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Crystal structure of 2-methoxy-4*b*,5,14,15-tetrahydro-6*H*-isoquinolino[2',1':1,6]pyrazino[2,3-*b*]quinoxaline, C₁₉H₁₈N₄O

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Abstract

C₁₉H₁₈N₄O, monoclinic, *P*2₁/*c* (no. 14), *a* = 11.3744(16) Å, *b* = 13.7367(15) Å, *c* = 11.208(2) Å, β = 118.51(2)°, *V* = 1538.9(5) Å³, *Z* = 4, *R*_{gt}(*F*) = 0.0494, *wR*_{ref}(*F*²) = 0.1327, *T* = 100(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.

Source of material

(6-Methoxy-1,2,3,4-tetrahydroisoquinolin-1-yl)methanamine (1.9 g, 10 mmol), 2,3-dichloroquinoxaline 2.0 g

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Table 1: Data collection and handling.

Crystal:	Colourless block
Size:	0.13 × 0.12 × 0.11 mm
Wavelength:	Mo Kα radiation (0.71073 Å)
μ:	0.09 mm ⁻¹
Diffractometer, scan mode:	SuperNova, ω
θ _{max} , completeness:	29.6°, 98% (up to 50° (2θ))
<i>N</i> (<i>hkl</i>) _{measured} , <i>N</i> (<i>hkl</i>) _{unique} , <i>R</i> _{int} :	7653, 3540, 0.022
Criterion for <i>I</i> _{obs} , <i>N</i> (<i>hkl</i>) _{gt} :	<i>I</i> _{obs} > 2 σ(<i>I</i> _{obs}), 2835
<i>N</i> (<i>param</i>) _{refined} :	218
Programs:	CrysAlis ^{PRO} [1], Olex2 [2], SHELX [3], WinGX/ORTEP [4]

10 mmol and DMF 20 mL were mixed in a round bottom flask. After all solids dissolved at room temperature, K₂CO₃ (4.15 g, 0.03 mol) was added. The reaction mixture was stirred for 10 h and after that slowly heated to 120 °C under nitrogen protection. The cooled reaction mixture was slowly poured into 500 mL purified water and filtered. The filter cake was washed with purified water (50 mL × 3) and then dried at 80 °C for 5 h. Recrystallization from methylene dichloride (250 mL) gave the title compound as a yellow solid.

Experimental details

Single crystal X-ray data of title compound was collected on a SuperNova four-circle diffractometer at 100 °C [1]. The structure was solved with the SHELX program using Olex2

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	0.39065 (13)	0.84986 (11)	0.25330 (14)	0.0238 (3)
C2	0.30697 (15)	0.90012 (11)	0.13258 (15)	0.0288 (3)
H2	0.292603	0.966470	0.136004	0.035*
C3	0.24604 (14)	0.85250 (11)	0.00945 (15)	0.0286 (3)
H3A	0.191521	0.886703	−0.069535	0.034*
C4	0.26645 (14)	0.75258 (11)	0.00364 (15)	0.0269 (3)
H4	0.226251	0.720477	−0.079486	0.032*
C5	0.34577 (13)	0.70171 (11)	0.12046 (15)	0.0251 (3)
H5	0.358139	0.635177	0.115738	0.030*
C6	0.40854 (13)	0.74907 (10)	0.24724 (14)	0.0224 (3)
C7	0.55751 (13)	0.74505 (10)	0.47618 (14)	0.0216 (3)
C8	0.54294 (13)	0.85032 (10)	0.48242 (14)	0.0222 (3)
C9	0.69934 (13)	0.84621 (10)	0.72710 (14)	0.0235 (3)
H9A	0.646656	0.833814	0.772659	0.028*
H9B	0.774680	0.886747	0.786098	0.028*
C10	0.75064 (13)	0.75025 (10)	0.70240 (14)	0.0240 (3)
H10	0.816517	0.763871	0.671741	0.029*
C11	0.81795 (13)	0.69200 (10)	0.83349 (14)	0.0223 (3)
C12	0.77887 (13)	0.59798 (10)	0.84365 (14)	0.0219 (3)
C13	0.67435 (13)	0.54580 (10)	0.71899 (14)	0.0244 (3)
H13A	0.589174	0.547550	0.719157	0.029*
H13B	0.700021	0.478155	0.721848	0.029*
C14	0.65894 (14)	0.59233 (10)	0.58978 (14)	0.0249 (3)
H14A	0.738714	0.581000	0.581137	0.030*
H14B	0.583280	0.563860	0.511659	0.030*
C15	0.92445 (13)	0.73421 (11)	0.94883 (15)	0.0258 (3)
H15	0.954642	0.795785	0.941912	0.031*
C16	0.98513 (13)	0.68632 (11)	1.07199 (15)	0.0262 (3)
H16	1.055712	0.715293	1.146952	0.031*
C17	0.93996 (13)	0.59441 (11)	1.08320 (14)	0.0246 (3)
C18	0.83964 (13)	0.54971 (10)	0.96884 (14)	0.0233 (3)
H18	0.812477	0.486993	0.975435	0.028*
C19	0.95060 (15)	0.46229 (12)	1.22612 (16)	0.0321 (4)
H19A	0.967454	0.414195	1.173985	0.048*
H19B	0.856051	0.466950	1.194274	0.048*
H19C	0.994858	0.443794	1.320114	0.048*
N1	0.45855 (12)	0.90011 (9)	0.37459 (12)	0.0248 (3)
N2	0.49226 (11)	0.69680 (8)	0.36234 (12)	0.0227 (3)
N3	0.61789 (12)	0.89751 (8)	0.60090 (12)	0.0250 (3)
H3	0.617244	0.960108	0.601431	0.030*
N4	0.63793 (11)	0.69668 (8)	0.59505 (12)	0.0231 (3)
O1	1.00010 (10)	0.55401 (8)	1.21128 (10)	0.0312 (3)

package [2, 3]. Finally, the crystal structure of title compound was visualized using Ortep3 software [4]. All of the hydrogen atoms were placed in the calculated positions.

Comment

Tetrazanbigen is a novel scaffold bearing quinoxaline core with anticancer activity *in vitro* and *in vivo*, which was

firstly reported by our team [5]. In order to improve the physical properties and biological activities, many efforts were made and a series of tetrazanbigen derivatives were designed and synthesized [6, 7]. In this study, the crystal structure of title compound is reported for the first time.

It is a novel tetrazanbigen derivative in which an electron donating group, methoxyl, was introduced at position C17 (see the Figure). The target compound was prepared from (6-methoxy-1,2,3,4-tetrahydroisoquinolin-1-yl)methanamine [8] and 2,3-dichloroquinoxaline [9] using mild condition. As we expected, this derivative showed greater anticancer activity. The single crystal structure verifies that all bond lengths and angles are in normal ranges. In conclusion, we have synthesized 2-methoxy-4*b*,5,14,15-tetrahydro- 6*H*- isoquinolino[2',1':1,6]pyrazino [2,3-*b*]quinoxaline, a quinoxaline derivative which showed better biological effect compared with tetrazanbigen.

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

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