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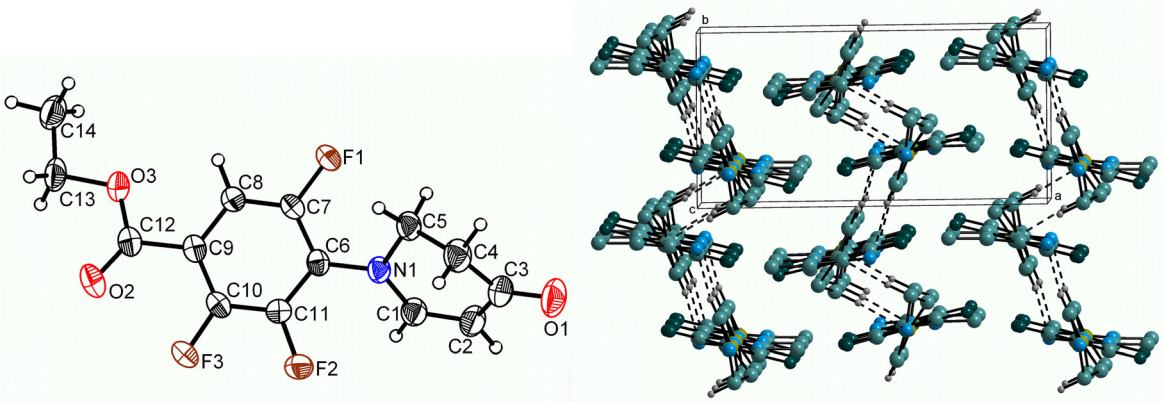
The crystal structure of ethyl 2,3,5-trifluoro-4-(4-oxo-3,4-dihydropyridin-1(2*H*)-yl)benzoate, $C_{14}H_{12}F_3NO_3$



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Abstract

$C_{14}H_{12}F_3NO_3$, monoclinic, $P2_1/n$ (no. 14), a = 14.4583(12) Å, b = 6.6553(5) Å, c = 14.8395(11) Å, β = 113.733(3)°, V = 1307.16(18) Å^3, Z = 4, $R_{gt}(F)$ = 0.0479, $wR_{ref}(F^2)$ = 0.1235, T = 170 K.

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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 1: Data collection and handling.

Crystal:	Colourless plate
Size:	0.49 × 0.35 × 0.10 mm
Wavelength:	Mo *K*α radiation (0.71073 Å)
μ:	0.14 mm^{-1}
Diffractometer, scan mode:	Bruker Apex-II, φ and ω
θ_{max}, completeness:	27.1°, >99%
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	14976, 2893, 0.034
Criterion for I_{obs}, $N(hkl)_{gt}$:	I_{obs} > 2 $\sigma(I_{obs})$, 2371
$N(param)_{refined}$:	195
Programs:	Bruker [1], Shelx [2, 3], Olex2 [4]

Source of material

In a representative experiment, the title compound commercially available was grown by the vapor diffusion method. Approximately 0.14 g (0.5 mmol) ethyl 2,3,5-trifluoro-4-(4-oxo-3,4-dihydropyridin- 1(2*H*)-yl)benzoate was dissolved in dichloromethane/methanol (1:1) solution dropwise in a well. Then *n*-pentane was added into another well. Both wells were sitting in a clear beaker sealed with tape for easy viewing and access. Over time the equilibrium of the vapor will exist between the solvents. During this equilibration process colorless plate crystals of the title compound were obtained within about a week.

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

Atom	*x*	*y*	*z*	U_{iso}*/U_{eq}
C1	0.56532(14)	0.1236(3)	0.82490(13)	0.0375(4)
H1	0.539511	0.010678	0.783091	0.045*
C2	0.56691(16)	0.1169(3)	0.91668(14)	0.0440(5)
H2	0.550094	−0.004842	0.939978	0.053*
C3	0.59367(16)	0.2911(3)	0.97965(14)	0.0449(5)
C4	0.60731(17)	0.4828(3)	0.93043(14)	0.0469(5)
H4A	0.540671	0.547446	0.895571	0.056*
H4B	0.650649	0.577144	0.981546	0.056*
C5	0.65411(15)	0.4432(3)	0.85873(13)	0.0399(4)
H5A	0.653172	0.567961	0.822004	0.048*
H5B	0.725410	0.402102	0.894832	0.048*
C6	0.59421(13)	0.2852(2)	0.69312(12)	0.0282(4)
C7	0.67659(12)	0.3364(3)	0.67109(12)	0.0303(4)
C8	0.67268(13)	0.3394(2)	0.57729(12)	0.0296(4)
H8[a]	0.730967	0.375863	0.566561	0.036*
C9	0.58365(13)	0.2893(2)	0.49755(12)	0.0286(4)
C10	0.50001(13)	0.2400(2)	0.51691(12)	0.0289(4)
H10[b]	0.437997	0.207169	0.463928	0.035*
C11	0.50581(12)	0.2381(2)	0.61215(13)	0.0289(4)
C12	0.57797(14)	0.2884(2)	0.39492(12)	0.0318(4)
C13	0.67172(17)	0.3126(3)	0.29616(13)	0.0454(5)
H13A	0.636642	0.434327	0.260246	0.054*
H13B	0.637732	0.192924	0.257314	0.054*
C14	0.78049(18)	0.3164(4)	0.31139(16)	0.0518(5)
H14A	0.785215	0.324143	0.247434	0.078*
H14B	0.813922	0.193768	0.345614	0.078*
H14C	0.813566	0.433898	0.351113	0.078*
F1	0.76544(7)	0.37929(19)	0.74621(7)	0.0409(3)
F2	0.42129(8)	0.19484(17)	0.62593(8)	0.0396(3)
F3[a]	0.41065(9)	0.19627(19)	0.44519(9)	0.0368(3)
F3A[b]	0.7544(4)	0.3951(10)	0.5745(4)	0.0368(3)
N1	0.59892(11)	0.2844(2)	0.78928(10)	0.0316(3)
O1	0.59685(14)	0.2919(3)	1.06346(11)	0.0600(5)
O2	0.50037(11)	0.2738(2)	0.32234(9)	0.0445(4)
O3	0.66926(10)	0.3057(2)	0.39382(9)	0.0399(3)

[a]Occupancy: 0.841(2), [b]Occupancy: 0.159(2).

Experimental details

A suitable crystal was selected and placed on a 'Bruker Apex–II CCD' diffractometer. Using Olex2 [4], the structure was solved with the ShelXT [2] structure solution program and refined with the ShelXT [3] refinement package.

U_{iso} values of hydrogen atoms were set to 1.2U_{eq} of the parent atoms for all C(H) groups, C(H,H) groups, and at 1.5U_{eq} for all C(H,H,H) groups. Secondary CH_2, C5(H5A,H5B), C13(H13A,H13B), C4(H4A,H4B), were refined with riding coordinates. Aromatic/amide H, C10(H10), C8(H8), C1(H1), C2(H2), were also refined with riding coordinates. Idealised Me, C14(H14A,H14B,H14C), were refined as rotating group. Statistical disorder is noted for the F3, F3A atom. The F3, F3A are disordered over two sites with occupancies 0.8414:0.1586. For this disorder, distances restraints of F3–C10 and F3A–C8, and U_{iso}/U_{aniso} restraints of U_{anis}(F3) = U_{anis}(F3A) were imposed. The disordered F atom in 1,2,4-trifluorobenzene group is also observed in related systems [5–8].

Comment

Contezolid with a strong potency against all major Gram-positive pathogens, including newer multidrug resistant strains, has gained a significant place as a last line antimicrobial agent [9, 10]. It is known that even very little structural changes to the oxazolidinone lead to drastic changes in biological activity [11, 12]. The title compound, a derivative of Contezolid, replaces its oxazolidinone group with a ethyl formate group which is expected to change conformations when they are bound to target nucleotides. The title compound is part of our continuing interest in the structure-activity relationship about the antimicrobial agent, and understanding of hydrogen bonding schemes of related compounds [13, 14].

The title compound has a trifluorinated benzyl group whose structure was determined without disorder by Refs. [15–17]. The trifluorinated benzyl group perhaps plays a part in toxicity and selective binding to bacteria according to cryo–EM results [9]. The structure of 2,3,5-trifluorobenzoic acid moiety, most similar to the title compound, has been reported by Refs. [18–20].

To the best of our knowledge, this is the first article to report a structure containing the ethyl 2,3,5-trifluorobenzoate group, and the first to report a structure containing the 2,3–dihydro-4-pyridinone group.

The asymmetric unit of the title structure contains one ethyl 2,3,5-trifluoro-4-(4-oxo-3,4-dihydropyridin-1(2H)-yl) benzoate (*cf*. left part of the figure, main part of the disorder is shown for clarity purpose). The bond lengths and angles within these moieties are in the expected ranges. The plane of 2,3–dihydro-4-pyridinone group (N1—C1—C2—C3—C4—C5—C6), encloses an angle of 53.87(9)° with the plane of the trifluorobenzoate group (C6—C7—C8—C9—C10—C11).

No classic hydrogen bond was found for the title compound, but two intermolecular non-classical hydrogen bonds.

Two hydrogen bonds (C4—H4A···O1′; ′ = 1–*x*, 1–*y*, 2–*z*; D···A = 3.344(3) Å) connect two adjacent molecules to form an eight-membered ring. The other two hydrogen bonds (C1—H1···O2″; ″ = 1–*x*, –*y*, 1–*z*; D···A = 3.317(2) Å) connect the next two adjacent molecules head-to-tail forming a large ring (*cf*. right part of the figure. Some hydrogen atoms are omitted for clarity). The two rings extend alternately,

constructing chains parallel to the diagonal of the *bc* plane (*cf*. right part of the figure).

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