

# An Economically and Environmentally Sustainable Synthesis and Characterization of Indole Pyrazole Carbothioamide Derivatives

Dnyandeve G. Bhosale<sup>1</sup>, Arun S. Chopade<sup>1</sup>, Dattatray G. Raut<sup>2</sup>, Anjana S. Lawand<sup>2</sup>

Department of Chemistry, Pratapsinh Mohite Patil Mahavidyalaya, Karmala, Solapur, Maharashtra, India<sup>1</sup>

School of Chemical Sciences, PAH Solapur University, Solapur, Maharashtra, India<sup>2</sup>

**Abstract:** *Indoles, both naturally occurring and synthetic, exhibit wide-ranging biological activity. Unusual and complex molecular architectures occur among their natural derivatives. As a result, this important ring system continues to attract attention from the international chemical community. The indole scaffold is found in a wide range of bioactive heterocycles and natural products. In the present work we have successfully synthesized and characterized some indole pyrazole carbothioamide derivatives.*

**Keywords:** Indole, Chalcones, Vilsmeier hack, Pyrazole Thiocarbamide

## REFERENCES

- [1]. Rao, Y. K.; Fang, S.H.; Tzeng, Y.M. Differential effects of synthesized 2'-oxygenated chalcone derivatives: modulation of human cell cycle phase distribution *Bioorg. Med. Chem.*, 2004, 12, 2679- 2686.
- [2]. Garcia, J.A.; Dreicer, R.J. Systemic chemotherapy for advanced bladder cancer: update and controversies. *Clin. Oncol.*, 2006, 24, 5545-5551.
- [3]. Lv, P.C.; Li, D.D.; Li, Q.S.; Lu, X.; Xiao, Z.P.; Zhu, H.L. Synthesis, molecular docking and evaluation of thiazolyl-pyrazoline derivatives as EGFR TK inhibitors and potential anticancer agents. *Bioorg. Med. Chem. Lett.*, 2011, 21, 5374-5377.
- [4]. Ozdemir1, A.; Altıntop, M.D.; Kaplancıkl, Z.A.; Turan-Zitouni, G.; Çiftçi, G.A.; Yıldırım S.U. Synthesis, molecular docking and evaluation of thiazolyl-pyrazoline derivatives as EGFR TK inhibitors and potential anticancer agents. *J. Enzyme Inhib. Med. Chem.*, 2012, 27(1), 51-57.
- [5]. Wang, H.H.; Qiu, K.M.; Cui, H.E.; Yang, Y.S.; Xing, Y.L.; Qiu, X.Y.; Bai, L.F.; Zhu, H.L. Synthesis, molecular docking and evaluation of thiazolyl-pyrazoline derivatives containing benzodioxole as potential anticancer agents. *Bioorg. Med. Chem.*, 2013, 21, 448-455.
- [6]. Qiu, K.M.; Wang, H.H.; Wang, L.M.; Luo, Y.; Yang, X.H.; Wang, X.M.; Zhu, H.L. Design, synthesis and biological evaluation of pyrazolyl-thiazolinone derivatives as potential EGFR and HER-2 kinase inhibitors. *Bioorg. Med. Chem.*, 2012, 20, 2010-2018.
- [7]. Awadallahm, F.M.; Piazza, G.A.; Gary, B.D.; Keeton, A.B.; Canzoneri, J.C. Synthesis of some dihydropyrimidine-based compounds bearing pyrazoline moiety and evaluation of their antiproliferative activity. *Eur. J. Med. Chem.*, 2013, 70, 273-279.
- [8]. El-Sayed, M.A.A.; Abdel-Aziz, N.I.; Abdel-Aziz, A.A.M.; ElAzab, A.S.; El-Tahir, K.E.H. Synthesis, biological evaluation and molecular modeling study of pyrazole and pyrazoline derivatives as selective COX-2 inhibitors and anti-inflammatory agents. Part 2. *Bioorg. Med. Chem.*, 2012, 20, 3306-3316.
- [9]. He, J.; Maa, L.; Wei, Z.; Zhu, J.; Peng, F.; Shao, M.; Lei, L.; He, L.; Tang, M.; He, L.; Wu, Y.; Chen, L. Synthesis and biological evaluation of novel pyrazoline derivatives as potent antiinflammatory agents. *Bioorg. Med. Chem. Lett.*, 2015, 25, 2429- 2433.
- [10]. Kumar, P.; Chandak, N.; Kaushik, P.; Sharma, C.; Kaushik, D.; Aneja, K.R.; Sharma, P.K. Benzenesulfonamide bearing pyrazolylpyrazolines: synthesis and evaluation as anti-inflammatory– antimicrobial agents. *Med. Chem. Res.*, 2014, 23, 882-895.

- [11]. Bandgar, B.P.; Adsul, L.K.; Chavan, H.V.; Jalde, S.S.; Shringare, S.N.; Shaikh, M.R.J.; Gacche, R.N.; Masand, V. Synthesis, biological evaluation, and docking studies of 3-(substituted)-aryl-5-(9-methyl-3-carbazole)-1H-2-pyrazolines as potent anti-inflammatory and antioxidant agents. *Bioorg. Med. Chem. Lett.*, 2012, 22, 5839-5844.
- [12]. Patel, M.V.; Bell, R.; Majest, S.; Henry, R.; Kolasa, T. Synthesis of 4,5-diaryl-1H-pyrazole-3-ol derivatives as potential COX-2 Inhibitors. *J. Org. Chem.*, 2004, 69, 7058-7065.
- [13]. Sharma, P.K.; Kumar, S.; Kumar, P.; Kaushik, P.; Kaushik, D.; Dhingra, Y.; Aneja, K.R. Synthesis and biological evaluation of some pyrazolylpyrazolines as anti-inflammatory-antimicrobial agents. *Eur. J. Med. Chem.*, 2010, 45, 2650-2655.
- [14]. Amir, M.; Kumar, H.; Khan, S.A. Synthesis and pharmacological evaluation of pyrazoline derivatives as new anti-inflammatory and analgesic agents. *Bioorg. Med. Chem. Lett.*, 2008, 18, 918-922.
- [15]. (a) Barsoum, F.F.; Hosni, H.M.; Girgi, A. Novel bis(1-acyl-2-pyrazolines) of potential anti-inflammatory and molluscicidal prop- Asymmetrical 1-thiocarbamoyl Pyrazole Derivatives as Potential Anticancer Anti-Cancer Agents in Medicinal Chemistry, 2018, Vol. 18, No. 15 7 erties. *Bioorg. Med. Chem.*, 2006, 14, 3929-3937. (b) Ibrahim, A.M.; Saleh, A.M.; Zohdi, H.F.; Ghorab, M.M.; Ismail, Z.H.; Abdel-Gawad, S.M.; Abdel-Aziem, A. Antimicrobial activity of amino acid, imidazole, and sulfonamide derivatives of pyrazolo [3,4-d] pyrimidine. *Heteroatom. Chem.*, 2004, 15, 57.
- [16]. Bharmal, F.M.; Kaneriya, D.J.; Parekh, H.H. Synthesis of some pyrazoline derivatives as biologically active agents. *Ind. J. Het. Chem.* 2000, 10, 189-192.
- [17]. Bekhit, A.A.; Abdel-Aziem, T. Design, synthesis and biological evaluation of some pyrazole derivatives as anti-inflammatory antimicrobial agents. *Bioorg. Med. Chem.*, 2004, 12, 1935-1945.
- [18]. Acharya, B.N.; Saraswat, D.; Tiwari, M.; Shrivastava, A.K.; Ghorpade, R.; Bapna, S.; Kaushik, K.P. Synthesis and antimalarial evaluation of 1, 3, 5-trisubstituted pyrazolines. *Eur J. Med Chem.*, 2010, 45, 430-438.
- [19]. Jeong, T.S.; Kim, K.S.; Kim, J.R.; Cho, K.H.; Lee, S.; Lee, W.S. Novel 3,5-diaryl pyrazolines and pyrazole as low-density lipoprotein (LDL) oxidation inhibitor. *Bioorg. Med. Chem. Lett.*, 2004, 14, 2719-2723.
- [20]. Karthikeyan, M.S.; Holla, B.S.; Kumari, N.S. Synthesis and antimicrobial studies on novel chloro-fluorine containing hydroxy pyrazolines. *Eur. J. Med. Chem.*, 2007, 42, 30-36.
- [21]. Shelke, S.N.; Mhaske, G.R.; Bonifácio, V.D.B.; Gawande, M.B. Green synthesis and anti-infective activities of fluorinated pyrazoline derivatives. *Bioorg. Med. Chem. Lett.*, 2012, 22, 5727-5730.
- [22]. Syed, A.N.; Kumar, P.S.A.; Marihal, S.C.; Gurusurthy, M. Antimicrobial study. *J. Adv. Pharm. Tech. Res.*, 2012, 3(2),14-19.
- [23]. Desai, N.C.; Joshi, V.V.; Rajpara, K.M.; Vaghani, H.V.; Satodiya, H.M. Facile synthesis of novel fluorine containing pyrazolebased thiazole derivatives and evaluation of antimicrobial activity. *J. Fluorine Chem.*, 2012, 142, 67-78.
- [24]. Ruhoglu, O.; Ozdemira, Z.; Çalis, U.; Gumusel, B.; Bilgin, A.A. Synthesis of and pharmacological studies on the antidepressant and anticonvulsant activities of some 1,3,5-trisubstituted Pyrazolines. *Arzneim.-Forsch Drug Res.*, 2005, 55(8), 431-436.
- [25]. Grosscurt, A.C.; Hes, R.V.; Wellinga, K. 1-Phenylcarbamoyl-2-pyrazolines, a new class of insecticides. 3. Synthesis and insecticidal properties of 3,4-diphenyl-1-phenylcarbamoyl-2-pyrazolines. *J. Agric. Food Chem.*, 1979, 27(2), 406-409.
- [26]. Palaska, E.; Aytemir, M.; Tayfun, U.I.; Erol, D. Synthesis and antidepressant activities of some 3,5-diphenyl-2-pyrazolines. *Eur. J. Med. Chem.*, 2001, 36, 539-543.
- [27]. Prasad, Y.R.; Rao, A.L.; Prasoon, L.; Murali, K.; Kumar, R.P. Synthesis and antidepressant activity of some 1,3,5-triphenyl-2-pyrazolines and 3-(2"-hydroxy naphthalen-1"-yl)-1,5-diphenyl-2-pyrazolines. *Bioorg. Med. Chem. Lett.*, 2005, 15, 5030-5034.
- [28]. Bijo, M.; Jerad, S.; Sockalingam, A.; Githa, E.M. Pyrazoline: A promising scaffold for the inhibition of monoamine oxidase. *Cent. Nerv. Sys. Agents Med. Chem.*, 2013, 13, 195-206.
- [29]. Can, O.D.; Ozkay, U.D.; Kaplanclkl, Z.A.; Ozturk, Y. *Arch. Pharm. Res.* 2009, 32, 9, 1293-1299.
- [30]. Ahmad, A.; Husain, A.; Khan, S.A.; Mujeeb, M.; Bhandari, A. Synthesis, antimicrobial and antitubercular activities of some novel pyrazoline derivatives. *J. Saudi Chem. Soc.*, 2014, 20(5), 577-584.

- [31]. Havrylyuk, D.; Zimenkovsky, B.; Vasylenko, O.; Day, C.W.; Smee, D.F.; Grellier, P.; Lesyk, R. Synthesis and biological activity evaluation of 5-pyrazoline substituted 4-thiazolidinones. *Eur. J. Med. Chem.*, 2013, 66, 228-237.
- [32]. Faisal, M.; Saeed, A.; Hussain, S.; Dar, P.; Larik, F.A. Recent developments in synthetic chemistry and biological activities of pyrazole derivatives. *Journal of Chemical Sciences* 2019, 131, 70, <https://doi.org/10.1007/s12039-019-1646-1>.
- [33]. Nozari, M.; Addison, A.W.; Reeves, G.T.; Zeller, M.; Jasinski, J.P.; Kaur, M.; Gilbert, J.G.; Hamilton, C.R.; Popovitch, J.M.; Wolf, L.M.; Crist, L.E.; Bastida, N. New Pyrazole- and Benzimidazole-derived Ligand Systems. *J. Heterocycl. Chem.* 2018, 55, 1291-1307, <https://doi.org/10.1002/jhet.3155>.
- [34]. Kelada, M.; Walsh, J.M.D.; Devine, R.W.; McArdle, P.; Stephens, J.C. Synthesis of pyrazolopyrimidinones using a “one-pot” approach under microwave irradiation. *Beilstein J. Org. Chem.* 2018, 14, 1222-1228, <https://doi.org/10.3762/bjoc.14.104>.
- [35]. Piltan, M. Preparation of 1H-pyrazolo[1,2-b]phthalazine-5,10-diones using ZrO<sub>2</sub> nanoparticles as a catalyst under solvent-free conditions. *Heterocycl. Commun.* 2017, 23, 401-403, <https://doi.org/10.1515/hc-2017-0142>.
- [36]. Zolfigol, M.A.; Afsharnadery, F.; Bagheri, S.; Salehzadeh, S.; Maleki, F. Catalytic applications of {[HMIM]C(NO<sub>2</sub>)<sub>3</sub>}: as a nano ionic liquid for the synthesis of pyrazole derivatives under green conditions and a mechanistic investigation with a new approach. *RSC Advances* 2015, 5, 75555-75568, <https://doi.org/10.1039/C5RA16289K>.
- [37]. Maddila, S.; Rana, S.; Pagadala, R.; Kankala, S.; Maddila, S.; Jonnalagadda, S.B. Synthesis of pyrazole-4-carbonitrile derivatives in aqueous media with CuO/ZrO<sub>2</sub> as recyclable catalyst. *Catal. Commun.* 2015, 61, 26-30, <https://doi.org/10.1016/j.catcom.2014.12.005>.