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# FACILE SYNTHESIS OF PHARMACEUTICALLY 1,3,4-THIADIAZOLES FROM ACYL HYDRAZIDES AND NITROALKANES WITH ELEMENTAL SULFUR

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## ABSTRACT

Due to their widespread use as antifungal, anti-inflammatory, antimicrobial, antiviral, and anticancer medicines, 1, 3, 4-Thiadizoles will prominent groups of organic heterocyclic composites with considerable biological properties. Innovative 1, 3, 4-thiadizole medication attributes will constantly attracting the attention of researchers. Even though there has been a lot of study on thiadizoles, attempts will currently be made to find new heterocyclic compounds with powerful biological activity. Our research's primary objective is to design effective coupling methods for the synthesis of novel 1, 3, 4-thiadizole members that may possess medicinal potential. The synthesized compounds will then have subjected towards column chromatography for purification, and their automated assets will be examined by DFT simulations. The structural chemical individualities of the synthesized composites will be identified via characterization approaches (NMR, FTIR, and Uv-Visible analysis).

**KEYWORDS:** Pharmaceutically 1, 3, 4-Thiadiazoles, Acyl Hydrazides, Nitroalkanes, Elemental Sulfur".

## 1. INTRODUCTION

The goal of pharmaceutical research is to create molecules with therapeutic qualities, and fresh methods will continually be being explored. One such class of compounds, the 1, 3, 4-thiadiazoles, has drawn a lot of interest due to its broad range of pharmacological uses. These compounds will attractive contestants for developing novel therapies because of their inclusive array of biological activities.[1-5]

Traditionally, 1, 3, 4-thiadizole synthesis will has been a difficult and time-consuming process. Recent advances in synthetic chemistry now make a simpler and more efficient synthesis possible.[6-11] This proposal would outline a research project to develop a simpler and effective method for synthesizing pharmaceutically relevant 1, 3, 4-thiadiazoles using acyl hydrazides and nitro alkanes with elemental Sulphur.

### 1.1. Research Problem & Relevance

Despite having surprisingly low yields, 1, 3, 4-thiadiazoles will crucial drug development intermediates, but their synthesis can be laborious and time-consuming. Some of the chemicals employed in conventional approaches may be costive or even dangerous. In order to manufacture 1, 3, 4-thiadiazoles with enhanced yields from affordable, widely available, and reasonably safe starting ingredients, a more simple and effective synthetic method is needed.

## 2. Literature review

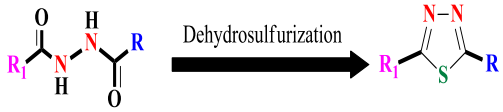
### 2.1. Modes of synthesis of 1, 3, 4-Thiadiazoles

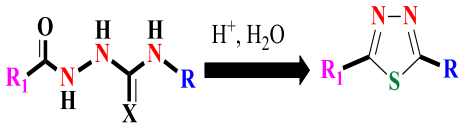
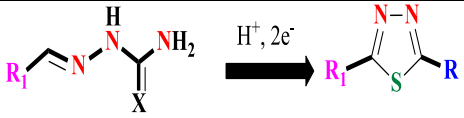
A variety of starting materials & reaction conditions will has been used in several arduous synthetic methods[2,8,12-16] for the synthesis of 1, 3, 4-thiadiazoles in the past as;

a. Sulphonyl acetic acid hydrazide.[17]
b. 1, 2-diacyl hydrazine.[18,19]
c. Acyl semi/thio-carbazide.[20]
d. semi/thio-carbazide.[21]

When it comes to production scale, safety, and environmental issues, such as complex techniques need to be addressed. There is an immediate need for a long-lasting and environmentally superior alternative to conventional chemical synthesis.

**Table: Modes of synthesis of 1, 3, 4-Thiadiazoles in literature.**

| S # | Author | Scheme of work | Major findings |
|---|---|---|---|
| 1. | Madhu et al; **(2019)** *Med Chem Research* |   | Synthesis from Sulfonyl Acetic Acid Hydrazide using $POCl_3$ |
| 2. | Kędzia et al; **(2020)** *Dyes & Pigments* |   | Synthesis from 1,2-Diacylhydrazines using *N,N′*-dicyclohexylcarbodiimide |

| | | | |
|---|---|---|---|
| 3. | Abu-Hashem et al; **(2021)***J. Het Chem* |  | Synthesis from Acyl Semi/Thiosemicarbazides using conc. Acids |
| 4. | Aksenov et al; **(2020)** *Chem Het Comp* |  | Synthesis from electronic Semi-/Thiosemicarbazides |

### 2.2. Therapeutic attributes of 1, 3, 4-Thiadizoles

The five-membered nitrogen based heterocyclic molecules, particularly 1, 3, 4- Due to their diverse biotic characteristics and potential uses in drug expansion, thiadizole has attracted a lot of research..[22-25] The Sulphur atom in 1,3,4-thiadizole contributes to better lipid dissolution, the amphoteric-ionic character of 1,3,4-thiadizole causes this family of derivatives display high tissue permeability, and these molecules will utilized as drug developers[26-28] owing to their encouraging metabolic contour and ability to establish H-bonds.[17]

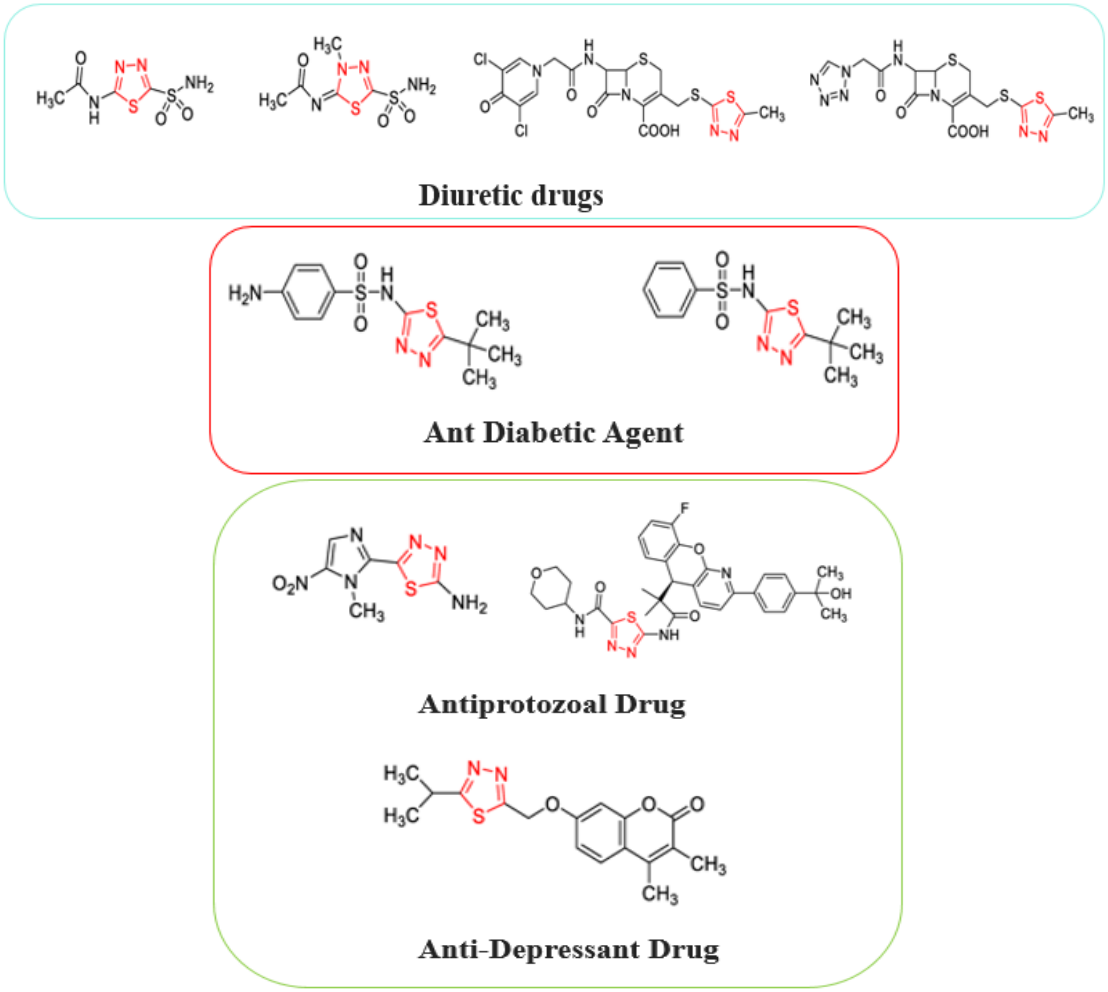



**Figure-a: Therapeutic attributes of 1, 3, 4-thiadiazoles.**

As a result, the 1, 3, 4-thiadiazole fragment may be found in a variety of therapeutically relevant medications. These include first-generation cephalosporin diuretics, the antidepressant medication Atibeprone, the ant diabetic medicines glybuthiazole and megazol, as well as glucocorticoid receptor modulators and glybuthiazole-based antiprotozoal medications (Figure-a). Aditionally, 1, 3, 4-thiadizole products are said to have antidepressant, antioxidant, antibacterial, anticancer, analgesic, and anti-inflammatory properties.[29-37]

## 3. Plan of work

### 3.1. Objectives of research

**Primary objectives**

The major goal of this research is to,

- Design and efficient way to synthesize 1,3,4-thiadiazoles using acyl hydrazides, nitro alkane and sulfuric acid.

**Secondary objectives**

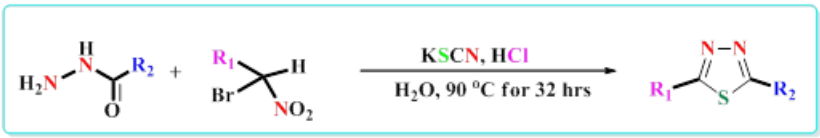
The secondary objective of this research is to,

- Test distinct hydrazides to test feasibility of the reaction procedure.
- Enhance product yield, while reducing waste by normalizing reaction conditions.
- Check quality and chemical integrity of synthesized products via stringent characterization procedures to ensure therapeutic applicability of the said compounds.

### 3.2. METHODOLOGY

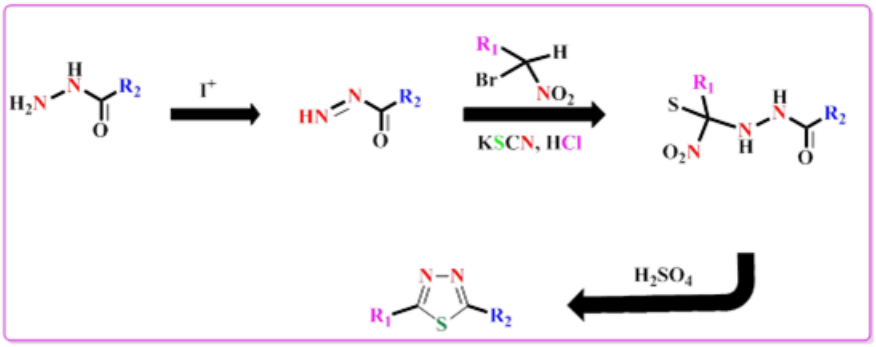
Our study will focus on efficiently synthesizing 1, 3, 4-thiadiazoles from acyl hydrazides and nitro alkanes using sulfur as the reducing agent. The optimal reaction conditions will reduce the amount of potentially dangerous chemicals while increasing the yield. In this synthesis, acyl hydrazides will be condensed with nitro alkanes before being cyclized with sulfur.

**General reaction**




**Scheme 1: General Reaction for synthesis of 1, 3, 4-thiadiazoles.**

**Mechanism**




**Scheme 2: Step-wise mechanistic approach of 1, 3, 4- thiadizoles.**

### 3.3. Reaction statistics

We will carefully adjust reaction parameters, such as temperature and reaction time, to find the ideal conditions for the synthesis. Spectroscopic and chromatographic techniques will be used to monitor the reaction course, and data will be logged at each stage. Calculations based on the information gathered will determine the kinetics, selectivity, and yield of the required 1, 3, and 4-thiadiazoles.

## 4. Anticipated Outcomes/Conclusion

Using acyl hydrazides and nitro alkanes to easily synthesize 1, 3, 4-thiadiazoles that will beneficial for pharmaceutical applications is fascinating since it might aid in the research of medicines. We can expect that this 1, 3, 4-thiadiazole synthetic process, which is simpler and more environmentally friendly, would help address some of the issues that have lately sprung up in the industry. The results of this study will have significant ramifications for the pharmaceutical sector, opening the door to the development of innovative therapeutic drugs with a variety of pharmacological characteristics. Through meticulous testing and data analysis, our study hopes to advance synthetic chemistry and pharmaceutical science. This concept is the starting point of our study, and we will hopeful about its potential uses in the synthesis of pharmaceuticals.

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