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COMMUNICATION

The Crystal Structure of DL-Lomenfloxacin Hydrate

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Abstract The DL-lomenfloxacin hydrate is an innersalt, which crystallizes in space group C2/c with cell parameters $a = 22.897(10)$, $b = 8.682(1)$, $c = 18.365(2)$ Å, $\beta = 93.633(9)°$, $V = 3{,}705(3)$ Å^3 and $Z = 8$. The piperazinyl ring adopts a chair conformation, and the quinolone ring is essentially planar. The plane defined by C atoms of the piperazinyl ring is not coplanar with the quinolone ring. The carboxylate group shows two disorder parts, and is not coplanar with the quinolone ring, the dihedral angle between them is 113.8°. The disorder carboxylate group is split into two parts, the planes of which are skewed at the dihedral angles of 24.5 and 21.6° with the plane of the quinolone ring, respectively. The IR of the title compound is measured and studied.

Keywords DL-Lomenfloxacin · Crystal structure · IR

Introduction

In recent years, a number of highly potent broad-spectrum antibacterial agents have been synthesized, and several have been introduced into clinical use. The lomefloxacin is one of the antimicrobial drugs, which has excellent activity against the Gram-positive and Gram-negative bacterial pathogens [1, 2]. This drug stops multiplication of bacteria by inhibiting the reproduction and repair of their DNA [3]. Previously, the structures of norfloxacin and sparfloxacin, which are similar with that of DL-lomenfloxacin, have been reported [4, 5]. There are several specifications of lomenfloxacin including hydrochloride salt and different optical forms in industry and market. The IR of the lomenfloxacin with unknown specification has been reported previously by Wang et al. [6]. This spectrum is exactly the same with that of lomenfloxacin HCl reported by Xu and Zun [7], but shows great difference with that of DL-lomenfloxacin in this study. This arises confusions which is needed to study carefully.

Experimental

The DL-lomenfloxacin HCl and triethylamine in 1:1 molar ratio were dissolved in water by heating to a temperature where a clear solution was resulted, and colorless crystals were obtained by standing the solution for several days at room temperature.

The IR spectrum shows bands: 3,415, 3,083, 1,612, 1,587, 1,519, 1,468, 1,402, 1,369, 1,347, 1,325, 1,274, 1,247, 1,141, 1,115, 1,068, 1,051, 1,019, 1,001, 914, 822, 800, 733, 654, and 513 cm^{-1}.

A single crystal of the title compound was mounted on a Bruker diffractometer with graphite monochromated MoKa radiation. The structure was solved by direct methods and expanded using Fourier techniques. The H atoms involved in hydrogen bonding were deduced from a difference Fourier map, while others were placed in calculated positions. Non-H atoms were refined anisotropically using the SHELX-93 program package [8], while all H atoms were fixed in the refinement. For the disorder water molecules in the crystal, no hydrogen bonds could be localized. The

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Table 1 Crystal data and structure refinement

Compound	$C_{16}H_{18}F_2N_3COOH{\cdot}4.78H_2O$
CCDC deposit no.	700791
Color/shape	Colorless/prism
Chemical formula	$C_{17}H_{19}F_2N_3O_{4.78}$
Cell weight	3,845.74
Temperature	273(2)K
Crystal system	Monoclinic
Space group	C2/c
Cell dimensions	$a = 22.897(3)$, $b = 14.147(4)$, $c = 11.460(3)$ and $\beta = 93.63(1)°$
Volume	3,705(3) Å^3
Z	8
Density (calculated)	1.724 g/cm^3
Absorption coefficient	0.194 mm^{-1}
Diffractometer/scan	Bruker Smart
θ Range for data collection (°)	1.69–26.87
Reflections measured	3,266
Independent/observed	10,915/3,975 [R(int) = 0.0323]
Data/restraints/parameters	3,975/5/286
Goodness of fit on F^2	1.057
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.0966$, $wR_2 = 0.2685$
R indices (all data)	$R_1 = 0.1141$, $wR_2 = 0.2845$
Largest diff. peak and hole	0.857 and −0.355 e Å^{-3}

carboxylate group was in disorder states, and was split into two parts with occupation of 46.3 and 53.7 in refinement, respectively. Scattering factors used were taken from international tables for X-ray crystallography [9]. Crystal data and refinement parameters were summarized in Table 1, and the selected bonds and angles were listed in Table 2, and hydrogen bonds detail was presented in Table 3.

Results and Discussion

As illustrated in Fig. 1, the DL-lomenfloxacin is an inner-salt, where the H atom of the carboxyl group is removed from the parent to the atom N(3) of the piperazinyl ring. Quinolone group itself is planar, except for the piperazinyl moiety and the ethyl group attached to the N(1) atom. The piperazinyl moiety is in a chair form. The dihedral angle between the quinolone and the plane that is consisted with the C atoms of the piperazinyl ring is 113.8°, and the plane of two parts of the disorder carboxylate group make the dihedral angles of 24.5 and 21.6° with the plane of the quinolinyl ring, respectively.

The two C–F bonds in quinolone ring, C(7)–F(2) and C(9)–F(1), have the same distance of 1.349(4) Å, which is different from those [1.356(3) and 1.360(3) Å] in the quinolone ring of the sparfloxacin reported [4]. The six bond lengths of the benzene ring in the quinolone group, falling in range from 1.357(4) to 1.414(4) Å, are abnormal, which indicates that the C–C bond lengths are not equal to the normal bond lengths of the benzene ring [1.390 Å]. These bond distances are reported to be in the range [1.389(3)–1.430(2) Å] in case of a quinolone group [4], hence deviation from the normal benzene ring geometry.

Table 2 Selected bond lengths [Å] and angles [°]

Atoms	Lengths	Atoms	Lengths
F(1)–C(9)	1.349(4)	C(1)–C(2)	1.499(8)
F(2)–C(7)	1.349(4)	C(2)–C(6)	1.370(5)
O(1)–C(1)	1.265(12)	C(2)–C(3)	1.428(4)
O(2)–C(1)	1.258(9)	C(3)–C(4)	1.477(4)
O(3)–C(3)	1.246(4)	C(4)–C(10)	1.390(4)
N(1)–C(6)	1.345(4)	C(4)–C(5)	1.408(4)
N(1)–C(5)	1.393(4)	C(5)–C(7)	1.414(4)
N(1)–C(16)	1.486(4)	C(7)–C(8)	1.381(5)
N(2)–C(8)	1.411(4)	C(8)–C(9)	1.402(5)
N(2)–C(11)	1.448(5)	C(9)–C(10)	1.357(4)
N(2)–C(14)	1.460(4)	C(11)–C(12)	1.496(5)
N(3)–C(13)	1.489(4)	C(12)–C(15)	1.498(5)
N(3)–C(12)	1.499(5)	C(13)–C(14)	1.509(4)
		C(16)–C(17)	1.497(7)
Atoms	**Angles**	**Atoms**	**Angles**
O(2)–C(1)–O(1)	121.9(13)	O(3)–C(3)–C(2)	125.7(3)
O(2)–C(1)–C(2)	118.7(16)	O(3)–C(3)–C(4)	119.2(3)
O(1)–C(1)–C(2)	117(2)	C(2)–C(3)–C(4)	115.1(3)
C(6)–N(1)–C(5)	118.4(3)	C(10)–C(4)–C(5)	120.1(3)
C(6)–N(1)–C(16)	116.5(3)	C(10)–C(4)–C(3)	117.8(3)
C(5)–N(1)–C(16)	125.1(3)	C(5)–C(4)–C(3)	122.1(3)
C(8)–N(2)–C(11)	116.0(3)	N(1)–C(5)–C(4)	118.8(3)
C(8)–N(2)–C(14)	119.7(3)	N(1)–C(5)–C(7)	124.2(3)
C(11)–N(2)–C(14)	112.7(3)	C(4)–C(5)–C(7)	116.9(3)
C(13)–N(3)–C(12)	112.0(3)	N(1)–C(6)–C(2)	127.0(3)
C(6)–C(2)–C(3)	118.4(3)	F(2)–C(7)–C(8)	116.4(3)
C(6)–C(2)–C(1)	117.3(10)	F(2)–C(7)–C(5)	120.0(3)
C(3)–C(2)–C(1)	124.2(9)	C(8)–C(7)–C(5)	123.6(3)
C(7)–C(8)–C(9)	116.2(3)	N(2)–C(11)–C(12)	110.9(3)
C(7)–C(8)–N(2)	124.9(3)	C(11)–C(12)–C(15)	114.3(4)
C(9)–C(8)–N(2)	118.8(3)	C(11)–C(12)–N(3)	111.1(3)
F(1)–C(9)–C(10)	120.1(3)	C(15)–C(12)–N(3)	110.3(3)
F(1)–C(9)–C(8)	117.4(3)	N(3)–C(13)–C(14)	111.0(3)
C(10)–C(9)–C(8)	122.6(3)	N(2)–C(14)–C(13)	107.8(3)
C(9)–C(10)–C(4)	120.6(3)	N(1)–C(16)–C(17)	112.5(4)

Table 3 Hydrogen bonds (distance, Å; angle, °)

D–H···A	D–H	H···A	D···A	D–H···A	Symmetry code
N3–H3A···O2	0.863	1.974	2.832	172.63	$x + 1/2, -y + 1/2, +z - 1/2$
N3–H3A···O2′	0.863	1.921	2.778	172.08	$x + 1/2, -y + 1/2, +z - 1/2$
N3–H3B···O2	0.916	2.191	2.844	127.63	$-x + 1/2, +y + 1/2, -z + 1/2$
N3–H3B···O3	0.916	2.057	2.860	145.55	$-x + 1/2, +y + 1/2, -z + 1/2$
C6–H6···O6	0.93	2.49	3.404	168.02	
C12–H12···O1	0.98	2.57	3.271	128.05	$x + 1/2, -y + 1/2, +z - 1/2$
C12–H12···O1′	0.98	2.37	3.072	127.84	$x + 1/2, -y + 1/2, +z - 1/2$
C14–H14A···O3	0.97	2.44	3.380	164.19	$-x + 1/2, +y + 1/2, -z + 1/2$
C14–H14B···O3	0.97	2.50	3.243	133.31	$-x + 1/2, +y + 1/2, -z + 1/2$
C16–H16A···O6	0.97	2.49	3.354	147.74	
C16–H16B···F1	0.97	2.47	3.157	127.48	$-x + 1/2, +y + 1/2, -z + 1/2$

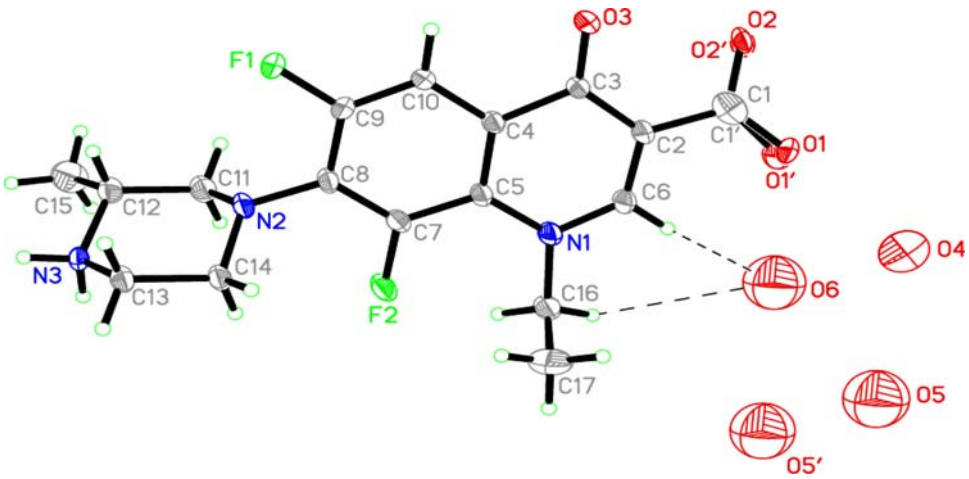

Fig. 1 Molecular structure of DL-lomenfloxcin showing 40% probability displacement ellipsoids

In the molecule of the DL-lomenfloxacin, the eight C–N bonds can be divided into three groups. Five bond lengths, falling in the range from 1.448(5) to 1.499(5) Å, are characterized of normal C–N single bonds. Two short C–N bonds, C(5)–N(1) [1.393(4) Å] and C(6)–N(1) [1.345(4) Å], and the other short C–N bond, C(8)–N(2) [1.411(4) Å], arises from the conjugation of the lone pair of electron on and N1 and N2 with the quinolone group, respectively. The bond angles around N1 and N2 are different.

In DL-lemenfloxacin, the bond lengths of C(1)–O(2) and C(1)–O(1) [1.258(9) and 1.265(12) Å] in the disorder carboxylate group are little longer than the C(3)–O(3) bond length [1.246(4) Å] which is the shortest length, and are in good agreement with the mean value observed for C–O bonds in carboxylate ions [1.268(4) and 1.253(4) Å, respectively] reported [5].

Figure 2 shows the crystal packing of the DL-lomenfloxacin viewed along the *b* axis. The protonated N(3) atom of the piperazinyl group is involved in hydrogen bonding with the quinolone carbonyl O(3) and the O(2) atom of the carboxylate group, and the structure exhibits intermolecular hydrogen bonds of the type C–H···O, the stability of the crystal structure can be accounted by these hydrogen bonds, and the intermolecular H-bonds link the neighboring molecules to form helical chains.

Figure 3 shows the IR spectrum of the title compound. The broad band from 3,300 to 3,500 cm^{-1} centering at 3,415 cm^{-1} is due O–H stretching of the disorder water molecules, and the strong peak at 3,083 cm^{-1} may be attributed to N–H stretching of the protonated piperazinyl group. It is interesting to note that there exist broad band ranging from 2,759 to 2,458 cm^{-1} for the lomenfloxacin

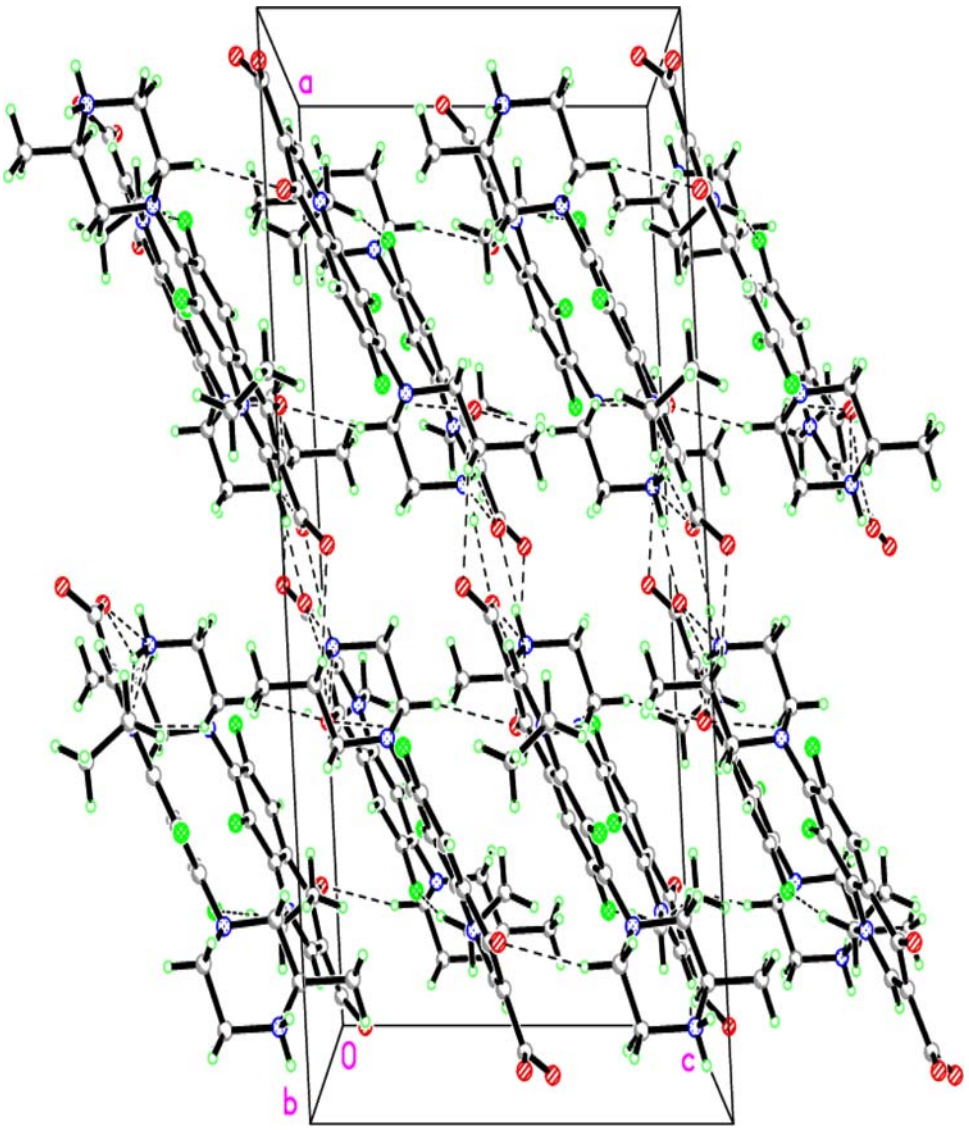

Fig. 2 Crystal packing viewed along the *b* axis. H-bonding for water molecules are omitted for clarity, and others are shown as *dashed lines*

[6], which is characteristic of *v*as(NH) stretching vibration; and that there is no such band for the DL-lomenfloxacin in this study. There strong peak of the title compound at 1,612 cm^{-1} may be attributed to C=O of the quinolone ring stretching, which as is conjugating with the benzene ring and carboxylate. There is also a moderate peak at 1,587 cm^{-1} which may be attributed to C=O of the carboxylate. There are two different C=O in the lomenfloxacin molecule, and there must have two different C=O peaks in the IR spectrum of lomenfloxacin. But, there is only one C=O peak at 1,725 cm^{-1} for lomenfloxacin in Wang's study [6]. In infrared spectra, the carboxylic group always show up at much higher wave number than the carboxylate does, the former ranging from 1,725 to 1,700 cm^{-1} and the later ranging from 1,550 to 1,630 cm^{-1}. The peak at 1,725 cm^{-1} is consistent with lomenfloxacin HCl where the carboxyl group may remain its carboxylic form. But, it is contradicted to lomenfloxacin, where, as it is revealed in this study, the carboxyl group turns to be a carboxylate. The CH_2 deformation vibration appears at 1,468 cm^{-1}. Besides, DL-lomenfloxacin has a moderate broad band in the region of 1,001–1,141 cm^{-1} which can be assigned to benzene and pyridine ring breathing. The bands between 654 and 822 cm^{-1} which is due to C–N and C–F stretching, are moderate. There is a moderate peak at 513 cm^{-1}, which attributes to ring deformation. In a sum, the title compound is different from Wang's and Xu's sample.

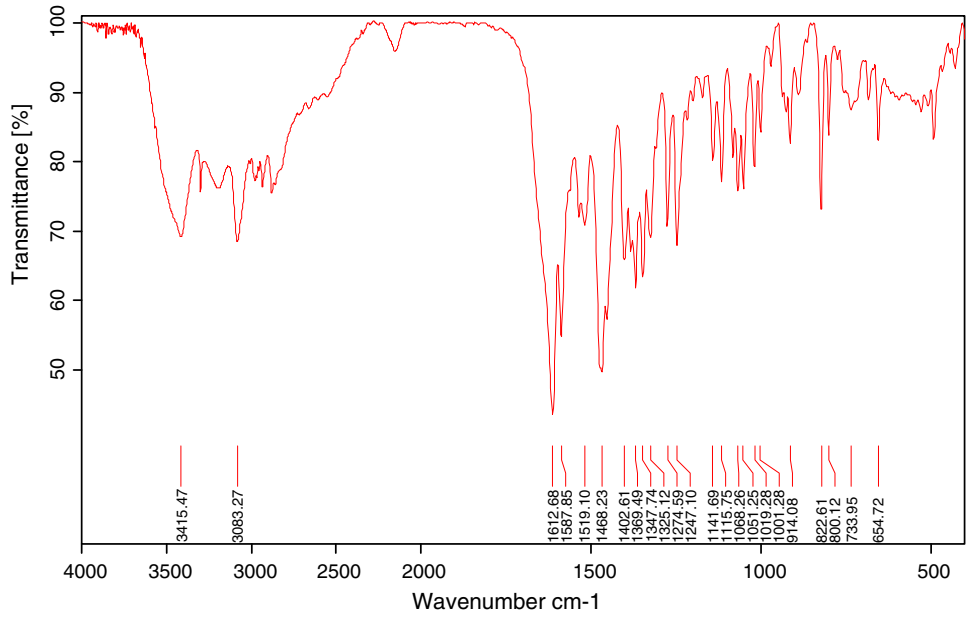

Fig. 3 IR spectrum of DL-lomefloxacin hydrate

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