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Crystal structure of 9-methoxy-2,3,4,4a,5,6-hexahydro-1*H*-pyrido [1',2':1,6]pyrazino[2,3-*b*]quinoxaline, C₁₅H₁₈N₄O

Table 1: Data collection and handling.

Crystal:	Colorless block
Size:	0.15 × 0.12 × 0.10 mm
Wavelength:	Mo K α radiation (0.71073 Å)
μ :	0.09 mm ⁻¹
Diffractometer, scan mode:	SuperNova, ω
$\theta_{\max}$, completeness:	25.0°, >99%
$N(hkl)_{\text{measured}}$, $N(hkl)_{\text{unique}}$, R_{int} :	4208, 2346, 0.021
Criterion for I_{obs} , $N(hkl)_{\text{gt}}$:	$I_{\text{obs}} > 2 \sigma(I_{\text{obs}})$, 1896
$N(\text{param})_{\text{refined}}$:	182
Programs:	CrysAlis ^{PRO} [1], Olex2 [2], SHELX [3], WinGX/ORTEP [4]

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Abstract

C₁₅H₁₈N₄O, triclinic, $P\bar{1}$ (no. 2), $a = 6.7562(5)$ Å, $b = 9.5520(6)$ Å, $c = 11.4227(8)$ Å, $\alpha = 97.206(5)^\circ$, $\beta = 102.335(6)^\circ$, $\gamma = 108.614(7)^\circ$, $V = 667.39(9)$ Å³, $Z = 2$, $R_{\text{gt}}(F) = 0.0480$, $wR_{\text{ref}}(F^2) = 0.1388$, $T = 150$ 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.

Source of material

Piperidin-2-ylmethanamine (1.1 g, 10 mmol), 2,3-dichloro-6-methoxyquinoxaline (2.3 g, 10 mmol) were added into a round bottom flask. K₂CO₃ (2.7 g, 20 mmol) was added after the solid was dissolved in 20 ml DMF. The mixture was stirred at 110 °C under a nitrogen atmosphere for 6 h. After cooling to room temperature, the reaction mixture was

slowly poured into 200 ml purified water and filtered. The filter cake was washed with purified water (50 ml*3) and desiccated at 80 °C for 5 h, then acquired the yellow solid product (yield 61.1%). Crystals were grown by slowly crystallization from methanol. The colorless crystals were obtained by filtration and desiccation.

Experimental details

Single crystal X-ray data was collected on a SuperNova four-circle diffractometer at 149.99 K [1]. Using Olex2, the structure was solved with SHELXT program and refined with the SHELXL refinement package [2, 3]. The crystal structure of title compound was visualized using Ortep3 software [4]. All hydrogen atoms were placed in their geometrically idealized positions.

Comment

Tetrazanbigen (TNBG) is an originally designed and synthesized leading compound bearing the quinoxaline core and showing anticancer activity *in vitro* and *in vivo* [5]. Based on SAR, our research team has reported a series of derivatives with improved physical properties and biological effect comparing to TNBG [6–8]. TNBG was synthesized from (1,2,3,4-tetrahydroisoquinolin-1-yl)methanamine [9] and 2,3-dichloro-6-methoxyquinoxaline [10] and its derivatives

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Table 2: Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å²).

Atom	x	y	z	U _{iso} */U _{eq}
O1	0.13061 (17)	0.42481 (12)	0.13536 (10)	0.0290 (3)
N1	0.6458 (2)	0.17601 (14)	0.69722 (11)	0.0211 (3)
N2	0.95986 (19)	0.36062 (14)	0.60444 (11)	0.0225 (3)
H2	1.057240	0.413802	0.574076	0.027*
N3	0.3767 (2)	0.19211 (14)	0.53973 (11)	0.0211 (3)
N4	0.69975 (19)	0.38572 (13)	0.45230 (11)	0.0195 (3)
C1	0.4747 (3)	0.05508 (18)	0.72461 (14)	0.0280 (4)
H1A	0.439908	−0.038301	0.666618	0.034*
H1B	0.344944	0.080452	0.714896	0.034*
C2	0.5431 (3)	0.0319 (2)	0.85271 (15)	0.0335 (4)
H2A	0.558185	0.120326	0.910888	0.040*
H2B	0.431362	−0.054031	0.864890	0.040*
C3	0.7540 (3)	0.0050 (2)	0.87684 (16)	0.0350 (4)
H3A	0.735549	−0.089384	0.825127	0.042*
H3B	0.798266	−0.002535	0.961657	0.042*
C4	0.9272 (3)	0.13371 (19)	0.85060 (14)	0.0290 (4)
H4A	1.058172	0.109911	0.858984	0.035*
H4B	0.960553	0.224401	0.911371	0.035*
C5	0.8621 (2)	0.16554 (17)	0.72356 (14)	0.0259 (4)
H5	0.859812	0.082446	0.662865	0.031*
C6	1.0276 (2)	0.30955 (18)	0.71385 (14)	0.0248 (4)
H6A	1.054731	0.387593	0.784598	0.030*
H6B	1.162729	0.293532	0.715075	0.030*
C7	0.7503 (2)	0.32845 (16)	0.54783 (13)	0.0179 (3)
C8	0.5820 (2)	0.22788 (16)	0.59313 (13)	0.0189 (3)
C9	0.3223 (2)	0.25400 (16)	0.44026 (13)	0.0204 (4)
C10	0.1034 (2)	0.22143 (17)	0.38113 (14)	0.0241 (4)
H10	−0.003985	0.158675	0.409732	0.029*
C11	0.0459 (3)	0.28071 (18)	0.28207 (14)	0.0263 (4)
H11	−0.099847	0.259365	0.244387	0.032*
C12	0.2066 (2)	0.37386 (17)	0.23708 (13)	0.0233 (4)
C13	0.4227 (2)	0.40793 (17)	0.29314 (13)	0.0221 (4)
H13	0.528474	0.469533	0.262840	0.027*
C14	0.4832 (2)	0.34936 (16)	0.39633 (13)	0.0188 (4)
C15	0.2883 (3)	0.5066 (2)	0.08046 (15)	0.0333 (4)
H15A	0.217304	0.532332	0.008607	0.050*
H15B	0.368249	0.445502	0.057984	0.050*
H15C	0.385878	0.597305	0.137671	0.050*

were substituted with alkaline side chains leaving basic structure of TNBG unchanged. In this study, in order to diminish molecular weight and structural rigidity, an attempt was carried out to modify the main scaffold of TNBG by deducting a benzene ring [11]. Hence, the title compound was synthesized possessing superior water solubility and equivalent anticancer activity to reported TNBG derivatives.

In conclusion, we report the synthesis and crystal structure of the title compound which is a pivotal anti-tumor intermediate for further derivation. There is one molecule in the asymmetric unit of the title structure

(see the Figure). All bond lengths and angles are in the expected ranges [12, 13].

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