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Review Article

Microwave-Assisted Organic Synthesis: An Efficient Green Synthesis

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ABSTRACT

Microwave-assisted organic synthesis in convergence with the principles of green chemistry is rapidly conquering its unending position in the modern era of chemical sciences. Microwave chemistry is science of using microwave radiation to perform chemical reactions. Microwaves heat medium containing polar molecules in a fluid or conducting ions in a solid, by acting as high-frequency electric fields. Polar solvents are heated because their constituent molecules rotate with the field and lose energy in collisions, therefore for the chemical reactions to continue, the dipole moments of molecules are necessary. The choice of microwave-assisted synthesis over conventional synthesis provides plethora of advantages to develop convenient cleaner synthetic routes such as higher yields in a fraction of time, minimum use of toxic starting materials and solvents, accelerated reaction rates and greater selectivity. The fundamental mechanisms operating in microwave reactors involve Dipolar-polarization and conduction. In recent times, the use of microwave reactors is popularly increasing in both industries and academia. Chemists are discovering microwave technology as a coping mechanism for hazardous, non-environmentally friendly chemical reactions. The present article highlights the advantages of microwave heating over conventional heating by giving examples of popular reactions which can be carried out easily and quickly by this technique, as well as synthesising environment friendly products.

Key words: Electric charges, Electric field, Green chemistry, Microwave technology.

1. INTRODUCTION

Green chemistry is a coping strategy for the environment as it looks for positive approaches to deal with the issues of hazardous chemical waste accumulation, which is becoming increasingly problematic [1]. Chemical waste that is improperly managed has the potential to harm and poison both land and aquatic sources [2]. This form of trash has a variety of origins, all of which have substantial and harmful consequences for aquatic and human life [3]. Furthermore, the use of toxic chemicals in laboratories is incredibly dangerous, and long-term exposure to these chemicals can result in a variety of health issues [4]. As a result, the noble concept of green chemistry opens many avenues in a new era of chemical science that has been proven to be environmentally beneficial: one such idea is microwave-assisted chemical reactions [5]. This technique offers clean, fast, efficient, and ecologically friendly synthesis of organic molecules [4,5]. Many traditional processes, such as refluxing, derivative preparations, and crystal preparation on a sand bath, can now be completed in a matter of minutes with microwave heating [6]. In comparison to conventional synthesis, the following Table 1 [7] summarises some of the most significant properties of microwave heating in comparison with conventional heating and comparison of reaction time and product yield for different reactions using both approaches may be compared and studied using Figures 1 and 2.

2. MICROWAVE-ASSISTED SYNTHESIS: HISTORY AND BASICS

Dr. Percy LeBaron Spencer's radar-related endeavor of producing magnetrons resulted in the first-ever microwave in 1946 in the United States [8]. While standing in front of the active radar, he witnessed three instances. He first noticed the melting of a candy in his pocket, and then he looked at it with some popcorn kernals. In a matter of seconds, they cracked, popped, and sprayed all over the surrounding area. Finally, he placed an egg near the active radar, which exploded. Spencer was enlightened by the light of the explosion with a rational, scientific thought: Could this idea be used to cook other foods? He researched, experimented, and in 1947, a commercial microwave oven with a height of 6 feet, a weight of 750 pounds, and a price range of \$2000–\$3000 was introduced. It was in 1967 that the first domestic, countertop microwave oven was introduced by Amana which was smaller in size and more reliable than previous models [9]. Microwave irradiation is a type of electromagnetic irradiation that ranges from 0.3 to 300 GHz in frequency [Figure 3]. Most of the microwaves, whether residential or microwave reactors mainly for chemical synthesis, functions at a specific wavelength of 12.24 cm (2.45 GHz- frequency range) to prevent obstruction with cellular and telephony frequencies. In this frequency range, the energy of a microwave photon (0.0016 eV) is less than the energy of Brownian movement, therefore, it cannot interrupt chemical bonds. As a result, microwaves are ruled out as a source of chemical reactions [10].

3. HEATING SYSTEM IN MICROWAVES

The fundamental concept of heating system in microwaves is based on "Microwave di-electric heating effects" which defines the ability of a specific material (solvents, reagent, or anything else) to absorb microwave radiation and convert it into heat [11]. The potential of a

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material to convert electromagnetic energy into heat is determined by loss tangent (loss factor/loss angle), tan δ at a specific temperature, and frequency [12]. More the value of tan δ, more will be the absorption by the medium and consequently rapid will be the heating. Generally, solvents are classified as high (tan 0.5 δ>), medium (tan δ 0.1–0.5), and low microwave absorbing (tanδ < 0.1) [13]. Table 2 summarizes the loss factor values of common solvents.

Microwave heating mechanism caused by the electric component of electromagnetic radiation (EMR) occurs mainly by following two mechanisms [11]:

3.1. Dipolar -polarization

The dipoles or ions try to realign themselves along the electric component of the field as the electric field is applied [11,12] [Figure 4]. As a result of molecular friction and dielectric loss, heat is generated. The most important criterion for dipolar polarization is that the quantity of heat generated by this process is proportional to the matrix's capacity to align itself with the applied field's frequency. The molecules assigned frequency of 2.45 GHz, which is utilized in all commercial systems, is in the middle of these two extremes.

3.2. Conduction

In conduction mechanism, a free ion or ionic species move translationally through space and tries to align with the moving electric field [11] [Figure 4]. By doing so, heat is generated as a result of molecular friction. Therefore, conduction mechanism generates heat through resistance to an electric field.

Table 1: Comparison between microwave heating and conventional heating [7].

S. No.	Conventional heating	Microwave heating
1.	Non- uniform heating through thermal or electrical sources	Uniform heating through electromagnetic waves
2.	The heating rate is lower	The heating rate is much higher
3.	Energy consumption is more	Energy consumption is less
4.	Slower reactions	Faster reactions
5.	Less yield %	High yield %
6.	The boiling point of a substrate limits the greatest temperature	The temperature can be elevated above the substrate's boiling point.
7.	Non-reproducible reactions	Reproducible reactions

Table 2: Loss factors (tan δ) of solvents at 2.45 GHz and 20°C [13].

Solvent	tan δ
Ethylene glycol	1.35
Ethanol	0.941
Methanol	0.659
Acetic acid	0.174
DMF	0.161
Water	0.123
Chloroform	0.091
Acetone	0.054
Toulene	0.04
Hexane	0.02

3.3. Di-electric Loss

When EMR reaches a substance, it promotes it to one of its excited energy levels. A Jablonski diagram is the easiest way to understand this. There are various vibrational levels within electrical levels, and rotational levels within vibrational levels, and so on. As a result, when EMR strikes matter, an energy exchange occurs between matter and radiation. As a result, matter moves to a higher energy level, but it cannot stay there indefinitely and must return to the ground state, which produces heat.

4. MICROWAVE-ASSISTED ORGANIC SYNTHESIS

Microwave technique aims at performing reactions with the least toxic starting materials to get cleaner, faster, and eco-friendly products. The microwave-assisted organic synthesis can be categorized into three types [14].

4.1. Reactions Using Neat Reactants

Reactions that uses pure or nearly pure starting materials are known as neat reactions and the starting materials are termed as neat reactants [14]. It is a positive step towards the goal of solvent-free reactions. One such example of neat reactions is MANNICH REACTION displayed in Figure 5.

4.2. Reactions Using Solid Mineral Support

The use of solid mineral support, in which chemicals are adsorbed onto mineral oxides and then irradiated with microwaves in dry media, is a widely popular approach of accomplishing solvent-free reactions [15]. Based on the type of organic processes involved, acidic or basic supports such as alumina, silica, clays, or zeolite are utilized. One such example is of HECK, SUZUKI, AND STILLE REACTION displayed in Figure 6.

4.3. Reactions Using Solid-liquid Phase Transfer Catalyst (PTC)

PTC is a type of catalyst which dissolves all reactants in one phase, eliminating the need for costly solvents. It is mostly employed for ionic reactants, which are soluble in the aqueous solution but insoluble in the organic solution, hence PTC aids in their solubility [16]. One such example of a reaction using PTC is the FORMATION OF CINNAMYL ACETATE displayed in Figure 7.

In Table 3 some more examples of common classical reactions are shown which can be carried out via microwave heating with no usage of solvents [9].

4.4. Beckmann Rearrangement

In the presence of acid (Figure 8), this reaction converts ketoximes to amides or lactams. To facilitate the rearrangement, very powerful acids have traditionally been utilized. Under microwave irradiation, Loupy and coworkers were able to perform simple Beckmann rearrangements on montmorillonite K10 clay with good yields (68–96%) [17].

4.5. 2- 1, 3 Cycloaddition Reaction

The use of microwave technology to perform 1,3-dipolar cycloaddition processes, a key tool for the production of five-membered heterocycles, is described in this paper. Microwave technology can be used to make 1,3-dipoles (nitrones, nitrile oxides, azomethine ylides, azomethine imines, nitrile imines, azides, and carbonyl ylides) and enhance

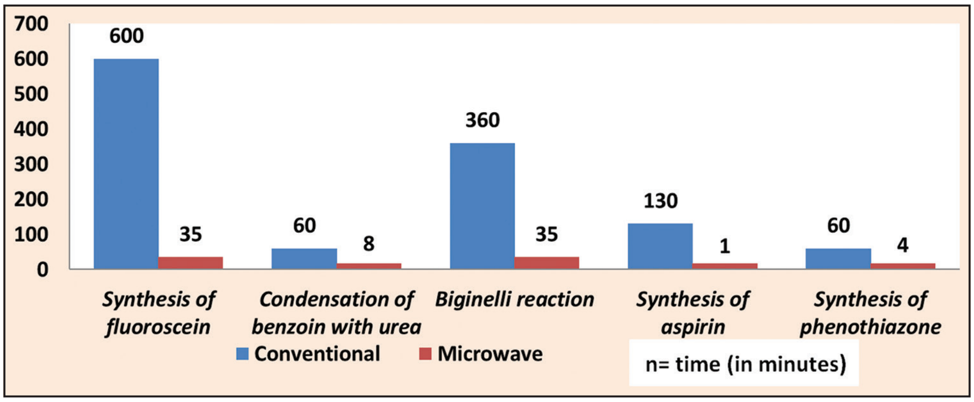

Figure 1: Comparative analysis of reaction times (in minutes) [8].

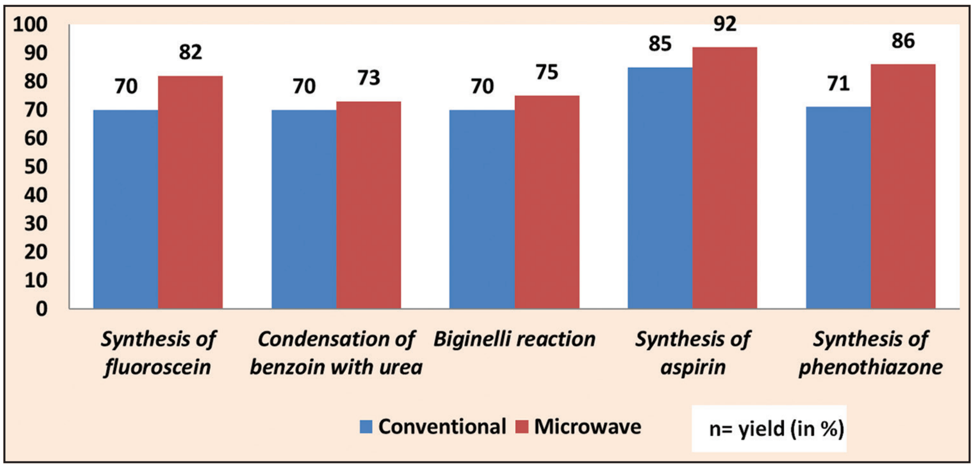

Figure 2: Comparative analysis of product yield (in percentage) [8].

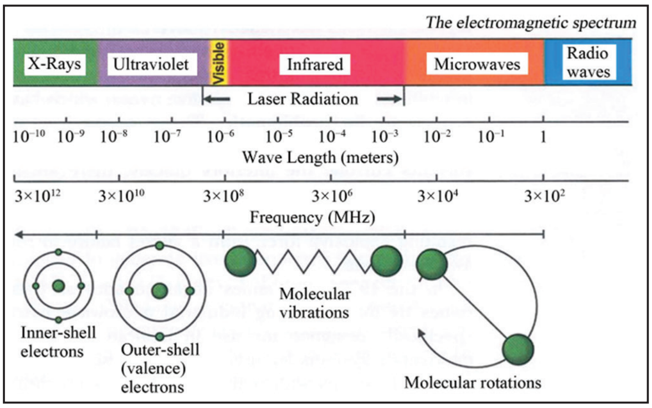

Figure 3: The EMR spectrum with microwave properties. Adapted from ref [5].

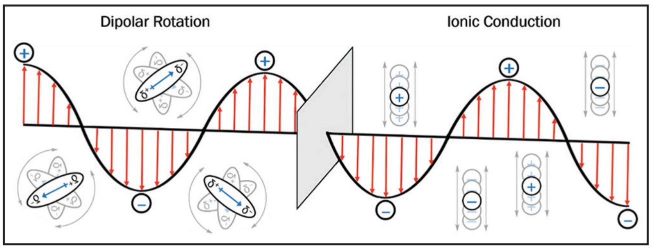

Figure 4: Pictorial representation of dipolar-polarization and condution mechanism. Adapted from ref [11].

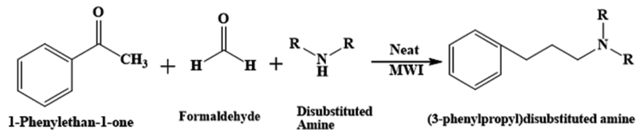

Figure 5: Microwave assisted synthesis Mannich reaction via neat reactants [14].

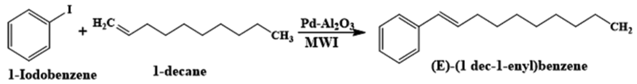

Figure 6: Microwave prom Heck, Suzuki and Stille reaction using Pd- Al203 [15].

subsequent cycloadditions while avoiding harsh reaction conditions in most cases.(Figure 9) [18].

4.6. 3-Synthesis of Quinoline

Synthesis of quinoline by conventional means requires glycerol solvent which on high temperature decomposes and forms a corrosive gas known as acrolein. By microwave technique, no solvent is required thereby, synthesizing eco-friendly product (Figure 10) [19].

4.7. 4- Synthesis of Salicylaldimines

The conventional synthesis of salicylaldimines requires THF, a highly flammable solvent whereas this reaction can be carried out

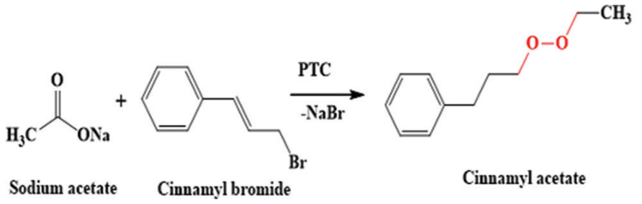

Figure 7: Microwave assisted synthesis of Cinnamyl acetate using PTC [16].

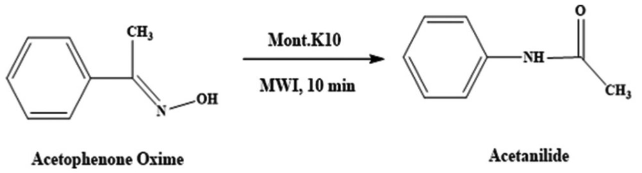

Figure 8: Microwave assisted Beckmann rearrangement [17].

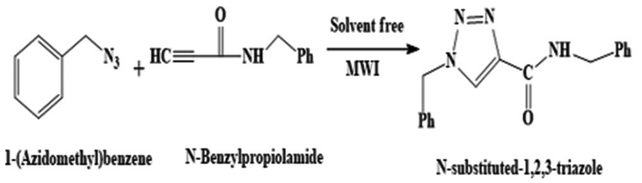

Figure 9: Microwave assisted 1,3 dipolar cycloaddition reaction [18].

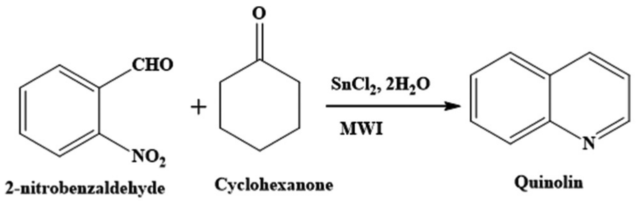

Figure 10: Microwave assisted synthesis of quinoline [19].

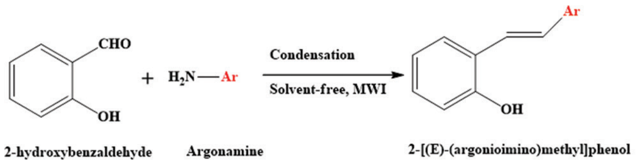

Figure 11: Microwave assisted synthesis of salicylaldimines [20].

in microwave within fraction of time and with no usage of solvents (Figure 11) [20].

5. APPLICATIONS OF MICROWAVE-ASSISTED SYNTHESIS

5.1. Microwave Synthesis: Newer Developments and Future Perspective

Many unique and significant advancements in this magnificent approach of microwave-assisted synthesis have been made in recent years [21]. Silicon carbide reactors are used, as well as an accurate temperature measurement utilizing a fiber optic temperature probe, a pressure regulator, and a tiny built-in integrated camera to keep an eye on the reaction [Figure 12] [22]. Figure 13 shows present experimental setup of microwave reactors. Given these advancements, it is clear that the convergence of MW reaction conditions and reaction medium will continue to provide various benefits in the development of future organic and nanomaterials synthesis methods.

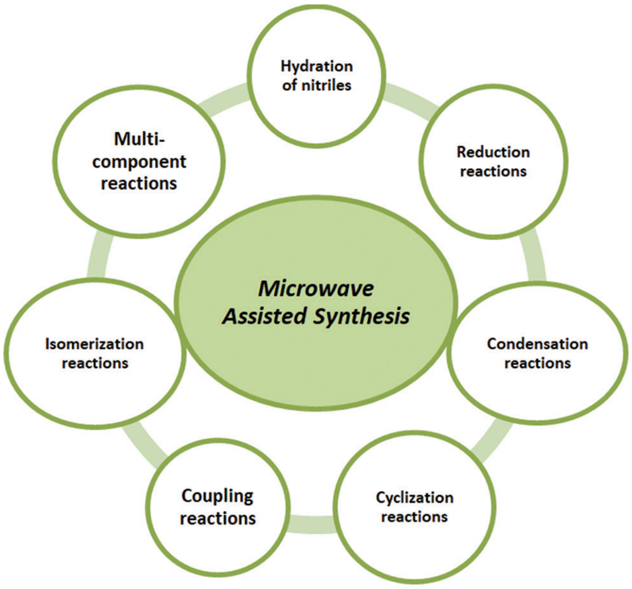

Figure 12: Applications of microwave assisted synthesis. Adapted from ref [22].

Table 3: Common reactions in microwave reactors with no usage of solvent

S. No.	Name of the reaction	Conventional heating	Microwave heating
1.	Beckmann rearrangement	Acetic acid, HCl, Acetic anhydride	No solvent
2.	1,3 Dipolar cycloaddition	Hexane	No solvent
3.	Synthesis of quinoline	Glycerol	No solvent
4.	Synthesis of salicylaldimines	THF, Methanol	No solvent

5.2. Limitations of Microwave Chemistry [23]

- Microwave chemistry is restricted to materials that absorb or are transparent to microwave radiation
- Temperature must be monitored since a quick rise in temperature might cause molecular deformation, resulting in an undesirable product
- Microwave reactors are typically difficult to conduct reactions involving bumping of materials or reactions involving effervescences
- Using a reaction medium containing concentrated sulphuric acid is challenging because sulphuric acid reacts aggressively with microwave radiation, increasing the temperature by several orders of magnitude. As a result, the reaction vessel may melt, posing a safety risk.

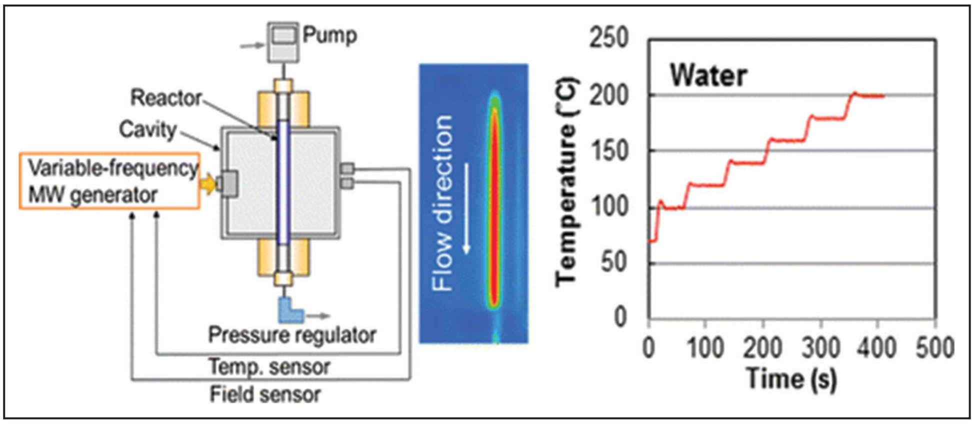

Figure 13: Demonstration of a MW-assisted flow reactor. Adapted from ref [21].

6. CONCLUSIONS

The novel concept of microwave chemistry is without a doubt revolutionary, but the question remains, Are we ready to adopt it and replace traditional practices? This technique has recently gained popularity due to its numerous benefits, including faster, cleaner, and environmentally friendly reactions [24]. As a result, it is a promising technology that has successfully conquered its unrivalled position in the modern period of chemical sciences. The benefits of this enabling technology have lately been used to complex complete synthesis and medicines' chemistry, as well as related domains such as polymer sciences, material sciences, nanoparticles, and biochemical interactions. It's worth mentioning that India appears to be the place where this technique is most widely adopted. Effort is needed on a couple of shortcomings of this technique in order to increase its usage level even more. Nevertheless, Microwave chemistry has a bright and hopeful future ahead of it, and it will be widely used in the upcoming years.

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*Bibliographical Sketch

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