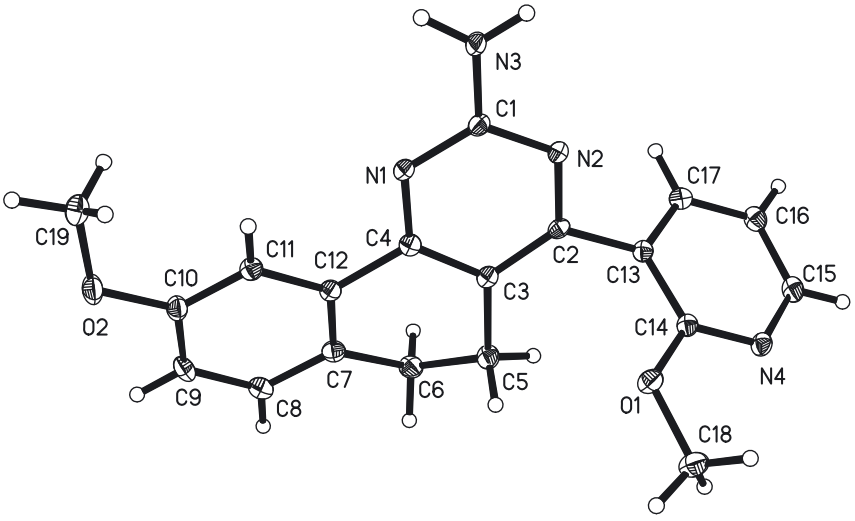
Mei-Lin Song, Xian-Rui Xie and Gui-Ge Hou*

Crystal structure of 9-methoxy-4-(2-methoxypyridin-3-yl)-5,6-dihydrobenzo[*h*]quinazolin-2-amine $C_{19}H_{18}N_4O_2$



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Abstract

$C_{19}H_{18}N_4O_2$, triclinic, $P\bar{1}$ (no. 2), a = 8.3712(10) Å, b = 9.6699(11) Å, c = 10.5323(12) Å, α = 77.24(1)°, β = 74.576(10)°, γ = 81.126(9)°, V = 797.42(17) Å^3, Z = 2, $R_{gt}(F)$ = 0.0564, $wR_{ref}(F^2)$ = 0.1540, T = 293.0 K.

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The crystal structure is shown in the figure. Displacement ellipsoids are drawn at the 30 % probability level.

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:	Yellow block
Size:	0.16 × 0.14 × 0.10 mm
Wavelength:	Mo *Kα* radiation (0.71073 Å)
μ:	0.09 mm^{-1}
Diffractometer, scan mode:	SuperNova, AtlasS2, CCD plate
θ_{max}, completeness:	25.5°, 100 %
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	6079, 2961, 0.041
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\sigma(I_{obs})$, 2,206
$N(param)_{refined}$:	230
Programs:	Rigaku[1], SHELX[2,3]

1 Source of material

Referring to the synthesis technique,[4,5] a 20 % sodium hydroxide solution (5.0 mL) was used as a catalyst. 7-Methoxy-3,4-dihydronaphthalen-1(2*H*)-one (0.70 g, 4.00 mmol) and 2-methoxynicotinaldehyde (0.55 g, 4.00 mmol) were dissolved in 25 mL of methanol and mixed by a Claisen–Schmidt condensation reaction at room temperature for 3 h, resulting in a yellow precipitate. The intermediate was filtered to obtain (*E*)-7-methoxy-2-((2-methoxypyridin-3-yl) methylene)-3,4-dihydronaphthalen-1(2*H*)-one. The intermediate (0.52 g, 1.76 mmol), guanidine hydrochloride (0.50 g,

***Corresponding author: Gui-Ge Hou**, School of Pharmacy, Binzhou Medical University, Yantai, 264003, P.R. China, E-mail: guigehou@163.com. https://orcid.org/0000-0002-9493-3981
Mei-Lin Song and Xian-Rui Xie, School of Pharmacy, Binzhou Medical University, Yantai, 264003, P.R. China

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

	x	*y*	*z*	U_{iso}*/U_{eq}
C1	0.3956 (3)	0.9973 (2)	0.21818 (19)	0.0200 (5)
C2	0.3075 (2)	0.7772 (2)	0.24523 (19)	0.0181 (5)
C3	0.2370 (2)	0.7765 (2)	0.37988 (19)	0.0192 (5)
C4	0.2532 (2)	0.8976 (2)	0.42677 (19)	0.0191 (5)
C5	0.1466 (3)	0.6558 (2)	0.4754 (2)	0.0246 (5)
H5A	0.101142	0.605208	0.425233	0.030*
H5B	0.225046	0.589204	0.517401	0.030*
C6	0.0070 (3)	0.7099 (2)	0.5827 (2)	0.0258 (5)
H6A	−0.085625	0.753961	0.543717	0.031*
H6B	−0.031308	0.629818	0.652281	0.031*
C7	0.0587 (3)	0.8162 (2)	0.6448 (2)	0.0222 (5)
C8	−0.0170 (3)	0.8337 (2)	0.7755 (2)	0.0248 (5)
H8	−0.094148	0.771975	0.828461	0.030*
C9	0.0186 (3)	0.9392 (2)	0.8290 (2)	0.0256 (5)
H9	−0.035046	0.948841	0.916504	0.031*
C10	0.1350 (3)	1.0317 (2)	0.75196 (19)	0.0240 (5)
C11	0.2157 (3)	1.0152 (2)	0.62286 (19)	0.0215 (5)
H11	0.296713	1.074437	0.572236	0.026*
C12	0.1759 (2)	0.9096 (2)	0.56801 (19)	0.0189 (5)
C13	0.2970 (2)	0.6602 (2)	0.17671 (19)	0.0187 (5)
C14	0.3654 (2)	0.5195 (2)	0.21249 (19)	0.0194 (5)
C15	0.2906 (3)	0.4468 (2)	0.0471 (2)	0.0251 (5)
H15	0.288513	0.374302	0.002507	0.030*
C16	0.2189 (3)	0.5795 (2)	0.0037 (2)	0.0252 (5)
H16	0.168114	0.596534	−0.067513	0.030*
C17	0.2239 (3)	0.6885 (2)	0.06883 (19)	0.0232 (5)
H17	0.178258	0.780370	0.040048	0.028*
C18	0.4981 (3)	0.3461 (2)	0.3597 (2)	0.0315 (6)
H18A	0.409772	0.287311	0.375098	0.047*
H18B	0.532394	0.337267	0.441384	0.047*
H18C	0.590830	0.316120	0.292026	0.047*
C19	0.2489 (3)	1.2497 (3)	0.7300 (2)	0.0340 (6)
H19A	0.361421	1.213836	0.693493	0.051*
H19B	0.249109	1.319185	0.782477	0.051*
H19C	0.196383	1.293337	0.658162	0.051*
N1	0.3330 (2)	1.00667 (17)	0.34736 (16)	0.0200 (4)
N2	0.3849 (2)	0.88611 (17)	0.16227 (16)	0.0199 (4)
N3	0.4750 (2)	1.10602 (19)	0.13626 (17)	0.0264 (5)
H3B	0.522919	1.100204	0.052174	0.034 (7)*
H3A	0.466399	1.188337	0.165583	0.034 (7)*
N4	0.3639 (2)	0.41487 (18)	0.15057 (16)	0.0221 (4)
O1	0.44040 (18)	0.49199 (15)	0.31557 (14)	0.0251 (4)
O2	0.1593 (2)	1.13532 (17)	0.81280 (14)	0.0319 (4)

5.28 mmol), and potassium hydroxide (0.30 g, 5.28 mmol) were dissolved in a solution of 15 mL ethanol and 15 mL dichloroethane. The mixture was stirred at 85 °C for 2 h and then filtered. After removing the solvent by concentrating under reduced pressure, 15 mL of ethanol and 5 mL of concentrated ammonia water were added at room temperature to eliminate hydrogen chloride. The mixture was extracted with dichloromethane. The organic phase was dried over anhydrous sodium sulfate, filtered, and the residue was dissolved in a mixture of dichloromethane and methanol (2:1, *v*/*v*). The product was then recrystallized using a solvent.

2 Experimental details

The H atoms were placed in idealized positions and treated as riding on their parent atoms, with *d*(C–H) = 0.96 Å (methyl), U_{iso}(H) = 1.5U_{eq}(C), and *d*(C–H) = 0.97 Å (methylene), U_{iso}(H) = 1.2U_{eq}(C) and *d*(C–H) = 0.98 Å (methyne), U_{iso}(H) = 1.2U_{eq}(C), and *d*(C–H) = 0.93 Å (aromatic), U_{iso}(H) = 1.2U_{eq}(C) H atoms on N atom were located in difference maps and treated as riding.

3 Comment

3,4-Dihydronaphthalen-1(2*H*)-one derivatives have been studied for their antitumor and anti-inflammatory activity, as well as their potential as regulators of allergy and inflammatory reactions. They have also been investigated as potential inhibitors of retinoic acid metabolism enzymes and have shown promise in the treatment of skin diseases and cancer.[6–9] However, 3,4-dihydronaphthalen-1(2*H*)-one derivatives have poor solubility in water. The water solubility and biological activity of 3,4-dihydronaphthalen-1(2*H*)-one derivatives can be further improved through the Michael addition reaction of their *α*, *β*-unsaturated ketones with guanidine hydrochloride. This study utilizes 7-methoxy-3,4-dihydronaphthalen-1(2*H*)-one as a starting material. The starting material underwent a Claisen–Schmidt condensation reaction with 2-methoxynicotinaldehyde to produce the intermediate (*E*)-7-methoxy-2-((2-methoxypyridin-3-yl)methylene)-3,4-dihydronaphthalen-1(2*H*)-one, which was subsequently condensed with guanidine hydrochloride to yield the desired product: 9-methoxy-4-(2-methoxypyridin-3-yl)-5,6-dihydrobenzo[*h*]quinazolin-2-amine.

The single crystal structure analysis shows that the crystal belongs to the triclinic crystal system. The central parent nucleus of the compound is 5,6-dihydrobenzo[*h*]quinazolin-2-amine. Carbon-nitrogen bonds vary in length. *i.e.* Bond length of C(1)–N(1), C(1)–N(2), C(1)–N(3), C(2)–C(4)–N(1), C(14)–N(4), C(15)–N(4) are 1.339(3), 1.360(3), 1.342(3), 1.340(2), 1.338(3), 1.323(3), and 1.345(3) Å, respectively. As a result of the 3,4-dihydronaphthalen-1(2*H*)-one torsion effect, the pyridine ring is not coplanar with the central mother nucleus, with a dihedral angle of approximately 65.4°. This distorted structure may increase the likelihood of interacting with biologically active molecules.[10,11] Notably, the N atom in the cross section of our pyridine ring, which can act as a hydrogen

bond donor, forms the foundation for increased biological activity (*cf.* the Figure). The bond lengths and angles were within the expected range.[12,13]

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