



**Highly Efficient Synthesis of New 3,5 Substituted (Isoxazolines) and
2,3,5-Trisubstituted (Pyrazolines) Mediated by Chloramin-T and their Evaluation
of Antioxidant and Antibacterial Activities**

**Ebraheem Abdu Musad^{a,1}, Abdullah Mohammed AL Dawsari^a, Zaki Eldin Ali Abdalla^a, Kakul
Husain^a, Razaz Saeed Saeed AL Sharabi^b, K. M. Lokanatha Rai^c**

^a*Department of Chemistry, Prince Sattam Bin Abdulaziz University, College of Arts and Science,
Wadi Al-Dawasir 11991, Saudi Arabia*

^b*Department of Mathematics, Prince Sattam Bin Abdulaziz University, College of Sciences and
Humanities – Slayel*

^c*Department of Studies in Chemistry, University of Mysore, Manasagangotri, Mysore 570 006, India*

Received 22.12.2019; revised 05.03.2020; accepted 08.03.2020

Abstract — Two short series of five membered heterocyclic 3,5-disubstituted–isoxazolines derivatives (**Va-f**) and 2,3,5-trisubstituted-pyrazolines derivatives (**VIIa-f**) were synthesized via 1,3-dipolar cycloaddition reaction of 2-(allyloxy)-4,6-dimethoxypyrimidine (**III**) with aromatic aldoximes (**IV**) which undergo oxidative–dehydrogenation with chloramine–T to give 3,5-disubstituted–isoxazolines derivatives (**Va-f**) and oxidative cyclization of diphenyl hydrazones (**VI**) using chloramine-T to give 2,3,5-trisubstituted-pyrazoline derivatives (**VIIa-f**) in good yield. The newly synthesized compounds were screened for anti-oxidant and anti-microbial activities. 2,3,5-trisubstituted-pyrazolines derivatives (**VIIb-e**) revealed higher antioxidant activity at 10µg/ml while 3,5-disubstituted–isoxazolines derivatives (**Va-c**) and 2,3,5-trisubstituted-pyrazolines derivatives (**VIIa-c**) showed better anti-microbial activity at 100µg/ml compared with standard vitamin C and ciprofloxacin, respectively. Structures of newly synthesized compounds were established on the basis of their elemental analysis and spectral IR, ¹H-NMR and ¹³C-NMR.

Keywords: isoxazolines, pyrazolines, chloramine–T, antioxidant, antibacterial

REFERENCES

1. Sridhara, A.M., Reddy, K.R.V., Keshavayya, J., Ambika, D.M.S., Gopinath, V.S., Bose, Goud, P.S.K., Peethambar, S.K., *J. Braz. Chem. Soc.*, 2011, vol. 22, pp. 849–856. doi 10.1590/50103-50532011000500006
2. Tully, W.R., Gardner, C.R., Gillespie, R.J., Westwood, R., *J. Med. Chem.*, 1991, vol. 34, pp. 2060–2067.
3. He, D.H., Zhu, Y.C., Yang, Z.R., Xihu, A., *J. Chin. Chem. Soc.*, 2009, vol. 56, pp. 268–270. doi 10.1002/jccs.200900039
4. Al-Mulla, A., *Der. Pharma. Chemica.*, 2017, vol. 9, pp. 141–147.
5. Angew, H.R., *Chem. Int. Ed.*, 1963, vol. 2, pp. 565–598.
6. Caramella, P., Gruenanger, P., *In 1,3-Dipolar Cycloaddition Chemistry*, vol. 1, Padwa, A., Ed., Wiley Interscience: New York, 1984, p. 337.
7. Patterson, J.W., Cheung, P.S., Ernest, M.J., *J. Med. Chem.*, 1992, vol. 35, pp. 507–510.

¹Corresponding author: phone: + (009) 665 09-30-25-82; , P.O. Box 56; e-mail: alhashmi.ibrahim@yahoo.com.

Полный текст статьи печатается в переводной версии журнала **Russian Journal of Bioorganic Chemistry** ([Springer](#))

8. Dannhardt, G., Kiefer, W., Kramer, G., Maehrlein, S., Nowe, U., Fiebich, B., *Eur. J. Med. Chem.*, 2000, vol. 35, pp. 499–510. doi 10.1016/S0223-5234(00)00150-1
9. Jayashankara, B., Lokanatha Rai., *Arkivoc.*, 2008, vol. (xi), pp. 75–85. doi 10.3998/ark.5550190.0009.b07
10. Kai, H., Matsumoto, H., Hattori, N., Takase, A., Fujiwara, T., Sugimoto, H., *Bioorg. Med. Chem. Lett.*, 2001, vol. 11, pp. 1997–2000. doi 10.1016/S0960-894X(01)00362-6
11. Basappa, M., Sadashiva, P., Mantelingu, K., Nanjunda, S.S., Rangappa, K.S., *Bioorg. Med. Chem.*, 2003, vol. 11, pp. 4539–4544. doi 10.1016/j.bmc.2003.08.007
12. Srivastava, S., Bajpai, L.K., Batra, S., Bhaduri, A.P., Maikhuri, J.P., Gupta, G., Dhar, J.D., *Bioorg. Med. Chem.*, 1999, vol. 7, pp. 2607–2613.
13. Groutas, W.C., Venkataraman, R., Chong, L.S., Yoder, J.E., Epp, J.B., Stanga, M.A., Kim, E.H., *Bioorg. Med. Chem.*, 1995, vol. 3, pp. 125–128.
14. Naim, M.J., Alam, O., Nawaz, F., Alam, M.J., Alam, P., *J. Pharm. Bio. Sci.*, 2016, vol. 8, pp. 2–17. doi 10.4103/0975-7406.171694
15. Singh, G., Jain, A., Halve, A., Sharma, N., Acharya, M., Dixit, A., *Indo Am. J. Pharm. Res.*, 2015, vol. 5, pp. 3480–3487. doi 10.1044/1980-iajpr.151106
16. Sivakumar, K., Rajasekaran, A., Ponnilaravaran, I., Somasundaram, A., Sivasakthi, R., Kamalaveni, S., *Der., Pharm. Lett.*, 2010 vol. 2, pp. 211–219.
<http://scholarsresearchlibrary.com/archive.html>
17. Fahmy, H.H., Khalifa, N.M., Ismail, M.M., El-Sahrawy, H.M., Nossier, E.S., *Molecules*, 2016, vol. 21, pp. 271–284. doi 10.3390/molecules21030271
18. Napoleon, A.A., Fazlur-Rahman, N.K., Jeong, E.D., *Chin. Chem. Lett.*, 2015, vol. 26, pp. 567–571. doi 10.1016/j.ccllet.2015.01.008
19. Lokanath Rai, K.M., Hassner, A., *Ind. J. Chem.*, 1997, vol. 36B, pp. 242–245.
20. Lokanath Rai, K.M., Hassner, A., *Synth. Commun.*, 1997, vol. 27, pp. 467–472.
21. Hassner, A., Lokanath Rai, K.M., *Synthesis*, 1989, vol. 1, pp. 57–59.
22. Lokanath Rai, K.M., Hassner, A., *Synth. Commun.*, 1989, vol. 19, pp. 2799–2807.
23. Vijay Kumar, H., Naik, N., *Eur. J. Med. Chem.*, 2010, vol. 45, pp. 2–10. doi 10.1016/j.ejmech.2009.09.016
24. Blois, M.S., *Nature*, 1957, vol. 181, pp. 1199–1200.
25. Ruberto, G., Baratta, M.T., Deans, S.G., Dorman, H., *J. Planta Med.*, 2000, vol. 66, pp. 687–693. doi 10.1055/s-2000-9773
26. Andrews, J., M.BSAC, *J. Antimicrob. Chemother.*, 2008, vol. 62, pp. 256–278. doi 10/1093/jac/dkn194