ELSEVIER

Journal of Molecular Structure 611 (2002) 73–81

Journal of
MOLECULAR
STRUCTURE

www.elsevier.com/locate/molstruc

Molecular structures of new ciprofloxacin derivatives

Zrinka Banić Tomišić[a], Nedjeljko Kujundžić[a], Mirjana Bukvić Krajačić[a], Aleksandar Višnjevac[b], Biserka Kojić-Prodić[b,*]

[a]*PLIVA, Pharmaceutical Industry, Incorporated, Research Division, Prilaz baruna Filipovića 25, HR-10000 Zagreb, Croatia*
[b]*Rudjer Bošković Institute, P.O. Box 180, Bijenicka 54, HR-10002 Zagreb, Croatia*

Received 3 October 2001; revised 28 January 2002; accepted 28 January 2002

Abstract

Two new derivatives from the ciprofloxacin fluoroquinoline family, 7-chloro-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-quinoline-3-methylcarbamate and 1-cyclopropyl-7-(4-ethyl-1-piperazinyl)-6-fluoro-1,4-dihydro-(3-oxopyrazolo)[4,3-c]quinoline, were synthesised, tested for antibacterial activity and crystallised. Their molecular and crystal structures were determined. Tests in vitro reveal lower activities than for ciprofloxacin. Characteristic structural features of these compounds are comparable to data for other known fluoroquinolines. The bicyclic quinoline ring is planar in both compounds; the carbamate side chain and five-membered pyrazolo ring are almost coplanar with it. A piperazinyl ring exhibits a chair conformation. In the crystal packing of the carbamate analogue, two C–H···O interactions form a dimer. The pyrazolo derivative crystallises as solvate with 1.5 water molecules per quinoline molecule. In its crystal structure donor and acceptor functionalities form dimers, via hydrogen bonds, which are connected into an infinite pattern through hydrogen bonded water molecules.

Keywords: Fluoroquinolines; Synthesis; Antimicrobial activity; X-ray structure; Hydrogen bonds; C–H···F intramolecular interaction

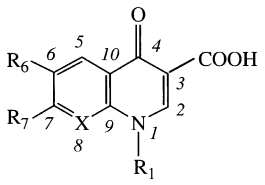
1. Introduction

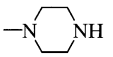
The 4-quinolones are a class of highly potent and orally active broad-spectrum antibacterial agents [1–3] which originate from a 1,8-naphthyridine precursor—nalidixic acid (Scheme 1), synthesised in the early 1960s [4]. It was the first clinically used quinolone antibiotic. Numerous quinolones have been synthesised since then and many are used as drugs today. To solve the problem of increasing antimicrobial resistance, especially the strong demand for treating drug-resistant *Streptococcus pneumoniae* and multi-resistant *Enterobacteriaceae*, the development of a new class of antimicrobials—fluoroquinolones was initiated.

The development from nalidixic acid (1,8-naphthyridine core, the first generation) to the second and the third generations of antimicrobial quinolone drugs involved basically modifications including piperazine substitution at the 7-position, fluorination at the 6-position and replacement of carbon with nitrogen at the 8-position (quinolone core). Norfloxacin (Scheme 1) was the first member of the fluoroquinolone series. Modifications such as 1-cyclopropyl substitution (ciprofloxacin, Scheme 1) and 1,8-cyclisation (ofloxacin, levofloxacin) produced the second generation of fluoroquinolones. In the next step, substitutions on the 6-fluoro-7-piperazinyl compound

* Corresponding author. Tel.: +385-1-4680126; fax: +385-1-4680245.
E-mail address: kojic@rudjer.irb.hr (B. Kojić-Prodić).

0022-2860/02/$ - see front matter
PII: S0022-2860(02)00062-5



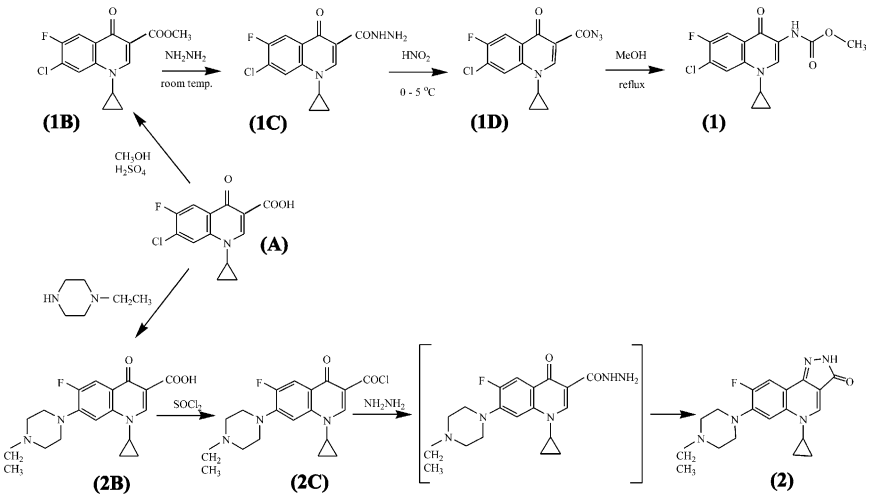
	R_1	R_6	R_7	X
nalidixic acid	$-CH_2CH_3$	-	$-CH_3$	N
norfloxacin	$-CH_2CH_3$	-F		C
ciprofloxacin		-F		C

Scheme 1. Examples of active quinolones.

produced an improved second generation of fluoroquinolones (sparfloxacin and clinafloxacin). The third generation, involving a 7-azabicyclo modification, yielded moxyfloxacin and gatifloxacin in the quinolone series and trovafloxacin in the 1,8-naphthyridine series. Ciprofloxacin, with the broadest spectrum of infective indications, is presently the reference agent for the new series of compounds to be compared with. Structure–activity relationship studies [5–7] and the known drug target [3 and the references therein] have facilitated the development of new more potent quinolone generations with broader spectrum activity, better pharmacokinetics, and good tolerability. The functional target of quinolone antimicrobials is the enzyme DNA gyrase, an essential adenosine triphosphate-hydrolyzing topoisomerase, inhibiting bacterial DNA replication and transcription causing rapid cell death. The drugs directly bind to DNA via hydrogen bonding to unpaired bases. In spite of the known molecular target and its interactions with these drugs, there are still open questions.

The most recent research findings on adverse reaction caused by quinolone antimicrobial agents and their photomutagenic activity [8] call for more attention to examine further significant tolerability problems. In this family of drugs, the most striking case is trovan® (trovafloxacin mesylate) which is associated with serious liver injuries and can hardly be used. Quite often quinolones interact with other drugs such as theophylline and non-steroidal antiinflammatory drugs producing effects on CNS [9]. So far, the molecular target or a receptor for such effects has not been known. Most probably, several mechanisms are responsible for effects on CNS and the problem of tolerability is still unresolved.

As part of an ongoing research project in the search for new pharmacologically active fluoroquinolones, we report synthesis, antimicrobial tests results and discuss molecular and crystal structures of two fluoroquinoline derivatives (Scheme 2): 7-chloro-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-quinoline-3-methylcarbamate **1** with the new carbamate functionality at position 3, and 1-cyclopropyl-7-(4-ethyl-1-piperazinyl)-6-fluoro-1,4-dihydro-(3-oxopyrazolo)[4,3-c]quinoline (named



Scheme 2. Synthetic routes.

Table 1
Crystalographic data, structure solution and refinement of **1** and **2**

Compound	**1**	2
Formula	$C_{14}H_{12}ClFN_2O_3$	$C_{38}H_{50}OF_2N_{10}O_5$
M_r	310.71	764.88
Crystal system	Monoclinic	Monoclinic
Space group	$P2_1/a$	$C2/c$
a (Å)	7.1667(2)	21.8583(8)
b (Å)	14.1663(2)	10.6637(1)
c (Å)	13.7385(2)	19.5774(6)
β (°)	90.570(5)	122.706(2)
V (Å^3)	1394.74(5)	3839.8(2)
Z	4	4
F_{000}	640	1624
D_x (mg m^{-3})	1.480	1.323
θ range (°) for cell det.	40.38–46.29	40.07–45.74
μ (mm^{-1})	2.656	0.802
Crystal form and colour	Colourless needle	Yellow prism
Crystal size (mm)	$0.18 \times 0.08 \times 0.07$	$0.20 \times 0.11 \times 0.11$
Absorption correction	Psi-scan	Psi-scan
Total data collected	2954	4027
Unique data	2840	3906
Observed data (criterion)	2192[$I > 2\sigma(I)$]	2949
R_{int}	0.0218	0.0222
θ_{max} (°) for data collection	74.15	74.13
Range of h, k, l	−8,8; −17,0; −17,0	−22.27; 0.13; −24,0
Refinement on	F^2	F^2
R_1 [$F_0 > 4\sigma$ (F_0)]	0.0783	0.0477
wR_2 (F^2), all data	0.2361	0.1460
S	1.045	1.057
Parameters	192	266
Weighting scheme[a]	$w = 1/[\sigma^2(F_0^2) + (0.1428P)^2 + 1.612P]$	$w = 1/[\sigma^2(F_0^2) + (0.0813P)^2 + 1.8779P]$
Max. and min. $\Delta\rho$ (eÅ^{-3})	1.53, −0.45	0.37, −0.36
Data reduction programme	HELENA [11]	HELENA
Structure solution programme	SIR97 [12]	SIR92 [13]
Structure refinement programme	SHEXL97 [14]	SHEXL97
Molecular graphics programme	PLATON98 [15]	PLATON98

[a] $P = (F_0^2 + 2F_c^2)/3$.

by IUPAC: 5-cyclopropyl-7-(4-ethyl-1-piperazinyl)-8-fluoro-2,5-dihydro-pyrazolo[4,3-c]quinoline-3-one) **2** with a fused pyrazolo ring at atoms C3 and C4 of the quinoline moiety.

2. Experimental

2.1. The synthesis of compounds *1* and *2*

The synthesis of the new fluoroquinolone derivatives **1** and **2**, including their intermediates, is outlined in Scheme 2. The compounds synthesised were characterised by elemental CHNS/O analysis, mass spectra, FT-IR, ^{1}H and ^{13}C NMR spectra (data not shown).

2.1.1. Preparation of compound *1*

A mixture of 7-chloro-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-quinoline-3-carboxylic acid (**A**) (9.8 g, 0.035 mol), methanol (140 ml) and sulphuric acid (2.2 ml) was refluxed for 24 h. The solution was cooled down to room temperature and the solid

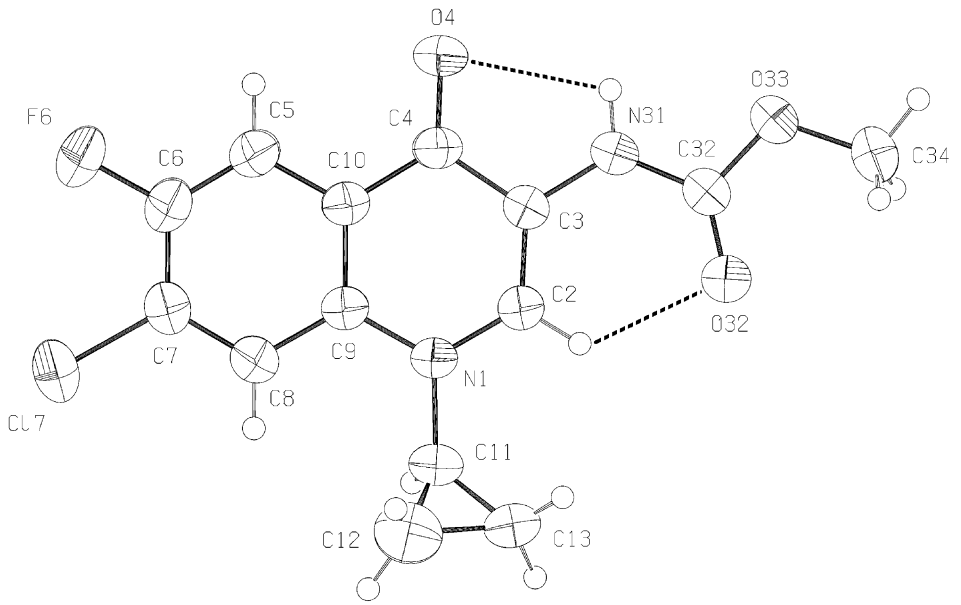


Fig. 1. Molecular structure of **1**, ORTEP plot, with atom numbering. Thermal ellipsoids are drawn at 50% probability level. Intramolecular hydrogen bonds N31–H31···O4 and C2–H2···O32 are indicated by dashed lines.

obtained diluted with water (80 ml). Acidic aqueous solution was neutralised with 10% NaOH to pH 10, cooled to 5 °C and then stirred for 1 h. The precipitate was filtered, washed with cold water (3 × 50 ml) and dried for 1 h at 100 °C to give 7-chloro-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-quinoline-3-carboxylic acid methyl ester (**1B**) (6.15 g, 59.8%).

A mixture of **1B** (6 g, 0.02 mol) and hydrazine-hydrate (25 ml, 0.514 mol) was stirred at room temperature for 10 h. The precipitated solid was collected by filtration and washed with water to give 7-chloro-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-quinoline-3-carboxylic acid hydrazide (**1C**) (4.6 g, 93.3%).

To the solution of **1C** (2.96 g, 0.01 mol) in 10 ml 3 M sulphuric acid, cooled to 0–5 °C, water solution of $NaNO_2$ (4.14 g, 0.06 mol) was added dropwise. After 30 min, reaction mixture was filtered to give 7-chloro-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-quinoline-3-carboxylic acid azide (**1D**).

A solution of **1D** (1.5 g, 0.0054 mol) in methanol (25 ml) was refluxed for 3 h. Reaction mixture was evaporated to dryness to yield 7-chloro-1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-quinoline-3-methyl-carbamate (**1**) (1.55 g, 92.3%).

*2.1.2. Preparation of compound **2***

1-Cyclopropyl-7-(4-ethyl-1-piperazinyl)-6-fluoro-1,4-dihydro-4-oxo-quinoline-3-carboxylic acid (**2B**) was synthesised from 1-cyclopropyl-7-chloro-6-fluoro-1,4-dihydro-4-oxo-quinoline-3-carboxylic acid (**A**) according to previously described procedure [10].

A solution of **2B** (5 g, 0.0139 mol) in $SOCl_2$ was refluxed for 10 h. The solvent was removed in vacuo to obtain 1-cyclopropyl-7-(4-ethyl-1-piperazinyl)-6-fluoro-1,4-dihydro-4-oxo-3-quinolinoyl chloride (**2C**) as a dark foam (5.2 g, 95.1%).

A mixture of **2C** (5.2 g, 0.0132 mol) and hydrazine-hydrate (25 ml, 0.514 mol) was stirred at room temperature for 1 h. The solvent was removed and the residue was dissolved in 20 ml 96% ethanol. After concentration of the reaction mixture under reduced pressure, the residue was recrystallised from 96% ethanol to give 1-cyclopropyl-7-(4-ethyl-1-piperazinyl)-6-fluoro-1,4-dihydro-(3-oxopyrazolo)[4,3-c]quinoline (**2**).

2.2. Activity

For antimicrobial activity tests in vitro, the following strains were used: *Staphylococcus aureus*

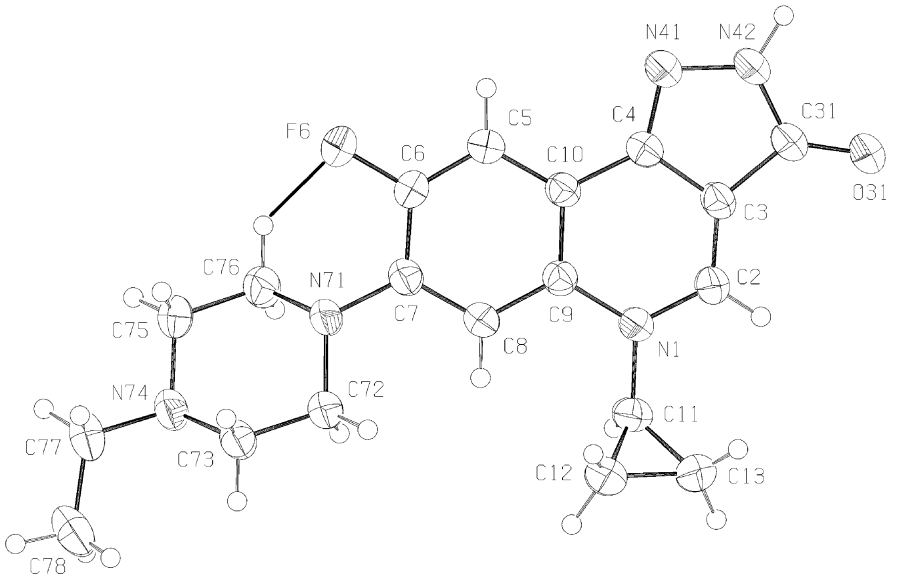


Fig. 2. Molecular structure of **2**, ORTEP plot, with atom numbering. Thermal ellipsoids are drawn at 50% probability level. Intramolecular hydrogen bond C76–H76···F7 is indicated by dashed line. For clarity, crystalline water molecules are not shown.

(ATCC29213), *Escherichia coli* (ATCC25922), *Enterococcus faecalis* (ATCC29212) and *S. pneumoniae* (ATCC6305). Ciprofloxacin was used as a reference substance. Unfortunately, both compounds showed lower activities than ciprofloxacin.

2.3. X-ray structure analysis

X-ray measurements were performed on an Enraf Nonius CAD4 diffractometer using a graphite monochromated Mo Kα radiation. For both compounds, crystals suitable for the X-ray structure determination were obtained from ethanol solution (96 vol%) by slow evaporation at room temperature. Details about data collection, structure solution, refinement and about software used are listed in Table 1 [11–15]. All hydrogen atoms in both compounds, except hydrogen at N42 and hydrogens of water molecules

Table 2
Selected geometric parameters for **1**

(a) *Bond lengths* (Å)			
F6–C6	1.351(5)	N1–C11	1.459(5)
Cl7–C7	1.729(4)	C11–C12	1.389(9)
N1–C2	1.355(5)	C11–C13	1.387(8)
N1–C9	1.378(4)	C12–C13	1.503(9)
(b) *Angles* (°)			
C2–N1–C9	120.6(3)	C12–C11–C13	65.6(4)
C2–N1–C11	118.8(3)	C11–C12–C13	57.2(4)
C9–N1–C11	120.0(3)	C11–C13–C12	57.3(4)
(c) *Torsion angles* (°)			
C2–N1–C11–C12	−113.2(6)	C2–C3–N31–C32	7.6(6)
C2–N1–C11–C13	−32.9(8)	C4–C3–N31–C32	−174.5(3)
C9–N1–C11–C12	74.9(7)	C3–N31–C32–O33	177.1(3)
C9–N1–C11–C13	155.2(5)	N31–C32–O33–C34	−179.8(4)

Table 3
Selected geometric parameters for **2**

(a) *Bond lengths* (Å)			
F6–C6	1.354(2)	C12–C13	1.491(3)
N1–C2	1.343(2)	C3–C4	1.424(2)
N1–C9	1.414(2)	N41–C4	1.316(1)
N1–C11	1.456(2)	N41–N42	1.400(2)
C11–C12	1.489(3)	N42–C31	1.354(2)
C11–C13	1.483(3)	C3–C31	1.448(2)
(b) *Angles* (°)			
C2–N1–C9	121.38(10)	C4–C3–C31	105.5(1)
C2–N1–C11	118.62(14)	N41–C4–C3	112.8(1)
C9–N1–C11	119.76(10)	N42–N41–C4	103.4(1)
C11–C12–C13	59.7(1)	N41–N42–C31	115.4(1)
C11–C13–C12	60.1(1)	N42–C31–C3	103.0(1)
C12–C11–C13	60.2(1)		
(c) *Torsion angles* (°)			
C2–N1–C11–C12	114.2(2)	C9–N1–C11–C12	−71.4(3)
C2–N1–C11–C13	44.0(3)	C9–N1–C11–C13	−141.5(2)

in compound **2**, were generated according to stereochemistry and refined using a riding model in SHELXL97 [14]. The hydrogen at N42 and the ones on water molecules (in compound **2**) were located in difference Fourier map. Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre, supplementary publication No. CCDC-171413 and CCDC-171414. Copies of data may be obtained free of charge on application to CSD, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-1223/336033, e-mail: deposit@ccdc.cam.ac.uk).

3. Results and discussion

The molecular structures of the studied compounds are shown in Figs. 1 and 2. Both molecules are achiral and crystallise in the centrosymmetric space groups (Table 1). The values observed for bond lengths and angles (Tables 2 and 3) are in agreement with the values found for the corresponding analogues [16–18]. An asymmetry in nitrogen to carbon C9–N1–C2 bond lengths is observed in compound **2** (Table 3), whereas in **1** it is less pronounced (Table 2). Thus, a bond N1–C9 in **2** (Table 3) is longer than the average value for $N_{sp2}–C_{sp2/aryl}$ value of 1.355(2) Å [19]. The cyclopropyl ring of **1** is slightly distorted; higher values of temperature factors for atoms C11, C12, C13 and higher residual density than usual ($\Delta\rho_{max} = 1.53$ eÅ^{-3}) near the cyclopropyl ring have been observed.

Table 4
Hydrogen bonding geometry for **1**

D–H···*A*	D–H (Å)	H···*A* (Å)	D···*A* (Å)	D–H···*A* (°)
N31–H···O4	0.86(1)	2.33(1)	2.690(4)	105(4)
C2–H···O32	0.93(1)	2.18(1)	2.812(5)	124(3)
C34–H···O4[a]	0.96(1)	2.45(2)	3.352(2)	157.2(1)

[a] Symmetry operation: $1-x, 1-y, 1-z$.

The bicyclic quinoline ring is planar in both compounds with the maximum displacement from the best least-squares plane of 0.020(4) Å for atom C3 of **1** and 0.028(2) Å for atom N1 of **2**. In both structures, fluorine atoms are shifted from the quinoline least-squares plane [0.020 Å in **1** and 0.068 Å in **2**]. The pyrazolo ring of **2** is almost coplanar with the quinoline ring plane. The dihedral angle between these planes is 2(1)°. The carbonyl oxygen O31 is significantly displaced (0.161 Å) from the quinoline ring plane as a consequence of its participation in hydrogen bond network. The cyclopropyl rings of both compounds are not coplanar with the quinoline ring; the angles between the quinoline and cyclopropyl least-squares planes are 46.1(5)° in **1** and 54.5(2)° in **2**. A piperazinyl ring of **2** is in a *chair* conformation $^{N}C_{N}$ with Cramer and Pople puckering parameters $Q = 0.583(2)$ Å, $\theta = 3.0(2)°$ and

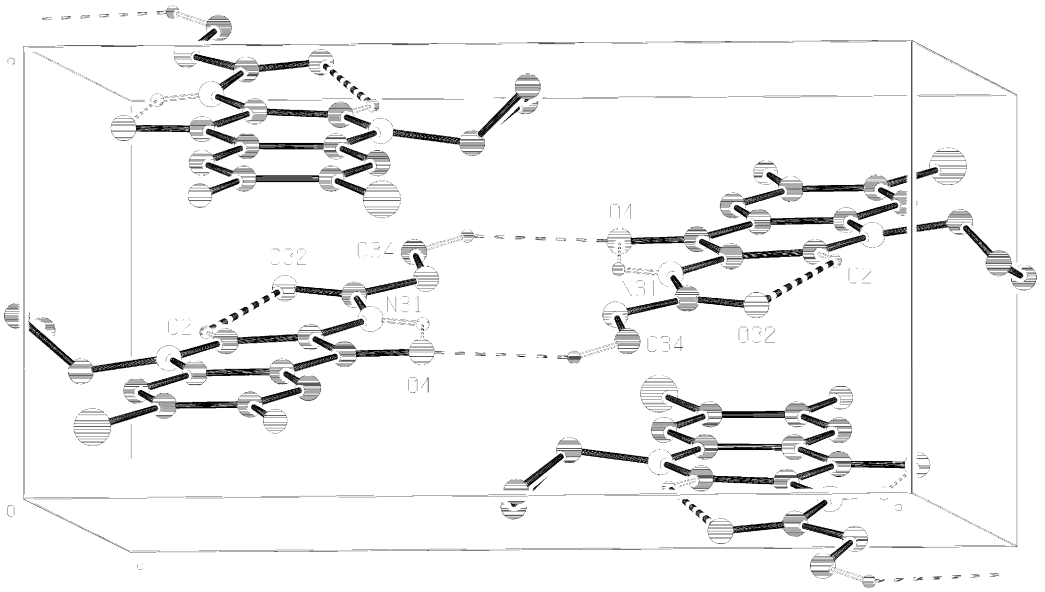


Fig. 3. In the crystal packing of **1**, the centorsymmetric dimer is created by two C–H···O interactions. Stacking of aromatic rings is pronounced along the axis-*a*.

$\varphi = 352(4)°$ [20]. The carbamate side chain of **1** adopts a zig-zag conformation almost in the plane of the quinoline ring with a characteristic torsion angle C3–N31–C32–O33 of 177.0(2)°. The overall conformation of both compounds is described by selected torsion angles in Tables 2 and 3.

Molecules of **1** are stabilised by intramolecular hydrogen bonds (Fig. 1). The carbonyl oxygen O4 and a hydrogen of the amino N31 group (N31–H31···O4) form a five-membered ring [graph-set notation S(5)] [21–23]. An intramolecular contact C2–H2···O32 satisfies criteria for a C–H···O hydrogen bond (Table 4) [24] forming a six-membered ring [graph-set notation S(6)]. In related 3-carboxylic acid analogues selected from the Cambridge Structural Database [25] carbonyl oxygen O4 acts as an acceptor of hydrogen from carboxyl group in formation of intramolecular hydrogen bond. The crystal packing comprises centrosymmetric dimers formed by C–H···O interactions between methyl groups and carbonyl oxygen atoms (Table 4, Fig. 3) forming the 16-membered ring with graph-set descriptor $R_2^2(16)$. π-Stacking of aromatic rings is pronounced along the crystallographic *a*-axis with the shortest separation distance of 3.64 Å (Fig. 3).

In the crystal packing of **2** intermolecular hydrogen

Table 5
Hydrogen bonding geometry for **2**

D–H···*A*	D–H (Å)	H···*A* (Å)	D···*A* (Å)	D–H···*A* (°)
N42–H···O31[a]	0.94(2)	1.87(2)	2.810(2)	171(3)
O1W–H1···O2W	1.01(4)	1.92(4)	2.817(2)	146(3)
O2W–H21···N74[b]	0.77(7)	2.16(7)	2.921(3)	166(5)
O2W–H22···O31[c]	0.97(4)	1.86(4)	2.826(2)	169(3)
C76–H76···F6	0.97(2)	2.31(4)	2.934(2)	121(4)

[a] Symmetry operation: $3/2 - x$, $1/2 - y$, $1 - z$.
[b] Symmetry operation: x, $-y$, $1/2 + z$.
[c] Symmetry operation: $x - 1/2$, $y - 1/2$, z.

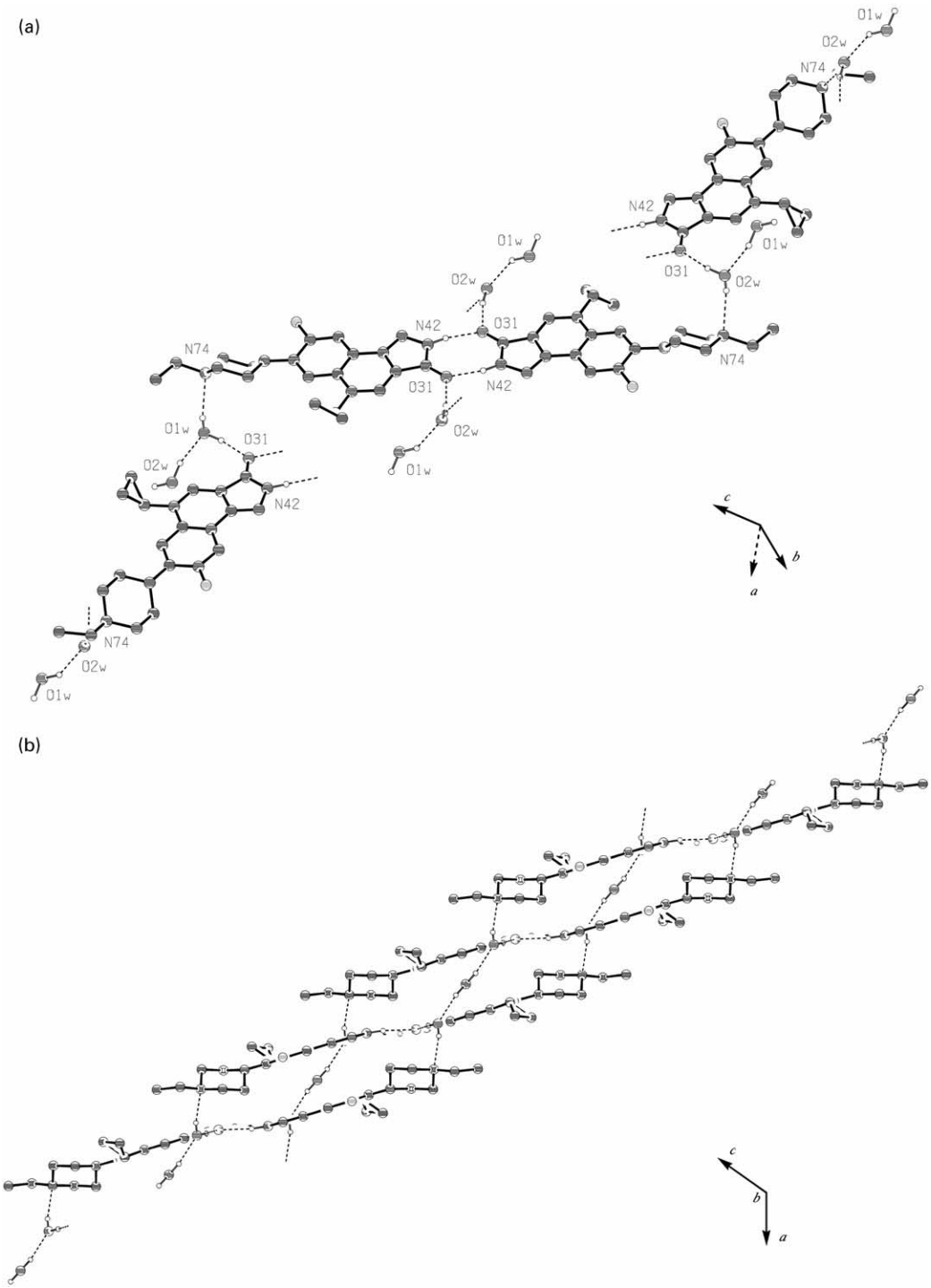


Fig. 4. Crystal packing of **2**: (a) Hydrogen bonded dimers of quinoline molecules are interconnected via hydrogen bonds with water molecules; (b) stacking is pronounced between the aromatic planes along the axis-*a* with a centroid distance of two nearest quinoline moieties of 3.525 Å.

bonds N42–H42···O31 create centrosymmetric dimers (Table 5, Fig. 4a) with an eight-membered ring of the graph-set descriptor $R_2^2(8)$ [21–23]. The hydrogen bonding is completed by cooperation of crystalline water molecules; compound **2** crystallises with 1.5 water molecules per quinoline molecule. One water molecule (O1W), of the two present in the asymmetric unit, is in special position at the twofold axis (4*e* special position in the *C*2/*c* space group). Water molecules O2W interconnect dimers of hydrogen bonded quinoline molecules by donating one of their hydrogen atoms to carbonyl oxygen O31 of the pyrazolo ring of one quinoline molecule (O2W–H22W···O31) and the other hydrogen to amino nitrogen N74 of piperazinyl ring of the other quinoline molecule (O2W–H21W···N74) (Fig. 4a). The waved chains of quinoline dimers parallel to [101] of the cell are formed with graph-set descriptor $C_2^2(15)$. Water molecules OW1 form bridges between these chains through O1W–H1W···O2W hydrogen bonds. Thus, the water molecules OW2 are three-coordinated, each molecule acting as a donor (to N74 and O31) in two hydrogen bonds and as an acceptor in one hydrogen bond, a feature which is commonly observed in the crystal structures of small molecule hydrates [26]. π···π interactions have been detected between quinoline moieties (Fig. 4b); centroids of the two neighbouring rings N1–C2–C3–C4–C10–C9 are separated by 3.525 Å. In the structure of **2** fluorine meets quite well geometrical criteria for an acceptor of hydrogen in the intramolecular interaction C76–H76A···F6 [graph-set notation S(6)]. According to the analysis reported by Shimoni and Glusker [27] for C–F as an acceptor group attached to an aromatic system, the mean H···F distance is 2.58 Å whereas the mean C–H···F angle is 129°. These values were obtained for a small statistical sample (seven structures) but they fit nicely in the ranges obtained by our analysis of data extracted from Cambridge Structural Database, version 5.21, April 2001 [25]. The restrictions to organic compounds and the structures with an *R* value <0.05, while searching met 325 structures with the C···F range from 2.480 to 3.169 Å and H···F from 2.072 to 2.669 Å. Our data for compound **2** (Table 5) are in agreement with these findings and data reported for analogous compound, ciprofloxacin lactate [28].

References

[1] T. Rosen, in: G.P. Ellis, G.B. West (Eds.), Progress in Medicinal Chemistry, vol. 27, Elsevier, Amsterdam, 1990, pp. 235–290 chapter 6.
[2] P. Ball, A. Fernald, G. Tillotson, Exp. Opin. Invest. Drugs 7 (1998) 761.
[3] J.M. Blondeau, Clin. Therapeut. 21 (1999) 3.
[4] G.Y. Lesher, E.J. Froelich, M.D. Gruett, J.H. Bailey, R.P. Brundage, J. Med. Chem. 5 (1962) 1063.
[5] T.D. Gootz, K.E. Brighty, Med. Res. Rev. 16 (1996) 433.
[6] J.M. Domagala, J. Antimicrob. Chemother. 33 (1994) 685.
[7] G.S. Tillotson, J. Med. Microbiol. 44 (1996) 320.
[8] E. Gocke, S. Albertini, A.A. Chetelat, S. Kirchner, W. Muster, Toxicol. Letts. 103 (1998) 375.
[9] A. De Sarro, G. De Sarro, Curr. Med. Chem. 8 (2001) 371.
[10] K. Grohe, U. Petersen, H.J. Zeiler, K. Metzger, Ger. Offen. DE 3, 525 (1986) 108.
[11] A.L. Spek, HELENA, Program for Data reduction, Utrecht University, The Netherlands, 1997.
[12] A. Altomare, G. Cascarano, C. Giacovazzo, A. Guagliardi, A.G.G. Moliterni, M.C. Burla, G. Polidori, M. Camalli, R. Spagna, SIR97: A Package for Crystal Structure Solution by Direct Methods and Refinement, University of Bari, Italy, 1997.
[13] A. Altomare, G. Cascarano, C. Giacovazzo, A. Guagliardi, A.G.G. Moliterni, M.C. Burla, G. Polidori, M. Camalli, R. Spagna, SIR92: A Package for Crystal Structure Solution by Direct Methods and Refinement, University of Bari, Italy, 1992.
[14] G. M. Sheldrick, SHELXL97. Program for crystal structure refinement, University of Goettingen, Germany, 1997.
[15] A.L. Spek, PLATON98. Version 1998, Utrecht University, The Netherlands, 1998.
[16] I. Turel, I. Leban, M. Zupančič, P. Bukovac, K. Gruber, Acta Cryst. C 52 (1996) 2443.
[17] M. Parvez, M.S. Arayne, N. Sultana, A.Z. Siddiqi, Acta Cryst. C 56 (2000) 910–912.
[18] A.J. Florence, A.R. Kennedy, N. Shankland, E. Wright, A. Al-Rubayi, Acta Cryst. C 56 (2000) 1372.
[19] F.H. Allen, O. Kennard, D.G. Watson, L. Brammer, A.G. Orpen, R. Taylor, J. Chem. Soc. Perkin Trans. 2 (1987) S1.
[20] D. Cremer, J.A. Pople, J. Am. Chem. Soc. 97 (1975) 1354.
[21] M.C. Etter, J. MacDonald, Acta Cryst. B 46 (1990) 256.
[22] J. Bernstein, M.C. Etter, J.C. MacDonald, J. Chem. Soc. Perkin Trans. 2 (1991) 695.
[23] J. Bernstein, R.E. Davis, L. Shimoni, N.L. Chang, Angew. Chem. Int. Ed. Engl. 34 (1995) 1555.
[24] G.R. Desiraju, T. Steiner, The Weak Hydrogen Bond in Structural Chemistry and Biology, Oxford University Press, Oxford, 2000.
[25] F.H. Allen, O. Kennard, Chem. Des. Autom. News 8 (1993) 31.
[26] G.A. Jeffrey, W. Saenger, Hydrogen Bonding in Biological Structures, Springer, Berlin, 1991 chapter 2, pp. 15–48.
[27] L. Shimoni, J.P. Glusker, Struct. Chem. 5 (1994) 383–397.
[28] M.D. Prasanna, T.N. Guru Row, J. Mol. Struct. 559 (2001) 255–261.