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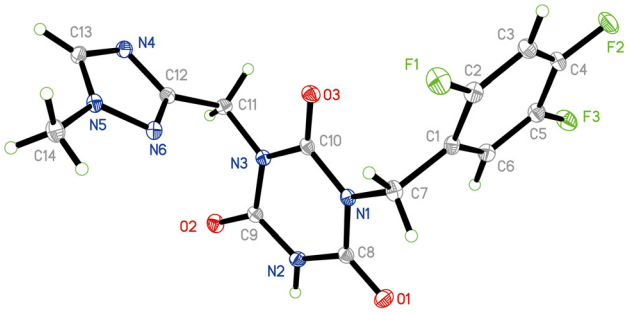
The crystal structure of 1-((1-methyl-1*H*-1,2,4-triazol-3-yl) methyl)-3-(2,4,5-trifluorobenzyl)-1,3,5-triazinane-2,4,6-trione, $C_{14}H_{11}F_3N_6O_3$



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Abstract

$C_{14}H_{11}F_3N_6O_3$, orthorhombic, *Pbca* (no. 61), a = 8.08620(10) Å, b = 15.4730(2) Å, c = 23.5892(2) Å, V = 2951.43(6) Å^3, Z = 8, $R_{gt}(F)$ = 0.0463, $wR_{ref}(F^2)$ = 0.1395, T = 293 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 × 0.10 × 0.10 mm
Wavelength:	Cu *K*α radiation (1.54178 Å)
μ:	1.28 mm^{-1}
Diffractometer, scan mode:	Rigaku Mercury
θ_{max}, completeness:	74.4°, >99%
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	50,285, 2991, 0.065
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 2712
$N(param)_{refined}$:	235
Programs:	Rigaku [1], Olex2 [2], SHELX [3, 4]

Source of material

All chemicals were obtained from commercial sources and used as purchased. To a solution of 6-(ethylthio)-3-((1-methyl-1*H*-1,2,4-triazol-3-yl)methyl)-1-(2,4,5-trifluorobenzyl)-1,3,5-triazine-2,4(1*H*,3*H*)-dione (0.41 g, 1 mmol) in dichloromethane (20 mL), 3-chloroperoxybenzoic acid (0.51 g, 3 mmol) was added. Then the mixture was stirred at room temperature for 3 h. After the reaction was completed, the solution was washed with saturated $NaHSO_3$ and $NaHCO_3$, respectively. The organic layer was dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. The crude products were purified by flash column chromatography. Colorless block crystals of the title compound were obtained by slow evaporation of a solution in ethyl acetate. **^{1}H NMR** (400 MHz, DMSO-d_6): δ 12.08 (s, 1H), 8.39 (s, 1H), 7.60 (m, 1H), 7.49 (m, 1H), 4.95 (s, 4H), 3.83 (s, 3H).

Experimental details

Absorption corrections were applied using a multi-scan program [1]. Using Olex2 [2], the structure was solved with the ShelXT [3] package and refined with the ShelXL [4] program. H atoms were positioned geometrically and allowed to ride on their parent atoms, with C–H = 0.93 Å (phenyl and triazolyl), 0.96 Å (methyl) or 0.97 Å (methylene) and with U_{iso}(H) = 1.2U_{eq}(C), and N–H = 0.86 Å and U_{iso}(H) = 1.2U_{eq}(N).

Comment

The 1,3,5-triazinane-2,4,6-trione, known as isocyanurate, is used to be a human gonadotropin-releasing hormone receptor antagonist [5, 6]. Many references showed crystal structures of the derivatives with 1,3,5-triazinane-

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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}
N1	0.20256 (18)	0.07419 (9)	0.36883 (6)	0.0180 (3)
N2	0.11187 (19)	0.02902 (10)	0.28007 (6)	0.0206 (3)
H2A	0.0939	−0.0120	0.2563	0.025*
N3	0.11168 (18)	0.17574 (9)	0.30152 (6)	0.0180 (3)
N4	−0.12391 (19)	0.38431 (10)	0.29917 (6)	0.0216 (3)
N5	−0.29975 (18)	0.31259 (10)	0.35155 (6)	0.0199 (3)
N6	−0.17560 (19)	0.25533 (10)	0.34046 (6)	0.0205 (3)
O1	0.21541 (18)	−0.06774 (9)	0.34285 (6)	0.0274 (3)
O2	−0.00009 (17)	0.12553 (9)	0.21859 (5)	0.0258 (3)
O3	0.19661 (16)	0.21725 (8)	0.38928 (5)	0.0229 (3)
F1	0.32191 (15)	0.14838 (9)	0.52638 (5)	0.0336 (3)
F2	0.89419 (15)	0.14513 (9)	0.49200 (5)	0.0351 (3)
F3	0.84506 (14)	0.05513 (8)	0.39638 (5)	0.0337 (3)
C1	0.4189 (2)	0.07909 (11)	0.44397 (7)	0.0204 (4)
C2	0.4512 (2)	0.12507 (12)	0.49312 (7)	0.0234 (4)
C3	0.6076 (3)	0.14877 (13)	0.51088 (8)	0.0266 (4)
H3A	0.6237	0.1798	0.5442	0.032*
C4	0.7382 (2)	0.12455 (13)	0.47719 (8)	0.0250 (4)
C5	0.7112 (2)	0.07786 (13)	0.42787 (8)	0.0243 (4)
C6	0.5551 (2)	0.05499 (12)	0.41111 (8)	0.0221 (4)
H6B	0.5397	0.0235	0.3779	0.027*
C7	0.2442 (2)	0.05469 (13)	0.42821 (7)	0.0224 (4)
H7A	0.2290	−0.0067	0.4348	0.027*
H7B	0.1681	0.0854	0.4528	0.027*
C8	0.1810 (2)	0.00649 (11)	0.33122 (7)	0.0196 (4)
C9	0.0687 (2)	0.11135 (12)	0.26347 (7)	0.0196 (4)
C10	0.1720 (2)	0.15992 (11)	0.35567 (7)	0.0180 (4)
C11	0.0846 (2)	0.26610 (11)	0.28568 (8)	0.0204 (4)
H11A	0.0826	0.2707	0.2447	0.025*
H11B	0.1761	0.3007	0.2995	0.025*
C12	−0.0737 (2)	0.30146 (11)	0.30907 (7)	0.0183 (4)
C13	−0.2670 (2)	0.38735 (12)	0.32676 (8)	0.0225 (4)
H13A	−0.3352	0.4357	0.3284	0.027*
C14	−0.4433 (2)	0.28671 (13)	0.38477 (8)	0.0264 (4)
H14A	−0.4301	0.2279	0.3970	0.040*
H14B	−0.4533	0.3237	0.4173	0.040*
H14C	−0.5411	0.2915	0.3619	0.040*

2,4,6-trione as parent structure [7–10]. In this work, we report the single crystal structure of 1-((1-methyl-1*H*-1,2,4-triazol-3-yl) methyl)-3-(2,4,5-trifluorobenzyl)-1,3,5-triazinane-2,4,6-trione, which is an intermediate for the synthesis of ensitrelvir, a novel oral drug for the treatment of coronavirus disease 2019 (COVID-19) [11].

Single-crystal structure analysis revealed that the asymmetric unit consists one 1-((1-methyl-1*H*-1,2,4-triazol-3-yl)methyl)-3-(2,4,5-trifluorobenzyl)-1,3,5-triazinane-2,4,6-trione molecule. The central six-membered heterocyclic ring lies on a general position, which is evidently different from that observed in the symmetric tri-substituted compounds (lying on a 3-fold totation axis) [7–9]. The dihedral angles between the least-squares plane of the central triazinane ring of the title molecule and those of the terminal triazole/benzene ring groups are 80.5(4)° (C12/N4/C13/N5/N6) and 78.0(2)° (C1–C6), respectively. The two planes of the terminal ring of the title molecule are oriented with respect to each other at 78.4(3)° [(C12/N4/C13/N5/N6) and (C1–C6)]. In the solid state structure, numerous classical N–H···N and weak C–H···F, C–H···N and C–H···O hydrogen-bonding interactions result in a one-dimensional supramolecular chain along the [0 1 0] direction.

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

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