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DEVELOPMENTS IN THE APPLICATIONS OF 1, 3, 4-OXADIAZOLE DERIVATIVES AND SYNTHETIC METHODS FOR 1, 3, 4-OXADIAZOLE 2-AMINE DERIVATIVES: A BRIEF REVIEW

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ABSTRACT: A brief review report examines recent advancements in the applications of 1, 3, 4-oxadiazole derivatives and synthetic methodologies for 1, 3, 4-oxadiazole 2-amine derivatives, which are important heterocyclic compounds in pharmaceutical chemistry. Oxadiazole, derived from furan by replacing two methane (-CH=) groups with pyridine-type nitrogen, serves as a structural key part in many drugs. Researchers explore novel methods to synthesize oxadiazole derivatives with potential medical applications, such as combating cancer, bacteria, and inflammation. Additionally, the synthetic strategies employed for the preparation of 1, 3, 4-oxadiazole 2-amine derivatives are thoroughly discussed, offering insights into their structural modifications and potential applications in medicine. A review article summarizes various approaches to produce oxadiazole derivatives and their biological activities, aiding researchers in developing new medicines. This overview aims to provide a detailed understanding of recent developments in this significant area of research.

KEYWORDS: 1, 3, 4oxadiazole, Biological activity, Antimicrobial, Fungicidal, Analgesic, Anti-inflammatory, Antimalarial, Antidepressant, 1, 3, 4-oxadiazole 2-amine derivatives

INTRODUCTION:

Heterocyclic compounds are widely recognized for their pharmacological potential, making them valuable in synthesizing new biologically active molecules. Recently, there has been significant progress in developing new poly-heterocyclic compounds. Compounds like thiazole, triazole, oxadiazole, and thiadiazole, known as azole derivatives, exhibit versatile pharmacological efficiency and have been extensively studied for various biological activities. These compounds hold promise in pharmaceutical chemistry due to their advantageous structures, facilitating effective drug design.

Out of the five members mentioned earlier, 1, 3, 4-oxadiazoles are very interesting in medicine. Studies show that 1, 3, 4-oxadiazole and its variations have many biological effects

like fighting bacteria and fungi, reducing inflammation, and even potentially fighting cancer. One such compound, furamizole, has a strong antibacterial effect. [i]

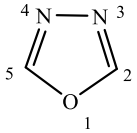


Fig-1:1,3,4oxadiazole

Oxadiazole (Fig: 1) is a type of ring with five members. It has two nitrogen atoms, one oxygen atom, and two double bonds in its aromatic ring. [ii, iii] This structure has many useful biological effects [iv]. The oxadiazole structure comes from replacing two methene groups (-CH=) in furan with two pyridine type nitrogen atoms (-N=) [iii] similar to those found in pyridine. Researchers have studied oxadiazole and its derivatives for many years. They have found that these compounds are powerful in treating various pharmacological and pathological conditions [v].

Four isomeric forms of oxadiazole exist, differing based on the position of the nitrogen atom within the ring, as illustrated below [vi]. (Fig-2)

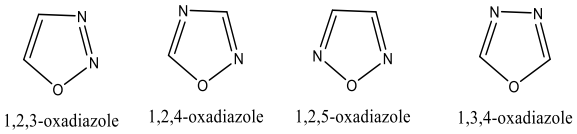


Fig 2: Isomeres of oxadiazole

In 1965, Ainsworth prepared 1, 3, 4-oxadiazole by the thermo-lysis of ethyl N-formyl formohydrazonate with hydrazine at regular air pressure [vii]. (Fig: 3)

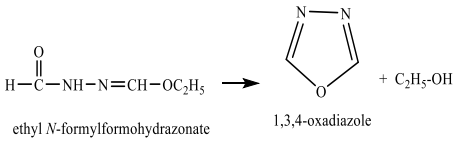


Fig:3 Ainsworth prepared 1,3,4-oxadiazole

The interaction of 1, 3, 4-oxadiazole ring is seen as a weak base. It contains two pyridine-like nitrogen atoms, which reduce its aromaticity. This makes it act like a conjugated diene. Because the carbon atom has lower electron density, it doesn't favor electrophilic substitution reactions. This is due to the electron-withdrawing nature of the pyridine-like nitrogen atoms [viii, ix]. In the realm of medicinal chemistry, the exploration of various heterocyclic compounds has been extensive. Among these, 1, 3, 4-oxadiazole derivatives have emerged as pivotal players. They serve as versatile foundations for crafting potential bioactive agents, making significant contributions to pharmaceutical development [x]. The oxadiazole ring's enhanced hydrolytic and metabolic constancy boosts interest in studying its pharmacokinetics, making it an important part of drug development [xi]. Oxadiazole chemistry has been extensively explored and is continuously evolving. Today, numerous drugs containing oxadiazole components combined with various heterocyclic rings are used in clinical practice. As a result, the 1,3,4-oxadiazole moiety is frequently targeted in drug discovery for various purposes such as anti-inflammatory, antibacterial, analgesic, fungicidal, antimalarial, antidepressant, hyperglycemic, and other activities [xii, xiii]. Prominent examples of compounds with the 1,3,4-oxadiazole structure include the antiretroviral drug Isentress [xiv], AZD3988 identified as DGAT-1 inhibitors for obesity and diabetes [xv] treatment, the antihypertensive nesapidil, and the antibiotic furamizole [xvi]. (Fig: 4)

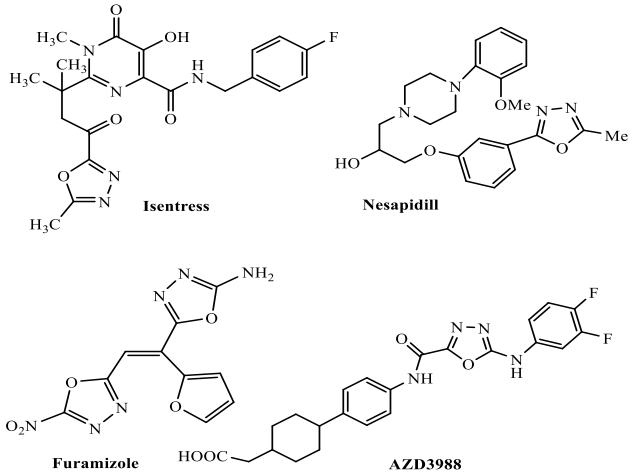
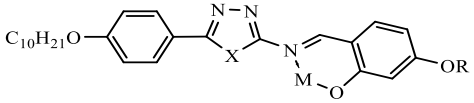


Fig:4 Perscribed agents featuring the 1,3,4-oxadiazoles Scafold

Chemists are interested in 1, 3, 4-oxadiazoles with various functional groups. They make new compounds with unknown or improved medicinal effects. For instance, 2-amino-1, 3, 4-oxadiazole compounds can act as muscle relaxants [xvii] and anti-mitotics [xviii]. For two decades, 1, 3, 4-oxadiazole heterocycles gained attention as antibacterial, insecticidal, fungicidal, herbicidal, analgesic, anti-inflammatory, antipyretic, sedative, anti-tubercular, hypnotic, hypoglycemic agents, and dyes, also used in x-ray contrast materials.

In 2003, Maria Parra [xix] and her colleagues conducted research on copper (II) and palladium (II) complexes created from ligands known as Schiff's bases, specifically incorporating 1, 3, 4-oxadiazole and 1, 3, 4-thiadiazole rings. They analyzed the complexes' thermal behavior using techniques like differential scanning calorimetry (DSC), thermogravimetric analysis (TGA), and polarizing optical microscopy. Among their findings, they observed that a single complex derived from schiff's base L1 displayed liquid crystalline properties. Furthermore, complexes Ic and IIc demonstrated an enantiotropic smectic C phase, while complexes IIa and IIb exhibited dimorphism smectic C-nematic phases. These discoveries shed light on the unique properties of these metal complexes and their potential applications. (Fig: 5)



L^1a,b,c a)X-S R-C_5H_{11}; b)X-S R-C_6H_{13}; c)X-S R-$C_{10}H_{21}$
L^2a,b,c a)X-O R-C_5H_{11}; b)X-O R-C_6H_{13}; c)X-O R-$C_{10}H_{21}$
L^3a,b,c a)X-S R-C_5H_{11}; b)X-S R-C_6H_{13}; c)X-S R-$C_{10}H_{21}$
L^4a,b,c a)X-O R-C_5H_{11}; b)X-O R-C_6H_{13}; c) X-O R-$C_{10}H_{21}$
Ia,b,c: M=Cu IIa,b,c: M=Pd
R: a=C_5H_{11}; b=C_6H_{13}; c=$C_{10}H_{21}$

Fig: 5 Copper (II) and Palladium (II) complexes derived from ligands of Schiff's bases (L1, L2, L3, L4)

P. Mishra (2005) [xx] and colleagues synthesized twenty Schiff bases via condensation reactions between 2-amino-5-aryl-1, 3, 4-oxadiazoles and various aromatic aldehydes. Structural confirmation was achieved through nitrogen analysis, IR, and ^{13}C-NMR spectral data. Antimicrobial activities were investigated against Proteus mirabilis (MTCC-425), Pseudomonas aeruginosa (MTCC-424), *Bacillus subtilis* (MTCC-619), and *Staphylococcus aureus* (MTCC-96) using the broth dilution method. The compounds displaying the highest activity levels were determined to be 4c (at 64 mg/mL), 4f (at 68 mg/mL), 4m (at 64 mg/mL), and 4q (at 62 mg/mL). The same method was employed for antifungal screening against *Aspergillus niger* (MTCC-1344) and *Candida albicans* (MTCC-227), revealing active compounds 4g (52 mg/mL), 4h (56 mg/mL), 4l (60 mg/mL), and 4m (58 mg/mL). (Fig: 6)

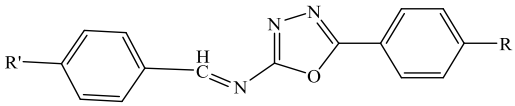


Fig:6: Schiff bases of 2-amino-5-aryl-1,3,4-oxadiazoles with different aromatic aldehydes

A study by A. K. Shaky (2008) [xxi] and colleagues synthesized several schiff' bases from 2-amino-5-(2-chlorophenyl)-1, 3, 4-oxadiazoles (Fig: 7) reacting with aromatic aldehydes. The chemical structures of these compounds were confirmed using elemental analysis, IR, and 13C NMR. They tested these compounds against Gram-positive bacteria like Staphylococcus aureus and Gram-negative bacteria such as Escherichia coli and Pseudomonas aeruginosa, as well as fungi like yeast; *Candida albicans* and mold *Aspergillus fumigatus*. They compared their effectiveness with standard drugs anti-microbiological ciprofloxacin and clotrimazole as antifungal. In vitro antibacterial and antifungal screening showed that compound 2e was the most active, followed by compounds 2b and 2a. Compounds with furan rings were less active compared to those with chlorophenyl or nitrophenyl derivatives.

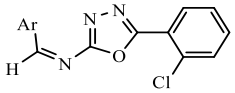


Fig:7 Ar= o-Cl; p-Cl;p-OMe; o-NO_2; p-NO_2; 5-nitrofuranyl;5-phenyl-2-furanyl and 5-(2-nitrophenyl)-2-furanyl

P.P. Naik (2013) [xxii] and coworkers synthesized some chemicals called 1, 3, 4-oxadiazole based Schiff's bases. (Fig: 8) They made these chemicals successfully and checked them using IR and NMR spectroscopy. The chemicals compound they synthesized were tested against cancer cells like K-562, MCF-7, and HCT-15 to see if they could stop cancer growth.

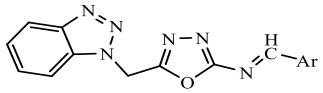


Fig:8 Schiff's bases of 1,3,4-oxadiazole

K. Zhang (2014) [xxiii] and their team designed new compounds with a mix of 1, 3, 4-oxadiazole and 1, 3, 4-thiadiazole along with a schiff base part. They then tested these compounds in the lab to see how well they could fight cancer cells in dishes. They used a method called CCK-8 assay to evaluate their effectiveness against three types of human tumor cells: SMMC-7721, MCF-7, and A549. They discovered that many of these new compounds were good at stopping tumor cell growth. In fact, some of them worked even better than a commonly used cancer drug called 5-fluorouracil (5-FU) when tested against various cancer cell lines. The substituents of phenyl ring on the 1, 3, 4-oxadiazole were studied and they displayed a role crucial in determining how well these compounds fought against different types of cancer cells.

S. Bala (2014) [xxiv] and colleagues have reported synthesis and biological assessment of new derivatives of 1, 3, 4-oxadiazole to fight bacteria as potential antibacterial agents. They confirmed the structures of these substances using UV, IR, ^{1}H NMR, ^{13}C NMR, and mass spectrometry. They tested the all derivatives against bacteria, comparing them to standard drugs like amoxicillin and cefixime. They used computer analysis to understand how the substances' properties relate to their ability to kill bacteria. They also studied how the active substances interact with bacteria to better understand their effectiveness. The derivatives exhibiting strong antibacterial properties underwent molecular docking analysis to explore how they interact with specific amino acid residues located within the active site of peptide deformylase. This assessment aimed to evaluate their potential as inhibitors of peptide deformylase and, consequently, their efficacy as antibacterial agents. (Fig: 9)

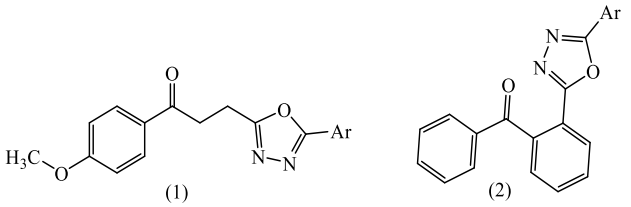


Fig:9 Novel 1,3,4-Oxadiazole Derivatives

1. 1-(4-methoxy-phenyl)-3-[5-(substituted phenyl)-1,3,4-oxadiazol-2-yl]propan-1-one.
2. (2-(5-aryl-1,3,4-oxadiazol-2-yl)phenyl)(phenyl)methanone

Y. Unver (2018) [xxv] and co-workers synthesized eight new compounds with thiophene, 1, 2, 4-triazolone, 1, 3, 4-oxadiazole, and morpholine parts. They confirmed the structures of these compounds by characterize elemental analyses, IR, ^{1}H NMR, and ^{13}C NMR. These new compounds were examined for how well they fight against oxidation and microbes. The compounds labeled 2(a-d), which had Schiff base, showed higher activity in tests like DPPH and FRAP compared to compounds labeled 3(a-d), which had both Schiff base and morpholine. Among compounds 2(a-c), the antioxidant potential was notable. Compound 2a displayed the most potent antimicrobial activity with the lowest MIC value of 31.25 µg/mL against Bacillus cereus RSKK 709.

J.N. Lalpara (2021) [xxvi] and coworkers undertook the task of designing and synthesized a series of novel 1, 3, 4-oxadiazol based Schiff base compounds (Fig: 10) employing a highly efficient strategy, resulting in exceptional yields. Newly synthesized molecules evaluated in vitro antibacterial studies against *Escherichia coli, Klebsiella pneumoniae, Bacillus subtilis,* and *Bacillus megaterium*. Each molecule was studied to understand its characteristics and how well it fought bacteria. This was done using a method called minimum inhibitory concentration (MIC). Additionally, in-silico parameters were used to look at other properties like drug-likeness, lipophilicity, and cytotoxicity. Some of the molecules, particularly those with a certain type of halogen called group 6d, 6f, 6g, and 6i, were found to be very powerful against bacteria and had good properties in-silico parameters.

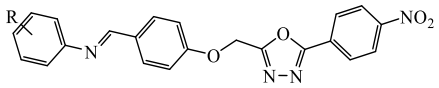


Fig:10 Synthesis of novel Schiff base derivatived 1,3,4-oxadiazole

Deshpande N.S. (2021) [xxvii] and colleagues created a new group of molecules called 1, 3, 4-oxadiazoles linked to Schiff bases. (Fig: 11) They aimed to investigate their potential against breast cancer by targeting the PARP-1 enzyme using computer simulations (in-silico). They analyzed how well these molecules fit into the enzyme using a method called molecular docking. They also checked their properties using computer-based tests like QikProp, Glide, and MM-GBSA binding free energy calculations by using Schrodinger suit 2019–2. The results showed that the molecules could bind well to the PARP-1 enzyme and had favorable properties for drug development. Some of these molecules showed promising activity against breast cancer, indicating their potential as future anticancer drugs.

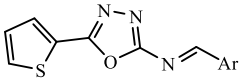


Fig:11 1,3,4-oxadiazole clubbed Schiff bases

1, 3, 4-Oxadiazole derivatives are really important in chemistry. They're a special type of compounds with unique properties. Scientists have discovered different ways to make these compounds, and available in the literature.

Consequently, there's a big need for easier ways to make 1, 3, 4-oxadiazole derivatives. One common method is the cyclodehydration of semi-carbazides, which requires

harsh reagents like phosphorous oxychloride [xxviii] or concentrated sulfuric acid [xxix]. Other options include Burgess-type reagents [xxx] or phosphonium salts[16], but they create a lot of by-products and are only good for solid-phase methods. However, some of these methods have problems like low yields, taking a long time, or needing strong, harmful chemicals. Concerning the synthesis of 1, 3, 4-oxadiazole derivatives several methods have been reported in the literature. The usually applicable route of synthesis for 1,3,4-oxadiazol involves reacting acid hydrizides or hydrazine with acid chlorides or carboxylic acids, then cyclizing diacylhydrazines using dehydrating agents like phosphorous oxychloride[4], phosphorous pentaoxide [xxxi], thionyl chloride [xxxii], polyphosphoric acid [xxxiii], triflic anhydride [xxxiv], or (Nisocyanimino-) triphenylphosphorane [xxxv-xxxviii]. Researchers have found that gram-positive bacteria are more susceptible to antimicrobial agents than gram-negative bacteria [xxxix].

SYNTHESIS STRATEGIES FOR 1, 3, 4-OXADIAZOLE 2-AMINE DERIVATIVES

Rakesh Singh (2014) [xl] and co-workers reviewed at different methods to synthesize 5-substituted-2-amino-1, 3, 4-oxadiazoles. They summarized these methods in Figure: 12. In the route a and b, they used acyl hydrazide intermediate reacted with cyanogen bromide or di-(benzotriazol-1-yl) methanimine. Method c involves dehydrating acyl semicarbazide, while method d uses semi-carbazones, which easily form the desired 1, 3, 4-oxadiazoles. Methods e and f utilize acyl thiosemicarbazide intermediates, which react differently to obtain the desired derivatives of 1, 3, 4-oxadiazole through oxidative cyclization reactions using iodine or carbodiimide derivatives.

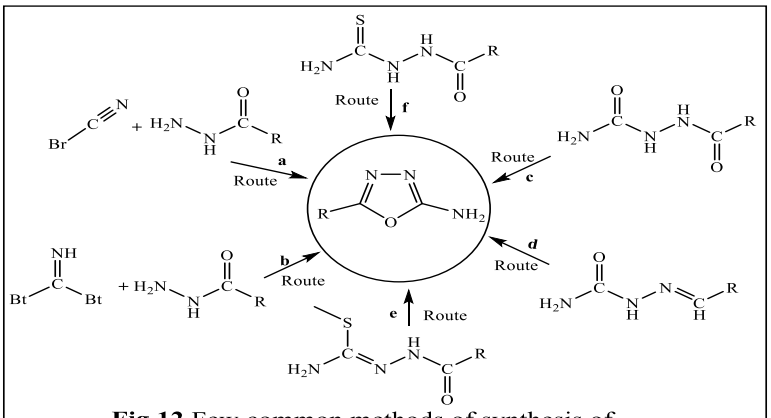
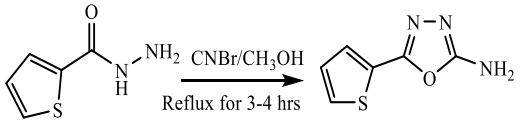


Fig.12 Few common methods of synthesis of 5-substituted-2-amino-1,3,4-Oxadiazole

M.A. El-Borai (1993) [xli] and his team by using the route (a) of above figure have reported the synthesis of 5-(thiophen-2-yl)-1, 3, 4-oxadiazol-2-amine. They mixed 2-thienyl hydrazide and CNBr together to make it. This method is good because it takes less time to react compared to other methods. (Fig: 13)



thiophene-2-carbohydrazide 5-(thiophen-2-yl)-1,3,4-oxadiazol-2-amine

Fig:13 Route for Synthesis of 5-(thiophen-2-yl)-1,3,4-oxadiazol-2-amine

A. Almasirad (2004) [xlii] and co-workers have been reported a series of synthesized new 2-substituted-5-[2-(2-fluorophenoxy) phenyl]-1, 3, 4-oxadiazoles and 1, 2, 4-triazoles. They carried out the Pharmacological evaluation of these compounds in the lab like anti-convulsant

activity by PTZ and MES models, and the compound established to have good anti-convulsant activity. (Fig: 14)

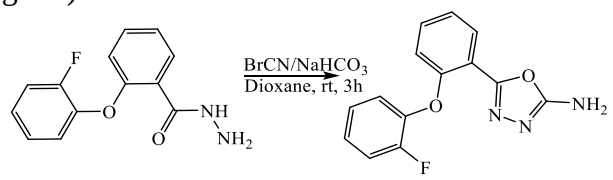


Fig:14 Synthesis of new 2-substituted-5- [2-(2-fluorophenoxy)phenyl] -1,3,4-oxadiazoles

N.B. Patel and J.C. Patel (2010) [xliii] successfully achieved the synthesis of 5-aryl-2-amino-1, 3, 4-oxadiazole compounds II with impressive yields ranging from 62 to 70 percent. (Fig: 15)

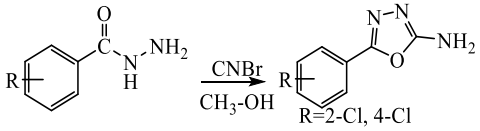


Fig: 15 Synthesis of 5-aryl-2-amino-1,3,4-oxadiazole

Kerimov (2012) [xliv] and co-workers synthesized a new group of compounds called 2-amino-1, 3, 4-oxadiazoles. They did this by reacting 2-(2-(4-substituted-phenyl)-1H-benzo[d]imidazol-1-yl) acetohydrazide with cyanogen bromide. The yield of these compounds ranged from 33% to 60%. (Fig: 16)

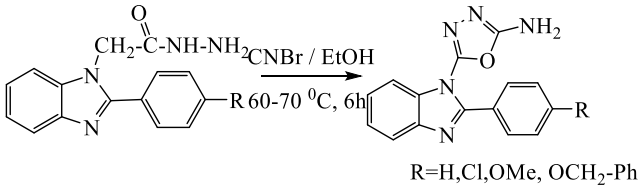


Fig:16 Synthesis of 2-amino-1,3,4-oxadiazoles

A.R. Katritzky (2002) [xlv] and co-workers obtained 5-aryl-2-amino-1, 3, 4-oxadiazole compounds using approach (b) with good yields; starting from di-(benzotriazol-1-yl) methanimine and arylhydrazides reaction**.** (Fig: 17).

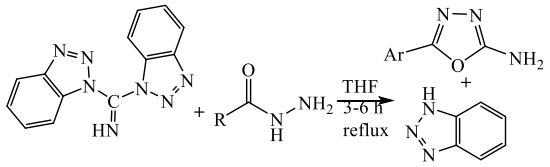


Fig:17 5-aryl-2-amino-1,3,4-oxadiazole compounds

Rajak H. (2011) [xlvi] and co-workers as well as **Gupta V. (2008)** [xlvii] and co-workers used the approach d frequently used for the synthesis of 5-substituted-1, 3, 4-oxadiazol-2-amines. It is the oxidative cyclization reaction of semicarbazones by using bromine in acetic acid. It forms a new compound. (Figure 18).

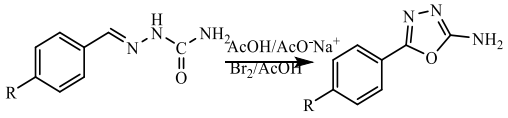


Fig: 18 Where, R=-H, -NO_2, -Me, -OH, -F, -OMe, -NH_2, -$N(CH_3)_2$

P.P. Roy (2017) [xlviii] and his team synthesized 2-Amino-5-aryl-1, 3, 4-oxadiazoles [3A-3G]. They followed a procedure (Fig: 19). They dissolved 0.01 M semicarbazone (2A-2G) and 0.02 M sodium acetate in 30–40 mL glacial acetic acid in a 100 mL round-bottomed flask. They added 0.7 mL Bromine drop by drop to 5 mL glacial acetic acid while stirring. They stirred for 30 minutes and then poured the content on crushed ice. They separated, dried, and recrystallized the solid product from free ethanol.

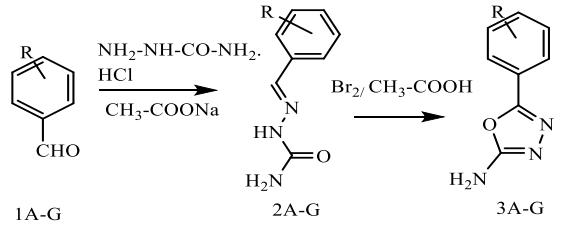


Fig:19 Synthetic pathway for compounds 3A-G

R= 4-OH, 2-Cl, 3-Br, 4-N(Me)$_2$,2-Cl, 3-Br, 4-OCH_3

L.K. Sharma (2010) [xlix] and his colleges, also the **B. Lotfi (2011)** [l] applied an alternate method to achieve the 5-aryl-2-amino-1, 3, 4-oxadiazoles from Semicarbazones by electro-cyclization. (Fig: 20)

R=-C_6H_5, 4-Cl-C_6H_4, 4-MeO-C_6H_4, 3-NO_2-C_6H_4,4-OH-C_6H_4, -CH_3

Fig:20 Electro-cyclization of semicarbazide into 5-aryl-2-amino-1, 3, 4-oxadiazoles

N.R. Rivera (2006) [li] and cyclized acylthiosemicarbazide to 5-aryl-2-amino-1, 3, 4-oxadiazoles in good yield using 1, 3-dibromo-5, 5-dimethylhydantoin which is efficient oxidizing agent for cyclization of the reactant. (Fig: 21) The best part about this method is that the chemicals they used are not expensive and they're safe to work with. This makes it easier for other scientists to try out this method in their own labs without worrying too much about cost or safety.

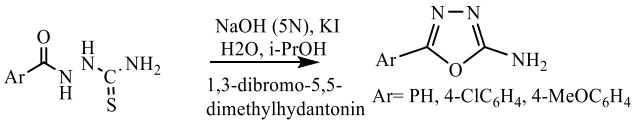
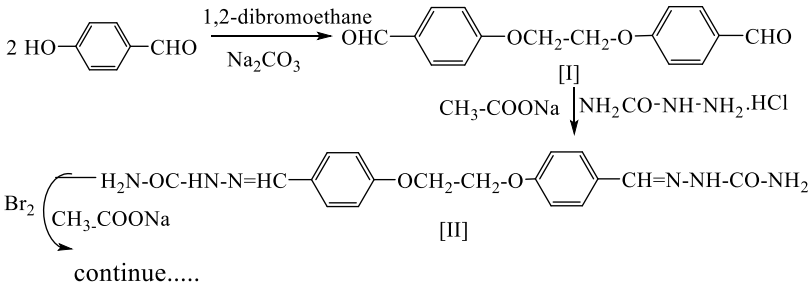


Fig:21 Synthesis of acylthiosemicarbazide to 5-aryl-2-amino-1,3,4- oxadiazoles

N. H. Karam (2010) [lii] and co-workers have synthesized new amides [IV] a-e and Schiff bases [V]f-h. These compounds came from 2-amino-1, 3, 4-oxadiazoles [III] and were identified using physical and spectral information. They prepared 2-amino-1, 3, 4-oxadiazoles by treating bromine with semicarbazide [II]. Semicarbazide was made by reacting dialdehyde [I] with semicarbazide hydrochloride. This reaction took place with sodium acetate and led to an intramolecular cyclization. (Fig: 22)



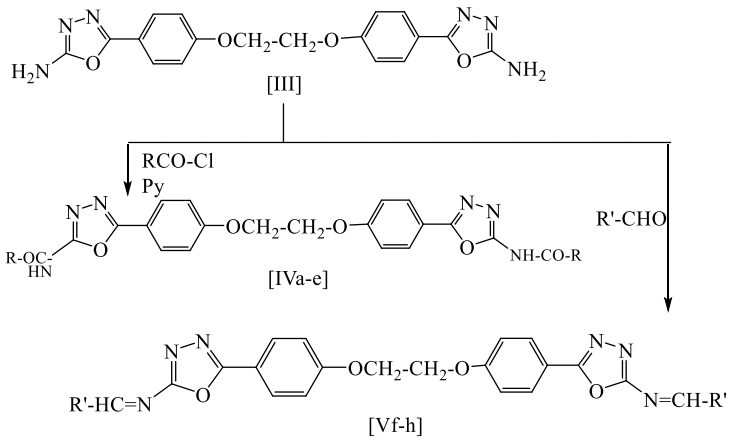


Fig:22 Synthesis of new amide compounds [IV]a-e and Schiff bases [V]f-h resulting from 2-amino-1,3,4-oxadiazoles [III]

G. Kaur (2012) [liii] and co-workers have been reported the synthesis of 1,3,4-oxadiazoes by reacting semicarbazide with conc. Sulphuric acid (H_2SO_4) and then it was kept overnight and then pour it into the ice-cold water. Then it is neutralized with ammonia and extracted with ether. (Fig: 23)

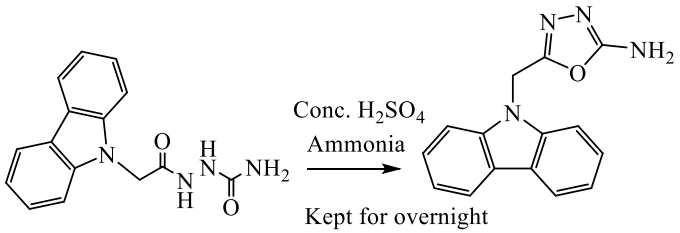


Fig:23 Synthesis of 1,3,4-oxadiazoes

I.A.G. El-Karim (2014) [liv] and his colleagues have synthesized 2-amino-5-heptadecyl-1, 3, 4-oxadiazole (1). Stearic acid (0.01 moles) and semi-carbazide hydrochloride (0.01 moles) were combined in 20 mL of $POCl_3$, and the resulting mixture was subjected to refluxing for a duration of 8 hours. After that, they concentrated the mixture and cooled it. Then, they poured it onto ice while stirring. They filtered off the solid produced and recrystallized it from ethanol. They obtained Compound 1 as a pale-yellow powder in 77% yield. Its melting point was between 102°C and 104°C. They calculated that Compound 1 should contain 70.54% carbon, 11.53% hydrogen, and 12.99% nitrogen. However, the actual percentages they found were slightly lower: 70.23% carbon, 11.29% hydrogen, and 12.81% nitrogen. (Fig: 24)

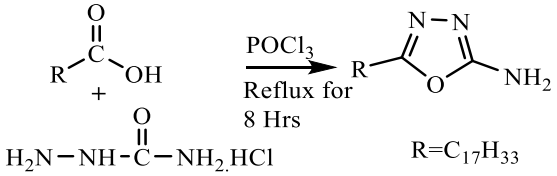


Fig:24 Synthetic routes of compounds-1

Riyadh (2019) [lv] and co-workers have synthesized the 1, 3, 4-oxadiazoles derivatives with the treatment of an appropriate 1, 2, 3-triazole derivative and semicarbazide hydrochloride dissolved in $POCl_3$. Further the obtained reaction mixture was refluxed for overnight. Then reaction mixture was cooled into room temperature and slowly poured onto crush-ice to get a precipitate. The obtained precipitate was stirred for 15 min in the same solution and further treated carefully with 50% aqueous sodium hydroxide solution. Finally, the precipitate was collected by filtration process under vacuum, washed with water and dried it. (Fig: 25)

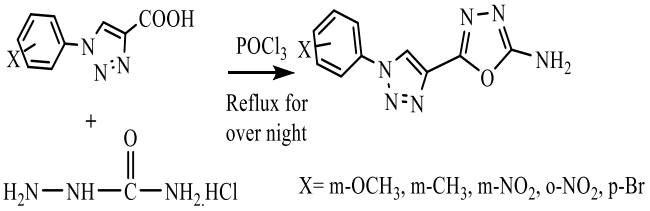


Fig:25 Synthesis of 1,3,4-oxadiazole derivatives

Hameed (2010) [lvi] and coworkers suggested a mechanism for the formation of 1, 3, 4-oxadiazole, (Fig: 26) as shown in Figure 24. Additionally, **S.K. Kolli (2016)** [lvii] proposed a mechanism for the same process.

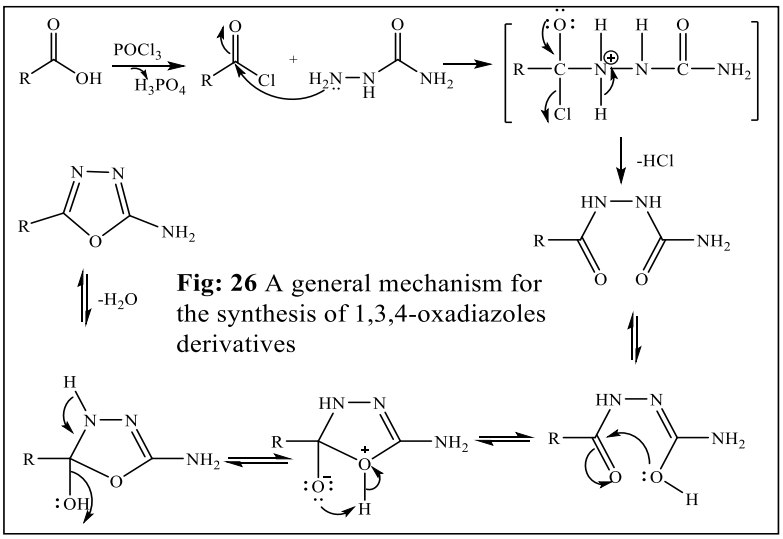


Fig: 26 A general mechanism for the synthesis of 1,3,4-oxadiazoles derivatives

Eid E. Salama (2020) [lviii] have been synthesized 5-(4-bromobenzyl)-1,3,4-oxadiazole-2-amine (**1**) and 5-(3-nitrophenyl)-1,3,4-oxadiazole-2-amine (**2**) (Fig: 26) starting from the mixture of 4-bromophenyl acetic acid and/or 3-nitro benzoic acid (1 mol) and semi-carbazide (0.455 grams, 1 mole equivalent) was dissolved in 3 milliliters of phosphorus oxychloride and subjected to reflux for a duration of 45 minutes. The reaction content was cooled to room temperature then 3 mL of water was added cautiously. Then the mixture was refluxed for four hours, filtered on hot condition and the solid washed by warm water and the filtrate was basified with potassium hydroxide saturated solution. The solid formed was separated by filtration and then purified through recrystallization using ethanol as the solvent. The colour, percentage yield, melting point, solubility and TLC profile were studied for all the eight synthesized compounds.

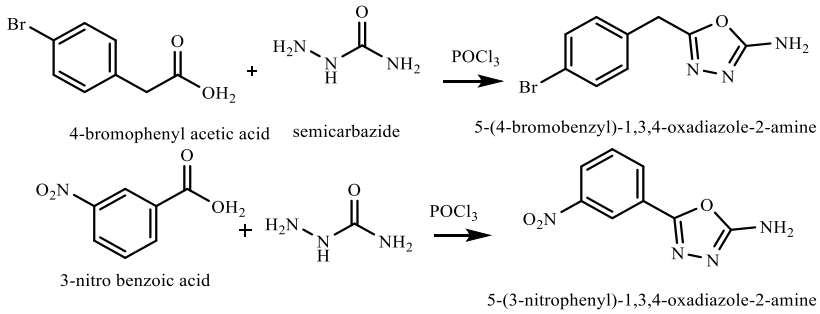


Fig:26 Synthetic routes of 2-Amino-5-aryl-1,3,4-Oxadiazoles

Iodine-Mediated Synthesis: Niu [lix] and colleagues have developed a method for synthesizing 2-amino-1, 3, 4-oxadiazoles using iodine as a mediator. (Fig: 27)

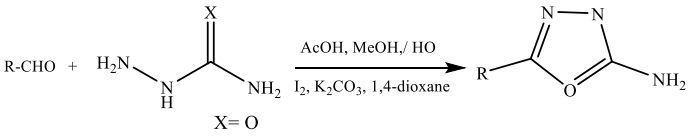


Fig.27: Synthesis of 2-amino-1, 3, 4-oxadiazole using iodine as a mediator

CONCLUSION:

The review has concluded with the background and significant pharmaceutical uses of the 1, 3, 4-oxadiazole nucleus. This compound shows various biological activities such as antimicrobial, anti-inflammatory, analgesic, fungicidal, antimalarial, antidepressant, hyperglycemic, antiretroviral, antibiotic, muscle relaxants, antihypertensive, anti-miotics, anticancer, antioxidant, inhibitors for obesity and diabetes. This review paper comprises various synthetic routes of 1, 3, 4-Oxadiazole-2-amines derivatives, and it can be used for further researches.

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COFLICT OF INTREST:

The authors affirm the absence of any competing financial interests.

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