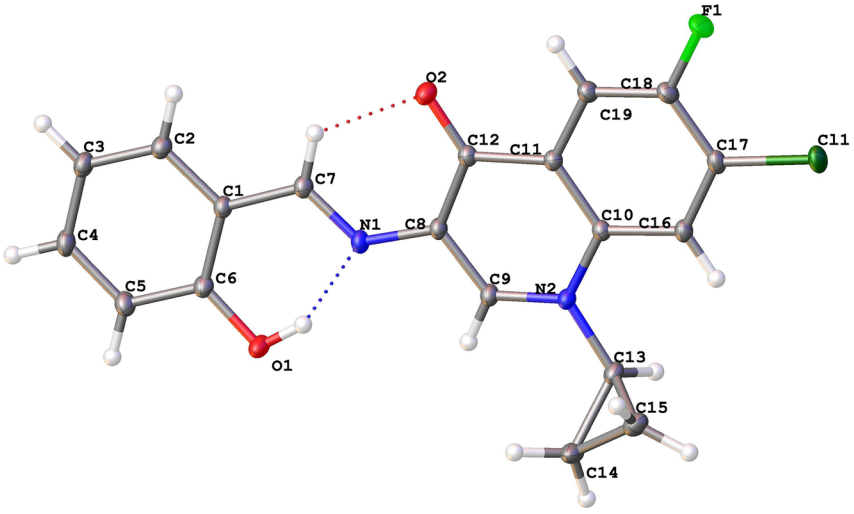
Iman M. Ibrahim, Kamrul Hasan, Urmila Ravi, Raed A. Al-Qawasmeh and Monther A. Khanfar*

The crystal structure of (*E*)-7-chloro-1-cyclopropyl-6-fluoro-3-((2-hydroxybenzylidene)amino) quinolin-4(1*H*)-one, $C_{19}H_{14}ClFN_2O_2$



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Abstract

$C_{19}H_{14}ClFN_2O_2$, triclinic, $P\bar{1}$ (no. 2), a = 8.9893(3) Å, b = 9.5324(3) Å, c = 10.1917(4) Å, α = 95.1780(10)°, β = 96.5320(1)°, γ = 116.3930(10)°, V = 767.42(5) Å^3, Z = 2, $R_{gt}(F)$ = 0.0355, $wR_{ref}(F^2)$ = 0.0966, T = 100(2) K.

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The molecular structure is shown in the figure. Table 1 contains crystallographic data. The list of the atoms including atomic coordinates and displacement parameters can be found in the cif-file attached to this article.

Table 1: Data collection and handling.

Crystal:	Yellow block
Size:	0.23 × 0.22 × 0.09 mm
Wavelength:	Mo *K*α radiation (0.71073 Å)
μ:	0.28 mm^{-1}
Diffractometer, scan mode:	Bruker Apex2, φ and ω scans
θ_{max}, completeness:	32.0°, 100 %
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	39,310, 5,348, 0.025
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\sigma(I_{obs})$, 4,787
$N(param)_{refined}$:	229
Programs:	Bruker,[1] Olex2,[2] SHELX[3,4]

1 Source of materials

The preparation of the target compound was performed under the Schiff base typical conditions: To a solution of 3-amino-7-chloro-1-cyclopropyl-6-fluoroquinolin-4(1*H*)-one (0.4 mmol, 1.0 eq.) in EtOH (4 mL) was added salicylaldehyde (0.436, 1.05 eq.) at room temperature. The reaction was stirred at reflux temperature overnight where no more amine was being observed through TLC. The solution was evaporated to dryness and the obtained crude residue was triturated in diethyl ether and pentane. The target compound was produced in 89 % yield. Crystals were obtained

***Corresponding author: Monther A. Khanfar**, Department of Chemistry, Pure and Applied Chemistry Group, College of Sciences, University of Sharjah, Sharjah-27272, UAE; and Department of Chemistry, The University of Jordan, Amman 11942, Jordan, E-mail: mkhanfar@sharjah.ac.ae. https://orcid.org/0000-0003-4718-4006
Iman M. Ibrahim, Kamrul Hasan and Urmila Ravi, Department of Chemistry, Pure and Applied Chemistry Group, College of Sciences, University of Sharjah, Sharjah-27272, UAE, E-mail: iibrahim2@sharjah.ac.ae (I.M. Ibrahim), khasan@sharjah.ac.ae (K. Hasan), y.urmilla@gmail.com (U. Ravi). https://orcid.org/0000-0003-4268-6381 (K. Hasan)
Raed A. Al-Qawasmeh, Department of Chemistry, Pure and Applied Chemistry Group, College of Sciences, University of Sharjah, Sharjah-27272, UAE; and Department of Chemistry, The University of Jordan, Amman 11942, Jordan, E-mail: ralqawasmeh@sharjah.ac.ae. https://orcid.org/0000-0002-9325-6229

through recrystallization from methanol. The structure of the compound was firstly determined by ^{1}H and ^{13}C NMR and further verified by XRD analyses. **^{1}H NMR** (500 MHz, $CDCl_3$, 298 K): δ 13.45 (s, 1H), 10.23 (s, 1H), 8.22 (d, J = 9.1 Hz, 1H), 8.03 (d, J = 5.9 Hz, 1H), 8.00 (s, 1H), 7.41 (dd, J = 7.6, 1.5 Hz, 1H), 7.32 (ddd, J = 8.8, 7.4, 1.6 Hz, 1H), 6.95 (d, J = 8.2 Hz, 1H), 6.92 (td, J = 7.5, 1.0 Hz, 1H), 3.56–3.43 (m, 1H), 1.39 (q, J = 6.8 Hz, 2H), 1.17 (q, J = 6.7 Hz, 2H). **^{13}C NMR** (125 MHz, $CDCl_3$, 298 K); δ 172.5, 165.3, 161.1, 155.3 (d, J_{C-F} = 249.6 Hz), 142.3, 136.3, 132.7, 132.5, 127.8 (d, J_{C-F} = 5.9 Hz), 126.9 (d, J_{C-F} = 20.5 Hz), 126.2, 120.2, 119.3, 118.7, 117.0, 113.3 (d, J_{C-F} = 22.7 Hz), 34.6, 8.6.

2 Experimental details

All chemicals and solvent were used as purchased without further purification. The starting material 3-amino-7-chloro-1-cyclopropyl-6-fluoroquinolin-4(1*H*)-one was prepared as described earlier[1] and used directly without crystallization. NMR spectra were recorded with a Bruker Avance III 500 spectrometer. All NMR spectra were reported in parts per million (ppm, δ) relative to tetramethylsilane for ^{1}H and ^{13}C NMR spectra, with the residual solvent proton and carbon resonances were used as internal standards. Coupling constants (J) were reported in Hertz (Hz), and integrations were reported as number of protons. The following abbreviations were used to describe peak patterns: s = singlet, d = doublet, m = multiplet, bs = broad singlet. All H atoms that were bonded to C atoms were refined as riding, with C–H distances of 0.93 Å (for aromatic rings).

3 Discussion

The fluoroquinolone scaffolds are among the most promising chemical agents to fight the bacterial infections world wide.[5,6] Structural modification of this scaffold is still an expanding area to generate new entities, which can be used to treat bacterial and fungal strains and mainly to overcome the bacterial resistance.[7] Current trends in this area are based on structural modifications of all position available while keeping the fluorine atom and the carboxylic acid moiety untouched at position 6 and 7, respectively.[5–7] Few approaches tackle the carboxylic acid replacements with heterocyclic rings and their derivatives.[8] In a continuation of our contribution on the fluoroquinolone to produce biologically active agents to combat bacterial infections as well as cancer,[9–11] we envision the introduction of the Schiff base components for their recognized activities.[12,13] In this regard the carboxylic acid moiety at position three in the compound 1-cyclopropyl-7-chloro-7-fluoro-quinolone-3-carboxylic acid is converted to nitro and thereafter reduced to get the 3-amine derivative, which herein reacts with salicylaldehyde to produce the desired compound. Eventually, the target compound has been isolated in high percentage yield and recrystallized into triclinic crystal system. The hydroxyl group in the salicylaldehyde shows a clear H-bonding with the imine nitrogen that forms an E isomer, which encouraged us to synthesize the target compound that features the salicylaldehyde and the fluoroquinolone moieties. The amine at position three of the quinolone compounds has been produced via successive decarboxylation-nitration and thereafter reduction to produce an amino group at that position as described in Ref. 14.

In the $C_{19}H_{14}ClFN_2O_2$ molecules all bond lengths are in normal ranges. The normal plane of the phenyl ring is almost coplanar with the normal plane of benzoquinolone ring with an angle of 4.46(3)°. This can be attributed to the strong intramolecular hydrogen bonding between H1···N1 with distance = 1.795(19) Å and weaker hydrogen bonding between H7···O2 with distance = 2.2234(7) Å. These interactions are accompanied by elongation of the O1–H1 to be 1.299(18) Å.

The crystal is stabilized by intramolecular interactions with halogen atom with the following distances: F···H (F1···H5, $+x$, $-1+y$, $1+z$) = 2.4601(7) Å and Cl···H interactions (Cl1···H15b, $2-x$, $1-y$, $2-z$) = 2.9534(2) Å. These interactions build up a two-dimensional arrangement of the molecules. These layers are connected to each other by O···H hydrogen bonding between O1···H14A ($-1x$, $-1+y$, $+z$) with distance equal 2.4792(7) Å.

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References

1. Bruker. APEX4, SAINT and SADABS; Bruker AXS Inc.: Madison, Wisconsin, USA, 2021.
2. Dolomanov, O. V.; Bourhis, L. J.; Gildea, R. J.; Howard, J. A. K.; Puschmann, H. OLEX2: A Complete Structure Solution, Refinement and Analysis Program. *J. Appl. Cryst.* **2009**, *42*, 339–341.
3. Sheldrick, G. M. SHELXT – Integrated Space-Group and Crystal-Structure Determination. *Acta Cryst.* **2015**, *A71*, 3–8.
4. Sheldrick, G. M. Crystal Structure Refinement with SHELXL. *Acta Cryst.* **2015**, *C71*, 3–8.

5. Nowakowska, J.; Radomska, D.; Czarnomysy, R.; Marciniec, K. Recent Development of Fluoroquinolone Derivatives as Anticancer Agents. *Molecules* **2024**, *29*, 3538.
6. Suaifan, G. A.; Mohammed, A. A. M.; Alkhawaja, B. A. Fluoroquinolones' Biological Activities against Laboratory Microbes and Cancer Cell Lines. *Molecules* **2024**, *27*, 1658.
7. Mohammed, H. H.; Abuo-Rahma, G. E.-D. A.; Abbas, S.; Abdelhafez, E.-S. M. Current Trends and Future Directions of Fluoroquinolones. *Curr. Med. Chem.* **2019**, *26*, 3132–3149.
8. Hryhoriv, H.; Kovalenko, S. M.; Georgiyants, M.; Sidorenko, L.; Georgiyants, V. A Comprehensive Review on Chemical Synthesis and Chemotherapeutic Potential of 3-Heteroaryl Fluoroquinolone Hybrids. *Antibiotics* **2023**, *12*, 625.
9. 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: Online J. Org. Chem.* **2009**, *12*, 322–336.
10. 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*. **2016**, *12l*, 563–573.
11. 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*. **2014**, *29*, 777–785.
12. Younus, H. A.; Saleem, F.; Hameed, A.; Al-Rashida, M.; Al-Qawasmeh, R. A.; El-Naggar, M.; Khan, K. M.; Saeed, M. Part-II: An Update of Schiff Bases Synthesis and Applications in Medicinal Chemistry-A Patent Review (2016–2023). *Expert Opin. Ther. Pat.* **2023**, *33*, 841–864.
13. Tomisic, Z. B.; Kujundzic, N.; Krajacic, M. B.; Visnjevac, A.; Kojic-Prodic, B. *J. Mol. Struct.* **2002**, *611*, 73.
14. Al-Qawasmeh, R. A.; Zahra, J. A.; Khanfar, M. A.; Al-Hiari, Y. M.; El-Abadelah, M. M.; Voelter, W. A Convenient Synthesis of 1-Alkyl-7-chloro-6- fluoro-3-nitro-4-quinolones. *Lett. Org. Chem*. **2009**, *6*, 511–514.