Indian Journal of Chemistry
Vol. 61, July 2022, pp. 723-731

Synthesis of some ethoxyphthalimide derivatives of pyrazoloisoxazoles and pyrazolopyrimidines and their antimicrobial and anticancer screening

Swati Joshi*[a] & G L Talesara[b]

[a] Department of Chemistry, Swami Keshvanand Institute of Technology, Management and Gramothan, Jaipur 302 017, Rajasthan, India

[b] Department of Chemistry, Mohan Lal Sukhadia University, Udaipur 313 001, Rajasthan, India

E-mail: swtojha@gmail.com

Received 27 September 2021; accepted (revised) 6 January 2022

Synthesis of 4-arylidene-5-methyl-2,4-dihydro-3*H*-pyrazol-3-one (**IIIa-d**) has been achieved by the condensation reaction between 5-methyl-2,4-dihydro-3*H*-pyrazol-3-one (**I**) and 4-substituted benzaldehydes (**IIa-d**). Ethyl acetoacetate and hydrazine hydrate in absolute alcohol undergo cyclization reaction to give (**I**). 4-Arylidene-5-methyl-2,4-dihydro-3*H*-pyrazol-3-ones (**IIIa-d**) have been converted to corresponding ethoxyphthalimide derivatives (**IVa-d**) by treatment with phthalimidoxyethyl bromide (**A**). 1-N-Ethoxyphthalimido-3-methyl-4-(4-substituted benzylidene) pyrazol-5-one (**IVa-d**) has been reacted with hydroxylamine hydrochloride and guanidine nitrate separately to yield ethoxyphthalimide substituted pyrazolo[3,4-c]isoxazoles (**Va-d**) and pyrazolo[3,4-d]pyrimidines (**VIa-d**) respectively. All the compounds have been characterized by elemental and spectral analysis mainly IR, ^{1}H NMR and mass spectroscopy. Synthesized compounds have also been screened for various biological activities *viz.* antibacterial, antifungal, antiviral and anticancer.

Keywords: Ethoxyphthalimide, pyrazoloisoxazoles, pyrazolopyrimidines, antimicrobial, anticancer

Many natural and synthetic products containing heterocyclic rings as isoxazoles[1] were reported to possess varied pharmacological activities. Isoxazoles are of considerable interest on account of their intriguing structural, chemical and biological properties. Among the wide variety of heterocycles that have been explored for developing pharmaceutically important molecules, isoxazoles[2] have played a dynamic role in the medicinal chemistry. Formation of isoxazoles from open chain hydroxy methylketones and hydroxylamine is well known[3]. Study of isoxazole derivatives is of considerable current interest as a result of their important biological and biophysical properties *i.e.* herbicidal[4], antitumor, antipsychotic, anticoagulant, antimicrobial[5] and antagonist. Isoxazoline derivatives elicit wide variety of biological activities as bactericides, fungicides, insecticides[6], analgesic and antipyretic agents and antioxidant[7], *etc*. The chemistry of isoxazoles has been reviewed and the importance of such heterocycles and their derivatives in medicinal chemistry is recognized as antiviral, bactericidal[8], anticancer[9], analgesic, antitubercular[10] and anti HIV[11] agents.

Pyrimidines are heterocyclic compounds, which serve as both biomimetic and reactive pharmacophores and many are key elements with potential biological activities. The chemistry of pyrimidines and their derivatives has been studied for over a century due to their diverse medicinal properties[12,13]. It has been associated with various medicinal applications *viz*. antitumor[14], immunodialator[15], anti tuberculosis, and radio protective. Condensed pyrazoles are biologically interesting compounds and their chemistry has received considerable attention. Pyrazolines are considered as useful synthon in organic reactions[16]. Synthetic method of these compounds involves the base catalyzed aldol condensation reaction of carbonyl compounds to give chalcones which upon cyclization reaction with hydrazine afford 2-pyrazolines[17].

A considerable number of pyrazolo[3,4-d]pyrimidines[18] are known to be bio-active and display antitumor, antiviral and antipyretic, anti-inflammatory, analgesic, anti-arthritic, antitumor[19], antiviral, antidepressant, anticonvulsant[20], antimicrobial[21], anticancer[22], hepatoprotective, antifungal[23], antihyperglycemic, antiproliferative[24] activities, *etc*.

Isoxazoles and their condensed derivatives form an important class of cyclic compounds with various