional supplements while oxovanadium(IV) and oxovanadium(V) complexes of picolinic acid and some of its derivatives are very promising candidates for insulinomimetic activity (Kucukbay *et al.* 2006, Lukaski *et al.* 2007, Yasumatsu *et al.* 2007). Picolinic acid has been shown to reduce intramacrophage growth of the *Mycobacterium avium* complex (Pais & Appelberg 2000, Cai *et al.* 2006, Tomioka *et al.* 2007).

The increasing resistance to antibiotics necessitates the search for new and more potent antimicrobial agents. Metal complexes of biologically active ligands are a target for the development of new drugs. We have reported the antimicrobial activity of some metal complexes of the ligands 1,10-phenanthroline and 2,2'-bipyridine (Agwara *et al.* 2010, Ndosiri *et al.* 2013), hexamethylenetetramine (Agwara *et al.* 2012) and 4,4'-bipyridine (Akum *et al.* 2014), where a general increase in antimicrobial activity was observed upon complexation.

In this paper we report the synthesis, X-ray crystal structure of an anhydrous Cu(II) picolinate complex as well as its antimicrobial properties against some resistant fungal and bacterial strains isolated from humans in Cameroon.

2. Method

2.1 Materials

All chemicals were of reagent grade and they were used as supplied without further purification.

2.2 Synthesis of the Complex

A solution of picolinic acid (0.49g; 4 mmol) in 5 mL of ethanol was added drop wise to a stirred solution of NaOH (0.16g; 4 mmol) in 5 mL of distilled water. To this solution was added drop wise a solution of $CuCl_2.2H_2O$ (0.48g; 2 mmol) in 20 mL of ethanol/water (3:1v/v) at room temperature. After stirring for 45 minutes, the resulting blue-green solution was filtered. The filtrate was left for nine days within which time blue crystals suitable for single crystal X-ray diffraction were obtained. These were filtered off, washed with diethyl ether and dried over silica gel in a desiccator under vacuum. *Yield* 64%; M.P. 116 ℃; *Anal. Calcd.:* C, 46.79; H, 2.59; N, 9.10. *Found;* C, 46.64; H, 2.76; N, 9.39. FTIR absorption bands (cm^{-1}): 1629m, 1595m, 1626m, 1374s, 764m, 446s, 295m. UV-vis 503 nm; magnetic moment 1.63 BM

2.3 Characterization Techniques

Elemental analyses (C,H,N) was carried out on a Perkin-Elmer automated model 2400 series II CHNS/O analyser at the University of Zululand (South Africa). The melting point/decomposition temperatures were recorded using the LEIC VMHB Kofler system. Conductivity measurement was carried out in distilled water using a HANNA multimeter H19811-5; pH/◦C/EC/TDS meter at room temperature. The FTIR spectrum was recorded on a Bruker FT-IR tensor 27 spectrophotometer directly on a small sample of the complex in the range 200 - 4000 cm^{-1} while the electronic spectrum was recorded on a Varian, Cary 50 UV-Visible spectrophotometer.

The magnetic susceptibility value of the complex was determined by the Gouy method at room temperature. The calibrant employed was $Hg[Co(SCN)_4]$ for which a magnetic susceptibility of 1.644×10^{-5} cm^3 g^{-1} was taken. Correction for diamagnetism of the constituent atoms was calculated using Pascal's constants (König 1966). The effective magnetic moment value, μ_{eff}, was calculated from the equation:

$$\mu_{eff} = 2.83(\chi_M T)^{1/2} \quad (1)$$

where χ_M is the magnetic susceptibility and T is the absolute temperature.

2.4 X-Ray Crystallography

A suitable single blue crystal with regular trigonal prismatic shape ($0.33\times0.31\times0.28$ mm^3) was selected and mounted on a glass fiber and fixed on a goniometer head. Data collection was performed at room temperature (293 K) on an Xcalibur3 diffractometer equipped with a CCD camera using Mo-Kα radiation (λ = 0.71073 Å) from an enhanced optic X-ray tube operating at 50 kV and 40 mA, and a detector-to-crystal distance of 50 mm, by means of omega scan of width 1 ° and an exposure time of 20 sec. Data integration and numerical absorption corrections were carried out with the *CrysAlis* software package yielding 2560 independent reflections out of the

4844 collected reflections. The final cell parameters were obtained using all measured reflections. The structure was solved by direct methods and full-matrix least-squares techniques based on F^2 values against all reflections and they converge to final $R_1 = 0.063$ for observed reflections ($I > 2\sigma(I)$) and $wR_2 = 0.162$ for all. The relatively high residuals are due to the difficulties encountered during absorption correction and racemic twin refinements. The thermal displacement of all non-hydrogen atoms was refined anisotropically. The H atoms bonded to C atoms were positioned geometrically and refined using a riding model with distance restraints of C–H = 0.93 Å, and with $U_{iso}(H) = 1.2U_{eq}(C)$.

2.5 Antimicrobial Tests

The antimicrobial tests were carried out in the Laboratory of Phytobiochemical and Medicinal Plant Study, University of Yaounde I. The tests were done on eight microorganisms, 4 yeasts, *Candida albicans* ATCC P37039, *Candida albicans* 194 B, *Candida glabrata* 44B, *Cryptococcus neoformans* and 4 bacterial strains *Staphylococcus aureus* CIP 7625, *Pseudomonas aeruginosa* CIP 76110, *Salmonella typhi* and *Escherichia coli* ATCC 25922 obtained from Centre Pasteur Yaoundé, Cameroon. Preliminary screening was carried out using Muller Hinton Agar. The disk diffusion method from the protocol described by the National Committee for Clinical Laboratory Standard (NCCLS, 2004) was used for preliminary screening. Mueller-Hinton agar was prepared from a commercially available dehydrated base according to the manufacturer's instructions. Several colonies of each microorganism was collected and suspended in saline (0.9% NaCl). Then, the turbidity of the test suspension was standardized to match that of a 0.5 McFarland standard (approximately 1.5×10^8 CFU/ml for bacteria or 1×10^6 - 5×10^6 cells/mL for yeast). Each compound or reference was accurately weighed and dissolved in the appropriate diluents (DMSO at 10%, Methanol at 10% or distilled water) to yield the required concentration (2 mg/mL for the compound or 1 mg/mL for the reference drug), using sterile glassware.

Whatman filter paper No. 1 was used to prepare disks approximately 6 mm in diameter, which were wrapped with aluminum paper and sterilized by autoclaving. Then, 25 µl of stock solutions of compound or positive control were delivered to each disk, leading to 50 µg of compound or 25 µg of reference drug.

The dried surface of a Müeller-Hinton agar plate was inoculated by flooding over the entire sterile agar surface with 500 µl of inoculum suspensions. The lid was left ajar for 3 to 5 minutes, but no more than 15 minutes, to allow for any excess surface moisture to be absorbed before applying the drug impregnated disks. Disks containing the complex or reference drugs were applied within 15 minutes of inoculating the MHA plate. Six disks per petri dish were plated. The plates were inverted and placed in an incubator set to 35 ℃. After 18 hours (for bacteria) or 24 hours (for yeasts) of incubation, each plate was examined. The diameters of the zones of complete inhibition (as judged by the unaided eye) were measured, including the diameter of the disk. Zones were measured to the nearest whole millimeter, using sliding calipers or a ruler, which was held on the back of the inverted petri plate. All experiments were carried out in duplicate. The compound was considered active against a microbe if the diameter of the inhibition zone was greater than 6 mm.

3. Results

3.1 Synthesis of the Complex

The reaction of picolinic acid with $CuCl_2.2H_2O$ in a water/ethanol mixture (3:1 v/v) yielded the complex of formula $Cu(Pic)_2$ which has the same molecular formula like that of the complexes $Cu(Pic)_2$ (Zurowska *et al.* 2007) and $Cu(Pic)_2$ (Zurowska *et al.* 2004) previously reported. Table 1 represents the physical data of the complex. The complex, obtained in moderate yield (64 %) has a sharp melting point of 116 ℃ and it undergoes a colour change from blue to brown around this temperature. The molar conductivity value of 60 $\Omega^{-1}cm^2mol^{-1}$ for the $Cu(Pic)_2$ complex corresponds to a non-electrolyte, suggesting the molecular nature of the complex. The complex has a room temperature magnetic moment of 1.63 BM, which is less than the spin-only value of 1.73 BM. This is consistent with the antiferromagnetic exchange coupling between the copper(II) ions (Zurowska *et al.* 2004).

Table 1. Physical data of the complex

Complex	Color	Yield (%)	Decomposition temp (◦C)
$Cu(Pic)_2$ $CuC_{12}H_8N_2O_4$	blue	64	116 (blue to brown)

3.2 Description of the Crystal Structure

Crystal structural data for $Cu(pic)_2$ are summarized in Table 2. The ORTEP view of the crystal structure together with the atom numbering scheme are shown in Fig. 1, the axial Cu-O interactions are shown in Fig. 2, while the packing diagram of the complex seen along the crystallographic a-axis is shown in Fig. 3.

Table 2. Crystal data and structure refinement for $[Cu(Pic)_2]$

Empirical formula	$C_{12}H_8CuN_2O_4$
Formula weight	307.74
Temperature	293(2) K
Wavelength (Mo-Kα)	λ = 0.71073
Crystal system	Triclinic
Space group	P1 (Nr 1)
Unit cell dimensions	
a	5.2044(9) Å
b	7.7996(16) Å
c	8.0936(17) Å
α	66.16(2) °
β	73.160(17) °
γ	70.600(17) °
Unit cell volume	V = 278.80(9) Å^3
Z	1
F_{000}	155
Density (calculated)	D_x = 1.833 Mg m^{-3}
Absorption coefficient	μ = 1.97 mm^{-1}
Crystal size	0.33 ×0.31 × 0.28
Theta range for data collection	θ = 3.3 – 29.0 °
Index ranges	$-7 \le h \le 6$
	$-10 \le k \le 10$
	$-10 \le l \le 10$
Reflections collected	4844
independent reflections	2560 [R_{int} = 0.048]
Observed reflections [$I > 2\sigma(I)$]	2038
Completeness to theta 29.0 °	92%
Absorption correction	Semi-empirical from equivalents
Refinement method	full-matrix least-squares on F^2
Data/restraints/parameters	2560/3/173
Goodness of fit on F^2	1.03
Final R indices [$I > 2\sigma(I)$]	R_1 = 0.0628 , wR_2 = 0.1618
Final R indices (all data)	R_1 = 0.0816 , wR_2 = 0.1463
Largest diff. Peak and hole	1.30 and −0.74 e Å^{-3}
Refinement on F^2	
	H atoms treated by constrained refinement
$R[F^2 > 2\sigma(F^2)]$ = 0.063	$w = 1/[\sigma^2(F_o^2) + (0.087P)^2]$
	where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2)$ = 0.162	$(\Delta/\sigma)_{max}$ = 2.792
S = 1.03	$\Delta\rho_{max}$ = 1.30 e Å^{-3}
2560 reflections	$\Delta\rho_{min}$ = −0.74 e Å^{-3}
173 parameters	Extinction correction: SHELXL,
	$Fc^*=kFc[1+0.001xFc^2\lambda^3/\sin(2\theta)]^{-1/4}$
3 restraints	Extinction coefficient: 0.000 (7)
constraints	Absolute structure: Flack H D (1983), Acta Cryst. A39, 876-881
Primary atom site location: structure-invariant direct methods	Flack parameter: 10 (10)

The complex crystallizes in the triclinic crystal system with space group *P*1 (Nr 1). This is different from the crystal system (monoclinic) and space group ($P2_1/c$) for $Cu(pic)_2$ complexes reported in the literature with similar molecular formulae (Zurowska *et al.* 2004, Zurowska *et al.* 2007). In the crystal structure of the complex, each Cu atom is covalently bonded to two picolinates through N- and O-atoms. The Cu-O (Cu-O1 = 1.953(9) Å, Cu-O2 = 1.954(10) Å) bond lengths are identical while the Cu-N (Cu-N1 = 1.970(14) Å, Cu-N2 = 1.966(14) Å) bond lengths are also similar but slightly longer than the Cu-O distance. These values are similar to those reported in the literature for Cu(II)-picolinate complexes (Zurowska *et al.* 2004, Zurowska *et al.* 2007, Dutta *et al.* 2008). The Cu(II) ion is in a distorted octahedral environment in which the basal plane is occupied by N_2O_2 from two picolinates and elongated in the axial direction by weak Cu-O (Cu-O3 = 2.777 Å; Cu-O5 = 2.822 Å) axial interactions (Fig. 2) between Cu atoms of one plane and carboxylate O-atoms of an adjacent plane. This type of

axial interaction (Cu-O = 2.745 and 2.770 Å) has been reported for a $Cu(pic)_2$ polymorph (Zurowska *et al.* 2007). The axial interaction leads to an infinite 1-D layered structure viewed along the crystallographic a-axis (Fig. 3).

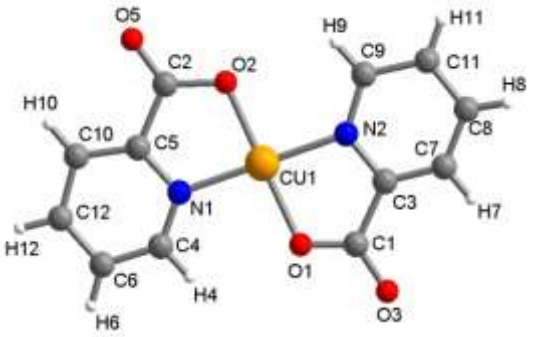

Figure 1. ORTEP view of the complex with atom numbering scheme

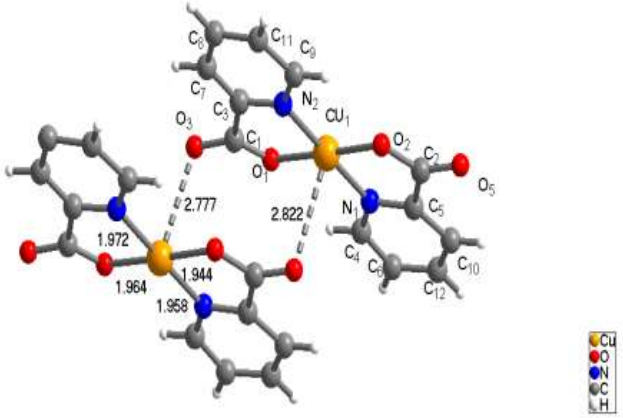

Figure 2. Crystal structure of the complex showing axial Cu-O interactions

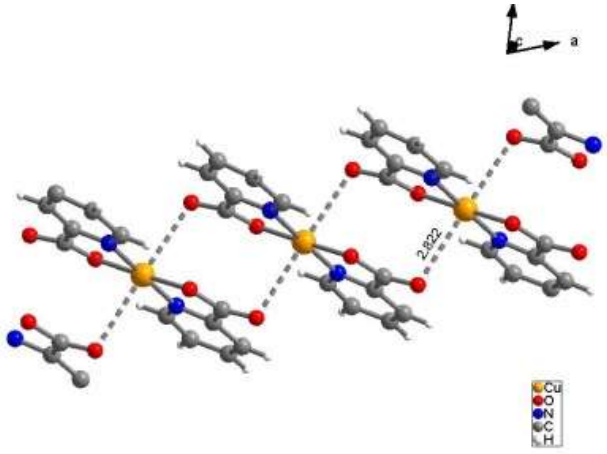

Figure 3. Packing diagram of the complex seen along the crystallographic a-axis

Selected crystal data of two identical complexes found in the literature (Zurowska *et al.* 2004, Zurowska *et al.* 2007) and which are polymorphic to each other are compared with crystal data of the title complex in Table 3. The title complex differs structurally from those in the literature (Zurowska *et al.* 2004, Zurowska *et al.* 2007) in terms of crystal system, space group and unit cell parameters. The methods of syntheses of these complexes also differ.

Table 3. Comparative crystal data of the complexes

Parameter	$Cu(pic)_2$ [this work]	$Cu(2\text{-pca})_2$ (Zurowska *et al.* 2007)	$Cu(2\text{-pca})_2$ (Zurowska *et al.* 2004)
Empirical formula	$C_{12}H_8CuN_2O_4$	$C_{12}H_8N_2O_4Cu$	$C_{12}H_8N_2O_4Cu$
Formula weight	307.74	307.74	307.74
Colour	blue	Blue-violet	violet
Crystal system	Triclinic	Monoclinic	Monoclinic
Space group	P1 (Nr 1)	$P2_1/c$	$P2_1/c$
Unit cell dimensions			
a	5.2044(9) Å	5.163(2)	3.697(7)
b	7.7996(16) Å	24.658(6)	11.989(19)
c	8.0936(17) Å	8.452(2)	11.888(19)
α	66.16(2) °		
β	73.160(17) °	92.22(3)	91.108(14)
γ	70.600(17) °		
Unit cell volume, *V*	278.80(9) $Å^3$	1075.2(6)	526.92(15)
Z	1	4	2

Bond lengths and angles for the complex are presented in Table 4.

Table 4. Bond lengths [Å] and bond angles [°] for $[Cu(pic)_2]$

Cu1—O1	1.953(9)	C4—H4	0.9300
Cu1—$O2^{i}$	1.954(10)	C5—$N1^{v}$	1.25(2)
Cu1—N2	1.966(14)	C5—$C10^{viii}$	1.398(18)
Cu1—$N1^{i}$	1.970(14)	C6—$C4^{ix}$	1.33(3)
O1—C1	1.243(18)	C6—C12	1.44(3)
N1—$C5^{ii}$	1.25(2)	C6—H6	0.9300
N1—$C4^{iii}$	1.30(3)	C7—C8	1.34(2)
N1—$Cu1^{iv}$	1.970(14)	C7—H7	0.9300
O5—C2	1.19(2)	C8—C11	1.32(3)
C1—O3	1.265(18)	C8—H8	0.9300
C1—C3	1.47(2)	C9—N2	1.31(2)
C2—$O2^{v}$	1.323(16)	C9—C11	1.46(2)
C2—C5	1.577(18)	C9—H9	0.9300
C3—C7	1.39(2)	C10—C12	1.37(2)
C3—N2	1.423(17)	C10—$C5^{x}$	1.398(18)
O2—$C2^{ii}$	1.323(16)	C10—H10	0.9300
O2—$Cu1^{iv}$	1.954(10)	C11—H11	0.9300
C4—$N1^{vi}$	1.30(3)	C12—H12	0.9300
C4—$C6^{vii}$	1.33(3)		
O1—Cu1—$O2^{i}$	178.5(5)	$C10^{viii}$—C5—C2	117.5(12)
O1—Cu1—N2	83.7(5)	$C4^{ix}$—C6—C12	116.9(16)
$O2^{i}$—Cu1—N2	95.6(5)	$C4^{ix}$—C6—H6	121.5
O1—Cu1—$N1^{i}$	97.8(5)	C12—C6—H6	121.6
$O2^{i}$—Cu1—$N1^{i}$	82.8(5)	C8—C7—C3	123.3(14)
N2—Cu1—$N1^{i}$	176.7(6)	C8—C7—H7	118.4
C1—O1—Cu1	113.9(7)	C3—C7—H7	118.3
$C5^{ii}$—N1—$C4^{iii}$	118.9(14)	C11—C8—C7	122.4(14)
$C5^{ii}$—N1—$Cu1^{iv}$	114.4(11)	C11—C8—H8	118.8
$C4^{iii}$—N1—$Cu1^{iv}$	125.7(12)	C7—C8—H8	118.8
O1—C1—O3	121.7(12)	N2—C9—C11	122.1(16)
O1—C1—C3	119.2(11)	N2—C9—H9	119.0
O3—C1—C3	118.8(14)	C11—C9—H9	118.9
O5—C2—$O2^{v}$	129.2(17)	C12—C10—$C5^{x}$	114.5(15)
O5—C2—C5	120.2(14)	C12—C10—H10	122.7
$O2^{v}$—C2—C5	110.2(12)	$C5^{x}$—C10—H10	122.7
C7—C3—N2	115.2(14)	C8—C11—C9	116.2(16)
C7—C3—C1	132.8(13)	C8—C11—H11	121.9
N2—C3—C1	111.8(13)	C9—C11—H11	121.9
$C2^{ii}$—O2—$Cu1^{iv}$	115.4(10)	C10—C12—C6	118.9(16)
$N1^{vi}$—C4—$C6^{vii}$	123.9(16)	C10—C12—H12	120.5
$N1^{vi}$—C4—H4	118.0	C6—C12—H12	120.6
$C6^{vii}$—C4—H4	118.2	C9—N2—C3	120.5(14)
$N1^{v}$—C5—$C10^{viii}$	126.1(11)	C9—N2—Cu1	128.8(11)
$N1^{v}$—C5—C2	115.7(12)	C3—N2—Cu1	110.8(12)

Symmetry codes: (i) *x*+1, *y*, *z*; (ii) *x*, *y*−1, *z*; (iii) *x*−1, *y*, *z*−1; (iv) *x*−1, *y*, *z*; (v) *x*, *y*+1, *z*; (vi) *x*+1, *y*, *z*+1; (vii) *x*+1, *y*−1, *z*; (viii) *x*, *y*, *z*−1; (ix) *x*−1, *y*+1, *z*; (x) *x*, *y*, *z*+1.*3.3 FTIR Analyses*

FTIR analysis on a powdered sample of the title compound shows that the characteristic absorption bands of C=O and C-O for the ligand at 1715 cm^{-1} and 1347 cm^{-1}, respectively have disappeared in the complex (Paraj ón-Costa *et al.* 2004). The asymmetric $\upsilon_{as}(COO^-)$ and symmetric $\nu_s(COO-)$ stretching vibrations of the carboxylate group have appeared in the 1629 cm^{-1} and 1374 cm^{-1} regions, respectively (Paraj ón-Costa *et al.* 2004, Zurowska *et al.* 2004, Zurowska *et al.* 2007, Kukovec *et al.* 2008). The difference ($\Delta\nu = \nu_{as} - \nu_{sym}$) of 256 cm^{-1} indicates monodentate carboxylate coordination (Zurowska *et al.* 2004, Zurowska *et al.* 2007). This high value of $\Delta\nu$ (> 200 cm^{-1}) suggests a highly asymmetrical bridging ("pseudo-monodentate" coordination) (Zurowska *et al.* 2007). This observation is consistent with the crystal structure of the complex. The $\upsilon_{C=N}$ band has shifted from 1657 cm^{-1} in the ligand to 1626 cm^{-1} in the complex. Absorption bands at 445 cm^{-1} and 293 cm^{-1} have been assigned to ν(Cu-O) and ν(Cu-N) vibrations, respectively (Paraj ón-Costa *et al.* 2004). The absence of a broad band in the 3100-3500 cm^{-1} region indicates the absence of water in the complex. This observation is consistent with the crystal structure.

3.4 Visible Spectroscopy

The electronic absorption spectrum of the complex shows a single broad band centred at 19880 cm^{-1} (503 nm). This single band is explained by a d-d transition in the Cu(II) ion which has been assigned to $^2E_g \rightarrow {}^2T_{2g}$ transition. The observed band is consistent with an octahedral geometry for Cu(II) complexes (Lee 2003).

3.5 Antimicrobial Tests

The assay compares the inhibition of fungal and bacterial cell growth with known antifungal and antibacterial agents, respectively. The ligand, metal salt and the complex were tested against resistant fungal and bacteria strains isolated from humans in Cameroon. The diameter of inhibition zones are presented in Table 5 and a histogram shown in Fig. 4. The higher the diameter of the inhibition zone (IZ) the more active the compound.

Table 5. Diameter of inhibition zones

Microorganism	**Zone of Inhibition (mm)**						
	Pic	$CuCl_2.2H_2O$	$Cu(pic)_2$	Amp.	Chloram.	Nyst.	Fluco.
***C. albicans ATCC* P37039**	6 ±0	0 ±0	6 ±0	6 ±0	7.5 ±1.5	6 ±0	6 ±0
***C. albicans* 194B**	10 ±2	7 ±0	9.5 ±1.5	30 ±0	14.5 ±0.5	7 ±0	7 ±0
***C. glabrata* 44B**	6 ±0	6 ±0	6 ±0	20.5 ±0.5	6 ±0	6 ±0	6 ±0
C. neoformans	6 ±0	7 ±0	11 ±1	15 ±0	10.5 ±0.5	9.5 ±0.5	6 ±0
E. coli	8 ±0	6 ±0	8 ±0	14.5 ±0.5	12 ±1	6 ±0	6 ±0
P. aeruginosa	6 ±0	9 ±0	10 ±0	15.5 ±0.5	11.5 ±1.5	6 ±0	6 ±0
S. typhi	8 ±1	10 ±0	6 ±0	17 ±1	10 ±0	6 ±0	6 ±0
S. aureus	6 ±0	9 ±0	6 ±0	26.5 ±3.5	14 ±1	10.5 ±0.5	6 ±0

Pic = picolinic acid; ***ATCC:*** *American Type Culture Collection*; Amp. = Ampicillin; Chloram. = Chloramphenicole; Nyst. = Nystatin; Fluco. = Fluconazole.

The ligand showed considerable activity only against the fungus C. *albicans* 194B while the metal complex showed increased activity against most of the pathogens. This indicates that the interaction of metal ions with the ligand plays an important role in enhancing its antimicrobial activity. The complex showed greater activity than the ligand and the metal salt. Generally, the Cu(II) complex exhibited its strongest antifungal effect against the fungi *C. neoformans* and C. *albicans* 194B, while an enhanced antibacterial activity was observed against the bacteria species P. *aeruginosa*. This observation is consistent with results found in the literature (Oladipo *et al.* 2013). This increase in activity could be due to the reduction of the polarity of the metal ion by partial sharing of the positive charge with the ligand's donor atoms so that there is electron delocalization within the metal complex. This may increase the hydrophobic and lipophilic character of the metal complex, enabling it to permeate the lipid layer of the organism killing them more effectively (Chohan *et al.* 2001, Nfor *et al.* 2013).

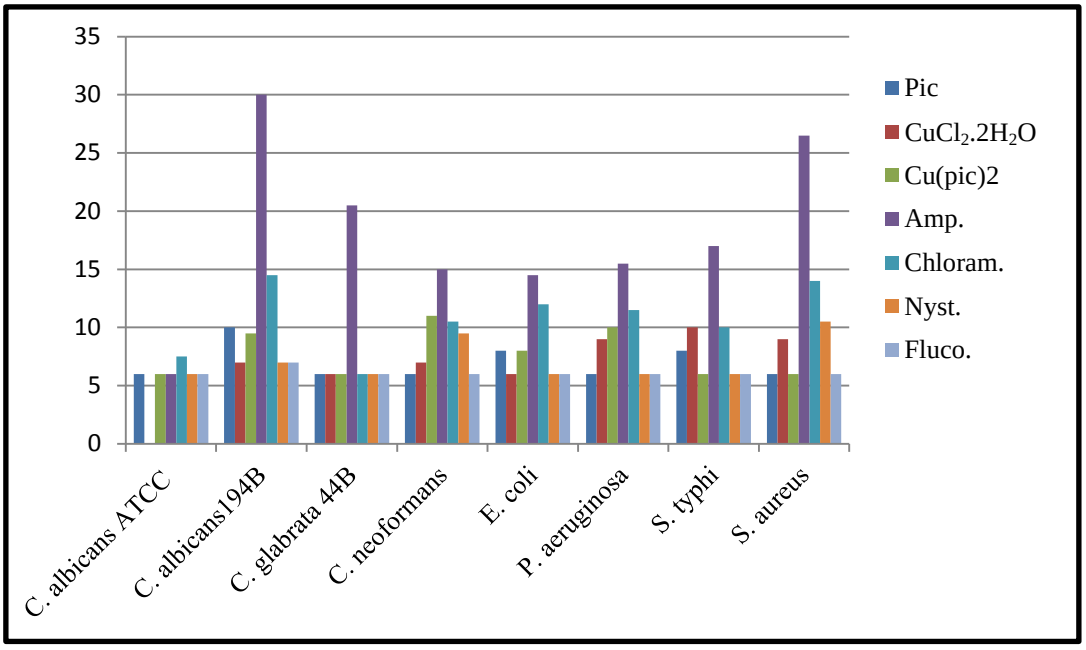

Figure 4. Histogram of inhibition zones

4. Conclusion

The compound $Cu(Pic)_2$ has been synthesised and characterised by elemental analysis, FTIR and XRD spectroscopic techniques. The coordination geometry around the copper(II) ion can be best described as a ‘‘Jahn Teller’’ distorted octahedron with two axial bonds elongated. The complex was screened for its antimicrobial activity against four resistant strains each of fungi and bacteria isolated from humans in Cameroon. The complex showed a greater activity than that of the ligand towards these pathogens.

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Conflict of Interests

The authors declare that there is no conflict of interests regarding the publication of this paper.

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