Anas J. Rasras, Mutasem Sinnokrot, Murad A. AlDamen, Monther A. Khanfar
and Raed A. Al-Qawasmeh*

The crystal structure of 3-(1*H*-benzo[*d*]imidazol-2-yl)-7-chloro-1-cyclopropyl-6-fluoro-1,4-dihydroquinolin – dimethylsulfoxide (1/1), $C_{21}H_{19}ClFN_3O_2S$

Table 1: Data collection and handling.

Crystal:	Yellow needle
Size:	0.60 × 0.40 × 0.10 mm
Wavelength:	Mo K α radiation (0.71073 Å)
μ :	0.33 mm ^{−1}
Diffractometer, scan mode:	Xcalibur, ω
$\theta_{\max}$, completeness:	29.4°, >99%
$N(hkl)_{\text{measured}}$, $N(hkl)_{\text{unique}}$, R_{int} :	10584, 4644, 0.020
Criterion for I_{obs} , $N(hkl)_{\text{gt}}$:	$I_{\text{obs}} > 2 \sigma(I_{\text{obs}})$, 3196
$N(\text{param})_{\text{refined}}$:	276
Programs:	Rigaku [1], Olex2 [2, 3], SHELX [4]

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

Atom	x	y	z	$U_{\text{iso}}^*/U_{\text{eq}}$
C2	0.3528(2)	0.3095(2)	0.49186(9)	0.0376(5)
H2	0.4045(2)	0.2305(2)	0.48204(9)	0.0451(6)*
C3	0.3528(2)	0.4377(2)	0.45878(9)	0.0357(5)
C4	0.2784(2)	0.5652(2)	0.47342(9)	0.0383(5)
C4A	0.20073(19)	0.5410(2)	0.52278(9)	0.0350(5)
C5	0.1217(2)	0.6571(3)	0.53862(10)	0.0422(5)
H5	0.1170(2)	0.7467(3)	0.51726(10)	0.0507(6)*
C6	0.0517(2)	0.6395(3)	0.58511(11)	0.0463(5)
C7	0.0592(2)	0.5071(3)	0.61840(10)	0.0424(5)
C8	0.1346(2)	0.3912(3)	0.60360(9)	0.0388(5)
H8	0.1388(2)	0.3027(3)	0.62568(9)	0.0466(6)*
C8A	0.20614(18)	0.4060(2)	0.55481(9)	0.0341(4)
C9	0.2981(2)	0.1514(3)	0.57275(10)	0.0433(5)
H9	0.3554(2)	0.1569(3)	0.61310(10)	0.0519(6)*
C10	0.1818(3)	0.0487(3)	0.56830(13)	0.0592(7)
H10a	0.1688(3)	−0.0038(3)	0.60508(13)	0.0711(8)*
H10b	0.1002(3)	0.0762(3)	0.54098(13)	0.0711(8)*
C11	0.3006(3)	0.0082(3)	0.54027(13)	0.0596(7)
H11a	0.3594(3)	−0.0692(3)	0.56000(13)	0.0715(8)*
H11b	0.2908(3)	0.0108(3)	0.49593(13)	0.0715(8)*
C2'	0.43115(19)	0.4420(3)	0.40932(9)	0.0368(5)
C3A'	0.5546(2)	0.3814(3)	0.34463(9)	0.0397(5)
C4'	0.6332(2)	0.3082(3)	0.30811(11)	0.0510(6)
H4'	0.6562(2)	0.2085(3)	0.31472(11)	0.0612(7)*
C5'	0.6757(2)	0.3878(3)	0.26208(11)	0.0547(6)
H5'	0.7289(2)	0.3412(3)	0.23745(11)	0.0656(8)*
C6'	0.6408(2)	0.5371(3)	0.25149(11)	0.0498(6)

<https://doi.org/10.1515/ncrs-2018-0599>

Received December 26, 2018; accepted February 8, 2019; available online March 11, 2019

Abstract

$C_{21}H_{19}ClFN_3O_2S$, monoclinic, $P2_1/n$ (no. 14), $a = 10.1495(4)$ Å, $b = 8.9769(5)$ Å, $c = 22.1431(10)$ Å, $\beta = 99.901(4)^\circ$, $V = 1987.43(16)$ Å³, $Z = 4$, $R_{\text{gt}}(F) = 0.0473$, $wR_{\text{ref}}(F^2) = 0.1418$, $T = 293(2)$ K.

CCDC no.: 1896105

The crystal asymmetric unit of the title structure 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: Raed A. Al-Qawasmeh, College of Science, Department of Chemistry, University of Sharjah, P.O. Box 27272, Sharjah, UAE, e-mail: ralqawasmeh@sharjah.ac.ae

Anas J. Rasras: Department of Chemistry, Faculty of Science, Al-Balqa Applied University, Al-Salt, Jordan

Mutasem Sinnokrot: The Petroleum Institute, Khalifa University of Science and Technology, Abu Dhabi 2533, UAE

Murad A. AlDamen and Monther A. Khanfar: Department of Chemistry, University of Jordan, Amman 11942, Jordan

Table 2 (continued)

Atom	x	y	z	U_{iso}^*/U_{eq}
H6'	0.6720(2)	0.5875(3)	0.22005(11)	0.0598(7)*
C7'	0.5616(2)	0.6123(3)	0.28619(9)	0.0423(5)
H7'	0.5380(2)	0.7116(3)	0.27890(9)	0.0507(6)*
C7A'	0.51900(19)	0.5306(3)	0.33279(9)	0.0369(5)
C12	0.1450(3)	0.9131(4)	0.34528(15)	0.0707(8)
C13	0.2776(3)	1.1254(4)	0.29612(15)	0.0652(8)
H13a	0.222(3)	1.205(4)	0.3059(15)	0.097(12)*
H13b	0.360(4)	1.172(4)	0.2944(15)	0.103(12)*
H13c	0.237(3)	1.069(4)	0.2585(15)	0.080(9)*
Cl1	-0.02682(7)	0.49377(9)	0.67890(3)	0.0654(2)
F1	-0.02457(16)	0.75200(18)	0.60041(7)	0.0724(5)
H12a	0.1234(9)	0.874(2)	0.3045(4)	0.1061(13)*
H12b	0.1423(6)	0.8344(17)	0.3744(7)	0.1061(13)*
H12c	0.0812(4)	0.9885(7)	0.3510(10)	0.1061(13)*
N1	0.28278(16)	0.28952(19)	0.53799(7)	0.0364(4)
N2'	0.44008(17)	0.5670(2)	0.37504(8)	0.0376(4)
H2'	0.40341(17)	0.6520(2)	0.37915(8)	0.0451(5)*
N3'	0.49877(17)	0.3276(2)	0.39319(8)	0.0421(4)
O1	0.27761(17)	0.68846(18)	0.44772(7)	0.0553(5)
O2	0.39546(19)	0.8753(2)	0.33618(10)	0.0778(6)
S1	0.30706(6)	0.99152(8)	0.35636(3)	0.0535(2)

Source of material

The title compound was synthesized according to similar procedure described earlier [5]. To a solution of 7-chloro-1-cyclopropyl-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid (281 mg, 1 mmol) in 10 mL dry DMF under nitrogen atmosphere at 0 °C was added (142 mg, 1.1 mmol) DIPEA (diisopropylethylamine). After 20 min, (352 mg, 1.1 mmol) TBTU (2-(1*H*-benzotriazole-1-yl)-1,1,3,3-tetramethylaminium tetrafluoroborate) was added and the mixture stirred for 20 min. Thereafter, (0.119 g, 1.1 mmol) of *o*-phenylenediamine was added and the mixture was stirred for 2 h at 0 °C. The resultant mixture was poured on ice and the solid was filtered off. The precipitated solid was filtered, washed with water and dissolved in EtOAc. The organic phase was washed with 1 N HCl aqueous solution, then with a saturated NaHCO₃ aqueous solution, and then H₂O. The organic layer was dried over MgSO₄, and concentrated *in vacuo*, which was used in the next stage without further purification. The solid was dissolved in 12 mL of dilute acetic acid and refluxed for 2 h. Upon completion, the mixture was poured on ice and the resultant solid was recrystallized from DMSO to produce 300 mg (85% yield) colorless crystals suitable for X-ray structure determination. *M.p.* = 281–282 °C. **HRMS-ESI (+)** (based on C₁₉H₁₄ClFN₃O) [*M*]⁺ *m/z* calcd.: 354.08039; found: 354.0790 (4 p.p.m.). **¹H-NMR** (500 MHz, DMSO-*d*₆, 318 K): 12.64 (1*H*, bs, NH), 9.00 (1*H*, s, H2), 8.34

(d, J_{H-F} = 6.15 Hz, 1*H*, H8), 8.14 (1*H*, d, J_{H-F} = 9.08 Hz, H5), 7.59/ 7.60 (2*H*, 2 d, H4', H7', J = 6.0 Hz), 7.12 and 7.11 (2*H*, 2 d, J = 6.0 Hz, H5'/H6'), 3.78 (1*H*, m, H9), 1.32, 1.17 (2*H*, m, 2*H*, bs, H10/H11). **¹³C-NMR** (125 MHz, DMSO-*d*₆, 318 K): 173.3 (C4), 155.0 (C6, J_{C-F} = 254 Hz), 148.5 (C2'), 144.8 (C2), 137.9 (C8A/C3A'/C7A'), 127.0 (C4A), 125.7 (C7, J_{C-F} = 20.4 Hz), 121.9/ 121.0 (C5'/C6'/C4'/C7'), 120.9 (C8), 112.2 (C5, J_{C-F} = 22.2), 109.8 (C3), 35.9 (C9), 8.1 (C10/C11).

Experimental details

General procedures: NMR spectra were recorded with a Bruker Avance III 500 spectrometer. All NMR spectra are reported in parts per million (ppm, d) relative to tetramethylsilane for ¹H and ¹³C-NMR spectra, with the residual solvent proton and carbon resonances used as internal standards. Coupling constants (*J*) are reported in Hertz (Hz), and integrations are reported as number of protons. The following abbreviations are used to described peak patterns: s = singlet, d = doublet, m = multiplet, bs = broad singlet. NMR experiments are given according to the numbering scheme of the molecular structure of the title compound. The ¹H and ¹³C-NMR chemical shift assignments are supported by data obtained from ¹H-¹H COSY, ¹H-¹³C HMQC and ¹H-¹³C HMBC. All H atoms bonded to C atoms were refined as riding, with C–H distances of 0.93 Å (for aromatic rings). **X-ray diffraction:** The highest difference electron peak (0.5 e/Å³) is located near the sulfur atom, indicating a non-refinable split position for the sulfur atom.

Comment

Fluoroquinolone derivatives have been widely investigated as drugs against bacterial infections. Various derivatives prove to be very potent against bacterial and fungal strains and currently in clinical use [6, 7]. In a program aimed to synthesize biologically active compounds, in detail we are searching for a hybridization of the fluoroquinolone with benzimidazole [8–11].

Herein, the carboxylic acid moiety was coupled with *o*-phenylenediamine and thereafter cyclized to produce the target compound. This title crystal structure consists of the C₁₉H₁₄ClFN₃O molecules, in which all bond lengths are in normal ranges. The asymmetric unit contains both the 3-(1*H*-benzo[*d*]imidazol-2-yl)-7-chloro-1-cyclopropyl-6-fluoroquinolin-4(1*H*)-one and DMSO as a crystallization solvent. The crystal is stabilized *via* weak CH⋯N and classical NH⋯O hydrogen bonds [N2'⋯O1 = 2.722(6) Å]. The compound except the cyclopropyl is almost planar. The quinolone and the benzimidazole moieties are coplanar due to the H-bonding between the NH and the carbonyl oxygen on C4 of the quinolone part.

Acknowledgements: The author gratefully acknowledges financial support from the Deanship of Scientific Research at the University of Jordan (grant No. 7/1005/2006). Professor Salim S. Sabri is highly acknowledged for his valuable discussion.

References

1. Rigaku Oxford Diffraction: CrysAlis^{PRO}. Rigaku Oxford Diffraction, Yarnton, England (2015).
2. Dolomanov, O. V.; Bourhis, L. J.; Gildea, R. J.; Howard, J. A. K.; Puschmann, H.: OLEX2: a complete structure solution, refinement & analysis program. *J. Appl. Crystallogr.* **42** (2009) 339–341.
3. Bourhis, L. J.; Dolomanov, O. V.; Gildea, R. J.; Howard, J. A. K.; Puschmann, H.: The anatomy of a comprehensive constrained, restrained refinement program for the modern computing environment, Olex2 dissected. *Acta Crystallogr.* **A71** (2015) 59–75.
4. Sheldrick, G. M.: SHELXT – integrated space-group and crystal-structure determination. *Acta Crystallogr.* **A71** (2015) 3–8.
5. Al-Tel, T. H.; Al-Qawasmeh, R. A.; Zaarour, R.: Design, synthesis and *in vitro* antimicrobial evaluation of novel imidazo[1,2-*a*]pyridine and imidazo[2,1-*b*][1,3]benzothiazole motifs. *Eur. J. Med. Chem.* **46** (2011) 1874–1881.
6. Li, Q.; Mitscher, L. A.; Shen, L. L.: The 2-pyridone antibacterial agents: bacterial topoisomerase inhibitors. *Med. Res. Rev.* **20** (2000) 231–293.
7. Mitscher, L. A.: Bacterial topoisomerase inhibitors: quinolone and pyridone antibacterial agents. *Chem. Rev.* **105** (2005) 559–592.
8. Al-Qawasmeh, R. A.; Zahra, J. A.; Zani, F.; Vicini, P.; Boese, R.; El-Abadelah, M. M.: Synthesis and antibacterial activity of 9-cyclopropyl-4-fluoro-6-oxo-6,9-dihydro-[1,2,5]thiadiazolo[3,4-*h*]quinoline-7-carboxylic acid and its ethyl ester. *ARKIVOC* **12** (2009) 322–336.
9. Abdel-Jalil, R. J.; Al-Qawasmeh, R. A.; Voelter, W.; Heeg, P.; El-Abadelah, M. M.: Synthesis and properties of some 2,3-disubstituted-6-fluoro-7(4-methyl-1-piperazinyl) quinoxalines. *J. Heterocycl. Chem.* **37** (2000) 1273–1275.
10. Al-Qawasmeh, R. A.; Abadleh, M. M.; Zahra, J. A.; El-Abadelah, M. M.; Albashiti, R.; Zani, F.; Incerti, M.; Vicini, P.: Design, synthesis and antibacterial activity studies of new thiadiazoloquinolone compounds. *J. Enzyme Inhib. Med. Chem.* **29** (2014) 785–777.
11. Al-Qawasmeh, R. A.; Huthail, B. B.; Sinnokrot, M. O.; Semreen, M. H.; Odeh, R. A.; Abu-Zarga, M. H.; Tarazi, H.; Yousef, I. A.; Al-Tel, T. H.: Design, synthesis and qualitative structure activity relationship evaluations of quinoline-based bisarylimidazoles as antibacterial motifs. *Med. Chem.* **12** (2016) 563–573.