Indian Journal of Heterocyclic Chemistry
Vol. 34 - Number 02 (Apr-Jun 2024) 195-203
https://connectjournals.com/01951.2024.34.195
https://doi.org/10.59467/IJHC.2024.34.195

ISSN (Print) : 0971-1627
ISSN (Online) : 2456-4311

"Click Chemistry" Inspired Synthesis and Antimicrobial Evaluation of 1,2,4-triazolo[4,3-a]pyridine linked 1,4-disubstituted 1,2,3-triazole Derivatives with Amide Functionalities

Rahul V. Parmar*, Milan S. Vadodaria and Prashant S. Gajera

Chemical Research Laboratory, Shri M. and N. Virani Science College, Rajkot, Gujarat, India

ABSTRACT In an attempt to rationalize the search for new potential antimicrobial agents, a new series of 1,2,4-triazolo[4,3-*a*] pyridine linked 1,4-disubstituted 1,2,3-triazoleswith amide linkage has been synthesized by the cyclization of 1,2,4-triazolo[4,3-*a*]pyridine-based alkynes and 2-azido *N*-phenylacetamide in the presence of $CuSO_4$ as catalyst *through* "Click Chemistry" approach. The newly synthesized scaffolds have been evaluated for their antimicrobial potential using eight microbial strains such as *Escherichia coli, Pseudomonas aeruginosa, Enterobacter aerogenes, Bacillus megaterium, Staphylococcus aureus, Bacillus subtilis, Aspergillus Niger, and Aspergillus flavus.* Results revealed that all synthesized scaffolds displayed superior activities than the standard drugs against various microbial strains. The synthesized compounds showed potential antimicrobial activity against Gram-positive, Gram-negative bacteria, and fungi.

KEYWORDS Antimicrobial activity, Click chemistry, Microwave irradiation, 1,4-Disubstituted 1,2,3-triazoles, 1,2,4-Triazolo[4,3-a]pyridine.

How to cite this article: Parmar, R.V., Vadodaria, M.S. and Gajera, P.S. "Click Chemistry" Inspired Synthesis and Antimicrobial Evaluation of 1,2,4-triazolo[4,3-a]pyridine linked 1,4-disubstituted 1,2,3-triazole Derivatives with Amide Functionalities, *Indian J. Heterocycl. Chem.*, **2024**, *34*, 195–203. (https://doi.org/10.59467/IJHC.2024.34.195)

INTRODUCTION

Microbial resistance is a threat to the health defense, it might turn into a next worldwide health emergency if serious and required actions are not taken to stop the microbial resistance.[1,2] To get control of this worse situation, the development of microbial drugs with novel method of action is extremely preferred. Scientists are using a variety of proposal to develop antimicrobial drugs for saving human life from the health emergencies of future and molecular hybridization approach is evolved as a main potential method to achieve this target.[3,4]

At present, the synthesis of nitrogen-containing heterocycles is significant in the fields of medicinal chemistry[5] and industrial chemistry.[6] Several reports found that fusing of triazole and pyridine rings is a good way to develop highly active compounds, such as antifungal[7,8] and antibacterial activity.[9]

The conjugation of functional molecules throughout 1,2,3-triazole has established great interest in drug design and discovery.[10,11] The formation of 1,2,3-triazole compounds through a Cu(I)-catalyzed alkyne azide 1,3-dipolar cycloaddition (CuAAC) reaction, frequently referred as click chemistry, is extensively used for the rapid assembly of heterocyclic molecules that may be later used as lead compound in drug development.[12] A wide range of biological activities such as antitubercular,[13] antifungal,[14] antioxidant,[15] antibacterial,[16] and anti-prostate cancer agent[17]are exhibited by 1,2,3-triazole based molecules.

Some 1,2,3-triazole-moiety containing molecules are accessible in the market or in clinical trials. Several of the 1,2,3-triazoles moiety-based potential pharmaceuticals include Rufinamide, Carboxyamidotriazole, tert-butyldime thylsilylspiroaminooxathioledioxide (TSAO), Tazobactam, Cefatrizine, and I-A09 [**Figure 1**].

*Corresponding author: Email: rahulparmar1313@gmail.com

Published & Hosted by :
Journal Homepage :
www.connectjournals.com/ijhc
www.connectjournals.com

REFERENCES

[1] Santos Ramos, M.A.D., Santos, K.C.D., da Silva, P.B., de Toledo, L.G., Marena, G.D., Rodero, C.F., de Camargo, B.A.F., Fortunato, G.C., Bauab, T.M. and Chorilli, M. Nanotechnological strategies for systemic microbial infections treatment: A review, *Int. J. Pharm*., **2020**, *589*, 119780.

[2] Cruz, M.P., Santos, E., Cervantes, M.A.V. and Juárez, M.L. COVID-19, a worldwide public health emergency, *Rev. Clín. Esp*., **2021**, *22*1, 55–61.

[3] Viegas-Junior, C., Danuello, A., Silva Bolzani, V., Barreiro, E.J. and Fraga, C.A.M. Molecular hybridization: A useful tool in the design of new drug prototypes, *Curr. Med. Chem*., **2007**, *14*, 1829–1852.

[4] Sunil, R.J., Pal, S. and Jayashree, A. Molecular hybridization-an emanating tool in drug design, *Med. Chem*., **2019**, *9*, 93–95.

[5] Cihan-Ustundag, G., Simsek, B., Ilhan, E. and Capan, G. Synthesis, characterization, antimycobacterial and anticancer evaluation of new 1, 2, 4-triazole derivatives, *Lett. Drug Des. Discov*., **2014**, *11*, 290–296.

[6] Shapiro, R., DiCosimo, R., Hennessey, S.M., Stieglitz, B., Campopiano, O. and Chiang, G.C. Discovery and development of a commercial synthesis of azafenidin, *Org. Process Res. Dev*., **2001**, *5*, 593–598.

[7] Yang, M.Y., Zhai, Z.W., Sun, Z.H., Yu, S.J., Liu, X.H., Weng, J.Q., Tan, C.X. and Zhao, W.G. A facile one-pot synthesis of novel 1, 2, 4-triazolo [4, 3-a] pyridine derivatives containing the trifluoromethyl moiety using microwave irradiation, *J. Chem. Res*., **2015**, *39*, 521–523.

[8] Liu, X.H., Sun, Z.H., Yang, M.Y., Tan, C.X., Weng, J.Q., Zhang, Y.G. and Ma, Y. Microwave assistant one pot synthesis, crystal structure, antifungal activities and 3D-QSAR of novel 1, 2, 4-triazolo [4, 3-a] pyridines, *Chem. Biol. Drug Des*., **2014**, *84*, 342–347.

[9] Sadana, A.K., Mirza, Y., Aneja, K.R. and Prakash, O.M. Hypervalent iodine mediated synthesis of 1-Aryl/ Hetryl-1, 2, 4-triazolo [4, 3-a] pyridines and 1-Aryl/ Hetryl 5-methyl-1, 2, 4-triazolo [4, 3-a] quinolines as antibacterial agents, *Eur. J. Med. Chem*., **2003**, *38*, 533–536.

[10] Wang, X., Huang, B., Liu, X. and Zhan, P. Discovery of bioactive molecules from CuAAC click-chemistry-based combinatorial libraries, *Drug Discov. Today*, **2016**, *21*, 118–132.

[11] Gao, P., Sun, L., Zhou, J., Li, X., Zhan, P. and Liu, X. Discovery of novel anti-HIV agents via Cu (I)-catalyzed azide-alkyne cycloaddition (CuAAC) click chemistry-based approach, *Expert Opin. Drug Discov*., **2016**, *11*, 857–871.

[12] Wang, C., Ikhlef, D., Kahlal, S., Saillard, J.Y. and Astruc, D. Metal-catalyzed azide-alkyne "click" reactions: Mechanistic overview and recent trends, *Coord. Chem. Rev*., **2016**, *316*, 1–20.

[13] Al-Ghulikah, H.,Ghabi, A., Mtiraoui, H., Jeanneau, E. and Msaddek, M. Synthesis of new 1, 2, 3-triazole linked benzimidazolidinone: Single crystal X-ray structure, biological activities evaluation and molecular docking studies, *Arab. J. Chem*., **2023**, *16*, 104566.

[14] Parmar, R.V. and Vadodaria, M.S. Synthesis, characterization and antimicrobial evaluation of novel imidazo [1, 2-a] pyrazine-linked 1, 2, 3-triazole derivatives via a click chemistry approach, *Russian J. Org. Chem*., **2023**, *59*, 1927–1939.

[15] Akolkar, S.V., Nagargoje, A.A., Shaikh, M.H., Warshagha, M.Z.A., Sangshetti, J.N., Damale, M.G. and Shingate, B.B. New N-phenylacetamide-linked 1, 2, 3-triazole-tethered coumarin conjugates: Synthesis, bioevaluation, and molecular docking study, *Arch. Pharm.* (*Weinheim*), **2020**, *353*, 2000164.

[16] Parmar, R.V. and Vadodaria, M.S. Click synthesis, characterization, mesomorphic properties, and antimicrobial evaluation of some novel imidazo [1, 2-a] pyrazine derivatives containing a 1, 2, 3-triazole ring, *Russian J. Org. Chem*., **2023**, *59*, 2186–2194.

[17] Cao, Y., Yang, Y., Ampomah-Wireko, M., Frejat, F.O.A., Zhai, H., Zhang, S., Wang, H., Yang, P., Yuan, Q. and Wu, G. Novel indazole skeleton derivatives containing 1, 2, 3-triazole as potential anti-prostate cancer drugs, *Bioorg. Med. Chem. Lett*., **2022**, *64*, 128654.

[18] Kumar, S., Wahl, A.K. and Singh, R. Synthesis and preliminary pharmacological evaluation of 2-[4-(Aryl substituted) piperazin-1-Yl]-nphenylacetamides: Potential antipsychotics, *Trop. J. Pharm. Res*., **2011**, *1010*, 265–291.

[19] Phatak, P.S., Sathe, B.P., Dhumal, S.T., Rehman, N.N.M.A., Dixit, P.P., Khedkar, V.M. and Haval, K.P. Synthesis, antimicrobial evaluation, and docking studies of substituted acetylphenoxymethyl-triazolyl-N-phenylacetamides, *J. Heterocycl. Chem*., **2019**, *56*, 1928–1938.

[20] National Committee for Clinical Laboratory Standards, 2002, *12th Informational Supplement*. National Committee for Clinical Laboratory Standards, Wayne, PA, M100-s12.

Received: 17 Dec 2023; Accepted: 17 Apr 2024