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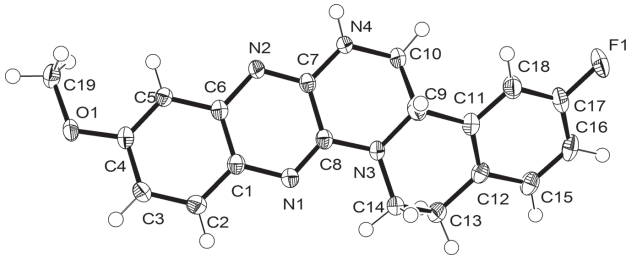
Crystal structure of 3-fluoro-9-methoxy-4*b*,5,14,15-tetrahydro-6*H*-isoquinolino [2′,1′:1,6]pyrazino [2,3-*b*]quinoxaline, $C_{19}H_{17}FN_4O$



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Abstract

$C_{19}H_{17}FN_4O$, orthorhombic, *Pbca* (no. 61), $a = 7.0607(2)$ Å, $b = 18.4459(5)$ Å, $c = 23.8955(7)$ Å, $V = 3112.17(15)$ Å^3, $Z = 8$, $R_{gt}(F) = 0.0543$, $wR_{ref}(F^2) = 0.1540$, $T = 100(2)$ 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.

Source of material

(7-Fluoro-1,2,3,4-tetrahydroisoquinolin-1-yl)methanamine (1.8 g, 10 mmol), 2,3-dichloro-6-methoxyquinoxaline (1.8 g, 8 mmol) and K_2CO_3 (4.15 g, 0.03 mol) were dissolved in DMF (20 mL). The mixture was stirred at 120 °C under an atmosphere of dry N_2 for 10 hours. After cooling to room temperature, the mixture was poured into 500 mL ice-water and filtered. The filter cake was washed with water (50 mL*3)

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Table 1: Data collection and handling.

Crystal:	Colourless block
Size:	$0.13 \times 0.12 \times 0.11$ mm
Wavelength:	Cu $K\alpha$ radiation (1.54184 Å)
μ:	0.83 mm^{-1}
Diffractometer, scan mode:	SuperNova, ω
θ_{max}, completeness:	73.4°, >99%
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	7304, 3064, 0.041
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 2487
$N(param)_{refined}$:	227
Programs:	CrysAlis^{PRO} [1], Olex2 [2], SHELX [3]

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

Atom	*x*	*y*	*z*	U_{iso}*/U_{eq}
C1	0.7725(3)	0.47235(10)	0.34176(8)	0.0161(4)
C2	0.9126(3)	0.49070(11)	0.30257(8)	0.0187(4)
H2	0.901149	0.474712	0.265810	0.022*
C3	1.0667(3)	0.53198(11)	0.31769(8)	0.0180(4)
H3	1.157475	0.544076	0.291079	0.022*
C4	1.0875(3)	0.55595(10)	0.37319(8)	0.0159(4)
C5	0.9500(2)	0.54038(10)	0.41260(8)	0.0147(4)
H5	0.962842	0.556866	0.449189	0.018*
C6	0.7895(3)	0.49913(10)	0.39680(8)	0.0144(4)
C7	0.5124(3)	0.44158(10)	0.42174(8)	0.0145(4)
C8	0.5011(3)	0.41067(10)	0.36528(8)	0.0151(4)
C9	0.1866(3)	0.36515(11)	0.38792(9)	0.0221(5)
H9	0.119976	0.410116	0.378469	0.027*
C10	0.2413(3)	0.36799(12)	0.44919(8)	0.0224(5)
H10A	0.128983	0.375583	0.471801	0.027*
H10B	0.297652	0.322172	0.460129	0.027*
C11	0.0545(3)	0.30193(11)	0.37700(9)	0.0202(4)
C12	0.0912(3)	0.24947(11)	0.33620(8)	0.0178(4)
C13	0.2700(3)	0.25356(11)	0.30203(9)	0.0230(5)
H13A	0.245921	0.234952	0.264734	0.028*
H13B	0.366849	0.223596	0.319174	0.028*
C14	0.3404(3)	0.33130(12)	0.29804(8)	0.0213(4)
H14A	0.461899	0.332479	0.279115	0.026*
H14B	0.251493	0.360171	0.276566	0.026*
C15	−0.0403(3)	0.19428(11)	0.32749(8)	0.0205(4)
H15	−0.016332	0.159589	0.300143	0.025*
C16	−0.2058(3)	0.18966(11)	0.35845(9)	0.0222(5)

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Table 2 (continued)

Atom	x	y	z	U_{iso}*/U_{eq}
H16	−0.292595	0.152509	0.352564	0.027*
C17	−0.2367(3)	0.24238(12)	0.39834(9)	0.0222(5)
C18	−0.1133(3)	0.29833(12)	0.40798(9)	0.0226(5)
H18	−0.140778	0.333404	0.434733	0.027*
C19	1.2755(3)	0.62196(11)	0.43916(8)	0.0208(4)
H19A	1.394435	0.647061	0.441208	0.031*
H19B	1.275121	0.582677	0.465519	0.031*
H19C	1.174512	0.654911	0.447881	0.031*
F1	−0.39778(17)	0.23897(7)	0.42986(6)	0.0314(3)
N1	0.6239(2)	0.42797(9)	0.32657(7)	0.0171(4)
N2	0.6523(2)	0.48466(9)	0.43648(7)	0.0150(3)
N3	0.3595(2)	0.36129(9)	0.35439(7)	0.0169(4)
N4	0.3750(2)	0.42620(9)	0.45906(7)	0.0182(4)
H4	0.366451	0.451380	0.489245	0.022*
O1	1.24949(18)	0.59398(8)	0.38385(6)	0.0202(3)

and dried at 80 °C for 5 hours. Recrystallization from methylene dichloride (250 mL) gave a yellow solid (yield 37.6%); m.p. 234–238 °C; **^{1}H NMR** (600 MHz, DMSO) δ [ppm] 7.83 (d, J = 3.8 Hz, 1H), 7.41–7.33 (m, 2H), 7.28 (dd, J = 8.3, 6.0 Hz, 1H), 7.10 (d, J = 2.5 Hz, 1H), 6.90–6.78 (m, 2H), 4.94 (ddd, J = 12.5, 4.8, 2.4 Hz, 1H), 4.73 (dd, J = 9.6, 2.9 Hz, 1H), 4.03 (dt, J = 11.6, 3.9 Hz, 1H), 3.79 (s, 3H), 3.35 (s, 2H), 3.06–2.97 (m, 1H), 2.91 (dd, J = 12.8, 6.3 Hz, 1H); **^{13}C NMR** (151 MHz, DMSO) δ [ppm] 162.04, 160.45, 157.07, 144.42, 142.08, 138.74, 136.50, 131.60, 131.23, 126.29, 114.50, 114.36, 113.62, 113.12–112.99, 112.90, 105.79), 55.62, 53.19, 45.52, 27.93. Crystals were obtained by evaporation within 3 days at room temperature.

Experimental details

The structure was solved with the SHELXL program using Olex2 [2, 3]. All hydrogen atoms were placed in the calculated positions.

Comment

Quinoxaline and its derivatives exhibit diverse biological activities, such as anticancer, antibacterial, antiviral, anti-inflammatory [4–6]. Tetrazanbigen (TNBG) was a creatively designed and synthesized leading compound bearing the quinoxaline core and showing anticancer activity [7]. Recently, a series of TNBG monosubstituted derivatives were developed with better physical properties and biological effect compared to TNBG [8]. The title compound is a disubstituted TNBG derivative, which was synthesized from (7-fluoro-1,2,3,4-tetrahydroisoquinolin-1-yl)methanamine [9] and 2,3-dichloro-6-methoxyquinoxaline [10]. It showed excellent anticancer activities against hepatoma cells, colon cancer cells and lung cancer cells *in vitro*, which can be deduced that the introduction of an electron-withdraw fluorine group and an electron-donating methoxy group at position C-3 and position C-9 of TNBG (see the figure) could improve their anticancer activities. All bond lengths and angles are in the normal ranges [11]. In conclusion the title compound is a potential antitumor agent, which can be used for further development.

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