**Benefits of Microwave-Assisted Organic Synthesis over Conventional methods in Synthetic Chemistry**

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**Abstract**
Microwave-assisted organic synthesis (MAOS) is a branch of Green Chemistry which has prolonged much deliberation in current age. Mainly, microwave-assisted chemical transformations are pollution free, environmental and offer high returns together with ease in processing and handling. This technique proposes a modest, renewed, efficient, fast and economic approach intended for the synthesis of large organic molecules. Currently, the microwave-assisted organic reaction has appeared as an advanced implement in organic synthesis.

In the current review, an attempt is made to focus on the benefits of microwave-irradiation in organic synthesis which reveal the Impact of MAOS over conventional method with the prominence in synthetic chemistry.

**Keywords:** Microwave-assisted organic synthesis (MAOS), Microwave irradiation, Green Chemistry, Conventional method.

**Introduction**
Microwave chemistry has come up with an advantage for the attention of environmental chemists. As an integral part of Green Chemistry, the field of Microwave-assisted organic synthesis (MAOS) has seen spectacular growth in the recent era. The microwave mediated organic reactions take place more rapid, safe and in an environmentally friendly manner with high yields. Such reactions not only reduce the amount of waste solvent generated, nonetheless the products often need very little or no purification1. These processes will hopefully be adopted by big industries as well by contributing to the betterment of the environment.

Concerning with the use of microwave irradiation in organic synthesis, significant reports have been published in 198645 for the synthesis of organic compounds. Robert Bunsen developed the burner which acts as an energy source for heating a reaction vessel, later most organic reactions were using old model heat transfer equipment such as oil baths, sandbaths and heating jackets1. These heating systems are laborious and develop temperature gradient within the sample, or sometimes lead to product, substrate or reagent decomposition whereas Microwave-Assisted Organic Synthesis (MAOS), developed in recent years, has been considered superior to traditional heating.

**Theory and Principle of MAOS:** In current ages, microwave irradiation is used comprehensively for resounding chemical reactions and developed as a convenient non-conventional energy source for organic synthesis91117 in the electromagnetic spectrum microwaves region situated among infrared and radio waves region. Microwaves take wavelengths amongst 1 mm and 1 meter and with an amount of 0.3-30 GHz, hence have similar frequencies to radar and telecommunication devices. Though, intended for laboratory reaction condition, 2.45 GHz frequency is preferred for its right penetration depth1. The microwave radiation passes through the vessels heating only the reactants and solvents. If the apparatus is sufficiently intended, the temperature increase will be uniform throughout the sample, which can lead to a smaller amount of by-products and or decomposition. In pressurized systems, it is possible to rapidly increase the temperature far above the standard boiling point of the solvent used.

Recently an alternative method for successive microwave-assisted organic reactions characterized by Enhanced Microwave Synthesis has been developed437. EMS is examined by superficially cooling the reaction vessel with compressed air, along with controlling microwave irradiation, more energy use to the reaction mixture. In Conventional Microwave Synthesis preliminary microwave power is high, increasing the bulk temperature TB to the preferred set point rapidly. However, upon getting this temperature, the microwave power cuts or shuts off wholly to uphold the anticipated bulk temperature. With Control Microwave Synthesis, microwave irradiation is principally used to reach TB earlier. Microwave improvement of chemical reactions takes place through the submission of microwave energy. This source of energy directly stimulates the molecules in a chemical reaction. EMS confirms that a high, constant level of microwave energy is applied.

**Mechanism of Heating:** The central principle behind the heating system in a microwave oven is an effect of the contact of a charged particle of the reaction material with electromagnetic irradiation. All the wave energy changes its polarity from positive to negative with each cycle of the wave, causes quick orientation and reorientation of the molecule. If the charged particles of material are allowed to travel, a current will persuade which travels in time through...
the field. If charge particles are bound within regions of the material, the electric field component will move till opposing force equivalent the electric force.

In dipolar polarization, it is a progression through which heat is produced by polar molecules. When polar molecules contact an oscillating electromagnetic field of suitable frequency, they attempt to track the field and bring into line with the phase. The use of microwave dielectric heating in organic, inorganic and organometallic chemistry has expanded identical rapidly. Microwave dielectric heating is promptly recognized procedure in synthetic chemistry. It includes distress of polar molecules or ions that oscillate below the effect of an oscillating electric or magnetic field. In the presence of an oscillating field, particles try to orient themselves or be in phase — however, the motion of these particles is restricted by resisting forces and generates random motion producing heat. The heating features of microwave irradiation conditions are dependent on its dielectric properties.

The advantages of microwave dielectric heating for analytical processes are also recognized for chemical analyses. The interactions amongst microwave energy at 2.45 GHz with water on the surface of the analytical models although in the conduction mechanism make heat over resistance to an electric current, the oscillating electric field produces an alternation of electrons in a conductor; follows an electric current, features internal resistance which heats the conductor. The conduction mechanism has much stronger interaction than the dipolar mechanism about heat generating capacity. However, this mechanism is not applicable to materials that have high conductivity.

It is to emphasize that the microwave heating effect depends on the frequency along with the power applied, the heat generated by this process is directly related to the ability of the matrix to align itself with the frequency of the field. If the particle does not have enough time to rearrange or reorient too quickly with the applied field, no heating occurs. The allocated frequency of 2.45GHz used in all commercial systems lies between these two extremes and gives time to rotate to the alternating electric field.

Effects of Solvents: In microwave-assisted synthesis, a homogeneous mixture is preferred to acquire a uniform heating pattern. Every solvent and reagent absorb microwave energy inversely having a different degree of polarity inside the molecule, moderately affected by altering microwave field. The frequency for maximum microwave device is 2.45 GHz, the dielectric constant merely changes with temperature. When a solvent is heated, the dielectric constant falls with the rise in temperature. For the complete mixture, adding a small amount of a polar solvent with considerable loss tangent indicates advanced heating rates, for instance, water, ethanol, acetonitrile, N, N-dimethylformamide (DMF), acetic acid, chloroform, dichloromethane, acetone, ethylene glycol. Those compounds have high dielectric constants and lean towards heat quickly beneath microwave irradiation, while less polar substances along with extremely well-ordered crystalline matters are poorly absorbing.

Operations of the Microwave: When microwaves enter a cavity, they are reflected by the walls. The reflection of the waves generates a three-dimensional immobile arrangement of perpendicular waves inside the cavity termed modes. The cavity in a domestic microwave oven intended characteristically 3-6 different modes projected to provide a uniform heating pattern although in multi-mode technique offers a field pattern with extent of high and low field strength, denoted as hot and cold spots. For small loads, the distinct heating pattern is required and for that single mode cavity microwave apparatus is preferred.

Single Mode Apparatus: It is designed for chemical synthesis consuming microwave acknowledged in domestic microwave ovens. It has the capability to generate a vertical wave pattern, created by the intervention of fields that have the same amplitude but different oscillating directions. This interface produces an array of nodes where microwave energy intensity is zero and an array of antinodes where the magnitude of microwave energy is at its highest. Distance of the sample from the magnetron should be appropriate to ensure the sample is placed at the antinodes of the vertical electromagnetic wave pattern.
Afterwards, the reaction mixture can quickly cool by compacted air; this is an inbuilt cooling feature of the device. Consequently, the apparatus can process volumes ranging from 0.2 to about 50 ml under sealed -vessel conditions and 150 ml under open-vessel reflux conditions. Now it is used for moderate drug discovery, automation and combinatorial chemical applications.

**Multi-Mode Apparatus:** In multi-mode apparatus, avoid generating a standing wave pattern inside it. Its goal is to generate as much chaos as possible inside the apparatus. Higher are the chaos, higher is the dispersion of radiation which increases the area that causes efficient heating inside the apparatus. Consequently, a multi-mode microwave heating apparatus can accommodate some samples simultaneously for heating. It is designed for bulk heating and carrying out chemical examinations such as ashing, extraction. In sizeable multi-mode apparatus, several liters of the reaction mixture are processed in both open and closed-vessel conditions.

**Profits of Microwave over Conventional Method:**
Microwave technology has become very important in the synthesis and it is reasonable to assert that there are now very few areas of synthetic organic chemistry that have not been shown to be enhanced using microwave heating\textsuperscript{16}. Microwave radiation is recognized as a tremendously efficient heating source for chemical reactions; it is one of the optimum procedure for shorter reaction time\textsuperscript{38}, reducing excess reagents, accelerates the reaction rate, delivers improved yields and uniform heating for sustenance in developing cleaner and greener synthetic routes:\textsuperscript{4,5,12-15}

a. Increased Rate of Reactions - microwave heating enhances the rate of specific chemical reactions repeatedly due to its ability to substantially increase the temperature of a reaction.

b. Efficient Source of Heating- Heating using microwave radiation is a highly efficient process and results in significant energy saving. Energy consumption is less.

c. Higher Yields - In individual chemical reactions, microwave radiation produces higher yields compared to conventional heating methods.

d. Uniform Heating System -Different to conventional heating methods. Microwave radiation provides uniform heating through a reaction mixture.

e. Environmentally approachable - Microwaves heat the compounds directly. Consequently, the practice of solvents in the chemical reaction is excluded and the usage of microwaves has also concentrated on the amount of purification vital for the end products of chemical reactions concerning toxic reagents. Hence, reactions through microwaves are cleaner and more environmentally friendly than conventional heating methods.

f. Superior Reproducibility of chemical reactions - Reactions with microwave heating are further reproducible associated with conventional heating because of uniform heating and improved regulator development parameters. The temperature of chemical reactions is efficiently monitored with relevance in the lead optimization phase of the drug development process.

**Benefits of Microwave-Assisted Organic Synthesis (MAOS):**

**Microwave in Heterocyclic Reactions:** Heterocyclic chemistry is recognized as discipline of general significance that touches almost all aspects of modern organic chemistry related to the search for new organic compound derivatives with desirable properties which are widely used in the pharmaceutical industry and nutraceutical applications\textsuperscript{46}, medicinal chemistry, biochemistry and synthetic organic chemistry. Heterocyclic compounds hold a special place among pharmaceutically important natural and synthetic materials\textsuperscript{30,45} — the remarkable ability of heterocyclic nuclei to serve as traditional vital elements of numerous drugs. Heterocycle molecules are widely deliberate for their synthesis and their uses are not only in medicinal chemistry but also in optics, electronics and material sciences.

Considerable attention is paid in scheming and resonant advanced synthetic protocols in heterocyclic chemistry to...
enhance more eco-sustainable approaches. These processes come under green chemistry. Also, the MW-assisted organic syntheses lead in short time to vast libraries of small-sized heterocyclic compounds. Microwave-assisted syntheses of heterocycles reported the synthesis of other modular reactions with 6-membered heterocycles and their fused analogs arranged according to the number of heteroatoms — for instance, Pyrimidines\textsuperscript{47,48} Quinazolines\textsuperscript{49,50} Pyridopyrimidines\textsuperscript{51} and Piperazines\textsuperscript{52} featuring high molecular diversity with potential bioactivities.

**Medicinal Chemistry and Drug Synthesis:** The use of microwave irradiation in organic synthesis has become increasingly popular within the pharmaceuticals and many other industries because it is a new enabling technology for drug discovery\textsuperscript{33} and developments. Mw assisted heating under the controlled condition is a unique technology for medicinal chemistry and drug discovery applications. It results from an increasing knowledge of fundamentals of the dielectric heating theory, availability of equipment designed especially for the laboratory use as well as for the discovery of the unique techniques of the microwave syntheses\textsuperscript{28}. Since it often intensely reduces reaction times, characteristically from days or hours to minutes. For instance, reaction temperature and time, variations in solvents, additives and catalysts, or the molar ratios of the substrates are evaluated in few hours to optimize the preferred chemistry\textsuperscript{2}.

Similarly, MAOS technology often facilitates the discovery of novel reaction pathways, because the extreme reaction conditions attainable by microwave heating sometimes lead to unusual reactivity that cannot always be duplicated by conventional heating. Currently, the microwave irradiation technique gets an exponential acceptance for improving chemical synthesis\textsuperscript{37}. Many industries approve MAOS to increase their productivity. Scaling up compounds for gram to kilograms extents is crucially bound for the synthesis of the drug. Several milligrams- and gram-scale synthesized drugs cannot be reproduced as safety issues on larger scales\textsuperscript{31}. Microwave expertise offers the opportunity empowering chemists to devote their treasured time to generate novel synthetic procedures, not reconstructing them.

**Microwave and continuous flow technologies in drug discovery:** An exemplary large-scale continuous flow microwave reactor was reported. Microwave and continuous flow microreactors are developed as conventional heating sources in new pharmaceutical industries\textsuperscript{28}. Through the introduction of microwave irradiation, reactions that acquired days to complete can be performed in minutes. Pharmaceutical companies take an easy-going way to advance the greenness and efficacy of many synthetic operations. The combined force of these technologies offers the potential to revolutionize discovery and manufacturing processes.

**Biochemical and clinical applications:** Microwave irradiation is a surprising source of energy for biochemical applications\textsuperscript{52}. The tentativeness of its onset, compared to organic synthesis, is most expected as a result of the high temperatures related to microwave-assisted alterations. Various biochemical molecules are temperature-profoun — many studies with recent technology, temperatures as low as 35–40°C supported by specific power input which approves a much more comprehensive range of chemistries to explore. Several studies are published on polysaccharides\textsuperscript{31} nucleosides, peptides\textsuperscript{32} proteins, peptoids, chitosan\textsuperscript{52} while in heterocyclic compounds, chromenes belong to a chemically important class having different biochemical prominence. Development of environmentally benign, efficient and economical methods for the synthesis of chromenes remains a significant challenge in synthetic chemistry\textsuperscript{27}.

In the recent biological applications of new chromenes, ready via microwave irradiation comprised to produce biologically and chemically essential chromenes in a time sensitive manner. Also, nuclear imaging using positron emission tomography (PET)\textsuperscript{19} is a dynamic method for clinical applications. It is very influential in vivo imaging modalities, proficiently guided and accelerated clinical trials of investigational new drugs. Conventional chemical syntheses of the short half-life radionuclides used in the process impose numerous limitations on the scope of available ligands. By utilizing microwave assisted synthesis methods, many of these limitations can be overcome.

**Homogeneous and Heterogeneous Catalysis:** The efficiency of microwave flash heating in accelerating organic transformations is proved in several different fields of organic chemistry\textsuperscript{11,25} The MW heated reactions in homogeneous media are performed at atmospheric pressure. Heterogeneous catalysis is favored by the chemical industry as it leads to ease separation and the likely usage of a fixed-bed reactor. MW irradiation can however actively enhance activity via the selective overheating of catalyst particles.

The combination of heterogeneous catalysts with microwaves has several advantages. Most of the positive catalysts highly absorb microwave irradiation and are considered as an internal heat source and reactions occur at the active surface of the catalyst and the direct coupling of the metal with microwaves can generate high (undetectable) local temperatures on the surface. This specific account is developing fast, vigorous and careful microwave-assisted transition metal-catalyzed reactions include selective Heck couplings, cross-couplings and asymmetric substitutions.

**Metal-Organic Frameworks (MOFs):** Metal-organic frameworks are a class of porous polymeric material, consisting of metal ions linked together by organic bridging ligands. Microwave irradiation is used to provide energy for the growth of MOFs\textsuperscript{32}. Microwave heating allows short reaction times, fast kinetics of crystal nucleation and growth.
and high yields of desirable products which isolate with limited or no minor products. The benefits of this technique include high efficiency, phase selectivity, particle size reduction and morphology control. Microwave heating, used in organic chemistry is now applied to the preparation of multi-dimensional coordination polymers, more commonly known as metal-organic frameworks (MOFs)\textsuperscript{20}. The synthetic routes towards MOFs, including microwave-assisted synthesis, are the recent development of MOFs for a wide variety of applications\textsuperscript{24}.

**Development of Eco-sustainable Novel Bio-inorganic Hybrid Materials:** A new organoclay, bio-inorganic hybrid material, was successfully prepared through the "green chemistry" principles. Use microwave irradiation together for the solvent-free synthesis of the organic filter (UVB filter) with hydrothermal intercalation in a sodium Bentonite clay. It signifies the use of Na-Bentonite cationic clay as an introducing agent of the manufactured quaternary UVB filter accompanied by the MW-assisted method\textsuperscript{23}.

**Applications of microwave heating in minerals processing:** Microwave heating is pragmatic to a quantity of minerals processing solicitations. Existing data on microwave heating are characteristic of some naturally occurring minerals and reagents grade compounds. Microwave investigation areas connected to mineral processing include waste immobilization using microwave vitrification and microwave combustion synthesis of ceramics. One of the most capable mineral processing applications, which touched the pilot plant scale, is the regeneration of granular activated carbon.

**Fluorescent Dyes:** When organic or inorganic specimens absorb and subsequently re-radiate light, the process is typically a result of fluorescence or phosphorescence. Fluorescence emission is thoroughly simultaneous with the absorption of the excitation light, as the time delay between photon absorption and emission is typically less than a microsecond. Fluorescents are a relatively new class of organics\textsuperscript{44}. These materials have many applications, as a penetrant liquid for crack detection, synthetic resins, plastics, printing inks, non-destructive testing and sports ball dyeing. Using microwave radiation for synthesis and design of fluorescent dyes is of great interest, as it decreases the time required for synthesis and the synthesized dyes for industrial scale.

There are so many fluorescent dyes, synthesized by applications of the microwave; fluorescein\textsuperscript{12,43} rhodamine\textsuperscript{39,40} coumarins\textsuperscript{41} naphthalimide, perylene and quinine.

**Biodiesel Production:** Microwave handling appeared as a tool in organic synthesis and displays an essential role for the transformation of biomass into chemicals and biofuels and switch with renewable resources\textsuperscript{18}. The microwave is processing a higher yield with a cleaner profile in comparison to other methods. Incorporation of processing methods with microwave irradiation has resulted in a significant reduction in the time required for many processes while the reaction efficiencies increased noticeably, the perspective of the microwave technology to achieve superior outcomes over the conventional methods in biodiesel production. The energy utilization for microwave-based biodiesel synthesis is lower and cost-effective.

**Conclusion**

Microwave-assisted organic synthesis (MAOS) appeared as an advanced procedure in synthetic organic chemistry including solvent-free reactions. The main reasons for the increasing practice of microwave equipment are intended for synthetic chemistry and the growth of solvent-free technique upgraded the safety features. A unique benefit of this technology includes the enhanced rate of the reaction, a decrease in reaction time with upgraded yield and superiority of the product. The choice offered by microwave-assisted organic synthesis is growing in the industry.

In the future, numerous other Microwave Assisted reactions will grow, simplify the time-consuming conventional procedures over microwave for assisting different organic reactions as a critical tool in synthetic organic chemistry.

**References**


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