International Journal for Multidisciplinary Research (IJFMR)
E-ISSN: 2582-2160 ● Website: www.ijfmr.com ● Email: editor@ijfmr.com

Occurrence, Chemistry and Synthesis of Various Novel Methods of Oxadiazole

Sandeep Kumar[1], Arvinder Pal Singh[2], Anshi Kumari[3], Dr. Amit Aggarwal[4]

Maharaja Agrasen School of Pharmacy, Maharaja Agrasen University, Baddi, Distt. Solan,Himachal Pradesh, India.

ABSTRACT

Oxadiazoles are a kind of heterocyclic molecule that can be identified by their five-membered ring structure, two azo groups, and a single oxygen atom in their make-up. These characteristics allow them to be distinguished from other heterocyclic compounds. Because of these features, it is possible to differentiate them from several other heterocyclic compounds. They have the highest importance and relevance in the area of heterocyclic chemistry, which is also where they have the most value. They are of the biggest significance. Research is being conducted on it in substantial amounts due to the fact that it has the potential to function as a starting point for the synthesis of bioactive molecules that are beneficial to the body. This article provides a brief discussion of the physicochemical features of oxadiazole, including its spectra and a few examples of how it may be synthesised. The article can be found here. The pharmacological effects of oxadiazole derivatives were investigated by our team of researchers, and the findings indicated that these compounds had a number of positive benefits, including anti-inflammatory, anti-cancer, anti-fungal, anti-osteoporotic, and anti-microbial properties. In this piece, we will have a brief discussion on both synthetic and naturally occurring medications that include the oxadiazole ring in addition to the moiety. This talk will focus on pharmaceuticals that have been manufactured. The production of these compounds may take place in a laboratory, or they maybe found occurring naturally in their natural environments.

Keywords: Oxadiazole, pharmacological activity Anti-microbial, Anticancer, Anti-osteoporotic.

INTRODUCTION

In case you were wondering, the molecular structure of oxadiazole is represented by the chemical formula $C_2H_2N_2O$, and it is categorised as a molecule that belongs to the family of heterocyclic aromatic compounds. For those who are interested in learning more, the oxadiazole molecule can be found here. Within each of the five members that comprise this ring, there are two nitrogen atoms, two carbon atoms, one oxygen atom, and two double bonds. All of these atoms are connected to one another by double bonds [1].

The 1, 2, 3-isomer, on the other hand, is inherently unstable and will continuously transform into the diazoketone tautomer. In 2008, it was discovered that oxadiazoles were useful in the fight against the parasite that is responsible for schistosomiasis. There was no evidence to suggest that any people had

any unfavourable impacts as a result of this [2]. Stable oxadiazoles may be found inthe chemical structures of a number of different pharmaceuticals, such as raltegravir, which is a medication used to treat viral infections; butalamine; fasiplon; oxolamine; and pleconaril; amongothers. Additional examples of drugs that are considered to be included in this group aretiodazosin, nosapidil, and furamizole [3]. The fact that oxadiazoles have been shown to be effective against a wide variety of diseases throughout the course of their clinical testing is the primary reason for their significance in the field of pharmaceutical chemistry. Oxadiazoles have been shown to be effective against a wide variety of diseases. Chemists that work in the syntheticfield nearly always have an interest in molecules that, in one form or another, include both nitrogen and oxygen [4]. This is because nitrogen and oxygen may be found in a broad range of compounds, both those that exist naturally and those that are synthesised, that have positive effects on living organisms. These compounds include those that occur naturally as well as those that are synthesized [5].

A study of the relevant literature revealed that some of the processes that 1, 3, 4 oxadiazole is exposed to include electrophilic substitution, nucleophilic substitution, thermochemical reactions, and photochemical reactions, among other processes. Because of this, it has been put to use in the manufacturing of a large number of pharmaceutical compounds that make use of 1, 3, and 4 oxadiazole. These compounds may be found in a wide variety of medicines. It has been shown that compounds based on 1,3,4-oxadiazole have specific anti-edema and anti-inflammatory effects, and these activities have been demonstrated [6].

NATURALLY OCURRING OXADIAZOLES:

Oxadiazole cores and the structures produced from them have the potential to be discovered in a very small number of naturally occurring molecules. As an example, we will utilise the 3- substituted indole alkaloids phidianidines A and B. These compounds are already known. These are provided for your convenience as a reference. The aeolid opisthobranch known as Phidiana militaris was successfully used for the extraction of phidianidines A and B by Carbone *et al.* [7]. They have a method of action that is selective for blocking the dopamine transporter, in addition to serving as partial agonists of the mu opioid receptor (DAT). Because neither phidianidine A nor phidianidine b have any cytotoxic properties, it is possible to utilise them against CNS targets without the danger of experiencing any negative side effects. There is a possibility that quisqualic acid, another molecule that belongs to the oxadiazole family, is found in nature. A metabolite that was developed as a result of an extraction procedure that used the seeds of the plants Quisqualis fructus and Quisqualis indica. It has been found that quisqualic acid can function as a potent agonist for group I metabotropic glutamate receptors as well as -amino-3-hydroxy-5- methyl-4- isoxazolepropionic acid receptors. This finding was made possible by the fact that quisqualic acid has a structure similar to that of amino-3-hydroxy-5- methyl-4- isoxazolepropionic acid. The fact that quisqualic acid has a structure that is comparable to that ofan amino acid made it feasible for researchers to make this discovery [8].

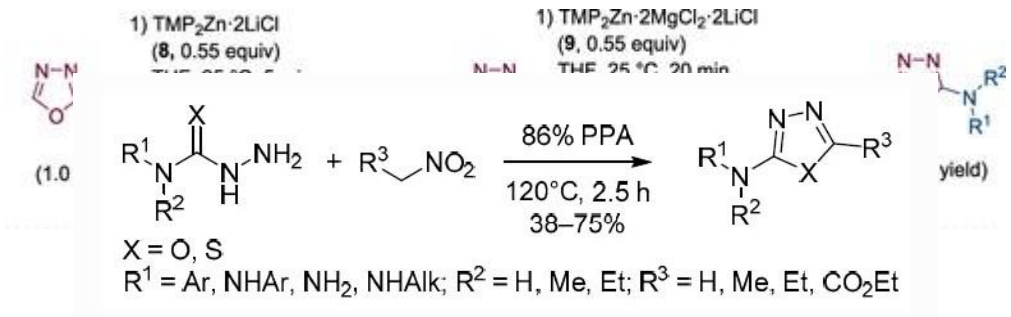
Chemistry

Oxadiazole does not meet the criteria for a strong base because of the inductive activity that it exhibits as a result of the presence of a heteroatom in the ring. This is caused by the presence ofa heteroatom.

As a consequence of this, its reactivity is much less than that of other bases. Oneof the characteristics that establishes it as a member of the category of conjugate dienes to which it belongs is the fact that it has two nitrogen atoms, just like pyridine does. This is another one of its qualities. Because carbon has a low electron density, the process of electrophilic substitutionat carbon is one that is very challenging to carry out. This may mostly be attributed to the presence of pyridine-like nitrogen in the ring, which has an action that is comparable to that of anelectron-drawing magnet [9].The absence of aromaticity in the molecule may be traced back to the existence of two nitrogens that are of the pyridine type. According to the findings of a number of studies that investigated the pairings of 1,2,4- and 1,3,4-oxadiazole compounds, the 1,3,4-oxadiazole isomer was found to always have a lower magnitude of lipophilicity (log D) compared to its 1,2,4-oxadiazole isomer. This was determined by comparing the two compounds' log D values. The fact that the 1,3,4- oxadiazole isomer had a lower log D value than the parent chemical was the starting point forour investigations, which led to the findings that you see here. In addition, they differ from one another in terms of the compounds' water solubility, metabolic stability, and the propensity to suppress hERG activity. The 1, 3, 4-oxadiazole isomers have been the primary focus of this study's examination for the great majority of its duration. The 1, 2, 4, and the 1, 3, 4 regioisomers each have charge distributions that are distinctively unlike those of the other, which is the primary factor that contributes to the distinctiveness of the profiles that each has. Additionally, the 1, 2, 4 and the 1, 3, 4 regioisomers each have their own unique profiles [10].

Reactions Using 2,2,6,6-Tetramethylpiperidyl Bases

This paper presents a thorough investigation into the regioselective zincation and magnesiation of 1,3,4-oxadiazole by the use of TMP bases. TMP stands for 2,2,6,6-tetramethylpiperidyl. When the concentration of THF was only mild, all of these compounds were formed: TMPMgClLiCl, TMPMgClLiCl, TMPZnClLiCl, and TMPZnClLiCl. All of these compounds are known as TMPZnClLiCl. The subsequent trapping of functionalized heterocycles with various electrophiles allows for access to the functionalized heterocycles that were previously inaccessible. One example of such an electrophile is the hydroxylamino benzoate, which is tolerant of a broad range of functional groups and is one kind of these electrophiles [11].

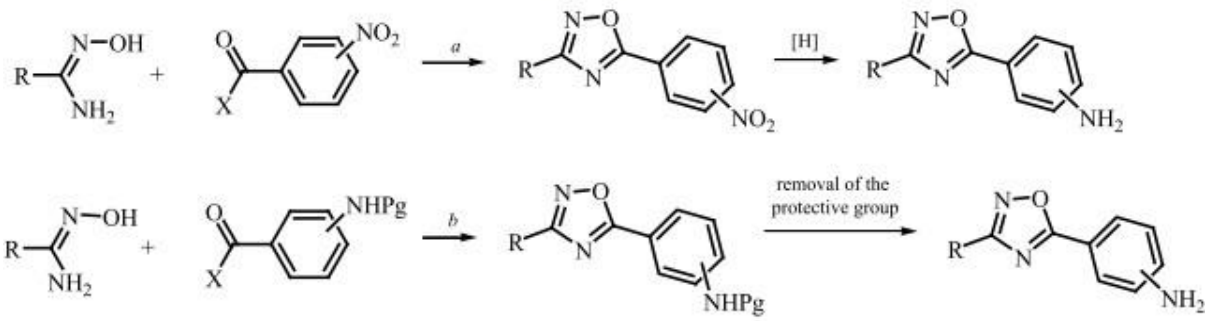


It has been shown that the presence of polyphosphoric acid in the presence of nitroalkanes leads to a unique reaction in which the nitroalkanes get electrophilically activated. This activation takes place as a result of the reaction. It has been shown that this activation of the nitroalkanes is really the case. After a subsequent nucleophilic attack with semicarbazides or thiosemicarbazides, it is possible to form 2-amino-1,3,4-oxadiazoles as well as 2-amino-1,3,4- thiadiazoles. This may be accomplished. These compounds all begin with the same element or substance as their parent [12].

The Structural Analysis of 1,2,4-Oxadiazole-Bound Palladium(II) Acyclic Diaminocarbene Complexes

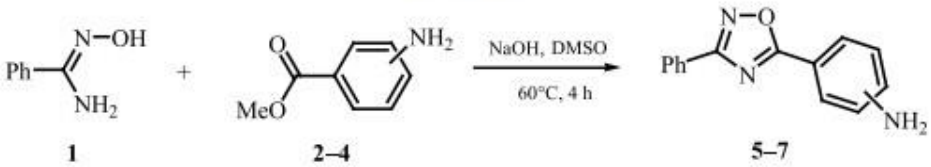
The formation of acyclic diaminocarbene complexes is the product of the reaction between 1,2,4-oxadiazolyl anilines and the bis(xylylisocyanide) Pd(II) complex. As a direct consequence of the reaction, these complexes are produced. At no point in time does the oxadiazole ring take part in any of the reactions that are taking place. Research was conducted using techniques such as mass spectrometry, nuclear magnetic resonance (NMR) spectroscopy, and X-ray diffraction of single crystals in order to confirm the identities of the compounds that had been found as well as the structures of those compounds [13].

Scheme 1.



X = Hlg, OH; Pg – protective group.

Scheme 2.



1 **2–4** **5–7**

p-amino (**2**, **5**), *m*-amino (**3**, **6**), *o*-amino (**4**, **7**).

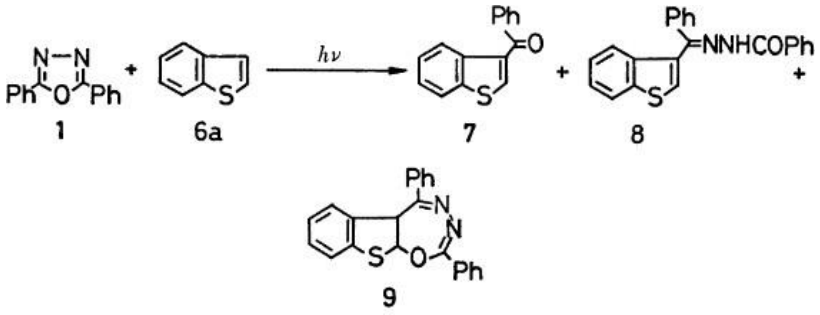
Photochemical Reactions with 2,5-Diphenyl-1,3,4-oxadiazole with Benzo[*b*]thiophenes

Irradiating 2,5-diphenyloxadiazole 1 with benzothiophene 6a led to the production of varied amounts of 3-benzoylbenzothiophene 7, in addition to the benzoylhydrazone 8 of that chemical and/or oxadiazepine 9. The compounds 1 and 6a go through a photochemical process that, when combined with the sensitizer benzophenone, results in the formation of the [2+2] cycloadduct 12.It has been revealed that the number nine may be broken down into the components one and six aby making use of photochemical processes. This discovery was made. When benzophenone is used in a sensitizer capacity, the [2+2] cycloadduct 19 is produced as a direct consequence. The 3-benzoyl-2-methylbenzothiophene benzoylhydrazone 18, which in turn was formed from the 2- methylbenzothiophene 6b, is what leads to the formation of this cycloadduct. When chemical 1 is irradiated with 3-methylbenzothiophene 6c, a product known as the [2+2] cycloadduct 20 is generated. This takes place regardless of whether or not benzophenone is present in the environment. Iodine catalyses a photochemical reaction between compound 1 and either compound 6a or 6b, producing the corresponding 3-benzoylbenzothiophene, 7 or 21, and benzoylhydrazone, 8 or 18, respectively. This reaction takes place in the presence of iodine. Compound 1 will undergo this reaction when it is brought into contact with either compound 6a or 6b. In contrast,

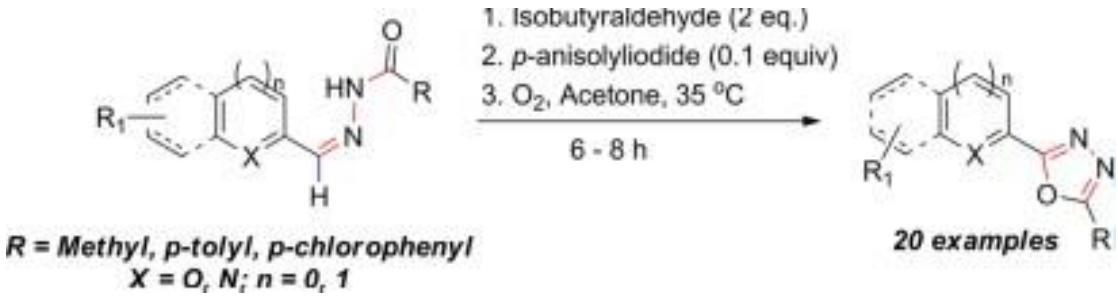
the formation of the [2+2] cycloadduct 23 is the result of the reaction between 6-c and 2-benzoyl-3-methylbenzothiophene 22, which was reported before. This reaction was carried out at room temperature. In addition to that, further information on the molecular underpinnings that underlie these reactions is supplied as well [14].

Synthesis of Substituted 1,3,4 Oxadiazoles:

In the absence of any metals and in the presence of molecular oxygen, isobutyraldehyde underwent auto-oxidation, which led to the formation of an acyloxy radical throughout the course of the reaction. After that, they were used on a regional scale in the synthesis of hypervalent iodines by the utilisation of p-anisolyl iodide. This process took place in Europe. This, in turn, led to the manufacture of N'-arylidene acetohydrazides, which were subsequently utilised in the synthesis of substituted 1,3,4-oxadiazoles with yields ranging from good to outstanding. Ultimately, this led to the production of substituted 1,3,4-



oxadiazoles. Due to the characteristics of the reaction process, it was able to carry out a wide variety of substrate substitutions on the hydrazides. These replacements included: Controlled experiments as well as previous studies have provided support for the concept that it is beneficial to generate an in situ iodosylarene complex, which accelerates product production [15].



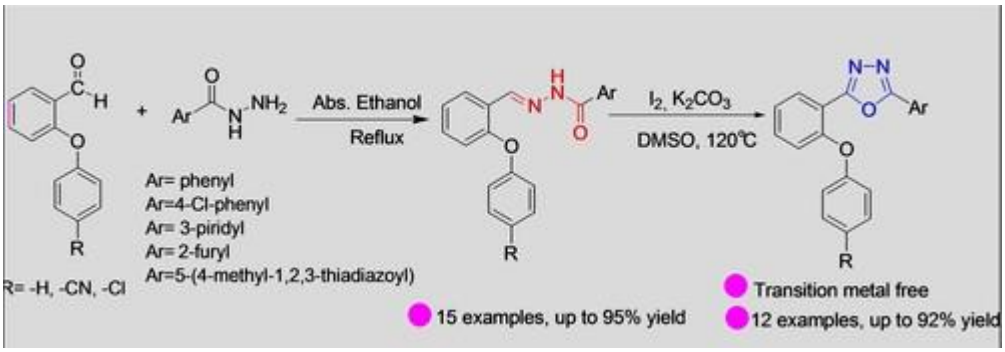
From N-Acyl Hydrazones

We have come up with a process for the production of carbon monoxide that is not only easy to carry out but also quite successful in its application. This technique makes use of a catalyst that is made up of iodine molecules at the molecular level. The condensation of 2- arenoxybenzaldehydes with substituted hydrazides results in the production of N-acyl hydrazones, which are the progenitors of a novel family of 2,5-disubstituted 1,3,4-oxadiazoles.

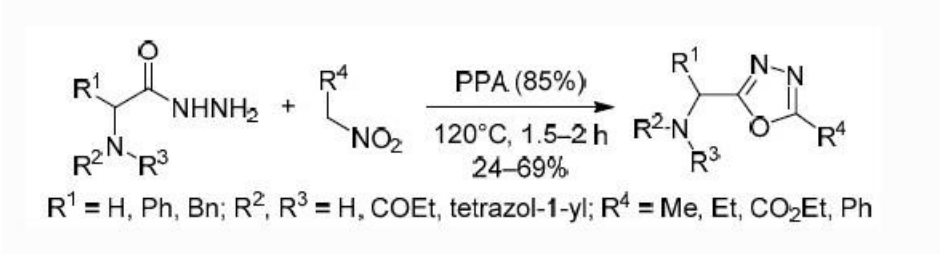
These N-acyl hydrazones were created as a byproduct of the reaction. This reaction occurred as a direct consequence of the reaction that took place between 2-arenoxybenzaldehydes and substituted hydrazides. These oxadiazoles were found by a process known as "accidental discovery"[16].

From amino acid derivatives

In the process of synthesising alkylamines having a 1,3,4-oxadiazole heterocyclic group, we made use of an unique preparative approach, which is outlined in the aforementioned piece of writing. This approach

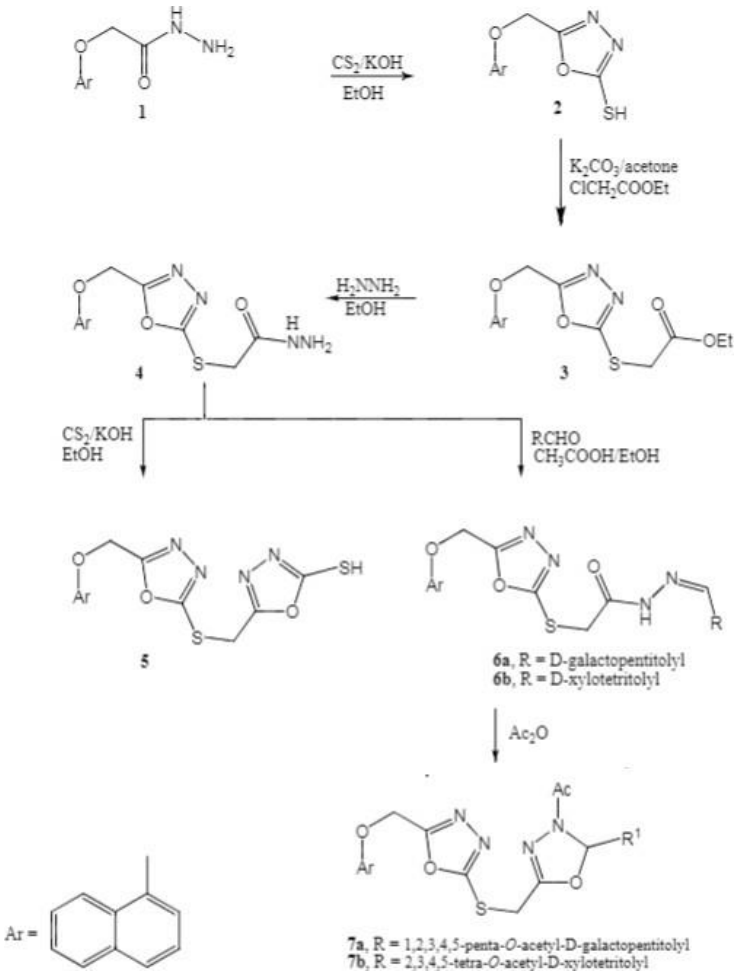


may be disassembled into its component parts, which include the formal (4+1) cyclocondensation of amino acid hydrazides with nitroalkanes that have been electrophilically activated in polyphosphoric acid. These are the method's essential building blocks [17].



From Acyclic Nucleoside

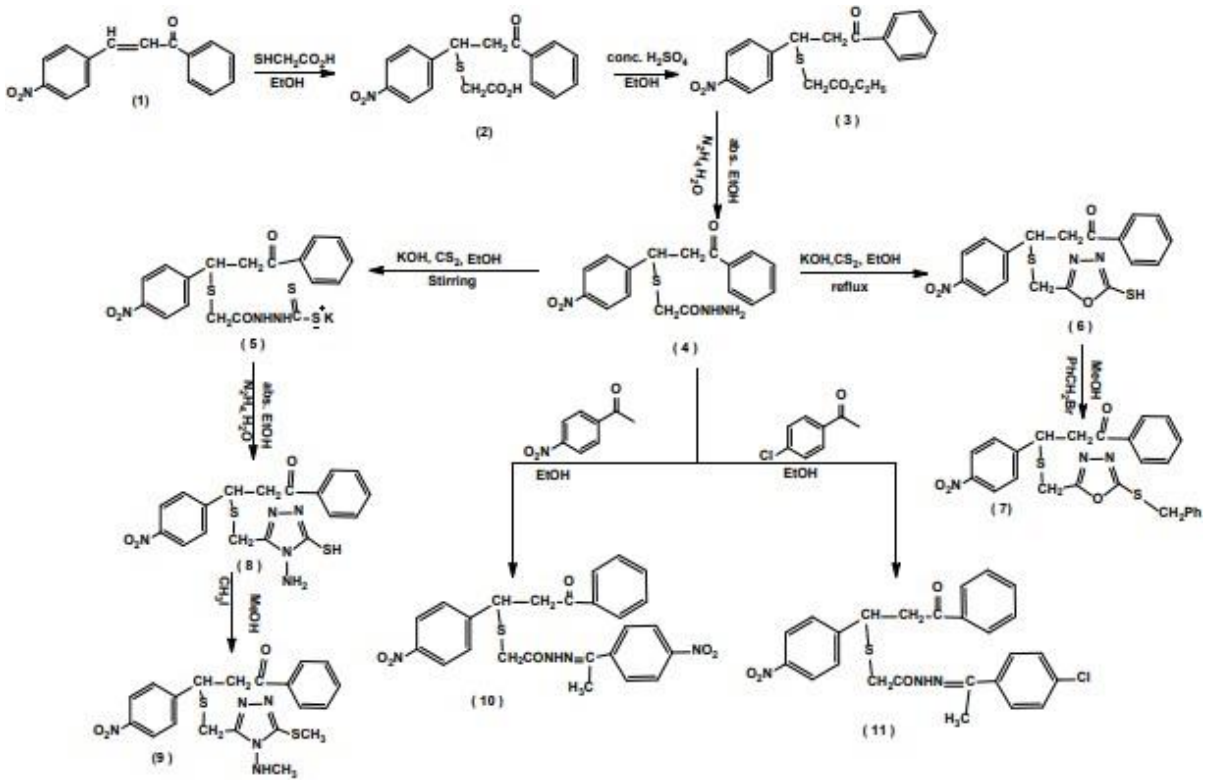
There is a diverse selection of unique 5-[(naphthalen-5-yloxy)methyl] compounds available for your consideration. The 1,3,4-oxadiazole compounds with the numbers 2 through 5 and 8 through 11 were created as a result of additional investigation. 2-5-[(naphthalen-5-yloxy)methyl is the name given to this particular chemical. The synthesis of 1,3,4-oxadiazol-2-ylthioace- tohydrazones 6a and 6b was the outcome of the reaction between hydrazide 4 and the monosaccharides that were suited for the reaction. In order to get the substituted oxadiazoline derivatives 7a and 7b, the sugar hydrazones 6a and 6b were subjected to a cyclization technique that was carried out using acetic anhydride as the catalyst. After conducting research on the antiviral potential of the compounds that were synthesised, the researchers found that several of the compounds exhibited moderate to high antiviral activity against the human immunodeficiency virus (HIV-1) [18].



From Chalcones

In the synthesis of substituted 1,3,4-oxadiazole, 1,2,4-triazole, and Schiff base, it has been shown to be highly productive to use chalcones as the starting material. Chalcones may be found in the following: The evidence suggests that this has been the case, with a significant amount of success. As a result of a reaction that was carried out with mercapto acetic acid, the chalcone compound (1) was transformed into a carboxylic acid. This change occurred as a consequence of the reaction (2). Compound 3 was made when compound 2 was esterified in an acidic environment, which led to the formation of the environment. Following the completion of its production, compound 3 was isolated (3). The reaction between the ester and $N_2H_4.H_2O$ resulted in the creation of the acid hydrazide, which is denoted by the number 4. (4). Oxadiazole was generated by the process of refluxing component 4 under the same conditions that were present before the production of compound 5, which was formed by the reaction of component 4 with CS2 and potassium hydroxide. Compound 5 was produced through the production of oxadiazole (6). Because of the reaction of (6) with benzyl bromide, we were able to get the substituted oxadiazole as a result (7). The 1,2,4-triazole (8) that was produced as a byproduct of the cyclization of molecule (5) was then subjected to treatment with methyl iodide in order to produce compound. This treatment was carried out in order to produce compound. The creation of compound was the end outcome of this procedure (9). (9). The production of Schiff bases occurred as a result of the interaction between component (4) and the substituted acetophenone. Infrared and proton nuclear magnetic resonance (IR and 1 H-NMR) tests were utilised to validate the structure of the compounds that were

synthesised. These tests produced data on both the physical and spectral properties of the compounds. In order to validate the structure of the compounds, several experiments were carried out [19].

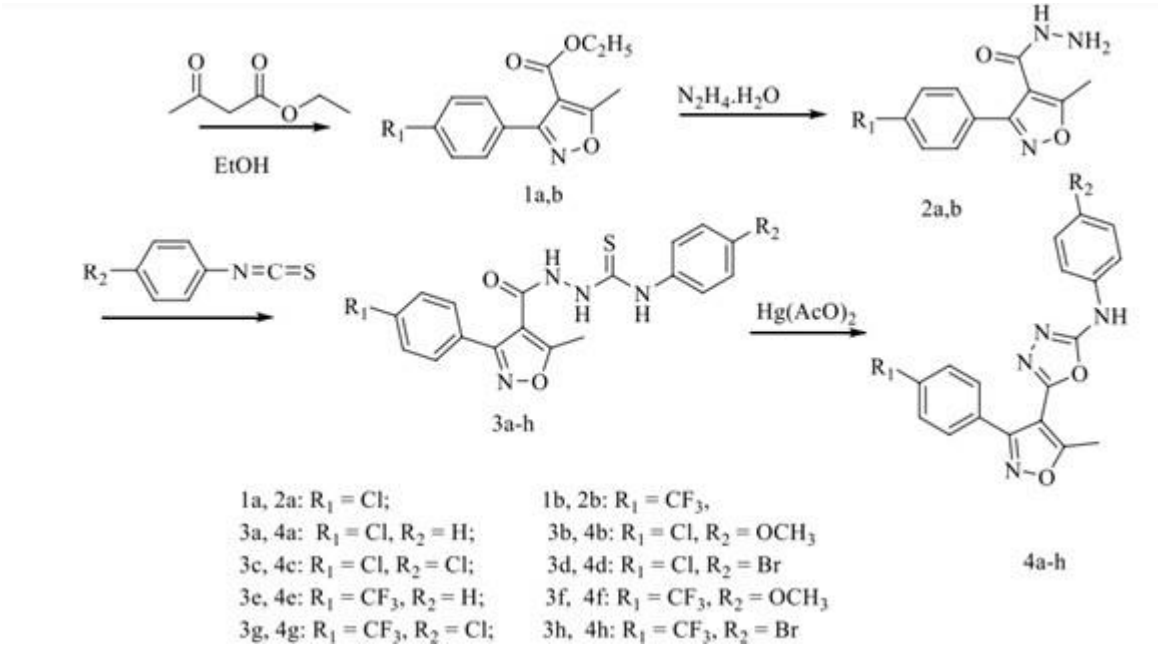


Synthesis of compound (1-11)

From 4-Chloro and 4-Trifuoromethyl Benzaldehyde by Multi-Step Reactions

2- (Substituted isoxazol-4-yl) Ethyl acetoacetate, 4-chloro and 4-trifluoromethyl benzaldehyde, hydrazine hydrate, aryl isocyanate, and hydroxylamine hydrochloride were the components that were utilised in the multi-step process that was utilised by Liu et al. (2014) in order to produce 5-arylamino-1,3,4-oxadiazole derivatives. This process was utilised in order to produce 5- arylamino the 5-aryla needed to be manufactured, therefore this procedure was carried out. A study was conducted to investigate whether or not the synthetic versions are effective antifungal agents against Rhizoctonia cerealis and Botrytis cinerea. The results of this study are currently being analysed. The aforementioned research has been carried out. The EC50 values of the compounds that were investigated ranged anywhere from 14.03 to 48.63 g/mL when the fungus Botrytis cinerea was used as a measuring stick. If you look at it one way, this places them at or below the same level as carbendazim, which has an EC50 value of 48.68 g/mL. Another way to look at it is that this puts them in the same ballpark. It would seem that the chemicals that were synthesised demonstrated antifungal effectiveness that ranged from moderate to high, if this finding is to be believed. At effective concentration levels that were significantly lower than 20 g/mL, compounds 4b, 4f, and 4g were proven to have significant antifungal activity. This wasthe case even though the concentrations were much higher. In comparison to carbendazim, the EC50 values against Rhizoctonia cerealis were discovered to be much higher, falling

somewhere in the range of 37.39-80.05 g/mL. The EC_{50} values for carbendazim might be found in the lower end of that range. Because of this fact, it would seem that the compounds that were produced hada very mild inhibitory impact on the reaction that was being studied.[20].



Scheme: Structure for the 2- (Substituted isoxazol-4-yl) derivatives of 5-arylamino-1,3,4-oxadiazoles

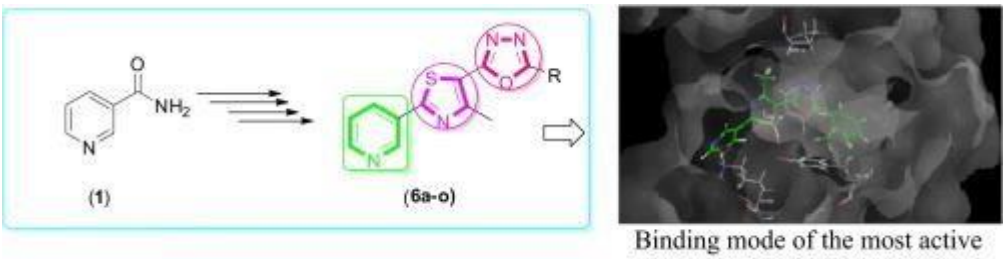
Cancer-fighting analogues of 2,5-disubstituted-1,3,4-oxadiazole

The current work marks a continuation of our examination into the possibility of developing new treatments for cancer. It does so by providing details regarding the design, synthesis, andevaluation of a variety of distinct oxadiazole analogues. The aryl core of IMC-038525, which is a tubulin polymerization inhibitor, NSC 776715, and NSC 776715 served as the basis for the design and synthesis of new oxadiazole analogues (4a-h) and NSC 776715. These results were published in the journal Biochemistry (4i-q). These counterparts were each assigned the numerals 4a through 4h or 4i through 4q, depending on which set they belonged to. Infrared, nuclear magnetic resonance (NMR), and mass spectrum data, in addition to elemental examinations, were employed in order to characterise and verify the absolute purity of each and every component. This was accomplished by using a combination of techniques. This was successfully completed (C, H, and N analysis). In accordance with the screening procedure developed by the National Cancer Institute, seven more compounds were subjected to a battery of tests to determine whether or not they had characteristics that may be able to fight cancer. These tests were performed on nine separate panels, each of which had sixty distinct cell lines in total (sixty cancer cell lines developed by the NCI). In accordance with the procedure that was published, ten distinct compounds were tested for the potential to either halt or significantly delay the growth of cancer in either the HeLa or the MDA-MB-435 cell lines. In the course of the research, these two different cell lines were analysed. Calculations of the GI_{50}, LC_{50}, and TGI dose-related parameters were performed for each of the four different drug concentrations (107, 106, 105, and 104 M). It was shown

that compound 4j was more vulnerable to the impacts of MOLT-4, IGROV1, HCT-116, and K-562, with comparable percent growth inhibitions of 50.38, 48.45, and 46.26 respectively. When the anticancer activity of compound 4j was evaluated, it indicated that it was most effective at a concentration of 10 million M. This value was determined by the results of the experiment. Imatinib is considered to be the "gold standard" therapy for cancer, yet the chemical 4j performed much better in comparison when it was tested against 41 distinct human cancer cell lines. HeLa cells had a GI50 value of 36.7 M when it came to the anticancer activity of 4p, but MDA-MB-435 cells had a value of 46.5 M. This difference was due to the fact that HeLa cells were more resistant to the effects of 4p. Both of these concentration levels are expressed in millimolar units [21].

Structure 1,3,4-oxadiazoles with pyridyl and thiazolyl backbones

In order to produce novel 2-pyridinyl substituted thiazolyl-5-aryl-1,3,4-oxadiazoles, an original multistep synthesis technique has been developed. This strategy used thionicotinamide as its primary



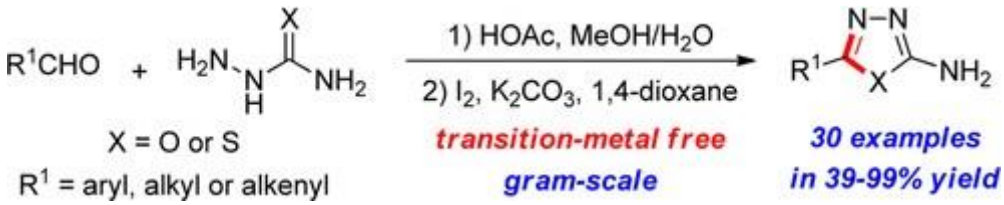
Binding mode of the most active compound (6l)

component from the beginning (6a-o). These chemicals have the potential to be effective antitubercular medications while still preserving a low risk of causing undesirable side effects. Chemicals have the potential to be effective antitubercular drugs. Outstanding to exceptional yields of the compounds referred to in the title were obtained by condensing pyridinyl- substituted thiazolyl acid hydrazide (4) with benzoic acids/nicotinic acids (5a-o) in the presence of silica-supported POCl3. This process was carried out in the presence of silica. The reactionhad to be carried out so that the compounds could be produced. The antitubercular activity of each of the compounds that were synthesised, from 6a to o, as well as the intermediate acid hydrazide, was evaluated in vitro. Both Mycobacterium tuberculosis H37Ra (MTB) and Mycobacterium bovis BCG were used as test organisms in this study. According to the results of the research, not a single one of the substances has any antitubercular action (4). Compounds 6f, 6j, 6l, and 6o have shown a potential capacity to be efficacious at doses that are lower than 3 g/mL against M. bovis BCG. The cytotoxicity of these compounds against four distinct human cancer cell lines is considered as being fairly substantial (the CC_{50} value is more than 100 g/mL), and this is because the value of the CC_{50} is greater than 100. The mycobacterial enoyl reductase (InhA) enzyme served as the target of the molecular docking research that was conducted inorder to obtain additional knowledge regarding the binding processes of these pharmaceuticals. This research was carried out so that more information regarding the binding processes of these pharmaceuticals could be gained. Because of this, we were able to acquire the data that was required. In addition to this, we have investigated the ADME characteristics of the many different commodities that were covered in the previous discussion [22].

Hybrids of the amino acids glycine and alanine, 2,5-disubstituted-1,3,4-oxadiazoles with HDAC8 inhibition and anticancer activity

Oxadiazole is a kind of heterocyclic molecule that consists of one oxygen atom, two nitrogen atoms, and a ring that has five members in it. These three components come together to createthe structure of the oxadiazole. It has been shown that compounds containing 1,3,4-oxadiazole cores display a broad spectrum of biological activity, and 1,3,4-oxadiazole has emerged as a crucial structural motif for the creation of new treatments. In this article, we provide the design, synthesis, and assessment of the biological activity of ten new 2,5-disubstituted 1,3,4- oxadiazoles (10a-10j). These substances have been shown to inhibit the activity of histone deacetylase class I. (HDAC). After having compounds developed and examined for their selectivity against HDAC8 using in silico docking software (Glide), the top 10 compounds that had a high dock score and complied with Lipinski's criteria were then organically synthesised. This was done after the compounds had been developed and analysed for their selectivity against HDAC8. Research was also carried out in a biological environment with the purpose of inhibiting the activity of HDAC and the proliferation of cells. Experiments that were conducted out in silico and in vitro indicated that all of the drugs (10a-10j) inhibited HDAC to a substantial degree and did so in a way that was selective for HDAC8. These results were found to be consistent across all of the medicines. 10b had the highest level of HDAC8 inhibitory activity and the most powerful anticancer activity, both of which were comparable to the positive control drug vorinostat, which is authorised by the FDA. 10b also had the highest level of HDAC8 inhibitory activity and the most powerful anticancer activity. When compared to the other pharmaceuticals that were looked at, 10b emerged as the undisputed victor in both of these categories (SAHA). It is investigated here to see whether there are any substitutions in the benzene ring that is linked on 1,3,4-oxadizole and glycine/alanine. In consideration of the structural activity of these compounds, this procedure is carried out. In light of the findings of this study, it is strongly suggested that additional research be carried out on the subject of the development of an HDAC8-selective inhibitory chemical as a therapeutic for the treatment of neoplastic diseases. This suggestion comes as a result of the fact that the results of this study suggest that such a chemical could be used. The inclusion of glycine and alanine into a new 1,3,4-oxadizole shown that HDAC8 might be inhibited by the compound [23].

Sequential Condensation and I2-Mediated Oxidative C-O/C-S Bond Formation of 2- Amino-1,3,4-Oxadiazoles and 2-Amino-1,3,4-Thiadiazoles

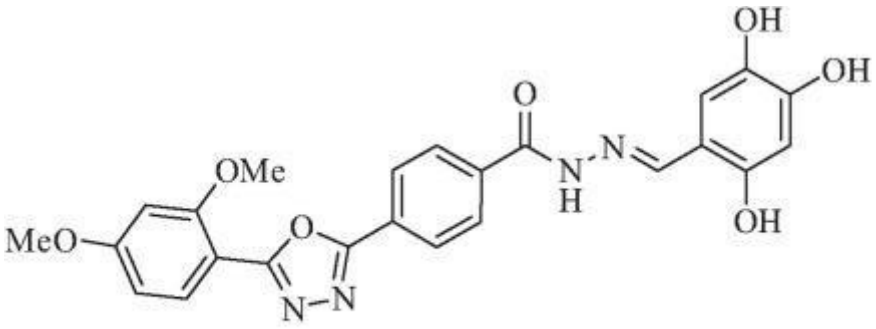


The oxidative C-O/C-S bond formation that is mediated by the ionisation of hydrogen dioxide was utilised in the process of creating 2-aminosubstituted 1,3,4-oxadiazoles and 1,3,4- thiadiazoles by the condensation of semicarbazide/thiosemicarbazide and the respective aldehydes. This was accomplished by the condensation of semicarbazide/thiosemicarbazide and the respective as a consequence of using this methodology, the final product consisted of 1,3,4- oxadiazoles as well as 1,3,4-thiadiazoles. This

sequential synthesis process does not require the use of any transition metals and can be used with aromatic, aliphatic, or cinnamic aldehydes to make a wide variety of diazole derivatives with a 2-amino substituent in a way that is both swift and uncomplicated. This process can also be used to make cinnamic aldehydes, which are cinnamyl aldehydes. The production of cinnamic aldehydes, also known as cinnamyl aldehydes, is another possible use of this technique [24].

Alternative oxadiazole compounds as α-glucosidase inhibitors

The use of benzohydrazide 5 in condensation reactions with a variety of benzaldehydes led to the production of oxadiazole derivatives (6-28) that included a hydrazone bond. These reactions tookplace in the presence of benzohydrazide 5. In order to get oxadiazole derivatives, these reactions have to be carried out. The ability of a variety of different oxadiazole compounds to suppress - glucosidase activity was investigated (6-28). The IC50 values, also known as the half-maximal inhibitory doses, may be anywhere from 2.640.05 to 4603.25 M. There is no set standard for these values. When compared to the compounds 6–9, 12, 13, 16, 18, 20, and 22–28, it was shownthat acarbose had a lower degree of activity. On the other hand, compounds 3–5 and 30–40 were found to be non-active. It was determined that the value of the half-maximal inhibitory concentration (IC50) for acarbose was 856.45 5.60 M. It would appear, based on the findings of structure-activity relationship (SAR) studies, that the inhibitory potential of oxadiazole benzohydrazones (6-28) is related to the degree of substitution that is present in the N- benzylidene section of the molecule. This is the case because these studies investigated the relationship between the structure of a molecule and its activity. This is because the molecule in question consists of a total of 28 carbon atoms. Compound 18, which has trihydroxy substitutions on the N-benzylidene moiety at positions C-2′, C-4′, and C-5′, demonstrated the highest level of inhibitory activity (IC50 = 2.64 0.05 M). The IC50 value for the traditional medication acarbose is 856.45 5.60 M, but this figure is about 300 times more potent than that value. Compound 23 was found to have the highest IC50 value, which showed that it was the most effective when compared to the other compounds that included just one hydroxyl substitution. This was observed when compounds that contained only one hydroxyl substitution were compared to one another. At a distance of 0.35 metres, this value was 34.64. When the hydroxyl group is moved from position C-2′ to places C-4′ (6) and C-3′, the inhibitory effect is greatly mitigated as a result. (7). Even though the activity levels of these substituted chlorine compounds (16, 28, and 27) were lower than the activity levels shown by their hydroxyl equivalents, substituted chlorine compounds showed high levels of activity. This was the case despite the fact that the activity levels of these compounds were lower. If a substituent such as a nitro or methyl group is introduced into the structure of an enzyme, anywhere in that structure, the inhibitory activity of the enzyme will be reduced. It makes no difference where in the phrase the substituents are placed; this will always be the case. In light of this, the importance of hydroxyl and halo groups as potential inhibitors of enzyme



18 (IC50 = 2.64 ± 0.05 µM)

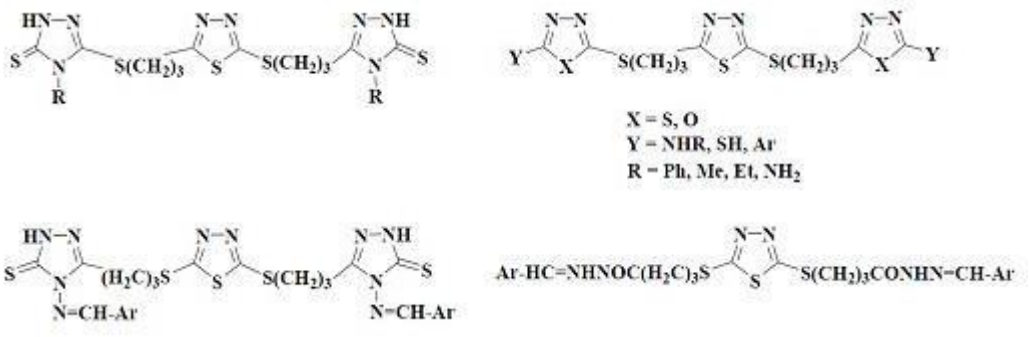
function is brought into sharperfocus. [25].

Ultrasound-assisted synthesis of completely substituted 1,3,4-oxadiazole derivatives: a novel, efficient, and rapid technique

Manufacturing completely substituted 1,3,4-oxadiazoles may be accomplished in a time- and cost-effective manner by using a technique that consists of three components and calls for the use of aromatic carboxylic acids, acenaphthoquinone, and (N-isocyanimino) triphenylphosphorane. Using a method that involves aromatic carboxylic acids is one way that this objective may be successfully met in an efficient manner. The directions on how to create this dish are included in this article. Methods such as melting point analysis, infrared spectroscopy, nuclear magnetic resonance, and mass spectrometry were used in the synthesis and characterization of a large number of compounds. In addition, a large number of compoundswere synthesised. This method has the potential to be of significant use due to the fact that it requires just the bare minimum of reaction conditions, it generates yields that vary from excellent to extraordinary, and it can be finished in an exceptionally short period of time [26].

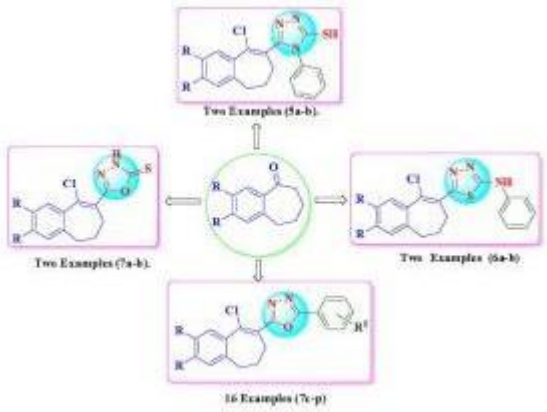
2,5-Disubstituted-1,3,4-thiadiazoles containing 1,2,4-triazole, 1,3,4-thiadiazole, 1,3,4- oxadiazole, and/or Schiff base may have antimicrobial and antiproliferative properties.

In this study, a new series of 2,5-disubstituted-1,3,4-thiadiazole linked 1,2,4-triazole, 1,3,4- thiadiazole, and 1,3,4-oxadiazole, as well as Schiff base derivatives, were synthesised and characterised using infrared spectroscopy, nuclear magnetic resonance (NMR), mass spectrometry (MS), and elemental analysis. Additionally, the Schiff base derivatives were characterised in addition to this, the Schiff base derivatives were investigated and characterised. In addition to bacteria and fungi, it was explored whether or not the substances were successfulin stopping the multiplication of cancer cells. It has been proven that a very large number of synthetic derivatives display biological activity. Some of these biological activities are fairly exciting to think about, and it has been shown that these activities occur in a very high number ofsynthetic derivatives [27].



Novel prospective antiproliferative drugs consisting of benzosuberone conjugated to 1,3,4-oxadiazole, 1,3,4-thiadiazole, or 1,2,4-triazole.

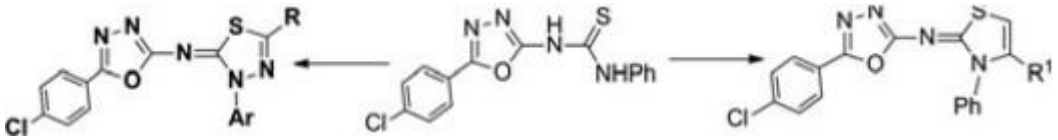
As part of our ongoing study into the creation of further anti-proliferative medications, our team has been successful in synthesising novel analogues of benzosuberone. These findings are being presented as part of our progress. There is a possibility that these analogues have a moiety that corresponds to 1,3,4-oxadiazole, 1,3,4-thiadiazole, or 1,2,4-triazole. Yields ranged between 82 and 93 percent. An in vitro test was carried out on the newly synthesised compounds using 1H NMR, 13C NMR, ESI/LC-MS, and HRMS in order to evaluate whether or not these compounds have the ability to inhibit the proliferation of four different types of human cancer cell lines. The results of these exams are shown in the following table (cervical, breast, pancreatic and alveolar).The fact that the GI50 values for compounds 4b, 6a, 7d, and 7l derived from these human cancer cell lines were all much lower than 1 mM lends credence to the notion that these compounds have a significant influence on the inhibition of the proliferation of cancer cells. The study was carried out on four different cell lines, all of which were taken from people who really had cancer. The value of the GI50 for the chemical 7d in the instance of the cervical cancer cell line was found to be 0.079 M, which is much lower than the value for the positive control colchicine. It was determined that this value was much lower than the value that was observed for the colchicine. The finding of this number was made possible by the use of colchicine as a comparison [28].



Derivatives of 1,3,4-Thiadiazole and 1,3-Thiazole Having Moiety of 1,3,4-Oxadiazole

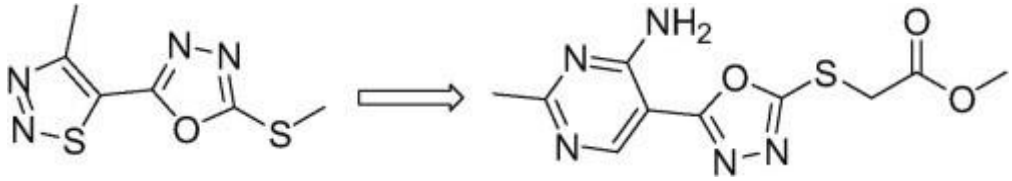
After going through a reaction with hydrazonoyl halides, the 1,3,4-oxadiazolyl-phenylthiourea 3 was able to form the required 1,3,4-oxadiazolylimino-1,3,4-thiadiazoles. It was shown that ethyl chloroacetate and -haloketones were both capable of converting 3 into an amount of thiazolidinone and

thiazole derivatives that was comparable to the original quantity. A approach similar to that one was used to achieve this. The recently synthesised compounds had their structures examined and validated using the spectrum data before they could be put to use. This allowed the newly created chemicals to be put to good use. In a cell line generated from colon cancer, ten different compounds were evaluated to see whether or not they might suppress the proliferation of malignant cells (HCT-116). 1,3,4-thiadiazole derivatives 13d and 19c indicated potential antitumor effectiveness against colon carcinoma (IC_{50} = 0.73 and 0.86 g/mL, respectively). This is despite the fact that the majority of the compounds that were evaluated showed very limited anti-cancer activity (HCT-116) [29].



Analogues of 2-methylthio-5-(4-amino-2-methylpyrimidin-5-yl)-1,3,4-oxadiazole

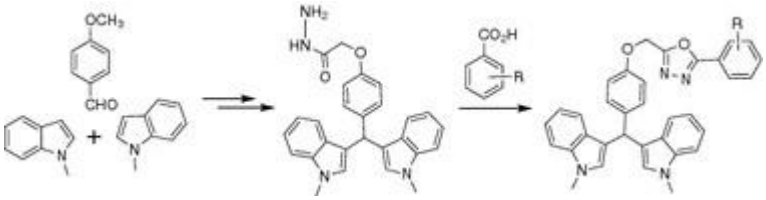
The tobacco mosaic virus was used as a test subject in order to determine whether or not avariety of newly synthesised 2-substituted methylthio-5-(4-amino-2-methylpyrimidin-5-yl-)- 1,3,4-oxadiazole derivatives have antiviral activity (TMV). Initial findings from the biological tests suggested that the compounds exhibited a significant level of antiviral activity against TMVin living organisms. There was evidence of this behaviour in live creatures. When tested against TMV, compounds 8f, 8h, 8k, and 8n in addition to compound 8q displayed anti-TMV activity with an EC_{50} value of 290.98-438.29 g/mL. This value was comparable to that of the commercial product Ningnanmycin, which had an EC_{50} value of 301.83 g/mL. Additionally, compound 8w demonstrated anti-TMV efficacy. The substantially greater therapeutic efficiency of Compound 8i against TMV (EC_{50} = 246.48 g/mL) stood out as particularly striking when contrasted with that of Ningnanmycin. In this investigation, for the very first time, a 2-substituted methylthio-5- (4-amino-2-methylpyrimidin-5-yl-)-1,3,4-oxadiazole derivative that exhibited significant antiviral activity against TMV was reported. To the best of our knowledge, the scenario is as follows: [30]



Bisindole derivatives related to 1,3,4-oxadiazole that inhibit cancer

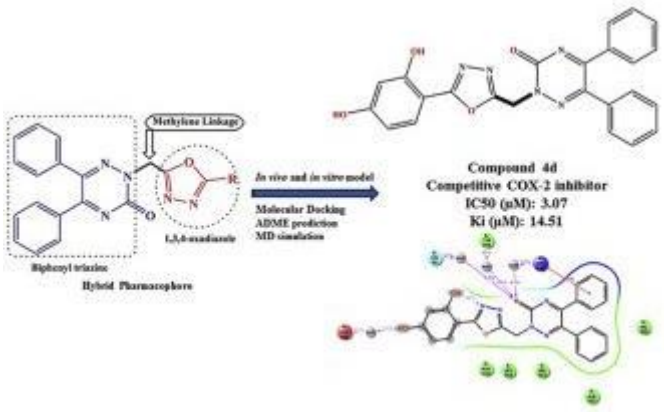
It has been shown that it is feasible to synthesise a sequence of ten 1,3,4-oxadiazole-linked bisindole derivatives without encountering any problems. It was possible to determine this sequence. During the course of the tests, the efficacy of the compounds was evaluated based on how well they eradicated four distinct human cancer cell types (MCF-7, KB, Colo-205, and A- 549). When compared to etoposide, the majority of these new compounds shown significant improvements in their capacity to eradicate cancer cells. The GI_{50} values for the chemicals that were used ranged anywhere from 0.1 to 3.9 M when they were supplied to the identical cell lines, but the GI_{50} values for the positive control etoposide varied anywhere from 0.13 to 3.08 M. Based on these findings, it seems that the chemicals that were utilised

had varied degrees of hazardous potential. When looking at the compounds in terms of their overall effectiveness, four of them performed much better than etoposide did [31].



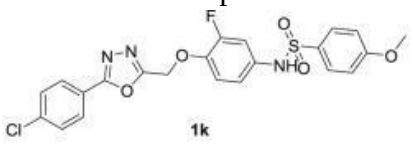
5,6-dimethyl-1,2,4-triazin-3(2H)-ones and their corresponding Possible anti-inflammatory and pain-relieving properties of 5-substituted 1,3,4-oxadiazole

The purpose of this research was to create a number of different triazin-3(2H)-one derivatives containing 1,3,4-oxadiazole and investigate the analgesic and anti-inflammatory properties of these compounds (4a-4o). A preliminary evaluation of the effectiveness of the anti-inflammatory medication was performed in vitro with the help of certain experiments that included denaturing albumin. The intriguing substances underwent further investigation utilising animal models of inflammation that ranged from acute to sub-chronic to chronic. The results of these tests provide reason to have positive expectations. When compared to the standard form of indomethacin, the anti-inflammatory effects of the indomethacin derivatives 4d, 4e, 4g, and 4j and 4l were significantly enhanced. In addition to this, these indomethacin derivatives shown a lower incidence of negative effects such as ulcerogenicity, toxicity to the liver, and damage to the kidneys. In order to test the analgesic effectiveness of these possible derivatives in mice that were participating in *in vivo* trials, a writhing paradigm as well as a formalin-induced paw licking response were used. Both of these reactions were caused by the administration of formalin. The goal of this test was to establish whether or not these derivatives were successful in easing the discomfort that the mice were feeling as a result of their painful experiences. Although the analgesic effects of compounds 4d, 4e, and 4g were comparable to one another, the effects of compounds 4j and 4l were about one-half as potent as those of the other compounds. An *in vitro* COX inhibition experiment was carried out in order to investigate the kinetics and selectivity of compounds 4d, 4e, 4g, and 4l for inhibiting (cyclooxygenase) COX-1 and (cyclooxygenase) COX-2 isozymes. This was done in order to determine whether compounds 4d, 4e, 4g, or 4l are more effective at inhibiting COX-1 or COX-2. Compounds 4d, 4e, 4g, and 4l areall included in this group. Molecular dynamics modelling allowed for the most effective chemical, 4d, which had an IC_{50} of 3.07 M for COX-2 to be docked into the active site of COX-
2. This was made possible mainly to the fact that molecular dynamics modelling was used. The findings of this experiment provide more support for the interaction that has been postulated to take place between the chemicals in issue and the enzyme in question. The proof was supplied bythe outcomes of the experiment [32].



Sulfonamide-containing 1,3,4-oxadiazole derivatives

The synthesis and characterization of a recently discovered class of chemicals known as sulfonamide-derivative 1,3,4-oxadiazoles are the topics of discussion in this article. Unintentional discovery led to the identification of this category of compounds. In order to examine the cancer-fighting capabilities of the nine different human cancer cell lines that make up the NCI-58, an *in vitro* examination of their antiproliferative potential was carried out. Compound 1k, which has a p-methoxybenzenesulfonamido moiety, was shown to have the greatest mean percent inhibition value across all 58 distinct cell lines that were investigated. This was the case regardless of the kind of cell line (10 M). It was shown to have a significant antiproliferative effect across a broad spectrum of cancer cell lines. [Cell lines] The growth of the T-47D breast cancer cell line was inhibited by 90.47 percent when compound 1k was administered to the T-47D breast cancer cell line at dosages of 10 millimolar. When it was tested at the same dosage, it was shown to suppress the development of cancer cell lines by more than 80 percent in three different types of cancer: SR leukaemia, SK-MEL-5 melanoma, and MDA- MB-468 breast cancer. Compound 1k was more effective than either Paclitaxel or Gefitinib against the cell lines that were particularly susceptible to the effects of the compound [33].



1k

At 10 μM concentration:

90.47% inhibition over T-47D breast cancer cell line

84.83% inhibition over MDA-MB-468 breast cancer cell line

84.32% inhibition over SK-MEL-5 melanoma cell line

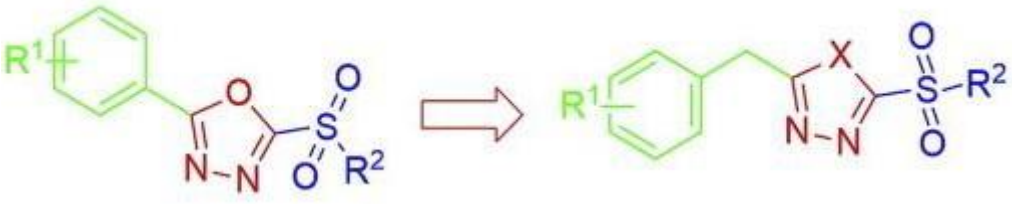
81.58% inhibition over SR leukemia cell line

Sonochemical synthesis of 2-aryl-1,3,4-oxadiazoles: a novel, rapid, and efficient one-pot method

It has been speculated that 2-aryl-1,3,4-oxadiazoles might be produced at room temperature with the use of ultrasonography. When the new tactic is used, the amount of time spent responding is reduced down, more is generated, the response profile is explained, and the experimental and workup stages are made more easy [34].

2-(2,5-dimethylamino)-1,3,4-oxadiazole/thiadiazole sulfone derivative

Both the bacterial infection known as Xanthomonas oryzae pv. oryzae and the bacterial infection known as Xanthomonas oryzicola are responsible for the rice illnesses known as leaf blight and leaf streak, respectively. Both of these diseases affect the leaves of the rice plant. Rice has the potential to harbour both of these diseases. An *in vitro* turbidimeter test was performed on a number of different 2,5-substituted-1,3,4-oxadiazole/thiadiazole sulfone derivatives that were synthesised in an effort to treat these conditions. The purpose of the test was to determine whether or not the derivatives possessed any antibacterial activity. According to the results of the antibacterial bioassays, the majority of the compounds that were evaluated had the capability to display antibacterial bioactivities against the microorganisms that are accountable for rice leaf blight and leaf streak. Compound 6c performed much better than Bismerthiazol and Thiediazole Copper in terms of its ability to inhibit the spread of rice bacterial leaf blight and leaf streak when compared to alternative treatments that are commercially available. This was the case when evaluating the effectiveness of Compound 6c. When these two scenarios were compared to one another, the EC50 values that were found to be appropriate were 1.07 and 7.14 g/mL, respectively. Compounds 6c (43.5 percent control) and 6g (42.4 percent control), according to the findings of tests that were conducted in a greenhouse, exhibited a greater degree of antibacterial activity against rice bacterial leaf blight. These findings were based on the findings of tests that were carried out. This was in contrast to the controls, Bismerthiazol (25.5 percent control) and Thiediazole Copper (25.8 percent control), both of which had a percentage of control of 25.8 percent (33.3 percent control) [35].



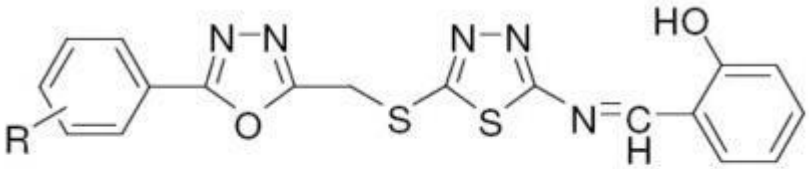
Inhibition of Corrosion of Mild Steel by 1,3,4-Oxadiazole Derivatives in 0.5 M Hydrochloric Acid

An investigation was carried out utilising mass loss and electrochemical techniques in order to determine the effect that three recently synthesised oxadiazole derivatives had on the prevention of corrosion of mild steel in a solution containing 0.5 M HCl. The goal of the investigation was to determine which of the three oxadiazole derivatives was more effective at preventing corrosion. Increasing the inhibitor concentration had the effect of slowing down the rate of corrosion, whereas increasing the temperature of the medium had the reverse impact and accelerated up the rate of corrosion. During the adsorption process, each of the three inhibitors operated in a way that could be characterised using a Langmuir isotherm. This was possible because of the structure of the Langmuir isotherm. According to the polarisation curves, it would seem that the inhibitors belong to the category of hybrids. [Citation needed] Experiments that are carried out with the use of electrochemical impedance spectroscopy give information on the method by which inhibitors act to stop the course of a process. As part of this work, a wide variety of thermodynamic parameters connected with activation and adsorption were investigated and analysed. In this examination of the surface-adsorbed layer, scanning electron microscopy and X-ray energy dispersive spectroscopy were both used as different methods of analysis (EDAX). To achieve the objective of determining the electronic properties of the inhibitors, the semiempirical AM1

quantum chemistry method was utilised as the method of analysis. It turned out that the theoretical predictions and the experimental observations were very compatible with one another [36].

Structures with a Schiff base moiety, such as 1,3,4-oxadiazole and 1,3,4-thiadiazole

The CCK-8 assay was used to develop, synthesise, and evaluate a series of novel hybrid compounds possessing Schiff base moiety for their in vitro anticancer activity against human tumour cell lines SMMC-7721, MCF-7, and A549. The results of these tests led to the identification of a series of novel hybrid compounds. The chemicals 1,3,4-oxadiazole and 1,3,4- thiadiazole were among these substances. These compounds shown the ability to inhibit the progression of human tumours when tested in the laboratory. The majority of the compounds thatwere tested showed significant anticancer activity in the bioassays, and some of these chemicals showed even stronger effects than the positive control medication 5-fluorouracil (5-FU) against anumber of different cell lines. The majority of the compounds that were tested were able to inhibit the growth of cancerous cells. The majority of the chemicals that were tested showed anticancer activity when they were put through the appropriate bioassays. It was found that among all of the compounds that were studied, the one that inhibited SMMC-7721 cells the most was compound 8d, with an IC50 value of 2.84 M. This was the case regardless of the compound. Compounds 8k and 8n showed significant anticancer activity against MCF-7 cells, with IC50 values of 4.56 and 4.25 M, respectively. The compounds were investigated for their effectiveness against cancer. Compounds 8a and 8n both shown substantial effectiveness against the proliferation of A549 cells in the laboratory. The fact that their IC50 values, respectively, were 4.11 and 4.13 M demonstrates that they are able to effectively suppress cell division. The antiproliferative effects of 1,3,4-oxadiazole are sensitive to being dramatically affected by the alteration of the phenyl ring substituents, as shown by the results of pharmacological research [37].

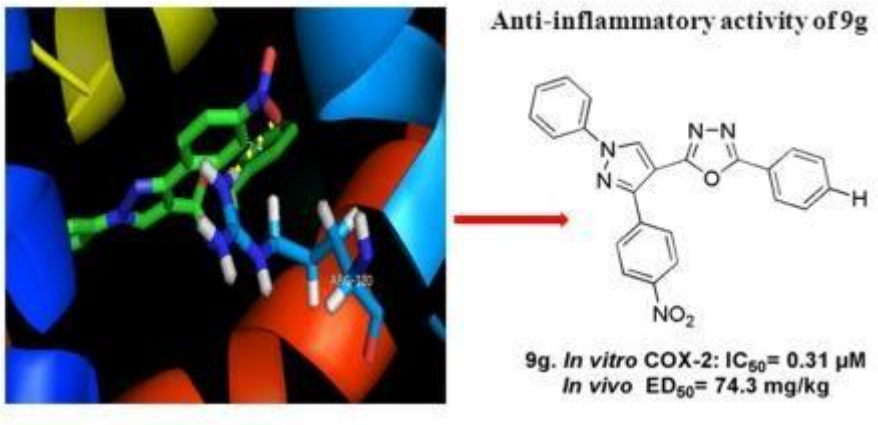


R= H, 4-F, 2-Cl, 4-Cl, 2-Br, 4-Br, 2-CH_3, 3-CH_3, 4-CH_3, 3-OCH_3, 4-OCH_3, 3,4,5-Tri-OCH_3, 3-NO_2, 4-NO_2

To inhibit COX-2 selectively and provide significant anti-inflammatory effects, 2-phenyl-5- (1,3-diphenyl-1H-pyrazol-4-yl)-1,3,4-oxadiazoles have been developed.

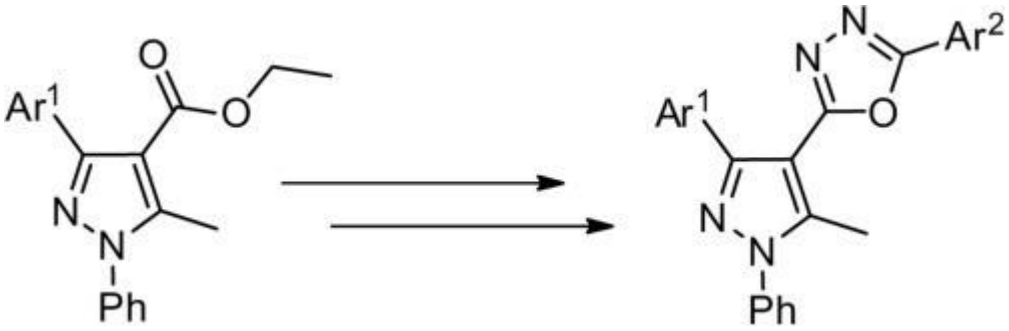
In order to precisely inhibit COX-2 and to provide a sizeable anti-inflammatory impact, a new class of 2-phenyl-5-(1,3-diphenyl-1H-pyrazol-4-yl)-1,3,4-oxadiazoles was conceived of, created,and manufactured in a laboratory. This class consists of compounds with the chemical formula 2-phenyl-5-(1,3-diphenyl-1H-pyrazol-4-yl). 2-phenyl-5-(1,3-diphenyl-1H-pyrazol-4-yl)-1,3,4-oxadiade is the name given to these compounds. In a model of carrageenan-induced rat paw edoema, the most potent COX-2 inhibitor, 2-(3-(4-nitrophenyl)-1-phenyl-1H-pyrazol-4-yl)-5- phenyl-1,3,4-oxadiazole, shown excellent anti-

inflammatory activities, with an ED50 value of
74.3 mg/kg for 9g. This chemical was put through its paces. This drug is known by its name, "3-nitropheny," which is a direct translation of its chemical nomenclature. The lead medication, 9g, had a higher gastro-sparing profile when compared to aspirin and a comparable decrease in the quantity of acetic acid-induced writhes. This was a significant achievement. By using molecular docking, researchers were able to determine that the propensity of ligands to bind to COX-2 is much higher than that of COX-1. This has been shown to be the case [38].



1-3,4-Oxadiazoles: Preparation, Characterization, and Antimicrobial Testing

The only collection of its sort consisting of 2-(5-methyl-1,3-diphenyl-1H-pyrazol-4-yl)-5- phenyl-1,3,4-oxadiazoles. The production of hydrazones required the use of a variety of different arylaldehydes in addition to (E)-N′-benzylidene-5-methyl-1,3-diphenyl-1H-pyrazole. After that, an oxidative cyclization procedure was carried out on these hydrazones, which resulted in the synthesis of the number 7. (a-m). Techniques such as infrared spectroscopy, nuclear magnetic resonance (1H and 13C), and liquid chromatography mass spectrometry (LC-MS) were used throughout the process of characterising freshly synthesised compounds. This was done so that the compounds might be better understood. The ability of the synthetic chemicals to thwart the growth of germs was put to the test, and the findings obtained from this endeavour were compared to those obtained from a wide variety of different treatments that are regarded as being conventional. The antibacterial activity of the compounds varied from being highly effective to being so weak that its effects were hardly detectable. This was due to the compounds' heterogeneous nature. Sevenm, one of the compounds that were created, turned out to be the most effective antibacterial agent, while compounds 7d, 7f, 7i, and 7l only demonstrated medium to moderate activity. Sevenm was one of the compounds that were developed. Sevenm proved to be the antibacterial agent with the greatest efficacy. The synthesised compounds included many antibacterial agents; however, the Sevenm was by far the most effective of these agents. The minimum inhibitory concentration (MIC) of the compounds was found to be between 20 and 50 micrograms per millilitre when the compounds were tested on bacteria. However, the minimum inhibitory concentration (MIC) was between 25 and 55 micrograms per millilitre when the compounds were tested on fungus. The term alludes to a class of antibacterial agents that was only recently discovered and has shown to be quite powerful. These compounds are members of that class [39].



CONCLUSION:

Oxadiazoles are a class of heterocyclic compounds that may be identified by the presence of a five-membered ring structure, two azo groups, and one oxygen atom as components of its overall chemical makeup. Oxadiazoles are further distinguished by the fact that they contain just one oxygen atom. Because of these characteristics, it is feasible to distinguish them from several other heterocyclic compounds. [Citation needed] They are the most prominent people in the fieldof heterocyclic chemistry, which is one of the reasons why they are of the utmost relevance and carry the most weight in the arguments that are conducted there. A substantial amount of research has been conducted on it because of the likelihood that it may serve as a starting point for the synthesis of beneficial bioactive chemicals. As a result of this possibility, a lot ofattention has been paid to it. As a direct result of this potential, there has been a great amount of inquiry placed into it. On this page, you will find a comprehensive discussion on the physical andchemical properties of oxadiazole, including its spectra as well as specific examples of its manufacturing. If you would want to learn more about oxadiazole, you may visit the following link. During the course of the investigation that our team carried out into the pharmacological effects of oxadiazole derivatives, we came across a variety of pharmacological activities that had not been discovered in the past. These activities included: This molecule has the ability to carry out a wide range of effects, some of which include those that are anti-inflammatory, anti-cancer, anti-fungal, anti-osteoporotic, and anti-microbial. These are only a few examples of the many other activities that may be done. In this part of the essay, we will have a short discussion on a variety of medicines that include the oxadiazole ring and moiety. These medicines vary from antidepressants to painkillers. Several different medical disorders have been successfully treated with the help of these medications. Some of these chemicals can be found in nature, whilst others can only be produced in an environment where there is strict quality control, such as in a laboratory. These compounds might have been created in a laboratory or discovered in their natural surroundings. Both possibilities are possible. Both scenarios are plausible. Both of these eventualities are quite conceivable at this point.

REFERENCES:

1. Birle R, Chaturvedi P, Dubey A, Engla G, Kushwah N. A Review on Substituted 1, 3, 4- Oxadiazole and its Biological Activities.
2. Küçükoğlu K, Acar Çevik U, Nadaroglu H, Celik I, Işık A, Bostancı HE, Özkay Y, Kaplancıklı ZA. Design, synthesis and molecular docking studies of novel benzimidazole-1, 3, 4-oxadiazole hybrids for their carbonic anhydrase inhibitory and antioxidant effects. Medicinal Chemistry Research. 2022 Oct;31(10):1771-82.

3. Nakra VK, Sharma M. Synthesis, charecterization and anti-microbial activity of substituted 5-(5-sulfanyl-1, 3, 4-oxadiazol-2-yl) benzene-1, 2, 3-triol derivatives. Journal of Drug Delivery and Therapeutics. 2019 Jul 15;9(4):357-65.
4. Luczynski M, Kudelko A. Synthesis and Biological Activity of 1, 3, 4-Oxadiazoles Used in Medicine and Agriculture. Applied Sciences. 2022 Apr 8;12(8):3756.
5. Zahrani NA, El-Shishtawy RM, Asiri AM. Recent developments of gallic acid derivatives and their hybrids in medicinal chemistry: A review. European journal of medicinal chemistry. 2020 Oct 15;204:112609.
6. Khan H, Zafar M, Patel S, Shah SM, Bishayee A. Pharmacophore studies of 1, 3, 4- oxadiazole nucleus: Lead compounds as α-glucosidase inhibitors. Food and Chemical Toxicology. 2019 Aug 1;130:207-18.
7. Voronin AA, Fedyanin IV, Churakov AM, Pivkina AN, Muravyev NV, Strelenko YA, Klenov MS, Lempert DB, Tartakovsky VA. 4 H-[1, 2, 3] Triazolo [4, 5-c][1, 2, 5] oxadiazole 5-oxide and Its Salts: Promising Multipurpose Energetic Materials. ACS Applied Energy Materials. 2020 Sep 3;3(9):9401-7.
8. Maftei CV, Fodor E, Jones PG, Daniliuc CG, Franz MH, Kelter G, Fiebig HH, Tamm M, Neda I. Novel 1, 2, 4-oxadiazoles and trifluoromethylpyridines related to natural products: Synthesis, structural analysis and investigation of their antitumor activity. Tetrahedron. 2016 Mar 3;72(9):1185-99.
9. Birle R, Pachore A, Hirve N, Mandloi N, Mahajan V, Engla G, Chaturvedi P. Synthesis Characterization and Antimicrobial Activity of Some Novel Oxadiazole Derivatives. International Journal of Research in Engineering, Science and Management. 2022 Apr 2;5(3):151-4.
10. Walker MA. Improvement in aqueous solubility achieved via small molecular changes. Bioorganic & Medicinal Chemistry Letters. 2017 Dec 1;27(23):5100-8.
11. Schwärzer K, Tüllmann CP, Graßl S, Górski B, Brocklehurst CE, Knochel P. Functionalization of 1, 3, 4-Oxadiazoles and 1, 2, 4-Triazoles via Selective Zincation or Magnesiation Using 2, 2, 6, 6-Tetramethylpiperidyl Bases. Organic letters. 2020 Feb 12;22(5):1899-902.
12. Aksenov NA, Arutiunov NA, Kirillov NK, Aksenov DA, Aksenov AV, Rubin M. Preparation of 1, 3, 4-oxadiazoles and 1, 3, 4-thiadiazoles via chemoselective cyclocondensation of electrophilically activated nitroalkanes to (thio) semicarbazides or thiohydrazides. Chemistry of Heterocyclic Compounds. 2020 Aug;56(8):1067-72.
13. Baikov SV, Trukhanova YA, Tarasenko MV, Kinzhalov MA. Synthesis and Study of the Structure of Palladium (II) Acyclic Diaminocarbene Complexes Containing a 1, 2, 4- Oxadiazole Moiety. Russian Journal of General Chemistry. 2020 Oct;90(10):1892-900.
14. Oe KO, Tashiro M, Tsuge O. Photochemistry of heterocyclic compounds. VII. Photochemical reaction of 2, 5-diphenyl-1, 3, 4-oxadiazole with benzo [b] thiophenes. Bulletin of the Chemical Society of Japan. 1977 Dec;50(12):3281-7.
15. Chauhan J, Ravva MK, Sen S. Harnessing Autoxidation of Aldehydes: In Situ Iodoarene Catalyzed Synthesis of Substituted 1, 3, 4-Oxadiazole, in the Presence of Molecular Oxygen. Organic letters. 2019 Aug 1;21(16):6562-5.
16. Başpınar Küçük H, Alhonaish A, Yıldız T, Güzel M. An efficient approach to access 2, 5-disubstituted 1, 3, 4-oxadiazoles by oxidation of 2-arenoxybenzaldehyde N-acyl hydrazones with molecular iodine. ChemistrySelect. 2022 Jul 14;7(26):e202201391.
17. Aksenov AV, Kirilov NK, Aksenov NA, Arutiunov NA, Aksenov DA, Rubin M. Electrophilically

activated nitroalkanes in the synthesis of substituted 1, 3, 4-oxadiazoles from amino acid derivatives. Chemistry of Heterocyclic Compounds. 2022 Jan;58(1):32-6.

18. El-Sayed WA, El-Essawy FA, Ali OM, Nasr BS, Abdalla MM, Adel AH. Anti-HIV activity of new substituted 1, 3, 4-oxadiazole derivatives and their acyclic nucleoside analogues. Zeitschrift für Naturforschung C. 2009 Dec 1;64(11-12):773-8.
19. Ahmed AA, Mahmood IQ, Aziz HS. Synthesis and Characterization of Few New Substituted 1, 3, 4-Oxadiazoles 1, 2, 4-Triazoles and Schiff Bases via Chalcone Compounds. Technology. 2022;12(3):1087-92.
20. Liu F, Wang M, Teng X, Zhang P, Jiang L. Synthesis and biological evaluation of novel 2-(substituted isoxazol-4-yl)-5-arylamino-1, 3, 4-oxadiazoles. Research on Chemical Intermediates. 2014 Apr;40(4):1575-81.
21. Agarwal M, Singh V, Sharma SK, Sharma P, Ansari M, Jadav SS, Yasmin S, Sreenivasulu R, Hassan M, Saini V, Ahsan MJ. Design and synthesis of new 2, 5- disubstituted-1, 3, 4-oxadiazole analogues as anticancer agents. Medicinal Chemistry Research. 2016 Oct;25(10):2289-303.
22. Dhumal ST, Deshmukh AR, Bhosle MR, Khedkar VM, Nawale LU, Sarkar D, Mane RA. Synthesis and antitubercular activity of new 1, 3, 4-oxadiazoles bearing pyridyl and thiazolyl scaffolds. Bioorganic & Medicinal Chemistry Letters. 2016 Aug 1;26(15):3646-51.
23. Pidugu VR, Yarla NS, Pedada SR, Kalle AM, Satya AK. Design and synthesis of novel HDAC8 inhibitory 2, 5-disubstituted-1, 3, 4-oxadiazoles containing glycine and alanine hybrids with anti cancer activity. Bioorganic & medicinal chemistry. 2016 Nov 1;24(21):5611-7.
24. Niu P, Kang J, Tian X, Song L, Liu H, Wu J, Yu W, Chang J. Synthesis of 2-amino-1, 3, 4-oxadiazoles and 2-amino-1, 3, 4-thiadiazoles via sequential condensation and I2- mediated oxidative C–O/C–S bond formation. The Journal of organic chemistry. 2015Jan 16;80(2):1018-24.
25. Taha M, Ismail NH, Imran S, Rokei MQ, Saad SM, Khan KM. Synthesis of new oxadiazole derivatives as α-glucosidase inhibitors. Bioorganic & medicinal chemistry. 2015 Aug 1;23(15):4155-62.
26. Rouhani M, Ramazani A, Joo SW. Ultrasonics in isocyanide-based multicomponent reactions: A new, efficient and fast method for the synthesis of fully substituted 1, 3, 4- oxadiazole derivatives under ultrasound irradiation. Ultrasonics sonochemistry. 2015 Jan 1;22:391-6.
27. Rezki N, Al-Yahyawi AM, Bardaweel SK, Al-Blewi FF, Aouad MR. Synthesis of novel 2, 5-disubstituted-1, 3, 4-thiadiazoles clubbed 1, 2, 4-triazole, 1, 3, 4-thiadiazole, 1, 3, 4- oxadiazole and/or Schiff base as potential antimicrobial and antiproliferative agents. Molecules. 2015 Sep 2;20(9):16048-67.
28. Yadagiri B, Gurrala S, Bantu R, Nagarapu L, Polepalli S, Srujana G, Jain N. Synthesis and evaluation of benzosuberone embedded with 1, 3, 4-oxadiazole, 1, 3, 4-thiadiazole and 1, 2, 4-triazole moieties as new potential anti proliferative agents. Bioorganic & medicinal chemistry letters. 2015 May 15;25(10):2220-4.
29. Dawood KM, Gomha SM. Synthesis and Anti-cancer Activity of 1, 3, 4-Thiadiazole and 1, 3-Thiazole Derivatives Having 1, 3, 4-Oxadiazole Moiety. Journal of Heterocyclic Chemistry. 2015 Sep;52(5):1400-5.
30. Wu W, Chen Q, Tai A, Jiang G, Ouyang G. Synthesis and antiviral activity of 2- substituted methylthio-5-(4-amino-2-methylpyrimidin-5-yl)-1, 3, 4-oxadiazole derivatives. Bioorganic & Medicinal Chemistry Letters. 2015 May 15;25(10):2243-6.

31. Hatti I, Sreenivasulu R, Jadav SS, Ahsan MJ, Raju RR. Synthesis and biological evaluation of 1, 3, 4-oxadiazole-linked bisindole derivatives as anticancer agents. Monatshefte für Chemie-Chemical Monthly. 2015 Oct;146(10):1699-705.
32. Banerjee AG, Das N, Shengule SA, Srivastava RS, Shrivastava SK. Synthesis, characterization, evaluation and molecular dynamics studies of 5, 6–diphenyl–1, 2, 4– triazin–3 (2H)–one derivatives bearing 5–substituted 1, 3, 4–oxadiazole as potential anti– inflammatory and analgesic agents. European journal of medicinal chemistry. 2015 Aug 28;101:81-95.
33. El-Din MM, El-Gamal MI, Abdel-Maksoud MS, Yoo KH, Oh CH. Synthesis and in vitro antiproliferative activity of new 1, 3, 4-oxadiazole derivatives possessing sulfonamide moiety. European journal of medicinal chemistry. 2015 Jan 27;90:45-52.
34. Rouhani M, Ramazani A, Joo SW. Novel, fast and efficient one-pot sonochemical synthesis of 2-aryl-1, 3, 4-oxadiazoles. Ultrasonics sonochemistry. 2014 Jan 1;21(1):262-7.
35. Li P, Shi L, Yang X, Yang L, Chen XW, Wu F, Shi QC, Xu WM, He M, Hu DY, Song BA. Design, synthesis, and antibacterial activity against rice bacterial leaf blight and leaf streak of 2, 5-substituted-1, 3, 4-oxadiazole/thiadiazole sulfone derivative. Bioorganic & medicinal chemistry letters. 2014 Apr 1;24(7):1677-80.
36. Gurudatt DM, Mohana KN. Synthesis of new pyridine based 1, 3, 4-oxadiazole derivatives and their corrosion inhibition performance on mild steel in 0.5 M hydrochloric acid. Industrial & Engineering Chemistry Research. 2014 Feb 12;53(6):2092-105.
37. Zhang K, Wang P, Xuan LN, Fu XY, Jing F, Li S, Liu YM, Chen BQ. Synthesis and antitumor activities of novel hybrid molecules containing 1, 3, 4-oxadiazole and 1, 3, 4- thiadiazole bearing Schiff base moiety. Bioorganic & medicinal chemistry letters. 2014 Nov 15;24(22):5154-6.
38. Bansal S, Bala M, Suthar SK, Choudhary S, Bhattacharya S, Bhardwaj V, Singla S, Joseph A. Design and synthesis of novel 2-phenyl-5-(1, 3-diphenyl-1H-pyrazol-4-yl)-1, 3, 4-oxadiazoles as selective COX-2 inhibitors with potent anti-inflammatory activity. European journal of medicinal chemistry. 2014 Jun 10;80:167-74.
39. Ningaiah S, Bhadraiah UK, Doddaramappa SD, Keshavamurthy S, Javarasetty C. Novel pyrazole integrated 1, 3, 4-oxadiazoles: Synthesis, characterization and antimicrobialevaluation. Bioorganic & medicinal chemistry letters. 2014 Jan 1;24(1):245-8.