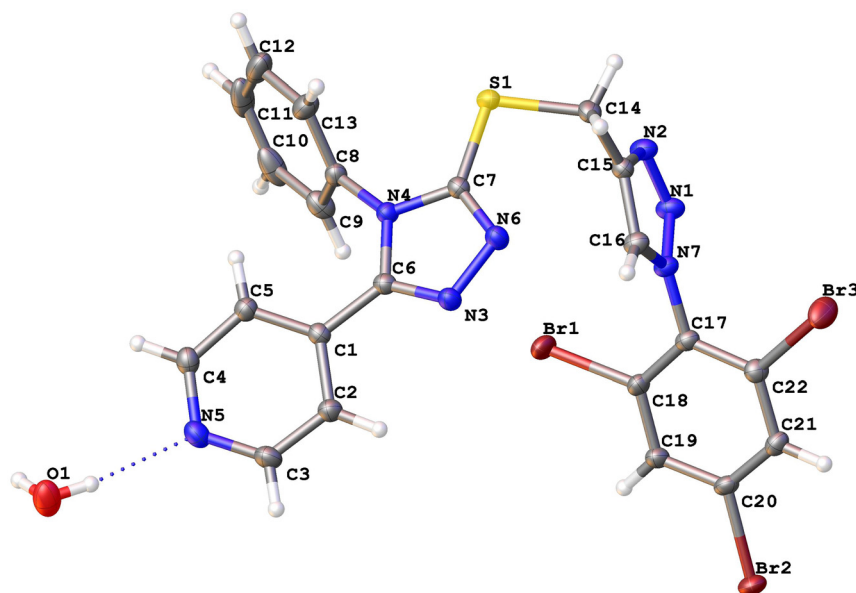


Haitham Al-Sa'doni, Mohamed El-Naggar, Ihsan A. Shehadi, Kamrul Hasan and Monther A. Khanfar*

The crystal structure of 4-(4-phenyl-5-(((1-(2,4,6-tribromophenyl)-1*H*-1,2,3-triazol-4-yl)methyl)thio)-4*H*-1,2,4-triazol-3-yl)pyridine, $C_{22}H_{14}Br_3N_7S$



<https://doi.org/10.1515/ncrs-2024-0301>

Received July 14, 2024; accepted August 21, 2024;

published online September 9, 2024

Abstract

$C_{22}H_{14}Br_3N_7S$, H_2O , triclinic, $P\bar{1}$ (no. 2), $a = 8.9098(17)$ Å, $b = 9.422(2)$ Å, $c = 15.702(4)$ Å, $\alpha = 86.453(9)^\circ$, $\beta = 78.382(7)^\circ$, $\gamma = 69.477(7)^\circ$, $V = 1209.1(5)$ Å³, $Z = 2$, $R_{gt}(F) = 0.0315$, $wR_{ref}(F^2) = 0.0802$, $T = 100(2)$ K.

CCDC no.: 2378891

Table 1: Data collection and handling.

Crystal:	Colourless needle
Size:	$0.36 \times 0.36 \times 0.13$ mm
Wavelength:	Mo $K\alpha$ radiation (0.71073 Å)
μ :	5.12 mm^{-1}
Diffractometer, scan mode:	Bruker D8-AVANCE, φ and ω
$\theta_{\max}$, completeness:	33.1° , >99 %
$N(hkl)_{\text{measured}}$, $N(hkl)_{\text{unique}}$, R_{int} :	65,262, 9136, 0.062
Criterion for I_{obs} , $N(hkl)_{\text{gt}}$:	$I_{\text{obs}} > 2\sigma(I_{\text{obs}})$, 7,458
$N(\text{param})_{\text{refined}}$:	314
Programs:	Bruker ¹ , Olex2 ² , SHELX ^{3,4}

*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>

Haitham Al-Sa'doni, Department of Chemistry, College of Sciences, Al al-Bayt University, Mafrq, Jordan, E-mail: haitham_alsadoni@aabu.edu.jo

Mohamed El-Naggar, Ihsan A. Shehadi and Kamrul Hasan, Department of Chemistry, Pure and Applied Chemistry Group, College of Sciences, University of Sharjah, Sharjah 27272, UAE, E-mail: melnaggar@sharjah.ac.ae (M. El-Naggar), ishehadi@sharjah.ac.ae (I.A. Shehadi), khasan@sharjah.ac.ae (K. Hasan)

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.

1 Source of materials

The title compound was prepared as follows: (438 mg, 1.5 mmol, 1.0 eq) from 4-(4-phenyl-5-(prop-2-yn-1-ylthio)-4*H*-1,2,4-triazol-3-yl)pyridine, and prepared according to the

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

Atom	x	y	z	U _{iso} [*] /U _{eq}
Br1	0.43362 (2)	0.36166 (2)	0.07683 (2)	0.03177 (6)
Br2	−0.13900 (2)	0.28661 (2)	0.02177 (2)	0.02894 (5)
Br3	0.31162 (3)	−0.18387 (2)	0.17679 (2)	0.03681 (6)
S1	0.85811 (5)	0.11124 (5)	0.30978 (3)	0.02185 (8)
O1	0.1579 (2)	1.25720 (19)	0.50739 (12)	0.0405 (4)
H1A	0.177 (4)	1.173 (4)	0.484 (2)	0.061 [*]
H1B	0.223 (4)	1.292 (4)	0.482 (2)	0.061 [*]
N1	0.64699 (17)	−0.01594 (17)	0.09509 (10)	0.0229 (3)
N2	0.75981 (17)	−0.05054 (17)	0.14230 (10)	0.0227 (3)
N3	0.41667 (17)	0.37427 (16)	0.40418 (10)	0.0208 (3)
N4	0.65443 (16)	0.39942 (15)	0.35044 (9)	0.0176 (2)
N5	0.24810 (19)	0.94764 (17)	0.43955 (10)	0.0256 (3)
N6	0.53061 (17)	0.23064 (16)	0.38249 (10)	0.0216 (3)
N7	0.50119 (16)	0.03971 (16)	0.15111 (9)	0.0193 (2)
C1	0.41213 (19)	0.63718 (17)	0.40209 (10)	0.0180 (3)
C2	0.2410 (2)	0.69992 (19)	0.41646 (12)	0.0220 (3)
H2	0.1776	0.6380	0.4142	0.026 [*]
C3	0.1662 (2)	0.8540 (2)	0.43407 (13)	0.0256 (3)
H3	0.0504	0.8956	0.4428	0.031 [*]
C4	0.4108 (2)	0.88549 (19)	0.42722 (11)	0.0234 (3)
H4	0.4707	0.9496	0.4318	0.028 [*]
C5	0.4979 (2)	0.73326 (19)	0.40810 (11)	0.0214 (3)
H5	0.6137	0.6954	0.3993	0.026 [*]
C6	0.49144 (18)	0.47352 (18)	0.38505 (10)	0.0180 (3)
C7	0.67038 (19)	0.24937 (18)	0.35057 (10)	0.0183 (3)
C8	0.78093 (19)	0.45655 (18)	0.30950 (11)	0.0199 (3)
C9	0.7648 (2)	0.5382 (2)	0.23347 (12)	0.0273 (4)
H9	0.6695	0.5593	0.2095	0.033 [*]
C10	0.8904 (3)	0.5887 (2)	0.19275 (15)	0.0387 (5)
H10	0.8802	0.6472	0.1414	0.046 [*]
C11	1.0302 (3)	0.5536 (2)	0.22733 (17)	0.0436 (6)
H11	1.1164	0.5870	0.1989	0.052 [*]
C12	1.0457 (3)	0.4706 (3)	0.30250 (17)	0.0401 (5)
H12	1.1428	0.4464	0.3251	0.048 [*]
C13	0.9198 (2)	0.4218 (2)	0.34565 (14)	0.0288 (4)
H13	0.9286	0.3664	0.3982	0.035 [*]
C14	0.7885 (2)	−0.04499 (18)	0.29702 (12)	0.0215 (3)
H14A	0.8847	−0.1385	0.2824	0.026 [*]
H14B	0.7228	−0.0615	0.3531	0.026 [*]
C15	0.68838 (19)	−0.01783 (17)	0.22807 (11)	0.0189 (3)
C16	0.52272 (19)	0.04105 (19)	0.23379 (11)	0.0205 (3)
H16	0.4411	0.0752	0.2846	0.025 [*]
C17	0.35256 (18)	0.09539 (18)	0.11971 (10)	0.0187 (3)
C18	0.30365 (19)	0.23936 (18)	0.08337 (11)	0.0199 (3)
C19	0.15813 (19)	0.29708 (19)	0.05335 (12)	0.0217 (3)
H19	0.1258	0.3948	0.0282	0.026 [*]
C20	0.06104 (18)	0.20782 (19)	0.06117 (11)	0.0198 (3)
C21	0.10396 (19)	0.06431 (19)	0.09682 (11)	0.0208 (3)
H21	0.0353	0.0055	0.1013	0.025 [*]
C22	0.2510 (2)	0.00968 (18)	0.12574 (11)	0.0200 (3)

literature,⁵ was dissolved and stirred in 10.0 mL of DMF. To this solution, 2-azido-1,3,5-tribromobenzene (692 mg,

1.95 mmol, 1.3 eq) along with sodium ascorbate (150 mg, 0.75 mmol) and CuSO₄ · 5H₂O (60 mg, 0.24 mmol) were added. The mixture was stirred overnight, and the reaction was monitored by TLC. The reaction was worked out by evaporation of the solvent under reduced pressure and the residue was subjected to column chromatography to produce the final compounds which was crystallized from methanol-dichloromethane.⁵ Melting point 138 °C–139 °C. ¹H-NMR (DMSO-*d*₆): δ (ppm) 8.70–8.50 (2H, m, ArH), 8.42 (1H, s, triazole H), 8.24 (2H, s, ArH), 7.65–7.55 (3H, m, ArH), 7.50–7.44 (2H, m, ArH), 7.35–7.25 (2H, m, ArH), 4.62 (2H, s, SCH₂); ¹³C-NMR (125 MHz, DMSO-*d*₆): δ 152.82, 152.75, 150.64, 143.15, 135.48, 135.40, 134.26, 133.83, 131.05, 130.72, 128.09, 126.50, 125.67, 123.75, 27.25; Anal. Calcd. (%) for C₂₂H₁₄Br₃N₇S: C, 40.77; H, 2.18; N, 15.13; Found: C, 40.75; H, 2.15; N, 15.10. ESI-MS 646.86 (M⁺) Calcd. for C₂₂H₁₄Br₃N₇S.

2 Experimental details

All chemicals and solvents were used as purchased without further purifications. The uncorrected melting point was determined using an electrothermal digital melting-point apparatus. The NMR spectra were recorded at room temperature in DMSO-*d*₆ solution on a Bruker Avance 500 MHz NMR spectrometer. Single crystal of C₂₂H₁₄Br₃N₇S was obtained through crystallization of the pure compound from slow evaporation of methanol-dichloromethane. The collected frames were integrated with the Bruker SAINT software package using a narrow-frame algorithm. Data corrections were performed for absorption effects using the multi-scan method (SADABS). The structure was solved and refined using the Bruker SHELXTL³ software package. Using Olex2,² the structure was further refined with the with the ShelXL⁴ refinement package using least squares minimization. All H atoms bonded to C atoms were refined as riding, with C–H distances of 0.93 Å (for aromatic ring).

3 Comment

Significant attention in synthetic chemistry was attributed to heterocyclic system with poly nitrogen containing compounds.^{6–8} Among these heterocyclic compounds, 1,2,4 and 1,2,3-triazole systems had proven to be of special interest due to the established biological activities and their existence in many modern drugs such as ribavirin, fluconazole, and tazobuctum which are currently used as antiviral, antifungals, and anti-bacterial activities, respectively.⁹ Diverse compounds containing these two moieties are proven to have anticancer activities.^{10,11} In a continuation

of our group interest in design and synthesize new biologically active system,^{12–16} we report the modification of both 1,2,4 and 1,2,3-triazole moieties tethered by the sulfur atom,⁵ the construction of the 1,2,3-triazole was successfully achieved via Cu(I) catalyzed click chemistry of the tribromophenylazide, which was prepared from the aniline derivative according to the published work,¹⁷ and the propargyl group constructed on the 1,2,4-triazole moiety prepared as described.⁵ Herein, we are reporting on the X-ray structure of the title compound.

The measurement shows that the crystal structure consists of the $C_{22}H_{14}Br_3N_7S$ monomeric molecule with one molecule of lattice water. The asymmetric unit shows one molecular unit, in which all bond lengths and angles are in normal ranges.¹⁸ The compound composed of five unsaturated rings, triazole and phenyl rings, twice each, and one pyridyl ring. The phenyl and pyridyl substituents on the 1,2,4-triazole ring are about perpendicular ($68.37(5)^\circ$) to each other due to steric repulsion between rings. The pyridyl group shows angle of $19.09(7)^\circ$ with the normal plane of the 1,2,4-triazole ring. On the other hand, the phenyl ring, attached to N4, shows an angle of $66.45(7)^\circ$ with the normal plane the 1,2,4-triazole ring. Conversely, in the 1,2,3-triazole ring the substituted phenyl ring, attached to N7 forms an angle of $79.66(6)^\circ$ with the normal plane of the 1,2,3-triazole. The N–N [N3–N6: 1.390(2), N1–N2: 1.306, N1–N7: 1.362 Å] and C–N [C6–N4: 1.382, C6–N3: 1.315, C7–N4: 1.370, C7–N6: 1.313, C15–N2: 1.372, C16–N7: 1.351 Å] bond lengths of both triazole rings are within the values reported for N–N and C–N in triazole rings. The substituents on sulfur atom (C7–S1–C14) show a normal bent angle of $99.29(8)^\circ$. Lattice water molecule link two moieties of the compound *via* hydrogen bonds with the pyridyl nitrogen (N4) with a distance of 2.115(4) Å and with the N3 (+x, 1 + y, +z) with a distance of 2.243 Å. Furthermore, the molecular packing of the title compound shows interaction between C20–Br2...H19 (–x, 1 – y, –z) with a distance 3.0913(7) Å to form centrosymmetric dimers.

Acknowledgments: ME acknowledge University of Sharjah, for financial support (grant No. 21021440109). Part of this work has been carried out during sabbatical leave granted to MAK from the University of Jordan during the academic year 2021–2022.

Author contribution: All the authors have accepted responsibility for the entire content of this submitted manuscript and approved submission.

Conflict of interest: The authors declare no conflicts of interest regarding this article.

Research funding: University of Sharjah (grant no. 21021440109).

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. Crystallogr.* **2009**, *42*, 339–341.
3. Sheldrick, G. M. SHELXT – Integrated Space-Group and Crystal-Structure Determination. *Acta Crystallogr.* **2015**, *A71*, 3–8.
4. Sheldrick, G. M. Crystal Structure Refinement with SHELXL. *Acta Crystallogr.* **2015**, *C71*, 3–8.
5. El-Naggar, M.; Hasan, K.; Khanfar, M.; Shehadi, I. A.; El-Awady, R.; Negm El-Dein, A.; Abdelmonsef, A. H.; Al-Qawasmeh, R. A. Synthesis, Biological Assessment and Molecular Docking Study of New Sulfur-Linked 1,2,4-Triazole and 1,2,3-Triazole Hybrid Derivatives as Potential DNA Gyrase Inhibitors. *Z. Naturforsch.* **2024**, *79*, 419–429.
6. Opsomer, T.; Dehaen, W. Triazoles. In *Comprehensive Heterocyclic Chemistry IV*; Black, D. S.; Cossy, J.; Stevens, C. V., Eds.; Elsevier: Oxford, 2022; pp. 78–121.
7. Abdelli, A.; Azzouni, S.; Plais, R.; Gaucher, A.; Efrat, M. L.; Prim, D. Recent Advances in the Chemistry of 1,2,4-Triazoles: Synthesis, Reactivity and Biological Activities. *Tetrahedron Lett.* **2021**, *86*, 153518.
8. Henary, M.; Kananda, C.; Rotolo, L.; Savino, B.; Owens, E. A.; Cravotto, G. Benefits Applications of Microwave-Assisted Synthesis of Nitrogen Containing Heterocycles in Medicinal Chemistry. *RSC Adv.* **2020**, *10*, 14170–14197.
9. Amjad, H.; Abbasi, M. A.; Siddiqui, S. Z.; Iqbal, J.; Rasool, S.; Ashraf, M.; Hussain, S.; Shah, S. A. A.; Imran, S.; Shahid, M.; Rasool, A.; Rehman, M. T.; Rehman, A. U. *In Vitro And In Silico* Assessment of Bioactivity Properties and Pharmacokinetic Studies of New 3,5-Disubstituted-1,2,4-Triazoles. *J. Mol. Struct.* **2023**, *1275*, 134720.
10. Bozorov, K.; Zhao, J.; Aisa, H. A. 1,2,3-Triazole-Containing Hybrids as Leads in Medicinal Chemistry: A Recent Overview. *Bioorg. Med. Chem.* **2019**, *27*, 3511–3531.
11. Gonnet, L.; Baron, M.; Baltas, M. Synthesis of Biologically Relevant 1,2,3- and 1,3,4-Triazoles: From Classical Pathway to Green Chemistry. *Molecules* **2021**, *26*, 5667.
12. 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**, *12*, 563–573.
13. Hersi, F.; Omar, H. A.; Al-Qawasmeh, R. A.; Ahmad, Z.; Jaber, A. M.; Zaher, D. M.; Al-Tel, T. H. Design and Synthesis of New Energy Restriction Mimetic Agents: Potent Anti-Tumor Activities of Hybrid Motifs of Amino-thiazoles and Coumarins. *Sci. Rep.* **2020**, *10*, 2893.
14. Al-Aboudi, A.; Al-Qawasmeh, R. A.; Shahwan, A.; Mahmood, U.; Khalid, A.; Ul-Haq, Z. In-Silico Identification of the Binding Mode of Synthesized Adamantyl Derivatives inside Cholinesterase Enzymes. *Acta Pharmacol. Sin.* **2015**, *36*, 879–886.

15. 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.
16. Shehadi, I. A.; Delmani, F. A.; Jaber, A. M.; Hammad, H.; AlDamen, M. A.; Al-Qawasmeh, R. A.; Khanfar, M. A. Synthesis, Characterization and Biological Evaluation of Metal Adamantyl 2-Pyridylhydrazone Complexes. *Molecules* **2020**, *25*, 2530.
17. Saber, S. W.; Al-Qawasmeh, R. A.; Abu-Qatouseh, L.; Shtaiwi, A.; Khanfar, M. A.; Al-Soud, Y. A. Novel Hybrid Motifs of 4-Nitroimidazole-Piperazinyl Tagged 1,2,3-Triazoles: Synthesis, Crystal Structure, Anticancer Evaluations, and Molecular Docking Study. *Heliyon* **2023**, *9*, e19327.
18. Sun, G.-X.; Min, L.-J.; Han, L.; Liu, X.-H. Crystal Structure of 2-((4-Phenyl-5-(pyridin-4-yl)-4*h*-1,2,4-triazol-3-yl)thio)acetonitrile, $C_{15}H_{11}N_5S$. *Z. Kristallogr. N. Cryst. Struct.* **2022**, *237*, 199–200.