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Crystal structure of 1-cyclopropyl-7-ethoxy-6,8-difluoro-4-oxo-1,4-dihydro-quinoline-3-carboxylic acid, $C_{15}H_{13}F_2NO_4$

Table 1: Data collection and handling.

Crystal:	Colorless block
Wavelength:	Size $0.20 \times 0.16 \times 0.12$ mm
μ :	MoK α radiation (0.71073 Å)
Diffraction mode:	0.13 mm ⁻¹
$\theta_{\max}$, completeness:	Bruker APEX-II, φ and ω
$N(hkl)_{\text{measured}}$, $N(hkl)_{\text{unique}}$, R_{int} :	25.5°, >99%
Criterion for I_{obs} , $N(hkl)_{\text{gt}}$:	10067, 2486, 0.031
$N(\text{param})_{\text{refined}}$:	$I_{\text{obs}} > 2 \sigma(I_{\text{obs}})$, 2020
Programs:	201
	Bruker [1], SHELX [2, 3],
	Diamond [4]

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Abstract

$C_{15}H_{13}F_2NO_4$, monoclinic, $P2_1/n$ (no. 14), $a = 5.1342(10)$ Å, $b = 9.6478(18)$ Å, $c = 27.192(5)$ Å, $\beta = 95.42^\circ$, $V = 1340.9(4)$ Å³, $Z = 4$, $R_{\text{gt}}(F) = 0.0434$, $wR_{\text{ref}}(F^2) = 0.1197$, $T = 296(2)$ 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.

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Source of material

To a stirred solution of 1-cyclopropyl-6,7,8-trifluoro-4-oxo-1,4-dihydro-quinoline-3-carboxylic acid ethyl ester (31.1 g, 0.1 mol) in ethanol (150 mL) was added sodium hydroxide (8.0 g, 0.2 mol), and then the reaction mixture was refluxed for about 0.5 h. After the reaction completed (monitored by TLC), the ethanol was distilled under reduced pressure to give crude product. The crude product was poured into water (40 mL) and extracted with EtOAc (50 mL $\times$ 3). The EtOAc solvent was evaporated to provide 1-cyclopropyl-7-ethoxy-6,8-difluoro-4-oxo-1,4-dihydro-quinoline-3-carboxylic acid being suitable for X-ray analysis in 75.0 % yield. ¹H NMR (400 MHz, CDCl₃) δ = 1.20–1.40 (m, 4H, CH₂CH₂), 1.49–1.52 (t, J = 12.0 Hz, 3H, CH₃), 3.97–4.07 (m, 1H, NCH), 4.42–4.48 (q, J = 8.0, 12.0 Hz, 2H, OCH₂), 8.02–8.05 (d, J = 12.0 Hz, 1H, ArH), 8.84 (s, 1H, NCH=C), 14.45 (br, 1H, COOH) ppm. ¹³C NMR (100 MHz, CDCl₃) δ = 176.60, 166.16, 149.68, 141.59, 139.39, 126.70, 124.25, 118.65, 108.48, 106.62, 71.21, 40.05, 15.57, 9.20, 9.12 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].

Table 2: Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å²).

Atom	x	y	z	<i>U</i> _{iso} [*] / <i>U</i> _{eq}
C1	0.9595 (3)	0.36199 (17)	0.10197 (6)	0.0380 (4)
C2	0.9755 (4)	0.44520 (19)	0.14452 (7)	0.0438 (4)
C3	1.1562 (4)	0.55082 (19)	0.15250 (7)	0.0493 (5)
C4	1.3231 (4)	0.57583 (19)	0.11607 (8)	0.0497 (5)
C5	1.3094 (4)	0.50276 (19)	0.07336 (7)	0.0456 (4)
H5	1.4208	0.5235	0.0493	0.055*
C6	1.1258 (3)	0.39576 (18)	0.06576 (6)	0.0390 (4)
C7	1.1095 (3)	0.32109 (18)	0.01888 (7)	0.0393 (4)
C8	0.9115 (3)	0.21779 (18)	0.01226 (6)	0.0390 (4)
C9	0.7630 (3)	0.18654 (18)	0.04983 (6)	0.0401 (4)
H9	0.6385	0.1167	0.0446	0.048*
C10	0.8716 (4)	0.13477 (19)	−0.03384 (7)	0.0455 (4)
C11	1.0776 (7)	0.7590 (3)	0.19501 (9)	0.0851 (9)
H11A	0.8878	0.7575	0.1917	0.102*
H11B	1.1347	0.8071	0.1666	0.102*
C12	1.1677 (7)	0.8317 (3)	0.23871 (9)	0.0927 (10)
H12A	1.1456	0.7748	0.2670	0.139*
H12B	1.0688	0.9157	0.2408	0.139*
H12C	1.3495	0.8540	0.2380	0.139*
C13	0.6410 (4)	0.19679 (19)	0.13365 (7)	0.0454 (5)
H13	0.4922	0.2526	0.1421	0.054*
C14	0.7899 (5)	0.1228 (2)	0.17531 (8)	0.0590 (6)
H14A	0.9770	0.1121	0.1742	0.071*
H14B	0.7343	0.1355	0.2081	0.071*
C15	0.6138 (5)	0.0439 (2)	0.13880 (8)	0.0600 (6)
H15A	0.4513	0.0087	0.1494	0.072*
H15B	0.6940	−0.0146	0.1155	0.072*
N1	0.7855 (3)	0.25053 (15)	0.09402 (5)	0.0395 (4)
O1	1.0316 (3)	0.16392 (16)	−0.06795 (5)	0.0577 (4)
H1	1.1304	0.2269	−0.0581	0.086*
O2	0.7089 (3)	0.04597 (17)	−0.04072 (5)	0.0666 (5)
O3	1.2607 (3)	0.34913 (15)	−0.01317 (5)	0.0555 (4)
O4	1.1725 (4)	0.62196 (15)	0.19580 (5)	0.0663 (5)
F1	1.5024 (3)	0.67760 (13)	0.12428 (5)	0.0693 (4)
F2	0.8092 (2)	0.42773 (12)	0.17943 (4)	0.0594 (3)

Comment

Quinolones are vitally synthetic broad-spectrum antibiotics and most significant breakthroughs after sulfonamide since the synthesis of naphthalic acid in the 1960s [5–8]. Caused by these characteristics of a wide antibacterial spectrum, a strong antibacterial activity, and no cross resistance with common antibiotics, quinolones have been popularized rapidly in clinic, and become the significant drug in the development, production and application all over the world [9]. Having been used or even abused for a long time, quinolones have been seriously resisted by bacteria through gene mutations. Therefore, it is urgent to obtain new effective quinolones against drug-resistant

bacteria [10]. Recently, an impactful and high-yielding method for the synthesis of fluoroquinolones is developed in our group, and single crystals of several key intermediates are achieved.

In the molecule of the title compound bond lengths and angles within 1-cyclopropyl-7-ethoxy-6,8-difluoro-4-oxo-1,4-dihydro-quinoline-3-carboxylic acid are very similar to those given in the literature for 1-(4-chlorophenyl)-7-ethoxyl-6,8-difluoro-4-oxo-1,4-dihydro-quinoline-3-carboxylic acid [11] and two other directly related structures [12, 13]. The atoms of quinoline ring are coplanar. The dihedral angles between the quinoline ring, the cyclopropane ring and the plane of carboxy group (C10–O1–O2) are 2.7°, 68.8° and 68.3°, respectively. The torsion angles of C4–C3–O4–C11 and C3–O4–C11–C12 are −164.5° and 75.2°, respectively.

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