

REVIEW ARTICLE

Recent Trend in the Chemistry of Triazolopyrimidines and their Applications

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Abstract: This review deals with the synthetic methods, chemical reactions, and applications of triazolopyrimidine derivatives. The synthetic methods and chemical reactions are subdivided into groups according to the junction between triazole and pyrimidine moieties for instance [1,2,4]triazolo[1,5-*a*]pyrimidine, [1,2,4]triazolo[1,5-*c*]pyrimidine, [1,2,3]triazolo[1,5-*a*]pyrimidine, [1,2,3]triazolo[1,5-*c*]pyrimidine, [1,2,4]triazolo[4,3-*c*]pyrimidine, and [1,2,4]triazolo[4,3-*a*]pyrimidine. Pharmacological activity of triazolopyrimidins is also reported.

Keywords: Triazolopyrimidine, pyrimidine, triazole, synthesis, heterocycles, pharmacological activities.

1. INTRODUCTION

Triazolopyrimidine is one of the fused heterocyclic compounds composed of two heterocycles, triazole and pyrimidine rings. Based on the structural arrangement and the position of nitrogen atoms, there are eight different positional isomers of triazolopyrimidine that may exist in nature, as given in Fig. (1). The skeleton of triazolopyrimidine was firstly obtained by Bulow and Haas in the early 20th century. Since it is rarely found in natural molecules, it presents an important synthetic intermediate and many attempts have been made to enhance its synthesis. Several methods are used for its synthesis, such as the Biginelli reaction and other effective multicomponent

[1,5-*a*]pyrimidines. Thus, the reaction of 5-amino-3-morpholino-1*H*-1,2,4-triazole (1) with diethyl 2-(ethoxymethylene)malonate (2) in glacial acetic acid gave ethyl 2-morpholino-7-oxo-4,7-dihydro-[1,2,4]triazolo[1,5-*a*]pyrimidine-6-carboxylate (3) in a good yield. Heating of the latter in phosphoryl chloride replaced the hydroxyl group with chlorine to furnish ethyl 7-chloro-2-morpholino-[1,2,4]triazolo[1,5-*a*]pyrimidine-6-carboxylate (4). Treatment of compounds 3 and 4 with either hydrazine hydrate or substituted hydrazine in ethanol resulted in the formation of 7-morpholino-2-(un)substituted-5*H*-pyrazolo[4,3-*e*] [1,2,4]triazolo[1,5-*a*]pyrimidin-3(2*H*)-ones 5a-e [14]