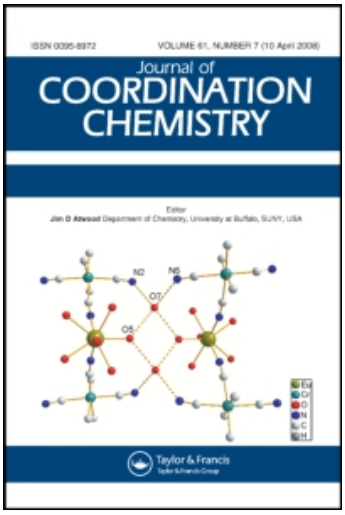

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Syntheses and crystal structure studies of two zinc complexes of enoxacin

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Two zinc complexes of enoxacin were synthesized and their crystal structures were determined. Compound **1**, $[Zn(H\text{-}Eno)\cdot Cl_2]\cdot 3H_2O$ (H-Eno = Enoxacin), crystallizes in the triclinic system, space group $P\bar{1}$, with lattice parameters $a = 8.7731(12)$, $b = 9.4976(14)$, and $c = 13.2033(19)$ Å, $\alpha = 86.319(7)^\circ$, $\beta = 71.912(7)^\circ$, and $\gamma = 80.604(7)^\circ$, $V = 1031.6(3)$ Å^3, $Z = 2$, $D_{Calcd} = 1.631\ Mg\,m^{-3}$; compound **2**, $[Zn(H\text{-}Eno)\cdot(H_2O)_2]\cdot 2NO_3$, also crystallizes in the triclinic system, space group $P\bar{1}$, with lattice parameters $a = 8.751(2)$, $b = 9.014(2)$, and $c = 12.594(3)$ Å, $\alpha = 92.277(14)^\circ$, $\beta = 109.867(12)^\circ$, and $\gamma = 111.469(12)^\circ$, $V = 854.1(3)$ Å^3, $Z = 1$, $D_{Calcd} = 1.684\ Mg\,m^{-3}$.

Keywords: Crystal structure; Zinc complexes; Enoxacin; Zwitterion

1. Introduction

Quinolones are synthetic antibacterial agents, structurally related to nalidixic acid, very active against aerobic Gram-negative microorganisms but less active against Gram-positive microorganisms [1]. 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 [1]. There are a number of reported drug interactions of enoxacin with milk and other foods, antacids and H2-receptor antagonists. Drug interactions have been reported when enoxacin is co-administered with magnesium and aluminium hydroxide, resulting in decreased levels of enoxacin in plasma and urine [2]. There is additional evidence for the formation of complexes with Mg and Ca cations at pH 7.4, the binding sites being first the carbonyl and carboxyl groups, and then the piperazine N4 atom [3]. In our previous articles, we described the syntheses and crystal structures of four metal complexes of the fluoroquinolone class [4–6]. In order to continue our work, we report here the syntheses and crystal structures of the compounds $[Zn(H\text{-}Eno)\cdot Cl_2]\cdot 3H_2O$ (**1**) and $[Zn(H\text{-}Eno)\cdot(H_2O)_2]\cdot 2NO_3$ (**2**).

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2. Experimental

2.1. *Materials and physical measurements*

Enoxacin was purchased from Fluka and all other chemicals were of reagent grade and used as purchased. C, H, and N data were obtained using a PE 2400 CHNS/O elemental analyzer. Infrared spectra were measured from KBr pellets using a Nicolet 5DXB system.

2.2. *Preparation of 1 and 2*

2.2.1. [Zn(H-Eno)·Cl_2]·$3H_2O$ (1). An aqueous mixture (10 mL) containing enoxacin (1 mmol), $ZnCl_2 \cdot 2H_2O$ (1 mmol), was placed in a Teflon-lined stainless steel vessel (25 mL). Ethanol (10 mL) was added to the mixture and the pH was adjusted to 6.5. The vessel was sealed and heated to 110°C for 3 days, cooled to room temperature, and yellow block-shaped crystals of compound **1** were obtained. Anal. Calcd for $C_{15}H_{19}Cl_2FN_4O_6Zn$: C, 35.53; H, 3.75; N, 11.05. Found: C, 35.51; H, 3.76; N, 11.07. IR data: (KBr pellet, cm^{-1}), 3424(s), 3129(s), 2845(m), 1642(s), 1556(s), 1520(s), 1447(s), 1370(m), 1349(m), 1326(m), 1261(m), 1219(w), 1192(w), 1145(w), 1093(w), 1034(w), 943(w), 907(w), 813(s), 789(w), 765(w), 650(w), 558(w), 516(w), 472(w).

2.2.2. [Zn(H-Eno)·$(H_2O)_2$]·$2NO_3$ (2). The procedure is similar to that of **1**, except that $Zn(NO_3)_2$ was used. Anal. Calcd for $C_{30}H_{38}F_2N_{10}O_{14}Zn$: C, 41.57; H, 4.39; N, 16.16. Found: C, 41.56; H, 4.38; N, 16.18. IR data (KBr pellet, cm^{-1}): 3387(m), 3228(m), 2979(w), 2935(w), 2863(w), 1637(s), 1577(s), 1475(s), 1444(s), 1346(m), 1368(m), 1274(s), 1185(m), 1126(m), 1074(w), 1034(w), 1013(W), 969(m), 948(m), 931(m), 907(m), 838(w), 826(w), 819(m), 789(m), 762(m), 742(m), 630(w), 633(m), 552(w), 506(w).

2.3. *Crystal structure determination*

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 ($\lambda = 0.71073$ Å). Multi-scan absorption corrections were applied using SADABS [7]. The structures were solved by direct methods using SHELXS-97 [8]. Refinements on F^2 were performed using SHELXL-97 [9] by full-matrix least-squares with anisotropic parameters for all non-hydrogen atoms. The hydrogens of enoxacin were generated geometrically. H atoms of one lattice water of **1** were not located. The crystal data are given in table 1.

3. Results and discussion

3.1. *Spectroscopic properties*

The IR spectra show two very strong peaks at 1642 and 1477 cm^{-1} for **1** and at 1637 and 1475 cm^{-1} for **2**, indicating that the carboxylic acid of quinolone is deprotonated

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

	1	**2**
Empirical formula	$C_{15}H_{19}Cl_2FN_4O_6Zn$	$C_{30}H_{38}F_2N_{10}O_{14}Zn$
Formula weight	506.61	866.07
Crystal system	Triclinic	Triclinic
Space group	$P\bar{1}$	$P\bar{1}$
Crystal size (mm^3)	$0.50 \times 0.28 \times 0.26$	$0.27 \times 0.10 \times 0.10$
Unit cell dimensions (Å, °)		
a	8.7731(12)	8.751(2)
b	9.4976(14)	9.014(2)
c	13.2033(19)	12.594(3)
α	86.319(7)	92.277(14)
β	71.912(7)	109.867(12)
γ	80.604(7)	111.469(12)
V (Å^3)	1031.6(3)	854.1(3)
Z	2	1
D_{Calcd} ($Mg\,m^{-3}$)	1.631	1.684
$F(000)$	516	448
Temperature (K)	296(2)	296(2)
Wavelength (Å)	0.71073	0.71073
h	$-10 \le h \le 9$	$-5 \le h \le 10$
k	$-11 \le k \le 11$	$-11 \le k \le 10$
l	$-16 \le l \le 16$	$-15 \le l \le 15$
Completeness	99.4	98.1
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.0324$, $wR_2 = 0.0911$	$R_1 = 0.0435$, $wR_2 = 0.1032$
R indices (all data)	$R_1 = 0.0375$, $wR_2 = 0.0946$	$R_1 = 0.0643$, $wR_2 = 0.1444$
Goodness-of-fit on F^2	1.053	1.020

and coordinated to the metal due to the absence of a strong ν(COOH) band at 1725 cm^{-1} for enoxacin. The ketone participates in bonding to the metal shifting to lower wavenumber at 1556 cm^{-1} for **1** and 1577 cm^{-1} for **2**.

3.2. *Crystal structures of 1 and 2*

Figure 1 shows an ORTEP of **1** with atomic numbering scheme. Selected bond distances and angles are given in table 2. The crystal is composed of [Zn(H-Eno)Cl_2] and uncoordinated water. Enoxacin (H-Eno) shows a zwitterion configuration with the carboxylic acid of quinolone deprotonated and coordinated to the metal, while the terminal N(1) of the piperazyl ring of enoxacin is protonated. Zn^{2+} is coordinated by two oxygens and two chlorides, forming a rather distorted tetrahedron. Two oxygens (O_{keto} and $O_{carboxylic}$) from one enoxacin coordinate Zn(1), forming a six-membered ring (Zn1/O1/C3/C2/C1/O2), with bond distances: Zn(1)–O(1) = 1.9584(15) Å and Zn(1)–O(2) = 1.9434(19) Å; obviously the Zn–O_{keto} bond length is longer than the Zn–$O_{carboxylic}$, similar to that of [Zn(Enox)$_2$)] · C_2H_5OH [10]. The difference between the carboxylate distance of O(2)–C(1) and O(3)–C(1) [1.275(3) and 1.281(3) Å] confirms the formation of a bond between the anionic carboxylate and Zn^{2+}; these bond distances are virtually identical in the uncoordinated quinolone ligand. The Zn–Cl bond distances are 2.2251(7) and 2.2302(8) Å; bond angles composed of C1–Zn–C1, O–Zn–C1, and O–Zn–C1 are from 93.88(7) to 114.55(6)° (table 2). There are many intramolecular hydrogen bonds, such as C(6)–H(6)···O(3), C(12)–H(12A)···F(1), and C(15)–H(15B)···N(3). The lattice water, the terminal N of the piperazyl

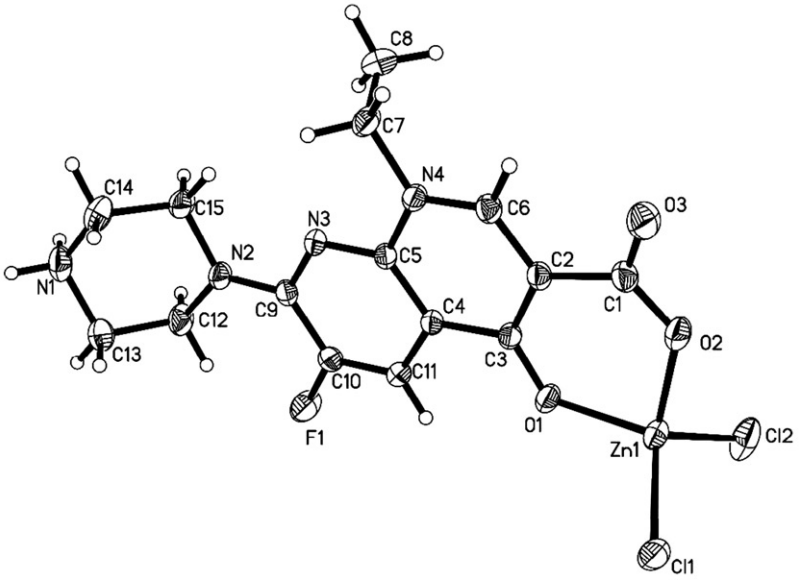

Figure 1. The coordination environment of Zn^{2+} in **1**. Atomic displacement ellipsoids are shown at the 30% probability level.

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

1			
Zn(1)–O(2)	1.9434(19)	Zn(1)–O(1)	1.9584(15)
Zn(1)–Cl(1)	2.2251(7)	Zn(1)–Cl(2)	2.2302(8)
O(1)–C(3)	1.281(3)	O(2)–C(1)	1.275(3)
O(3)–C(1)	1.221(3)		
O(2)–Zn(1)–O(1)	93.88(7)	O(2)–Zn(1)–Cl(1)	113.71(7)
O(1)–Zn(1)–Cl(1)	112.81(5)	O(2)–Zn(1)–Cl(2)	107.61(7)
O(1)–Zn(1)–Cl(2)	114.55(6)	Cl(1)–Zn(1)–Cl(2)	112.81(3)
2			
Zn(1)–O(1)	2.026(3)	Zn(1)–O(3)	2.055(2)
Zn(1)–O(4)	2.125(3)	O(2)–C(3)	1.251(5)
O(1)–C(3)	1.259(4)		
O(1)–Zn(1)–O(3)	87.59(10)	O(1)–Zn(1)–O(3A)	92.41(10)
O(1)–Zn(1)–O(4)	87.20(12)	O(1A)–Zn(1)–O(4)	92.80(12)
O(3A)–Zn(1)–O(4)	89.28(12)	O(3)–Zn(1)–O(4)	90.72(12)
O(1)–Zn(1)–O(4A)	92.80(12)	O(1A)–Zn(1)–O(4A)	87.20(12)

ring of enoxacin, some carbons of enoxacin, uncoordinated carboxylate and coordinated Cl^- form intermolecular hydrogen bonds, such as N(1)–H(1A)···O(5)#1, N(1)–H(1B)···Cl(2)#2, O(5)–H(5A)···Cl(1)#3, O(5)–H(5B)···O(3)#4, C(7)–H(7B)···Cl(1)#3, C(13)–H(13A)···O(4)#5, C(14)–H(14A)···O(2)#3 (table 3), which assemble the complex to 3-D networks (figure 2 and table 3).

The X-ray crystal analysis of **2** revealed that Zn(II) is coordinated in a distorted octahedral geometry with an equatorial plane composed of four oxygens [O(1), O(3), O(1A), and O(3A)], as shown in figure 3. Two oxygens are from the quinolone ring and the others from two carboxylates, forming two stable six-membered

Table 3. Hydrogen bonds for **1** and **2**.

D–H···A	d(D–H)	d(H···A)	d(D···A)	∠(DHA)
1				
N(1)–H(1A)···O(5)#1	0.90	1.94	2.775(3)	154
N(1)–H(1B)···Cl(2)#2	0.90	2.49	3.330(3)	155
O(5)–H(5A)···Cl(1)#3	0.85(3)	2.34(3)	3.174(2)	170(3)
O(5)–H(5B)···O(3)#4	0.84(3)	1.88(3)	2.670(3)	156(6)
C(6)–H(6)···O(3)	0.93	2.34	2.709(3)	104
C(7)–H(7B)···Cl(1)#3	0.97	2.77	3.578(3)	141
C(12)–H(12A)···F(1)	0.97	2.01	2.777(3)	134
C(13)–H(13A)···O(4)#5	0.97	2.53	3.254(5)	131
C(14)–H(14A)···O(2)#3	0.97	2.43	3.368(4)	163
C(15)–H(15B)···N(3)	0.97	2.24	2.704(3)	108
2				
O(4)–H(4)···O(7)#2	0.82	2.08	2.829(6)	152.2
N(1)–H(1A)···O(2)#3	0.90	1.84	2.682(4)	155.0
N(1)–H(1B)···O(2)#4	0.90	1.95	2.807(4)	158.3
O(4)–H(4B)···O(6)#5	0.841(10)	1.927(16)	2.741(5)	162(4)

Symmetry transformations used to generate equivalent atoms: #1: $1-x,-y,1-z$; #2: $-x,-y,1-z$; #3: $1-x,1-y,-z$; #4: $1-x,1-y,1-z$; #5: $x,y,-1+z$ for **1**; #1 $-x,-y,-z$; #2: $x-1,y,z$; #3: $x,y,z+1$; #4: $-x+1,-y+1,-z+1$; #5: $-x+1,-y+1,-z$ for **2**.

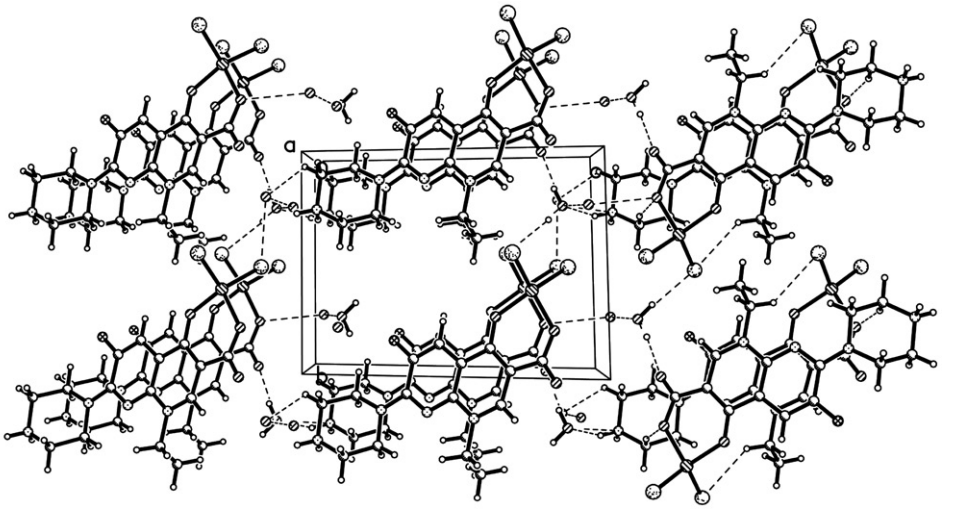

Figure 2. Crystal packing perspective view of **1** showing supramolecular weak aromatic π–π stacking interactions and hydrogen-bonds.

chelating rings. The Zn–O bond distances are in the range 2.026(3)–2.055(2) Å and the bite angle O(1)–Zn(1)–O(3) is 93.88(7)°, as shown in table 2. The carboxylate of enoxacin in **2** is monodentate with one oxygen of carboxylate uncoordinated. The apical positions are occupied by two [O(4) and O(4A)] water molecules with bond distance of 2.125(3) Å. The terminal N of the piperazyl ring of enoxacin, uncoordinated carboxylate, water molecules, and uncoordinated NO_3^- form intermolecular hydrogen bonds, such

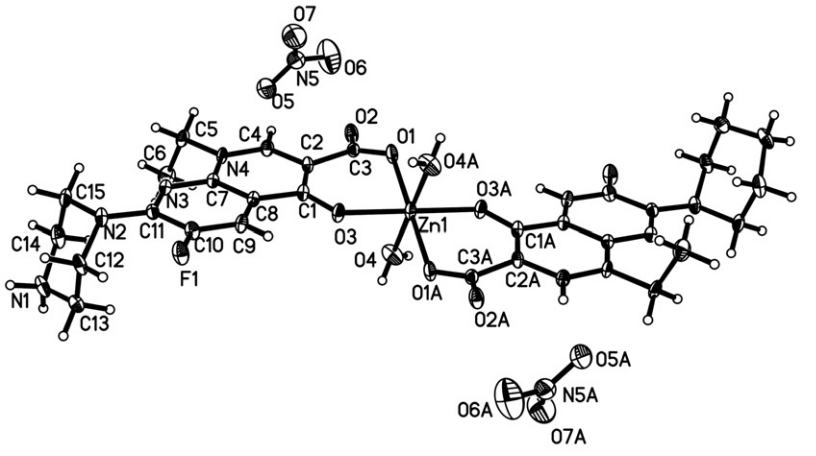

Figure 3. The coordination environment of Zn^{2+} in **2**. The thermal ellipsoids are drawn at 30% probability level.

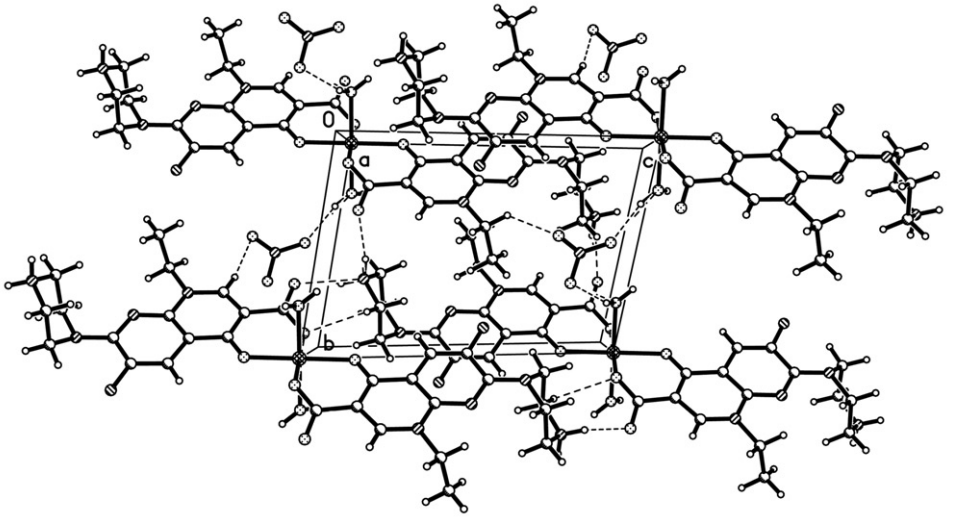

Figure 4. Crystal packing perspective view of **2** along the *a*-axis.

as O(4)–H(4)···O(7)#2, N(1)–H(1A)···O(2)#3, N(1)–H(1B)···O(2)#4, and O(4)–H(4B)···O(6)#5, assembling the complex to a 3-D network (figure 4 and table 3).

Supplementary material

Crystallographic data for **1** and **2** have been deposited with the Cambridge Crystallographic Data Center with deposition numbers CCDC 711869 and 707668, respectively.

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