Acta Crystallographica Section E
Structure Reports Online
ISSN 1600-5368

A methanol hemisolvate of ciprofloxacin

X. Li,[a] Y. Hu,[b] Y. Gao,[c] G. G. Z. Zhang[d] and R. F. Henry[e]*

[a]Department of Chemistry and Chemical Engineering, Minjiang University, Fuzhou, People's Republic of China, [b]School of Life Sciences, Nanjing University, Nanjing, People's Republic of China, [c]Pharmaceutics Center, Global Pharmaceuticals R&D, Abbott Laboratories, 100 Abbott Park Road, Abbott Park, IL 60064, USA, [d]Solid State Sciences, Global Pharmaceuticals R&D, Abbott Laboratories, 1401 Sheridan Road, North Chicago, IL 60064, USA, and [e]Structural Chemistry, Global Pharmaceuticals R&D, Abbott Laboratories, 100 Abbott Park Road, Abbott Park, IL 60064, USA

Correspondence e-mail: rodger.henry@abbott.com

Key indicators

Single-crystal X-ray study
T = 193 K
Mean σ(C–C) = 0.002 Å
Disorder in solvent or counterion
R factor = 0.050
wR factor = 0.132
Data-to-parameter ratio = 17.2

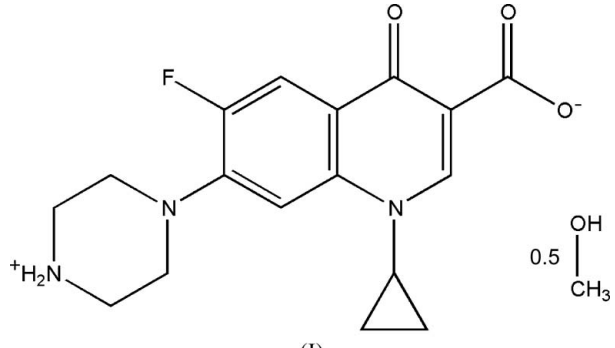
For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

Received 24 October 2006
Accepted 16 November 2006

The title compound [systematic name: 1-cyclopropyl-6-fluoro-4-oxo-7-(piperazin-4-ium-1-yl)-1,4-dihydroquinoline-3-carboxylate methanol hemisolvate], $C_{17}H_{18}FN_3O_3\cdot0.5CH_4O$, is an antibacterial fluoroquinolone. The molecule exists as a zwitterion in the solid state. The methanol molecule is disordered across a twofold rotation axis.

Comment

1-Cyclopropyl-6-fluoro-4-oxo-7-(piperazin-1-yl)-1,4-dihydro-3-quinolinecarboxylic acid, commonly known as ciprofloxacin, is a widely prescribed broad-spectrum oral fluoroquinolone antibiotic available in more than 100 countries and has been approved for the treatment of 14 types of infections (CIPRO, 2005). Several structures containing ciprofloxacin have been reported, including several salts and metal complexes (Drevensek *et al.*, 2002, 2003, 2005; Prasanna & Row, 2001; Saha *et al.*, 2002, 2003, 2004; Turel *et al.*, 1994, 1999; Turel & Golobic, 2003; Turel, Leban & Bukovec, 1997; Turel *et al.*, 1996; Wallis *et al.*, 1995; Zupancic *et al.*, 2001). The most relevant for comparison to the hemimethanolate, (I), is the hexahydrate, (II) (Turel, Bukovec & Quiros, 1997). Compounds (I) and (II) are similar in many ways but have several notable differences. In (I) the ciprofloxacin molecule adopts a zwitterionic state (Fig. 1), just as it does in (II). The hydrogen bonding and conformation of ciprofloxacin, however, differs in the two forms.



(I)

The hydrogen-bonding network in (I) consists of interactions between the positively charged piperazinium N atom, one of the two carboxylate O atoms and the ketone O atom of the quinolone system. These interactions organize the ciprofloxacin molecules into hydrogen-bonded sheets parallel to the $(10\bar{1})$ crystallographic plane. The first of these interactions is between the equatorial piperazinium H atom and carboxylate atom O1, forming a continuous chain in the $(10\bar{1})$

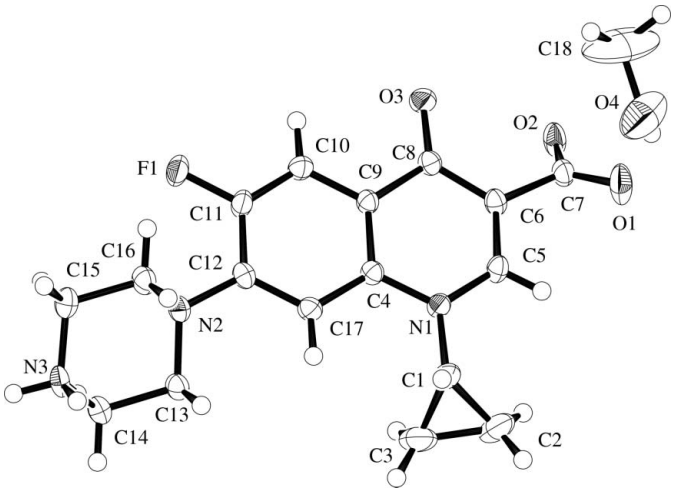


Figure 1
The molecular structure of (I) with the atomic numbering scheme. Displacement ellipsoids are drawn at the 50% probability level.

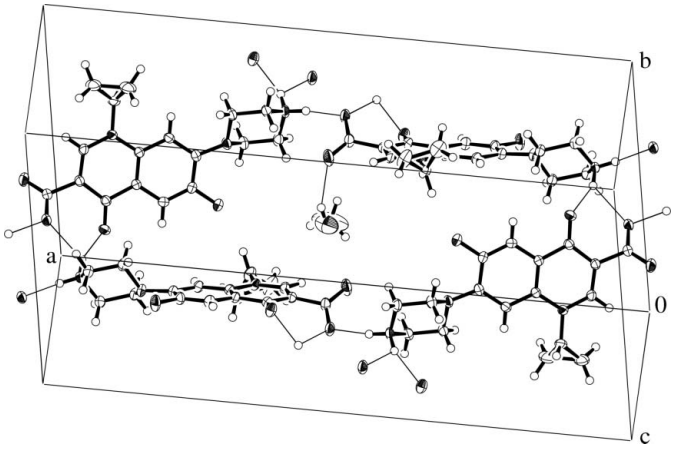


Figure 2
A view of the hydrogen bonding (dashed lines) in (I).

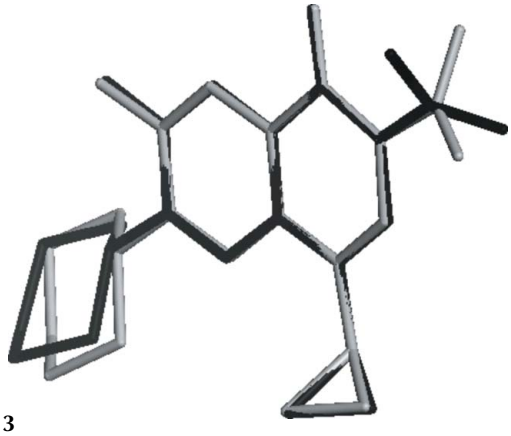


Figure 3
Overlay of ciprofloxacin molecules in (I) and (II).

plane perpendicular to the crystallographic *b* axis. The second interaction consists of a bifurcated hydrogen bond between the axial piperazinium H atom and both the ketone O3 and the carboxylate O1 atoms, forming a continuous chain parallel to the *b* crystallographic axis. A section of this network is shown in Fig. 2. This degree of ciprofloxacin-to-ciprofloxacin interaction is in strong contrast to (II) in which there is no ciprofloxacin-to-ciprofloxacin interaction at all.

The methanol molecule does not contribute to the hydrogen-bonding network but forms a discrete hydrogen bond with carboxylate atom O2. The methanol molecule lies in a pocket centered on a twofold rotational axis, over which it is disordered. The proximity of the methanol C atom to the crystallographic twofold axis necessitated the restraint of the C—O distance of 1.40 (1) Å.

Conformationally, the ciprofloxacin molecule in (I) is very similar to that in (II). The most significant difference between them is in the torsion angle of the acid group, which differs by more that 60° [define the torsion angle by atom labels and give the actual values]. An overlay of the ciprofloxacin molecules in the two solvates can be seen in Fig. 3.

Experimental

Solid ciprofloxacin (8.1 mg), purchased from LKT Laboratories Inc., was dissolved in methanol (2.5 ml) at ambient temperature in a vial. The vial was then sealed with Parafilm. Several holes were punctured through the Parafilm allowing the methanol to evaporate slowly. After four days of standing, needle-shaped colorless crystals formed at the bottom of the vial.

Crystal data

$C_{17}H_{18}FN_3O_3\cdot0.5CH_4O$
$M_r = 347.37$
Monoclinic, $C2/c$
$a = 26.036\ (11)$ Å
$b = 12.697\ (5)$ Å
$c = 10.235\ (4)$ Å
$\beta = 100.941\ (7)^\circ$
$V = 3322\ (2)$ Å^3
$Z = 8$
$D_x = 1.389$ Mg m^{-3}
Mo $K\alpha$ radiation
$\mu = 0.11$ mm^{-1}
$T = 193\ (2)$ K
Needle, colorless
0.4 × 0.1 × 0.1 mm

Data collection

Bruker APEX CCD diffractometer
ω scans
Absorption correction: none
19542 measured reflections
4067 independent reflections
3174 reflections with $I > 2\sigma(I)$
$R_{int} = 0.054$
$\theta_{max} = 28.4^\circ$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.050$
$wR(F^2) = 0.132$
$S = 1.01$
4067 reflections
236 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0834P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.004$
$\Delta\rho_{max} = 0.42$ e Å^{-3}
$\Delta\rho_{min} = -0.27$ e Å^{-3}

Table 1
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
O4—H4···O1	0.82	2.27	3.029 (4)	155
N3—H1A···O2^{i}	0.90	1.73	2.6209 (17)	171
N3—H1B···O3^{ii}	0.90	1.99	2.8247 (18)	154
N3—H1B···O2^{ii}	0.90	2.27	2.8422 (17)	121

Symmetry codes: (i) $x+\frac{1}{2}, -y+\frac{1}{2}, z+\frac{1}{2}$; (ii) $-x+\frac{1}{2}, y-\frac{1}{2}, -z+\frac{1}{2}$.

H atoms were treated with a riding model (C—H = 0.93–0.98 Å, N—H = 0.90 Å and O—H = 0.82 Å). U_{iso}(H) values were fixed at $1.5U_{eq}$ of the parent atom for methyl and hydroxyl H atoms, and $1.2U_{eq}$ of the parent atom for all other cases.

Data collection: *SMART* (Bruker, 2001); cell refinement: *SAINT-Plus* (Bruker, 1999); data reduction: *SAINT-Plus*; program(s) used to solve structure: *SHELXTL* (Sheldrick, 2000); program(s) used to refine structure: *SHELXTL*; molecular graphics: *ORTEPII* (Johnson 1976) and *MS Modeling* (Accelrys, 2004); software used to prepare material for publication: *SHELXTL*.

References

Accelrys (2004). *MS Modeling.* Version 3.1.0.0. Accelrys Inc., San Diego, CA, USA.

Bruker (1999). *SAINT-Plus*. Version 6.02. Bruker AXS Inc., Madison, Wisconsin, USA.

Bruker (2001). *SMART*. Version 5.624. Bruker AXS Inc., Madison, Wisconsin, USA.

CIPRO (2005). *Physician's Desk Reference*, 59th ed. Montvale, NJ, USA: Thomson PDR..

Drevensek, P., Golobic, A., Turel, I., Poklar, N. & Sepcic, K. (2002). *Acta Chim. Slov*. **49**, 857–870.

Drevensek, P., Leban, I., Turel, I., Giester, G. & Tillmanns, E. (2003). *Acta Cryst.* C**59**, m376–m378.

Drevensek, P., Zupancic, T., Pihlar, B., Jerala, R., Kolitsch, U., Plaper, A. & Turel, I. (2005). *J. Inorg. Biochem.* **99**, 432–442.

Johnson, C. K. (1976). *ORTEPII.* Report ORNL-5138. Oak Ridge National Laboratory, Tennesse USA.

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

Saha, D. K., Padhye, S., Anson, C. E. & Powell, A. K. (2002). *Inorg. Chem. Commun.* **5**, 1022–1027.

Saha, D. K., Padhye, S., Anson, C. E. & Powell, A. K. (2003). *Transition Met. Chem.* **28**, 579–584.

Saha, D. K., Sandbhor, U., Shirisha, K., Padhye, S., Deobagkar, D., Anson, C. E. & Powell, A. K. (2004). *Bioorg. Med. Chem. Lett.* **14**, 3027–3032.

Sheldrick, G. M. (2000). *SHELXTL.* Version 6.10. Bruker AXS Inc., Madison, Wisconsin, USA.

Turel, I., Bukovec, P. & Quiros, M. (1997). *Int. J. Pharm.* **152**, 59–65.

Turel, I., Golic, L. & Ramirez, O. L. R. (1999). *Acta Chim. Slov.* **46**, 203–211.

Turel, I. & Golobic, A. (2003). *Anal. Sci.* **19**, 329–330.

Turel, I., Leban, I. & Bukovec, N. (1994). *J. Inorg. Biochem.* **56**, 273–282.

Turel, I., Leban, I. & Bukovec, N. (1997). *J. Inorg. Biochem.* **66**, 241–245.

Turel, I., Leban, I., Zupancic, M., Bukovec, P. & Gruber, K. (1996). *Acta Cryst.* C**52**, 2443–2445.

Wallis, S. C., Gahan, L. R., Charles, B. G. & Hambley, T. W. (1995). *Polyhedron*, **14**, 2835–2840.

Zupancic, M., Turel, I., Bukovec, P., White, A. J. P. & Williams, D. J. (2001). *Croat. Chem. Acta*, **74**, 61–74.