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A Review on Synthesis and Biological Activities of Substituted 1, 3, 4 Thiadiazole Derivatives

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ABSTRACT

The 1, 3, 4-thiadiazole and its derivatives are the most important compound among heterocyclic atoms in the field of research due to their wide range of pharmaceutical and industrial significance. Thiadiazole nucleus exists as a principal structural element in the combination of drug categories such as antimicrobial, anti-inflammatory, analgesic, antiepileptic, antiviral, antineoplastic, antitubercular agents. In this review article, attempted at showing the various synthetic procedure of thiadiazole derivatives and its various pharmacological activities.



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INTRODUCTION

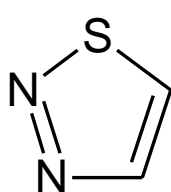
Heterocyclic compounds are the cyclic compounds possessing one or more atom(s) of other elements in company with carbon atoms in the ring system. Nitrogen, sulfur, oxygen are the most commonly used heteroatoms. They are widespread in nature and are significant to our life¹.

Heterocyclic compounds can be classified into aliphatic or aromatic. The aromatic heterocyclic compounds are the compound, which has a heteroatom in the ring and acts in a manner similar to benzene in most of their properties. Thiadiazole is one of the aromatic heterocyclic compounds. Thiadiazole is a five-membered cyclic system possessing hydrogen-binding domain, the sulfur atom, and nitrogen atoms. 1, 3, 4-thiadiazoles have become a considerable class of heterocycles and a great area for researchers because of their wide range of biological activity².

1,3,4-thiadiazole derivatives possess interesting biological activity probably discussed with them due to strong aromaticity of the ring system. The important biological activities inspired several research groups to catch out different methods for synthesis of new thiadiazoles using different synthonnes, such as thiosemicarbazides, thiocarbazides, dithiocarbamates, thioacylhydrazines, acylhydrazines³.

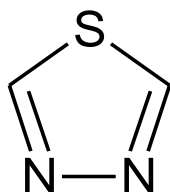
Chemistry of Thiadiazole:

Thiadiazole moiety behaves as a “hydrogen binding domain” and “two-electron donor system”. Thiadiazole acts as a bioisosteric replacement of thiazole nucleus. Therefore, it follows as third and fourth generation cephalosporin. Thiadiazole is a five-membered ring system possessing sulfur and nitrogen atom. They exist in four isomeric forms viz., 1, 2, 3-thiadiazole (1), 1, 2, 4-thiadiazole (2), 1, 2, 5-thiadiazole (3), 1, 3, 4-thiadiazole (4).



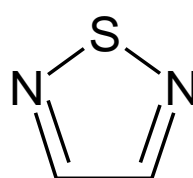
1, 2, 3-Thiadiazole

(1)



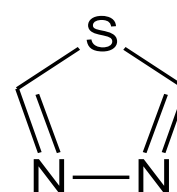
1, 2, 4-Thiadiazole

(2)



1, 2, 5-Thiadiazole

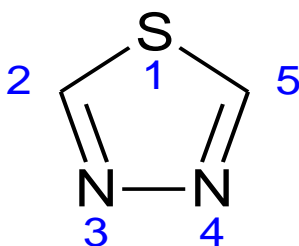
(3)



1, 3, 4- Thiadiazole

(4)

The numbering of monocyclic azole system starts with the heteroatom that is in the highest group in the periodic table and with the element of lowest atomic weight in that group. The numbering in thiadiazole starts from sulphur atom⁴.

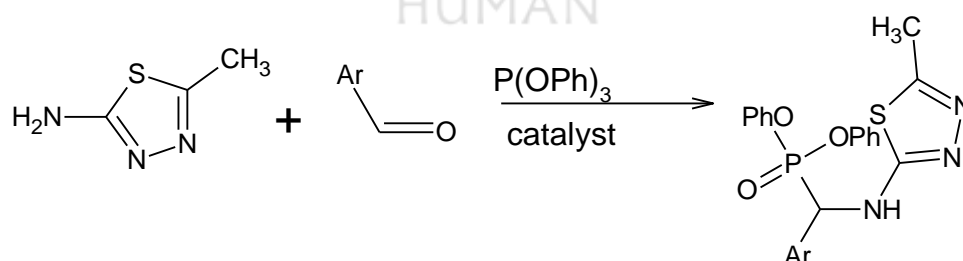


1, 3, 4-thiadiazole

(5)

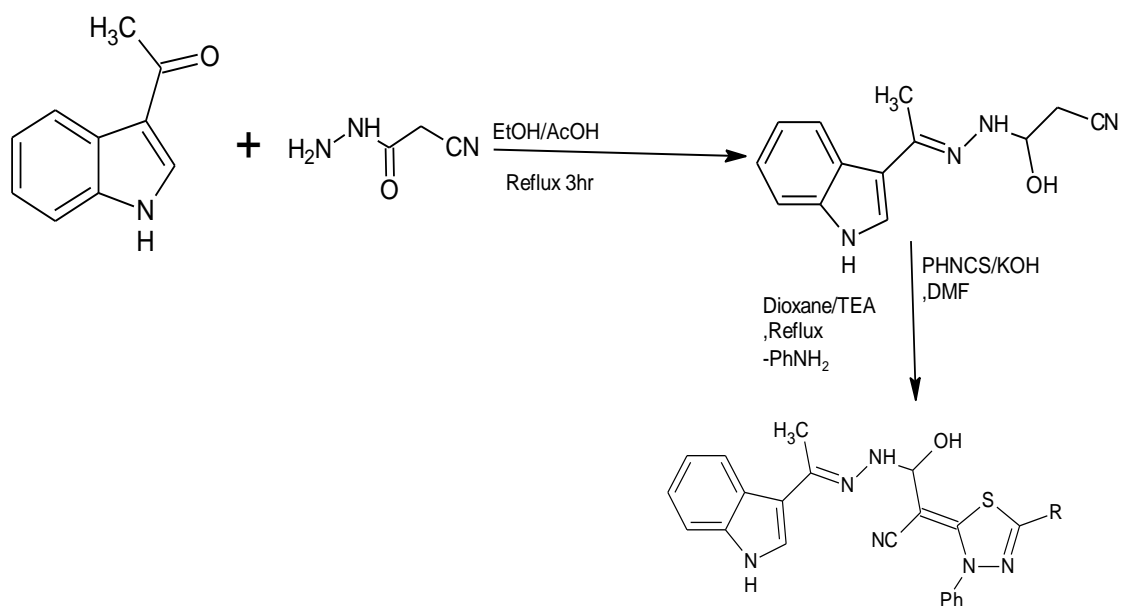
LITERATURE REVIEW

➤ Azaam M M *et al.*, (2018) An α -aminophosphonate containing thiadiazole was synthesized by reacting 2-amino-5-methyl-1,3,4-thiadiazole with various aldehydes, triphenyl phosphite and mixed valence Cu(I)/Cu(II) inorganic coordination polymer as a catalyst., characterized and their anticancer activity was carried out on human hepatocellular carcinoma and breast adenocarcinoma cell lines using MTT assay method⁵.



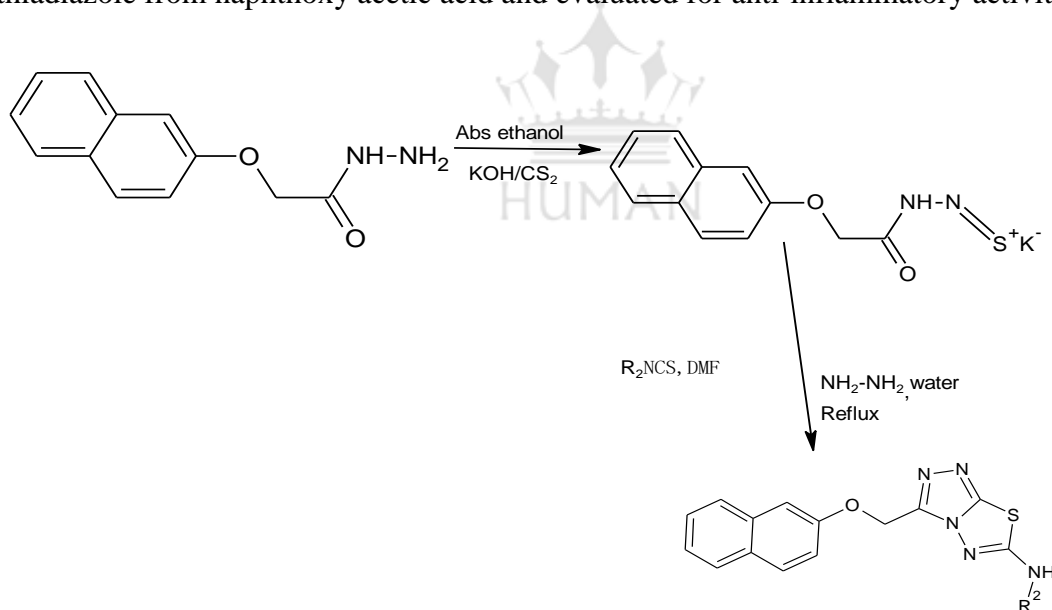
Scheme 1

➤ Abdelhamid A O *et al.*, (2016) synthesized some 1, 3, 4-thiadiazole derivatives by the reaction of hydrazonoyl halides with 3-(1H-indol-2-yl)-5-(p-tolyl)-4,5-dihydro-1H-pyrazole-1-carbothioamide, hydrazonoyl halides were reacted with N'-((1H-indol-3-yl)ethylidene)-2-cyanoacetohydrazide to form 1,3,4-thiadiazole derivatives. The compounds have been identified for their antitumor activity against the MCF-7 human breast carcinoma cell line⁶.



Scheme 2

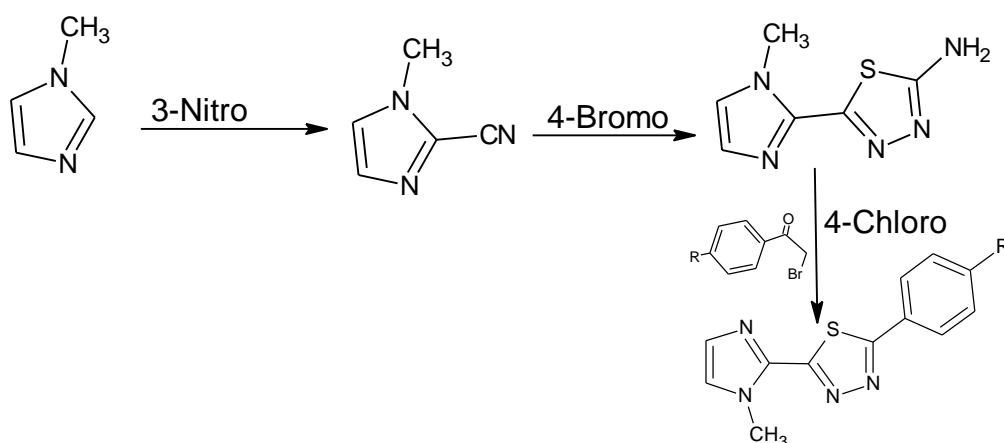
- Amir M *et al.*, (2017) Synthesized 6-substituted-1, 2, 4-triazolo [3, 4-b]-1, 3, 4-thiadiazole from naphthoxy acetic acid and evaluated for anti-inflammatory activity⁷.



R=phenyl,methyl,propyl...

Scheme 3

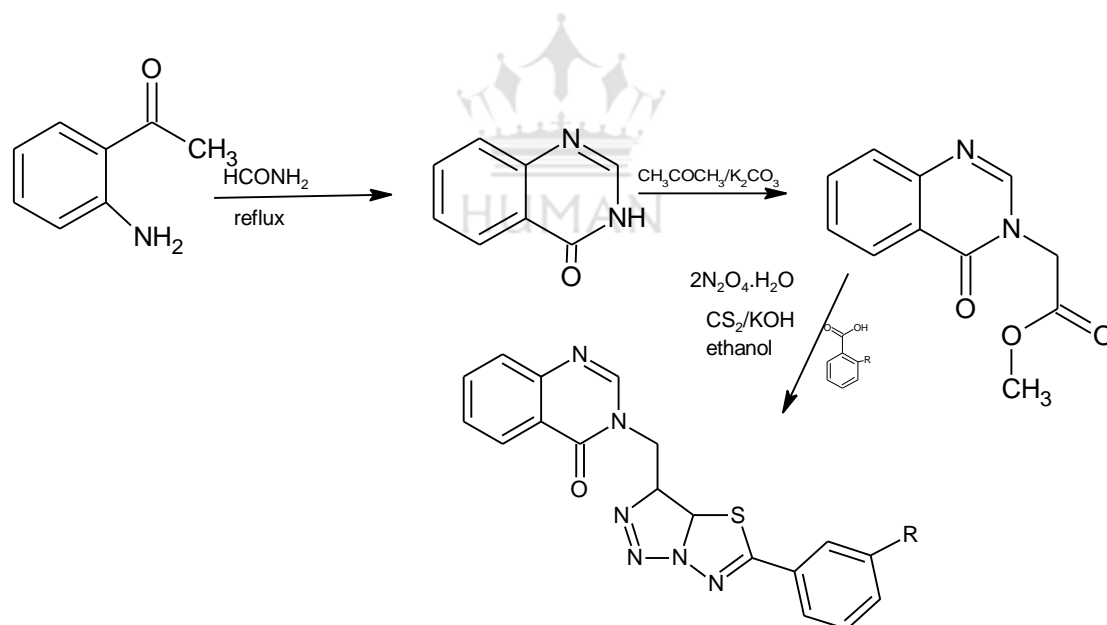
- Patel H M, Noolvi M N, Sethi N S, Gadad A K, Cameotra S S *et al.*,(2017) Synthesized imidazo [2, 1-b][1, 3, 4] thiadiazole derivatives and evaluated for its antitubercular activity⁸.



R=methyl,ethyl,phenyl

Scheme 4

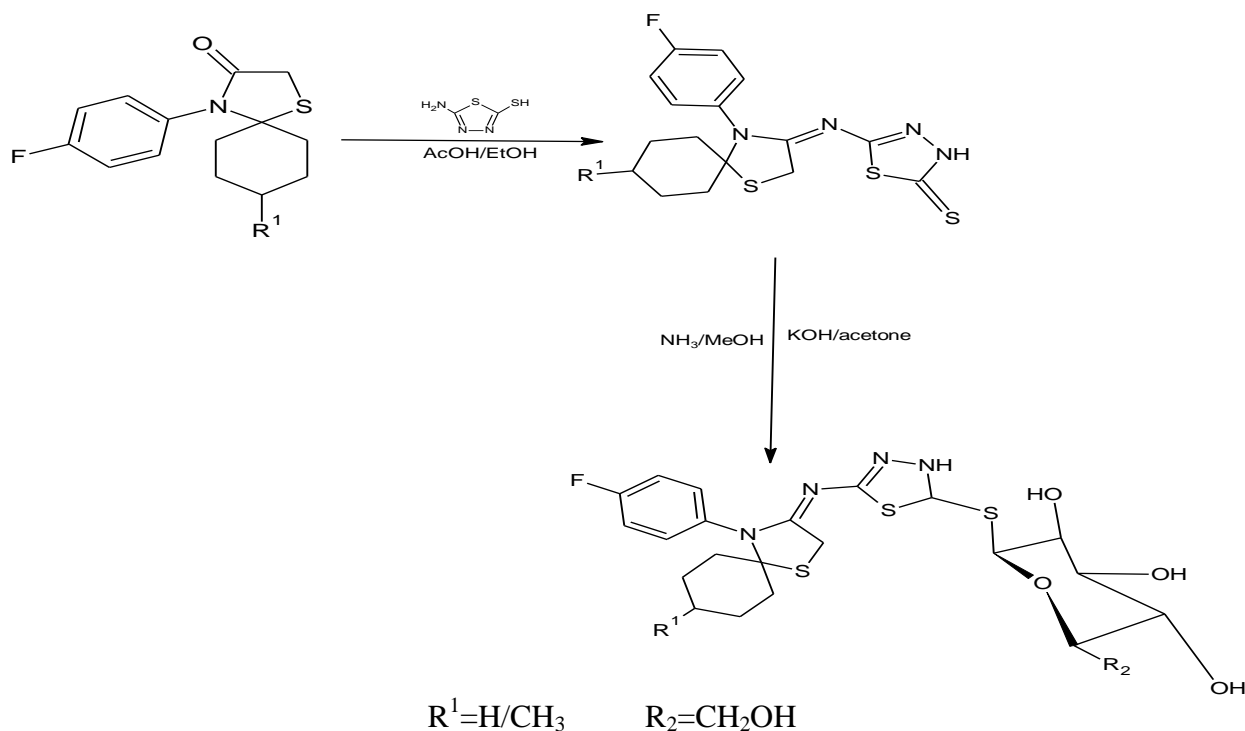
➤ Lv X, Yang L, Fan Z, Bao X *et al.*, (2017) Synthesized quinazolin-4 (3H)-one derivatives containing a 1, 2, 4-triazolo [3, 4-b][1, 3, 4] thiadiazole moiety and evaluated its antimicrobial activities⁹.



R=Phenyl, methoxy

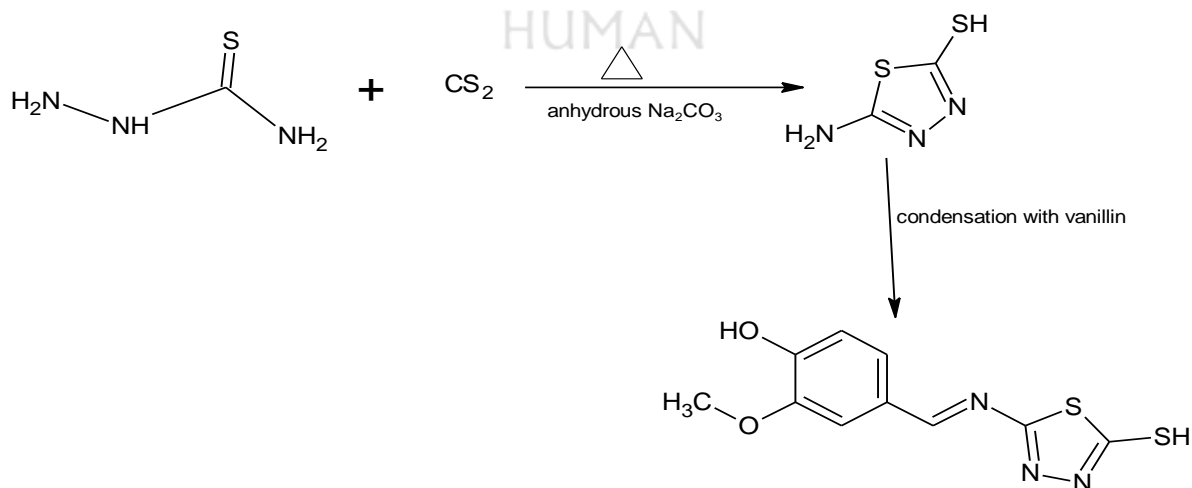
Scheme 5

➤ Ffefel E M, El-Sayed W A, Mohamed A M, El-Sofany W I, Awad H M *et al.*, (2017) Synthesized new 1-thia-4-azaspiro [4.5] decane, derived thiazolopyrimidine and 1, 3, 4-thiadiazole thioglycosides. And evaluated their anticancer activity¹⁰.



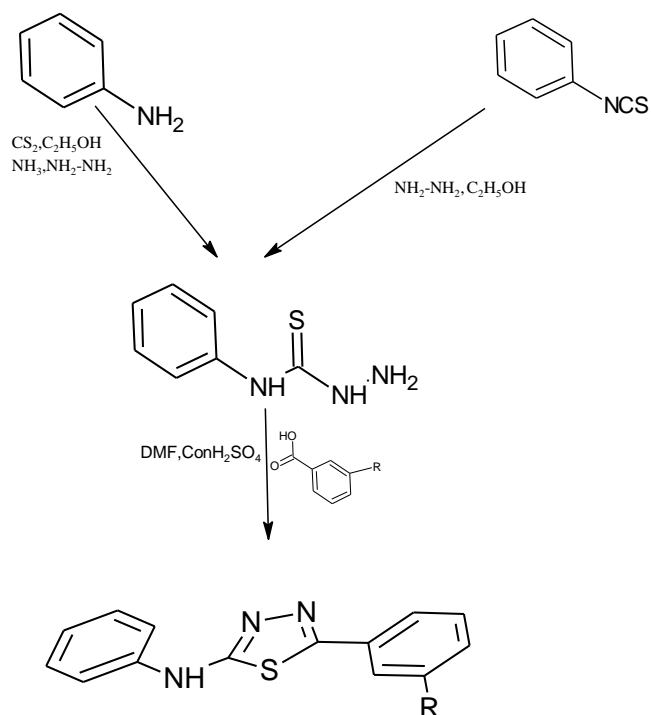
Scheme 6

- Ameen H A, Qasir A J *et al.*, (2017) Synthesized 2-amino-5-mercapto-1, 3, 4-thiadiazole derivatives and evaluated for its antimicrobial activity¹¹.



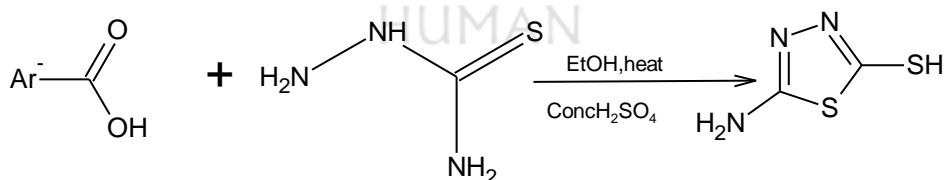
Scheme 7

- Kumari R, Sharma B B, Dubey V *et al.*, (2017) synthesized 1, 3,4-thiadiazole derivatives and evaluated for its anti-inflammatory activities¹².



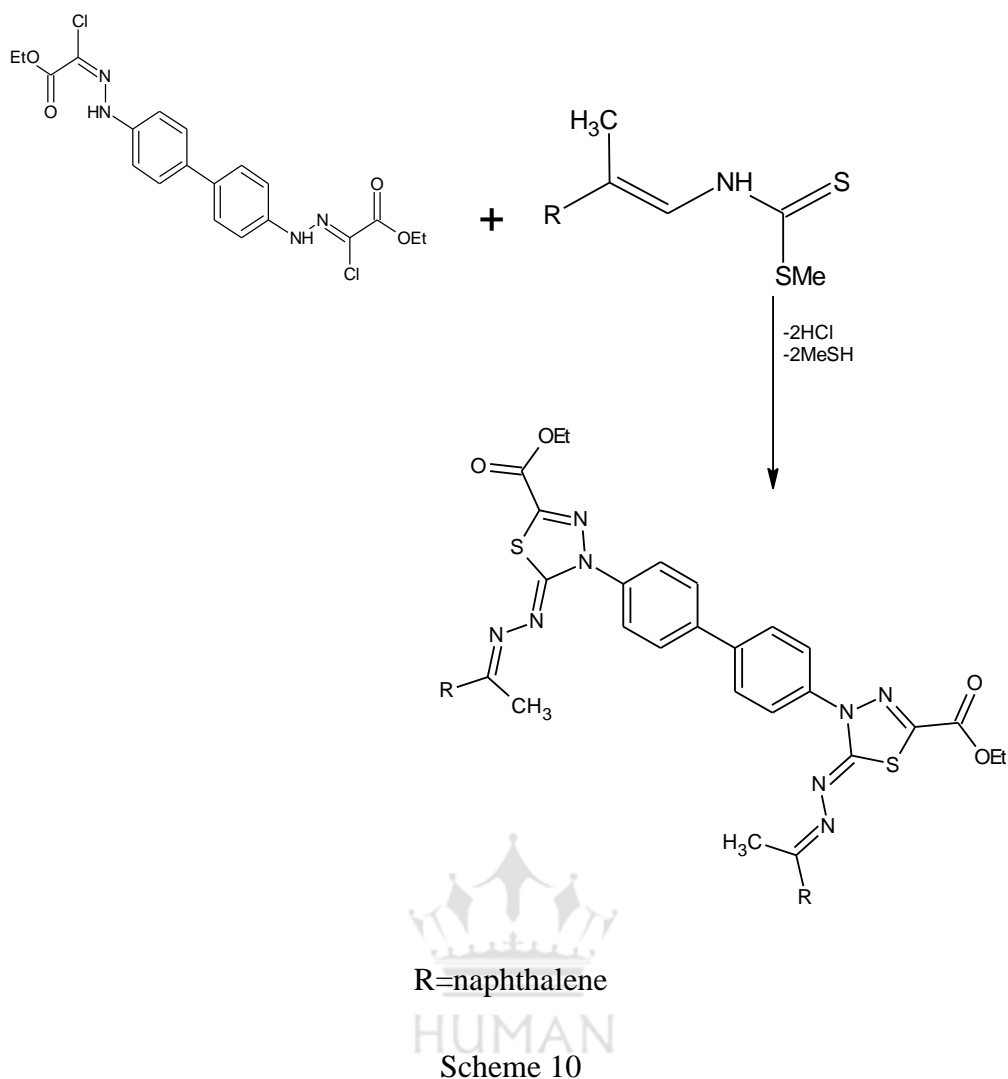
Scheme 8

- Kothawade P, Bhalerao R, Kulkarni G *et al.*, (2017) synthesized 1, 3, 4- thiadiazole derivatives and evaluated for its antidiabetic and antioxidant activity¹³.

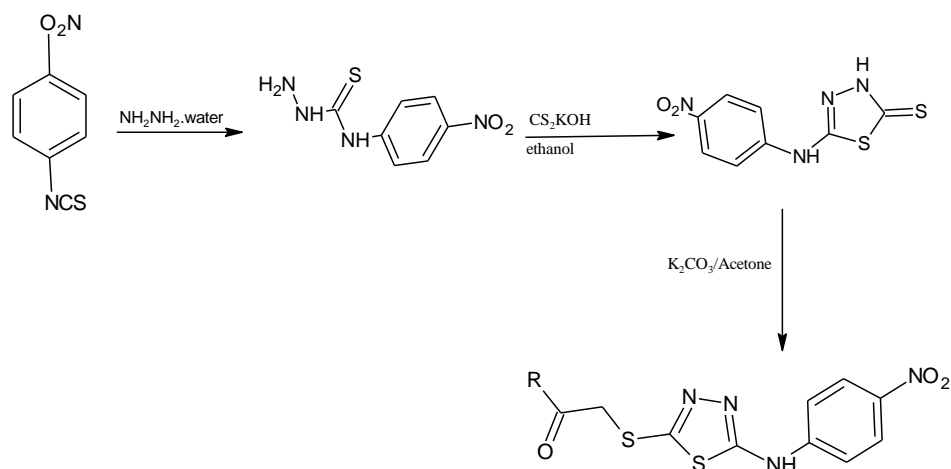


Scheme 9

- Gomha S M, Kheder N A, Abdelhamid A O, Mabkhot Y N *et al.*,(2016) synthesized bis (1, 3, 4-thiadiazole) derivatives and evaluated for its anticancer activity¹⁴.

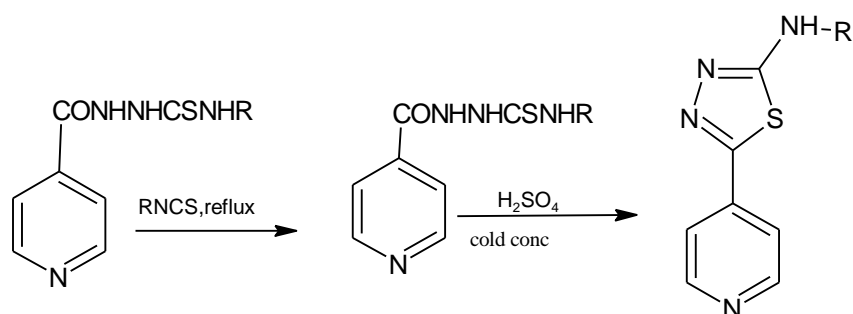


- Altıntop M D, Can Ö D, Demir Özkay Ü, Kaplancıklı Z A *et al.*, (2016) Synthesized new 1, 3, 4-thiadiazole derivatives and evaluated for its antinociceptive agents¹⁵.



Scheme 11

➤ Abdo N Y, Kamel M M. *et al.*, (2015) synthesized 1, 3, 4-thiadiazole derivatives and evaluated for its anticancer activity¹⁶.



R=anisole/toluene

Scheme 12

CONCLUSION

This review article indicates the various synthetic procedures and pharmacological activities of 1, 3, 4-thiadiazole derivatives. The activities include anticancer activity, Anti-tubercular activity, Anti-diabetic activity, Antifungal activity, Anti-inflammatory activity, Antibacterial activity, Anticonvulsant activity.

Acknowledgment

I, Shadiha Saheed K, the student of M-Pharm-Pharmaceutical Chemistry at the Kerala University of Health Science like to express my thanks to Almighty for giving me power and patience to complete the review article in a successful way. I, express my sincere gratitude to my HOD Mr.Akash Marathakam who is the source of inspiration for achieving greater height in the perusal of excellence. And also the great pleasure to acknowledge my sincere gratitude to my project guide Mrs.Thushara B S for her valuable guidance during the preparation of this review article. And also thanks to my batch mates Midhula C C and Baijika P for the co-operation to this article.

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