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Different Method for the Production of Oxadiazole Compounds.

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Abstract

The creation of procedures for the environmentally friendly synthesis of materials and chemicals is referred to as "green synthetic protocol." The synthesis of different biologically active compounds is done through energy-efficient and environmentally safe processes like microwave irradiation technology, ultrasound-mediated synthesis, photo-catalysis (ultraviolet, visible, and infrared irradiation), molecular sieving, grinding, and milling techniques, etc. These procedures are regarded as sustainable technology and have gained value as green protocols for the synthesis of novel medicinal compounds because they have several advantages over traditional synthetic techniques.On the basis of this idea, Oxadiazole derivatives are made using a microwave irradiation approach to decrease the amount of byproduct generated and boost the product yield quantitatively in a shorter amount of reaction time. Because of this, the synthesis of pharmacological molecules under microwave irradiation adheres to a green chemistry strategy, which uses a set of guidelines to reduce or eliminate the use of dangerous and toxic ingredients in the design, production, and use of chemicals. By using cleaner solvents, catalysts, and appropriate reaction conditions, this strategy helps to reduce environmental pollution and boosts energy efficiency and atom economy. Oxadiazole is a heterocyclic molecule with five members that has two nitrogen and one oxygen atoms in its ring system. The oxadiazole moiety is garnering a lot of interest in the development of novel drug candidates due to its potential therapeutic activities, which include antibacterial, antifungal, antiviral, anticonvulsant, anticancer, antimalarial, antitubercular, anti-asthmatic, antidepressant, anti-diabetic, antioxidant, antiparkinsonian, analgesic, and anti-inflammatory properties. This review focuses on the many synthesis methods for oxadiazole derivatives that are heated using a microwave and the investigation of their diverse biological functions.

Keywords: Drug, green chemistry, microwave, oxadiazole, synthesis, biological activities.

INTRODUCTION

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The application of a set of guidelines that lessens the production of chemical hazards during the creation, production, and usage of chemical substances is known as the "green chemistry approach." By employing cleaner solvents, catalysts, and appropriate reaction conditions, this procedure significantly reduces environmental pollution while also improving the synthesis process's energy efficiency and atom economy. Because microwave-assisted synthesis reduces environmental contamination throughout the synthetic process, it adheres to the green chemistry approach. There are several advantages of using microwave radiation energy for medication production involving faster reaction rates, higher

product yields, and more pristine reactions. Chemical reactions that traditionally required hours or even days can now be completed in minutes thanks to microwave heating [1].

The implementing of a set of guidelines that lessens the production of chemical hazards during the creation, production, and usage of chemical substances is known as the "green chemistry approach." By employing cleaner solvents, catalysts, and appropriate reaction conditions, this procedure significantly reduces environmental pollution while also improving the synthesis process's energy efficiency and atom economy. Because microwave-assisted synthesis reduces environmental contamination throughout the synthetic process, it adheres to the green chemistry approach. In order to carry out drug synthesis, microwave radiation energy offers several advantages, such as improved product yields, faster reaction speeds, and cleaner processes. Chemical reactions that used to take hours or even days to complete can now be completed in minutes because to microwave heating [2].

These facts lead to the synthesis of oxadiazole derivatives, which decrease byproduct production and boost product yield in a shorter reaction time. Owing to structural similarities with oxadiazole, there is also great interest in the development of novel drug candidates with potential therapeutic activities, such as those that are antibacterial, antifungal, antiviral, anticonvulsant, anticancer, antimalarial, antitubercular, anti-asthmatic, antidepressant, antidiabetic, antioxidant, antiparkinsonian, analgesic, and anti-inflammatory [3].

Few calorie crops, such as rice, wheat, and maize, provide two thirds of the calories in the average human diet. These three crops alone account for most of the world's food security (Cassman, 1999).The greatest "weapon" we have to protect crops from fungal diseases is fungicide (Leadbeater, 2015; Oliver and Hewitt, 2014). Fungal crop pathogens constitute the biggest danger to this supply (Fisher et al., 2012) [4].

These variables cause the synthesis of oxadiazole derivatives, which decrease the production of byproducts and boost product yield in a reduced reaction time. The development of novel drug candidates with potential therapeutic activities is also receiving a lot of attention. Examples of these include those that are antibacterial, antifungal, antiviral, anticonvulsant, anticancer, antimalarial, antitubercular, anti-asthmatic, antidepressant, antidiabetic, antioxidant, antiparkinsonian, analgesic, and anti-inflammatory, and that share a structural motif with oxadiazole [5].

THE OXADIAZOLE MOIETY'S CHEMISTRY

Oxadiazoles are heterocyclic compounds with five members that have two nitrogen atoms and one oxygen atom in their ring structure. There are various isomeric forms of the oxadiazole moiety, such as 1,2,3-oxadiazole, 1,2,4-oxadiazole, 1,2,5-oxadiazole, and 1,3,4-oxadiazole, depending on the position of heteroatoms (oxygen or nitrogen) (Figure 2). These substances have the molecular formula C2H2N2O and belong to the azole family of chemicals. Among these isomers, the diazoketone tautomer is produced by the unstable isomer 1,2,3-oxadiazole ring-opening.

On the other hand, 1,3,4-oxadiazole is an aromatic compound that is thermally stable and is important in the development of novel therapeutic candidates with a variety of biological activities, including antitubercular, antibacterial, antifungal, anticancer, and anti-inflammatory properties [6].

The electrophilic substitution process in the oxadiazole ring is very challenging due to the very low electron density on the carbon atom.

On the other hand, if the oxadiazole ring is replaced with an electron-releasing group, the electrophilic assault happens at nitrogen. Analogously, the oxadiazole ring typically withstands nucleophilic assault. On the other hand, nucleophiles replace the halogen atom in the halogen-substituted oxadiazole, causing it to undergo nucleophilic substitution [7].

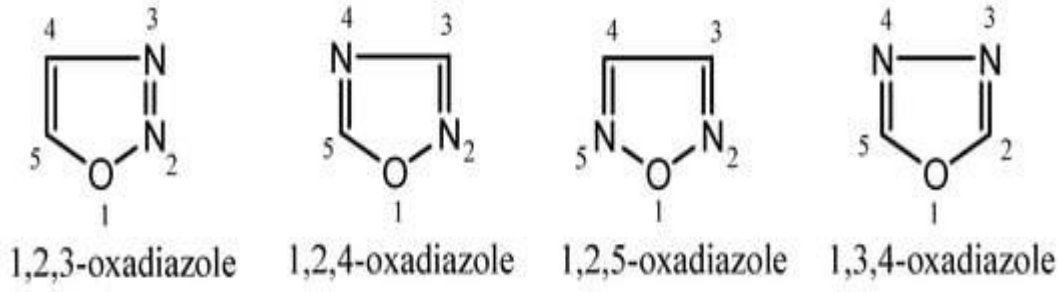

Figure 1. Chemical compositions of isomers of oxadiazole.

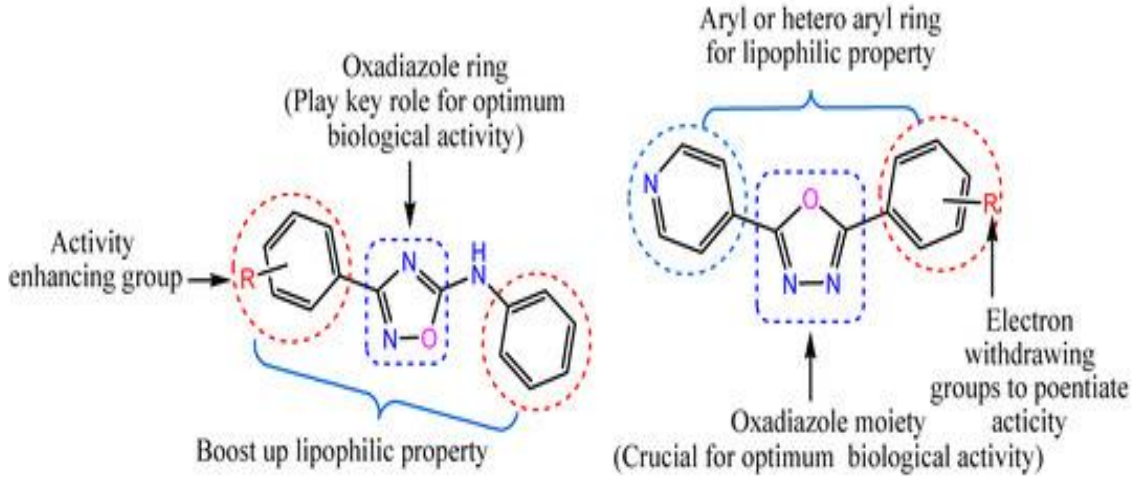

Figure 2. SAR analysis of derivatives of oxadiazole.

GREEN CHEMISTRY METHODOLOGIES

A variety of green chemistry techniques, such as microwave irradiation, ultrasonication, photo-catalysis, grinding, and milling, can be used to perform diverse chemical reactions (Figure 1). By increasing the rate of reaction with a shorter reaction time and a higher product yield, these technologies make organic processes more productive and economical. Mechanochemistry is used in synthetic procedures such as grinding and milling techniques to synthesize a variety of physiologically active chemicals quickly, cleanly, and efficiently without the need for solvents [8].

Oxadiazole Derivatives Synthesised by Ultrasound Mediation

Ultrasound-mediated organic synthesis is a strong technology that can be used to increase reaction rate and product yield in an environmentally friendly manner. The creation of high energy intermediates increases the ultrasonic irradiation.Compared to conventional procedures, this synthetic method can be regarded as an environmentally beneficial process for energy reduction and waste minimization. Similar to this, the prospective application of molecular sieves assisted synthesis in catalysis has garnered a lot of interest [9].

The synthesis, molecular docking, and antifungal evaluation of 5-(4-(benzyloxy)-substituted-phenyl)-3-((phenylamino)methyl)-1,3,4-oxadiazole-2(3H)-thiones were described by Nikalje et al. with the assistance of ultrasonography and molecular sieves. Using molecular sieves under ultrasound irradiation, these oxadiazole derivatives were effectively synthesized with superior product yields of 78–90% in shorter reaction durations than with standard heating procedures, which need 15–20 hours for refluxing. The compounds with the same name showed encouraging antifungal activity, and the scaffold that was created offers a useful model for producing antifungal medicines [10].

Research on the Structure-Activity Relationship (SAR)

The oxadiazole moiety is necessary for biological action such as antibacterial, antifungal, anticancer, antitubercular, antioxidant, analgesic, and anti-inflammatory qualities.

For alterations to result in distinct oxadiazole derivatives, positions C2 and C5 are necessary. By granting high affinity and selectivity towards the receptor's target binding site, the presence of electron-withdrawing substituents (nitro, methoxy, hydroxyl, chloro, bromo, and fluoro) amplifies the activity. The degree of activation or deactivation as well as the placement of the groups or substituents on the ring have a significant impact on a compound's high level of biological activity [11].

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The National Science Foundation and the Environmental Protection Agency launched the Green Chemistry Program in 1991.

Twelve key green chemistry concepts were developed by P.T. Anastas and J.C. Warner to lessen or completely eradicate the risk of chemical risks and environmental contamination [14].

1. Waste and byproduct prevention: It is crucial to conduct the synthesis in a way that minimizes or completely eliminates the production of waste and byproducts.
2. Atom economy: This refers to the creation of artificial processes that optimize the addition of reactants, or beginning materials and reagents, to produce the desired end products.
3. Use of less toxic and hazardous chemicals: Different synthetic processes should be appropriately planned to minimize or completely eliminate the harmful effects of drug use and generation on the environment and human health. 4. Creating Safer Chemicals: Chemical products should be designed to maintain their effectiveness while lowering their toxicity [15]. Figure 3

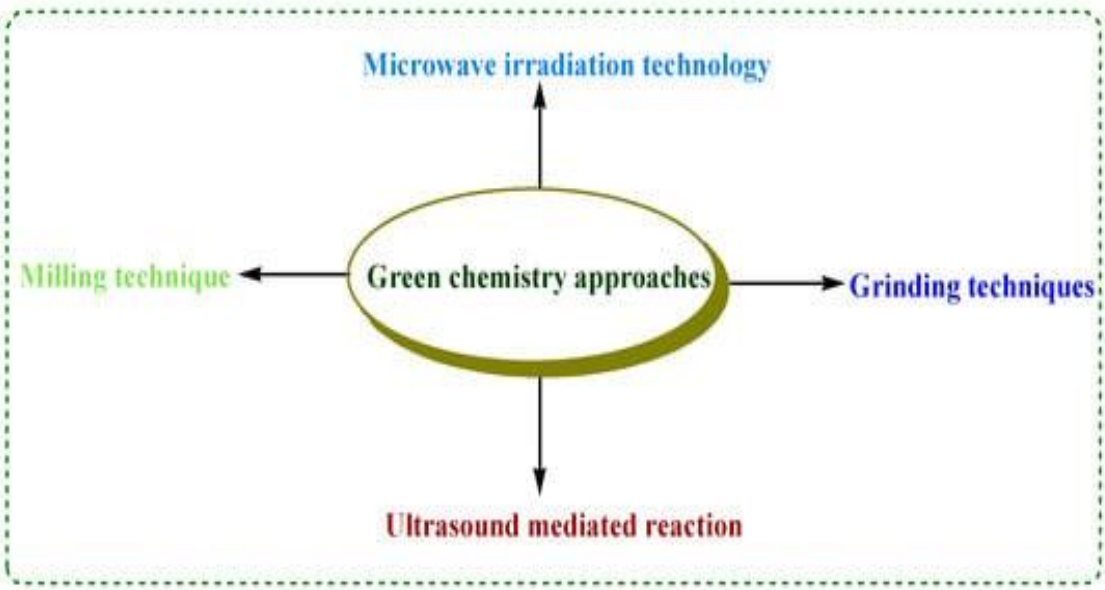

Figure 3. Green chemistry methods.

LITERATURE

Upcoming Development

Compared to traditional heating methods, microwave radiation works as a nonconventional energy source that can be employed to accomplish a wide range of drug synthesis with high yields in a short amount of time.Using the high energy of MWI, chemical processes that are sometimes impossible to perform using traditional methods can be carried out. Different oxadiazole derivatives can be produced and screened using microwave technology to identify novel therapeutic compounds with a range of biological activities, including antibacterial, antifungal, antidepressant, antitubercular, and anti-inflammatory properties. Because of its ability to participate in binding interactions with many targets or receptors that have the right metabolic profile, oxadiazole is therefore regarded as a crucial heterocyclic core and serves as a key scaffold for the development of new drug candidates. Because of its ability to participate in binding interactions with many targets or receptors that have the right metabolic profile, oxadiazole is therefore regarded as a crucial heterocyclic core and serves as a key scaffold for the development of new drug candidates [16].

Agents Antimicrobial

Over 1400 distinct species of microorganisms, including bacteria, viruses, protozoa, fungus, and helminthes, have been identified in literature to date. These organisms can cause illnesses in humans that frequently result in death. Remarkably, hardly 20 of them—mostly bacteria—are in charge of almost two thirds of the fatal instances. In high-developed nations, the number of estimated infections-related deaths has been steadily declining, from 16 million in 1990 to roughly 15 million in 2050, with projections of 13 million. However, the burden of pneumonia, HIV/AIDS, and other illnesses continues to weigh heavily on individuals. diarrhea, malaria, TB, and numerous other illnesses. Finding novel, efficient antibacterial/antiviral medications and developing cutting-edge therapies are two problems of utmost importance given the various pandemic dangers facing Europe and the rest of the world, including the recent infections with the SARS-CoV-2 virus that causes COVID-19 [16].

Anti-Insomnia Substances

A health disturbance known as insomnia is linked to inadequate or poor sleep duration. It typically manifests as a loss of sleep, difficulty concentrating, difficulty learning, negative mood, irritability, and occasionally even as a risk factor for heart disease, hypertension, dementia, or melancholy. According to estimates, up to 70% of adults worldwide suffer from sleeplessness, making it a serious public health issue. GABA antagonists were the mainstay of treatment for insomnia for many years, but the increased risk of addiction and worsened mood the following day prompted the development of new anti-insomniac medications. After the neuropeptides known as orexin A and orexin B were identified in 1998, their antagonists, such as The clinical trials for lemborexant and almorexant are complete. The FDA approved suvorexant, the first Dual-Orexin Receptor Antagonist (DORA) for treating insomnia, in 2014. Suvorexant is sold under the Belsomra brand.

More stronger molecules with a better pharmacological profile and safety are still needed, though, as common side effects include muscle weakness, strange nightmares, sleepwalking, and somnolence the next morning [17].

Identification of Fungal Infections in Plants

The pinnacle of plant pathology is the precise detection, identification, and quantification of plant infections. Before implementing disease control techniques, it is imperative to accurately identify the organisms causing a plant disease. As a result, using an accurate disease detection procedure is crucial for the identification of fungal infections in plants. It is crucial to be able to do so because many fungal infections exhibit symptoms that are similar to one another [18].

Commercially Accessible Biosensors for the Identification of Fungi

These days, on-site detection is becoming more significant in the diagnosis of plant diseases. Plant disease may now be detected in the field, even by growers themselves, thanks to the development of

quick and sensitive test kits and devices that address the need for on-site detection. Only a few number of the aforementioned methods have a strong chance of becoming commercial items at this time. The development of on-site gadgets that function better for plants is underway [19].

Difficulties and Hopes for the Future

The necessity for prompt, precise, and on-site plant infection examination has increased significantly, and it is predicted that the development of on-site testing technologies will revolutionize plant pathogen detection in the upcoming years. While the creation of LFDs has marked the beginning and is likely to remain a significant technology, new tests are probably going to use DNA sequencing technologies for real-time detection. creation of the following generation [20].

IN CONCLUSION

When compared to traditional synthetic methods, the synthesis of diverse heterocyclic compounds, such as derivatives of oxadiazole, under microwave irradiation exhibits a number of benefits, including exceptionally quick reaction times, high product yields, and straightforward purification procedures. Additionally, MWI is an environmentally favorable synthetic method because it uses less solvents in chemical reactions. Furthermore, because they have a variety of chemical configurations, oxadiazole derivatives have drawn the attention of medicinal chemists looking for novel therapeutic agents. The pharmacological activities of oxadiazole rings have been thoroughly investigated in order to create selective drug molecules, wherein the pharmacological activities of the molecule are determined by the presence of distinct substituents or groups. This paper compares the efficacious synthetic techniques of the traditional and microwave methods for the synthesis of oxadiazole derivatives, and then examines the various therapeutic actions of these compounds. A chemical library with a variety of biological functions can be produced by structurally altering or functionalizing oxadiazole scaffolds, according to a number of findings. The best antibacterial drugs against any chosen microbial strain were found to be among all the produced compounds.

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