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Synthesis of triazolo-thiadiazine and their derivatives by hydrazine hydrate, thiocarbohydrazine and thiosemicarbazide: A review

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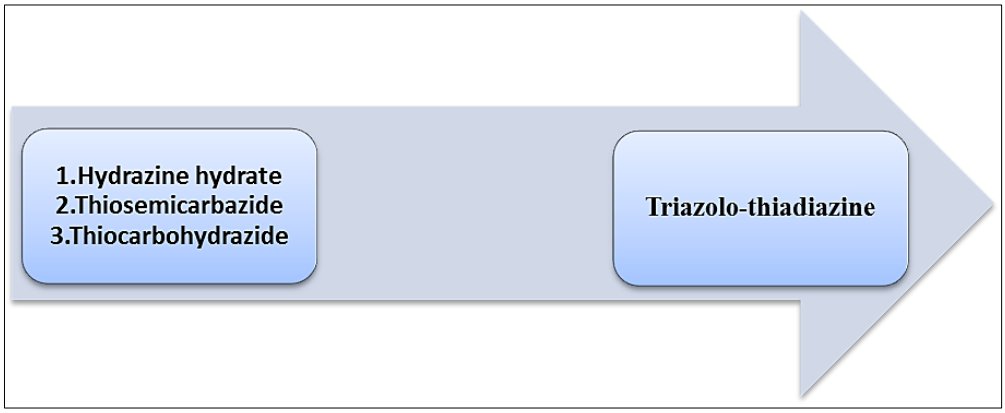
Abstract
Synthesis of triazolo-thiadiazine and their derivatives using the reaction to produce triazolo-thiadiazines by treating with hydrazine hydrate, thiocarbohydrate, and thiosemicarbazide, produced the traiazoles in good yields and the newly synthesised compounds were tested for their pharmacological activity.



Keywords: Triazolo-thaidiazine, hydrazine hydrate, thiosemicarbazide, thiocarbohydrazide

Introduction
The 1,2,4-triazole substituted with amino and mercapto groups have been reported to possess a variety of biological activities such as antibacterial [1], antifungal [2], antitubercular [3], anticancer [4], diuretic [5], and hypoglycemic [6]. The amino and mercapto groups are readymade nucleophilic centers for synthesis of fused heterocyclic systems [7]. Further, the triazole fused with thiadiazine have promising biological activities such as anti-HIV [8], CNS stimulant [9], antifungal [10], and anti-inflammatory [11] and anti-Candidal activity [12]. Further the detailed activities of triazoles are discussed in the following section.

Materials and Methods
Figure 1: Sahu *et al*. [13] described that, a series of 6-aryl-3-(3,4-dialkoxyphenyl)-7H-[1,2,4] triazolo [3,4-b] [1,3,4] thiadiazine was prepared using a one-pot process involving the condensation of 4-amino-5-(3,4-dialkoxyphenyl)-4H-[1,2,4]-triazole-3-thiol with different aromatic carboxylic acids. Antimicrobial evaluations were performed on all synthesised compounds. Some of the compounds showed antibacterial action that was promising. The results of the current study allow us to draw the conclusion that synthetic chemicals are advantageous due to their innovative structural characteristics and distinct biological activities. These compounds could be further modified to develop potential and safer antifungal agents.

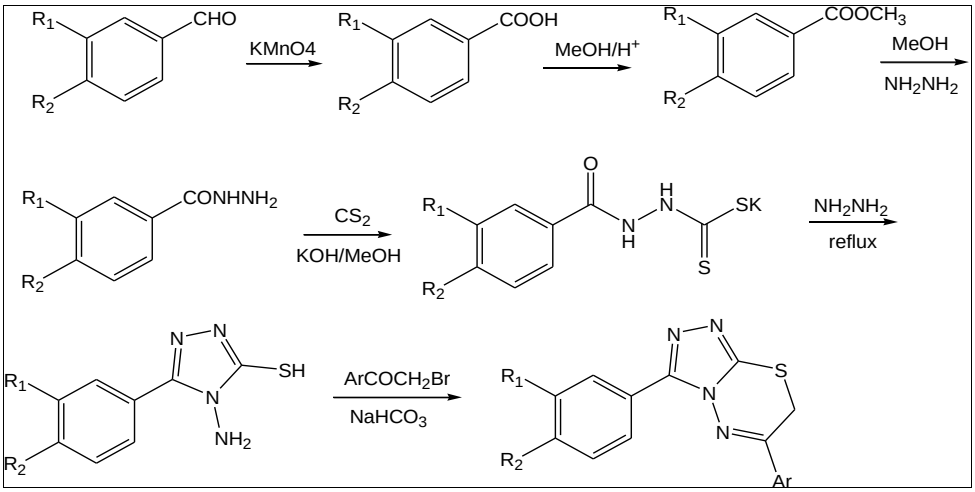


Figure 1

Figure 2: Zafer *et al*. [14] synthesised the new 1,2,4-triazole and 1,2,4-triazolo [3,4-b] [1,3,4] thiadiazine compounds as novel antibacterial agents. The 4-amino-3-mercapto-5-[(1*H*-indol-3-yl)methyl]-4*H*-1,2,4-triazole was produced *via* the reaction of 1*H*-indol-3-acetic acid with thiocarbohydrazide. The 4-arylideneamino-3-mercapto-5-[(1*H*-indol-3-yl)methyl]-4H-1,2,4-triazoles was produced *via* the reaction of triazole with arylaldehydes in ethanol. The 1-[(1*H*-indol-3-yl)methyl]-3,2-,4-triazolo [3,4-b]-6-aryl-triazole and phenacyl bromides were combined and condensed in 100% ethanol to produce [1,3,4] thiadiazines. Significant antibacterial action was shown against *Candida albicans*, *Candida glabrata*, *Bacillus cereus* (NRRL B-3711), *Salmonella typhimurium* (NRRL B-4420), *Staphylococcus aureus* (NRRL B-767), *Micrococcus luteus* (NRLL B-4375), *Proteus vulgaris* (NRRL B-123), and *Staphylococcus aureus*.

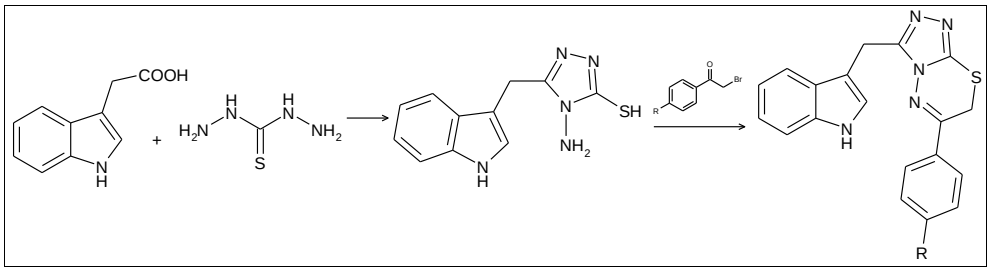


Figure 2

Figure 3: The hydroxybenzophenones were the first stage in a multistep chemical sequence that produced the triazolothiadiazine analogues. Hydroxybenzophenones produce ethyl (2-aroylaryloxy) acetates upon reaction with ethyl chloroacetate, which upon reaction with hydrazine hydrate produces 2-(2-aroylaryloxy) aceto- hydrazides, which upon intramolecular cyclization with carbon disulfide produces 5-(2-aroylaryloxy)methyl-1,3,4-oxadiazole-2-(3H) thiones, which upon three-(2-aroylaryloxy)methyl-6-phenyl-1,2,4-triazolo [3,4-b] [1,3,4] thiadiazine analogues are produced by condensation with halocarbonyls. These compounds were evaluated in contrast to fluconazole and chloramphenicol against a range of bacterial and fungal species [15].

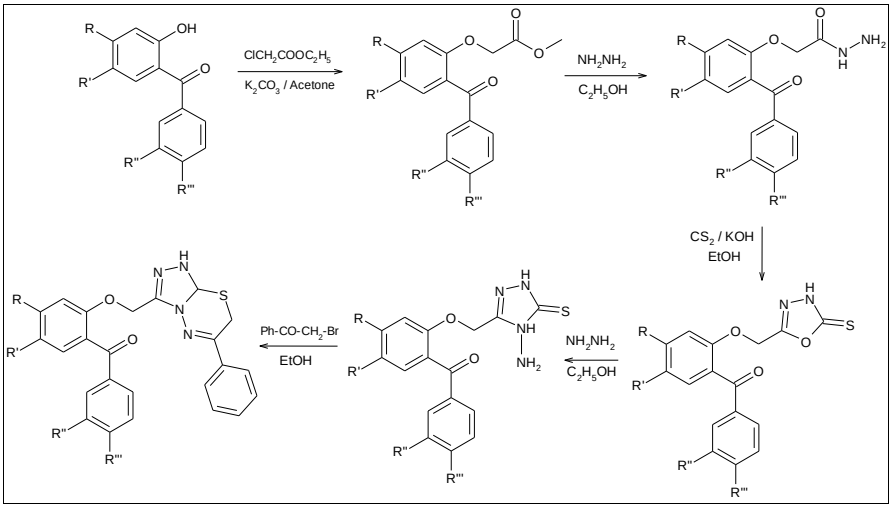


Figure 3

Figure 4: Jin *et al*. [16] synthesised a number of novel 1,2,4-triazole derivatives to find new ones that may have important biological activity. 6-aryl-3-(D-galactopentitol-1-yl) - 7,2,4-triazolo [3,4-*b*] [1,3,4] thiadiazines from 4-amino-3-(D-galactopentitol-1-yl)-5-mercapto-1,2,4-triazole, one can obtain and 4-(arylmethylidene) amino-5-(D-galacto-pentitol-1-yl)-3-mercapto-4H-1,2,4-triazoles. These compounds have extraordinary impacts on the growth of wheat and radish, according to experiments on the activity of chemicals that regulate plant growth.

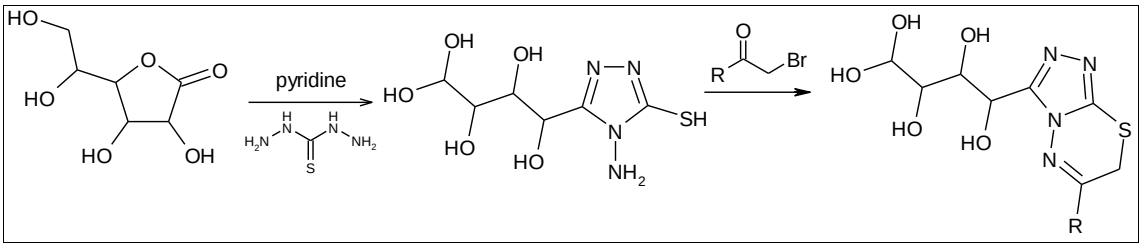


Figure 4

Figure 5: According to Jian *et al*. [17] there are several 6-aryl-3-(3-hydroxypropyl)-7H-1,2,4-triazolo [3,4-b] [1,3,4] thiadiazines were synthesised by reacting 4-amino-3-(3-hydroxypropyl)-5-mercapto-1,2,4-triazole with substituted haloacetophenones. The title compounds have extraordinary growth-inhibitory activities on the growth of wheat and radish, according to tests of their effects on controlling plant development.

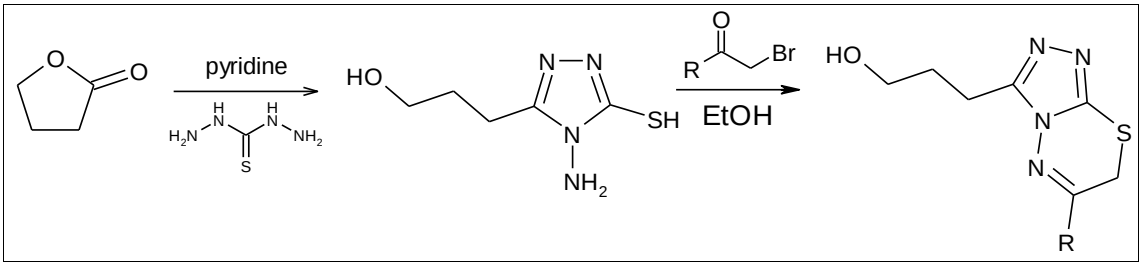


Figure 5

Figure 6: 5-aryl-2-acetyl-2-furans were prepared through the Meerwein reaction between 2-acetylfuran and arenediazonium chlorides. These compounds were brominated to produce 2-bromo-1-(5-aryl-2-furyl)-ethanones which on reaction with 4-amino-3-R-6-4*H*-5-R-1,2,4-triazole-3-thiols form triazolo [3,4-b] [1,3,4] thiadiazines [18].

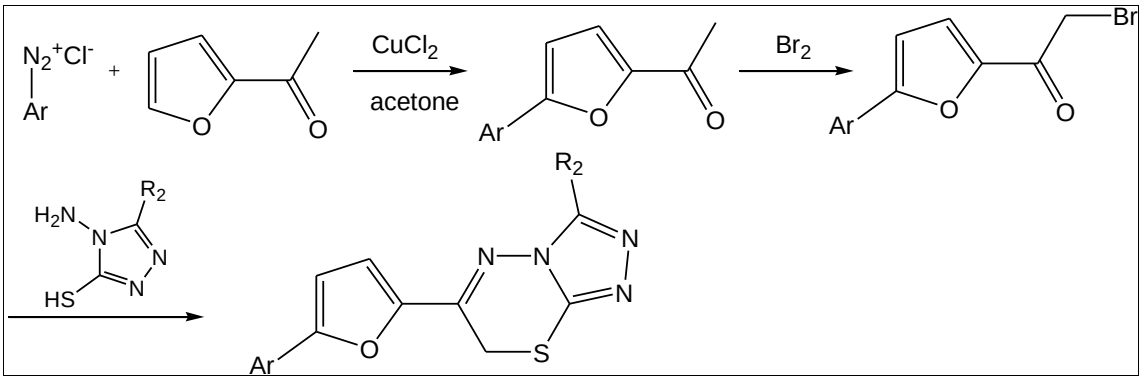


Figure 6

Figure 7: Holla *et al.* [19] reported the synthesis of a series of 1,2,4-triazolo [3,4-b]-1,3,4-thiadiazines by the condensation of 3-aryl-1-(2,4-dichloro-5-fluorophenyl)-2-bromo-propen-1-one and 4-amino-5-mercapto-3-aryloxymethyl/anilinomethyl-1,2,4-triazoles is described. These compounds were tested for their antimicrobial activities against *Escherichia coli*, *Staphyococcus aerugnosa Bacillus subtilis* and *Candida albicans*. Some of the newly synthesized compounds were also screened for their anticancer activity.

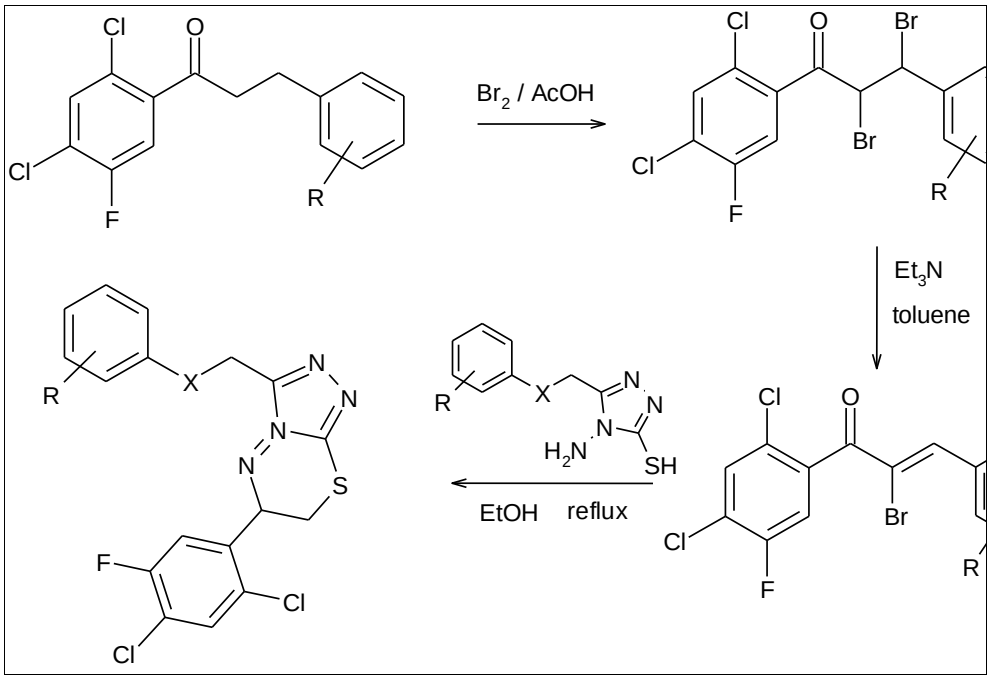


Figure 7

Figure 8: A new series of 2-phenyl-3-(6-aryl-7H-[1,2,4] triazolo [3,4-b] [1,3,4] thiadiazin-3-yl)-4H-4-chromenone 10(a-j) has been synthesized by the reaction of 3(4-amino-5-sulfanyl-4H-1,2,4-triazol-3-yl)-2-phenyl-4H-4-chromenone 7 with a variety of phenacyl bromides in ethanol under reflux.Nagaraj *et a l* [19]. All newly synthesized compounds were screened for their *in vitro* antibacterial activities against S. aureus, B. cereus and P. aeruginosa. Compounds 10d, and 10h were highly active against Bacillus cereus, compound 10a was highly active whereas compounds 10b and 10d were moderately active against Staphylococcus aureus, compounds 10f and 10h was moderately active against Pseudomonas aureginosa.

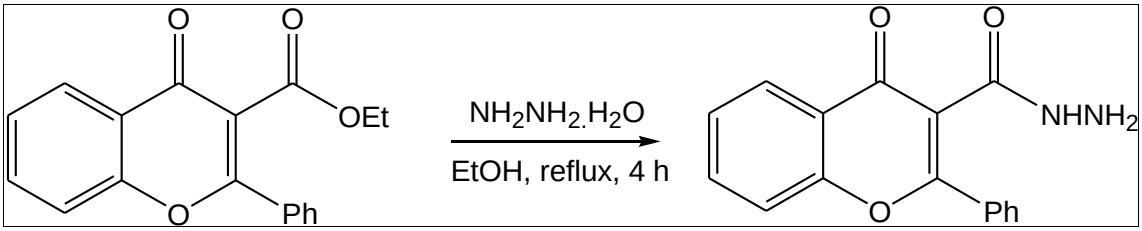


Figure 8

Conclusion

This review outlined the triazoles-thiadiazines and their derivatives served as a resource for both basic and applied research on the subject.

Acknowledgments

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