Green Synthetic Approach: An Efficient Eco-Friendly Tool for Synthesis of Biologically Active Oxadiazole Derivatives

HemlataTamrkar, Research Scholar
Dr. Shiv Brat Singh, Supervisor
Shri Krishna University, Chhatarpur (M.P)

Abstract

Green synthetic protocol refers to the development of processes for the sustainable production of chemicals and materials. For the synthesis of various biologically active compounds, energy-efficient and environmentally benign processes are applied, such as microwave irradiation technology, ultrasound-mediated synthesis, photo-catalysis (ultraviolet, visible and infrared irradiation), molecular sieving, grinding and milling techniques, etc. Thesemethods are considered sustainable technology and become valuable green protocol to synthesize new drug molecules as theyprovidenumerous benefits over conventional synthetic methods.Based on this concept, oxadiazole derivatives are synthesized under microwave irradiation technique to reduce the formation of byproduct so that the product yield can be increased quantitatively in less reaction time. Hence, the synthesis of drug molecules under microwave irradiation follows a green chemistry approach that employs a set of principles to minimize or remove the utilization and production of hazardous toxic materials during the design, manufacture and application of chemical substances.This approach plays a major role in controlling environmental pollution by utilizing safer solvents, catalysts, suitable reaction conditions and thereby increases the atom economy and energy efficiency. Oxadiazole is a five-membered heterocyclic compound that possesses one oxygen and two nitrogen atoms in the ring system.Oxadiazole moiety is drawing considerable interest for the development of new drug candidates with potential therapeutic activities including antibacterial, antifungal, antiviral, anticonvulsant, anticancer, anti malarial, anti tubercular, anti-asthmatic, antidepressant, anti diabetic, antioxidant, anti parkinsonian, analgesic and anti inflammatory, etc. This review focuses on different synthetic approaches of oxadiazole derivatives under microwave heating method and study of their various biological activities.

Keywords

drug; **green chemistry**; **microwave**; **oxadiazole**; **synthesis**; **biological activities**

Introduction

The green chemistry approach refers to the utilization of a set of principles that reduces the generation of chemical hazardous during the design, manufacture and use of chemical

substances. This protocol plays a major role in controlling environmental pollution by using safer solvents, catalysts, suitable reaction conditions and thereby increases the atom economy and energy efficiency of the synthetic process. Hence, microwave-assisted synthesis followsthe green chemistry approach as it makes the synthetic process eco-friendly by reducing environmental pollution. Microwave radiation energy offers significant benefits to carry out drug synthesis, including increased reaction rates, product yield enhancements, and cleaner reactions.The chemical transformations which take hours, or even days, to complete can now be completed in minutes with the help of microwave heating .

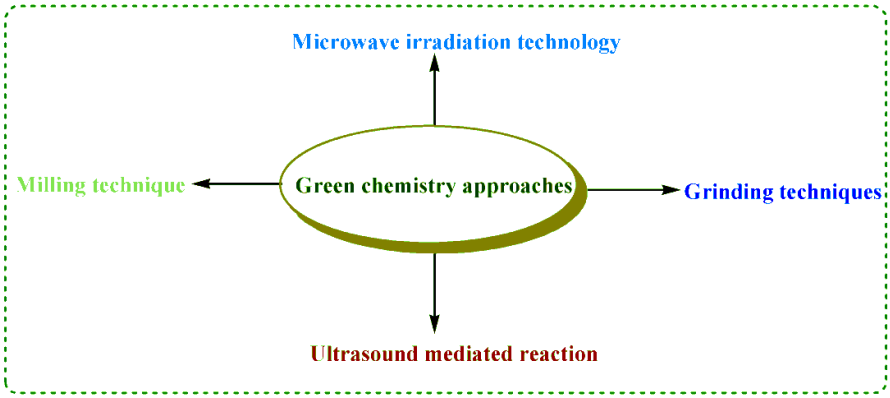
Similarly, the ultrasonic irradiation method is applied to accelerate various chemical reactions, including both homogeneous and heterogeneous systems. The use of ultrasound in organic synthesis involves specific activation based on the physical phenomenon, i.e., acoustic cavitations.In contrast, photo-catalytic reactions involve the use of ultra-violet, visible light and infrared radiation to generate new medicinally active compounds with diverse molecular structures. To carry out a photochemical reaction, the UV-visible spectra of the photoactive compounds are recorded. The photoactive compound is the molecule that can be electronically excited and undergoes chemical reaction from its excited state.

The grinding technique is also considered a green synthetic method to perform chemical reactions under solvent-free conditions with high product yield. Grinding of the recanting substances for a chemical reaction can be carried out by using mortar and pestle or by using a high-speed vibrating mill. Due to the collision between the reacting molecules, the chemical reaction is carried forward. A milling technique like ball milling is considered to be one of the automated forms of mortar and pestle. In the case of the ball mill, the reacting materials are placed in a reaction vessel equipped with grinding balls and covered with a lid. The vessel is allowed to shake at high-speed to carry out the chemical reactions.

Green Chemistry Approaches

There are various green chemistry approaches to carry out different chemical reactions that include microwave irradiation (MWI), ultra sonication, photo-catalysis, grinding and milling methods. By applying these technologies, organic reactions become more efficient and economic by enhancing the rate of reaction with reduced reaction time and high product yield. Synthetic approaches like grinding or milling techniques involve the application of mechano chemistry for the rapid, clean, efficient and solvent-free synthesis of various biologically active compounds.

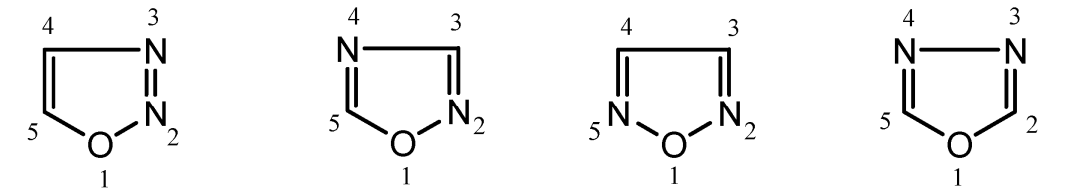
(Figure 1)



Chemistry of OxadiazoleMoiety

Oxadiazoles are five-membered heterocyclic compounds that possess one oxygen atom and two nitrogen atoms in the ring system. Depending on the position of heteroatoms (oxygen or nitrogen), there are different isomeric forms of oxadiazole moiety such as 1,2,3-oxadiazole, 1,2,4-oxadiazole, 1,2,5-oxadiazole, 1,3,4-oxadiazole. These chemical compounds are of the azole family with the molecular formula $C_2H_2N_2O$. Among these isomers, 1,2,3-oxadiazole is unstable and ring-opens to form the diazoketone tautomer. However, 1,3,4-oxadiazole is a thermally stable aromatic molecule and plays a major role in developing new drug candidates with diverse biological activities such as anticancer, antiparasitic, antifungal, antibacterial, antidepressant, antitubercular and antiinflammatory, etc.

(Figure 2)



Microwave-Assisted Synthesis of Biologically Active Oxadiazoles

Microwave-assisted drug synthesis is a Green technology that utilizes microwave radiation as a heating source to perform various synthetic reactions. The microwave radiation is used as an alternative energy source to complete various organic transformations in minutes instead of hours or even days. Microwaves are electromagnetic radiation with wavelengths ranging from one meter to one millimeter with frequencies between 300 MHz and 300 GHz . These high-frequency electric fields of the microwave are applied to heat the reacting substances of an organic reaction with electric charges. In the case of the polar reaction medium, these are

heated due to their dipolar rotation with the electric field and loose energy during collisions between reacting molecules. With the help of microwave heating technology, the rate of organic synthesis can be improved, and the drug products can be manufactured selectively by utilizing suitable microwave parameters. Thus, microwave technology provides several advantages such as instantaneous, rapid heating, homogeneity and selective heating as compared to conventional heating techniques like water bath, oil bath or sand batch, etc.

Future Development

Microwave radiation acts as a nonconventional energy source that can be used to perform a wide range of drug synthesis within a short period of time with high yields as compared to conventional heating methods.The chemical reactions which are not possible under conventional techniques can sometimes be carried out by utilizing the high energy of MWI. By applying microwave technology, different oxadiazole derivatives can be synthesized and also screened to find out new therapeutic molecules with diverse biological activities such as antibacterial, antifungal, antidepressant, antitubercular and antiinflammatory, etc. Hence, oxadiazole is considered a significant heterocyclic core and becomes a major scaffold for the development of new drug candidates because of its potential to be involved in the binding interactions with different targets or receptors with suitable metabolic profile.

9. Conclusions

The synthesis of various heterocyclic compounds like oxadiazole derivatives under microwave irradiation demonstrates several advantages in terms of remarkably short reaction time, high product yields and a simple purification process in comparison with the classical synthetic strategies. Moreover, also, the volume of solvents used during a chemical reaction is reduced, which makes MWI an environmentally friendly synthetic approach. Further, oxadiazole derivatives have attracted medicinal chemists in search of new therapeutic agents due to the presence of diverse molecular structures. The therapeutic potentials of oxadiazole rings have been extensively studied to develop selective drug molecules inwhich the presence of different substituents or groups in the molecule is responsible for displaying different pharmacological activities. In this review, the synthesisofoxadiazole derivatives by the conventional method and the microwave method is reported to compare their effective synthetic strategies followed by a study of their different therapeutic activities. From various results, it reveals that the structural modification or functionalization of oxadiazolescaffoldsto generate a compound library with diverse biological activities.

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