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Pefloxacinium methanesulfonate 0.10-hydrate

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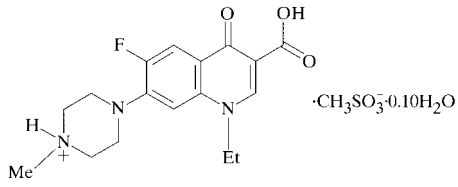
The crystal structure of 4-(3-carboxy-1-ethyl-6-fluoro-1,4-dihydro-4-oxo-7-quinolyl)-1-methylpiperazinium methanesulfonate 0.10-hydrate, $C_{17}H_{21}FN_3O_3^+\cdot CH_3O_3S^-\cdot 0.10H_2O$, contains pefloxacinium cations, methanesulfonate anions and a partially occupied water of solvation. The quinoline ring system in the cation is essentially planar. The anions lie parallel to each other about inversion centers. The structure is stabilized by strong hydrogen bonds involving the terminal piperazinyl-N atom of the cation and an O atom of the anion [N···O 2.739 (2) Å], and a strong intramolecular hydrogen bond between carbonyl and carboxyl groups [O···O 2.523 (2) Å].

Comment

Pefloxacin belongs to the second generation quinolone antimicrobial agents. These antimicrobials exert their action by inhibiting enzyme DNA-gyrase which is responsible for the continuous introduction of negative supercoils into DNA (Alfred *et al.*, 1996). Pefloxacin gives satisfactory clinical responses in the treatment of respiratory tract infections, including Gram-negative bacillary, staphylococcal pneumonia (Lauwers *et al.*, 1986), Gram-negative pneumonia (Giamarellou *et al.*, 1989) and chronic bronchitis (Maesens *et al.*, 1987). It is also used in the treatment of prostatitis (Guibert *et al.*, 1990), neisseria and gonorrhea (Ridgway, 1993), and possesses excellent activity against several Gram-negative meningeal pathogens (Scheld & Sande, 1983). It may cause headaches, dizziness, insomnia, rashes and gastrointestinal symptoms like nausea, vomiting and diarrhea (John & Hooper, 1989). The crystal structures of pefloxacinium methanesulfonate dihydrate (Toffoli *et al.*, 1987), silver pefloxacin hexahydrate (Baenziger *et al.*, 1986) and dipefloxacinium tetrachloroplatinum(II) dihydrate (Toffoli *et al.*, 1988) have already been reported. In this article, we report the crystal and molecular structure of pefloxacinium methanesulfonate 0.10-hydrate, (I).

The asymmetric unit of (I) contains a pefloxacinium cation, a methanesulfonate anion and a partially occupied water of



(I)

solvation with a site-occupancy factor of 0.10 (Fig. 1). The cation is composed of an essentially planar quinoline ring system [maximum deviation 0.029 (2) Å] which is substituted with ethyl, fluoro, oxo, carboxyl and methylpiperazinium groups. The bond distances and angles in the pefloxacinium ion are in excellent agreement with the corresponding dimensions reported in the structures of pefloxacinium methanesulfonate dihydrate (Toffoli *et al.*, 1987), silver pefloxacin hexahydrate (Baenziger *et al.*, 1986) and dipefloxacinium tetrachloroplatinum(II) dihydrate (Toffoli *et al.*, 1988); the mean values being: Csp^3—N (ammonium N3) 1.491 (2), Csp^3—N 1.462 (10), Csp^2—N 1.37 (3), Csp^3—Csp^3 1.505 (2) and C—$C_{aromatic}$ 1.39 (2) Å. The carboxyl group in (I) lies in the plane of the quinolyl moiety [angle between the two planes being 3.3 (3)°], while the plane composed of the N1,C10,C11 atoms is inclined at 80.5 (1)° to the quinolyl moiety. The six-membered piperazinyl ring adopts a chair conformation with puckering parameters (Cremer & Pople, 1975) Q = 0.566 (2) Å, θ = 177.3 (2) and φ = 60 (6)°. The methanesulfonate anion also exhibits normal molecular

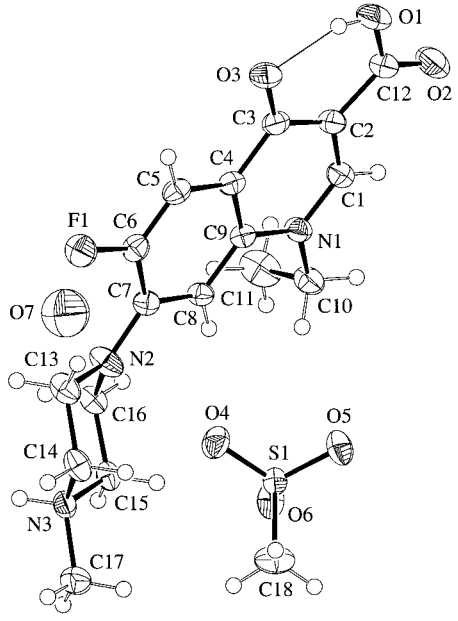


Figure 1
*ORTEP*II (Johnson, 1976) drawing of (I) with the atomic numbering scheme and 30% probability displacement ellipsoids.

dimensions with a mean S═O distance of 1.450 (8) Å and the longest distance associated with the O6 atom involved in a hydrogen bond [1.462 (2) Å].

The structure is stabilized by hydrogen bonds involving the terminal piperazinyl-N atom of the pefloxacinium and an O atom of the methanesulfonate ion, with strong N—H···O interactions [N3···O6 2.739 (2) Å and N3—H3···O6 159°]. The carbonyl and carboxyl groups are also involved in a strong intramolecular O—H···O hydrogen bond [O···O 2.523 (2) Å and O1—H1···O3 155°]. The pefloxacinium ions in (I) lie parallel to each other about inversion centers with *N*-ethyl groups oriented inwards (Fig. 2), similar to the packing observed in dipefloxacinium tetrachloroplatinum(II) dihydrate (Toffoli *et al.*, 1988). In the structures of pefloxacinium methanesulfonate dihydrate (Toffoli *et al.*, 1987) and silver pefloxacin hexahydrate (Baenziger *et al.*, 1986), the pefloxacinium moieties lie parallel to each other in a head-to-tail manner, with the *N*-ethyl groups oriented in the opposite directions. The 'outwards' motif is also present in (I). The separation of the quinoline rings in the 'inwards' and 'outwards' motifs in (I) is 3.35 and 3.34 Å, respectively.

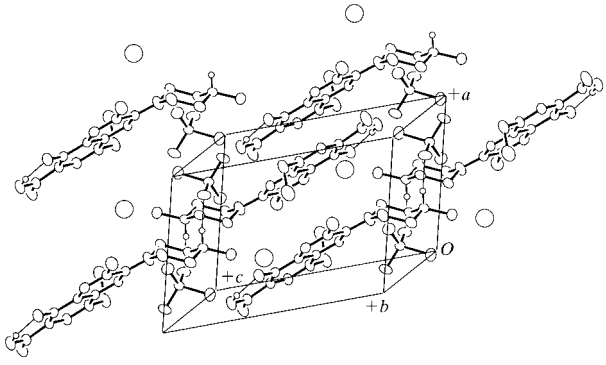


Figure 2
Packing diagram for (I) showing the hydrogen bonds.

The O7 atom of the partially occupied water of solvation lies at distances between 3.13 (3) and 3.38 (3) Å from the O2, O3, C16 and N1 atoms. There is a short intramolecular contact, H8···H16*A* (2.01 Å), which does not seem to influence the geometry about the atoms in the close proximity of these atoms.

The crystal structures of the quinolones related to (I) which have been reported include: an adduct of magnesium sulfate with ciprofloxacin (Turel *et al.*, 1996), norfloxacin 2DCl·D_2O (Wallis *et al.*, 1994), and an iron(III) complex of ciprofloxacin (Wallis *et al.*, 1995).

Experimental

Pefloxacinium methanesulfonate was a gift from Rhone-Poulenc Rorer Pakistan (Pvt) Ltd, Wah Cant., Pakistan. It was recrystallized from dimethylformamide as colorless crystals [m.p. 543–544 K (dec.)].

Crystal data

$C_{17}H_{21}FN_3O_3^+\cdot CH_3O_3S^-\cdot 0.10H_2O$
M_r = 431.26
Triclinic, $P\overline{1}$
a = 8.111 (3) Å
b = 10.013 (1) Å
c = 13.277 (3) Å
α = 101.22 (1)°
β = 102.85 (2)°
γ = 102.01 (1)°
V = 994.9 (4) Å^3
Z = 2
D_x = 1.44 Mg m^{-3}
Cu $K\alpha$ radiation
Cell parameters from 25 reflections
θ = 10–25°
μ = 1.91 mm^{-1}
T = 293 (2) K
Prismatic, colorless
0.30 × 0.23 × 0.20 mm

Data collection

Enraf–Nonius CAD-4 diffractometer
ω–2θ scans
Absorption correction: empirical ψ scan (3 reflections; North *et al.*, 1968)
T_{min} = 0.60, T_{max} = 0.70
3886 measured reflections
3612 independent reflections
3167 reflections with $I > 2\sigma(I)$
R_{int} = 0.012
θ_{max} = 68°
$h = 0 \rightarrow 9$
$k = -12 \rightarrow 11$
$l = -15 \rightarrow 15$
3 standard reflections
every 200 reflections
intensity decay: <0.2%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.040
$wR(F^2)$ = 0.111
S = 1.10
3612 reflections
266 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0535P)^2 + 0.4415P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.35 e Å^{-3}
$\Delta\rho_{min}$ = −0.41 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

S1—O5	1.444 (2)	N1—C9	1.401 (3)
S1—O4	1.444 (2)	N1—C10	1.475 (3)
S1—O6	1.462 (2)	N2—C7	1.370 (3)
S1—C18	1.754 (2)	N2—C16	1.453 (2)
F1—C6	1.360 (2)	N2—C13	1.457 (3)
O1—C12	1.322 (3)	N3—C17	1.488 (3)
O2—C12	1.206 (3)	N3—C14	1.490 (3)
O3—C3	1.264 (2)	N3—C15	1.494 (2)
N1—C1	1.336 (3)		
O5—S1—O4	113.06 (10)	C9—N1—C10	121.13 (16)
O5—S1—O6	111.81 (9)	C7—N2—C16	122.13 (16)
O4—S1—O6	112.36 (10)	C7—N2—C13	125.47 (17)
O5—S1—C18	106.28 (12)	C16—N2—C13	111.88 (16)
O4—S1—C18	106.79 (12)	C17—N3—C14	111.99 (17)
O6—S1—C18	105.95 (11)	C17—N3—C15	111.94 (17)
C1—N1—C9	120.01 (17)	C14—N3—C15	109.78 (15)
C1—N1—C10	118.77 (17)		

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

D—H···A	D—H	H···A	D···A	D—H···A
N3—H3···O6^{i}	0.91	1.87	2.739 (2)	159
O1—H1···O3	0.82	1.76	2.523 (2)	155

Symmetry code: (i) $1-x, 1-y, 2-z$.

Towards the end of the refinement, a void area was indicated by the program *PLATON* (Spek, 1990) which was consistent with the position of the largest peak in the difference map suggesting water of solvation. Atom O7 was included in the refinement initially allowing its site-occupancy factor to refine in order to determine its percentage

in the crystal. In the final round of calculations, the O7 atom was included at 10% occupancy and refined isotropically ignoring the H atoms attached to it. The distances used in the H-atom calculations were C—H 0.93–0.97, N—H 0.91 and O—H 0.82 Å.

Data collection: *CAD*-4 *Software* (Enraf–Nonius, 1989); cell refinement: *CAD*-4 *Software*; data reduction: *TEXSAN* (Molecular Structure Corporation, 1994); program(s) used to solve structure: *SAPI*91 (Fan, 1991); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *TEXSAN*; software used to prepare material for publication: *SHELXL*97.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: FR1263). Services for accessing these data are described at the back of the journal.

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