Mohcine Missiou, El Mokhtar Essassi, Joel T. Mague and Youssef Ramli*

Synthesis and crystal structure of (*E*)-1-benzyl-3-(4-methoxystyryl)quinoxalin-2(1*H*)-one, $C_{24}H_{20}N_2O_2$

<https://doi.org/10.1515/ncrs-2020-0300>

Received June 18, 2020; accepted July 8, 2020; available online July 15, 2020

Abstract

$C_{24}H_{20}N_2O_2$, monoclinic, $P2_1/c$ (no. 14), $a = 11.1713(3)$ Å, $b = 17.7718(5)$ Å, $c = 10.9852(3)$ Å, $\beta = 118.990(1)^\circ$, $V = 1907.67(9)$ Å³, $Z = 4$, $R_{gt}(F) = 0.0538$, $wR_{ref}(F^2) = 0.1582$, $T = 296(2)$ K.

CCDC no.: 2006147

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

To a solution of 3-methylquinoxalin-2(1*H*)-one (3.59 mmol) in *N,N*-dimethylformamide (20 mL) was added potassium carbonate (5.38 mmol) and the mixture was stirred at 80 °C for

Table 1: Data collection and handling.

Crystal:	Yellow block
Size:	0.37 × 0.36 × 0.28 mm
Wavelength:	Cu $K\alpha$ radiation (1.54178 Å)
μ :	0.66 mm ⁻¹
Diffractometer, scan mode:	Bruker D8 VENTURE PHOTON 100 CMOS, ω
θ_{max} , completeness:	72.5°, 99%
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int} :	14266, 3708, 0.032
Criterion for I_{obs} , $N(hkl)_{gt}$:	$I_{obs} > 2 \sigma(I_{obs})$, 3032
$N(param)_{refined}$:	255
Programs:	Bruker [1, 2], SHELX [3, 4], Diamond [5]

1 h. After cooling benzylchloride (5.38 mmol) and a catalytic amount of tetrabutylammonium bromide was added and stirring was continued at room temperature for 24 h. After completion of the reaction (monitored by TLC), the solution was concentrated and the residue was purified by column chromatography on silica gel using a hexane/ethyl acetate mixture (7/3, v/v) as eluent. A portion of the product was dissolved in hot ethanol, the solution was filtered and the filtrate was left undisturbed for 10 days to form clear, colorless block crystals.

Experimental details

Hydrogen atoms attached to carbon were placed in calculated positions ($C-H = 0.95 - 0.99$ Å) and included as riding contributions with isotropic displacement parameters 1.2 – 1.5 times those of the attached atoms. A Hirshfeld Test Diff for C21–C22 indicated 7.5 s.u. This may be the result of some minor disorder at this point but it was not enough to model effectively.

Comment

Quinoxaline and its derivatives have received considerable attention due to their biological and industrial properties [6, 7]. These molecules exhibit a wide range of pharmacological applications and are potentially useful in medicinal chemistry research and have therapeutic applications because of their anticancer [8], antimicrobial [9–11], anti-inflammatory [12], antihistaminic [13] and antidiabetic activities [14]. As a continuation of our research on the synthesis of quinoxaline

*Corresponding author: Youssef Ramli, Laboratory of Medicinal Chemistry, Drug Sciences Research Center, Faculty of Medicine and Pharmacy, Mohammed V University in Rabat, Morocco, e-mail: y.ramli@um5s.net.ma. <https://orcid.org/0000-0002-6885-5692>

Mohcine Missiou: Laboratory of Medicinal Chemistry, Drug Sciences Research Center, Faculty of Medicine and Pharmacy, Mohammed V University in Rabat, Morocco

El Mokhtar Essassi: Laboratory of Heterocyclic Organic Chemistry, Mohammed V University, Agdal-Rabat, Morocco

Joel T. Mague: Department of Chemistry, Tulane University, New Orleans, LA, 70118, USA

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

Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> _{iso} [*] / <i>U</i> _{eq}
O1	0.42090(14)	0.30337(7)	0.50175(14)	0.0800(4)
O2	0.11095(17)	0.34160(10)	−0.38584(15)	0.0973(5)
N1	0.42507(12)	0.39399(7)	0.64889(13)	0.0583(3)
N2	0.31361(13)	0.49376(7)	0.42404(13)	0.0612(3)
C1	0.34999(14)	0.51788(9)	0.55669(16)	0.0574(4)
C2	0.32838(18)	0.59338(10)	0.57641(19)	0.0692(4)
H2	0.290102	0.625748	0.500394	0.083*
C3	0.3627(2)	0.62020(11)	0.7056(2)	0.0802(5)
H3	0.346227	0.670241	0.717464	0.096*
C4	0.4219(3)	0.57247(12)	0.8182(2)	0.0878(6)
H4	0.446893	0.591029	0.906516	0.105*
C5	0.4448(2)	0.49811(11)	0.80297(19)	0.0776(5)
H5	0.485506	0.466916	0.880559	0.093*
C6	0.40724(14)	0.46935(9)	0.67173(16)	0.0575(4)
C7	0.39769(15)	0.36851(9)	0.52022(17)	0.0603(4)
C8	0.33550(15)	0.42407(9)	0.40464(16)	0.0584(4)
C9	0.46967(16)	0.33806(9)	0.76112(17)	0.0644(4)
H9A	0.435264	0.289123	0.719840	0.077*
H9B	0.428360	0.350405	0.818530	0.077*
C10	0.62167(15)	0.33245(8)	0.85298(16)	0.0559(4)
C11	0.67210(19)	0.29902(9)	0.98287(17)	0.0675(4)
H11	0.611875	0.282658	1.013157	0.081*
C12	0.8114(2)	0.28995(11)	1.0673(2)	0.0831(6)
H12	0.844562	0.268132	1.154743	0.100*
C13	0.9013(2)	0.31302(12)	1.0228(2)	0.0866(6)
H13	0.994963	0.306624	1.079677	0.104*
C14	0.85219(19)	0.34547(12)	0.8941(2)	0.0808(5)
H14	0.912700	0.360749	0.863401	0.097*
C15	0.71331(17)	0.35553(10)	0.80997(18)	0.0676(4)
H15	0.680993	0.378108	0.723292	0.081*
C16	0.29872(16)	0.39615(10)	0.26666(17)	0.0648(4)
H16	0.322149	0.346868	0.258784	0.078*
C17	0.23374(17)	0.43660(10)	0.15108(18)	0.0670(4)
H17	0.208470	0.485162	0.160732	0.080*
C18	0.19795(16)	0.41265(10)	0.01056(17)	0.0656(4)
C19	0.21993(19)	0.33988(11)	−0.02119(19)	0.0744(5)
H19	0.258075	0.304593	0.050111	0.089*
C20	0.1878(2)	0.31831(12)	−0.15244(19)	0.0786(5)
H20	0.203089	0.268950	−0.169508	0.094*
C21	0.13372(18)	0.36854(12)	−0.25801(19)	0.0750(5)
C22	0.1077(2)	0.44130(13)	−0.2344(2)	0.0891(6)
H22	0.068815	0.475568	−0.307383	0.107*
C23	0.1407(2)	0.46317(12)	−0.0987(2)	0.0847(5)
H23	0.123831	0.512328	−0.082150	0.102*
C24	0.0463(2)	0.38768(18)	−0.5028(2)	0.1077(8)
H24A	0.102723	0.430717	−0.491422	0.162*
H24B	−0.040288	0.404026	−0.513763	0.162*
H24C	0.031888	0.360020	−0.583903	0.162*

derivatives [15–21] we report the molecular and crystal structures of the title compound. For directly related structures, see: [22, 23].

The asymmetric unit consists of one molecule of (*E*)-1-benzyl-3-(4-methoxystyryl)quinoxalin-2(1*H*)-one. The quinoxaline moiety is not exactly planar as indicated by the dihedral angle of 1.64(5)° between its constituent planes. The C10...C15 and C18...C23 benzene rings are inclined to the mean plane of the heterocyclic ring by 82.78(6) and 2.00(6)°, respectively. The latter indicates that the styryl moiety is nearly coplanar with the quinoxaline unit while the C6–N1–C9–C10 torsion angle of −85.40(17)° indicates the benzyl substituent to be oriented well out of the above plane (see the Figure). All bond distances and interbond angles appear as expected for the given formulation. In the crystal, chains of molecules extending along the *c*-axis direction are formed by C11–H11...O1 and C20–H20...O1 hydrogen bonds reinforced by C24–H24A...Cg1 interactions. The chains are linked along the *a*-axis direction by C14–H14...Cg4 interactions to form layers parallel to the *ac* plane. The layers pack with inversion-related C1...C6 rings appearing to overlap but the centroid...centroid distance of 3.8871(10) Å and the slip-page of 1.734 Å suggest that this is more to minimize void space rather than any significant π -stacking interaction.

References

1. Bruker. APEX3 – Diffractometer control and data reduction software package. Bruker AXS Inc., Madison, WI, USA, 2016.
2. Krause, L.; Herbst-Irmer, R.; Sheldrick, G. M.; Stalke, D.: Comparison of silver and molybdenum microfocus X-ray sources for single-crystal structure determination. *J. Appl. Crystallogr.* **48** (2015) 3–10.
3. Sheldrick, G. M.: SHELXT – Integrated space-group and crystal-structure determination. *Acta Crystallogr.* **A71** (2015) 3–8.
4. Sheldrick, G. M.: Crystal structure refinement with SHELXL. *Acta Crystallogr.* **C71** (2015) 3–8.
5. Brandenburg, K.: DIAMOND. Visual Crystal Structure Information System. Ver. 4.0. Crystal Impact, Bonn, Germany, 2015.
6. Ramli, Y.; Essassi, E. M.: Advances in synthetic approaches, functionalization and biological properties of quinoxaline derivatives. In: *Advances in Chemistry Research* 27 (Ed. James C. Taylor), p. 109–160. Nova Science Publishers, New York 2015.
7. Ramli, Y.; Moussaif, A.; Karrouchi, K.; Essassi, E. M.: Pharmacological profile of quinoxalinone. *J. Chem.* **2014** Article ID 563406(2014) 1–21.
8. Abbas, H. S.; Al-Marhabi, A. R.; Eissa, S. I.; Ammar, Y. A.: Molecular modeling studies and synthesis of novel quinoxaline derivatives with potential anticancer activity as inhibitors of c-Met kinase. *Bioorg. Med. Chem.* **23** (2015) 6560–6572.
9. Attia, A. S.; Abdel Aziz, A. A.; Alfallos, K. A.; El-Shahat, M. F.: New diethoxo-bridged dinuclear Cr(III) complexes with derivatives of the quinoxaline-2,3-dione ligand and 2,2-bipyridine as a co-ligand: syntheses, spectral characterizations, magnetic properties, antimicrobial inhibitory activities and interpretation of the electronic absorption spectra using the

- ZINDO/S-CI semi-empirical method. *Polyhedron* **51** (2013) 243–254.
10. Vieira, M.; Pinheiro, C.; Fernandes, R.; Noronha, J. P.; Prudêncio, C.: Antimicrobial activity of quinoxaline 1,4-dioxide with 2- and 3-substituted derivatives. *Microbiol. Res.* **169** (2014) 287–293.
 11. Teja, R.; Kapu, S.; Kadiyala, S.; Dhanapal, V.; Raman, A. N.: Heterocyclic systems containing bridgehead nitrogen atom: synthesis and antimicrobial activity of thiadiazolo[2,3:2,3]imidazo[4,5-*B*] quinoxaline. *J. Saudi Chem. Soc.* **20** (2016) S387–S392.
 12. Guirado, A.; Lopez Sanchez, J. I.; Ruiz-Alcaraz, A. J.; Bautista, D.; Galvez, J.: 1. Synthesis and biological evaluation of 4-alkoxy-6,9-dichloro[1, 3, 5]triazolo[4,3-*a*]quinoxalines as inhibitors of TNF- α and IL-6. *Eur. J. Med. Chem.* **54** (2012) 87–94.
 13. Sridevi, K. B. C. H.; Naidu, A.; Sudhakaran, R.: Synthesis of some phenylpyrazolo benzimidazolo quinoxaline derivatives as potent antihistaminic agents. *Eur. J. Chem.* **7** (2010) 234–238.
 14. Kulkarni, N. V.; Revankar, V. K.; Kirasur, B. N.; Hugar, M. H.: Transition metal complexes of thiosemicarbazones with quinoxaline hub: an emphasis on antidiabetic property. *Med. Chem. Res.* **21** (2012) 663–671.
 15. Ramli, Y.; Essassi, E. M.: Condensation study of hydrazonoyl chloride with 3-methylquinoxalin-2-one and 3-styrylquinoxalin-2-one. *J. Mar. Chim. Heterocycl.* **18** (2019) 39–47.
 16. Abad, N.; Hajji, M.; Ramli, Y.; Belkhira, M.; Elmgirhi, S. M. H.; Habib, M. A.; Guerfel, T.; Mague, J. T.; Essassi, E. M.: A newly synthesized nitrogen-rich derivative of bicyclic quinoxaline—structural and conceptual DFT reactivity study. *J. Phys. Org. Chem.* **33** (2020) e4055.
 17. Missioui, M.; El Fal, M.; Taoufik, J.; Essassi, E. M.; Mague, J. T.; Ramli, Y.: 2-(3-Methyl-2-oxo-1,2-dihydroquinoxalin-1-yl)acetic acid dihydrate. *IUCrData* **3** (2018) x180882.
 18. Ramli, Y.; El Bakri, Y.; El Ghayati, L.; Essassi, E. M.; Mague, J. T.: 1-Benzyl-3-methylquinoxalin-2(1*H*)-one. *IUCrData* **3** (2018) x180390.
 19. Missioui, M.; Mague, J. T.; El Fal, M.; Taoufik, J.; Essassi, E. M.; Ramli, Y.: Ethyl 2-[(3-methylquinoxalin-2-yl)sulfanyl]acetate. *IUCrData* **2** (2017) x171763.
 20. Ramli, Y.; Karrouchi, K.; Essassi, E. M.; El Ammari, L.: *N'*-Phenyl-*N'*-[3-(2,4,5-triphenyl-2,5-dihydro-1*H*-pyrazol-3-yl)quinoxalin-2-yl]benzohydrazide. *Acta Crystallogr.* **E69** (2013) o1320.
 21. Ramli, Y.; Slimani, R.; Zouihri, H.; Lazar, S.; Essassi, E. M.: 3-Methyl-1-(prop-2-en-1-yl)quinoxalin-2(1*H*)-one. *Acta Crystallogr.* **E66** (2010) o1767.
 22. Ramli, Y.; Moussaif, A.; Zouihri, H.; Lazar, S.; Essassi, E. M.: 1-Benzyl-3-methylquinoxalin-2(1*H*)-one. *Acta Crystallogr.* **E66** (2010) o1922.
 23. Ramli, Y.; Missioui, M.; El Fal, M.; Ouhcine, M.; Essassi, E. M.; Mague, J. T.: 2-{3-[2-(2-Chlorophenyl)ethyl]-2-oxo-1,2-dihydroquinoxalin-1-yl} acetohydrazide. *IUCrData* **2** (2017) x171424.