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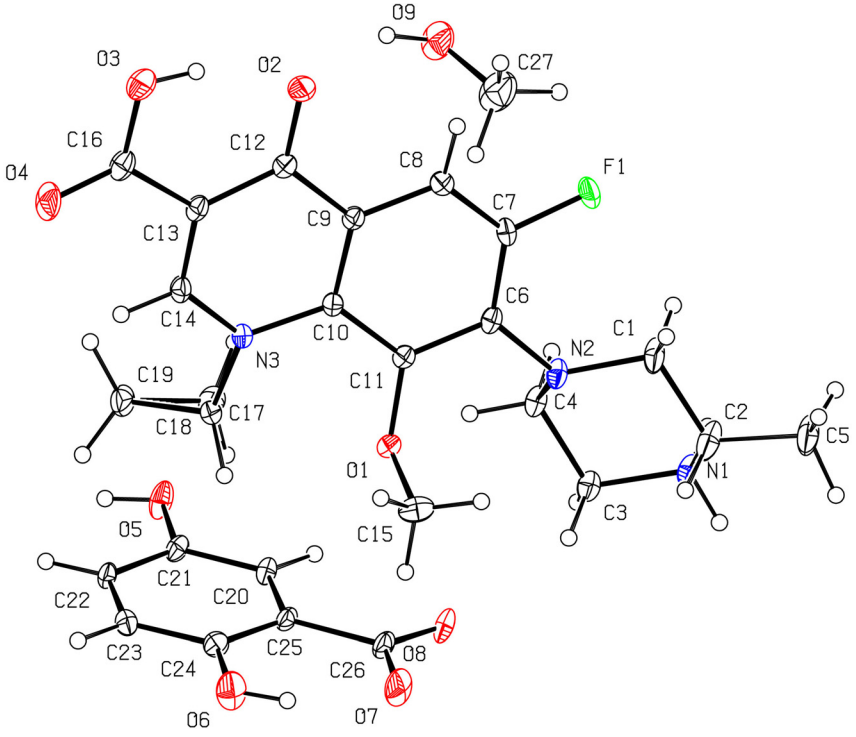
The crystal structure of 4-(3-carboxy-1-cyclopropyl-6-fluoro-8-methoxy-4-oxo-1,4-dihydroquinolin-7-yl)-2-methylpiperazin-1-ium 2,5-dihydroxybenzoate methanol solvate, $C_{27}H_{32}FN_3O_9$



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Abstract

$C_{27}H_{32}FN_3O_9$, triclinic, $P\bar{1}$ (no. 2), a = 8.0932(4) Å, b = 11.8392(7) Å, c = 14.6782(8) Å, α = 87.860(3)°, β = 76.795(2)°, γ = 78.317(2)°, V = 1340.81(13) Å^3, Z = 2, R_{gt} (F) = 0.0559, wR_{ref} (F^2) = 0.1537, T = 170 K.

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Table 1: Data collection and handling.

Crystal:	Needle, colourless
Size:	0.07 × 0.04 × 0.03 mm
Wavelength:	Ga *K*α radiation (1.34139 Å)
μ:	0.59 mm^{-1}
Diffractometer, scan mode:	Zju Bruker D8 Venture, φ and ω-scans
θ_{max}, completeness:	60.6°, >99 %
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	25,694, 6034, 0.049
Criterion for I_{obs}, $N(hkl)_{gt}$:	I_{obs}° >° 2 $\sigma(I_{obs})$, 4834
$N(param)_{refined}$:	379
Programs:	Bruker programs [1], Olex2 [2], Shelx [3, 4]

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Table 1 contains crystallographic data and Table 2 contains the list of the atoms including atomic coordinates and displacement parameters.

Table 2: Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2).

Atom	*x*	*y*	*z*	U_{iso}*/U_{eq}
F1	0.17243 (16)	0.55645 (10)	0.21156 (8)	0.0393 (3)
O1	0.09648 (15)	0.17812 (10)	0.30827 (8)	0.0230 (3)
O2	−0.27009 (18)	0.62348 (11)	0.51238 (9)	0.0290 (3)
O3	−0.47802 (19)	0.59090 (13)	0.66231 (10)	0.0355 (3)
H3	−0.414411	0.622037	0.619636	0.053*
O4	−0.5197 (2)	0.41360 (14)	0.69978 (10)	0.0423 (4)
N1	0.48541 (19)	0.21299 (15)	0.00895 (11)	0.0277 (4)
H1A	0.447158	0.260427	−0.035340	0.033*
H1B	0.575405	0.158000	−0.020707	0.033*
N2	0.25881 (19)	0.31199 (14)	0.17688 (10)	0.0247 (3)
N3	−0.19096 (18)	0.27729 (12)	0.45385 (10)	0.0197 (3)
C1	0.3949 (3)	0.36975 (19)	0.12547 (14)	0.0331 (5)
H1C	0.434045	0.413872	0.169678	0.040*
H1D	0.348778	0.424623	0.080479	0.040*
C2	0.5470 (3)	0.2812 (2)	0.07322 (16)	0.0392 (5)
H2A[a]	0.584666	0.226090	0.121296	0.047*
H2B[b]	0.618236	0.329129	0.029642	0.047*
C3	0.3428 (2)	0.15661 (17)	0.06044 (13)	0.0268 (4)
H3A	0.386933	0.099132	0.104350	0.032*
H3B	0.300451	0.115798	0.015509	0.032*
C4	0.1959 (2)	0.24602 (17)	0.11406 (12)	0.0255 (4)
H4A	0.144275	0.298973	0.069650	0.031*
H4B	0.104789	0.207531	0.151026	0.031*
C6	0.1349 (2)	0.36578 (16)	0.25373 (12)	0.0219 (4)
C7	0.0934 (2)	0.48511 (16)	0.27314 (13)	0.0254 (4)
C8	−0.0226 (2)	0.53359 (16)	0.35079 (13)	0.0241 (4)
H8	−0.039231	0.613791	0.363129	0.029*
C9	−0.1173 (2)	0.46428 (15)	0.41234 (12)	0.0198 (3)
C10	−0.0878 (2)	0.34473 (14)	0.39432 (11)	0.0182 (3)
C11	0.0469 (2)	0.29594 (15)	0.31892 (12)	0.0196 (3)
C12	−0.2417 (2)	0.51656 (15)	0.49504 (12)	0.0209 (3)
C13	−0.3270 (2)	0.43861 (16)	0.55594 (12)	0.0220 (4)
C14	−0.2995 (2)	0.32512 (16)	0.53172 (12)	0.0217 (4)
H14	−0.361915	0.276703	0.573032	0.026*
C15	0.2429 (3)	0.13175 (19)	0.34798 (16)	0.0375 (5)
H15A	0.341061	0.166977	0.317833	0.056*
H15B	0.274627	0.048058	0.337843	0.056*
H15C	0.212718	0.148669	0.415281	0.056*
C16	−0.4498 (2)	0.47880 (18)	0.64523 (13)	0.0283 (4)
C17	−0.1975 (2)	0.16028 (15)	0.42865 (13)	0.0248 (4)
H17	−0.101324	0.097270	0.439418	0.030*
C18	−0.2704 (2)	0.14664 (18)	0.34617 (14)	0.0312 (4)
H18A	−0.218962	0.077086	0.306268	0.037*
H18B	−0.309459	0.217166	0.312188	0.037*
C19	−0.3737 (3)	0.13052 (18)	0.44290 (16)	0.0367 (5)
H19A	−0.385353	0.051088	0.462579	0.044*
H19B	−0.475908	0.191257	0.468503	0.044*
C5[a]	0.7011 (4)	0.3261 (3)	0.0251 (3)	0.0471 (11)
H5A[a]	0.794666	0.261653	−0.001370	0.071*
H5B[a]	0.738690	0.368780	0.070004	0.071*
H5C[a,b]	0.672370	0.377693	−0.025207	0.071*
C5A[b]	0.6588 (8)	0.2245 (6)	0.1246 (5)	0.038 (2)
H5AA[b]	0.596026	0.182661	0.175304	0.057*
H5AB[b]	0.709498	0.280460	0.151105	0.057*
H5AC[b]	0.751195	0.169837	0.084135	0.057*
O5	−0.42524 (16)	−0.06653 (14)	0.14809 (9)	0.0340 (3)
H5	−0.517897	−0.086701	0.175011	0.051*
O6	0.06314 (19)	−0.18091 (16)	0.36160 (11)	0.0437 (4)
H6	0.160874	−0.171982	0.331122	0.066*
O7	0.28458 (17)	−0.13235 (15)	0.22160 (12)	0.0426 (4)
O8	0.21267 (16)	−0.08015 (13)	0.08635 (10)	0.0332 (3)
C20	−0.1354 (2)	−0.08775 (15)	0.16279 (12)	0.0214 (4)
H20	−0.104927	−0.061998	0.100251	0.026*
C21	−0.3055 (2)	−0.09712 (16)	0.20128 (12)	0.0220 (4)
C22	−0.3482 (2)	−0.13669 (15)	0.29261 (13)	0.0233 (4)
H22	−0.463720	−0.144807	0.319070	0.028*
C23	−0.2241 (2)	−0.16421 (16)	0.34505 (13)	0.0263 (4)
H23	−0.254927	−0.190832	0.407297	0.032*
C24	−0.0541 (2)	−0.15309 (16)	0.30701 (13)	0.0251 (4)
C25	−0.0088 (2)	−0.11568 (15)	0.21483 (12)	0.0210 (4)
C26	0.1749 (2)	−0.10775 (16)	0.17019 (14)	0.0265 (4)
O9	−0.3516 (2)	0.61947 (16)	0.11429 (10)	0.0478 (4)
H9	−0.417198	0.615858	0.167221	0.072*
C27	−0.1757 (4)	0.5955 (3)	0.12276 (19)	0.0612 (8)
H27A	−0.100121	0.608220	0.062467	0.092*
H27B	−0.144294	0.515090	0.141407	0.092*
H27C	−0.162032	0.646771	0.170242	0.092*

Occupancies: [a]0.684 (7); [b]0.316 (7).

1 Source of materials

Gatifloxacin (GAT) (15.0 mg, 0.04 mmol) and 2,5-dihydroxy benzoic acid (15.0 mg, 0.07 mmol) were dissolved in methanol (5 mL) and water (1.5 mL) at 50 °C. Then, the solution was filtered and the filtrate placed in a 10 mL glass bottle. The glass bottle was covered with a porous film. Single crystal of the title compound were obtained after 7 days.

2 Experimental details

Absorption corrections were applied by using multi-scan program [1]. Using Olex2 [2], the structure was solved with the Shelxt [3] structure solution program and refined with the SHELXL [4] refinement package.

3 Comment

Gatifloxacin is a novel extended-spectrum fluoroquinolone with improved Gram-positive and anaerobe coverage compared with older agents such as ciprofloxacin [5]. The drug is available as tablets and aqueous solutions for intravenous therapy as well as eye drop formulation

(Zymar). The crystal structure of 1-cyclopropyl-6-fluoro-8-methoxy-7-(3-methyl-1-piperazinyl)-1,4-dihydro -4-oxo-3-quinolinecarboxylic acid hydrochloride, $[C_{19}H_{23}FN_3O_4]Cl$ (CCDC:692347) was reported [6]. As one of the fourth-generation quinolones, due to its poor solubility and easy to develop drug resistance, it is difficult to give full play to its clinical effects. In order to improve the physiochemical properties of gatifloxacin, salts were designed and synthesized by pharmaceutical salt forming technology. For example, the solubility of GAT with the pharmaceutical salts of 2,3-dihydroxybenzoic acid increased its solubility, the hygroscopic stability and the antibacterial activities *in vitro* of GAT-dihydroxybenzoic is also superior to GAT [7]. To improve the solubility of the fluoroquinolone drug gatifloxacin, a pharmaceutical salt of GAT with 2,5-dihydroxybenzoic acid is designed, synthesized, and characterized.

The title structure cystallizes in the triclinic $P\bar{1}$ space group with two asymmetric units in the unit cell, each containing a GAT cation and a 2,5-dihydroxybenzoate anion, where a proton is transferred from 2,5-dihydroxy benzoic acid to the piperazine N atom of GAT. N1H1A in the piperazine group participates in a classical N1–H1A···O9[1] hydrogen bond with methanol molecule ([1] = $-x$, $1-y$, $-z$; d(N1···O9) = 2.5162(19) Å; N1–H1A···O9 = 153.9°); N1H1B in the piperazine group is involved in a N1–H1B···O8[2] hydrogen bond to the oxygen atom in 2,5-dihydroxybenzoic acid ([2] = $1-X$, $-Y$, $-Z$; d(N1···O8) = 2.729(2) Å; N1–H1A···O8 = 164.4°); O9H9 in the carboxyl group of GAT participates in O9–H9···O4[4] hydrogen bond with methanol molecule ([4] = $-1-x$, $1-y$, $1-z$; d(O9···O4) = 2.734(2) Å; O9–H9···O4 = 157.4°). Two oxygen atoms in two molecule of 2,5-dihydroxybenzoic acid form one hydrogen bonds: O5–H5···O7[3] ([3] = $-1+x$, $+y$, $+z$; d(O5···O7) = 2.6091(19) Å; O5–H5···O7 = 174.8°).

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Conflict of interest statement: The authors declare no conflicts of interest regarding this article.

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