Zhi Hong*, Sha-sha Zhao, Hong Pan, Qian Jin, Xiao-qin Tang and Jun-li Liu

Crystal structure of 3-cyclohexyl-2-(cyclohexylimino)-2,3-dihydro-6,8-diiodo-4*H*-1,3-benzoxazin-4-one, C₂₀H₂₄I₂N₂O₂

Table 1: Data collection and handling.

Crystal:	Colourless block
Size:	0.30 × 0.28 × 0.26 mm
Wavelength:	Mo K α radiation (0.71073 Å)
μ :	30.0 cm ⁻¹
Diffractometer, scan mode:	Bruker APEXII, φ and ω -scans
2 $\theta_{\max}$, completeness:	55°, >98%
$N(hkl)_{\text{measured}}$, $N(hkl)_{\text{unique}}$, R_{int} :	18798, 4763, 0.025
Criterion for I_{obs} , $N(hkl)_{\text{gt}}$:	$I_{\text{obs}} > 2 \sigma(I_{\text{obs}})$, 4119
$N(\text{param})_{\text{refined}}$:	235
Programs:	Bruker [1], SHELX [2], DIAMOND [3]

Source of material

The title compound was obtained according to the literature-known method for the preparation of 3-cyclohexyl-2-cyclohexylimino-3,4-dihydro-4-oxo-2*H*-1,3-benzoxazine [4–6]. To obtain the title compound a mixture of 3,5-diiodo-2-hydroxybenzoic acid (3.90 g, 10 mmol) and *N,N'*-dicyclohexylcarbodiimide (2.06 g, 10 mmol) dissolved in dry THF (40 mL) was stirred at room temperature for 0.5 h, then it was refluxed for 2 h. Colorless powder precipitates during the cooling to room temperature. After filtration, the filtrate was evaporated to dryness giving a residue that crystallized from methanol. Yield 1.42 g (24.5%). Crystals were obtained by slow evaporation of mixed solution of dichloromethane and ethanol (volume 1:1) at room temperature.

Experimental details

Hydrogen atoms were placed geometrically and refined using a riding model with $d(\text{C-H}) = 0.93\text{--}0.97$ Å, $U_{\text{iso}}(\text{H}) = 1.2 U_{\text{eq}}(\text{C})$ for CH groups.

Discussion

The benzo[*e*]-1,3-oxazin-4-ones and their derivatives are reported to have pharmaceutically interesting properties, such as allosteric mitogen-activated kinase (MEK) inhibition [7], osteoclast differentiation and bone resorption inhibition

DOI 10.1515/ncrs-2017-0027

Received January 23, 2017; accepted June 21, 2017; available online July 14, 2017

Abstract

C₂₀H₂₄I₂N₂O₂, monoclinic, $P2_1/c$ (no. 14), $a = 17.5052(10)$ Å, $b = 12.7846(7)$ Å, $c = 9.4663(5)$ Å, $\beta = 94.899(1)^\circ$, $V = 2110.8(2)$ Å³, $Z = 4$, $R_{\text{gt}}(F) = 0.0321$, $wR_{\text{ref}}(F^2) = 0.0996$, $T = 291$ K.

CCDC no.: 1557557

There is one molecule in the asymmetric unit of the title crystal structure, which is shown in the figure. Tables 1 and 2 contain details on crystal structure and measurement conditions and a list of the atoms including atomic coordinates and displacement parameters.

***Corresponding author: Zhi Hong**, School of Pharmaceutical and Chemical Engineering, Taizhou University, Taizhou 318000, Zhejiang Province, P. R. China, e-mail: zhihong@tzc.edu.cn
Sha-sha Zhao, Hong Pan, Qian Jin, Xiao-qin Tang and Jun-li Liu: School of Pharmaceutical and Chemical Engineering, Taizhou University, Taizhou 318000, Zhejiang Province, P. R. China

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}
I1	0.607746(15)	0.08603(2)	0.04186(3)	0.04630(10)
I2	0.361425(15)	0.18745(3)	0.42753(4)	0.05878(12)
O1	0.69760(14)	0.0655(2)	0.3435(3)	0.0361(5)
O2	0.64463(17)	0.1270(3)	0.7404(3)	0.0567(8)
N1	0.73514(16)	0.0976(2)	0.5860(3)	0.0327(6)
N2	0.81591(16)	0.0131(2)	0.4407(3)	0.0327(6)
C1	0.5264(2)	0.1365(3)	0.5172(4)	0.0376(7)
H1A	0.5111	0.1480	0.6076	0.045*
C2	0.47484(19)	0.1443(3)	0.4000(4)	0.0380(8)
C3	0.4963(2)	0.1273(3)	0.2643(4)	0.0383(7)
H3A	0.4604	0.1332	0.1865	0.046*
C4	0.5717(2)	0.1016(3)	0.2451(4)	0.0350(7)
C5	0.62399(19)	0.0930(3)	0.3637(4)	0.0312(7)
C6	0.75238(18)	0.0558(2)	0.4556(3)	0.0292(6)
C7	0.6610(2)	0.1117(3)	0.6199(4)	0.0371(7)
C8	0.60234(19)	0.1110(3)	0.4978(4)	0.0336(7)
C9	0.8012(2)	0.1053(3)	0.6961(4)	0.0340(7)
H9A	0.8476	0.1047	0.6449	0.041*
C10	0.8073(2)	0.0119(3)	0.7934(4)	0.0411(8)
H10A	0.8067	−0.0519	0.7379	0.049*
H10B	0.7639	0.0105	0.8505	0.049*
C11	0.8819(3)	0.0188(3)	0.8896(5)	0.0533(10)
H11A	0.8839	−0.0383	0.9573	0.064*
H11B	0.9251	0.0116	0.8327	0.064*
C12	0.8879(3)	0.1215(4)	0.9682(5)	0.0582(12)
H12A	0.9375	0.1255	1.0223	0.070*
H12B	0.8487	0.1243	1.0346	0.070*
C13	0.8788(3)	0.2146(3)	0.8697(5)	0.0495(10)
H13A	0.9208	0.2161	0.8093	0.059*
H13B	0.8806	0.2785	0.9250	0.059*
C14	0.8028(3)	0.2088(3)	0.7779(5)	0.0461(9)
H14A	0.7984	0.2672	0.7123	0.055*
H14B	0.7602	0.2118	0.8371	0.055*
C15	0.83213(19)	−0.0297(3)	0.3025(4)	0.0356(7)
H15A	0.8120	0.0174	0.2266	0.043*
C16	0.7953(2)	−0.1374(3)	0.2820(5)	0.0477(10)
H16A	0.7405	−0.1312	0.2884	0.057*
H16B	0.8033	−0.1631	0.1880	0.057*
C17	0.8279(3)	−0.2153(3)	0.3914(6)	0.0597(12)
H17A	0.8047	−0.2833	0.3722	0.072*
H17B	0.8158	−0.1933	0.4849	0.072*
C18	0.9145(3)	−0.2237(4)	0.3881(7)	0.0674(14)
H18A	0.9348	−0.2710	0.4621	0.081*
H18B	0.9264	−0.2523	0.2976	0.081*
C19	0.9520(2)	−0.1175(4)	0.4096(5)	0.0518(10)
H19A	0.9445	−0.0922	0.5041	0.062*
H19B	1.0067	−0.1241	0.4022	0.062*
C20	0.9188(2)	−0.0392(3)	0.3011(4)	0.0425(8)
H20A	0.9312	−0.0607	0.2074	0.051*
H20B	0.9421	0.0287	0.3208	0.051*

[8], antimycobacterial activity [9] and antimycobacterial properties [10].

Bond lengths and angles are generally in the normal ranges. The C6, N2 and C15 atoms form a bond angle of 120.1°. The surprising magnitude of this angle may have sterical reasons. Both cyclohexyl rings exhibit a slightly distorted chair conformation.

Acknowledgements: This work was supported by School Foundation of Taizhou University (grant no. 2015PY016) and Zhejiang Open Foundation of the Key Subjects of Applied Chemistry.

References

1. Bruker. APEX2, SAINT and SADABS. Bruker AXS Inc., Madison, Wisconsin, USA, 2009.
2. Sheldrick, G. M.: A short history of SHELX. *Acta Crystallogr. A* **64** (2008) 112–122.
3. Brandenburg, K.: DIAMOND. Visual Crystal Structure Information System. Version 3.2i. Crystal Impact, Bonn, Germany 2012.
4. Steyn, P. S.; Holzapfel, C. W.: The synthesis of ochratoxins A and B metabolites of *aspergillus ochraceus* wilh. *Tetrahedron* **23** (1967) 4449–4461.
5. Ried, W.; Oremek, G.; Pauli, R.: Synthesis of potentially biologically active 1,3-oxazinones. *Arch. Pharm.* **315** (1982) 324–330.
6. May, E. L.: 3,4-Dihydro-1,3-oxazines from dicyclohexylcarbodiimide. *J. Med. Chem.* **10** (1967) 505–506.
7. Sun, J.; Niu, Y.; Wang, C.; Zhang, H.; Xie, B.-Y.; Xu, F.-R.; Jin, H.-W.; Peng, Y.-H.; Liang, L.; Xu, P.: Discovery of 3-benzyl-1,3-benzoxazine-2,4-dione analogues as allosteric mitogen-activated kinase (MEK) inhibitors and anti-enterovirus 71(EV71) agents. *Bioorgan. Med. Chem.* **24** (2016) 3472–3482.
8. Chen, C.-L.; Liu, F.-L.; Lee, C.-C.; Chen, T.-C.; Ahmed Ali, A. A.; Sytwu, H.-K.; Chang, D.-M.; Huang, H.-S.: Modified salicylanilide and 3-phenyl-2*H*-benzo[e][1, 3]oxazine-2,4(3*H*)-dione derivatives as novel inhibitors of osteoclast differentiation and bone resorption. *J. Med. Chem.* **57** (2014) 8072–8085.
9. Waisser, K.; Matyk, J.; Kunes, J.; Skala, P.; Kaustova, J.: Antimycobacterial activity of 3-pyridin-2-yl-2*H*-1,3-benzoxazine-2,4(3*H*)-diones. *Folia Pharm. Univ. Carol.* **38** (2010) 31–34.
10. Petrlikova, E.; Waisser, K.; Divisova, H.; Husakova, P.; Vrabцова, P.; Kunes, J.; Kolar, K.; Stolarikova, J.: Highly active antimycobacterial derivatives of benzoxazine. *Bioorgan. Med. Chem.* **18** (2010) 8178–8187.