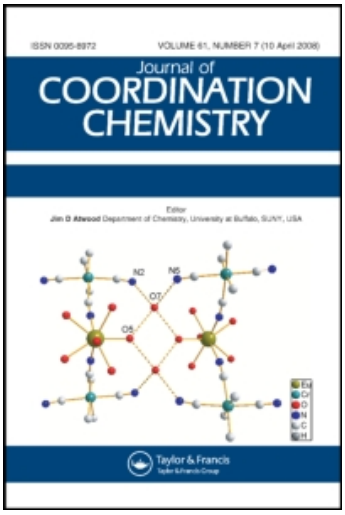

Journal of Coordination Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713455674

Hydrothermal syntheses, crystal structures and antibacterial activities of two Cu(II) complexes with quinolones

Liang-Cai Yu[a]; Zi-Long Tang[a]; Pin-Gui Yi[a]; Sheng-Li Liu[a]; Xia Li[a]
[a] College of Chemistry & Chemical Engineering, Hunan University of Science and Technology, Xiangtan 411201, P.R. China

First published on: 22 September 2010

To cite this Article Yu, Liang-Cai , Tang, Zi-Long , Yi, Pin-Gui , Liu, Sheng-Li and Li, Xia(2008) 'Hydrothermal syntheses, crystal structures and antibacterial activities of two Cu(II) complexes with quinolones', Journal of Coordination Chemistry, 61: 18, 2961 — 2967, First published on: 22 September 2010 (iFirst)
To link to this Article: DOI: 10.1080/00958970801993052
URL: http://dx.doi.org/10.1080/00958970801993052

Journal of Coordination Chemistry
Vol. 61, No. 18, 20 September 2008, 2961–2967

Taylor & Francis
Taylor & Francis Group

Hydrothermal syntheses, crystal structures and antibacterial activities of two Cu(II) complexes with quinolones

LIANG-CAI YU*, ZI-LONG TANG, PIN-GUI YI, SHENG-LI LIU and XIA LI

College of Chemistry & Chemical Engineering, Hunan University of Science and Technology, Xiangtan 411201, P.R. China

(*Received 30 May 2007; in final form 3 December 2007*)

Hydrothermal reactions of ciprofloxacin with $Cu(ClO_4)_2 \cdot 6H_2O$, and ofloxacin with $Cu(CH_3COO)_2 \cdot 4H_2O$, yield two metal complexes: $[Cu(H\text{-}Cip)_2] \cdot (ClO_4)_2 \cdot 6H_2O$ (**1**) and $[Cu(Ofl)_2 \cdot H_2O] \cdot 2H_2O$ (**2**), which were characterized by elemental analysis, IR and single crystal diffraction analyses. Compounds **1** and **2** were screened for antibacterial activities against *Staphylococcus aureus*, *Escherichia coli*, *Candida albicans* and *pseudomonas aeruginosa*.

Keywords: Copper(II); Ciprofloxacin; Ofloxacin; Crystal structure; Antibacterial activity

1. Introduction

Many copper complexes are biologically active due to their chelating ability and positive redox potential. In particular, some copper(II) complexes possess a wide range of biological activity as antivirals, fungicides, pesticides and even tracers [1–4] depending on ligand binding sites. Quinolones are a group of synthetic antibacterial agents structurally related to nalidixic acid, which are very active against aerobic Gram-negative microorganisms but less active against Gram-positive microorganisms [5]. They are extremely useful for the treatment of a variety of infections including urinary tract infections, soft tissue infections, respiratory infections, bone-joint infections, sexually transmitted diseases, prostatitis, acute bronchitis and sinusitis [5]. The most active representatives of this class of compounds, designated as "fluoroquinolones," include ciprofloxacin [H-cip = 1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7(1-piperazinyl)-3-quinolone carboxylic acid], ofloxacin [H-ofl = 9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-7H-pyrido[1,2,3-de][1,4]-benzoxazine-6-carboxylic acid], norfloxacin, enoxacin and perfloxacin. Many drugs possess modified pharmacological and toxicological properties when administered in the form of metallic complexes. Studies on the antibacterial activity of metal compounds with quinolones have been reported [6–11]. It was also established that Cu(II) is effective in induction of the

*Corresponding author. Email: ylcphd@gmail.com

Journal of Coordination Chemistry
ISSN 0095-8972 print/ISSN 1029-0389 online © 2008 Taylor & Francis
DOI: 10.1080/00958970801993052

cytotoxicity of quinolones against leukemia *in vitro*, whereas Mg(II) is not effective. We report here the syntheses and crystal structures of two copper complexes, $[Cu(H\text{-}Cip)_2]\cdot(ClO_4)_2\cdot 6H_2O$ (**1**) and $[Cu(Ofl)_2\cdot H_2O]\cdot 2H_2O$ (**2**).

2. Experimental

2.1. *Materials and apparatus*

$Cu(ClO_4)_2\cdot 6H_2O$ was prepared by reaction of CuO with $HClO_4$; all other chemicals were purchased and used as received without further purification. All solvents were of analytical grade. C, H and N data were obtained using an American PE 2400 CHNS/O elemental analyzer. An infrared spectrum was measured from a KBr pellet using a Nicolet 5DXB system. The single-crystal structure data were collected on Smart Apex CCD with graphite-monochromated Mo-Kα ($\lambda = 0.71073$ Å) radiation at 296(2)K.

Caution: Perchlorate salts of metal complexes are potentially explosive.

2.2. *Preparation of 1 and 2*

Blue block crystalline **1** and **2** were obtained by the hydrothermal reactions of ciprofloxacin with $Cu(ClO_4)_2\cdot 6H_2O$, and ofloxacin with $Cu(CH_3COO)_2\cdot 4H_2O$.

2.2.1. $[Cu(H\text{-}Cip)_2]\cdot(ClO_4)_2\cdot 6H_2O$ (1). An aqueous mixture (15 mL) containing ciprofloxacin (1 mmol, 0.4150 g) and $Cu(ClO_4)_2\cdot 6H_2O$ (1 mmol, 0.02640 g) was placed in a Teflon-lined stainless steel vessel (25 mL) and ethanol (5.0 mL) added to the mixture. The vessel was sealed and heated to 110°C for 4 days. Upon cooling to room temperature, blue block crystals of **1** were obtained. Anal. Calcd. for $C_{34}H_{48}C_{l2}CuF_2N_6O_{20}$: C, 39.39; H, 4.63; N, 8.11. Found: C, 39.16; H, 4.67; N, 8.01. IR (KBr pellet, cm^{-1}): 419(s), 2972(w), 2850(w), 2536(w), 1628(s), 1576(s), 1554(s), 1524(s), 1489(s), 1385(m), 1354(m), 1338(m), 1306(s), 1272(s), 1226(m), 1184(w), 1114(m), 1090(s), 1031(w), 949(m), 897(m), 866(m), 842(m), 816(m), 787(w), 715(w), 627(s), 585(w), 557(w), 544(w), 513(w).

2.2.2. $[Cu(Ofl)_2\cdot H_2O]\cdot 2H_2O$ (2). Complex **2** was prepared by the same procedure as **1** except that ofloxacin and $Cu(CH_3COO)_2\cdot 4H_2O$ was used, blue block crystals of **2** were obtained. Anal. Calcd for $C_{36}H_{38}CuF_2N_6O_{11}$: C, 51.92; H, 4.57; N, 10.10. Found: C, 51.42; H, 4.59; N, 9.83. IR (KBr pellet, cm^{-1}): 3429(s), 2925(w), 1622(s), 1589(s), 1557(w), 1524(s), 1464(s), 1404(m), 1370(w), 1349(w), 1273(s), 1202(w), 1132(w), 1055(w), 1008(w), 983(w), 813(w), 769(w), 747(w), 699(w), 637(w), 518(w).

2.3. *Crystal structure determination*

The X-ray single crystal data collections for **1** and **2** were performed on a Bruker Smart CCD diffractometer equipped with graphite monochromated Mo-Kα radiation

Table 1. Summary of crystallographic data for **1** and **2**.

Parameter	**1**	**2**
Formula	$C_{34}H_{48}C_{12}CuF_2N_6O_{20}$	$C_{36}H_{38}CuF_2N_6O_{11}$
Formula weight	1033.22	832.23
Crystal system	Triclinic	Triclinic
Space group	$P\bar{1}$	$P\bar{1}$
a (Å)	9.2234(3)	9.2972(3)
b (Å)	9.7481(3)	11.2513(3)
c (Å)	11.7164(4)	17.9051(6)
α (°)	91.7960(10)	92.110(2)
β (°)	99.7470(10)	95.405(2)
γ (°)	93.0530(10)	91.743(2)
v (Å^3)	1035.88(6)	1862.30(10)
Z	1	2
$F(000)$	535	854
P_{Calcd} (Mg m^{-3})	1.656	1.477
T (K)	296(2)	296(2)
Reflections collected Independent reflections	8791	16938
Goodness-of-fit on F^2	3646	8835
Final R index [$I>2\sigma(I)$]	1.098	1.087
	$R_1=0.0425$	$R_1=0.0614$
	$wR_2=0.1254$	$wR_2=0.1665$

($\lambda=0.71073$ Å) (table 1). Multi-scan absorption corrections were applied using the SADABS program. The structure was solved by direct methods using the SHELXS-97 program. Refinement on F^2 was performed using SHELXS-97 by full-matrix least-squares with anisotropic parameters for all non-hydrogen atoms. There is disorder of atoms (C29 and C31) in **2**, which were refined with restraints. H atoms of ligands are located in calculated positions and H atoms of coordinated water of **2** were located from the difference Fourier map; H atoms of lattice water of **1** and **2** were not fixed.

2.4. *Antibacterial tests*

Samples were suspended in distilled water and the orbicular filter scrip method was used for testing all samples. The process is similar to that of antibacterial tests of bismuth(III)-quinolone against *Helicobacter pylori* and some other bacteria [13, 14]. All tested strains (*Streptococcus haemolyticus*, *Staphylococcus aureus*, *Escherichia coli* and *Pseudomonas aeruginosa*) were freshly isolated from clinical material and dissolved in 15 mL of sterilized agar culture media at 40°C, and were inoculated on a sterilized culture dish. After being stirred to homodisperse, kept horizontal, and cooled, the culture medium of strains were obtained.

The suspensions of the samples and orbicular filter scrip with diameter of 6 mm were sterilized at 120°C under high pressure. The minimum of suspensions were dropped in filter scrip and put into a culture dish containing culture medium of strains after drying at room temperature. Then the culture dish was placed into a culture box at 37°C for 18 h. The results showed the average ranges (mm) of inhibiting bacteria and are listed in table 2.

Table 2. Comparative *in vitro* activities of two tested compounds against four bacteria.

	Final concentrations of the tested substances ($\mu g\,mL^{-1}$)					
	1			Ciprofloxacin		
	0.5	0.25	0.125	0.5	0.25	0.125
Staphylococcus aureus	22	20	18	23	21	19
E. coli	37	34	33	36	33	31
pseudomonas aeruginosa	28	25	22	27	24	21
Candida albicans	13	12	11	12	10	9

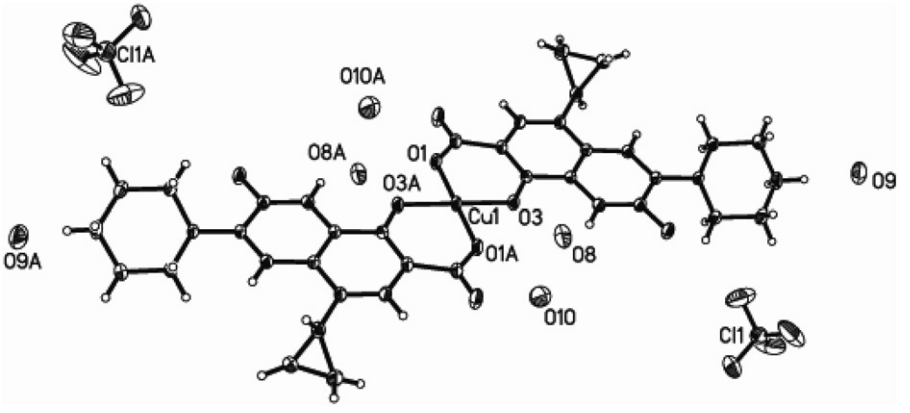

Figure 1. The coordination environment of Cu^{2+} in **1**. The thermal ellipsoids are drawn at 30% probability level.

3. Results and discussion

3.1. *Spectroscopic properties*

IR spectra show two very strong peaks at 1628 and 1489 cm^{-1}, for **1**, and at 1622 and 1464 cm^{-1} for **2**, indicating that the carboxylic acid of quinolones are deprotonated and coordinated to the metal ions as also shown by the absence of a strong ν(COOH) band above 1700 cm^{-1} for ciprofloxacin and 1710 cm^{-1} for ofloxacin. A strong and broad peak at 1090 cm^{-1} for **1** indicates the presence of uncoordinated ClO_4^-.

3.2. *Crystal structure of [Cu(H-Cip)$_2$]·(ClO$_4$)$_2$·6H$_2$O (1)*

The molecular structure of **1** is shown in figure 1 and selected bond lengths and angles are listed in table 3. The crystal structure of **1** is mononuclear with copper(II) coordinated to two ciprofloxcinate ions through a carboxylate oxygen O(1) and carbonyl oxygen O(3), forming a CuO_4 chromophore in a crystallographically planar configuration with two six-membered chelate rings. The Cu(1)–O(1) bond distance (1.9157(19) Å) is slightly shorter than that of Cu(1)–O(3) (1.9360(17) Å); the bond angles of O(1)–Cu(1)–O(3)#1 and O(1)–Cu(1)–O(3) vary from 86.31(8) to 93.69(8), slightly deviating from the normal value of 90°. The protonated N atoms of the

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

Cu(1)–O(1)	1.9157(19)	Cu(1)–O(3)	1.9360(17)
O(1)#1–Cu(1)–O(1)	180.000(1)	O(1)#1–Cu(1)–O(3)	86.31(8)
O(1)–Cu(1)–O(3)	93.69(8)	O(1)#1–Cu(1)–O(3)#1	93.69(8)
O(1)–Cu(1)–O(3)#1	86.31(8)	O(3)–Cu(1)–O(3)#1	180.000(1)

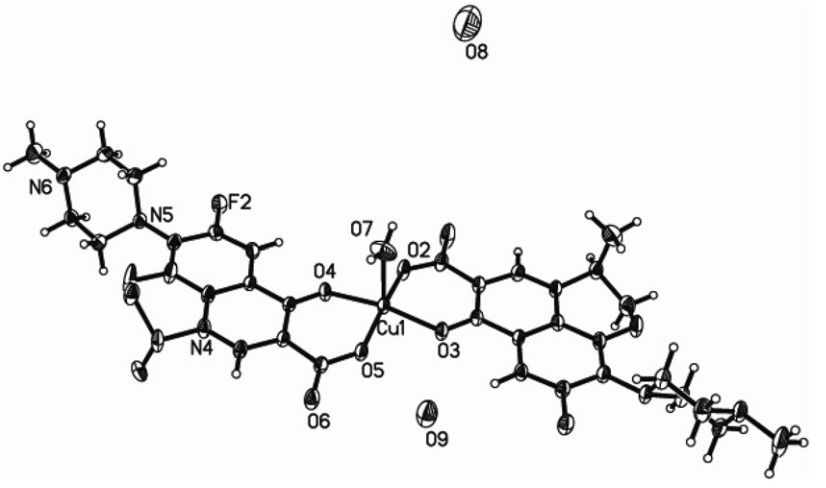

Figure 2. The coordination environment of Cu^{2+} in **2**. The thermal ellipsoids are drawn at 30% probability level.

piperidyl ring lose coordination capacity. The ClO_4^- remains uncoordinated as counter ion. Hydrogen bonds assembly **1** into a very complicated network, all possible hydrogens participate actively, lattice water, the protonated amino group, uncoordinated carboxylate O atoms and perchlorate O atoms.

3.3. *Crystal structure of [Cu(Ofl)$_2$·H$_2$O]·2H$_2$O (2)*

Crystal structure of **2** is different from **1** (see figure 2) with the coordination around Cu(II) in **2** a slightly distorted square based pyramid with ordinary chelate bonding of quinolone to the metal through ring carbonyl [Cu(1)–O(3) = 1.944(2) Å, Cu(1)–O(4) = 1.963(2) Å] and one carboxylic oxygen [Cu(1)–O(2) = 1.907(2) Å, Cu(1)–O(5) = 1.931(2) Å]. Additionally, a water is coordinated to copper(II) [Cu(1)–O(5) = 1.931(2) Å], see table 4. The lattice water, coordinated and uncoordinated carboxylate O atoms participate in hydrogen bonds, thus forming the three-dimensional network.

3.4. *Antibacterial activities*

As shown in table 2, the activity of **1** was similar to that of ciprofloxacin against *Staphylococcus aureus*, *E. coli* and *Candida albicans*. Nevertheless, **1** showed stronger antibacterial activities against *pseudomonas aeruginosa* at all concentrations.

Table 4. Selected bond lengths (Å) and angles (°) for **2**.

Cu(1)–O(2)	1.907(2)	Cu(1)–O(3)	1.944(2)
Cu(1)–O(4)	1.963(2)	Cu(1)–O(5)	1.931(2)
Cu(1)–O(7)	2.221(3)		
O(2)–Cu(1)–O(3)	92.91(10)	O(5)–Cu(1)–O(3)	86.21(9)
O(2)–Cu(1)–O(4)	86.17(10)	O(5)–Cu(1)–O(4)	92.06(10)
O(3)–Cu(1)–O(4)	165.38(11)	O(2)–Cu(1)–O(7)	94.30(12)
O(5)–Cu(1)–O(7)	96.08(11)	O(3)–Cu(1)–O(7)	101.11(14)
O(4)–Cu(1)–O(7)	93.50(13)	O(2)–Cu(1)–O(5)	169.56(11)

Complex **2** is insoluble and shows no bio–activity against the four bacteria. It is difficult to compare these results for the antibacterial activities with those reported by other authors because of the different methodology and strains assayed. Generally, the action mechanism proposed is that transition metal complexes with quinolones interfere with the transport of substrates and ions through the cell membrane resulting in antibacterial activity [15]. Enhancement of ligand activity upon metal coordination from increased liposolubility of the ligand may contribute to the facile transport into the bacterial cell [16]. The better activity of **1** than **2** may be related to the different solubility. However, at this stage it as impossible to find a simple explanation for the antibacterial effect of metal-ciprofloxacin and further studies will be needed to elucidate this phenomenon.

Supplementary material

Crystallographic data for complexes **1** and **2** were deposited to the Cambridge Crystallographic Data Center with deposition numbers CCDC 614254 and 614007, respectively.

Acknowledgements

This work was supported by the Doctor Foundation of Hunan University of Science and Technology (E55106).

References

[1] S. Padhye, G.B. Kauffman. *Coord. Chem. Rev.*, **63**, 127 (1985).
[2] D.X. West, A.E. Liberta, S.B. Chinate, P.B. Sonawane, A.S. Kumbhar, R.G. Yerande. *Coord. Chem. Rev.*, **123**, 49 (1993).
[3] D.X. West, S.B. Padhye, P.B. Sonawane. *Struct. Bond.*, **76**, 1 (1991).
[4] N.J.M. Campbell. *Coord. Chem. Rev.*, **15**, 279 (1975).
[5] O. Paulsen. *Drugs Today*, **23**, 269 (1987).
[6] F. Gao, P. Yang, J. Xie, H. Wang. *J. Inorg. Biochem.*, **60**, 61 (1995).
[7] M. Ruiz, L. Perelló, J. Server-Carrió, R. Ortiz, S. García-Grand, M.R. Díaz, E. Cantón. *J. Inorg. Biochem.*, **69**, 231 (1998).

[8] G.C. Crumplin, J.T. Smith. *Antimicrob. Agents Chemother.*, **8**, 251 (1985).
[9] D.I. Annear. *J. Antimicrob. Chemother.*, **10**, 260 (1982).
[10] E. Cantón, M.T. Jimenez, M.S. Ramón, M. Gobernado. *J. Chemother.*, **3**, 65 (1991).
[11] E. Cantón, M.S. Romón, M.T. Jimenez, J.P. Martinez. *Chemotherapy*, **39**, 394 (1993).
[12] L.C. Yu, Z.F. Chen, L. Hong, C.S. Zhou, H.K. Fun. *J. Coord. Chem.*, **59**, 953 (2006).
[13] I. Turel, L. Golič, P. Bukovec, M. Gubina. *J. Inorg. Biochem.*, **71**, 53 (1998).
[14] Z.F. Chen, S.M. Shi, R.X. Hu, M. Zhang, H. Liang, Z.Y. Zhou. *Chinese J. Chem.*, **21**, 1059 (2003).
[15] I. Turel, A. Golbič, A. KLavžar, B. Philar, P. Buglyó, E. Tolis, D. Rehder, K. Sepčić. *J. Inorg. Biochem.*, **95**, 199 (2003).
[16] D.K. Saha, S. Padhye, C.E. Anson, A.K. Powell. *Inorg. Chem. Commun.*, **5**, 1022 (2002).