INTRODUCTION

Organic chemists are required to generate a diverse array of organic molecules using eco-friendly conditions, including short reaction times. A primary driver of synthetic organic chemistry is the development of efficient and environmentally benign synthetic protocols. A central driving force in this increasing awareness is that Green Chemistry accomplishes both economic and environmental goals, simultaneously through the use of sound, fundamental scientific principles. In the field of chemistry and chemical technology, Green Chemistry provides a set of clear guidelines for the development of new synthetic methodologies, chemical processes and the evaluation of their potential for environmental impact.

In recent years, environmentally benign synthetic methods have received considerable attention and some solvent-free protocols have been developed by many researchers. Ultrasound method is an efficient and virtually innocuous means of activation in synthetic chemistry, has been employed for decades with varied success. Since it is an upcoming and a recent field of interest, there is a great deal more to explore in ultrasonics as an important tool in order to tap its full potential for the discovery of new reactions utilizing highly energetic sound waves. The sonochemistry is turning out to be a real boon for synthetic chemistry. Sonochemistry is nothing but the chemical effects and applications of ultrasonic waves and sustainable (green) chemistry both aim to use less hazardous chemicals and solvents, reduce energy consumption and increase product selectivity.

Ultrasonic irradiation and the associated sonochemical effect is complementary technique for driving more efficient chemical reactions and yields. This high-energy input enhances mechanical effect not only in heterogeneous
processes, but it is also known to induce new reactivities leading to the formation of unexpected chemical species. Sonochemistry makes unique and is the remarkable phenomenon of **cavitation** (shown in fig 1), currently the subject of intense research which has already yielded thought-provoking results. This **critical review** is aimed at discussing the present status of **cavitational chemistry** and some of the underlying phenomena, and to highlight some recent applications and trends in organic sonochemistry, especially in combination with other sustainable technologies.

![Cavitation Diagram](image_url)

**Fig: 1 Application of cavitation in organic sonochemistry**

A comprehensive collection of ultrasound knowledge covers the most relevant aspects linked to and linking green chemistry practices to environmental sustainability through the uses and applications of ultrasound-mediated and ultrasound-assisted biological, biochemical, chemical and physical processes. Sonochemistry has some important environmental **connotations**. Thus, the following sonochemical effects can be observed in chemical reactions and processes,

1. Increase in reaction speed
2. Increase in reaction output
3. More efficient energy usage
4. Sonochemical methods for switching of reaction pathway
5. Avoidance of phase transfer catalysis
6. Use of crude or technical reagents
7. Activation of metals and solids
8. Increase in the reactivity of reagents or catalysis
9. Improvement of particle synthesis
10. Coating of nanoparticles
11. Reduces the formation of side products (waste minimization)
12. It is friendly and non-toxic

Overall this results in simplified and milder procedures accompanied by energy savings. Essentially ultrasound can often be considered to offer a cheaper ‘Green’ route. Now a day, ultrasound is widely used for improving the traditional reactions that use expensive reagents, strongly acidic conditions, long reaction times, high temperatures, unsatisfactory yields and incompatibility with other functional groups.

Nitrogen and sulphur containing heterocycles, especially five-membered rings, are of great interest as they are found in natural products and used frequently in Medicinal chemistry. Among these heterocycles, 1,3,4-oxadiazole and 1,3,4-thiadiazole motif are particular value in material science, agro chemistry and in pharmaceutical chemistry as it can be used as a bioisosteric replacement of acid, ester and amide functionalities. Due to increase hydrolytic and metabolic stability of oxadiazole ring improved pharmacokinetic and in-vitro performance is often observed.
1,3,4-Oxadiazole and 1,3,4-thiadiazole derivatives have so far been synthesized mainly because of their wide range of biological activities. These compounds play an important role in medicinal chemistry, serving as key templates central to the development of numerous important therapeutic agents. Because of these interesting features several routes to the synthesis of 1,3,4-oxadiazoles have been developed. A majority of the 1,3,4-oxadizoles have been synthesized from cyclodehydration of diacylhyrazines or diarylhydrazines by strong or mild dehydrating agents or unprotected acylhydrazones and aldehydes by oxidation with variety of oxidizing agents.

Among the new synthetic transformations, cyclocondensation reactions are the most attractive methodologies for synthesizing heterocyclic compounds and the need for improved cyclocondensation reactions are evident. In particular, oxadiazole and their derivatives have attracted increasing interest as versatile intermediates for the synthesis of biologically active compounds. So the construction of this type of molecule has received great attention.

According to the above mentioned facts and in continuation of our interest in the synthesis and bioassay of different heterocyclic compounds, we focused our attention to synthesize some new 1,3,4-oxadiazole and 1,3,4-thiadiazole derivatives via ultrasound irradiation method.

1.1. REVIEW OF LITERATURE

1.1.1. ULTRASOUND IN ORGANIC SYNTHESIS

Sonochemical synthesis is a novel technique adopted by various researchers for synthesis\(^1\text{-}\text{2}\). The first report about the effect of ultrasound to chemical reactions is from 1927, by Richards and Loomis involving rate studies on the hydrolysis of
dimethyl sulfate and the iodine “clock” reaction (the reduction of potassium iodate by sulfurous acid)\(^3\).

In 1938, Porter and Young reported that ultrasound increased the rate of the Curtius rearrangement\(^4\). In 1950, Renaud prepared an organometallic compound using ultrasound\(^5\). Since 1982 when Han and Boudjouk (Ph.D from UW-Madison, 1971) significantly increased the yields and rates of Reformatsky reactions\(^6-7\), ultrasound has been investigated intensively in organic synthesis.

The use of ultrasound irradiation technique for activating various reactions is well documented in the literature such as synthesis of azoles and diazones\(^8\), oxidation of substrates such as hydroquinones\(^9\), conversion of nitro compounds to carbamates\(^10\), Pinacol coupling\(^11\), Ullmann condensation\(^12\), Suzuki cross coupling\(^12\) and Hantzsch condensation\(^13\). Moreover, ionic liquids with the acidic counter ions are also found to be an efficient medium in synthetic chemistry\(^14-15\). To date, many valuable organic compounds have been synthesized under ultrasound irradiation without need to potent conditions like the traditional methods\(^16-20\).

Ultrasonic irradiation accelerates the reactivity million fold and many synthetically useful reactions were successfully accomplished as compared to conventional conditions. As compared to conventional conditions, viz. strong base and long reaction time, the ultrasonic irradiation procedure is milder and more conventional leading to higher yields in shorter reaction time\(^21\).

In this chapter we have shown, several convenient ultrasound-promoted synthetic methodologies have been established for the preparation of the title class of compounds\(^22-31\). The main advantages of the use of ultrasound in organic synthesis are evident when compared with classical methodologies i.e., a reduction in the reaction
times and an improvement in yields. Most of the papers covered by this review employed simple ultrasonic cleaning baths as energy sources. Hence, the purpose of this review is to synthesize 1,3,4-oxadiazole and 1,3,4-thiadiazole derivatives via Ultrasonic irradiation. Oxadiazoles\textsuperscript{32-33} and thiadiazoles\textsuperscript{34-36} are cyclic compounds containing one oxygen or one sulphur with two nitrogen atoms in a five membered ring respectively.

1.1.2. 1,3,4-OXADIAZOLE AND THIADIAZOLE DERIVATIVES

1,3,4-Oxadiazole and thiadiazole are important classes of heterocyclic chemistry due to the broad range of new theraptics they possess, which will be discussed in the following sections.

1.1.2.1. 1,3,4-Oxadiazole derivatives

The Moussebios et. al.,\textsuperscript{37} was reported the first of four possible isomeric unsubstituted oxadiazoles (1-4). Who made the thermally unstable 1,2,4-oxadiazole (4). Recently, Olofson et. al.,\textsuperscript{38} prepared the thermally stable 1,2,5-oxadiazole parent nucleus (3). Anisworth\textsuperscript{39} recorded the preparation of the thermally stable 1,3,4-oxadiazole (1), the only isomer not containing an oxygen-nitrogen bond. The sequence of these atoms may be different as follows:

![Diagram of oxadiazole isomers](image-url)

The four possible isomeric unsubstituted oxadiazoles

Maggio and co-workers were the first to find the formation of an oxadiazole by oxidation with aqueous sodium hypobromite\textsuperscript{40-41} and iodine in sodium carbonate\textsuperscript{41}. 

6
Thereafter, the oxidative cyclization of semicarbazones was studied with several oxidizing agents, such as iodine-potassium iodide, bromine and lead tetraacetate. In contrast, oxidation of semicarbazones by heating with alcoholic ferric chloride was found long ago to give the isomeric triazolinones.

Scott and co-workers have discussed whether a 1,3,4-oxadiazole or triazolinone should be formed in oxidation of a semicarbazone with bromine in acetic acid solution. They observed that reaction led to the formation of an oxadiazole in the presence of either (or both) sodium acetate or water, but led mostly to a triazolinone and small amounts of oxadiazole in anhydrous acetic acid (scheme-1).

1,3,4-Oxadiazole is the most common out of these structures. It is thermally stable neutral aromatic molecule with resonance energy 167.4 KJ/mol. The bond length in 1,3,4-oxadiazole reflect π-electron delocalization. However, the C=N bond length are very close to that in acyclic compounds and therefore indicate some dienic character in 1,3,4-oxadiazole. All these triatomic heterocycles are of purely synthetic origin. Most 1,3,4-oxadiazole are best obtained by synthesis from acyclic...
precursors. Such reactions are mainly “one bond” or two bond cyclisation. For convenience, cyclisation of intermediate formed two reactants are classed as one bond cyclizations of intermediate can be isolated.

1. **Cyclisation with the formation of one bond**

   The only common mode of cyclisation is formation of the O-C (2) bond, usually by nucleophilic attack of the carbonyl oxygen of an amide group at the carbon atom which becomes C-2 in the 1,3,4-oxadiazole ring (scheme-2).

   ![Cyclisation with the formation of one bond](image)

   **SCHEME-2**

2. **From 1,2-diacylhydrazines and related compounds**

   The most widely applicable route to 2,5-dialkyl-5-aryl and 2,5-diaryl-1,3,4-oxadiazoles is the thermal or acid catalyzed cyclisation of 1,2-diacylhydrazines (scheme-3). The method may also be used for monosubstituted oxadiazole and esters.

   ![From 1,2-diacylhydrazines and related compounds](image)

   **SCHEME-3**

   Where,
   \[
   R^1 = \text{H, Alkyl, Aryl, Hetaryl} \quad \text{and} \quad R^2 = \text{Alkyl, Aryl, Hetaryl}
   \]

   1-Phenyl-1,2-diacylhydrazines cyclize in acetic acid in the presence of acid HX to form oxadiazolium salts (7) in scheme-4.
As 1,3,4-oxadiazoles (in structure 5) have relatively low electron density at carbon (2 & 5) and a relatively high electron density at nitrogen (3 & 4). The major reactions are nucleophilic attack at carbon, generally followed by ring cleavage and electrophillic attack at nitrogen. The ring is more stable when substituted by one or more aryl groups. 1,3,4-oxadiazoles have a wide variety of uses, in particular, as biologically active compounds in medicine and in agricultural, as dyestuff, uv absorbing and fluorescent materials, heat resistant polymer and scintillators.

1,3,4-oxadiazole have been prepared through various procedures in the past and new techniques and methodologies to prepare 1,3,4-oxadiazole derivatives are quickly growing. A brief account of the methods adopted so far for the synthesis of substituted-1,3,4-oxadiazoles is outlined below.

a) From Aldehydes

Aldehydes have been used with trichloroacetic acid hydrazide in the presence of a base yield 1,3,4-oxadiazoles\textsuperscript{48} (scheme-5).
b) From Trichloromethylarenes

Symmetrical 2,5-diaryl-1,3,4-oxadiazoles have been prepared by making use of trichloromethylarenes\textsuperscript{49} with excess of hydrazine hydrate in alcohol with 68-69 % yield (scheme-6).

c) From Acid hydrazides

Four different routes from acid hydrazides are known to lead to the formation of 1,3,4-oxadiazoles.

i. N-Acylhydrazines are known to react with ortho formic ester to yield intermediate imino derivatives, which are at correct oxidation level to cyclize directly to the respective 1,3,4-oxadiazoles\textsuperscript{50} (scheme-7).

ii. Ladva\textsuperscript{51} and his coworkers have utilized the reaction of acid hydrazides with aromatic acids in the presence of phosphoryl chloride. This lead to the formation of corresponding 2,5-disubstituted-1,3,4-oxadiazoles (scheme-8).
iii. Chloroacetic acid reacts with phenol to give phenoxyacetic acid. This acid after conversion to phenoxy acetic acid hydrazide has been cyclised in the presence of cynogen bromide to give 2-amino-5-substituted-1,3,4-oxadiazole (scheme-9).

iv. Carboxylic acid hydrazides when treated with carbon disulphide in the presence of potassium hydroxide in ethanol, yielded 5-substituted-2-mercapto-1,3,4-oxadiazoles (scheme-10).

v. Lee et. al., have reported the synthesis of 1,3,4-oxadiazoles having phenol or thiophenol group. This was achieved by the treatment of suspension of salicylic acid hydrazide in toluene with acetic anhydride in the presence of equimolar methanesulphonic acid (scheme-11).
d) From substituted thiosemicarbazides

A general method\textsuperscript{24} of synthesis of 2-substituted-5-aryl-1,3,4-oxadiazole starts with 4-substituted-1-arylthiosemicarbazides which are obtained by the reaction of arylisothiocyanates with arylhydrazines. The cyclisation is achieved by lead oxide and sodium azide in ethanol (scheme-12).

\[
\begin{align*}
\text{R} & \quad \text{C} \quad \text{N} \quad \text{N} \quad \text{C} \quad \text{H} \quad \text{N} \quad \text{R}^1 \\
\text{O} & \quad \text{S}
\end{align*}
\]

2-substituted-1-aryl thiosemicarbazides

\[
\begin{align*}
\text{PbO} & \quad \text{sodium azide} \\
\text{R} & \quad \text{C} \quad \text{N} \quad \text{N} \quad \text{C} \quad \text{H} \quad \text{N} \quad \text{R}^1 \\
\text{O} & \quad \text{S}
\end{align*}
\]

2-substituted-5-aryl-1,3,4-oxadiazole

Where
\[\text{R} = \text{Aryl} \quad ; \quad \text{R}^1 = \text{Arylamino}\]

SCHEME-12

2-Amino-5-phenyl-1,3,4-oxadiazole\textsuperscript{25} was obtained by heating 1-benzoyl-S-methylisothiosemicarbazide at 200°C for ten minutes (scheme-13).

\[
\begin{align*}
\text{C}_6\text{H}_5 & \quad \text{C} \quad \text{N} \quad \text{N} \quad \text{C} \quad \text{H} \quad \text{N} \quad \text{NH}_2 \\
\text{O} & \quad \text{S} \quad \text{CH}_3
\end{align*}
\]

200°C

\[
\begin{align*}
\text{C}_6\text{H}_5 & \quad \text{N} \quad \text{N} \quad \text{C} \quad \text{H} \quad \text{N} \quad \text{NH}_2 \\
\text{O} & \quad \text{NH}_2
\end{align*}
\]

SCHEME-13

The convenient of synthesis of 1,3,4-oxadiazoles introduced by Silberg and Cosma involves the oxidative cyclisation of thiosemicarbazide with iodine in potassium iodide solution. Using the same method, a number of 2,5-disubstituted-1,3,4-oxadiazoles have been prepared\textsuperscript{26-28} (scheme-14).
Yale and Losee\textsuperscript{29} synthesized 2-amino-5-subsituted-1,3,4-oxadiazoles from 1-acyl-3-thiosemicarbazides using Lead dioxide as the cyclising agent. Certain derivatives of 5-aryl-2-anilino-1,3,4-oxadiazoles were prepared by treating 1-aroyl-4-X-arylthiosemicarbazides with dimethyl sulphate and excess of aqueous sodium hydroxide (10%).

\textbf{e) From N,N’-diacylhydrazine}

The common synthetic approaches to oxadiazole involve cyclisation of diacylhydrazines. A variety of reaction conditions and anhydrous reagents as mentioned below, have been used to induce cyclisation of N,N’-diacylhydrazine to their respective 1,3,4-oxadiazoles. The general reaction is represented by following (scheme-15).

\textbf{i.} Iodobenzene has been found to be an excellent reagent for the oxidation of a variety of hydrazides to N,N’–diacylhydrazines which undergo readily cyclisation to yield corresponding oxadiazoles\textsuperscript{54}.

\textbf{ii.} A novel and efficient means of affecting the cyclodehydration of N,N’-diacyl hydrazines is reported by Brain and Co-workers\textsuperscript{55} by using polymer supported Burgess Reagent in combination with single mode microwave heating.
iii. Pd$^0$-catalyzed cyclization of N,N’-diacetylhydrazines is successfully done by Lutuns and his co-workers$^{56}$. 

iv. N,N’-diacetylhydrazines on reaction with bis-silyl (MeSiCl$_2$) in the presence of triflic acid catalyst have been reported$^{57}$ to yield 1,3,4-oxadiazoles.

**f) From Aryl Hydrazines**

2,5-Diaryl-1,3,4-oxadiazoles were prepared by the cyclisation of the corresponding 1,2-diarylhydrazines in presence of dehydrating agent such as acetic anhydride$^{30}$ (scheme-16).

\[
\begin{align*}
\text{R} - &- C - H - N - N - C - R^1 \\
| & | & | & | & | & \text{Acetic anhydride} \\
O & & O & & & \\
\text{1,2-diarylhydrazines} & & & & & \\
\rightarrow & & & & & \\
N & & N & & & R^1 \\
\text{2,5-diaryl-1,3,4-oxadiazole} & & & & & \\
\end{align*}
\]

Where, $R = R^1$ = Substituted Phenyl

**SCHEME-16**

The formation of substituted 1,3,4-oxadiazoles and 1,3,4-thiadiazoles was achieved by the condensation of acid hydrazides or carbothionic acid hydrazides with triethyl orthoformate has been reported$^{31}$ (scheme-17).

\[
\begin{align*}
\text{R} - &- C - X - H - N - H_2 \quad + \quad \text{R}^1 - C(OC_2H_5)_3 \\
| & | & | & | & | & \text{Triethylorthoformate} \\
\text{Acidhydrazides} & & & & & & 3 \text{EtOH} \\
\rightarrow & & & & & & \\
N & & N & & & X & R^1 \\
\text{Substituted 1,3,4-oxadiazole} & & & & & & \\
\end{align*}
\]

Where  
- $X = O \quad R = o$-methoxy Ph, p-chloro  
- $R = C_2H_4 \quad R^1 = H \quad R^1 = 4$-Pyridyl  
- $X = S \quad R = Ph \quad R^1 = H, \text{CH}_3$

From condensation reaction of acidhydrazides with triethylformate

**SCHEME-17**

2-(p-tolyl)-5-(3-pyridyl)-1,3,4-oxadiazole was obtained when 1-(p-tolyl)-2-nicotinoyl hydrazine was refluxed with phosphoryl chloride$^{32}$ (scheme-18).
Kempter et al.\textsuperscript{33} during their search for better pharmacologically active compounds synthesized various 2-amino-5-(2-thiazolyl)-1,3,4-oxadiazoles by treating thiazole-2-carboxylic acid hydrazide with cyanogens bromide (scheme-19).

\begin{center}
\includegraphics[width=\textwidth]{scheme-18.png}
\end{center}

\textbf{SCHEME-18}

\begin{center}
\includegraphics[width=\textwidth]{scheme-19.png}
\end{center}

\textbf{SCHEME-19}

\textbf{g) From semicarbazones}

2-Amino-5-phenyl-1,3,4-oxadiazole was prepared from benzaldehyde semicarbazone and sodium hypoiodide or hypobromite\textsuperscript{58} (scheme-20).

\begin{center}
\includegraphics[width=\textwidth]{scheme-20.png}
\end{center}

\textbf{SCHEME-20}

Gibson\textsuperscript{43} synthesized 2-amino-5-aryl-1,3,4-oxadiazoles by oxidative cyclisation of aldehyde semicarbazones with bromine and anhydrous sodium acetate in glacial acetic acid.
Aryldenesemicarbazones when treated with bromine an acetic acid furnished triazolone derivatives. The insoluble triazolone derivatives were filtered and the filtrate on basification gave the corresponding 1,3,4-oxadiazoles (scheme-21).

Where

- $R = \text{Ph, p-Chloro phenyl, p-Bromo phenyl, p-Tolyl, p-Methoxy phenyl}$
- $R^1 = H, \text{CH}_3$

h) From Schiff’s bases

Saikachi et. al., prepared 5-substituted-2-(2-furyl)-1,3,4-oxadiazoles by oxidative cyclisation of Schiff’s bases by lead tetra acetate (scheme-22).

Where

- $R = \text{2-Furyl, 2-Thienyl and substituted phenyl}$

Anisworth et. al., reported the synthesis of monosubstituted-1,3,4-oxadiazoles, prepared by heating 1-acyl-2-ethoxymethylene hydrazine, this was prepared from alkylcarboxylic acid hydrazides and triethylorthoformate (scheme-23).
Where $R = \text{Alkyl}$

**SCHEME-23**

i) **From Heterocyclic esters**

Due to biological importance of pyridazines and 1,3,4-oxadiazoles, Bakhite and coworkers\(^6\) synthesized derivatives containing both the entities in one molecule. Treatment of Ethyl-5-hydroxyl-3,4-diphenylthieno-[2,3-c]-pyridazine--6-carboxylate with hydrazine hydrate in ethanol to carbohydrazide. Furthermore, refluxing of carbohydrazide in glacial acetic acid resulted in the formation of the corresponding 1,3,4-oxadiazole (scheme-24).

**SCHEME-24**

j) **From Di(benzotriazole-1-yl)methanimine**

Katritzky and coworkers\(^6\) synthesized 2-amino-5-phenyl-1,3,4-oxadiazole by the reaction of benzene carbohydrazide with di-(benzotriazol-1-yl)methanimine in THF (scheme-25).
k) From Trichloroacetic acid hydrazones

Kaim and coworkers\textsuperscript{48} developed novel route for the synthesis of new 1,3,4-oxadiazoles from hydrazones. This was achieved by the reaction of 4-nitrophenol trichloroacetate with hydrazine and in situ trapping with carbonyl derivative. This was followed by the treatment of these hydrazones with potassium carbonate under phase transfer conditions to new 1,3,4-oxadiazoles (scheme-26).

\[
\text{NH}_2\text{NH}_2 + \text{PhCONH}_2 \rightarrow \text{Ph} \overset{\text{O}}{\text{O}} \overset{\text{N}}{\text{N}} \text{NH}_2
\]

\text{di(1H-benzo[d][1,2,3]triazol-1-yl)methanimine}

\text{5-phenyl-1,3,4-oxadiazol-2-amine}

SCHEME-25

l) From polar salts

It has been observed the polar structure material such as acylthiocarbazinate salts gave very rapid conversion to the desired products, mercapto-1,3,4-oxadiazoles, in dipolar-aprotic, high boiling solvents (DMF/DMSO). This synthesis has been reported by Sachin Joshi and Karnik\textsuperscript{63} under microwave irradiation (scheme-27).

SCHEME-26

Reddy et al.,\textsuperscript{64} reported the synthesis of 2-(2-(methylamino)-phenyl)-5-aryl-1,3,4-oxadiazole derivatives from oxidation of N-(2-methylaminobenzoyl)-N’-benzylidenehydrazide (scheme-28).
Shaban et al., have been synthesized bis-(3-acetyl-5-aryl-2,3-dihydro-1,3,4-oxadiazol-2-yl) and bis-(3-benzoyl-5-aryl-2,3-dihydro-1,3,4-oxadiazol-2-yl) derivatives were obtained by condensative cyclization of glyoxal bis-(aryldrazones) with acetic anhydride.

Mekuskien et al., have been synthesized 5-(4,6-dimethyl-2-pyrimidinyl)-1,3,4-oxadiazole-2-thione (8) and its alkylation, aminomethylation and acylation.

Kalluraya et al., synthesized some 5-substituted-1,3,4-oxadiazole-2-hydrazones (9).

Barbery et al., synthesized 5-aryl-2-amino-1,3,4-oxadiazoles (10) and 2-(2,5-dihydroxyphenylthio)-5-aryl-1,3,4-oxadiazoles (11) by treating 2-mercapto-5-substituted-1,3,4-oxadiazoles with primary and secondary amine in absolute ethanol and p-benzoquinone in anhydrous xylene respectively (scheme-29).
Mogilaiah et al.,70 synthesized conveniently 5-Aryl-2-[p-(1,8-Naphthyridin-2-yl)phenoxyethyl]-1,3,4-oxadiazoles (12) from the reaction of a solution of 2-(p-hydroxyphenyl)-1,8-naphthyridin with ethyl chloroacetate under microwave irradiation.

\[
\text{Ar} = \text{C}_6\text{H}_5; \text{p-CH}_3\text{-C}_6\text{H}_5
\]

Pandey et al.,71 synthesized tweezers incorporating 2-mercapto-5-aryl-1,3,4-oxadiazoles (13) as heterocyclic subunits (scheme-30).
Wang et. al.,\textsuperscript{72} reported that 1,3,4-oxadiazoles can be rapidly and efficiently synthesized from variety of carboxylic acid and acid hydrazides in one simple step. The use of commercially available PS-PPh$_3$ resin combined with microwave heating delivered product 1,3,4-oxadiazoles (scheme-31) in high yields and purity.

$$
\begin{align*}
R & \text{COOH} + R' \text{C}&& \text{NH}_2 \xrightarrow{\text{CCl}_3\text{CN}, \text{CH}_3\text{CN}} R \text{N}&& \text{O} \quad \begin{array}{c}
\text{SCHEME-31}
\end{array}
\end{align*}
$$

Where
$$R \text{ & } R' = \text{Aryl or Alkyl}$$

Rivera et. al.,\textsuperscript{73} reported 5-substituted-2-amino-1,3,4-oxadiazoles via oxidative cyclisation using 1,3-dibromo-5,5-dimethyl hydantoin as the primary oxidant, in the presence of KI to give variety of oxadiazoles (scheme-32) in good yields.

$$
\begin{align*}
\text{Ar} & \text{C} && \text{HN} \text{H}&& \text{N} && \text{C} && \text{NH}_2 \xrightarrow{\text{KI}} \text{Ar} \text{N}&& \text{O} \quad \begin{array}{c}
\text{SCHEME-32}
\end{array}
\end{align*}
$$

Dabiri et. al.,\textsuperscript{74} reported unsymmetrically 2,5-disubstituted-1,3,4-oxadiazoles (scheme-33) efficiently synthesized from the cyclisation-oxidation of acyl hydrazones also, the synthesis of the acyl hydrazides and aromatic aldehydes in the presence of ceric ammonium nitrate in dichloromethane.

$$
\begin{align*}
R & \text{C} && \text{NH}_2 + R' \text{C}&& \text{H} \xrightarrow{\text{CAN}, \text{CH}_2\text{Cl}_2} R \text{N}&& \text{O} \quad \begin{array}{c}
\text{SCHEME-33}
\end{array}
\end{align*}
$$

Where
$$R = \text{Acyl} \quad R' = \text{Alkyl}$$

Nagalakshmi et. al.,\textsuperscript{75} have synthesized series of 2-(4-methoxyphenyl)-5-(substitutedphenyl)- 1,3,4-oxadiazole \textbf{(14)} derivatives.
Husain et. al.,\textsuperscript{76} have been synthesized a novel series of 2-[3-(4-bromophenyl)-propan-3-one]-5-(substitutedphenyl)-1,3,4-oxadiazoles (scheme-34) from 3-(4-bromobenzoyl)propionic acid.

Bhattacharya Joyashis et. al.,\textsuperscript{77} synthesized and characterized novel 1,3,4-oxadiazole dimmers (15) from benzoic acids.

Jayachandran et. al.,\textsuperscript{78} have been synthesized various substituted 3-amino-1-(2,4-dinitrophenyl)-5-[(5-substituted-1,3,4-oxadiazol-2-yl)-amino]-1H-pyrazole-4-carboxyamide(16) and (5E)-5-[4-(dimethyamino)-benzylidene]-3-(5-substituted-1,3,4-oxadiazol-2-yl)-2-phenyl-3,5-dihydro-4H-imidazol-4-one containing different functional groups by using different aromatic aldehydes and semicarbazide.
Take a mixture of disubstituted hydrazine carboxamide and sodium iodine / carbonate to formed 5-substituted-1,3,4-oxadiazol-2-amine (step 2), condensation of step 2 solution with N,N'-dimethylaminobenzaldehyde, benzyl glycine, dry acetic acid, anhydrous sodium acetate. The mixture has liquefied completely, ethanol was added slowly to the solution to get oxazolone\textsuperscript{78} (17).

Vijay Dabholkar et. al.,\textsuperscript{79} have been synthesized diethyladipate on reaction with hydrazine hydrate gave succinohydrazide (18) which on further treatment with carbon disulfide (19), aromatic aldehydes (20) and cynogen bromide(21) yielded 2-substituted-1,3,4-oxadiazole derivatives (scheme-35).
Benmekhbi Lotifi et. al.,\textsuperscript{80} have been synthesized some 2,5-disubstituted-1,3,4-oxadiazole by electro synthesis in methanol containing Lithium perchlorate as a supporting electrolyte (scheme-36).

Harish Rajak et. al.,\textsuperscript{81} have been synthesized 2,5-disubstituted-1,3,4-oxadiazole from semicarbazone using bromine in acetic acid.

Sanjeev Kumar et. al.,\textsuperscript{82} synthesized 2-amino-5-substituted-1,3,4-oxadiazoles through the electro oxidation. 5-Substituted-2-amino-1,3,4-oxadiazoles were synthesized directly from the semicarbazone at a platinum electrode under controlled potential electrolysis in an undivided cell assembly in acetonitrile (scheme-37).
Sharma et. al.,\textsuperscript{83} have been synthesized 1,3,4-oxadiazole derivatives by treating with acetic anhydride with Schiff’s bases under the microwave irradiation (scheme-38).

Suman Bala et. al.,\textsuperscript{84} synthesized a new series of substituted 1,3,4-oxadiazole derivatives (22) from Aryl hydrazide in phosphorous oxychloride (scheme-39).
Jean-Francis Paquin et. al.,\textsuperscript{85} described 1,3,4-oxadiazoles from 1,2-diacyl hydrazines using XtalFluor-E ([Et$_2$NSF$_2$]BF$_4$) as cyclodehydration reagent (scheme-40).

\begin{center}
\includegraphics[width=0.5\textwidth]{scheme-40.png}
\end{center}

Nirav Joshi et. al.,\textsuperscript{86} synthesized the new 1-(2,3-dichlorophenyl)-4-((5-aryl-1,3,4-oxadiazol-2-yl)methyl)piperazine (23).

Alan Aitken et. al.,\textsuperscript{87} have been described a new synthetic approaches to 1,3,4-oxadiazole and an improved method involving dehydration of N,N'-diformylhydrazine with P$_2$O$_5$ in poly phosphoric acid.

1.1.2.2. 1,3,4-Thiadiazole derivatives

The five-member heterocyclic compounds; particularly nitrogen and sulphur heterocycles; thiadiazoles have been successfully tested against several diseases and therefore received special attention in pharmaceutical and medicinal chemistry due to their diverse potential applications. Thiadiazoles and their derivatives can be considered as simple five membered heterocycles possessing one sulphur and two nitrogen atoms. The thiadiazoles exist in different isomeric forms such as
1,3,4-, 1,2,3-, 1,2,5- and 1,2,4-thiadiazoles\textsuperscript{35-36} (24-27). Among the different thiadiazoles; more information about the synthesis and applications of 1,3,4-thiadiazoles is available in the literature.

![Thiadiazole structures]

The four possible isomeric unsubstituted Thiadiazoles

Thiadiazoles continuously draws interest for development of newer drug moiety. Researchers have demonstrated a broad spectrum of biological properties of thiadiazoles in both pharmaceutical and agrochemical fields. Literature reveals that compounds having thiadiazole nucleus have wide spectrum of pharmacological activities. For instances, 1,3,4-thiadiazole derivatives have also demonstrated a broad spectrum of biological properties in both pharmaceutical and agrochemical fields. They have known to exhibit diverse biological activities such as in vitro inhibition of cyclo-oxygenase and 5-lipoxygenase activities\textsuperscript{88}.

New acylated 5-thio-beta-D-glucopyranosylimino-disusbstituted-1,3,4-thiadiazoles prepared by cycloaddition of the glycosyl iso-thiocyanate with the reactive intermediates 1-aza-2-azoniaallene hexachloroantimonates and have been tested in vitro antiviral activity against HIV-1, HIV-2, human cytomegalovirus (HMCV)\textsuperscript{89}. Apart from the pharmacological applications, thiadiazoles and their derivatives have been known to exhibit varied physical properties such as exhibit anticorrosion, liquid crystal, optical brightening and fluorescent properties\textsuperscript{90}.

The usual or classical method of synthesis of thiadiazoles involves the condensation of thiosemicarbazide with carboxylic acids or carboxylic acid chlorides
or carboxylic acid esters with cyclising or condensing agents such as phosphorus oxychloride, phosphorus pentachloride, acetic anhydride, sulphuric acid<sup>91</sup>, hydrogen peroxide<sup>92</sup> etc. While substituted 1,3,4-thiadiazoles were synthesized from acid hydrazide by their reaction with carbon disulphide in pyridine<sup>93</sup>. Substituted hydrazine was treated with phosphorous oxychloride to give the corresponding 1,3,4-thiadiazoles<sup>94</sup>.

Yadav et. al.,<sup>95</sup> have been synthesized a facile ring transformation of 5-oxazolone derivative of new 1,3,4-oxa (thia)diazole (3,2-a)pyrimidin-5-one (28).

![Chemical Structure](image)

(28)

Reddy et. al.,<sup>96</sup> synthesized 1,3,4-benzotriazepinones-1,3,4-thiadiazole and 1,3,4-oxadiazoles<sup>29</sup> by cyclization by dehydro sulphurization of 1-(-aminobenzoyl)-4-aryl-3-thiosemicarbazide.

![Chemical Structure](image)

(29)

Thiosemicarbazides reacted with tetracyanoethene in ethyl acetate with admission of air to form the 7-amino-2-organylmino-2,3-dihydro-1,3,4-thiadiazepine-5,6-dicarbonitrides (30), 7-amino-1-organylmino-3-oxopyrazolo-[1,2-c]-1,3,4-thiadiazole-5,5,6-tricarbonitriles (31), 7-amino-1-organyl-imino-pyrazolo-[1,2-c]-1,3,4-thiadiazole-3,3,5,5,6-pentacarbonitriles (32) in moderate yields. Rationales for the observed conversations are presented (scheme-41)<sup>97</sup>.
Sangpure et al.,\textsuperscript{98} synthesized some 1,3,4-oxadiazole, thiadiazole, triazole and related compounds possessing benzofuran moiety and evaluated for antibacterial and antifungal activity.

Rai and co-workers\textsuperscript{99} introduced thiourea as a new reagent for the direct conversion of 2,5-diaryl-1,3,4-oxadiazole to 2,5-diaryl-1,3,4-thiadiazole. They observed that, when the reaction of 1,3,4-oxadiazoles with thiourea was carried out at reflux temperature for 3 to 4 days, only 2 to 5\% of oxadiazoles gets converted to thiadiazoles. In order to reduce the reaction time and to increase the yield, they carried out in a sealed tube at water bath temperature for 10-15 hr and obtained the yield in 65-72\% (scheme-42).

Mulwad et al.,\textsuperscript{100} have been synthesized thiaadiazolo-1,3,4-oxadiazole derivative.

Rai and coworkers method of using thiourea as thionating agent for the transformation of oxadiazoles to thiadiazoles has been widely accepted and implemented. For instance, the unsymmetrical 1,3,4-oxadiazole (33) when treated with
two fold excess thiourea in tetrahydrofuran produced 2-(benzylsulfonylmethyl)-5-(arylsulfonylmethyl)-1,3,4-thiadiazole\textsuperscript{101} (34)(scheme-43).

![Chemical structure](image)

The reaction of 6-chloro-1,3-benzothiazol-2-yl semicarbazide, aromatic acid in phosphorus oxychloride (POCl\textsubscript{3}) produces 2-aryl-5-(6-chloro-1,3-benzothiazol-2-yl-amino-1,3,4-thiadiazoles\textsuperscript{102} (35) in good yield (scheme-44).

![Chemical structure](image)

A series of $N$-(5-phenyl)-1,3,4-thiadiazole-2-yl-benzamide derivatives synthesized from thiosemicarbazide and benzoyl chloride in phosphorous pentachloride\textsuperscript{103}.

2-Amino-5-aryl-1,3,4-thiadiazole synthesized by the reaction of thiosemicarbazide, aromatic carboxylic acid in conc. sulphuric acid. Then the compound was converted to chloroacetyl derivative by its reaction with chloroacetyl
chloride in the presence of sodium acetate in acetic acid. Finally it was transformed into $N$-(5-(4-aminophenyl)-1,3,4-thiadiazole-2-yl)-2-chloroacetamide\textsuperscript{104} (scheme-45).

\[
\text{ArCHO} + \text{NH}_2\text{NHCONH}_2 + \text{H}_2\text{SO}_4 \rightarrow \text{H}_2\text{SO}_4 \\
\text{Ar} + \text{NH}_2\text{NHCONH}_2 \rightarrow \text{Cl-CO-CH}_2\text{Cl} \\
\text{Ar} + \text{NHCH}_2\text{COR} \rightarrow \text{Ar} + \text{HN}_2\text{CH}_2\text{COCl}
\]

Scheme-45

4-(Substitutedbenzylidene)-1-(5-mercapto-1,3,4-thiadiazol-2-yl)-2-phenyl-1H-imidazol-5-(4H)-one (36) was prepared by the condensation reaction of 4-arylidene-2-phenyloxazol-5-(4H)-one and 5-amino-1,3,4-thiadiazole-2-thiol\textsuperscript{105} using this MW irradiation technique.

Cyclization of the thiosemicarbazones with acetic anhydride produced 4,5-dihydro-1,3,4-thiadiazolyl derivatives\textsuperscript{106}.

\[
\text{Ar} \text{CH} \rightarrow \text{N} \text{N} \text{O} \text{N} \text{N} \text{S} \text{SH} \\
\text{O} \text{O} \text{XY} \text{R} \text{Ar} \text{R} \text{Ar} \text{X} , \text{Y} = \text{NH} \\
\text{P} \text{S} \text{P} \text{S} \text{Ar} \text{Ar} \text{S} \text{S} \text{S} \text{S}
\]

Lawesson's Reagent

THF , 55°C

Scheme-46

5-(4-Fluoro-3-nitrophenyl)-1,3,4-thiadiazol-2-ylamine (37), on reflux with 4-methoxyphenacyl bromide in ethanol as solvent yielded 2-(4-fluoro-3-nitrophenyl)-6-(4-methoxyphenyl)-imidazo[2,1-b]-1,3,4-thiadiazole (38) (scheme-47)\textsuperscript{107}.

31
A series of $S$-[5-(phenylamino)-1,3,4-thiadiazole-2-yl]benzenecarbothioate and $S$-[5-(phenylamino)-1,3,4-thiadiazole-2-yl]ethanethioate were prepared by refluxing benzoyl chloride and acetyl chloride in presence of potassium carbonate with 5-(phenylamino)-1,3,4-thiadiazole-2-thiol and 5-(Phenylamino)-1,3,4-thiadiazole-2-thiol were prepared by cyclization of arylthiosemicarbazide with carbondisulphide$^{108}$.

A series of fluorine-containing thiadiazoles were synthesized from thiosemicarbazides by conventional method by heating mixture of thiosemicarbazide and 2N sodium hydroxide, by green synthesis such as ultrasonification and microwave irradiation. The study reports that the green synthesis yielded more percentage of yield. Other than these methods are environment friendly and economically cheaper$^{109}$. A variety of methods have been reported for the preparation of this class of compounds.

Some of these reactions were allowed to occur under thermal conditions (i.e., the reaction mixture refluxed for more than 8 hours$^{77,86,110}$ and in presence of POCl$_3$) and vigorous stirring. These reaction conditions suffer from economic and environmental concerns. Ultrasound has increasingly been used in organic synthesis.
in the last three decades compared with traditional methods; the procedure is more convenient and can be carried out in higher yields, shorter reaction time or milder conditions under ultrasound irradiation\textsuperscript{111-113}.

Continuing out investigation on the application of ultrasound in organic synthesis, we wish to report an efficient and practical procedure for the synthesis of 1,3,4-oxadiazole and thiadiazole derivatives. Ultrasound Assisted Organic Synthesis (UAOS) exploits a variety of factors such as milder and more efficient conditions, high yields of 1,3,4-oxadiazole and thiadiazole derivatives. The reaction time was drastically reduced by sonication with good yields.

With the review of literature biological significance of oxadiazole and thiadiazole derivatives are evident. Among all, the compounds bearings 1,3,4-oxadiazole and thiadiazole nucleus have been reported to have significant anti-inflammatory activity. There are several methods available in literature for the synthesis of 1,3,4-oxadiazole and thiadiazole. However, some of these methods suffer from disadvantages such as long reaction times, lower yield, requirement of severe conditions and using strong or toxic or costly reagent. Therefore, synthesis of new derivatives with greater efficacy and better yield still is desirables. Therefore, synthesis and characterization of oxadiazole and thiadiazole derivatives have been planned in the present work by using ultrasound.
1.2 MATERIALS AND METHODS

1.2.1 CHEMICALS

The chemicals and reagents required for the synthesis and evaluation of the proposed compounds have been procured from reputed chemical suppliers like Merck, Fischer Scientific and Himedia etc. and were used without further purification. Solvents are distilled wherever mentioned.\textsuperscript{114}

1.2.2 MELTING POINTS

The synthesized compounds have been characterized by melting point. Melting points were determined by open capillary method and are uncorrected.

1.2.3 SPECTROSCOPIC TECHNIQUES

1.2.3.1 IR SPECTROSCOPY

The peaks in the IR spectra give an idea about the probable structure of the compound. IR region ranges 4000-400 cm\textsuperscript{-1}. The IR spectra were recorded on SHIMADZU FT-IR spectrophotometer (Thermo Nicolet), the sample was mixed with KBr and the pellet technique was adopted to record the spectra. Various peaks obtained for different functional groups of individual compounds. The characteristic peaks confirmed 1,3,4-oxadiazole and thiadiazole derivatives.

1.2.3.2 NMR SPECTROSCOPY

PROTON NMR: The proton NMR spectrum enables us to know how many different kinds of environment are there in the molecules and also which atoms are present in neighboring groups.

The proton NMR was recorded at room temperature using TMS an internal reference. The spectra were recorded on BRUKER AMX 400 spectrometer. Samples were prepared by dissolving about 10mg of compounds in 0.5mole of CDCl\textsubscript{3} and DMSO.\textsuperscript{1}H-NMR chemical shifts were measured in ppm.
**13C-NMR SPECTRA:** 13C-NMR spectra were recorded on BRUKER AMX-400 spectrometer in proton decoupled mode samples were prepared by dissolving 50mg of the compound in 0.5ml of CDCl₃ and DMSO. All the spectral values from NMR spectra confirms the structure of 1,3,4-oxadiazole and thiadiazole derivatives.

**1.3 EXPERIMENTAL PROCEDURE**

The present investigation involves the preparation of 1,3,4-oxadiazole and thiadiazole via ultrasound irradiation method. The starting compound, 1-(substitutedbenzylidene)semicarbazide and thiosemicarbazide were prepared by the reaction of semicarbazide and thiosemicarbazide and appropriate disubstituted aromatic aldehydes in the presence of sodium acetate under ultrasound irradiation. 1-(substitutedbenzylidene)semicarbazide and thiosemicarbazide on treatment with distilled acetic anhydride under ultrasound irradiation resulted in the formation of the desired compound. The preparation of above mentioned compounds involves the following steps.

**1.3.1 STEP-IPREPARATION OF 1-(SUBSTITUTED)ALDEHYDES OF SEMICARBAZIDES AND THIOSEMICARBAZIDES**

The first step of the synthesis strategy involved preparation of 1-(substituted)aldehydes of semicarbazide with various aldehydes. Similarly 1-(substituted)aldehydes of thiosemicarbazide were prepared.

**1.3.1.1 Preparation of 1-benzylidenesemicarbazide (39)**

0.1 mole of semicarbazide hydrochloride in water and 0.1 mole of benzaldehyde in alcohol were taken, sodium acetate as catalyst, stirred few minutes with glass rod and then irradiated with ultrasound wave. The mixture was allowed to attain room temperature and then poured over ice water mixture. The solid thus
separated was filtered, dried and purified by TLC. The dried sample was further recrystallized from absolute ethanol as shining solid melts at 220°C.

\[
\text{Benzaldehyde} + \text{Semicarbazide} \rightarrow (E)-1\text{-benzylidenesemicarbazide (39)}
\]

**Scheme - 49**

### 1.3.1.2 Preparation of 1-(3-(trifluoromethyl)benzylidene)semicarbazide (40)

A solution of 0.1 mol of semicarbazide hydrochloride and 0.1 mol of sodium acetate trihydrate in 10 ml of water was added to a solution of 0.1 mol of 3-trifluoromethylbenzaldehyde in 5 ml of ethanol and stirred few minutes with glass rod and then irradiated with ultrasound wave. The mixture was allowed to attain room temperature and then poured over ice water mixture. The solid thus separated was filtered, dried and purified by TLC. The dried sample was further recrystallized from absolute ethanol as glittering solid melts at 192°C.

\[
\text{3-(trifluoromethyl)benzaldehyde} + \text{Semicarbazide} \rightarrow (E)-1\text{-}(3\text{-}(trifluoromethyl)benzylidene)semicarbazide (40)}
\]

**Scheme - 50**
1.3.1.3 Preparation of 1-(2,4-dimethoxybenzylidene)semicarbazide (41)

0.1 mole of semicarbazide hydrochloride in water and 0.1 mole of 2,4-dimethoxybenzaldehyde in alcohol was taken, sodium acetate as catalyst, stirred few minutes with glass rod and then irradiated with ultrasound wave. The mixture was allowed to attain room temperature and then poured over ice water mixture. The solid thus separated was filtered, dried and purified by TLC. The dried sample was further recrystallized from absolute ethanol as shining solid melts at 176°C.

![Scheme - 51](image)

1.3.1.4 Preparation of 1-(2,6-dichlorobenzylidene)semicarbazide (42)

A solution of 0.1 mol of semicarbazide hydrochloride and 0.1 mol of sodium acetate trihydrate in 10 ml of water was added to a solution of 0.1 mol of 2,6-dichlorobenzaldehyde in 5 ml of ethanol, stirred few minutes with glass rod and then irradiated with ultrasound wave. The mixture was allowed to attain room temperature and then poured over ice water mixture. The solid thus separated was filtered, dried and purified by TLC. The dried sample was further recrystallized from absolute ethanol as shining solid melts at 232°C.
1.3.1.5 Preparation of 1-(3,4-dimethoxybenzyldiene)semicarbazide (43)

Take 0.1 mole of semicarbazide hydrochloride in water and 0.1 mole of 3,4-dimethoxybenzaldehyde in alcohol, sodium acetate as catalyst, stirred few minutes with glass rod and then irradiated with ultrasound wave. The mixture was allowed to attain room temperature and then poured over ice water mixture. The solid thus separated was filtered, dried and purified by TLC. The dried sample was further recrystallized from absolute ethanol as shining solid melts at 178°C.
1.3.1.6 Preparation of 1-((1H-indol-3-yl)methylene)semicarbazide (44)

Take 0.1 mole of semicarbazide hydrochloride in water and 0.1 mole of Indole-3-carboxyaldehyde in alcohol, sodium acetate as catalyst, stirred few minutes with glass rod and then irradiated with ultrasound wave. The mixture was allowed to attain room temperature and then poured over ice water mixture. The solid thus separated was filtered, dried and purified by TLC. The dried sample was further recrystalized from absolute ethanol as shining solid melts at 224°C.

\[
\text{Indole-3-carboxyaldehyde} + \text{Semicarbazide} \rightarrow (E)-1-((1H-indol-3-yl)methylene)semicarbazide (44)
\]

Scheme - 54

1.3.1.7 Preparation of 1-benzylidenethiosemicarbazide (45)

0.1 mole of thiosemicarbazide in water and 0.1 mole of benzaldehyde in alcohol were taken, sodium acetate as catalyst, stirred few minutes with glass rod and then irradiated with ultrasound wave. The mixture was allowed to attain room temperature and then poured over ice water mixture. The solid thus separated was filtered, dried and purified by TLC. The dried sample was further recrystalized from absolute ethanol as shining solid melts at 200°C.
1.3.1.8 Preparation of 1-((trifluoromethyl)benzylidene)thiosemicarbazide (46)

A solution of 0.1 mol of thiosemicarbazide and 0.1 mol of sodium acetate trihydrate in 10 ml of water was added to a solution of 0.1 mol of 3-trifluoromethylbenzaldehyde in 5 ml of ethanol, then stir few minutes with glass rod and irradiated with ultrasound wave. The mixture was allowed to attain room temperature and then poured over ice water mixture. The solid thus separated was filtered, dried and purified by TLC. The dried sample was further recrystallized from absolute ethanol as shining solid melts at 218°C.
1.3.1.9 Preparation of 1-(2,4-dimethoxybenzylidene)thiosemicarbazide (47)

Take 0.1 mole of thiosemicarbazide in water and 0.1 mole of 2,4-dimethoxybenzaldehyde in alcohol, sodium acetate as catalyst, stirred few minutes with glass rod and then irradiated with ultrasound wave. The mixture was allowed to attain room temperature and then poured over ice water mixture. The solid thus separated was filtered, dried and purified by TLC. The dried sample was further recrystallized from absolute ethanol as shining solid melts at 176°C.

\[
\begin{align*}
\text{H}_3\text{CO} & \quad \text{OCH}_3 \\
\text{2,4-dimethoxybenzaldehyde} & \quad \text{H}_2\text{N} \quad \text{-} \quad \text{C} \quad \text{-} \quad \text{NH}_2 \\
\downarrow & \\
\text{H}_3\text{CO} & \quad \text{OCH}_3 \\
\text{(E)-1-(2,4-dimethoxybenzylidene)thiosemicarbazide (47)}
\end{align*}
\]

Scheme - 57

1.3.1.10 Preparation of 1-(2,3-dichlorobenzylidene)thiosemicarbazide (48)

A solution of 0.1 mol of thiosemicarbazide and 0.1 mol of sodium acetate trihydrate in 10 ml of water was added to a solution of 0.1 mol of 2,3-dichlorobenzaldehyde in 5 ml of ethanol then stirred few minutes with glass rod and irradiated with ultrasound wave. The mixture was allowed to attain room temperature and then poured over ice water mixture. The solid thus separated was filtered, dried and purified by TLC. The dried sample was further recrystallized from absolute ethanol as shining solid melts at 230°C.
1.3.1.11 Preparation of 1-(3,4-dimethoxybenzylidene)thiosemicarbazide (49)

0.1 mole of thiosemicarbazide in water and 0.1 mole of 3,4-dimethoxybenzaldehyde in alcohol was taken, sodium acetate as catalyst, stirred few minutes with glass rod and then irradiated with ultrasound wave. The mixture was allowed to attain room temperature and then poured over ice water mixture. The solid thus separated was filtered, dried and purified by TLC. The dried sample was further recrystallized from absolute ethanol as shining solid melts at 179°C.

\[
\text{Scheme - 58}
\]
1.3.1.12 Preparation of 1-(2,4-difluorobenzylidene)thiosemicarbazide (50)

0.1 mole of thiosemicarbazide in water and 0.1 mole of 2,4-difluorobenzaldehyde in alcohol was taken, sodium acetate as catalyst, stirred few minutes with glass rod and then irradiated with ultrasound wave. The mixture was allowed to attain room temperature and then poured over ice water mixture. The solid thus separated was filtered, dried and purified by TLC. The dried sample was further recrystallized from absolute ethanol as shining solid melts at 197°C.

\[
\begin{align*}
\text{2,4-difluorobenzaldehyde} & \quad + \quad \text{H}_2\text{N} - \text{NH} - \text{C} \quad \equiv \quad \text{NH}_2 \\
\text{Thiosemicarbazide} & \\
\text{(E)-1-(2,4-difluorobenzylidene)thiosemicarbazide (50)}
\end{align*}
\]

Scheme - 60

1.3.2 STEP-II PREPARATION OF AUTHENTIC 1,3,4-OXADIAZOLE AND THIADIAZOLE DERIVATIVES FROM SEMICARBAZIDE DERIVATIVES

The second step of the synthesis strategy involves preparation of 1-(5-amino-2-(substituted)phenyl-1,3,4-oxadiazol-3(2H)-yl)ethanone from authentic 1-(substituted)benzylidene semicarbazide with acetic anhydride. Similarly thiaiazole derivatives were prepared from 1-(substituted)benzylidenethiosemicarbazide.
1.3.2.1 Preparation of 1-(5-amino-2-phenyl-1,3,4-oxadiazol-3(2H)-yl)ethanone (51)

1-(5-amino-2-phenyl-1,3,4-oxadiazol-3(2H)-yl)ethanone (51) prepared from 1-benzylidene semicarbazide on treatment with excess acetic anhydride under ultrasound irradiation for 80 minutes. Reaction mixture was cooled to room temperature and poured in ice. The precipitate obtained was filtered off, washed with water and purified by recrystallization with ethanol to give 1-(5-amino-2-phenyl-1,3,4-oxadiazol-3(2H)-yl)ethanone.

(E)-1-benzylidene semicarbazide (39)

\((\text{CH}_3\text{CO})_2\text{O})\), 80 min

1-(5-amino-2-phenyl-1,3,4-oxadiazol-3(2H)-yl)ethanone (51)

1.3.2.2 Preparation of 1-(5-amino-2-(3-(trifluoromethyl)phenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (52)

1-(5-Amino-2-(3-(trifluoromethyl)phenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (52) was prepared from 1-(3-trifluoromethyl)benzylidene semicarbazide on treatment with excess acetic anhydride under ultrasound irradiation for 88 minutes. Reaction mixture was cooled to room temperature and poured in ice. The precipitate obtained was filtered off, washed with water and purified by recrystallization with ethanol to give 1-(5-amino-2-(3-(trifluoromethyl)phenyl)-1,3,4-oxadiazole-3(2H)-yl)ethanone.
1.3.2.3 Preparation of 1-(5-amino)-2-(2,4-dimethoxyphenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone(53)

This can be prepared from 1-(2,4-dimethoxybenzylidene)semicarbazide on treatment with excess acetic anhydride under ultrasound irradiation for 96 minutes. Reaction mixture was cooled to room temperature and poured in ice. The precipitate obtained was filtered off, washed with water and purified by recrystallization with ethanol to give 1-(5-amino)-2-(2,4-dimethoxyphenyl)-1,3,4-oxadiazole-3(2H)-yl)ethanone.
1.3.2.4 Preparation of 1-(5-amino)-2-(2,6-dichlorophenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone

1-(2,6-dichlorobenzylidene)semicarbazide on treatment with excess acetic anhydride under ultrasound irradiation for 100 min. Reaction mixture was cooled to room temperature and poured in ice. The precipitate obtained was filtered off, washed with water and purified by recrystallization with ethanol to give 1-(5-amino)-2-(2,6-dichlorophenyl)-1,3,4-oxadiazole-3(2H)-yl)ethanone.

![Diagram](image)

Scheme - 64

1.3.2.5 Preparation of 1-(5-amino)-2-(3,4-dimethoxyphenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone

1-(3,4-Dimethoxybenzylidene)semicarbazide on treatment with excess acetic anhydride under ultrasound irradiation for 96 minutes. Reaction mixture was cooled to room temperature and poured in ice. The precipitate obtained was filtered off, washed with water and purified by recrystallization with ethanol to give 1-(5-amino)-2-(3,4-dimethoxyphenyl)-1,3,4-oxadiazole-3(2H)-yl)ethanone.
1.3.2.6 Preparation of 1-(5-amino)-2-(1H-indol-3-yl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (56)

1-(1H-indol-3-yl)methylene)semicarbazide on treatment with excess acetic anhydride under ultrasound irradiation for 104 minutes. Reaction mixture was cooled to room temperature and poured in ice. The precipitate obtained was filtered off, washed with water and purified by recrystallization with ethanol to give 1-(5-amino)-2-(1H-indol-3-yl)-1,3,4-oxadiazole-3(2H)-yl)ethanone.
1.3.2.7 Preparation of 1-(5-(amino)-2-phenyl-1,3,4-thiadiazol-3(2H)-yl)ethanone (57)

1-Benzylidenethiosemicarbazide on treatment with excess acetic anhydride under ultrasound irradiation for 90 minutes. Reaction mixture was cooled to room temperature and poured in ice. The precipitate obtained was filtered off, washed with water and purified by recrystallization with ethanol to give 1-(5-(amino)-2-phenyl-1,3,4-thiadiazole-3(2H)-yl)ethanone.

\[
\begin{align*}
\text{(E)-1-benzylidenethiosemicarbazide (45)} & \quad \text{[(CH}_3\text{CO)}_2\text{O]} \\
& \quad \text{)))}, \quad 90 \text{ min} \\
\text{1-(5-amino-2-phenyl-1,3,4-thiadiazol-3(2H)-yl)ethanone (57)}
\end{align*}
\]

**Scheme - 67**

1.3.2.8 Preparation of 1-(5-(amino)-2-(3-trifluoromethyl)phenyl-1,3,4-thiadiazol-3(2H)-yl)ethanone (58)

1-(3-Trifluoromethyl)benzylidenethiosemicarbazide on treatment with excess acetic anhydride under ultrasound irradiation for 96 minutes. Reaction mixture was cooled to room temperature and poured in ice. The precipitate obtained was filtered off, washed with water and purified by recrystallization with ethanol to give 1-(5-(amino)-2-(3-trifluoromethyl)phenyl-1,3,4-thiadiazole-3(2H)-yl)ethanone.
1.3.2.9 Preparation of 1-(5-amino)-2-(2,4-dimethoxyphenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (59)

1-(2,4-Dimethoxybenzylidene)thiosemicarbazide on treatment with excess acetic anhydride under ultrasound irradiation for 104 minutes. Reaction mixture was cooled to room temperature and poured in ice. The precipitate obtained was filtered off, washed with water and purified by recrystallization with ethanol to give 1-(5-amino)-2-(2,4-dimethoxyphenyl)-1,3,4-thiadiazole-3(2H)-yl)ethanone.
1.3.2.10 Preparation of 1-(5-amino)-2-(2,3-dichlorophenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (60)

1-(2,3-Dichlorobenzylidene)thiosemicarbazide on treatment with excess acetic anhydride under ultrasound irradiation for 112 minutes. Reaction mixture was cooled to room temperature and poured in ice. The precipitate obtained was filtered off, washed with water and purified by recrystallization with ethanol to give 1-(5-amino)-2-(2,3-dichlorophenyl)-1,3,4-thiadiazole-3(2H)-yl)ethanone.

1.3.2.11 Preparation of 1-(5-amino)-2-(3,4-dimethoxyphenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (61)

1-(3,4-Dimethoxybenzylidene)thiosemicarbazide on treatment with excess acetic anhydride under ultrasound irradiation for 108 minutes. Reaction mixture was cooled to room temperature and poured in ice. The precipitate obtained was filtered off, washed with water and purified by recrystallization with ethanol to give 1-(5-amino)-2-(3,4-dimethoxyphenyl)-1,3,4-thiadiazole-3(2H)-yl)ethanone.
1.3.2.12 Preparation of 1-(5-amino)-2-(2,4-difluorophenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (62)

1-(2,4-Difluorobenzylidene)thiosemicarbazide on treatment with excess acetic anhydride under ultrasound irradiation for 88 minutes. Reaction mixture was cooled to room temperature and poured in ice. The precipitate obtained was filtered off, washed with water and purified by recrystallization with ethanol to give 1-(5-amino-2-(2,4-difluorophenyl)-1,3,4-thiadiazole-3(2H)-yl)ethanone.
1.4 RESULTS AND DISCUSSION

The synthesis of the 1,3,4-oxadiazole and thiadiazole derivatives were carried out according to procedures reported in the literature and the two synthetic stages were outlined by following schemes. The physical data of 1,3,4-oxadiazole and thiadiazole derivatives are given in table 1.5.1.

Table 1.4.1 Physical data of 1,3,4-oxadiazole and thiadiazole derivatives

<table>
<thead>
<tr>
<th>Sl. no</th>
<th>Compound</th>
<th>Molecular formula</th>
<th>Molecular Weight</th>
<th>Sonication time in minutes</th>
<th>Melting point (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,3,4-Oxadiazole derivatives</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>51</td>
<td>C₁₁H₁₁N₃O₂</td>
<td>205.21</td>
<td>80</td>
<td>210</td>
</tr>
<tr>
<td>2</td>
<td>52</td>
<td>C₁₁H₁₀F₃N₃O₂</td>
<td>273.21</td>
<td>88</td>
<td>188</td>
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<tr>
<td>3</td>
<td>53</td>
<td>C₁₂H₁₅N₃O₄</td>
<td>265.27</td>
<td>96</td>
<td>166</td>
</tr>
<tr>
<td>4</td>
<td>54</td>
<td>C₁₀H₉Cl₂N₃O₂</td>
<td>274.1</td>
<td>100</td>
<td>220</td>
</tr>
<tr>
<td>5</td>
<td>55</td>
<td>C₁₂H₁₅N₃O₄</td>
<td>265.27</td>
<td>96</td>
<td>172</td>
</tr>
<tr>
<td>6</td>
<td>56</td>
<td>C₁₂H₁₂N₄O₂</td>
<td>244.25</td>
<td>104</td>
<td>209</td>
</tr>
<tr>
<td>1,3,4-Thiadiazole derivatives</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>57</td>
<td>C₁₀H₁₁N₃OS</td>
<td>221.28</td>
<td>90</td>
<td>196</td>
</tr>
<tr>
<td>2</td>
<td>58</td>
<td>C₁₁H₁₀F₃N₃OS</td>
<td>289.29</td>
<td>96</td>
<td>186</td>
</tr>
<tr>
<td>3</td>
<td>59</td>
<td>C₁₂H₁₅N₃O₃S</td>
<td>281.33</td>
<td>104</td>
<td>180</td>
</tr>
<tr>
<td>4</td>
<td>60</td>
<td>C₁₀H₉Cl₂N₃OS</td>
<td>290.17</td>
<td>112</td>
<td>212</td>
</tr>
<tr>
<td>5</td>
<td>61</td>
<td>C₁₂H₁₅N₃O₃S</td>
<td>281.33</td>
<td>108</td>
<td>170</td>
</tr>
<tr>
<td>6</td>
<td>62</td>
<td>C₁₀H₉F₂N₃OS</td>
<td>257.26</td>
<td>104</td>
<td>182</td>
</tr>
</tbody>
</table>
1.4.1 SPECTRAL CHARACTERIZATION OF 1,3,4-OXADIAZOLE DERIVATIVES

1.4.1.1 General scheme for preparation of 1-(5-amino-2-phenyl-1,3,4-oxadiazol-3(2H)-yl)ethanone (51)

The following scheme was adopted for the synthesis of 1-(5-amino-2-phenyl-1,3,4-oxadiazol-3(2H)-yl)ethanone (51) from (E)-1-benzylidenesemicarbazide (39) (scheme 48).

1.4.1.1.1 Spectral data of the synthesized compound 1-benzylidenesemicarbazide(39)

Analysis of FT-IR spectrum of 1-benzylidenesemicarbazide (39) in cm\(^{-1}\)

The compound 1-benzylidenesemicarbazide (39) characterized by FT-IR spectroscopy (Table–1.4.2). The FT-IR spectrum of 1-benzylidenesemicarbazide (39) is displayed in plate 1.
Table-1.4.2 IR absorption frequencies for selected functional group of 1-benzylidenesemicarbazide (39) in cm$^{-1}$

<table>
<thead>
<tr>
<th>Vibration mode</th>
<th>Frequency in cm$^{-1}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>–C=O</td>
<td>1687</td>
</tr>
<tr>
<td>–C=N coupled with –C=O</td>
<td>1597</td>
</tr>
<tr>
<td>–N-H-</td>
<td>3456</td>
</tr>
<tr>
<td>–N-H-NH$_2$</td>
<td>3286</td>
</tr>
<tr>
<td>Aromatic –C-H</td>
<td>3066</td>
</tr>
<tr>
<td>Aliphatic –C-H</td>
<td>2931</td>
</tr>
</tbody>
</table>

The IR spectra of synthesized 1-benzylidenesemicarbazide (39) compound showed –C=N stretching band at 1597 cm$^{-1}$ and C=O absorption band at around 1687 cm$^{-1}$ respectively. Sharma et. al.,$^{115}$ reported νC=O skeletal bands at 1685 - 1642 cm$^{-1}$ range. The C=N stretching skeletal bands$^{116-118}$ are observed in the range 1650 – 1550 cm$^{-1}$. Absorption at 3066 cm$^{-1}$ and 2931 cm$^{-1}$ may due to aromatic and aliphatic –CH stretching vibrations. The NH stretching vibration$^{119}$ appears as a strong and broad band in the region 3390 ± 60 cm$^{-1}$ and symmetry NH$_2$ stretching in the region 3210 ± 60 cm$^{-1}$. In the present study, the NH stretching band appeared at 3456 cm$^{-1}$ and symmetry NH$_2$ stretching band appeared at 3286 cm$^{-1}$.
1.4.1.1.2 Spectral data of the synthesized compound 1-(5-amino-2-phenyl-1,3,4-oxadiazol-3(2H)-yl)ethanone (51)

Analysis of FT-IR spectrum of 1-(5-amino-2-phenyl-1,3,4-oxadiazole-3(2H)-yl)ethanone(51) in cm⁻¹

The compound 1-(5-amino-2-phenyl-1,3,4-oxadiazole-3(2H)-yl)ethanone (51) characterized by FT-IR spectroscopy (Table–1.4.3). The FT-IR spectrum of 1-(5-amino-2-phenyl-1,3,4-oxadiazole-3(2H)-yl)ethanone (51) is displayed in plate 2.

Table-1.4.3 IR absorption frequencies for selected functional group of 1-(5-amino-2-phenyl-1,3,4-oxadiazole-3(2H)-yl)ethanone (51) in cm⁻¹

<table>
<thead>
<tr>
<th>Vibration mode</th>
<th>Frequency in cm⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetyl –C=O</td>
<td>1687</td>
</tr>
<tr>
<td>–C=N in ring</td>
<td>1649</td>
</tr>
<tr>
<td>–NH₂</td>
<td>3286 &amp; 3458</td>
</tr>
<tr>
<td>Aromatic –C-H</td>
<td>3066</td>
</tr>
<tr>
<td>Aliphatic –C-H</td>
<td>2931</td>
</tr>
<tr>
<td>C-O-C in Oxadiazole ring (sym)</td>
<td>1091</td>
</tr>
</tbody>
</table>

IR data showed that 1-(5-amino-2-phenyl-1,3,4-oxadiazole-3(2H)-yl)ethanone (51) have strong absorption around 3066 cm⁻¹ which is evidence for the presence of aromatic –C-H bonds. Munther A.J. Mohammed Ali et. al.,¹²⁰ reported medium-weak adsorption band at 3054 – 3137 cm⁻¹ which are characteristic of aromatic stretching for 1,3,4-oxadiazole derivative. Presence of aliphatic C-H bonds was confirmed by presence of absorption band around 2931 cm⁻¹. The synthesized oxadiazole analogues clearly showed C=N stretching band around 1649 cm⁻¹ and C=O stretching band around 1687 cm⁻¹. Singh et. al.,¹²¹ reported the C-O-C absorption
band at around 1010 – 1091 cm\(^{-1}\) and 1239 - 1282 cm\(^{-1}\) indicating formation of the 1,3,4-oxadiazole ring. In the present case, the C-O-C absorption band observed at 1091 cm\(^{-1}\) and 1274 cm\(^{-1}\) which indicates ring closure of 1,3,4-oxadiazole ring. IR data confirmed the presence of specific functional groups present in the final synthesized compounds.

**Analysis of \(^1\)H-NMR spectrum of 1-(5-amino-2-phenyl-1,3,4-oxadiazol-3(2H)-yl)ethanone (51)**

The \(^1\)H-NMR chemical shift values are given in **Table-1.4.4**. The \(^1\)H-NMR spectrum has been displayed in **Plate-3**.

**Table-1.4.4 \(^1\)H-NMR chemical shift values of 1-(5-amino-2-phenyl-1,3,4-oxadiazol-3(2H)-yl)ethanone (51) in ppm**

<table>
<thead>
<tr>
<th>Signal No.</th>
<th>Signal Position, ((\delta \text{ ppm}))</th>
<th>Relative No. of Protons</th>
<th>Multiplicity</th>
<th>Inference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6.42</td>
<td>2H</td>
<td>Singlet</td>
<td>Amine protons</td>
</tr>
<tr>
<td>2</td>
<td>2.54</td>
<td>3H</td>
<td>Singlet</td>
<td>Aliphatic methyl protons</td>
</tr>
<tr>
<td>3</td>
<td>8.11</td>
<td>1H</td>
<td>singlet</td>
<td>-C-H in 1,3,4-oxadiazole ring</td>
</tr>
<tr>
<td>4</td>
<td>7.69 – 7.93</td>
<td>5H</td>
<td>Multiplet</td>
<td>Aromatic protons</td>
</tr>
</tbody>
</table>

In \(^1\)H-NMR spectrum of 1-(5-amino-2-phenyl-1,3,4-oxadiazol-3(2H)-yl)ethanone (51), signal at 6.42 ppm singlet may due to –NH\(_2\). Benmekhbi et. al.,\(^8\) reported a singlet in the region of 6.2 – 7.52 ppm for amino protons in 1,3,4-oxadiazole derivatives. Appearance of singlet at 2.54 ppm may due to aliphatic –CH\(_3\). A singlet at 8.11 ppm due to –CH present in 1,3,4-oxadiazole ring. Similar type of proton was also reported by T.C.Frank and coworkers\(^1\) at 8.09 ppm. A characteristic signal at 7.69 – 7.93 ppm represents the aromatic protons.
Analysis of $^{13}$C-NMR spectrum of 1-(5-amino-2-phenyl-1,3,4-oxadiazole-3(2H)-yl) ethanone (51)

The $^{13}$C-NMR chemical shift values of given in Table-1.4.5. The $^{13}$C-NMR spectrum is displayed in plate-4.

![Diagram of 1-(5-amino-2-phenyl-1,3,4-oxadiazole-3(2H)-yl)ethanone (51)](image)

**Table-1.4.5 $^{13}$C-NMR chemical shift values of 1-(5-amino-2-phenyl-1,3,4-oxadiazole-3(2H)-yl)ethanone (51) in ppm**

<table>
<thead>
<tr>
<th>Position</th>
<th>Chemical shift values, δ in ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbonyl carbon at C-1</td>
<td>170.37</td>
</tr>
<tr>
<td>Methyl proton at C-2</td>
<td>20.77</td>
</tr>
<tr>
<td>C-4</td>
<td>59.77</td>
</tr>
<tr>
<td>C-7</td>
<td>156.67</td>
</tr>
<tr>
<td>Aromatic carbons C-8 to C-13</td>
<td>122.68 – 137.53</td>
</tr>
</tbody>
</table>

In the $^{13}$C-NMR spectra, signals characteristic of C=O around 170.37 ppm and alkyl around 20.77 ppm, as well as the oxadiazole ring signal (C-4) around 59.77 ppm and (C-7) about 156.67 ppm were observed, thus confirming the formation of the 1,3,4-oxadiazole ring. Aromatic carbon signal appeared at 122.68 - 137.53 ppm.
1.4.1.2 General scheme for preparation of 1-(5-amino-2-(3-(trifluoromethyl)-phenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (52)

The following scheme was adopted for the synthesis of 1-(5-amino-2-(3-(trifluoromethyl)phenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (52) from (E)-1-(3-(trifluoromethyl)benzylidene)semicarbazide (40).

\[
\begin{align*}
\text{3-(trifluoromethyl)benzaldehyde} & + \text{H}_{2}\text{N}-\text{NH}-\text{C}-\text{NH}_2 \\
\text{Semicarbazide} & \\
\text{7 min} & \\
\text{(E)-1-(3-(trifluoromethyl)benzylidene)semicarbazide (40)} & \\
\text{88 min} & \\
\text{1-(5-amino-2-(3-(trifluoromethyl)phenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (52)} & \\
\end{align*}
\]

1.4.1.2.1 Spectral data of the synthesized compound (E)-1-(3-(trifluoromethyl)-benzylidene)semicarbazide (40)

Analysis of FT-IR spectrum of 1-(3-trifluoromethyl)benzylidene-semicarbazide (40) in cm\(^{-1}\)

The compound 1-(3-trifluoromethyl)benzylidenesemicarbazide (40) characterized by FT-IR spectroscopy (Table–1.4.6). The FT-IR spectrum of (E)-1-(3-(trifluoromethyl)benzylidene)semicarbazide (40) is displayed in plate 5.
Table-1.4.6 IR absorption frequencies for selected functional group of 1-(3-trifluoromethyl)benzylidenesemicarbazide (40) in cm\(^{-1}\)

<table>
<thead>
<tr>
<th>Vibration mode</th>
<th>Frequency in cm(^{-1})</th>
</tr>
</thead>
<tbody>
<tr>
<td>–C=O</td>
<td>1695</td>
</tr>
<tr>
<td>–C=N coupled with –C=O</td>
<td>1600</td>
</tr>
<tr>
<td>–N-H-</td>
<td>3464</td>
</tr>
<tr>
<td>–N-H-NH(_2)</td>
<td>3290</td>
</tr>
<tr>
<td>Aromatic –C-H</td>
<td>3068</td>
</tr>
<tr>
<td>Aliphatic –C-H</td>
<td>2935</td>
</tr>
<tr>
<td>–C-F</td>
<td>1327</td>
</tr>
</tbody>
</table>

IR spectral data of 1-(3-trifluoromethyl)benzylidenesemicarbazide (40) revealed bands at 3068 cm\(^{-1}\) (Aromatic –C-H str), 2935 cm\(^{-1}\) (Aliphatic –C-H str), 3464 cm\(^{-1}\) (–N-H str), 3290 cm\(^{-1}\) (–NH\(_2\) str), 1600 cm\(^{-1}\) (–C=N str) and 1695 cm\(^{-1}\) (–C=O str frequency).

1.4.1.2.2 Spectral data of the synthesized compound 1-(5-amino-2-(3-trifluoromethyl)phenyl-1,3,4-oxadiazol-3(2H)-yl)ethanone (52)

Analysis of FT-IR spectrum of 1-(5-amino-2-(3-trifluoromethyl)phenyl-1,3,4-oxadiazol-3(2H)-yl)ethanone (52) in cm\(^{-1}\)

The compound 1-(5-amino-2-(3-trifluoromethyl)phenyl-1,3,4-oxadiazol-3(2H)-yl)ethanone (52) characterized by FT-IR spectroscopy (Table-1.4.7).
The FT-IR spectrum of 1-(5-amino-2-(3-trifluoromethyl)phenyl-1,3,4-oxadiazole-3(2H)-yl)ethanone (52) is displayed in plate-6.

**Table-1.4.7 IR absorption frequencies for selected functional group of 1-(5-amino-2-(3-trifluoromethyl)phenyl-1,3,4-oxadiazole-3(2H)-yl) ethanone (52) in cm⁻¹**

<table>
<thead>
<tr>
<th>Vibration mode</th>
<th>Frequency in cm⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetyl –C=O</td>
<td>1693</td>
</tr>
<tr>
<td>–C=N in ring</td>
<td>1647</td>
</tr>
<tr>
<td>–NH₂</td>
<td>3464 &amp; 3290</td>
</tr>
<tr>
<td>Aromatic –C-H</td>
<td>3068</td>
</tr>
<tr>
<td>Aliphatic –C-H</td>
<td>2935</td>
</tr>
<tr>
<td>C-O-C in Oxadiazole ring (sym)</td>
<td>1076</td>
</tr>
<tr>
<td>–CF₃</td>
<td>1327</td>
</tr>
</tbody>
</table>

In the IR spectrum of 1-(5-amino-2-(3-trifluoromethyl)phenyl-1,3,4-oxadiazole-3(2H)-yl)ethanone (52), a stretching vibration observed at 3068 cm⁻¹ which indicates the presence of aromatic –C-H bonds. An aliphatic C-H bond was confirmed by presence of absorption band around 2935 cm⁻¹. The synthesized oxadiazole analogues clearly showed C=N stretching band around 1647 cm⁻¹. Broad stretching band at 3290 cm⁻¹ and a sharp band at 3464 cm⁻¹ was due to -NH while strong stretching band around 1693 cm⁻¹ was attributed to the carbonyl of acetyl group. 1076 cm⁻¹ and 1215 cm⁻¹ which could be attributed the C-O-C symmetry and asymmetry respectively, which indicates ring closure of 1,3,4-oxadiazole ring. Mohamed Amir et. al.,¹²³ reported the C-O-C symmetry at 1071 cm⁻¹ for 2-substituteddiaryl-5-(2,4,6-trichlorophenoxymethyl)-1,3,4-oxadiazole compound. IR data confirmed the presence of specific functional groups present in the final synthesized compounds.
Analysis of $^1$H-NMR spectrum of 1-(5-amino-2-(3-trifluoromethyl)phenyl-1,3,4-oxadiazole-3(2H)-yl)ethanone (52)

The $^1$H-NMR chemical shift values are given in Table-1.4.8. The $^1$H-NMR spectrum has been displayed in Plate-7.

Table-1.4.8 $^1$H-NMR chemical shift values of 1-(5-amino-2-(3-trifluoromethyl)-phenyl-1,3,4-oxadiazole-3(2H)-yl)ethanone (52) in ppm

<table>
<thead>
<tr>
<th>Signal No.</th>
<th>Signal Position, (δ ppm)</th>
<th>Relative No. of Protons</th>
<th>Multiplicity</th>
<th>Inference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6.67</td>
<td>2H</td>
<td>Singlet</td>
<td>Amine protons</td>
</tr>
<tr>
<td>2</td>
<td>2.49</td>
<td>3H</td>
<td>Singlet</td>
<td>Aliphatic methyl protons</td>
</tr>
<tr>
<td>3</td>
<td>8.14</td>
<td>1H</td>
<td>Singlet</td>
<td>-C-H in 1,3,4-oxadiazole ring</td>
</tr>
<tr>
<td>4</td>
<td>7.56 – 7.97</td>
<td>4H</td>
<td>Multiplet</td>
<td>Aromatic protons</td>
</tr>
</tbody>
</table>

In $^1$H-NMR spectrum of 1-(5-amino-2-(3-trifluoromethyl)phenyl-1,3,4-oxadiazole-3(2H)-yl)ethanone (52) showed a singlet at 6.67 ppm due to $\text{–NH}_2$, appearance of singlet at 2.49 ppm due to aliphatic $\text{–CH}_3$ protons and 8.14 ppm due to $\text{–CH}$ present in 1,3,4-oxadiazole ring. A singlet at 8.1 ppm was observed by Vijey Aanandhi and coworkers$^{124}$ for $\text{–CH}$ proton present in 1,3,4-oxadiazole ring. Other characteristic multiple signals at 7.56 – 7.97 ppm represents the aromatic protons.

Analysis of $^{13}$C-NMR spectrum of 1-(5-amino-2-(3-trifluoromethyl)phenyl-1,3,4-oxadiazole-3(2H)-yl)ethanone (52)

The $^{13}$C-NMR chemical shift values of given in Table-1.4.9. The $^{13}$C-NMR spectrum is displayed in plate-8.
Table-1.4.9 $^{13}$C-NMR chemical shift values of 1-(5-amino-2-(3-trifluoromethyl)phenyl)-1,3,4-oxadiazole-3(2H)-yl)ethanone (52) in ppm

<table>
<thead>
<tr>
<th>Position</th>
<th>Chemical shift values, δ in ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbonyl carbon at C-1</td>
<td>169.76</td>
</tr>
<tr>
<td>Methyl proton at C-2</td>
<td>21.20</td>
</tr>
<tr>
<td>C-4</td>
<td>79.95</td>
</tr>
<tr>
<td>C-7</td>
<td>155.75</td>
</tr>
<tr>
<td>Aromatic carbons C-8 to C13</td>
<td>122.56 – 138.95</td>
</tr>
</tbody>
</table>

In the $^{13}$C-NMR spectra, signals characteristic of C=O around 169.76 ppm and alkyl around 21.20 ppm, as well as the oxadiazole ring signal (C-4) around 79.95 ppm and (C-7) about 155.75 ppm were observed, thus confirming the formation of the 1,3,4-oxadiazole ring. Aromatic carbon signal appeared at 122.56 – 138.95 ppm.

1.4.1.3 General scheme for preparation for 1-(5-amino-2-(2,4-dimethoxyphenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (53)

The following scheme was adopted for the synthesis of 1-(5-amino-2-(2,4-dimethoxyphenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (53) from (E)-1-(2,4-dimethoxybenzylidene)semicarbazide (41).
1.4.1.3.1 Spectral data of the synthesized compound (E)-1-(2,4-dimethoxybenzylidene)semicarbazide (41)

Analysis of FT-IR spectrum of (E)-1-(2,4-dimethoxybenzylidene)semicarbazide (41) in cm$^{-1}$

The compound (E)-1-(2,4-dimethoxybenzylidene)semicarbazide (41) characterized by FT-IR spectroscopy (Table–1.4.10). The FT-IR spectrum of 1-(2,4-dimethoxybenzylidene)semicarbazide (41) is displayed in plate 9.
Table 1.4.10 IR absorption frequencies for selected functional group of (E)-1-(2,4-dimethoxybenzylidene)semicarbazide (41) in cm\(^{-1}\)

<table>
<thead>
<tr>
<th>Vibration mode</th>
<th>Frequency in cm(^{-1})</th>
</tr>
</thead>
<tbody>
<tr>
<td>–C=O</td>
<td>1678</td>
</tr>
<tr>
<td>–C=N coupled with –C=O</td>
<td>1597</td>
</tr>
<tr>
<td>–N-H-</td>
<td>3475</td>
</tr>
<tr>
<td>–N-H-NH(_2)</td>
<td>3269</td>
</tr>
<tr>
<td>Aromatic –C-H</td>
<td>3047</td>
</tr>
<tr>
<td>Aliphatic –C-H</td>
<td>2924</td>
</tr>
<tr>
<td>–OCH(_3)</td>
<td>1274</td>
</tr>
</tbody>
</table>

The IR spectrum of 1-(2,4-dimethoxybenzylidene)semicarbazide (41) exhibited two absorption bands at 3475 cm\(^{-1}\) and 3269 cm\(^{-1}\) representing –NH and –NH\(_2\) groups. The absorption bands revealed at 3047 cm\(^{-1}\) (Aromatic –C-H str), 2924 cm\(^{-1}\) (Aliphatic –C-H str), 3269 cm\(^{-1}\) (-NH\(_2\) str), 1597 cm\(^{-1}\) (-C=N str) and 1678 cm\(^{-1}\) (carbonyl str).

1.4.1.3.2 Spectral data of the synthesized compound 1-(5-amino-2-(2,4-dimethoxyphenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (53)

Analysis of FT-IR spectrum of 1-(5-amino-2-(2,4-dimethoxyphenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (53) in cm\(^{-1}\)

The compound 1-(5-amino-2-(2,4-dimethoxyphenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (53) characterized by FT-IR spectroscopy (Table 1.4.11). The FT-IR spectrum of 1-(5-amino-2-(2,4-dimethoxyphenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (53) is displayed in Plate 10.
Table 1.4.11 IR absorption frequencies for selected functional group of 1-(5-amino-2-(2,4-dimethoxyphenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (53) in cm$^{-1}$

<table>
<thead>
<tr>
<th>Vibration mode</th>
<th>Frequency in cm$^{-1}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetyl –C=O</td>
<td>1674</td>
</tr>
<tr>
<td>–C=N in ring</td>
<td>1608</td>
</tr>
<tr>
<td>–NH$_2$</td>
<td>3477 &amp; 3267</td>
</tr>
<tr>
<td>Aromatic –C-H</td>
<td>3064</td>
</tr>
<tr>
<td>Aliphatic –C-H</td>
<td>2920</td>
</tr>
<tr>
<td>C-O-C in Oxadiazole ring (sym)</td>
<td>1028</td>
</tr>
<tr>
<td>–OCH$_3$</td>
<td>1271</td>
</tr>
</tbody>
</table>

In the IR spectrum of 1-(5-amino-2-(2,4-dimethoxyphenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (53), a stretching vibration observed at 3064 cm$^{-1}$ which indicates the presence of aromatic –C-H bonds. An aliphatic -CH bond was confirmed by presence of absorption band around 2920 cm$^{-1}$. The synthesized oxadiazole analogues clearly showed C=N stretching band around 1608 cm$^{-1}$. Broad and sharp stretching bands at 3267 cm$^{-1}$ and 3477 cm$^{-1}$ was due to –NH moiety while strong stretching band around 1674 cm$^{-1}$ was attributed to the carbonyl of acetyl group. Sarathkumar$^{125}$ observed a characteristic bands in the region of 3477 – 3348 cm$^{-1}$ due to –NH for 5-{1-methyl-2-(o-nitroanilino)ethyl}-1,3,4-oxadiazole-2-thiol. 1028 cm$^{-1}$ and 1215 cm$^{-1}$ which could be attributed the C-O-C symmetry and asymmetry respectively, which indicates ring closure of 1,3,4-oxadiazole ring. Sanjeev Kumar$^{126}$ elucidated the C-O-C symmetry band at 1032 cm$^{-1}$ in 2-amino-5-(2-chloro-5-nitrophenyl)-1,3,4-oxadiazole. IR data confirmed the presence of specific functional groups present in the final synthesized compounds.
Analysis of $^1$H-NMR spectrum of 1-(5-amino-2-(2,4-dimethoxyphenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (53)

The $^1$H-NMR chemical shift values are given in Table-1.4.12. The $^1$H-NMR spectrum has been displayed in Plate-11.

**Table-1.4.12 $^1$H-NMR chemical shift values of 1-(5-amino-2-(2,4-dimethoxy-phenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (53) in ppm**

<table>
<thead>
<tr>
<th>Signal No.</th>
<th>Signal Position, ($\delta$ ppm)</th>
<th>Relative No. of Protons</th>
<th>Multiplicity</th>
<th>Inference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6.56</td>
<td>2H</td>
<td>Singlet</td>
<td>Amine protons</td>
</tr>
<tr>
<td>2</td>
<td>2.54</td>
<td>3H</td>
<td>Singlet</td>
<td>Aliphatic methyl protons</td>
</tr>
<tr>
<td>3</td>
<td>7.79</td>
<td>1H</td>
<td>Singlet</td>
<td>-C-H in 1,3,4-oxadiazole ring</td>
</tr>
<tr>
<td>4</td>
<td>6.9 – 7.4</td>
<td>3H</td>
<td>Multiplet</td>
<td>Aromatic protons</td>
</tr>
<tr>
<td>5</td>
<td>3.42</td>
<td>6H</td>
<td>Singlet</td>
<td>Methoxy protons</td>
</tr>
</tbody>
</table>

In $^1$H-NMR spectrum of 1-(5-amino-2-(2,4-dimethoxyphenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (53), singlet at 6.56 ppm for two protons due to amino group, appearance of singlet at 2.54 ppm for three protons and 7.79 ppm for one proton (in 1,3,4-oxadiazole ring) due to aliphatic –CH$_3$ and –CH respectively. Mohamed M. El. Sadek et. al.,$^{127}$ observed a singlet for –CH in the range 7.12 – 8.24 ppm. A characteristic signal at 6.9 – 7.4 ppm represents the aromatic protons. The appearance of signal at 3.42 ppm for 6 protons may due to two methoxy groups present in aromatic ring.

Analysis of $^{13}$C-NMR spectrum of 1-(5-amino-2-(2,4-dimethoxyphenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (53)

The $^{13}$C-NMR chemical shift values of given in Table-1.4.13. The $^{13}$C-NMR spectrum is displayed in plate-12.
Table-1.4.13 $^{13}$C-NMR chemical shift values of 1-(5-amino-2-(2,4-dimethoxyphenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (53) in ppm

<table>
<thead>
<tr>
<th>Position</th>
<th>Chemical shift values, $\delta$ in ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbonyl carbon at C-1</td>
<td>170.76</td>
</tr>
<tr>
<td>Methyl proton at C-2</td>
<td>29.69</td>
</tr>
<tr>
<td>C-4</td>
<td>82.97</td>
</tr>
<tr>
<td>C-7</td>
<td>152.00</td>
</tr>
<tr>
<td>Aromatic carbons C-8 to C13</td>
<td>113.82 – 131.09</td>
</tr>
</tbody>
</table>

In the $^{13}$C-NMR spectra, signals characteristic of C=O around 170.76 ppm and alkyl around 29.69 ppm, as well as the oxadiazole ring signal (C-4) around 82.97 ppm and (C-7) about 152.00 ppm were observed, thus confirming the formation of the 1,3,4-oxadiazole ring. Aromatic carbon signal appeared at 113.82 – 131.09 ppm. Cledualdo Soares de Oliveria et. al.,\textsuperscript{128} has reported the characteristic signal range at 167.16 – 167.49 ppm for carbonyl carbon and 152.94 – 155.04 ppm for –N-C-O carbon in oxadiazole ring.

1.4.1.4 General scheme for preparation of 1-(5-amino-2-(2,6-dichlorophenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (54)

The following scheme was adopted for the synthesis of 1-(5-amino-2-(2,6-dichlorophenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (54) from (E)-1-(2,6-dichlorobenzylidene)semicarbazide (42).
1.4.1.4.1 Spectral data of the synthesized compound

(E)-1-(2,6-dichlorobenzylidene)semicarbazide (42) from stage-I

Analysis of FT-IR spectrum of (E)-1-(2,6-dichlorobenzylidene)semicarbazide (42) in cm⁻¹

The compound (E)-1-(2,6-dichlorobenzylidene)semicarbazide (42) characterized by FT-IR spectroscopy (Table 1.4.14). The FT-IR spectrum of (E)-1-(2,6-dichlorobenzylidene)semicarbazide (42) is displayed in plate 13.
Table-1.4.14 IR absorption frequencies for selected functional group of 
(E)-1-(2,6-dichlorobenzylidene)semicarbazide (42) in cm⁻¹

<table>
<thead>
<tr>
<th>Vibration mode</th>
<th>Frequency in cm⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>–C=O</td>
<td>1726</td>
</tr>
<tr>
<td>–C=N coupled with –C=O</td>
<td>1579</td>
</tr>
<tr>
<td>–N-H-</td>
<td>3462</td>
</tr>
<tr>
<td>–N-H-NH₂</td>
<td>3226</td>
</tr>
<tr>
<td>Aromatic –C-H</td>
<td>3082</td>
</tr>
<tr>
<td>Aliphatic –C-H</td>
<td>2922</td>
</tr>
<tr>
<td>–C-Cl</td>
<td>775</td>
</tr>
</tbody>
</table>

IR spectrum of (E)-1-(2,6-dichlorobenzylidene)semicarbazide (42) showed amide -C=O stretching absorption bands around 1726 cm⁻¹ and -C=N absorption at around 1579 cm⁻¹. At 3082 cm⁻¹ and 2922 cm⁻¹ vibrations were due to aromatic and aliphatic –C-H stretching respectively. Sharp and broad bands are appeared at 3462 cm⁻¹ and 3226 cm⁻¹ which is attributed the presence of -NH and -NH₂ group. C-Cl group showed an absorption band at 775 cm⁻¹.

1.4.1.4.2 Spectral data of the synthesized compound 1-(5-amino-2-(2,6-
dichlorophenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (54)

Analysis of FT-IR spectrum of 1-(5-amino-2-(2,6-dichlorophenyl)-
-1,3,4-oxadiazol-3(2H)-yl)ethanone(54) in cm⁻¹

The compound 1-(5-amino-2-(2,6-dichlorophenyl)-1,3,4-oxadiazol-3(2H)-yl) 
ethanone (54) characterized by FT-IR spectroscopy (Table–1.4.15). The FT-IR 
spectrum of 1-(5-amino-2-(2,6-dichlorophenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (54) is displayed in plate 14.
Table 1.4.15: IR absorption frequencies for selected functional group of 1-(5-amino-2-(2,6-dichlorophenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (54) in cm⁻¹

<table>
<thead>
<tr>
<th>Vibration mode</th>
<th>Frequency in cm⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetyl –C=O</td>
<td>1730</td>
</tr>
<tr>
<td>–C=N in ring</td>
<td>1656</td>
</tr>
<tr>
<td>–NH₂</td>
<td>3462 &amp; 3228</td>
</tr>
<tr>
<td>Aromatic –C-H</td>
<td>3070</td>
</tr>
<tr>
<td>Aliphatic –C-H</td>
<td>2920</td>
</tr>
<tr>
<td>C-O-C in Oxadiazole ring (sym)</td>
<td>1024</td>
</tr>
<tr>
<td>–C-Cl</td>
<td>773</td>
</tr>
</tbody>
</table>

The IR spectrum of 1-(5-amino-2-(2,4-dimethoxyphenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (54) is, a stretching vibration observed at 3070 cm⁻¹ which indicates the presence of aromatic –CH bonds. Mohamed Amir and coworkers¹²³ observed aromatic –CH band at 3072 cm⁻¹ for 1,3,4-oxadiazole derivatives. An aliphatic C-H bond was confirmed by presence of absorption band around 2920 cm⁻¹. The synthesized oxadiazole analogues clearly showed C=N stretching band around 1656 cm⁻¹. Broad and sharp stretching bands at 3228 cm⁻¹ and 3462 cm⁻¹ was due to –NH moiety while strong stretching band around 1730 cm⁻¹ was attributed to the carbonyl of acetyl group. 1024 cm⁻¹ and 1271 cm⁻¹ which could be attributed the C-O-C symmetry and asymmetry respectively, which indicates ring closure of 1,3,4-oxadiazole ring. Sanjeev Kumar¹²⁶ reported the C-O-C symmetry band at 1024 cm⁻¹. Appearance of absorption band at 773 cm⁻¹ represents C-Cl group. IR data confirmed the presence of specific functional groups present in the final synthesized compounds.
Analysis of $^1$H-NMR spectrum of 1-(5-amino-2-(2,6-dichlorophenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (54)

The $^1$H-NMR chemical shift values are given in Table-1.4.16. The $^1$H-NMR spectrum has been displayed in Plate-15.

Table-1.4.16 $^1$H-NMR chemical shift values of 1-(5-amino-2-(2,6-dichlorophenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (54) in ppm

<table>
<thead>
<tr>
<th>Signal No.</th>
<th>Signal Position, (δ ppm)</th>
<th>Relative No. of Protons</th>
<th>Multiplicity</th>
<th>Inference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5.99</td>
<td>2H</td>
<td>Singlet</td>
<td>Amine protons</td>
</tr>
<tr>
<td>2</td>
<td>2.50</td>
<td>3H</td>
<td>Singlet</td>
<td>Aliphatic methyl protons</td>
</tr>
<tr>
<td>3</td>
<td>7.27</td>
<td>1H</td>
<td>Singlet</td>
<td>-C-H in 1,3,4-oxadiazole ring</td>
</tr>
<tr>
<td>4</td>
<td>7.19 – 8.28</td>
<td>3H</td>
<td>Multiplet</td>
<td>Aromatic protons</td>
</tr>
</tbody>
</table>

In $^1$H-NMR spectra of 1-(5-amino-2-(2,6-dichlorophenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (54), the signals of the respective protons at 5.99 (s, 2H, -NH$_2$), 2.50 ppm (s, 3H, -CH$_3$), 7.27 ppm (s, 1H, -C-H in 1,3,4-oxadiazole ring) were verified on the basis of their chemical shifts. Multiple signals between 7.19 – 8.28 ppm confirmed the presence of aromatic protons.

Analysis of $^{13}$C-NMR spectrum of 1-(5-amino-2-(2,6-dichlorophenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (54)

The $^{13}$C-NMR chemical shift values of given in Table-1.4.17. The $^{13}$C-NMR spectrum is displayed in plate-16.
Table-1.4.17 $^{13}$C-NMR chemical shift values of 1-(5-amino-2-(2,6-dichlorophenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (54) in ppm

<table>
<thead>
<tr>
<th>Position</th>
<th>Chemical shift values, $\delta$ in ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboxyl carbon at C-1</td>
<td>169.45</td>
</tr>
<tr>
<td>Methyl proton at C-2</td>
<td>23.89</td>
</tr>
<tr>
<td>C-4</td>
<td>79.19</td>
</tr>
<tr>
<td>C-7</td>
<td>156.35</td>
</tr>
<tr>
<td>Aromatic carbons C-8 to C-13</td>
<td>129.29 – 134.48</td>
</tr>
</tbody>
</table>

In the $^{13}$C-NMR spectra, signals characteristic of C=O around 169.45 ppm and alkyl around 23.89 ppm, as well as the oxadiazole ring signal (C-4) around 79.19 ppm and (C-7) about 156.35 ppm were observed, thus confirming the formation of the 1,3,4-oxadiazole ring. Aromatic carbon signal appeared at 129.29 – 134.48 ppm.  

1.4.1.5 General scheme for preparation of 1-(5-amino-2-(3,4-dimethoxyphenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (55)

The following scheme was adopted for the synthesis of 1-(5-amino-2-(3,4-dimethoxyphenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (55) from (E)-1-(3,4-dimethoxybenzylidene)semicarbazide (43).
1.4.1.5.1 Spectral data of the synthesized compound
(E)-1-(3,4-dimethoxybenzylidene)semicarbazide (43)

Analysis of FT-IR spectrum of (E)-1-(3,4-dimethoxybenzylidene)semicarbazide (43) in cm\(^{-1}\)

The compound (E)-1-(3,4-dimethoxybenzylidene)semicarbazide (43) characterized by FT-IR spectroscopy (Table 1.4.18). The FT-IR spectrum of (E)-1-(3,4-dimethoxybenzylidene)semicarbazide (43) is displayed in plate-17.
Table-1.4.18 IR absorption frequencies for selected functional group of (E)-1-(3,4-dimethoxybenzylidene)semicarbazide (43) in cm⁻¹

<table>
<thead>
<tr>
<th>Vibration mode</th>
<th>Frequency in cm⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>–C=O</td>
<td>1678</td>
</tr>
<tr>
<td>–C=N coupled with –C=O</td>
<td>1593</td>
</tr>
<tr>
<td>–N-H-</td>
<td>3408</td>
</tr>
<tr>
<td>–N-H-NH₂</td>
<td>3284</td>
</tr>
<tr>
<td>Aromatic –C-H</td>
<td>3064</td>
</tr>
<tr>
<td>Aliphatic –C-H</td>
<td>2926</td>
</tr>
<tr>
<td>–OCH₃</td>
<td>1263</td>
</tr>
</tbody>
</table>

IR spectrum of (E)-1-(3,4-dimethoxybenzylidene)semicarbazide (43) showed amide -C=O stretching absorption bands around 1678 cm⁻¹ and -C=N absorption at around 1593 cm⁻¹. At 3064 and 2926 cm⁻¹ vibrations were due to aromatic –CH stretching and aliphatic –CH stretching respectively. Sharp and broad bands are appeared at 3408 cm⁻¹ and 3284 cm⁻¹ which is attributed the presence of -NH and -NH₂ group. C-O- stretching absorption band for Methoxy is appeared at 1263 cm⁻¹.

1.4.1.5.2 Spectral data of the synthesized compound 1-(5-amino-2-(3,4-dimethoxyphenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (55)

Analysis of FT-IR spectrum of 1-(5-amino-2-(3,4-dimethoxyphenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone(I) in cm⁻¹

The compound 1-(5-amino-2-(3,4-dimethoxyphenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (55) characterized by FT-IR spectroscopy (Table–1.4.19). The FT-IR spectrum of 1-(5-amino-2-(3,4-dimethoxyphenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (55) is displayed in plate 18.
Table-1.4.19 IR absorption frequencies for selected functional group of 1-(5-amino-2-(3,4-dimethoxyphenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (55) in cm⁻¹

<table>
<thead>
<tr>
<th>Vibration mode</th>
<th>Frequency in cm⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetyl –C=O</td>
<td>1672</td>
</tr>
<tr>
<td>–C=N in ring</td>
<td>1598</td>
</tr>
<tr>
<td>–NH₂</td>
<td>3414 &amp; 3286</td>
</tr>
<tr>
<td>Aromatic –C-H</td>
<td>3068</td>
</tr>
<tr>
<td>Aliphatic –C-H</td>
<td>2918</td>
</tr>
<tr>
<td>C-O-C in Oxadiazole ring (sym)</td>
<td>1074</td>
</tr>
<tr>
<td>–OCH₃</td>
<td>1261</td>
</tr>
</tbody>
</table>

The IR spectrum of 1-(5-amino-2-(3,4-dimethoxyphenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (55) is showed a stretching vibration at 3068 cm⁻¹ which indicates the presence of aromatic –CH bonds. An aliphatic C-H bond was confirmed by presence of absorption band around 2918 cm⁻¹. The synthesized oxadiazole analogues clearly showed C=N stretching band around 1598 cm⁻¹. Broad and sharp stretching bands at 3286 cm⁻¹ and 3414 cm⁻¹ was due to –NH moiety while strong stretching band around 1672 cm⁻¹ was attributed to the carbonyl of acetyl group. 1074 cm⁻¹ and 1267 cm⁻¹ which could be attributed the C-O-C symmetry and asymmetry respectively, which indicates ring closure of 1,3,4-oxadiazole ring. IR data confirmed the presence of specific functional groups present in the final synthesized compounds.

Analysis of ¹H-NMR spectrum of 1-(5-amino-2-(3,4-dimethoxyphenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (55)

The ¹H-NMR chemical shift values are given in Table-1.4.20. The ¹H-NMR spectrum has been displayed in Plate-19.
Table-1.4.20 $^1$H-NMR chemical shift values of 1-(5-amino-2-(3,4-dimethoxy-phenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (55) in ppm

<table>
<thead>
<tr>
<th>Signal No.</th>
<th>Signal Position, (δ ppm)</th>
<th>Relative No. of Protons</th>
<th>Multiplicity</th>
<th>Inference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7.28</td>
<td>2H</td>
<td>Singlet</td>
<td>Amine protons</td>
</tr>
<tr>
<td>2</td>
<td>2.4</td>
<td>3H</td>
<td>Singlet</td>
<td>Aliphatic methyl protons</td>
</tr>
<tr>
<td>3</td>
<td>9.16</td>
<td>1H</td>
<td>Singlet</td>
<td>–C-H in 1,3,4-oxadiazole ring</td>
</tr>
<tr>
<td>4</td>
<td>6.3-7.01</td>
<td>3H</td>
<td>Multiplet</td>
<td>Aromatic protons</td>
</tr>
<tr>
<td>5</td>
<td>3.7</td>
<td>3H</td>
<td>Singlet</td>
<td>Methoxy protons (meta sub)</td>
</tr>
<tr>
<td>6</td>
<td>3.83</td>
<td>3H</td>
<td>Singlet</td>
<td>Methoxy protons (para sub)</td>
</tr>
</tbody>
</table>

In the $^1$H-NMR of 1-(5-amino-2-(3,4-dimethoxyphenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (55), singlet at 7.28 ppm for two protons due to amino group, appearance of singlet at 2.4 ppm for three protons and 9.16 ppm for one proton in 1,3,4-oxadiazole ring due to aliphatic –CH$_3$ and –CH respectively. Sanjeev Kumar$^{129}$ reported a singlet at 7.2 – 7.5 ppm for NH$_2$ group in 5-substituted-2-amino-1,3,4-oxadiazole derivative. Seranthimata Samshuddin et. al.,$^{130}$ reported a singlet for –CH proton present in ring for 4,4’’-Difluoro-4’-(1,3,4-oxadiazol-2-yl)-1,1’:3’,1”-terphenyl-5’-ol. A characteristic multiple signal at 6.3 – 7.01 ppm represents the aromatic protons. The appearance of signal at 3.7 ppm for three protons and 3.83 ppm for three protons may due to –OCH$_3$ present in aromatic ring at meta and para positions respectively.

**Analysis of $^{13}$C-NMR spectrum of 1-(5-amino-2-(3,4-dimethoxyphenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (55)**

The $^{13}$C-NMR chemical shift values of given in Table-1.4.21. The $^{13}$C-NMR spectrum is displayed in plate-20.
Table-1.4.21 $\text{^{13}C}$-NMR chemical shift values of 1-(5-amino-2-(3,4-dimethoxy-phenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (55) in ppm

<table>
<thead>
<tr>
<th>Position</th>
<th>Chemical shift values, $\delta$ in ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbonyl carbon at C-1</td>
<td>164.63</td>
</tr>
<tr>
<td>Methyl proton at C-2</td>
<td>25.35</td>
</tr>
<tr>
<td>C-4</td>
<td>85.05</td>
</tr>
<tr>
<td>C-7</td>
<td>147.32</td>
</tr>
<tr>
<td>Aromatic carbons C-8 to C13</td>
<td>123.54 – 139.65</td>
</tr>
</tbody>
</table>

In the $\text{^{13}C}$-NMR spectra, signals characteristic of C=O around 164.63 ppm and alkyl around 25.35 ppm, as well as the oxadiazole ring signal (C-4) around 85.05 ppm and (C-7) about 147.32 ppm were observed, thus confirming the formation of the 1,3,4-oxadiazole ring. Aromatic carbon signal appeared at 123.54 – 139.65 ppm. Cledualdo Soares de Oliveria et. al.,$^{128}$ has reported the characteristic signal at 55.89 ppm for methoxy carbon and 84.34 – 85.09 ppm range for -CH carbon present in oxadiazole ring.

1.4.1.6 General scheme for preparation of 1-(5-amino-2-(1H-indol-3-yl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (56)

The following scheme was adopted for the synthesis of 1-(5-amino-2-(1H-indol-3-yl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (56) from (E)-1-(((1H-indol-3-yl)methylene)semicarbazide (44).
1.4.1.6.1 Spectral data of the synthesized compound (E)-1-((1H-indol-3-yl)methylene)semicarbazide (44)

Analysis of FT-IR spectrum of (E)-1-((1H-indol-3-yl)methylene)semicarbazide (44) in cm⁻¹

The compound (E)-1-((1H-indol-3-yl)methylene)semicarbazide (44) characterized by FT-IR spectroscopy (Table–1.4.22). The FT-IR spectrum of (E)-1-((1H-indol-3-yl)methylene)semicarbazide (44) is displayed in plate 21.
Table-1.4.22 IR absorption frequencies for selected functional group of (E)-4-((1H-indol-3-yl)methylene)semicarbazide (44) in cm⁻¹

<table>
<thead>
<tr>
<th>Vibration mode</th>
<th>Frequency in cm⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>–C=O</td>
<td>1641</td>
</tr>
<tr>
<td>–C=N coupled with –C=O</td>
<td>1573</td>
</tr>
<tr>
<td>–N-H-</td>
<td>3404</td>
</tr>
<tr>
<td>–N-H-NH₂</td>
<td>3170</td>
</tr>
<tr>
<td>Indole –N-H-</td>
<td>3491</td>
</tr>
<tr>
<td>Aromatic –C-H</td>
<td>3043</td>
</tr>
<tr>
<td>Aliphatic –C-H</td>
<td>2926</td>
</tr>
</tbody>
</table>

IR spectral data of (E)-1-((1H-indol-3-yl)methylene)semicarbazide (44) is revealed bands at 3043 cm⁻¹ (Aromatic –C-H str), 2926 cm⁻¹ (Aliphatic –C-H str), 3404 cm⁻¹ (-N-H str), 3170 cm⁻¹ (-NH₂ str), 1573 cm⁻¹ (-C=N str) and 1641 cm⁻¹ (-C=O str frequency). Aggrawal Navneet and Mishra Pradeep¹³¹ reported the IR spectra of semicarbazones show bands in the region 1578 – 1571 cm⁻¹ as stretching C=N. Indole itself absorbs 3491 cm⁻¹ and has been studied by Fuson et al.,¹³² Witkop & Marion¹³³-¹³⁵ and Vampiri et al.,¹³⁶.

1.4.1.6.2 Spectral data of the synthesized compound 1-(5-amino-2-(1H-indol-3-yl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (56)

Analysis of FT-IR spectrum of 1-(5-amino-2-(1H-indol-3-yl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (56) in cm⁻¹

The compound 1-(5-amino-2-(1H-indol-3-yl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (56) characterized by FT-IR spectroscopy (Table-1.4.23). The FT-IR spectrum of 1-(5-amino-2-(1H-indol-3-yl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (56) is displayed in plate 22.
Table-1.4.23 IR absorption frequencies for selected functional group of 1-(5-amino-2-(1H-indol-3-yl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (56) in cm⁻¹

<table>
<thead>
<tr>
<th>Vibration mode</th>
<th>Frequency in cm⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetyl –C=O</td>
<td>1635</td>
</tr>
<tr>
<td>–C=N in ring</td>
<td>1573</td>
</tr>
<tr>
<td>–NH₂</td>
<td>3396 &amp; 3167</td>
</tr>
<tr>
<td>Aromatic –C-H</td>
<td>3043</td>
</tr>
<tr>
<td>Aliphatic –C-H</td>
<td>2978</td>
</tr>
<tr>
<td>C-O-C in Oxadiazole ring (sym)</td>
<td>1083</td>
</tr>
</tbody>
</table>

The IR spectrum of 1-(5-amino-2-(1H-indol-3-yl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (56) characterized, a stretching vibration at 3043 cm⁻¹ which indicates the presence of aromatic –C-H bonds. Sanjeev Kumar and coworker¹³⁷ reported the aromatic range from 3030 cm⁻¹ to 3060 cm⁻¹ for 1,3,4-oxadiazole derivatives. An aliphatic C-H bond was confirmed by presence of absorption band around 2978 cm⁻¹. The synthesized oxadiazole analogues clearly showed C=N stretching band around 1573 cm⁻¹. Broad stretching band at 3167 cm⁻¹ and around 3403 cm⁻¹ was due to NH while strong stretching band around 1635 cm⁻¹ was attributed to the carbonyl of acetyl group. 1083 cm⁻¹ and 1240 cm⁻¹ which could be attributed the C-O-C symmetry and asymmetry respectively, which indicates ring closure of 1,3,4-oxadiazole ring. Shashikant et. al.,¹³⁸ reported the C-O-C symmetry value at 1080 cm⁻¹ for 1,3,4-oxadiazole derivative. IR data confirmed the presence of specific functional groups present in the final synthesized compounds.

Analysis of "H-NMR spectrum of 1-(5-amino-2-(1H-indol-3-yl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (56)

The "H-NMR chemical shift values are given in Table-1.4.24. The "H-NMR spectrum has been displayed in Plate-23.
Table-1.4.24 $^1$H-NMR chemical shift values of 1-(5-amino-2-(1H-indol-3-yl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (56) in ppm

<table>
<thead>
<tr>
<th>Signal No.</th>
<th>Signal Position, (δ ppm)</th>
<th>Relative No. of Protons</th>
<th>Multiplicity</th>
<th>Inference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6.27</td>
<td>2H</td>
<td>Singlet</td>
<td>Amine protons</td>
</tr>
<tr>
<td>2</td>
<td>2.28</td>
<td>3H</td>
<td>Singlet</td>
<td>Aliphatic methyl protons</td>
</tr>
<tr>
<td>3</td>
<td>8.83</td>
<td>1H</td>
<td>Singlet</td>
<td>-C-H in 1,3,4-oxadiazole ring</td>
</tr>
<tr>
<td>4</td>
<td>7.28 - 8.36</td>
<td>5H</td>
<td>Multiplet</td>
<td>Aromatic protons</td>
</tr>
<tr>
<td>5</td>
<td>10.10</td>
<td>1H</td>
<td>Singlet</td>
<td>Indole N-H</td>
</tr>
</tbody>
</table>

In $^1$H-NMR spectra of 1-(5-amino-2-(1H-indol-3-yl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (56), the signals of the respective protons at 6.27 (s, 2H, -NH$_2$), 2.28 (s, 3H, -CH$_3$), 8.83 ppm (s, 1H, -C-H in 1,3,4-oxadiazole ring) were verified on the basis of their chemical shifts. Multiple signals between 7.28 – 8.36 ppm confirmed the presence of aromatic protons. Abdel Rahman and coworker$^{139}$ reported a singlet at 2.2 ppm for aliphatic methyl protons in 1,3,4-oxadiazole derivative. Arun Dureja et. al.,$^{140}$ reported a singlet at 8.7 ppm in 3-(4-acetyl-5H-5-phenyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)-2H-chromen-2-one. Zaied et. al.,$^{141}$ reported a singlet for indole –NH at 11.12 ppm. In the present investigation the indole –NH appeared at 10.10 ppm.

Analysis of $^{13}$C-NMR spectrum of 1-(5-amino-2-(1H-indol-3-yl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (56)

The $^{13}$C-NMR chemical shift values of given in Table-1.4.25. The $^{13}$C-NMR spectrum is displayed in plate-24.
Table-1.4.25 $^{13}$C-NMR chemical shift values of 1-(5-amino-2-(1H-indol-3-yl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (56) in ppm

<table>
<thead>
<tr>
<th>Position</th>
<th>Chemical shift values, $\delta$ in ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbonyl carbon at C-1</td>
<td>158.01</td>
</tr>
<tr>
<td>Methyl proton at C-2</td>
<td>29.69</td>
</tr>
<tr>
<td>C-4</td>
<td>79.95</td>
</tr>
<tr>
<td>C-7</td>
<td>155.43</td>
</tr>
<tr>
<td>Aromatic carbons C-9 to C-16</td>
<td>119.41 – 137.64</td>
</tr>
</tbody>
</table>

In the $^{13}$C-NMR spectra, signals characteristic of C=O around 158.01 ppm and alkyl around 29.69 ppm, as well as the oxadiazole ring signal (C-4) around 79.25 ppm and (C-7) about 155.43 ppm were observed, thus confirming the formation of the 1,3,4-oxadiazole ring. Aromatic carbon signal appeared at 119.41 – 137.64 ppm.

1.4.2 SPECTRAL CHARACTERIZATION OF 1,3,4-THIADIAZOLE DERIVATIVES

1.4.2.1 General scheme for preparation of 1-(5-amino-2-phenyl-1,3,4-thiadiazol-3(2H)-yl)ethanone (57)

The following scheme was adopted for the synthesis of 1-(5-amino-2-phenyl-1,3,4-thiadiazol-3(2H)-yl)ethanone (57) from (E)-1-benzylidenesemicarbazide (45).
1.4.2.1.1 Spectral data of the synthesized compound

(E)-1-benzylidenethiosemicarbazide (45)

Analysis of FT-IR spectrum of (E)-1-benzylidenethiosemicarbazide (45) in cm\(^{-1}\)

The compound (E)-1-benzylidenethiosemicarbazide (45) characterized by FT-IR spectroscopy (Table–1.4.26). The FT-IR spectrum of (E)-1-benzylidenethiosemicarbazide (45) is displayed in plate 25.
Table-1.4.26 IR absorption frequencies for selected functional group of (E)-1-benzylidenethiosemicarbazide (45) in cm\(^{-1}\)

<table>
<thead>
<tr>
<th>Vibration mode</th>
<th>Frequency in cm(^{-1})</th>
</tr>
</thead>
<tbody>
<tr>
<td>–C=S</td>
<td>1373</td>
</tr>
<tr>
<td>–C=N coupled with –C=S</td>
<td>1591</td>
</tr>
<tr>
<td>–N-H-</td>
<td>3421</td>
</tr>
<tr>
<td>–N-H-NH(_2)</td>
<td>3253</td>
</tr>
<tr>
<td>Aromatic –C-H</td>
<td>3028</td>
</tr>
<tr>
<td>Aliphatic –C-H</td>
<td>2981</td>
</tr>
</tbody>
</table>

The IR spectrum of the (E)-1-benzylidenethiosemicarbazide (45) is showed absorption peaks at 1373 cm\(^{-1}\) due to the stretching of –C=S. The characteristic aromatic group in 1,3,4-thiadiazole moiety is observed at 3028 cm\(^{-1}\). The C=N stretching vibration appeared at 1591 cm\(^{-1}\). The IR spectra of the reported thiosemicarbazones\(^{142-144}\) show bands in the region 1538 – 1647 cm\(^{-1}\) as stretching for C=N. Aliphatic –CH stretching absorption is appeared at 2981 cm\(^{-1}\). NH and NH\(_2\) group shows an absorption peak at 3421 cm\(^{-1}\) and 3253 cm\(^{-1}\) respectively.

1.4.2.1.2 Spectral data of the synthesized compound 1-(5-amino-2-phenyl-1,3,4-thiadiazol-3(2H)-yl)ethanone (57)

Analysis of FT-IR spectrum of 1-(5-amino-2-phenyl-1,3,4-thiadiazole-3(2H)-yl)ethanone(I) in cm\(^{-1}\)

The compound 1-(5-amino-2-phenyl-1,3,4-thiadiazole-3(2H)-yl)ethanone (57) characterized by FT-IR spectroscopy (Table–1.4.27).
The FT-IR spectrum of 1-(5-amino-2-phenyl-1,3,4-thiadiazole-3(2H)-yl)ethanone (57) is displayed in plate 26.

Table-1.4.27 IR absorption frequencies for selected functional group of 1-(5-amino-2-phenyl-1,3,4-thiadiazole-3(2H)-yl)ethanone (57) in cm\(^{-1}\)

<table>
<thead>
<tr>
<th>Vibration mode</th>
<th>Frequency in cm(^{-1})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetyl –C=O</td>
<td>1693</td>
</tr>
<tr>
<td>–C=N in ring</td>
<td>1608</td>
</tr>
<tr>
<td>–NH(_2)</td>
<td>3471 &amp; 3215</td>
</tr>
<tr>
<td>C-S-C in 1,3,4-thiadiazole ring (sym)</td>
<td>727</td>
</tr>
<tr>
<td>Aromatic –C-H</td>
<td>3057</td>
</tr>
<tr>
<td>Aliphatic –C-H</td>
<td>2914</td>
</tr>
</tbody>
</table>

The IR spectrum of 1-(5-amino-2-phenyl-1,3,4-thiadiazole-3(2H)-yl)ethanone (57) is characterized, a stretching vibration at 3057 cm\(^{-1}\) which indicates the presence of aromatic –C-H bonds. An aliphatic C-H bond was confirmed by presence of absorption band around 2914 cm\(^{-1}\). The synthesized thiadiazole analogues clearly showed C=N stretching band around 1608 cm\(^{-1}\). Broad stretching band at 3215 cm\(^{-1}\) and around 3471 cm\(^{-1}\) was due to -NH while strong stretching band around 1693 cm\(^{-1}\) was attributed to the carbonyl of acetyl group. 727 and 1274 cm\(^{-1}\) which could be attributed the C-S-C symmetry and asymmetry respectively, which indicates ring closure of 1,3,4-thiadiazole ring. Harish Rajak et. al.,\(^{145}\) have been reported the C-S-C symmetry range at 737 – 742 cm\(^{-1}\) in semicarbazones containing 1,3,4-thiadiazole and quinazoline ring. IR data confirmed the presence of specific functional groups present in the final synthesized compounds.
Analysis of $^1$H-NMR spectrum of 1-(5-amino-2-phenyl-1,3,4-thiadiazol-3(2H)-yl)ethanone (57)

The $^1$H-NMR chemical shift values are given in Table-1.4.28. The $^1$H-NMR spectrum has been displayed in Plate-27.

Table-1.4.28 $^1$H-NMR chemical shift values of 1-(5-amino-2-phenyl-1,3,4-thiadiazol-3(2H)-yl)ethanone (57) in ppm

<table>
<thead>
<tr>
<th>Signal No.</th>
<th>Signal Position, (δ ppm)</th>
<th>Relative No. of Protons</th>
<th>Multiplicity</th>
<th>Inference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6.83</td>
<td>2H</td>
<td>Singlet</td>
<td>Amine protons</td>
</tr>
<tr>
<td>2</td>
<td>2.23</td>
<td>3H</td>
<td>Singlet</td>
<td>Aliphatic methyl protons</td>
</tr>
<tr>
<td>3</td>
<td>8.05</td>
<td>1H</td>
<td>Singlet</td>
<td>-C-H in 1,3,4-thiadiazole ring</td>
</tr>
<tr>
<td>4</td>
<td>6.98 - 7.04</td>
<td>5H</td>
<td>Multiplet</td>
<td>Aromatic protons</td>
</tr>
</tbody>
</table>

In $^1$H-NMR spectrum of 1-(5-amino-2-phenyl-1,3,4-thiadiazol-3(2H)-yl)ethanone (57), signal at 6.83 ppm singlet may due to $–\text{NH}_2$, appearance of singlet at 2.23 ppm and 8.05 ppm due to aliphatic $–\text{CH}_3$ and $–\text{CH}$ (present in 1,3,4-thiadiazole ring) respectively. Multiple signals at 6.98 – 7.04 ppm revealed the presence of aromatic protons.

Analysis of $^{13}$C-NMR spectrum of 1-(5-amino-2-phenyl-1,3,4-thiadiazol-3(2H)-yl)ethanone (57)

The $^{13}$C-NMR chemical shift values of given in Table-1.4.29. The $^{13}$C-NMR spectrum is displayed in plate-28.
Table 1.4.29 $^{13}$C-NMR chemical shift values of 1-(5-amino-2-phenyl-1,3,4-thiadiazole-3(2H)-yl)ethanone (57) in cm$^{-1}$

<table>
<thead>
<tr>
<th>Position</th>
<th>Chemical shift values, $\delta$ in ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbonyl carbon at C-1</td>
<td>168.83</td>
</tr>
<tr>
<td>Methyl proton at C-2</td>
<td>23.30</td>
</tr>
<tr>
<td>C-4</td>
<td>67.81</td>
</tr>
<tr>
<td>C-7</td>
<td>145.85</td>
</tr>
<tr>
<td>Aromatic carbons C-8 to C-13</td>
<td>125.68 – 140.22</td>
</tr>
</tbody>
</table>

In the $^{13}$C-NMR spectra, signals characteristic of C=O around 168.83 ppm and alkyl around 23.30 ppm, as well as the thiadiazole ring signal (C-4) around 67.81 ppm and (C-7) about 145.85 ppm were observed, thus confirming the formation of the 1,3,4-thiadiazole ring. Aromatic carbon signal appeared at 125.68 – 140.22 ppm.

1.4.2.2 General scheme for preparation of 1-(5-amino-2-(3-(trifluoromethyl)phenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (58)

The following scheme was adopted for the synthesis of 1-(5-amino-2-(3-(trifluoromethyl)phenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (58) from (E)-1-(3-(trifluoromethyl)benzylidene)thiosemicarbazide (46)
1.4.2.2.1 **Spectral data of the synthesized compound**

**(E)-1-(3-trifluoromethyl)benzylidenethiosemicarbazide (46)**

**Analysis of FT-IR spectrum of (E)-1-(3-trifluoromethyl)benzylidene thiosemicarbazide (46) in cm\(^{-1}\)**

The compound (E)-1-(3-trifluoromethyl)benzylidenethiosemicarbazide (46) characterized by FT-IR spectroscopy (Table 1.4.30). The FT-IR spectrum of (E)-1-(3-(trifluoromethyl)benzylidene)thiosemicarbazide (46) is displayed in plate 29.
Table-1.4.30 IR absorption frequencies for selected functional group of (E)-1-(3-trifluoromethyl)benzylidenethiosemicarbazide (46) in cm⁻¹

<table>
<thead>
<tr>
<th>Vibration mode</th>
<th>Frequency in cm⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>–C=S</td>
<td>1301</td>
</tr>
<tr>
<td>–C=N coupled with –C=S</td>
<td>1598</td>
</tr>
<tr>
<td>–N-H-</td>
<td>3400</td>
</tr>
<tr>
<td>–N-H-NH₂</td>
<td>3246</td>
</tr>
<tr>
<td>Aromatic –C-H</td>
<td>3082</td>
</tr>
<tr>
<td>Aliphatic –C-H</td>
<td>2981</td>
</tr>
<tr>
<td>–C-F</td>
<td>1365</td>
</tr>
</tbody>
</table>

IR data showed that (E)-1-(3-(trifluoromethyl)benzylidene)thiosemicarbazide (46) have strong absorption around 3082 cm⁻¹ which is evidence for the presence of aromatic –C-H bonds. Presence of aliphatic C-H bonds was confirmed by presence of absorption band around 2981 cm⁻¹. The synthesized thiadiazole analogues clearly showed C=N stretching band around 1598 cm⁻¹, C=S stretching band around 1365 cm⁻¹ and N-H and NH₂ absorption bands appeared at 3400 cm⁻¹ and 3246 cm⁻¹.

1.4.2.2.2 Spectral data of the synthesized compound 1-(5-amino-2-(3-trifluoromethyl)phenyl-1,3,4-thiadiazol-3(2H)-yl)ethanone (58)

Analysis of FT-IR spectrum of 1-(5-amino-2-(3-trifluoromethyl)phenyl-1,3,4-thiadiazol-3(2H)-yl)ethanone(58) in cm⁻¹

The compound 1-(5-amino-2-(3-trifluoromethyl)phenyl-1,3,4-thiadiazole-3(2H)-yl)ethanone (58) characterized by FT-IR spectroscopy (Table–1.4.31). The FT-IR spectrum of 1-(5-amino-2-(3-trifluoromethyl)phenyl-1,3,4-thiadiazole-3(2H)-yl)ethanone (58) is displayed in plate 30.
Table 1.4.31 IR absorption frequencies for selected functional group of 1-(5-amino-2-(3-trifluoromethyl)phenyl-1,3,4-thiadiazole-3(2H)-yl)ethanone (58) in cm$^{-1}$

<table>
<thead>
<tr>
<th>Vibration mode</th>
<th>Frequency in cm$^{-1}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetyl –C=O</td>
<td>1710</td>
</tr>
<tr>
<td>–C=N in ring</td>
<td>1608</td>
</tr>
<tr>
<td>–NH$_2$</td>
<td>3223 &amp; 3145</td>
</tr>
<tr>
<td>Aromatic –C-H</td>
<td>3070</td>
</tr>
<tr>
<td>Aliphatic –C-H</td>
<td>2956</td>
</tr>
<tr>
<td>C-S-C in Oxadiazole ring (sym)</td>
<td>692</td>
</tr>
<tr>
<td>–C-F</td>
<td>1371</td>
</tr>
</tbody>
</table>

IR data showed that 1-(5-amino-2-(3-trifluoromethyl)phenyl-1,3,4-thiadiazole-3(2H)-yl)ethanone (58) have strong absorption around 3070 cm$^{-1}$ which is evidence for the presence of aromatic –C-H bonds. Presence of aliphatic C-H bonds was confirmed by presence of absorption band around 2956 cm$^{-1}$. The synthesized thiadiazole analogues clearly showed C=N stretching band around 1608 cm$^{-1}$, C=O stretching band around 1710 cm$^{-1}$ and C-S-C sym absorption band around 692 cm$^{-1}$ which indicates ring closure of 1,3,4-oxadiazole ring. Aras Abdullah Hassan$^{146}$ reported the C-S-C symmetry at 660 – 700 cm$^{-1}$ in 2-(4-(substitutedphenyl)-amino-5-(4-pyridyl)-4H-1,3,4-oxadiazole. IR data confirmed the presence of specific functional groups present in the final synthesized compounds.
Analysis of $^1$H-NMR spectrum of 1-(5-amino-2-(3-trifluoromethyl)phenyl-1,3,4-thiadiazole-3(2H)-yl)ethanone(58)

The $^1$H-NMR chemical shift values are given in **Table-1.4.32**. The $^1$H-NMR spectrum has been displayed in **Plate-31**.

**Table-1.4.32** $^1$H-NMR chemical shift values of 1-(5-amino-2-(3-trifluoromethyl)-phenyl-1,3,4-thiadiazole-3(2H)-yl)ethanone (58) in ppm

<table>
<thead>
<tr>
<th>Signal No.</th>
<th>Signal Position, (δ ppm)</th>
<th>Relative No. of Protons</th>
<th>Multiplicity</th>
<th>Inference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6.87</td>
<td>2H</td>
<td>Singlet</td>
<td>Amine protons</td>
</tr>
<tr>
<td>2</td>
<td>2.5</td>
<td>3H</td>
<td>Singlet</td>
<td>Aliphatic methyl protons</td>
</tr>
<tr>
<td>3</td>
<td>7.18</td>
<td>1H</td>
<td>Singlet</td>
<td>-C-H in 1,3,4-thiadiazole ring</td>
</tr>
<tr>
<td>4</td>
<td>6.95 - 7.33</td>
<td>4H</td>
<td>Multiplet</td>
<td>Aromatic protons</td>
</tr>
</tbody>
</table>

In $^1$H-NMR spectrum of 1-(5-amino-2-(3-trifluoromethyl)phenyl-1,3,4-thiadiazole-3(2H)-yl)ethanone (58) showed a singlet at 6.87 ppm due to –NH$_2$, appearance of singlet at 2.5 ppm and 7.18 ppm due to aliphatic –CH$_3$ and –CH present in 1,3,4-thiadiazole ring respectively. A characteristic signal at 6.95 – 7.33 ppm represents the aromatic protons.

Analysis of $^{13}$C-NMR spectrum of 1-(5-amino-2-(3-trifluoromethyl)phenyl-1,3,4-thiadiazole-3(2H)-yl)ethanone(58)

The $^{13}$C-NMR chemical shift values of given in **Table-1.4.33**. The $^{13}$C-NMR Spectrum is displayed in **plate 32**.
Table-1.4.33 $^{13}$C-NMR chemical shift values of 1-(5-amino-2-(3-trifluoromethyl)phenyl)-1,3,4-thiadiazole-3(2H)-yl)ethanone (58) in ppm

<table>
<thead>
<tr>
<th>Position</th>
<th>Chemical shift values, δ in ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbonyl carbon at C-1</td>
<td>169.04</td>
</tr>
<tr>
<td>Methyl proton at C-2</td>
<td>21.97</td>
</tr>
<tr>
<td>C-4</td>
<td>67.16</td>
</tr>
<tr>
<td>C-7</td>
<td>145.60</td>
</tr>
<tr>
<td>Aromatic carbons C-8 to C-13</td>
<td>122.59 – 131.47</td>
</tr>
</tbody>
</table>

In the $^{13}$C-NMR spectra, signals characteristic of C=O around 169.04 ppm and alkyl around 21.97 ppm, as well as the thiadiazole ring signal (C-4) around 67.16 ppm and (C-7) about 145.60 ppm were observed, thus confirming the formation of the 1,3,4-thiadiazole ring. Aromatic carbon signal appeared at 122.59 – 131.47 ppm.

1.4.2.3 General scheme for preparation of 1-(5-amino-2-(2,4-dimethoxyphenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (59)

The following scheme was adopted for the synthesis of 1-(5-amino-2-(2,4-dimethoxyphenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (59) from (E)-1-(2,4-dimethoxybenzylidene)thiosemicarbazide (47).
1.4.2.3.1 Spectral data of the synthesized compound

(E)-1-(2,4-dimethoxybenzylidene)thiosemicarbazide (47)

Analysis of FT-IR spectrum of (E)-1-(2,4-dimethoxybenzylidene)thiosemicarbazide (47) in cm\(^{-1}\)

The compound (E)-1-(2,4-dimethoxybenzylidene)thiosemicarbazide (47) characterized by FT-IR spectroscopy (Table–1.4.34). The FT-IR spectrum of (E)-1-(2,4-dimethoxybenzylidene)thiosemicarbazide (47) is displayed in plate 33.
Table-1.4.34 IR absorption frequencies for selected functional group of (E)-1-(2,4-dimethoxybenzylidene)thiosemicarbazide (47) in cm\(^{-1}\)

<table>
<thead>
<tr>
<th>Vibration mode</th>
<th>Frequency in cm(^{-1})</th>
</tr>
</thead>
<tbody>
<tr>
<td>–C=S</td>
<td>1327</td>
</tr>
<tr>
<td>–C=N coupled with –C=S</td>
<td>1604</td>
</tr>
<tr>
<td>–N-H-</td>
<td>3442</td>
</tr>
<tr>
<td>–N-H-NH(_2)</td>
<td>3248</td>
</tr>
<tr>
<td>Aromatic –C-H</td>
<td>3008</td>
</tr>
<tr>
<td>Aliphatic –C-H</td>
<td>2964</td>
</tr>
<tr>
<td>–OCH(_3)</td>
<td>1278</td>
</tr>
</tbody>
</table>

The IR spectrum of (E)-1-(2,4-dimethoxybenzylidene)thiosemicarbazide (47) exhibited two absorption bands at 3442 cm\(^{-1}\) and 3248 cm\(^{-1}\) representing –NH and –NH\(_2\) groups. The absorption bands revealed at 3008 cm\(^{-1}\) (Aromatic –C-H str), 2964 cm\(^{-1}\) (Aliphatic –C-H str), 1604 cm\(^{-1}\) (-C=N str) and 1327 cm\(^{-1}\) (C=S str).

1.4.2.3.2 Spectral data of the synthesized compound 1-(5-amino-2-(2,4-dimethoxyphenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (59)

Analysis of FT-IR spectrum of 1-(5-amino-2-(2,4-dimethoxyphenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (59) in cm\(^{-1}\)

The compound 1-(5-amino-2-(2,4-dimethoxyphenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (59) characterized by FT-IR spectroscopy (Table–1.4.35). The FT-IR spectrum of 1-(5-amino-2-(2,4-dimethoxyphenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (59) is displayed in plate 34.
Table-1.4.35 IR absorption frequencies for selected functional group of 1-(5-amino-2-(2,4-dimethoxyphenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (59) in cm⁻¹

<table>
<thead>
<tr>
<th>Vibration mode</th>
<th>Frequency in cm⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetyl –C=O</td>
<td>1701</td>
</tr>
<tr>
<td>–C=N in ring</td>
<td>1647</td>
</tr>
<tr>
<td>–NH₂</td>
<td>3444 &amp; 3209</td>
</tr>
<tr>
<td>Aromatic –C-H</td>
<td>3045</td>
</tr>
<tr>
<td>Aliphatic –C-H</td>
<td>2943</td>
</tr>
<tr>
<td>C-S-C in Oxadiazole ring (sym)</td>
<td>700</td>
</tr>
<tr>
<td>–OCH₃</td>
<td>1294</td>
</tr>
</tbody>
</table>

The IR spectrum of 1-(5-amino-2-(2,4-dimethoxyphenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (59) is characterized a stretching vibration at 3045 cm⁻¹ which indicates the presence of aromatic –CH bonds. An aliphatic C-H bond was confirmed by presence of absorption band around 2943 cm⁻¹. The synthesized thiadiazole analogues clearly showed C=N stretching band around 1647 cm⁻¹. Broad and sharp stretching bands at 3209 cm⁻¹ and 3441 cm⁻¹ was due to –NH moiety while strong stretching band around 1701 cm⁻¹ was attributed to the carbonyl of acetyl group. 700 and 1247 cm⁻¹ which could be attributed the C-S-C symmetry and asymmetry respectively, which indicates ring closure of 1,3,4-thiadiazole ring. IR data confirmed the presence of specific functional groups present in the final synthesized compounds.

Analysis of ¹H-NMR spectrum of 1-(5-amino-2-(2,4-dimethoxyphenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (59)

The ¹H-NMR chemical shift values are given in Table-1.4.36. The ¹H-NMR spectrum has been displayed in Plate-35.
In $^1$H-NMR spectrum of 1-(5-amino-2-(2,4-dimethoxyphenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (59), singlet at 6.90 ppm for two protons due to amino group, appearance of singlet at 2.46 ppm for three protons and 8.46 ppm for one proton in 1,3,4-thiadiazole moiety due to aliphatic –CH$_3$ and –CH respectively. A signal at 7.28 – 7.58 ppm represents the aromatic protons. The appearance of signal at 4.00 ppm for 6 protons may due to two –OCH$_3$ group present in aromatic ring.

**Analysis of $^{13}$C-NMR spectrum of 1-(5-amino-2-(2,4-dimethoxyphenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (59)**

The $^{13}$C-NMR chemical shift values of given in Table-1.4.37. The $^{13}$C-NMR Spectrum is displayed in plate-36.

![Diagram of 1-(5-amino-2-(2,4-dimethoxyphenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (59)](image-url)
Table-1.4.37 $^{13}$C-NMR chemical shift values of 1-(5-amino-2-(2,4-dimethoxy-phenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone in ppm

<table>
<thead>
<tr>
<th>Position</th>
<th>Chemical shift values, $\delta$ in ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbonyl carbon at C-1</td>
<td>161.88</td>
</tr>
<tr>
<td>Methyl proton at C-2</td>
<td>22.81</td>
</tr>
<tr>
<td>C-4</td>
<td>65.94</td>
</tr>
<tr>
<td>C-7</td>
<td>145.28</td>
</tr>
<tr>
<td>Aromatic carbons C-8 to C-13</td>
<td>127.44 – 137.25</td>
</tr>
</tbody>
</table>

In the $^{13}$C-NMR spectra, signals characteristic of C=O around 161.88 ppm and alkyl around 22.81 ppm, as well as the thiadiazole ring signal (C-4) around 65.94 ppm and (C-7) about 145.28 ppm were observed, thus confirming the formation of the 1,3,4-thiadiazole ring. Aromatic carbon signal appeared at 127.44 – 137.25 ppm.

1.4.2.4 General scheme for preparation of 1-(5-amino-2-(2,3-dichlorophenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (60)

The following scheme was adopted for the synthesis of 1-(5-amino-2-(2,3-dichlorophenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (60) from (E)-1-(2,3-dichlorobenzylidene)thiosemicarbazide (48).
1.4.2.4.1 Spectral data of the synthesized compound (E)-1-(2,3-dichlorobenzylidene)thiosemicarbazide (48)

Analysis of FT-IR spectrum of (E)-1-(2,3-dichlorobenzylidene)thiosemicarbazide (48) in cm\(^{-1}\)

The compound (E)-1-(2,3-dichlorobenzylidene)thiosemicarbazide (48) characterized by FT-IR spectroscopy (Table–1.4.38). The FT-IR spectrum of (E)-1-(2,3-dichlorobenzylidene)thiosemicarbazide (48) is displayed in plate 37.

(E)-1-(2,3-dichlorobenzylidene)thiosemicarbazide (48)
Table-1.4.38 IR absorption frequencies for selected functional group of (E)-1-(2,3-dichlorobenzylidene)thiosemicarbazide (48) in cm\(^{-1}\)

<table>
<thead>
<tr>
<th>Vibration mode</th>
<th>Frequency in cm(^{-1})</th>
</tr>
</thead>
<tbody>
<tr>
<td>–C=S</td>
<td>1359</td>
</tr>
<tr>
<td>–C=N coupled with –C=S</td>
<td>1595</td>
</tr>
<tr>
<td>–N-H-</td>
<td>3408</td>
</tr>
<tr>
<td>–N-H-NH(_2)</td>
<td>3275</td>
</tr>
<tr>
<td>Aromatic –C-H</td>
<td>3151</td>
</tr>
<tr>
<td>Aliphatic –C-H</td>
<td>3005</td>
</tr>
<tr>
<td>–C-Cl</td>
<td>786</td>
</tr>
</tbody>
</table>

IR spectrum of (E)-1-(2,3-dichlorobenzylidene)thiosemicarbazide (48) showed amide -C=S stretching absorption bands around 1359 cm\(^{-1}\) and -C=N absorption at around 1595 cm\(^{-1}\). At 3151 cm\(^{-1}\) and 3005 cm\(^{-1}\) vibrations were due to aromatic –C-H stretching and aliphatic –C-H stretching respectively. Sharp and broad bands are appeared at 3408 cm\(^{-1}\) and 3275 cm\(^{-1}\) which is attributed the presence of -NH and -NH\(_2\) group. Absorption band around 786 cm\(^{-1}\) represents the C-Cl group.

1.4.2.4.2 Spectral data of the synthesized compound 1-(5-amino-2-(2,3-dichlorophenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (60)

Analysis of FT-IR spectrum of 1-(5-amino-2-(2,3-dichlorophenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (60) in cm\(^{-1}\)

The compound 1-(5-amino-2-(2,3-dichlorophenyl)-1,3,4-thiadiazol-3(2H)-yl) ethanone (60) characterized by FT-IR spectroscopy (Table-1.4.39). The FT-IR spectrum of 1-(5-amino-2-(2,3-chlorophenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (60) is displayed in plate 38.
Table-1.4.39 IR absorption frequencies for selected functional group of 1-(5-amino-2-(2,3-dichlorophenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (60) in cm\(^{-1}\)

<table>
<thead>
<tr>
<th>Vibration mode</th>
<th>Frequency in cm(^{-1})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetyl –C=O</td>
<td>1691</td>
</tr>
<tr>
<td>–C=N in ring</td>
<td>1625</td>
</tr>
<tr>
<td>–NH(_2)</td>
<td>3439 &amp; 3209</td>
</tr>
<tr>
<td>Aromatic –C-H</td>
<td>3064</td>
</tr>
<tr>
<td>Aliphatic –C-H</td>
<td>2939</td>
</tr>
<tr>
<td>C-S-C in Oxadiazole ring (sym)</td>
<td>723</td>
</tr>
<tr>
<td>–C-Cl</td>
<td>781</td>
</tr>
</tbody>
</table>

The IR spectrum of 1-(5-amino-2-(2,3-dichlorophenyl)-1,3,4-thiadiazol-3(2H)-yl) ethanone (60), a stretching vibration observed at 3064 cm\(^{-1}\) which indicates the presence of aromatic –CH bonds. An aliphatic C-H bond was confirmed by presence of absorption band around 2939 cm\(^{-1}\). The synthesized thiadiazole analogues clearly showed C=N stretching band around 1625 cm\(^{-1}\). Broad and sharp stretching bands at 3209 cm\(^{-1}\) and 3439 cm\(^{-1}\) was due to –NH moiety while strong stretching band around 1691 cm\(^{-1}\) was attributed to the carbonyl of acetyl group. 723 cm\(^{-1}\) and 1271 cm\(^{-1}\) which could be attributed the C-S-C symmetry and asymmetry respectively, which indicates ring closure of 1,3,4-thiadiazole ring. Absorption band around 781 cm\(^{-1}\) representing C-Cl group. IR data confirmed the presence of specific functional groups present in the final synthesized compounds.
Analysis of $^1$H-NMR spectrum of 1-(5-amino-2-(2,3-dichlorophenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (60)

The $^1$H-NMR chemical shift values are given in Table-1.4.40. The $^1$H-NMR spectrum has been displayed in Plate-39.

Table-1.4.40 $^1$H-NMR chemical shift values of 1-(5-amino-2-(2,3-dichlorophenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (60) in ppm

<table>
<thead>
<tr>
<th>Signal No.</th>
<th>Signal Position, (δ ppm)</th>
<th>Relative No. of Protons</th>
<th>Multiplicity</th>
<th>Inference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6.88</td>
<td>2H</td>
<td>Singlet</td>
<td>Amine protons</td>
</tr>
<tr>
<td>2</td>
<td>2.21</td>
<td>3H</td>
<td>Singlet</td>
<td>Aliphatic methyl protons</td>
</tr>
<tr>
<td>3</td>
<td>7.2</td>
<td>1H</td>
<td>Singlet</td>
<td>-C-H in 1,3,4-thiadiazole ring</td>
</tr>
<tr>
<td>4</td>
<td>7.03 - 7.28</td>
<td>3H</td>
<td>Multiplet</td>
<td>Aromatic protons</td>
</tr>
</tbody>
</table>

In $^1$H-NMR spectra of 1-(5-amino-2-(2,3-dichlorophenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (60), the signals of the respective protons at 6.88 (s, 2H, -NH$_2$), 2.21 ppm (s, 3H, -CH$_3$), 7.2 ppm (s, 1H, -C-H in 1,3,4-thiadiazole ring) were verified on the basis of their chemical shifts. Multiple signals between 7.03 – 7.28 ppm confirmed the presence of aromatic protons.

Analysis of $^{13}$C-NMR spectrum of 1-(5-amino-2-(2,3-dichlorophenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (60)

The $^{13}$C-NMR chemical shift values of given in Table-1.4.41. The $^{13}$C-NMR Spectrum is displayed in plate-40.
Table-1.4.41 $^{13}$C-NMR chemical shift values of 1-(5-amino-2-(2,3-dichlorophenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (60) in ppm

<table>
<thead>
<tr>
<th>Position</th>
<th>Chemical shift values, δ in ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbonyl carbon at C-1</td>
<td>165.18</td>
</tr>
<tr>
<td>Methyl proton at C-2</td>
<td>21.85</td>
</tr>
<tr>
<td>C-4</td>
<td>65.72</td>
</tr>
<tr>
<td>C-7</td>
<td>144.05</td>
</tr>
<tr>
<td>Aromatic carbons C-8 to C13</td>
<td>121.16 – 136.85</td>
</tr>
</tbody>
</table>

In the $^{13}$C-NMR spectra, signals characteristic of C=O around 165.18 ppm and alkyl around 21.85 ppm, as well as the thiaadiazole ring signal (C-4) around 65.72 ppm and (C-7) about 144.05ppm were observed, thus confirming the formation of the 1,3,4-thiadiazole ring. Aromatic carbon signal appeared at 121.16 – 136.85 ppm.

1.4.2.5 General scheme for preparation of 1-(5-amino-2-(3,4-dimethoxyphenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (61)

The following scheme was adopted for the synthesis of 1-(5-amino-2-(3,4-dimethoxyphenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (61) from (E)-1-(3,4-dimethoxybenzylidene)thiosemicarbazide (49).
1.4.2.5.1 Spectral data of the synthesized compound

(E)-1-(3,4-dimethoxybenzylidene)thiosemicarbazide (49)

Analysis of FT-IR spectrum of (E)-1-(3,4-dimethoxybenzylidene)thiosemicarbazide (49) in cm⁻¹

The compound (E)-1-(3,4-dimethoxybenzylidene)thiosemicarbazide (49) characterized by FT-IR spectroscopy (Table–1.4.42). The FT-IR spectrum of (E)-1-(3,4-dimethoxybenzylidene)thiosemicarbazide (49) is displayed in plate-41.
Table-1.4.42 IR absorption frequencies for selected functional group of (E)-4-(3,4-dimethoxybenzylidene)thiosemicarbazide (49) in cm\(^{-1}\)

<table>
<thead>
<tr>
<th>Vibration mode</th>
<th>Frequency in cm(^{-1})</th>
</tr>
</thead>
<tbody>
<tr>
<td>(-C=S)</td>
<td>1328</td>
</tr>
<tr>
<td>(-C=N) coupled with (-C=S)</td>
<td>1610</td>
</tr>
<tr>
<td>(-N-H-)</td>
<td>3350</td>
</tr>
<tr>
<td>(-N-H-NH_2)</td>
<td>3263</td>
</tr>
<tr>
<td>Aromatic (-C-H)</td>
<td>3113</td>
</tr>
<tr>
<td>Aliphatic (-C-H)</td>
<td>2960</td>
</tr>
<tr>
<td>(-OCH_3)</td>
<td>1269</td>
</tr>
</tbody>
</table>

IR spectrum of (E)-1-(3,4-dimethoxybenzylidene)thiosemicarbazide (49) showed amide \(-C=S\) stretching absorption bands around 1328 cm\(^{-1}\) and \(-C=N\) absorption at around 1610 cm\(^{-1}\). At 3020 cm\(^{-1}\) and 2960 cm\(^{-1}\) vibrations were due to aromatic \(-CH\) stretching and aliphatic \(-CH\) stretching respectively. Sharp and broad bands are appeared at 3350 cm\(^{-1}\) and 3263 cm\(^{-1}\) which is attributed the presence of \(-NH\) and \(-NH_2\) group. C-O- stretching absorption band is appeared at 1269 cm\(^{-1}\).

1.4.2.5.2 Spectral data of the synthesized compound 1-(5-amino-2-(3,4-dimethoxyphenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (61)

Analysis of FT-IR spectrum of 1-(5-amino-2-(3,4-dimethoxyphenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (61) in cm\(^{-1}\)

The compound 1-(5-amino-2-(3,4-dimethoxyphenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (61) characterized by FT-IR spectroscopy (Table–1.4.43). The FT-IR spectrum of 1-(5-amino-2-(3,4-dimethoxyphenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (61) is displayed in plate 42.
Table 1.4.43: IR absorption frequencies for selected functional group of 1-(5-amino-2-(3,4-dimethoxyphenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (61) in cm⁻¹

<table>
<thead>
<tr>
<th>Vibration mode</th>
<th>Frequency in cm⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetyl –C=O</td>
<td>1668</td>
</tr>
<tr>
<td>–C=N in ring</td>
<td>1610</td>
</tr>
<tr>
<td>–NH₂</td>
<td>3431 &amp; 3228</td>
</tr>
<tr>
<td>Aromatic –C-H</td>
<td>3072</td>
</tr>
<tr>
<td>Aliphatic –C-H</td>
<td>2943</td>
</tr>
<tr>
<td>C-S-C in Oxadiazole ring (sym)</td>
<td>723</td>
</tr>
<tr>
<td>–OCH₃</td>
<td>1300</td>
</tr>
</tbody>
</table>

The IR spectrum of 1-(5-amino-2-(3,4-dimethoxyphenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (61) is showed a stretching vibration at 3072 cm⁻¹ which indicates the presence of aromatic –CH bonds. An aliphatic C-H bond was confirmed by presence of absorption band around 2943 cm⁻¹. The synthesized thiadiazole analogues clearly showed C=N stretching band around 1610 cm⁻¹. Broad and sharp stretching bands at 3228 cm⁻¹ and 3431 cm⁻¹ was due to –NH moiety while strong stretching band around 1668 cm⁻¹ was attributed to the carbonyl of acetyl group. 723 and 1267 cm⁻¹ which could be attributed the C-S-C symmetry and asymmetry respectively, which indicates ring closure of 1,3,4-thiadiazole ring. IR data confirmed the presence of specific functional groups present in the final synthesized compounds.
Analysis of $^1$H-NMR spectrum of 1-(5-amino-2-(3,4-dimethoxyphenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (61)

The $^1$H-NMR chemical shift values are given in Table-1.4.44. The $^1$H-NMR spectrum has been displayed in Plate-43.

**Table-1.4.44 $^1$H-NMR chemical shift values of 1-(5-amino-2-(3,4-dimethoxyphenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (61) in ppm**

<table>
<thead>
<tr>
<th>Signal No.</th>
<th>Signal Position, (δ ppm)</th>
<th>Relative No. of Protons</th>
<th>Multiplicity</th>
<th>Inference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6.82</td>
<td>2H</td>
<td>Singlet</td>
<td>Amine protons</td>
</tr>
<tr>
<td>2</td>
<td>2.32</td>
<td>3H</td>
<td>Singlet</td>
<td>Aliphatic methyl protons</td>
</tr>
<tr>
<td>3</td>
<td>8.32</td>
<td>1H</td>
<td>Singlet</td>
<td>$\text{-C-H in 1,3,4-thiadiazole ring} $</td>
</tr>
<tr>
<td>4</td>
<td>7.26 – 7.34</td>
<td>3H</td>
<td>Multiplet</td>
<td>Aromatic protons</td>
</tr>
<tr>
<td>5</td>
<td>3.33</td>
<td>3H</td>
<td>Singlet</td>
<td>Methoxy protons (meta)</td>
</tr>
<tr>
<td>6</td>
<td>3.43</td>
<td>3H</td>
<td>Singlet</td>
<td>Methoxy protons (para)</td>
</tr>
</tbody>
</table>

In the $^1$H-NMR of 1-(5-amino-2-(3,4-dimethoxyphenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (61), singlet at 6.82 ppm for two protons due to amino group, appearance of singlet at 2.32 ppm for three protons and 8.32 ppm for one proton (in1,3,4-thiadiazole ring) due to aliphatic $\text{–CH}_3$ and $\text{–CH}$ respectively. A characteristic multiple signal at 7.26 – 7.34 ppm represents the aromatic protons. The appearance of signal at 3.33 ppm for three protons and 3.43 ppm for three protons may due to $\text{–OCH}_3$ present in aromatic ring at meta and para positions respectively.

Analysis of $^{13}$C-NMR spectrum of 1-(5-amino-2-(3,4-dimethoxyphenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (61)

The $^{13}$C-NMR chemical shift values of given in Table-1.4.45. The $^{13}$C-NMR spectrum is displayed in plate-44.
Table-1.4.45 13C-NMR chemical shift values of 1-(5-amino-2-(3,4-dimethoxyphenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (61) in ppm

<table>
<thead>
<tr>
<th>Position</th>
<th>Chemical shift values, δ in ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carboxyl carbon at C-1</td>
<td>170.64</td>
</tr>
<tr>
<td>Methyl proton at C-2</td>
<td>23.59</td>
</tr>
<tr>
<td>C-4</td>
<td>64.50</td>
</tr>
<tr>
<td>C-7</td>
<td>151.28</td>
</tr>
<tr>
<td>Aromatic carbons C-8 to C-13</td>
<td>123.02 – 141.29</td>
</tr>
</tbody>
</table>

In the $^{13}$C-NMR spectra, signals characteristic of C=O around 170.64 ppm and alkyl around 23.59 ppm, as well as the thiadiazole ring signal (C-4) around 64.50 ppm and (C-7) about 151.28 ppm were observed, thus confirming the formation of the 1,3,4-thiadiazole ring. Aromatic carbon signal appeared at 123.02 – 141.29 ppm.

1.4.2.6 General scheme for preparation of 1-(5-amino-2-(2,4-difluorophenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (62)

The following scheme was adopted for the synthesis of 1-(5-amino-2-(2,4-dimethoxyphenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (62) from (E)-1-(2,4-difluoro benzylidene)thiosemicarbazide (50).
1.4.2.6.1 Spectral data of the synthesized compound

(E)-1-(2,4-difluorobenzylidene)thiosemicarbazide (50)

Analysis of FT-IR spectrum of (E)-1-(2,4-difluorobenzylidene)thiosemicarbazide (50) in cm⁻¹

The compound (E)-1-(2,4-difluorobenzylidene)thiosemicarbazide (50) characterized by FT-IR spectroscopy (Table–1.4.46). The FT-IR spectrum of (E)-1-(2,4-difluorobenzylidene)thiosemicarbazide (50) is displayed in plate 45.
Table-1.4.46 IR absorption frequencies for selected functional group of (E)-1-(2,4-difluorobenzylidene)thiosemicarbazide (50) in cm⁻¹

<table>
<thead>
<tr>
<th>Vibration mode</th>
<th>Frequency in cm⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>–C=S</td>
<td>1373</td>
</tr>
<tr>
<td>–C=N coupled with –C=S</td>
<td>1600</td>
</tr>
<tr>
<td>–N-H-</td>
<td>3425</td>
</tr>
<tr>
<td>–N-H-NH₂</td>
<td>3250</td>
</tr>
<tr>
<td>Aromatic –C-H</td>
<td>3028</td>
</tr>
<tr>
<td>Aliphatic –C-H</td>
<td>2985</td>
</tr>
<tr>
<td>–C-F</td>
<td>1062</td>
</tr>
</tbody>
</table>

The IR spectrum of (E)-1-(2,4-difluorobenzylidene)thiosemicarbazide (50) exhibited two absorption bands at 3425 cm⁻¹ and 3250 cm⁻¹ representing –NH and –NH₂ groups. The characteristic absorption bands revealed at 3028 cm⁻¹ (Aromatic –C-H stretches), 2985 cm⁻¹ (Aliphatic –C-H str), 1600 cm⁻¹ (-C=N stretches), 1373 cm⁻¹ (C=S stretches) and 1062 cm⁻¹ (C-F stretches).

1.4.2.6.2 Spectral data of the synthesized compound 1-(5-amino-2-(2,4-difluorophenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (62)

Analysis of FT-IR spectrum of 1-(5-amino-2-(2,4-difluorophenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (62) in cm⁻¹

The compound 1-(5-amino-2-(2,4-difluorophenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (62) characterized by FT-IR spectroscopy (Table–1.4.47). The FT-IR spectrum of 1-(5-amino-2-(2,4-difluorophenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (62) is displayed in plate 46.
Table-1.4.47 IR absorption frequencies for selected functional group of 1-(5-amino-2-(2,4-difluorophenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (62) in cm⁻¹

<table>
<thead>
<tr>
<th>Vibration mode</th>
<th>Frequency in cm⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetyl –C=O</td>
<td>1703</td>
</tr>
<tr>
<td>–C=N in ring</td>
<td>1631</td>
</tr>
<tr>
<td>–NH₂</td>
<td>3439 &amp; 3223</td>
</tr>
<tr>
<td>Aromatic –C-H</td>
<td>3086</td>
</tr>
<tr>
<td>Aliphatic –C-H</td>
<td>2968</td>
</tr>
<tr>
<td>C-S-C in Oxadiazole ring (sym)</td>
<td>721</td>
</tr>
<tr>
<td>–C-F</td>
<td>1033</td>
</tr>
</tbody>
</table>

The IR spectrum of 1-(5-amino-2-(2,4-difluorophenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (62), a stretching vibration observed at 3086 cm⁻¹ which indicates the presence of aromatic –CH bonds. An aliphatic C-H bond was confirmed by presence of absorption band around 2968 cm⁻¹. The synthesized thiadiazole analogues clearly showed C=N stretching band around 1631 cm⁻¹. Broad and sharp stretching bands at 3223 cm⁻¹ and 3439 cm⁻¹ was due to –NH moiety while strong stretching band around 1703 cm⁻¹ was attributed to the carbonyl of acetyl group. 721 cm⁻¹ and 1271 cm⁻¹ which could be attributed the C-S-C symmetry and asymmetry respectively, which indicates ring closure of 1,3,4-thiadiazole ring. Appearance of absorption band at 1033 represents the presence of C-F group. IR data confirmed the presence of specific functional groups present in the final synthesized compounds.

Analysis of ¹H-NMR spectrum of 1-(5-amino-2-(2,4-difluorophenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (62)

The ¹H-NMR chemical shift values are given in Table-1.4.48. The ¹H-NMR spectrum has been displayed in Plate-47.
### Table-1.4.48

<table>
<thead>
<tr>
<th>Signal No.</th>
<th>Signal Position, (δ ppm)</th>
<th>Relative No. of Protons</th>
<th>Multiplicity</th>
<th>Inference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6.87</td>
<td>2H</td>
<td>Singlet</td>
<td>Amine protons</td>
</tr>
<tr>
<td>2</td>
<td>2.27</td>
<td>3H</td>
<td>Singlet</td>
<td>Aliphatic methyl protons</td>
</tr>
<tr>
<td>3</td>
<td>7.05</td>
<td>1H</td>
<td>Singlet</td>
<td>-C-H in 1,3,4-oxadiazole ring</td>
</tr>
<tr>
<td>4</td>
<td>7.07 – 7.92</td>
<td>3H</td>
<td>Multiplet</td>
<td>Aromatic protons</td>
</tr>
</tbody>
</table>

In $^1$H-NMR spectra of 1-(5-amino-2-(2,4-difluorophenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (62), the signals of the respective protons at 6.87 (s, 2H, -NH$_2$), 2.27(s, 3H, -CH$_3$), 7.05 ppm (s, 1H, -C-H in 1,3,4-thiadiazole ring) were verified on the basis of their chemical shifts. Multiple signals between 7.07–7.92ppm confirmed the presence of aromatic protons.

**Analysis of $^{13}$C-NMR spectrum of 1-(5-amino-2-(2,4-difluorophenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (62)**

The $^{13}$C-NMR chemical shift values of given in Table-1.4.49. The $^{13}$C-NMR spectrum is displayed in plate-48.

![Chemical Structure](image-url)

1-(5-amino-2-(2,4-difluorophenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (62)
Table-1.4.49 $^{13}$C-NMR chemical shift values of 1-(5-amino-2-(2,4-difluorophenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (62) in ppm

<table>
<thead>
<tr>
<th>Position</th>
<th>Chemical shift values, $\delta$ in ppm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbonyl carbon at C-1</td>
<td>164.48</td>
</tr>
<tr>
<td>Methyl proton at C-2</td>
<td>21.57</td>
</tr>
<tr>
<td>C-4</td>
<td>64.03</td>
</tr>
<tr>
<td>C-7</td>
<td>145.54</td>
</tr>
<tr>
<td>Aromatic carbons C-8 to C-13</td>
<td>120.49 – 141.38</td>
</tr>
</tbody>
</table>

In the $^{13}$C-NMR spectra, signals characteristic of C=O around 164.48 ppm and alkyl around 21.57 ppm, as well as the oxadiazole ring signal (C-4) around 64.03 ppm and (C-7) about 145.54 ppm were observed, thus confirming the formation of the 1,3,4-oxadiazole ring. Aromatic carbon signal appeared at 120.49 – 141.38 ppm.

1.5 CONCLUSION

1,3,4-Oxadiazole and thiadiazole derivatives were synthesized via ultrasound irradiation method. Ultrasound irradiation for synthesis of the title compounds offers reduction in reaction time, operation simplicity, cleaner reaction, easy work up and improved yields. The procedure clearly highlights the advantages of ultrasound.

The structures of the synthesized compounds were elucidated from results obtained from various characterizations i.e., IR, $^1$H-NMR and $^{13}$C-NMR.

The compounds 1,3,4-oxadiazole derivatives exhibits characteristic bands in the region at 3070 – 2918 cm$^{-1}$ (for aromatic –CH), 1674 – 1631 cm$^{-1}$ (C=O, stretching for acetyl), 1647 – 1631 cm$^{-1}$ (C=N stretching), 1082 – 1024 cm$^{-1}$ (C-O-C, stretching of 1,3,4-oxadiazole) and 3477 – 3157 cm$^{-1}$ (for -NH stretching).
For thiadiazole derivatives the IR spectral values revealed at 3086 – 3045 cm⁻¹ (for aromatic –CH), 1710 – 1668 cm⁻¹ (C=O, stretching for acetyl), 1647 – 1608 cm⁻¹ (C=N stretching), 723 – 692 cm⁻¹ (C=S-C, stretching of 1,3,4-oxadiazole) and 3471 – 3145 cm⁻¹ (for -NH stretching).

¹H-NMR and ¹³C-NMR spectroscopy data was sufficient to confirm the formation of 1,3,4-oxadiazole and thiadiazole ring, as these compounds have very characteristic signals. Thus, in the ¹H-NMR spectra of compounds from 51 to 62 two typical signals were observed, one assigned to the methyl protons (from acyl) in the aliphatic region of 2.28 – 2.54 ppm and another assigned to methinic proton present in diazole moiety observed at region 7.27 – 9.16 ppm. Multiple signals between 6.3 – 8.39 ppm confirmed the presence of aromatic protons. A characteristic signal is observed in the region of 6.08 – 7.28 ppm indicated the presence of –NH₂.

In the ¹³C-NMR spectra, characteristic signal of C=O appeared in the range of 158.01 – 170.76 ppm and alkyl in 20.77 – 29.69 ppm, as well as the oxadiazole ring signal (C-4) at 59.77 – 85.05 ppm and (C-7) at 147.32 – 156.67 ppm were observed, thus confirming the formation of the 1,3,4-oxadiazole ring. Aromatic carbon signal appeared at 113.82 – 139.65 ppm. For thiadiazole derivatives, the ¹³C-NMR spectra, signals characteristic of C=O appeared in the range of 161.88 – 170.64 ppm and alkyl in 21.57 – 23.59 ppm, as well as the oxadiazole ring signal (C-4) at 64.03 – 67.81 ppm and (C-7) at 144.05 – 151.28 ppm were observed, thus confirming the formation of the 1,3,4-thiadiazole ring. In the present study the aromatic carbon signal is appeared at 120.49 - 141.38 ppm.
Plate 1: The FT-IR spectrum of 1-benzylidenesemicarbazide (39)
Plate 2: The FT-IR spectrum of 1-(5-amino-2-phenyl-1,3,4-oxadiazole-3(2H)-yl)ethanone (51)
Plate 3: $^1$H-NMR spectrum of 1-(5-amino-2-phenyl-1,3,4-oxadiazol-3(2H)-yl)ethanone (51)
Plate 4: $^{13}$C-NMR spectrum of 1-(5-amino-2-phenyl-1,3,4-oxadiazol-3(2H)-yl)ethanone (51)
Plate 5: The FT-IR spectrum of (E)-1-(3-(trifluoromethyl)benzylidene)semicarbazide (40)
Plate 6: The FT-IR spectrum of 1-(5-amino-2-(3-trifluoromethyl)phenyl)-1,3,4-oxadiazole-3(2H)-yl)ethanone (52)
Plate 7: $^1$H-NMR spectrum of 1-(5-amino-2-(3-trifluoromethyl)phenyl-1,3,4-oxadiazole-3(2H)-yl)ethanone (52)
Plate 8: $^{13}$C-NMR spectrum of 1-(5-amino-2-(3-trifluoromethyl)phenyl-1,3,4-oxadiazole-3(2H)-yl)ethanone (52)
Plate 9: The FT-IR spectrum of 1-(2,4-dimethoxybenzylidene)semicarbazide (41)
Plate 10: The FT-IR spectrum of 1-(5-amino-2-(2,4-dimethoxyphenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (53)
Plate 11: $^1$H-NMR spectrum of 1-(5-amino-2-(2,4-dimethoxyphenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (53)
Plate 12: $^{13}$C-NMR spectrum of 1-(5-amino-2-(2,4-dimethoxyphenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (53)
Plate 13: The FT-IR spectrum of (E)-1-(2,6-dichlorobenzylidene)semicarbazide (42)
Plate 14: The FT-IR spectrum of 1-(5-amino-2-(2,6-dichlorophenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (54)
Plate 15: $^1$H-NMR spectrum of 1-(5-amino-2-(2,6-dichlorophenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (54)
Plate 16: $^{13}$C-NMR spectrum of 1-(5-amino-2-(2,6-dichlorophenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (54)
Plate 17: The FT-IR spectrum of (E)-1-(3,4-dimethoxybenzylidene)semicarbazide (43)
Plate 18: The FT-IR spectrum of 1-(5-amino-2-(3,4-dimethoxyphenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (55)
Plate 19: $^1$H-NMR spectrum of 1-(5-amino-2-(3,4-dimethoxyphenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (55)
Plate 20: $^{13}$C-NMR spectrum of 1-(5-amino-2-(3,4-dimethoxyphenyl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (55)
Plate 21: The FT-IR spectrum of \((E)-1-((1H\text{-indol-3-yl})\text{methylene})\text{semicarbamide}\) (44)
Plate 22: The FT-IR spectrum of 1-(5-amino-2-(1H-indol-3-yl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (56)
Plate 23: $^1$H-NMR spectrum of 1-(5-amino-2-(1H-indol-3-yl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (56)
Plate 24: $^{13}$C-NMR chemical shift values of 1-(5-amino-2-(1H-indol-3-yl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (56)
Plate 25: The FT-IR spectrum of (E)-1-benzylidenethiosemicarbazide (45)
Plate 26: The FT-IR spectrum of 1-(5-amino-2-phenyl-1,3,4-thiadiazole-3(2H)-yl)ethanone (57)
Plate 27: $^1$H-NMR spectrum of 1-(5-amino-2-phenyl-1,3,4-thiadiazol-3(2H)-yl)ethanone (57)
Plate 28: $^{13}$C-NMR spectrum of 1-(5-amino-2-phenyl-1,3,4-thiadiazol-3(2H)-yl)ethanone (57)
Plate 29: The FT-IR spectrum of (E)-1-(3-(trifluoromethyl)benzylidene)thiosemicarbazide (46)
Plate 30: The FT-IR spectrum of 1-(5-amino-2-(3-trifluoromethyl)phenyl-1,3,4-thiadiazole-3(2H)-yl)ethanone (58)
Plate 31: $^1$H-NMR spectrum of 1-(5-amino-2-(3-trifluoromethyl)phenyl-1,3,4-thiadiazole-3(2H)-yl)ethanone (58)
Plate 32: $^{13}$C-NMR spectrum of 1-(5-amino-2-(3-trifluoromethyl)phenyl-1,3,4-thiadiazole-3(2H)-yl)ethanone(58)
Plate 33: The FT-IR spectrum of (E)-1-(2,4-dimethoxybenzylidene)thiosemicarbazide (47)
Plate 34: The FT-IR spectrum of 1-(5-amino-2-(2,4-dimethoxyphenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (59)
Plate35: $^1$H-NMR spectrum of 1-(5-amino-2-(2,4-dimethoxyphenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (59)
Plate 36: $^{13}$C-NMR spectrum of 1-(5-amino-2-(2,4-dimethoxyphenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (59)
Plate 37: The FT-IR spectrum of (E)-1-(2,3-dichlorobenzylidene)thiosemicarbazide (48)
Plate 38: The FT-IR spectrum of 1-(5-amino-2-(2,3-chlorophenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (60)
Plate 39: $^1$H-NMR spectrum of 1-(5-amino-2-(2,3-dichlorophenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (60)
Plate 40: $^{13}$C-NMR spectrum of 1-(5-amino-2-(2,3-dichlorophenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (60)
Plate 41: The FT-IR spectrum of (E)-1-(3,4-dimethoxybenzylidene)thiosemicarbazide (49)
Plate 42: The FT-IR spectrum of 1-(5-amino-2-(3,4-dimethoxyphenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (61)
Plate 43: $^1$H-NMR spectrum of 1-(5-amino-2-(3,4-dimethoxyphenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (61)
Plate 44: $^{13}$C-NMR spectrum of 1-(5-amino-2-(3,4-dimethoxyphenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (61)
Plate 45: The FT-IR spectrum of (E)-1-(2,4-difluorobenzylidene)thiosemicarbazide (50)
Plate 46: The FT-IR spectrum of 1-(5-amino-2-(2,4-difluorophenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (62)
Plate 47: $^1$H-NMR spectrum of 1-(5-amino-2-(2,4-difluorophenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (62)
Plate 48: $^{13}$C-NMR spectrum of 1-(5-amino-2-(2,4-difluorophenyl)-1,3,4-thiadiazol-3(2H)-yl)ethanone (62)
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