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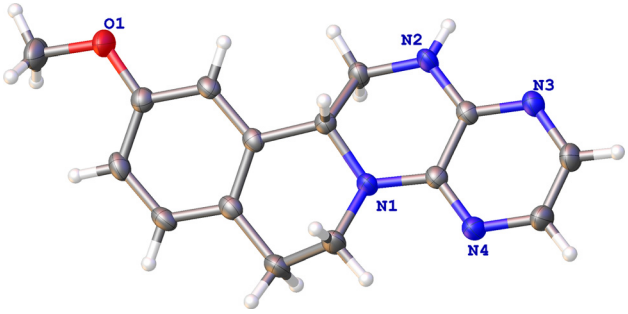
Crystal structure of 10-methoxy-7,11*b*,12,13-tetrahydro-6*H*-pyrazino [2′,3′:5,6] pyrazino[2,1-*a*]isoquinoline, $C_{15}H_{16}N_4O$



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Abstract

$C_{15}H_{16}N_4O$, monoclinic, $P2_1/c$ (no. 14), a = 10.3021(8) Å, b = 15.7835(13) Å, c = 8.3052(7) Å, β = 90.894 (7)°, V = 1350.29(19)

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Tables 1 and 2 contain details on crystal structure and measurement conditions and a list of the atoms including atomic coordinates and displacement parameters.

Table 1: Data collection and handling.

Crystal:	Bronze block
Size:	0.14 × 0.12 × 0.10 mm
Wavelength:	Mo *K*α radiation (0.71073 Å)
μ:	0.09 mm^{-1}
Diffractometer, scan mode:	SuperNova, ω
θ_{max}, completeness:	25.0°, >99 %
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	6234, 2378, 0.019
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 2027
$N(param)_{refined}$:	186
Programs:	CrysalisPRO [1], Olex2 [2], Shelx [3], WinGX/Ortep [4]

1 Source of material

(7-Methoxy-1,2,3,4-tetrahydroisoquinolin-1-yl)methanamine (20 g, 10 mmol), K_2CO_3 (28.75 g, 20 mmol) were added into a round bottom flask. 2,3-Dichloropyrazine (7.6 g, 5 mmol) were added after the solid dissolved in 250 mL DMF. The mixture was stirred at 150 °C in nitrogen atmosphere for 8 h. After cooling to room temperature, the reaction solution was poured into 500 mL water and stirred. The organic phase was extracted three times with EA, and 20 % HCL solution was added. After mixing, the aqueous phase was kept, and the pH was adjusted to alkaline by adding NaOH solution, then extracted three times with DCM (100 mL*3), dried with Na_2SO_4 and concentrated under reduced pressure. After separation and purification, 10.31 g of a yellow solid was obtained (yield 38.9 %). Crystals were grown by slow crystallization in methanol solution. Yellow crystals were obtained by filtration and drying.

2 Experimental details

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.

3 Comment

Tetrazanbigen (TNBG) is a non-cytotoxic antitumor compound with an innovative configuration containing tetrahydroisoquinoline and quinoxaline structures, with good anti-tumor activity and low toxic side effects, and no cross-resistance with other anti-tumor drugs [5]. To overcome its poor water solubility, our team modified the side chains of its parent nucleus to obtain a range of compounds with enhanced water solubility and better anti-tumor activity [6, 7]. In previous experiments, structural modification was carried out by changing the group connected to the side chain.

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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}
O1	0.70720 (9)	0.47185 (7)	0.94100 (14)	0.0412 (3)
N1	0.33424 (10)	0.67681 (7)	0.52689 (14)	0.0267 (3)
N2	0.16576 (11)	0.54125 (8)	0.56779 (15)	0.0282 (3)
H2	0.1172 (15)	0.4977 (11)	0.5641 (19)	0.037 (4)*
N3	0.00745 (10)	0.60944 (7)	0.41658 (14)	0.0287 (3)
N4	0.17557 (11)	0.74581 (7)	0.37256 (15)	0.0313 (3)
C1	0.50513 (12)	0.60736 (8)	0.69016 (15)	0.0218 (3)
C2	0.54736 (12)	0.54561 (9)	0.79711 (16)	0.0254 (3)
H2A	0.486925	0.510128	0.844664	0.030*
C3	0.67792 (13)	0.53569 (9)	0.83463 (17)	0.0273 (3)
C4	0.76831 (13)	0.58913 (9)	0.76582 (18)	0.0301 (4)
H4	0.856316	0.583145	0.789802	0.036*
C5	0.72541 (13)	0.65137 (9)	0.66112 (17)	0.0288 (3)
H5	0.786139	0.687277	0.615283	0.035*
C6	0.59539 (13)	0.66241 (9)	0.62169 (17)	0.0257 (3)
C7	0.55136 (14)	0.73255 (10)	0.5110 (2)	0.0368 (4)
H7A	0.561528	0.714918	0.399991	0.044*
H7B	0.605064	0.782218	0.529164	0.044*
C8	0.41089 (14)	0.75471 (9)	0.5396 (2)	0.0338 (4)
H8A	0.401707	0.779442	0.645718	0.041*
H8B	0.380828	0.795573	0.460140	0.041*
C9	0.21211 (12)	0.67971 (8)	0.45824 (16)	0.0233 (3)
C10	0.12615 (12)	0.60846 (8)	0.47876 (16)	0.0227 (3)
C11	0.05397 (14)	0.74456 (10)	0.30746 (19)	0.0347 (4)
H11	0.026200	0.790159	0.244930	0.042*
C12	−0.02799 (13)	0.67898 (9)	0.33083 (19)	0.0333 (4)
H12	−0.111393	0.681657	0.286639	0.040*
C13	0.30269 (12)	0.52998 (8)	0.60266 (17)	0.0256 (3)
H13A	0.346172	0.509162	0.507759	0.031*
H13B	0.314525	0.488764	0.688269	0.031*
C14	0.36054 (12)	0.61452 (8)	0.65372 (16)	0.0227 (3)
H14	0.317234	0.633199	0.751765	0.027*
C15	0.84039 (14)	0.45816 (12)	0.9796 (2)	0.0448 (5)
H15A	0.887323	0.447976	0.882545	0.067*
H15B	0.848666	0.409931	1.049437	0.067*
H15C	0.875163	0.507326	1.032909	0.067*

In this experiment, the main scaffold of TNBG was changed by deducting the benzene ring, so as to reduce the molecular weight and structural stiffness [8]. Thus, the synthesized title compound showed superior water solubility and equivalent anticancer activity compared to the reported TNBG derivatives. The single crystal structure verified that all bond lengths and bond angles of the compound were within the expected range [9]. In summary, we report the synthesis and crystal structure of this compound, which is further derived as a key antitumor intermediate.

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

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