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Microwave Assisted Drug Synthesis (MADS): A Green Technology in Medicinal Chemistry

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Introduction

Drug therapies for various diseases are developed based on their biological targets. However, the development of new drug molecule with their desired biological properties is time consuming and expensive. In order to identify the potential drug candidates, rational drug design along with combinatorial chemistry has emerged to speed up the lead identification and optimization during drug discovery process. So, it is thought of interest toward technologies that allow rapid synthesis and screening of chemical substances to identify lead compounds with suitable potency and less toxicity. Thus, microwave accelerated drug synthesis (MADS) is considered as an emerging green technology with environmental friendly chemical processes in medicinal chemistry. Most of the drug synthesis proceeds faster with higher yields under microwave irradiation as compared to conventional heating method. Microwave technology possesses several advantages such as high efficiency, yield, selectivity, easy separation and purification [1,2].

History of Development of Microwave Technology

The first microwave oven was introduced by Tappan in 1955 but the widespread use of domestic microwave ovens occurred during the 1970s and 1980s. The first application of microwaves irradiation in chemical synthesis was published in 1986 by the groups of Richard Gedye and Raymond J. Giguere/George Majetich. Several research groups started experiments with solvent free microwave synthesis to eliminate the chemical hazards in the year 1990. Since the year 2000, commercial microwave reactors for chemical synthesis have become available to carry out the various chemical transformations in the research laboratories [3].

Types of microwave reaction

- Microwave assisted reactions using solvents
- Microwave assisted reactions under solvent free conditions
- Microwave assisted reactions using solid phase
- Microwave assisted reactions on mineral supports in dry media

Heating Mechanism of Microwave Synthesis

Microwaves are the form of electromagnetic radiation or energy. The microwave region of the electromagnetic spectrum lies between infrared and radio frequencies. Electromagnetic wave consists of both electric field and magnetic field. In typical microwave ovens, the magnetrons (microwave generators) produce a microwave wavelength of 12.25 cm which corresponds to a frequency of 2.45 GHz. Microwave irradiation elicits heating by two main mechanisms such as dipolar polarization and ionic conduction. When irradiated at microwave frequencies, electromagnetic waves pass through the dipoles or ions of the sample and cause the molecules to oscillate. In this process, energy is lost in the form of heat through molecular friction and dielectric loss. Because microwave radiation is introduced into the reaction system remotely without direct physical contact with reaction materials, this can lead to a rapid temperature increase throughout the sample that cause less by-products formation and decomposition of products. Every solvents and reagent also absorb microwave energy differently. So, the organic solvents are categorized into three types such as low, medium and high absorber of microwave radiation. The low absorbers are generally hydrocarbons while the high absorbers are more polar compounds like alcohols and medium absorbers are water, dimethyl formamide, acetonitrile, acetone, acetic acid etc [4].

Advantages of microwaves synthesis

Microwave assisted drug synthesis provides following benefits over conventional synthesis

- Increased reaction rate with less usage of energy for chemical reaction
- High efficiency and uniform heating throughout the reacting medium
- Selectivity of chemical reaction with improved reproducibility
- Reduced reaction time with high yield and purity of the product
- Reduced environmental heat loss
- Reduction in unwanted side reaction
- Reduced wastage of heating reaction vessel
- Low operating cost

Applications of Microwave Assisted Organic Synthesis

Most of the peptide synthesis is carried out on a solid phase and it has been observed that microwave irradiation enhances the deprotection, coupling, cyclization, condensation, isomerization, oxidation, reduction, cycloaddition, rearrangement, nucleophilic substitution and cleavage of chemical reactions. Based on the highly efficient microwave heating technology, a series of potent and selective allosteric AKT kinase inhibitors were developed. These inhibitors were derived from a 2,3-diphenylquinoxaline [5].

Conclusion

Rapid synthesis and quick construction of diverse compound libraries are essential to speed up the drug discovery and development process. For high speed synthesis, microwave irradiation heating technology has gained its importance as an instrumental tool in the

drug discovery programs. So microwave technology is emerging as an alternative powerful energy source to accomplish chemical transformations in minutes, instead of hours or even days.

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