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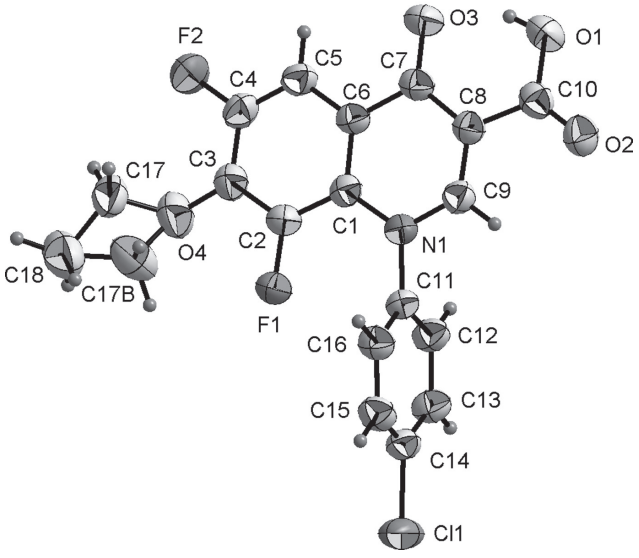
Crystal structure of 1-(4-chloro-phenyl)-7-ethoxyl-6,8-difluoro-4-oxo-1,4-dihydro-quinoline-3-carboxylic acid, $C_{18}H_{12}ClF_2NO_4$



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Abstract

$C_{18}H_{12}ClF_2NO_4$, monoclinic, $P2_1/c$ (no. 14), $a = 13.544(5)$ Å, $b = 9.344(3)$ Å, $c = 13.545(5)$ Å, $\beta = 109.86°$, $V = 1612.4(10)$ Å^3, $Z = 4$, $R_{gt}(F) = 0.0393$, $wR_{ref}(F^2) = 0.1058$, $T = 296(2)$ K.

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The molecular structure is shown in the figure. Table 1 contains crystallographic data and Table 2 contains the list of the atoms including atomic coordinates and displacement parameters.

Table 1: Data collection and handling.

Crystal:	Colorless block
Size:	0.20 × 0.16 × 0.13 mm
Wavelength:	Mo $K\alpha$ radiation (0.71073 Å)
μ:	0.28 mm^{-1}
Diffractometer, scan mode:	Bruker APEX-II, φ and ω
θ_{max}, completeness:	25.5°, >99%
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	12053, 2988, 0.033
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 2251
$N(param)_{refined}$:	249
Programs:	Bruker [1], SHELX [2, 3], Diamond [4]

Source of material

To a stirred solution of 1-(4-chloro-phenyl)-6,7,8-trifluoro-4-oxo-1,4-dihydro-quinoline-3-carboxylic acid ethyl ester (38.2 g, 0.1 moL) in ethanol (200 mL) was added sodium hydroxide (4.0 g, 0.1 moL), and then the reaction mixture was refluxed for about 0.5 h. After the reaction was completed (monitored by TLC), the ethanol was evaporated under reduced pressure to give a crude product. The crude product was poured into water (40 mL) and extracted with EtOAc (50 mL × 3). The EtOAc solvent was evaporated to provide crystals of the title compound suitable for X-ray analysis in 84.5% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.37–1.40 (t, $J = 8.0$ Hz, 3 H, CH3), 4.29–4.35 (q, $J = 8.0$, 16.0 Hz, 2 H, OCH2), 7.36–7.55 (m, 4 H, PhH), 8.05–8.07 (d, $J = 8.0$ Hz, 1 H, ArH), 8.58 (s, 1 H, NCH), 14.30 (br, 1 H, COOH) ppm. **^{13}C NMR**

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

Atom	*x*	*y*	*z*	U_{iso}*/U_{eq}
C1	0.83318(14)	0.0732(2)	0.43218(14)	0.0421(4)
C2	0.74913(15)	−0.0206(2)	0.39365(15)	0.0481(5)
C3	0.72053(16)	−0.1151(2)	0.45689(17)	0.0537(5)
C4	0.78124(18)	−0.1169(2)	0.56385(16)	0.0561(5)
C5	0.86451(17)	−0.0301(2)	0.60473(16)	0.0510(5)
H5	0.9037	−0.0348	0.6759	0.061*
C6	0.89194(15)	0.0670(2)	0.54009(14)	0.0421(4)
C7	0.97992(15)	0.1630(2)	0.58605(15)	0.0451(5)
C8	1.00360(15)	0.2577(2)	0.51487(15)	0.0437(4)
C9	0.94274(15)	0.2596(2)	0.41129(15)	0.0459(5)
H9	0.9597	0.3246	0.3676	0.055*
C10	1.09032(16)	0.3617(2)	0.55004(17)	0.0519(5)
C11	0.79339(15)	0.2046(2)	0.26158(14)	0.0429(4)
C12	0.72062(16)	0.3114(2)	0.24645(16)	0.0509(5)
H12	0.7163	0.3639	0.3032	0.061*
C13	0.65381(17)	0.3405(2)	0.14633(16)	0.0547(5)
H13	0.6035	0.4121	0.1349	0.066*
C14	0.66227(16)	0.2626(2)	0.06386(15)	0.0499(5)
C15	0.73762(17)	0.1596(2)	0.07809(16)	0.0533(5)
H15	0.7440	0.1105	0.0209	0.064*
C16	0.80398(16)	0.1295(2)	0.17837(15)	0.0503(5)
H16	0.8553	0.0593	0.1896	0.060*
C17[a]	0.6243(3)	−0.3329(4)	0.4318(4)	0.0703(16)
H17A[a]	0.5980	−0.3463	0.4895	0.084*
H17B[a]	0.6936	−0.3755	0.4520	0.084*
C18	0.5549(2)	−0.4072(3)	0.3393(3)	0.0987(10)
H18A	0.5857	−0.4066	0.2851	0.148*
H18B	0.4882	−0.3596	0.3146	0.148*
H18C	0.5453	−0.5043	0.3574	0.148*
Cl1	0.57505(5)	0.29522(8)	−0.06195(4)	0.0741(2)
F1	0.69051(10)	−0.02017(14)	0.29174(9)	0.0693(4)
F2	0.75266(13)	−0.20755(17)	0.62604(11)	0.0861(5)
N1	0.86015(12)	0.17355(17)	0.36877(12)	0.0440(4)
O1	1.14296(13)	0.36268(19)	0.65210(12)	0.0709(5)
H1	1.1213	0.2983	0.6805	0.106*
O2	1.11349(12)	0.44157(17)	0.49151(13)	0.0653(4)
O3	1.03103(12)	0.16004(17)	0.68288(11)	0.0612(4)
O4	0.63224(14)	−0.1920(2)	0.41624(15)	0.0800(5)
C17B[d]	0.6119(7)	−0.2834(10)	0.3329(6)	0.089(4)
H17C[b]	0.6781	−0.3126	0.3264	0.107*
H17D[b]	0.5729	−0.2318	0.2695	0.107*

[a]Occupancy: 0.635(8), [b]Occupancy: 0.365(8).

(100 MHz, $CDCl_3$) $\delta = 176.03$, 165.07, 149.57, 140.68, 135.70, 129.44, 126.39, 107.72, 107.53, 70.41, 14.76 ppm.

Experimental details

All H atoms were included in calculated positions and refined as riding atoms, with O—H = 0.82 Å with U_{iso} (H) = 1.2 U_{eq} (O), C—H = 0.93–0.98 Å) with U_{iso}(H) = 1.2–1.5 U_{eq}(C) [3].

Comment

Since the advent of naphthalic acid in the 1960s, quinolones are very important synthetic broad-spectrum antibiotics and the most important breakthroughs in antibiotic synthesis after sulfonamide [5–8]. Owing the characteristics of wide antibacterial spectrum, strong antibacterial activity, convenient administration and no cross resistance with commonly used antibiotics, quinolones have been popularized rapidly in clinic, and become the key drug in the development, production and application in the world [9]. However, quinolones have been used or even abused for a long time, and bacteria have become seriously resistant to the quinolones through mutation and chromosome medium. Therefore, it is urgent to develop new quinolones effective against drug-resistant bacteria [10]. Recently, an expedient and high-yielding method for the synthesis of fluoroquinolones is explored in our group, and single crystals of several key intermediates are achieved. We have reported the synthesis and single crystals of a key intermediate 7-ethoxyl-6,8-difluoro-4-oxo-1-phenyl-1,4-dihydroquinoline-3-carboxylic acid [11]. Herein, the synthesis and crystal structure of a key intermediate 1-(4-chloro-phenyl)-7-ethoxy-6,8-difluoro-4-oxo-1,4-dihydro-quinoline-3-carboxylic acid is disclosed.

In the molecule of the title compound bond lengths and angles are very similar to those given in the literature for directly related ones [12–14]. The molecule consists of two moieties: quinoline and substituted chloro-phenyl group. The chloro-phenyl group is connected to the nitrogen atom (N1) of the quinoline moiety. The dihedral angle of quinoline chlorophenyl group and the carboxylate group C10-O1-O2 plane are 85.42(5)°, 3.35(10)° and 85.97(11)°, respectively. The torsion angles of C4-C3-O4-C17 and C3-O4-C17-C18 are −51.1(4)° and −143.3(3)°, respectively.

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