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Crystal structure of 4-(2,2-difluoroethyl)-2,4,6-trimethylisoquinoline-1,3(2*H*,4*H*)-dione, $C_{14}H_{15}F_2NO_2$

Table 1: Data collection and handling.

Crystal:	Colourless block
Size:	0.23 × 0.20 × 0.18 mm
Wavelength:	Mo K α radiation (0.71073 Å)
μ :	0.11 mm ⁻¹
Diffractometer, scan mode:	D8-APEX2, φ and ω
$\theta_{\max}$, completeness:	27.8°, 99%
$N(hkl)_{\text{measured}}$, $N(hkl)_{\text{unique}}$, R_{int} :	7513, 2688, 0.036
Criterion for I_{obs} , $N(hkl)_{\text{gt}}$:	$I_{\text{obs}} > 2 \sigma(I_{\text{obs}})$, 1886
$N(\text{param})_{\text{refined}}$:	274
Programs:	Bruker [1], Olex2 [2], SHELX [3]

Source of material

According to the literature method [4], the title compound was obtained in 72% yield. The title compound was recrystallized from anhydrous tetrahydrofuran at room temperature to obtain the colorless block crystals.

Experimental details

All H atoms were located by geometrical calculations and refined as riding atoms, and their positions and thermal parameters were fixed during the structure refinement. Some atoms are disordered over two positions. The two parts overlapped each other with site occupation factors of 0.788 and 0.212. The disorder is omitted in the figure for clarity.

Comment

Isoquinoline-1,3-dione and its derivatives have been widely investigated due to their excellent pharmaceutical and biological activities, such as anti-tumor and HIV-1 integrase inhibitors [5–10]. Especially, the isoquinoline-1,3-diones containing a difluoromethyl moiety (CF_2H) often show special biological properties [4, 11, 12]. However, the synthesis and crystal structure of difluoromethylated isoquinoline-1,3-diones remains limited. In order to investigate the structural and biological properties of difluoromethylated isoquinoline-1,3-diones, the structure of the title compound was analyzed in detail.

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Abstract

$C_{14}H_{15}F_2NO_2$, monoclinic, $P2_1/c$ (no. 14), $a = 11.5474(10)$ Å, $b = 11.0737(7)$ Å, $c = 11.4311(10)$ Å, $\beta = 114.979(11)^\circ$, $V = 1325.0(2)$ Å³, $Z = 4$, $R_{\text{gt}}(F) = 0.0738$, $wR_{\text{ref}}(F^2) = 0.2034$, $T = 293(2)$ 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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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 ^a	0.3381 (4)	0.2220 (3)	0.6764 (4)	0.0424 (9)
C1A ^b	0.309 (2)	0.2344 (18)	0.7149 (18)	0.063 (4)
C2	0.1206 (3)	0.2426 (3)	0.5044 (3)	0.0499 (7)
C3	0.14746 (19)	0.36866 (16)	0.48370 (19)	0.0438 (6)
C4 ^a	0.26464 (17)	0.4227 (2)	0.5567 (2)	0.0374 (9)
C4A ^b	0.2437 (19)	0.4292 (19)	0.5913 (18)	0.063 (5)
C5 ^a	0.3726 (3)	0.3513 (3)	0.6581 (3)	0.0370 (7)
C5A ^b	0.3353 (17)	0.3682 (15)	0.7129 (15)	0.061 (3)
C6 ^a	0.4896 (7)	0.3449 (8)	0.6261 (6)	0.0507 (12)
H6A ^a	0.556342	0.299340	0.691633	0.076*
H6B ^a	0.519585	0.425103	0.622734	0.076*
H6C ^a	0.465712	0.306211	0.543993	0.076*
C6A ^b	0.329 (3)	0.456 (3)	0.823 (4)	0.069 (7)
H6AA ^b	0.251067	0.501618	0.788107	0.104*
H6AB ^b	0.400531	0.510650	0.852032	0.104*
H6AC ^b	0.332302	0.408580	0.894532	0.104*
C7	0.05091 (15)	0.43441 (18)	0.38855 (18)	0.0563 (7)
H7	−0.027483	0.398238	0.339692	0.068*
C8	0.0715 (2)	0.55423 (18)	0.3664 (2)	0.0588 (8)
H8A ^a	0.006941	0.598223	0.302756	0.071*
H8B ^b	0.019846	0.589992	0.287992	0.071*
C9 ^a	0.1887 (3)	0.60829 (18)	0.4394 (3)	0.0490 (15)
C9A ^b	0.1726 (18)	0.6245 (17)	0.464 (2)	0.048 (4)
C10 ^a	0.2853 (2)	0.5425 (2)	0.5346 (3)	0.0471 (11)
H10 ^a	0.363663	0.578714	0.583448	0.056*
C10A ^b	0.2533 (17)	0.5515 (18)	0.564 (2)	0.063 (5)
H10A ^b	0.325853	0.590211	0.623566	0.075*
C11 ^a	0.2099 (8)	0.7392 (6)	0.4190 (10)	0.075 (2)
H11A ^a	0.203857	0.750053	0.333255	0.113*
H11B ^a	0.293119	0.763442	0.480688	0.113*
H11C ^a	0.146102	0.787517	0.429835	0.113*
C11A ^b	0.183 (4)	0.760 (3)	0.440 (5)	0.090 (10)
H11D ^b	0.259637	0.774047	0.428523	0.136*
H11E ^b	0.185264	0.805206	0.511943	0.136*
H11F ^b	0.110237	0.783817	0.363068	0.136*
C12 ^a	0.4183 (3)	0.4144 (3)	0.7916 (3)	0.0417 (8)
H12A ^a	0.482532	0.364469	0.856423	0.050*
H12B ^a	0.457919	0.490891	0.788453	0.050*
C12A ^b	0.4682 (18)	0.3829 (15)	0.7371 (19)	0.074 (4)
H12C ^b	0.521538	0.332796	0.809461	0.088*
H12D ^b	0.493714	0.466403	0.758745	0.088*
C13 ^a	0.3088 (9)	0.4373 (9)	0.8314 (9)	0.0568 (12)
H13 ^a	0.247933	0.493367	0.769502	0.068*
C13A ^b	0.488 (5)	0.342 (5)	0.603 (5)	0.107 (6)
H13A ^b	0.438219	0.383208	0.520989	0.129*
C14	0.1886 (4)	0.0518 (3)	0.6244 (4)	0.0773 (11)
H14A	0.239775	−0.001354	0.599200	0.116*
H14B	0.099829	0.034741	0.573610	0.116*
H14C	0.208731	0.039699	0.714090	0.116*
F1 ^a	0.2497 (3)	0.3426 (3)	0.8359 (3)	0.0807 (9)
F1A ^b	0.6286 (14)	0.3575 (16)	0.6669 (19)	0.155 (7)
F2 ^a	0.3601 (3)	0.4912 (3)	0.9509 (3)	0.0985 (11)
F2A ^b	0.4822 (15)	0.2247 (13)	0.6108 (16)	0.126 (5)
N1	0.2156 (2)	0.1779 (2)	0.6035 (2)	0.0538 (6)
O1 ^a	0.4173 (4)	0.1580 (4)	0.7576 (4)	0.0680 (11)

Table 2: (continued)

Atom	x	y	z	<i>U</i> _{iso} */ <i>U</i> _{eq}
O1A ^b	0.379 (2)	0.1726 (18)	0.8021 (18)	0.112 (8)
O2	0.0203 (2)	0.1934 (2)	0.4379 (2)	0.0784 (8)

^aOccupancy: 0.788 (4), ^bOccupancy: 0.212 (4).

In the asymmetric unit of the crystal structure, the C=O bond lengths of 1.218(5) and 1.213(3) Å show typical double-bond character. The central six-membered ring [C1/N1/C2/C3/C4/C5] is slightly deviated from planarity, the mean deviation from the plane of 0.0225 Å (see the Figure). The deviation of N1 is the highest, 0.0344 Å. In the crystal structure, the molecules are linked into three-dimensional frameworks by weak C—H...F and C—H...O hydrogen bonds. All geometric parameters may be slightly affected by the disorder in this structure.

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