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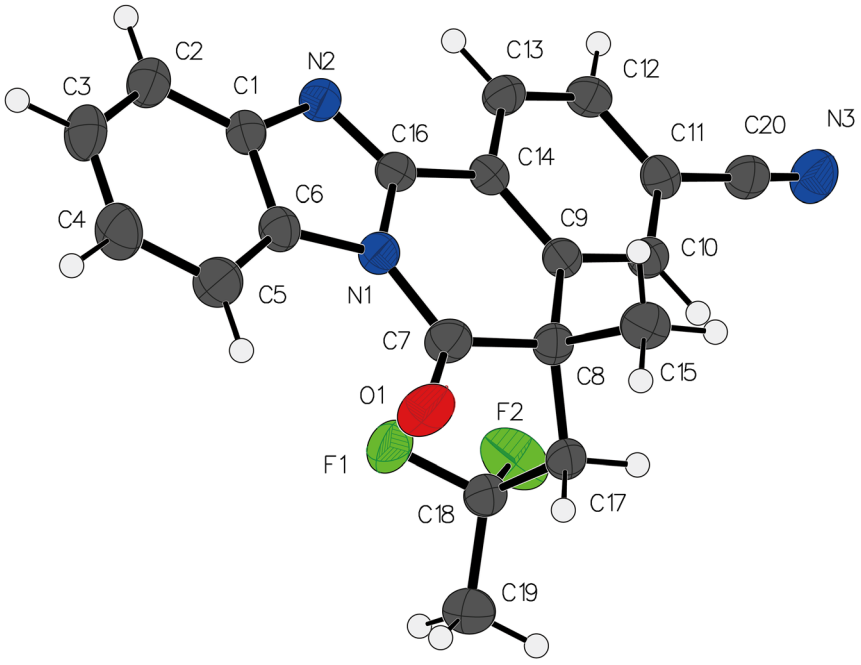
Crystal structure of 5-(2,2-difluoropropyl)-5-methyl-6-oxo-5,6-dihydrobenzo[4,5]imidazo[2,1-*a*]isoquinoline-3-carbonitrile, $C_{20}H_{15}F_2N_3O$



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Abstract

$C_{20}H_{15}F_2N_3O$, monoclinic, $P2_1/c$ (no. 14), a = 7.2737(2) Å, b = 9.5461(3) Å, c = 24.0298(8) Å, β = 91.5320(10)°, V = 1,667.92(9) Å^3, Z = 4, $R_{gt}(F)$ = 0.0459, $wR_{ref}(F^2)$ = 0.1164, T = 150 K.

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The molecular structure is shown in the figure. Table 1 contains the crystallographic data. The list of the atoms including atomic coordinates and displacement parameters can be found in the cif-file attached to this article.

Table 1: Data collection and handling.

Crystal:	Colourless block
Size:	0.15 × 0.09 × 0.05 mm
Wavelength:	Mo *K*α radiation (0.71073 Å)
μ:	0.10 mm^{-1}
Diffractometer, scan mode:	Rigaku SuperNova, ω scans
θ_{max}, completeness:	26.4°, 99 %
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	16209, 3363, 0.072
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\sigma(I_{obs})$, 2,631
$N(param)_{refined}$:	237
Programs:	Rigaku[1], SHELX[2,3], Olex2[4]

1 Source of materials

A 20 mL test tube equipped with a magnetic stir bar was charged with 4-(1-methacryloyl-1H-benzo[d]imidazol-2-yl) benzonitrile (1 equiv., 0.2 mmol), $NaSO_2CF_2Me$ (3 equiv., 0.6 mmol), $LiClO_4$ (0.3 M in $MeCN/H_2O$), and a mixed solvent

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system of MeCN (4.5 mL) and H_2O (1.5 mL) under an inert atmosphere. A carbon plate served as the anode, while a platinum plate functioned as the cathode. The reaction mixture was electrolyzed in an undivided cell at room temperature using a constant voltage of 2.1 V for 3 h. Post-electrolysis, the crude product was extracted thrice with EtOAc (10 mL each). The combined organic layers were dried over anhydrous Na_2SO_4, concentrated under reduced pressure, and purified via silica gel column chromatography (eluent: gradient of hexanes/EtOAc) to yield the final products.

2 Experimental details

Initial phase determination was achieved via the ShelXT algorithm,[2] followed by iterative refinement and constrained least-squares optimization using ShelXL[3] within the Olex2 platform.[4]

3 Comment

Isoquinoline derivatives constitute a structurally diverse and biologically significant class of heterocyclic compounds, serving as fundamental building blocks in numerous alkaloids and pharmaceutical agents.[5] Despite extensive studies on their synthetic pathways and biological applications, the precise structural elucidation of complex isoquinoline derivatives-particularly those incorporating multiple stereocenters, fluorine-containing substituents, or fused ring systems-remains challenging yet critical for understanding molecular recognition mechanisms and reactivity patterns.[6–9] The present study focuses on the crystallographic characterization of 5-(2, 2-difluoropropyl)-5-methyl-6-oxo-5,6-dihydro benzo[4,5]imidazo[2,1-*a*] isoquinoline-3-carbonitrile, a multifunctional heterocycle exhibiting intriguing features.

The molecular architecture exhibits a central fused bicyclic framework comprising a benzimidazole ring and an isoquinoline ring. This fused system establishes a planar, electron-rich heterocyclic core.[10–14] A carbonyl double bond (C7=O) with a bond length of 1.208 Å is present at the 6-oxo substituent located at position C7.

The nitrile group at C11 resides in the same plane as the fused rings, maintaining coplanarity with the central heterocyclic system. Attaching to the fused ring junction are two substituents: a methyl group (–CH_3) and a 2-difluoropropyl group (–$CH_2CF_2CH_3$) at position C8. Notably, the fluorine atoms (F1/F2) exhibit significant electron-withdrawing effects, which destabilize ground-state conformations and exert substantial influence on intermolecular interactions.

Crystal structure analysis reveals the absence of pronounced hydrogen bonding networks. The molecules aggregate through π–π stacking interactions between adjacent aromatic rings, with interplanar distances between stacked layers measuring approximately 3.6 Å. These π–π interactions, combined with van der Waals forces, constitute the primary stabilizing mechanisms for the crystal lattice.

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