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A Review On 1,2,4-Triazoles

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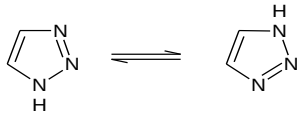
ABSTRACT

Triazole is a five membered heterocyclic system consisting of two carbon atoms and three nitrogen atoms shows wide range of biological activities. Triazoles can be synthesized using Einhorn-Brunner reaction or the Pellizzari reaction from acyl hydrazides and various different method. Triazole derivatives are showing very promising and excellent therapeutic effectiveness. The major activities exhibited by these derivatives include insecticial, antifungal, antiviral, antibacterial, sedative,hypnotic, anticonvulsant and anti-inflammatory action. In recent year heterocyclic compounds analogues and derivatives have attracted strong interest due to their useful biological and pharmacological properties. The small and simple triazole nucleus is present in compounds involved in research aimed at evaluating new products that possess biological activities, such as,anti-microbial, anti-tumor, anthelmintic, anti-leishmanial, anti-convulsant and anti-inflammatory.

Key words: *Triazole, 1H-1, 2,4-Triazole, Heterocycle, Total synthesis, Biological activities.*

INTRODUCTION

Triazoles are heterocyclic compounds featuring five member ring of two carbon atoms and three nitrogen atoms as part of the aromatic five-member ring. Triazole refers either one of a pair of isomeric chemical compounds with molecular formula C2H3N3.



1*H*-1,2,3-triazole

4*H*-1,2,4-triazole

During the last few decades, a considerable attention has been devoted to synthesis of 1,2,4 triazole derivatives due to their wide spectrum of biological activities such as anticonvulsant [1], antidepressant [2], antibacterial [3], antifungal [4], anti-inflammatory [5], analgesic [6], anticancer [7] and anti viral [8] activities. The anticonvulsant drug design is based on the presumption that for the activity in maximal electroshock seizure (MES) evaluation, at least one phenyl or similar aromatic group in close proximity to a two electron donor atom is required. For activity in pentylenetetrazole (PTZ) evaluation, an alkyl or amine group close to a two electron donor atom is needed [9]. In view of the above findings, it was thought worthwhile to synthesize a series of ten compounds containing the features of 1,2,4-triazole moiety with different substituents and studied their anticonvulsant activity by electroshock and chemo shock methods.The chemistry of 1,2,4-triazoles described briefly in the literature [9, 10]. The first 1,2,4-triazole derivatives have been synthesised by Bladin in 1885. 1,2,4-triazole derivatives are also useful as analytical reagents [11], photographic chemicals[12] and in polymer synthesis [13].

Synthetic Aspect:

1. Base-catalyzed, direct synthesis of 3,5-disubstituted 1,2,4-triazoles:

A convenient and efficient one step, base-catalyzed synthesis of 3,5-disubstituted 1,2,4-triazoles by the condensation of a nitrile and a hydrazide is presented. A diverse range of functionality and heterocycles are tolerated under the reaction conditions developed, and the reactivity of the nitrile partner is relatively insensitive to electronic effects [14].

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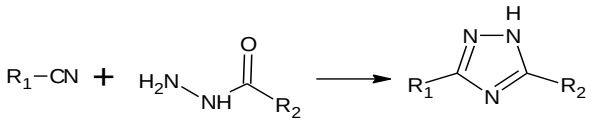
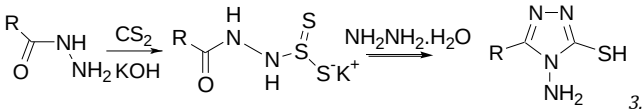
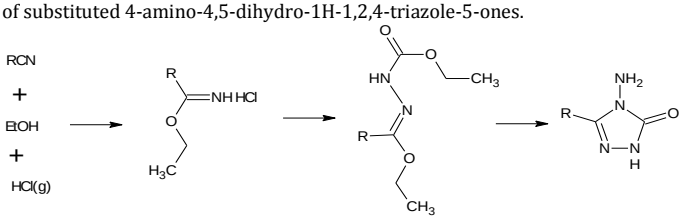


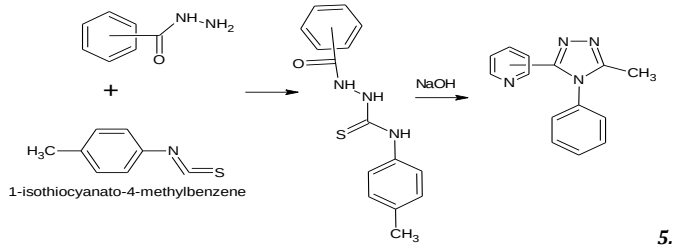
2. Reid and Heindel[15] have reported the reaction of aryl acid hydrazide with CS2/KOH and Hydrazine hydrate furnished triazoles:



3. ***Bahittin Kahveci*** [16] have reported that the iminoester hydrochlorides are converted into ester ethoxycarbonyl hydrazones, which turn into a new series of substituted 4-amino-4,5-dihydro-1H-1,2,4-triazole-5-ones.



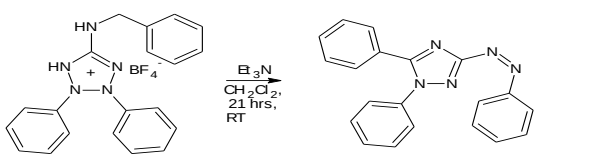
4. ***Khosrow Zamani and co-worker*** [17] have prepared triazole derivatives from respective substituted pyridine carboxylic acid hydrazides and 4-methylphenyl isothiocyanate.



1-isothiocyanato-4-methylbenzene

5. ***Li-Li Liu and Guang Yang*** [18] were described a facile method to prepare 1,2,4-triazole by the reaction of isonicotinonitrile with excess amount of hydrazine.

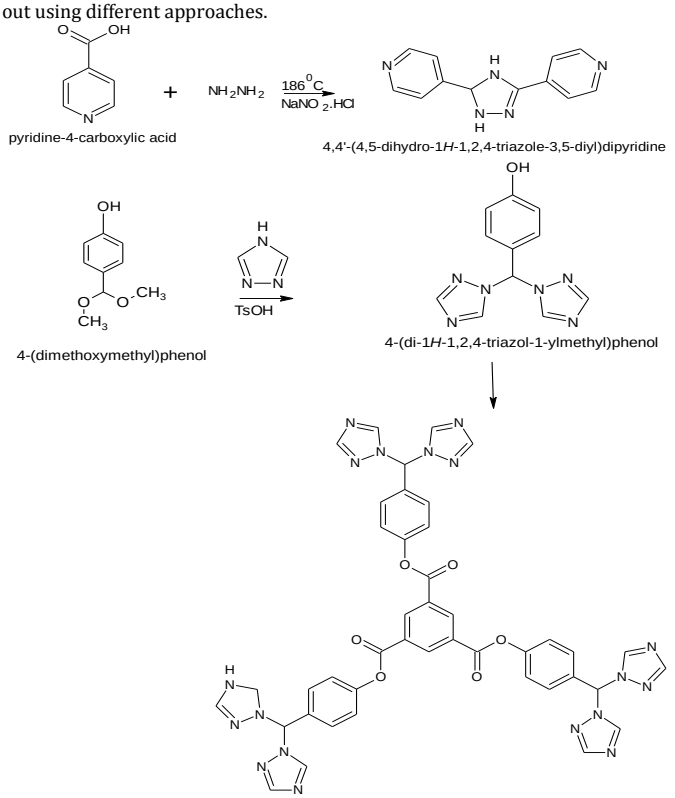
6. Shuki Araki and co-worker [19] have synthesized 1,2,4-triazoles from 2,3-diphenyltetrazolium salt. using triethylamine as a base.



1,5-diphenyl-3-[(*Z*)-phenyldiazenyl]-1*H*-1,2,4-triazole

DOI: https://doi.org/10.5281/zenodo.1098645

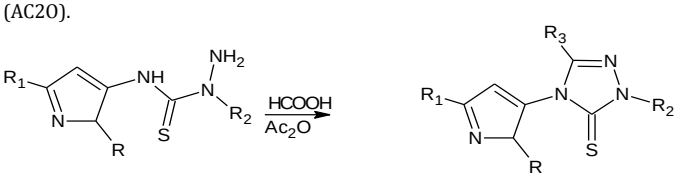
7. The synthesis of dendrons bearing 1,2,4-triazoles moiety is described by Enrique Diez-Barra et al. [20] The synthesis of these compounds was carried out using different approaches.



8. Kee-Jung lee et al. [21] have reported 1,2,4-triazole from the electrocyclic reaction of conjugated heterocumulenes.

8. Chande et al.[22] have reported 4-anilino-5-mercapto-5-triazoles from -acyl dithiocarbazinate and phenyl hydrazine at 140-160oC.

9. Shin-ichi Nagai [23] have synthesised triazole by the reaction of thiosemicarbazide with formic acid in the presence of acetic anhydride (AC2O).



10. Yan Shiquaing [24] have prepared triazole by the treatment of ferrocenecarboxylic acid hydrazide with aryl isothiocyanate and cyclization of the product gave 3,4-disubstituted 4H-1,2,4-triazole-5-thiol.

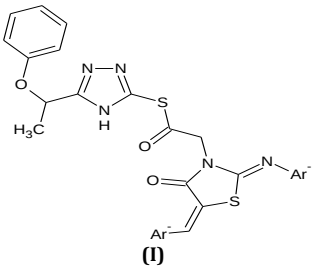
11. B. J. Rai and Co-workers [25] have synthesised 3-amino-5-aryl-2-phenyl-2H-1,2,4-triazole by reaction of aroyl-cyanide with phenyl hydrazine.

Therapeutic Importance:

1,2,4-triazole derivatives have been associated with diverse biological activities. Therapeutic activity of 1,2,4-triazoles are listed as under.

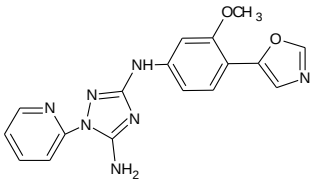
1. Antiinflammatory [26]
2. Diuretic [27]
3. Antiviral [28]
4. Antihypertensive [29]
5. Anthelmintics [30]
6. Bactericidal [31]
7. Anticonvulsant [32]
8. Herbicidal [33]
9. Insecticidal & Acaricidal [34]
10. Fungicidal [35]
11. Antimicrobial [36]
12. Anticancer and anti-HIV [37]
13. Plant growth regulator [38]
14. Antileishmanial [39]
15. Antitumor [40]
16. Antidepressant and Anxiolytic [41]

A new series of clubbed thiazolidinone–triazole derivatives(I) were synthesized by Mahendra R. Shiradkar et al. [42] The compounds were evaluated for their anticonvulsant activity in two animal models of seizures.



(I)

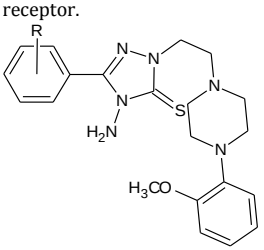
Rossi Carla [43] was investigated 1,2,4-triazoles having antigestative immunosuppressant and antitumor activity. Michael et al. [44] have reported triazoles as potential antibacterial agents. H. Mikali et al. [45] have documented triazoles as antimicrobial agents. Subdtituted 1,2,4-triazole have been reported for their pharmacological activity by Bahittin Kahveci et al. [46] and antifungal activity [47]. Liu. Chanjian et al. [48] have investigated triazoles (II) as IMPDH inhibitors.

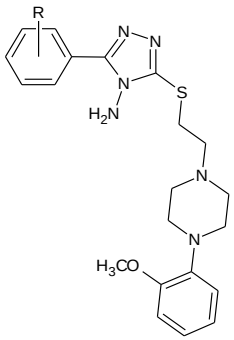


N^3-[3-methoxy-4-(1,3-oxazol-5-yl)phenyl]-1-(pyridin-2-yl)-1*H*-1,2,4-triazole-3,5-diamine

(II)

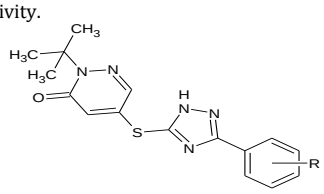
A series of 4-amino-5-(substituted phenyl) [1,2,4]triazoles(III) and (IV) were synthesized by Loredana Salerno et al. [49] with the aim of to obtaining new selective 5-HT1A ligands. All New compounds were tested in radioligand binding experiments, from many of them showed a preferential affinity for the 5 - HT1A receptor.



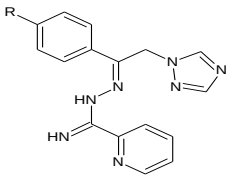


(III) & (IV)

Mari Makoto et al. [50] have prepared water soluble triazoles as fungicides. Laddawahetty et al [51]. have synthesised triazole as selective human GABA receptor for the treatment of anxiety and enhancing cognition. Eight novel compounds like (V) were synthesized and their insecticidal activities were tested by Bing Chai and co-workers [52]. The newly designed substituted triazole derivatives (VI) were synthesized by Maria Grazia Mamolo et al. [53] and tested for their *in vitro* antifungal and a n t i mycobacterial activity.

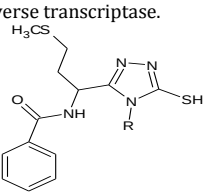


(V)

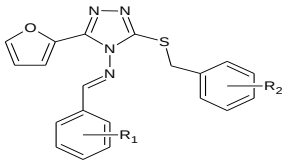


(VI)

New 1,2,4-triazole compounds (VII), containing a *D,L*-methionine moiety were synthesized by Otilia Pintilie et al [54]. All compounds exhibited promising antimicrobial activities. A series of 4amino-3-(2-furyl)-5-mercapto-1,2,4-triazole (VIII) were prepared by Jingde Wu and co worker [55]. All the synthesized substituted triazole derivatives were reported as an anti-HIV-1 agents by examined their inhibition activity of HIV-1-induced cytopathogenicity in MT-4 cells and by determined their inhibitory effect on HIV-1 reverse transcriptase.

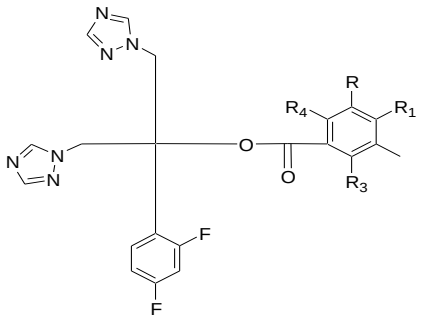


(VII)

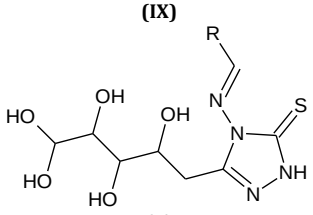


(VIII)

A variety of fluconazole derivatives were synthesized by Ruchita Ohlan and co workers [56]. The synthesized compounds (IX) were evaluated for their in vitro antifungalactivity against C.albicans and A. niger. Jian-yu Jin and co workers [57] have discovered new 1,2,4-triazole derivatives (X), which may possess significant biological activities, Plant growth-regulating activity tests of all compounds showed remarkable effects on the growth of radish and wheat.

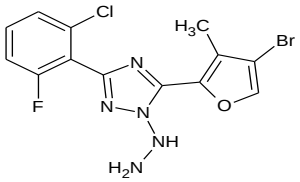


(IX)

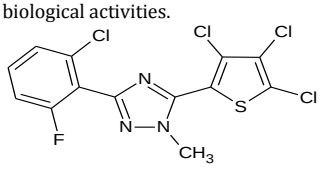


(X)

John W. Hull Jr. et al. [58] have investigated a new family of functionalized 2,6-dihaloaryl 1,2,4 triazole (XI) & (XII) insecticides featuring. Ibtehal A. Al-Juwaiser et al. [59] have been synthesized anhydronucleosides of 1,2,4-Triazoles which showed pronounce biological activities.

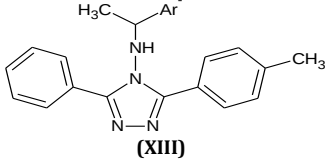


(XI)

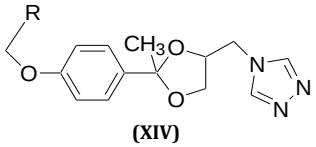


(XII)

Mevlut Serdar and co worker [60] have synthesized a new series of triazole(XIII) and the all compounds were screened for their antimicrobial and antifungal activities.Thirteen new triazoles (XV) containing 1,3-dioxolane rings were synthesized by Liang-Zhong Xu et al. [61] and their results of preliminary biological tests show that all of these compounds possess some fungicidal and plant growth regulant activities.



(XIII)



(XIV)

Giorgia pastorin et al. [62] have documented 1,2,4-triazoles as adenosine receptor antagonist and also as human A3 and A2B adenosine receptor. B.Shivarama Holla et al. [63] have screened 1,2,4 triazoles for anticancer property. Uesaka et al. [64] documented triazoles as adrenergic *a*2C receptor antagonists. Biologically active triazole were reported by P. V. Chepal et al. [65] Aoki Satosh et al. [66] have investigated triazoles as potent cyclooxygenase inhibitor.

CONCLUSION

Triazole is a unique template that is associated with several biological activities. This article highlightened research work of many researchers reported in literature for different pharmacological activities on triazole compounds synthesized. This review has presented comprehensive details of triazole analogues, potent compounds reported for particular pharmacological activity and the method or technique involved in evaluation process. More investigations must be carried out to evaluate more activities of triazole for many diseases whose treatment are difficult in the medical sciences.

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