Acta Crystallographica Section E
Structure Reports Online
ISSN 1600-5368

2-Hydroxyethanaminium enrofloxacinate

Hong-Xiang Sun,[a,b]* Yuan Li[a] and Yuan-Jiang Pan[b]

[a]College of Animal Sciences, Zhejiang University, Hangzhou 310029, People's Republic of China, and [b]Department of Chemistry, Zhejiang University, Hangzhou 310027, People's Republic of China

Correspondence e-mail: sunhx@zju.edu.cn

Key indicators

Single-crystal X-ray study
T = 298 K
Mean σ(C–C) = 0.002 Å
R factor = 0.037
wR factor = 0.102
Data-to-parameter ratio = 12.7

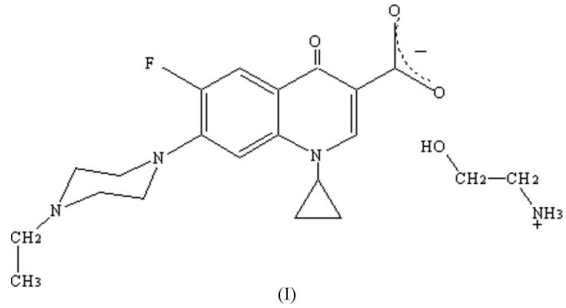
For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

Received 24 May 2004
Accepted 31 August 2004
Online 11 September 2004

The title compound hydroxyethylammonium enrofloxacinate [systematic name: 2-hydroxyethanaminium 1-cyclopropyl-7-(4-ethylpiperazin-1-yl)-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylate], $C_2H_8NO^+\cdot C_{19}H_{21}FN_3O_3^-$, contains enrofloxacinate anions and 2-hydroxyethanaminium cations. The quinoline ring system in the anions is essentially planar. The piperazine moiety adopts a chair conformation. The cations lie parallel to each other about inversion centers. The structure is stabilized by strong intermolecular hydrogen bonds involving the carbonyl, carboxyl and terminal piperazine N groups of the anion and the hydroxyl and ammonium groups of the cation.

Comment

Fluoroquinolone antibiotics display a wide spectrum of activity against both gram positive and gram negative bacteria. These antibiotics stop the multiplication of bacteria by inhibiting the reproduction and repair of their DNA (Bauditz, 1990; Cinquina *et al.*, 2003). 4-Oxo and 3-carboxylic groups are essential for antibacterial activity of quinolones (Dax, 1997). According to the most convincing and commonly accepted model of the molecular mechanism of the antibacterial activity of quinolones (Shen *et al.*, 1989), the two groups interact with guanine of bacterial DNA in the gyrase–DNA complex (Główka *et al.*, 2003; Souza *et al.*, 2004). The same groups are also capable of intramolecular hydrogen-bond formation, which enables a quinolone to mask the acidic H atom of the carboxylic acid group and thus enhance permeability of quinolones through lipophilic biological membranes. On the other hand, the intramolecular hydrogen bond decreases the concentration of quinolone forms capable of a specific interaction with DNA. Therefore, the analysis of various interactions in fluorquinolone drugs is of particular importance to drug action. Enrofloxacin is a fluoroquinolone marketed for use in veterinary medicine. We report here the crystal structure of enrofloxacin in its anionic form, enrofloxacinate with 2-hydroxyethanaminium as the cation.



(I)

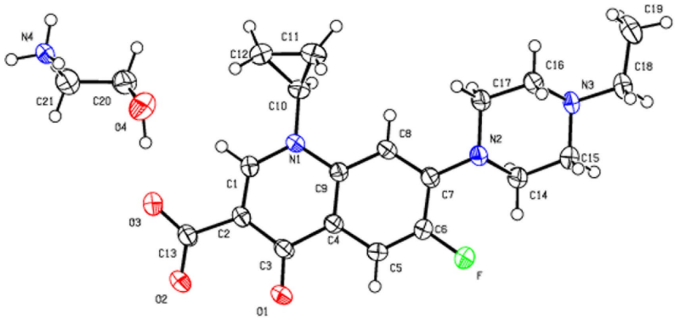


Figure 1
A view of (I), with the atomic numbering scheme. Displacement ellipsoids are drawn at the 50% probability level.

The title compound, (I), was obtained as colorless prismatic crystals in the triclinic space group $P\overline{1}$. X-ray data allowed determination of the relative stereochemistry of the molecules in the crystal studied; a view of the structure, with the numbering scheme, is shown in Fig. 1, and selected dimensions are given in Table 1. The structure is composed of an enrofloxacinate anion and a 2-hydroxyethanaminium cation. The quinoline ring system is essentially planar and the cyclopropyl ring makes an angle of 54.6 (5)° with the quinolonyl unit. The piperazinyl moiety adopts a chair conformation. The 2-hydroxyethanaminium cations lie parallel to each other about inversion centers.

The carbonyl (O1), carboxyl (O2 and O3) and terminal piperazinyl N atoms of the cation, and the hydroxyl (O4) and aminium (N2) atoms of the cation, participate in hydrogen bonding. The aminium and hydroxyl groups of the 2-hydroxyethanaminium cation serve as hydrogen-bond donors, and carbonyl and carboxyl O atoms and terminal piperazinyl N atoms as hydrogen-bond acceptors (Table 2), resulting in five intermolecular hydrogen bonds. As the enrofloxacin is present in its deprotonated anionic form in this crystal structure there is no H atom available to form the strong intramolecular hydrogen bond between carbonyl and carboxyl groups observed in most cases of fluoroquinolone crystal structures found in the literature (Prasanna & Guru Row, 2001; Główka *et al.*, 2003). The enrofloxacinate anion and 2-hydroxyethanaminium cation are linked by O4—H4O···O3 hydrogen bonds. The other hydrogen bonds are between adjacent symmetry-equivalent ions. In the solid state, the molecules are linked by N4—H4*C*···O1^{i}, N4—H4*C*···O2^{i} and N4—H4*B*···O2^{ii} [symmetry codes: (i) $1+x$, y, z; (ii) $2-x$, $1-y$, $-z$] hydrogen bonds to form two-dimensional sheet-like structures, which stack approximately perpendicular to the *b* axis. The sheet-like structure is further stabilized by N4—H4*A*···N3($1+x$, y, $z-1$) hydrogen bonds.

Experimental

The sample of enrofloxacin was obtained from Haizheng Pharma Ltd Co., Zhejiang, China. Crystals of enrofloxacin and ethanolamine suitable for diffraction work were grown from an aqueous solution of ethanolamine by slow evaporation.

Crystal data

$C_2H_8NO^+\cdot C_{19}H_{21}FN_3O_3^-$
M_r = 420.48
Triclinic, $P\overline{1}$
a = 9.791 (2) Å
b = 9.858 (1) Å
c = 12.274 (2) Å
α = 69.12 (1)°
β = 75.74 (1)°
γ = 89.54 (1)°
V = 1068.5 (3) Å^3
Z = 2
D_x = 1.307 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 34 reflections
θ = 4.3–15.9°
μ = 0.10 mm^{-1}
T = 298 (2) K
Prism, colorless
0.54 × 0.32 × 0.24 mm

Data collection

Siemens *P*4 diffractometer
ω scans
Absorption correction: none
4509 measured reflections
3932 independent reflections
2733 reflections with $I > 2\sigma(I)$
R_{int} = 0.009
θ_{max} = 25.5°
$h = 0 \rightarrow 11$
$k = -11 \rightarrow 11$
$l = -14 \rightarrow 14$
3 standard reflections
every 97 reflections
intensity decay: 5.3%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.037
$wR(F^2)$ = 0.102
S = 0.95
3932 reflections
309 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.06P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.20 e Å^{-3}
$\Delta\rho_{min}$ = −0.15 e Å^{-3}
Extinction correction: *SHELXL*97
Extinction coefficient: 0.041 (3)

Table 1
Selected geometric parameters (Å, °).

F—C6	1.3639 (17)	N1—C9	1.3948 (18)
O1—C3	1.2405 (18)	N1—C10	1.4564 (18)
O2—C13	1.2495 (18)	N2—C7	1.4071 (18)
O3—C13	1.2522 (19)	N3—C18	1.4805 (18)
N1—C1	1.3539 (18)	N4—C21	1.480 (2)
C1—N1—C9	119.35 (12)	C12—C10—C11	60.02 (12)
C1—N1—C10	119.96 (12)	C12—C11—C10	59.90 (12)
C9—N1—C10	120.60 (12)	C10—C12—C11	60.08 (12)
N1—C1—C2	125.49 (14)	O2—C13—O3	124.18 (14)
O1—C3—C2	125.29 (13)		
C1—N1—C10—C12	41.7 (2)	C9—N1—C10—C11	−71.92 (19)
C9—N1—C10—C12	−141.65 (16)	C3—C2—C13—O2	−23.4 (2)
C1—N1—C10—C11	111.40 (17)	C1—C2—C13—O3	−22.3 (2)

Table 2
Hydrogen-bonding geometry (Å, °).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O4—H4O···O3	0.98 (3)	1.69 (3)	2.6687 (19)	175 (2)
N4—H4*C*···O1^{i}	0.901 (9)	2.033 (13)	2.7973 (17)	141.8 (15)
N4—H4*C*···O2^{i}	0.901 (9)	2.216 (14)	2.9171 (19)	134.3 (14)
N4—H4*B*···O2^{ii}	0.906 (9)	1.888 (10)	2.7937 (18)	179.1 (17)
N4—H4*A*···N3^{iii}	0.915 (9)	2.185 (10)	3.085 (2)	167.6 (18)

Symmetry codes: (i) $1+x$, y, z; (ii) $2-x$, $1-y$, $-z$; (iii) $1+x$, y, $z-1$.

H atoms attached to the hydroxyl (O4), aminium (N4) and cyclopropyl C atoms (C10, C11 and C12) were located in difference Fourier syntheses. These were refined with distance restraints. Other H atoms were placed in calculated positions and included in a riding model, with C—H = 0.93–0.97 Å and U_{iso}(H) = 1.2U_{eq}(carrier atom). .

Data collection: *XSCANS* (Siemens, 1994); cell refinement: *XSCANS*; data reduction: *SHELXTL*/*PC* (Siemens, 1991); program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *SHELXTL*/*PC*; software used to prepare material for publication: *SHELXTL*/*PC*.

References

Bauditz, R. (1990). *Enrofloxacin, Clinical Evolution in Several Animal Species. Veterinary Pharmacology, Toxicology and Therapy in Food Producing Animals*, p. 21. University of Veterinary Science, Unipharma, Budapest.

Cinquina, A. L., Roberti, P., Giannetti, L., Longo, F., Draisci, R. A., Fagiolo, R. & Brizioli, N. R. (2003). *J. Chromatogr. A*, **987**, 221–226.

Dax, S. L. (1997). *Antibacterial Chemotherapeutic Agents*, pp. 298–345. Glasgow, Scotland: Blackie.

Główka, M. L., Martynowski, D., Olczak, A., Bojarska, J., Szczesio, M. & Kozłowska, K. (2003). *J. Mol. Struct.* **658**, 43–50.

Prasanna, M. D. & Guru Row, T. N. (2001). *J. Mol. Struct.* **559**, 255–261.

Shen, L. L., Mitscher, L. A., Sharma, P. N., O'Donnell, T. J., Chu, D. T. W., Cooper C. S., Rosen, T. & Pernet, A. G. (1989). *Biochemistry*, **28**, 3886–3894.

Sheldrick, G. M. (1997). *SHELXS*97 and *SHELXL*97. University of Göttingen, Germany.

Siemens (1991). *SHELXTL*/*PC*. Version 4.2. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.

Siemens (1994). *XSCANS*. Version 2.10*b*. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.

Souza, M. J., Bittencourt, C. F. & Filho, P. S. S. (2004). *J. Pharm.* **271**, 287–291.