International Journal of Advance and Innovative Research
Volume 6, Issue 1 (XVI): January - March, 2019
ISSN 2394 - 7780

AN OVERVIEW ON BIOLOGICAL IMPORTANCE AND SYNTHETIC METHODOLOGY OF TRIAZOLOPYRIMIDINES

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ABSTRACT
Among the four triazolopyrimidine forms, 1, 2, 4-triazolo [1, 5-a] pyrimidine derivatives are thermodynamically more stable and the mainly studied ones. Recently, 1, 2, 4-triazolo [1, 5-a] pyrimidines have been received a growing attention from the biological view points, due to their various pharmaceutical properties. The 1, 2, 4-triazolopyrimidin-5-one has shown significant activities. The present review endeavor to give a information about the various biological importance and synthesis of triazolopyrimidines

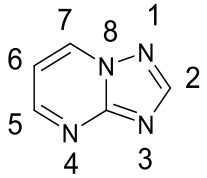
Keywords: Biological importance, synthetic methods, triazolopyrimidines.

INTRODUCTION

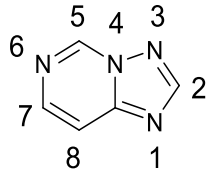
Heterocyclic compounds have been received special attention in medicinal chemistry because of their abundance in natural products and their diverse biological properties [1]. Pyrimidine derivatives have been familiar as important heterocyclic compounds due to their diversity of chemical and biological importance to medicinal chemistry [2-6].

In the past decade, various fused pyrimidines like purines, indenopyrimidines, pyrazolopyrimidines, triazolopyrimidines, furopyrimidines, pyridopyrimidines, and pyrrolopyrimidines were highly studied and were found to possess noteworthy pharmaceutical properties [7-17].

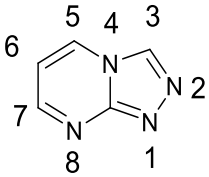
It is well known that the condensation of triazole ring and pyrimidine give rise to the formation of bicyclic heterocycles known as 1, 2, 4- triazolopyrimidines [18]. The triazolopyrimidine exist in four different structural isomeric forms (Fig. 1) [19-20].



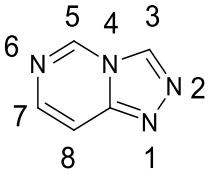
a).1,2,4-triazolo[1,5-a]pyrimidine



b).1,2,4-triazolo[1,5-c]pyrimidine



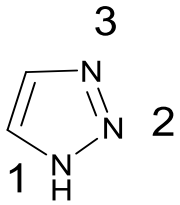
c).1,2,4-triazolo[4,3-a]pyrimidine



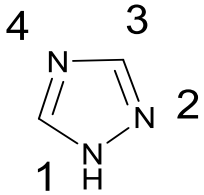
d).1,2,4-triazolo[4,3-c]pyrimidine

Fig-1: Structural isomers of triazolopyrimidine

Triazoles are five member important heterocycles among the azole heterocycles. Triazole ring is mostly of two types, the 1, 2, 3-triazole and the 1, 2, 4-triazole and used as an intermediate for the synthesis of bioactive molecules.



1,2,3-triazole



1,2,4-triazole

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Biological Importance

Before few decades, the chemistry of 1, 2, 4-triazoles and their fused heterocyclic compounds have received significant attention due to their synthetic and useful biological importance [21]. The incorporation of two bioactive motifs like triazole and pyrimidine into a single carbon skeleton leads to formation of wide variety of pharmaceutical interesting fused molecules [22-27]. (Fig-2)

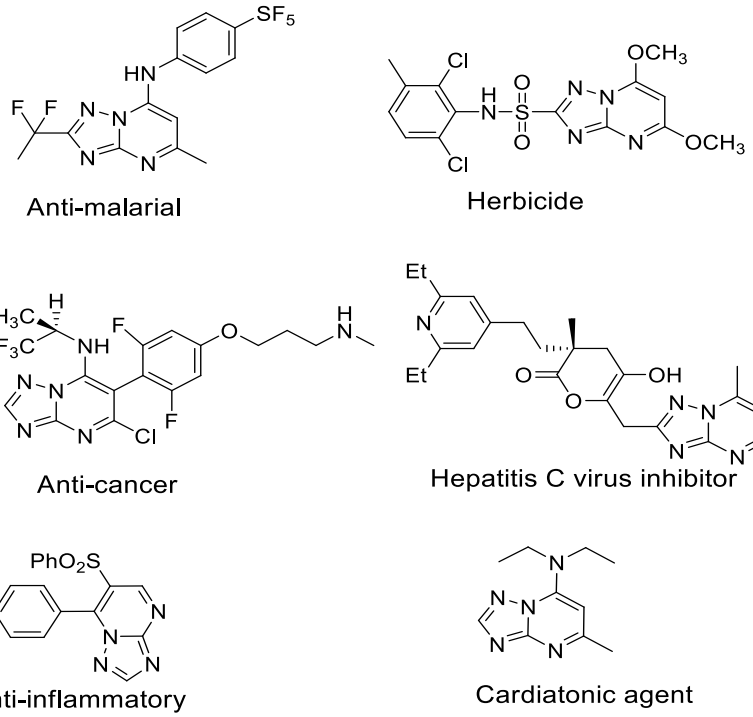
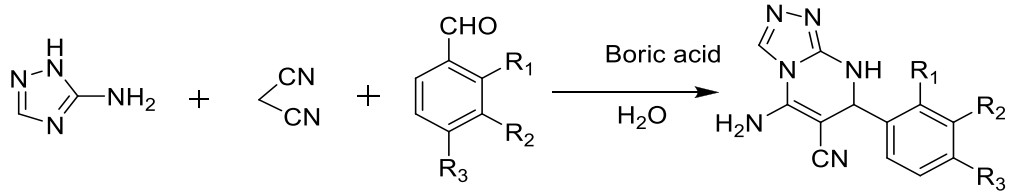


Fig-2: Examples of bioactive triazolopyrimidines

METHODS OF SYNTHESIS

Literature survey revealed that various bioactive triazolopyrimidines are synthesized using amino heterocycles

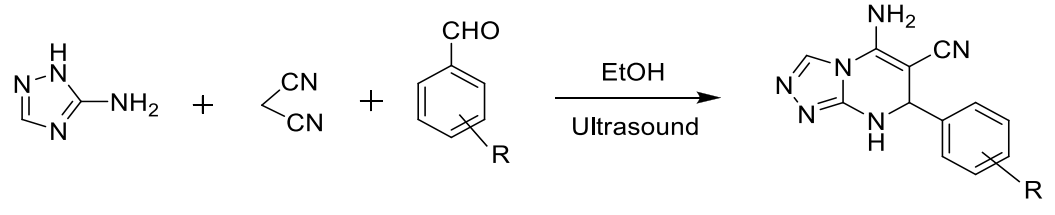
M. Singh et al. reported boric acid catalyzed simple, green, and efficient protocol for the synthesis of aryl-7,8-dihydro[1,2,4]triazolo[4,3-a] pyrimidine-6-carbonitriles derivatives through one-pot multi-component reaction using substituted aromatic aldehydes, malononitrile, and 3-amino[1,2,4]triazole [28].(Scheme-.1)



R_1= -H, -Cl. R_2= -H, -OH, -OMe.
R3= $-NO_2$, -Cl, -F etc.

Scheme-1

K. Ablajan and his coworkers synthesized triazolo pyrimidine derivatives by a one-pot reaction of 3-amino-1, 2, 4-triazole, malononitrile and aromatic aldehydes in ethanol under heating or ultrasonic irradiation in the presence of NaOH [29]. (Scheme-2)



R= $-NO_2$, -Cl, $-OCH_3$ etc.

Scheme-2

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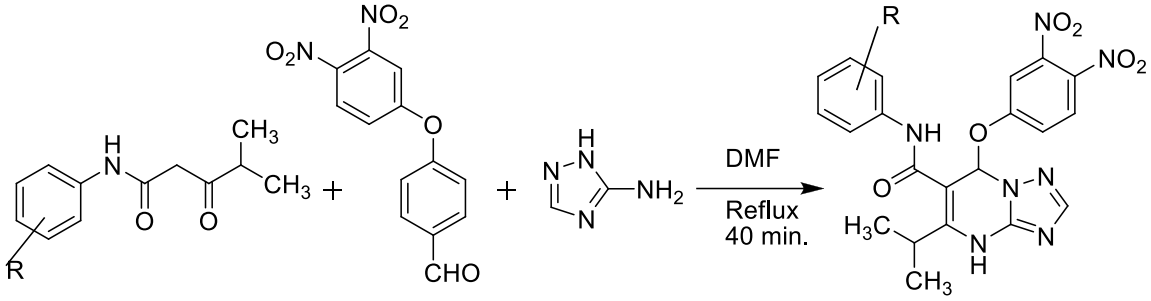
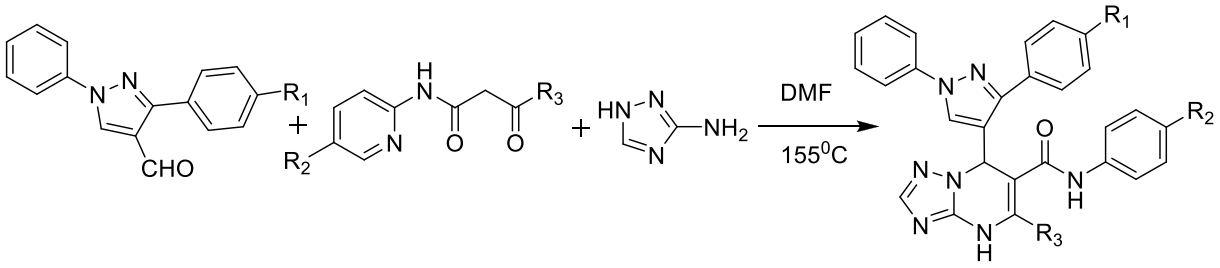
P. D. Fadadu et al. synthesized new derivatives of triazolopyrimidines using acetoacetamides, aldehyde and triazole using DMF as a solvent at reflux condition in good yield [30]. (Scheme-3)



R= -Cl, -F, -OH, -NO_2 etc.

Scheme-3

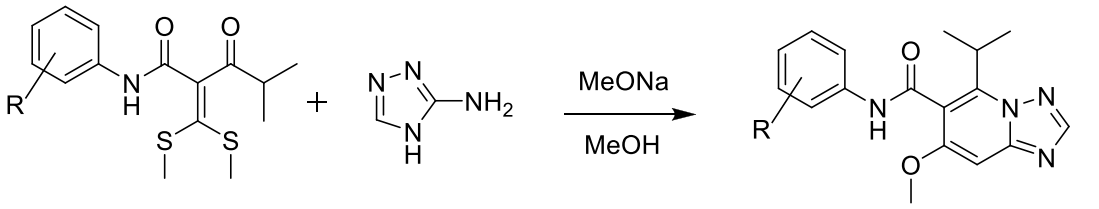
Jaimin D. Bhatt and his coworkers prepared series of novel triazolo pyrimidine derivatives. They also evaluated anti-tuberculosis activity of synthesized pyrimidine derivatives against M.tb H37Rv strain and some of them shown excellent anti-tuberculosis activity [31]. (Scheme-4)



R1= -H, -CH_3, -NO_2. R_2= -H, -CH_3, -Br.
R_3= -CH_3, -$CH(CH_3)_2$

Scheme-4

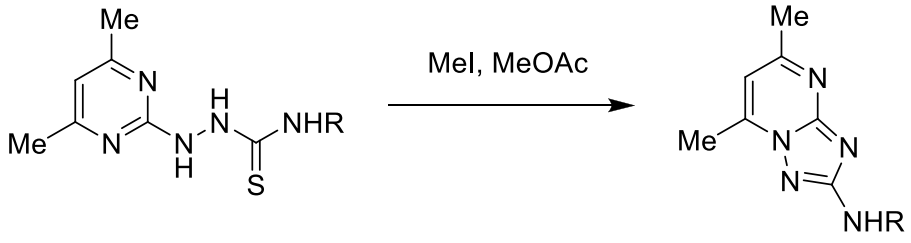
S. P. Gami et al. described the synthesis of substituted triazolopyrimidine derivatives in moderate to good yield and all the synthesized compounds were evaluated for their anti-microbial activity [32]. (Scheme-5)



R= -CH_3, -NO_2 , -Cl etc.

Scheme-5

R. I. Vas'kevich et al. reported the synthesis of amino derivatives of triazolopyrimidine from 1-(4, 6-dimethylpyrimidin-2-yl)-4-R-thiosemicarbazides by using Dimroth rearrangement [33]. (Scheme-6)



R=Me, Ph etc.

Scheme-6

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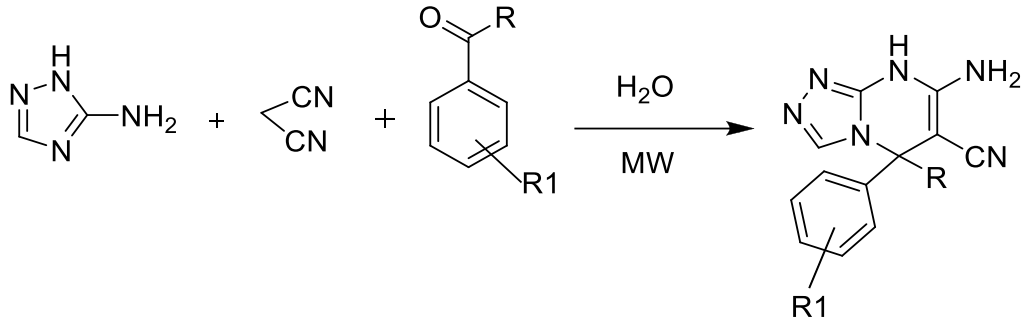
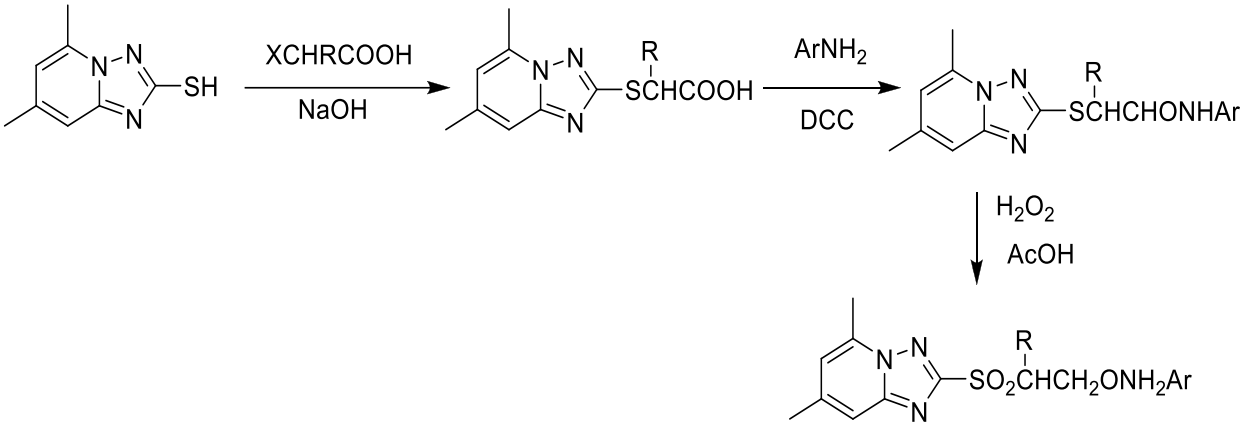
A. Dandia et al. developed an efficient and environmentally benign microwave assisted method for synthesis of 1, 2, 4-triazolo [4, 3- a] pyrimidines by using amino triazole, carbonyl compounds and alkene nitrile derivatives in an aqueous medium [34]. (Scheme: 7)



R= -H, -CH_3 etc. R1= -Cl, -NO_2 etc.

Scheme-7

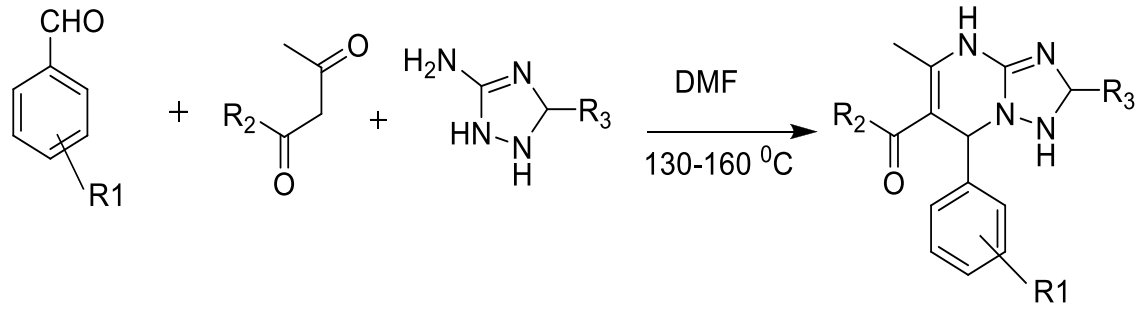
G. Yang et al. synthesized novel 1, 2, 4-triazolo [1, 5-a] pyrimidine derivatives. The synthesized compounds were screened for their herbicidal activity and most of the compounds shown good said activity [35]. (Scheme-8)



X= -Cl, -Br. R= -H, -CH_3

Scheme-8

H. Wang and coworkers synthesised 1, 2, 4-triazolo[1,5-a]pyrimidines using aldehydes, active methylene compounds and aminoazoles in DMF and synthesized compounds were assessed as anti-bacterial agents against Enterococcus faecium [36] (Scheme-9)



R_1=H, -NO_2, -F, -CF_3 etc. R_2= -OC_2H_5, -$NHCH_3$
R_3= -SCH2Ph.

Scheme-9

N. Jianga et al. reported the synthesis of new triazolopyrimidine derivatives and also screened for their anticonvulsant activity [37]. (Scheme-10)

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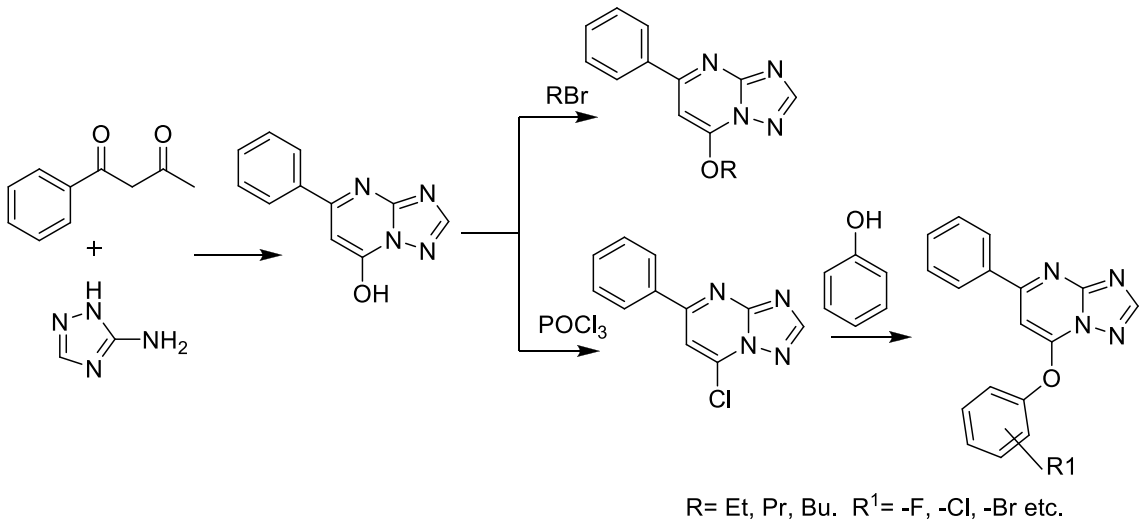
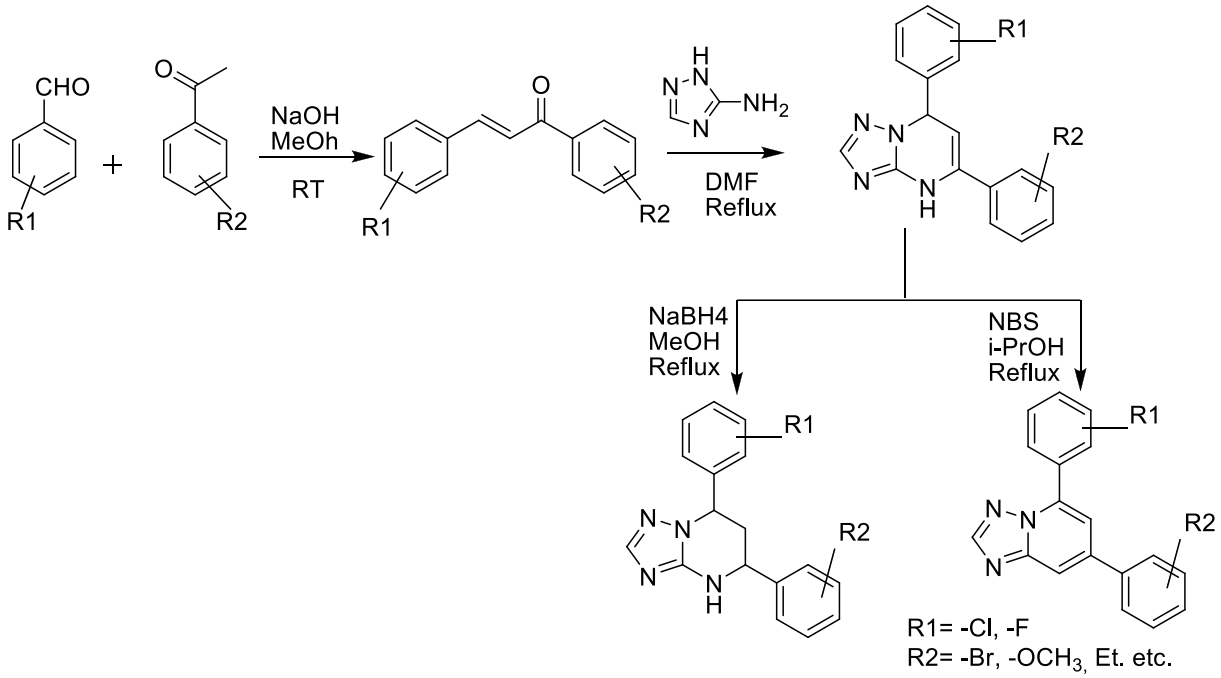


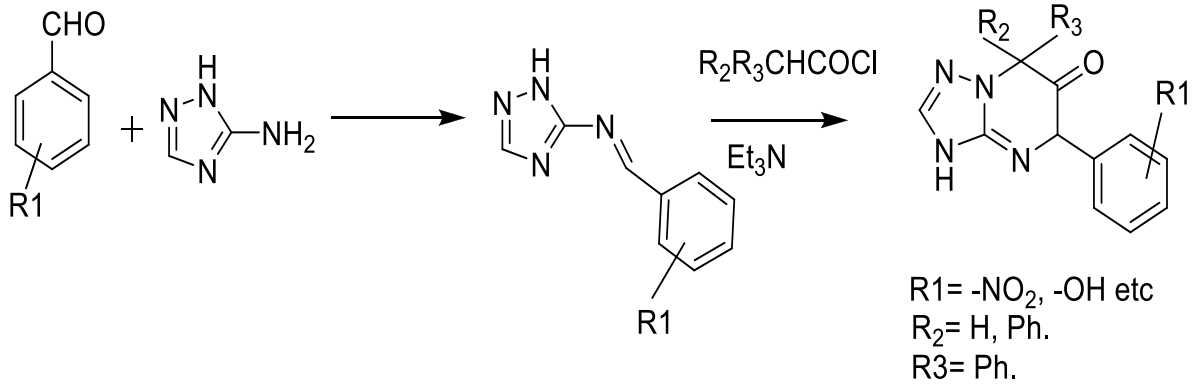
Scheme-10

W. Yu and his coworkers designed and synthesized triazolopyrimidine derivatives and assessed as novel inhibitors of Hepatitis B surface antigen secretion (HBsAg) [38]. (Scheme-11)



Scheme-11

S. K. Borthakur has been described the synthesis of a new series of [1, 2, 4] triazolo [1, 5-a pyrimidin-6-one using triethylamine as a catalyst and newly synthesized compounds were tested for anti-fungal activities against Rhizoctonia solani and Trichoderma species [39]. (Scheme-12)



Scheme-12

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CONCLUSION

Among all heterocyclic compounds, pyrimidines are one of the most important heterocycles shows remarkable biological and pharmaceutical activities because it is an essential constituent of all cells. In medicinal chemistry pyrimidine derivatives have been very well known for their therapeutic applications. The presence of a pyrimidine unit in nucleic acids, DNA and RNA is one possible reason for their biological activities. The versatile synthetic applicability and biological importance of the triazolopyrimidine derivatives will help the chemists to develop new approaches towards finding of new drugs.

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