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RECENT ADVANCES IN MICROWAVE- ASSISTED SYNTHESIS

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ABSTRACT

Microwave synthesis is the major breakthrough in the synthetic organic chemistry where as the conventional heating is the inefficient and time consuming. Microwave synthesis is the new lead which is being used as the source of heating in the organic synthesis reaction. The present article will give an idea about microwave assisted synthesis.

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INTRODUCTION

MICROWAVE SYNTHESIS

The great invention of burner was done In organic chemistry 1899 by Robert Bunsel. This invention was so useful that it lead to provide heat in a much focused manner required to carry out any chemical synthesis but this Bunsen burner was later superseded by microwave energy since the first published reports on the use of microwave irradiation to carry out organic chemical transformation by the groups of Gedye and Ginguere\Majeticn in 1986 microwave heating has been show to dramatically reduce reaction times, increase product yield and enhance product purities by reducing unwanted side reaction compared to conventional heating method.

a) Single mode microwave resonators
b) Multi mode microwave resonators

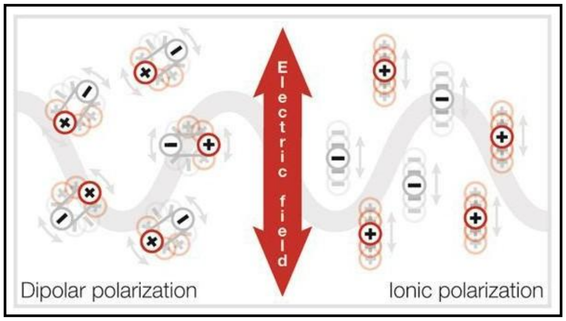
PRINCIPLES OF MICROWAVE HEATING

Dipole interaction

Polar ends of molecules tend to align themselves and oscillate in a step with the oscillating electrical field of the microwave collisions and friction between the moving molecule results in heating.

Ionic condition

It result if there are free ions or ionic species present in the substances being the electric field generates ionic motion as the molecule try to orient themselves to the rapidly changing field. This causes the instantaneous super heating.



ADVANTAGES

1. Time saving
2. Uniform heating occurs throughout the material
3. Process speed is increased
4. High efficiency of heating
5. Reduction in unwanted side reaction
6. Purity in final product
7. Improve reproducibility

Microwave oven can be classified into two types

Microwave synthesizer components

MICROWAVE CONSIST OF FOUR PARTS

High power source

A magnetron is a thermo ionic diode having anode and directly heated cathode which generate microwave.

Wave guide feed

It is a rectangular channel which causes transmission of microwave from magnetron to microwave cavity. It is have reflective wall made of sheet metal. This wall prevents leakage of radiation by increasing the efficiency of the oven.

The oven cavity

The area of oven cavity is designed in such a way so that it receives large amount energy In the form of electrical energy.

Reaction vessel

The reaction vessel for microwave induced organic reaction is a tall beaker loosely covered which is having the capacity greater than volume of the reaction mixture. Teflon and polystyrene vessel can be used as these are transparent to microwaves metallic container gets heated soon due to preferential absorption and reflected of rays. Hence those are avoided.

WORKING.

- In a microwave oven, microwaves are generated by a magnetron. A magnetron is a thermo-ionic diode having an anode and a directly heated cathode. As the cathode is heated, electrons are released and are attracted towards the anode. The anode is made up of an even number of small cavities, each of which acts as a tuned circuit. The anode is, therefore, a series of circuits, which are tuned to oscillate at a specific frequency or at its overtones.
- A very strong magnetic field is induced axially through the anode assembly and has the effect of bending the path of electrons as they travel from the cathode to the anode. As the deflected electrons pass through the cavity gaps, they induce a small charge into the tuned circuit, resulting in the oscillation of the cavity. Alternate cavities are linked by two small wire straps, which ensure the correct phase relationship. This process of oscillation continues until the oscillation has achieved sufficiently high amplitude. It is then taken off by the anode via an antenna.
- The variable power available in domestic ovens is produced by switching the magnetron on and off according to the duty cycle. Microwave dielectric heating is effective when the matrix has a sufficiently large dielectric loss tangent (i.e. contains molecules possessing a dipole moment).
- The use of a solvent is not always mandatory for the transport of heat.10 Therefore, reactions performed under solvent-free conditions present an alternative in the microwave chemistry and constitute an environmentally benign technique, which avoids the generation of toxic residues, like organic solvents and mineral acids, and thus allows the attainment of high yields of products at reduced environmental costs. This emerging environmentally benign technique belongs to the upcoming area of green chemistry.

EFFECTS OF SOLVENTS

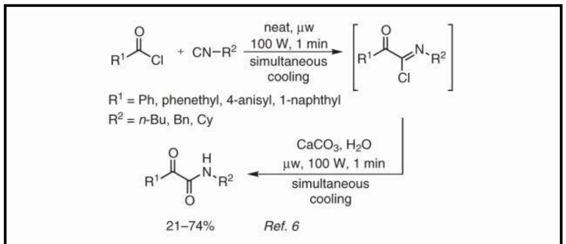
Every solvent and reagent will absorb microwave energy differently. They each have a different degree of polarity within the molecule, and therefore, will be affected either more or less by the changing microwave field. A solvent that is more polar, for example, will have a stronger dipole to cause more rotational movement in an effort to align with the changing field. A compound that is less polar.

However, will not be as disturbed by the changes of the field and, therefore, will not absorb as much microwave energy. Unfortunately, the polarity of the solvent is not the only factor in determining the true absorbance of microwave energy, but it does provide a good frame of reference. Most organic solvents can be broken into three different categories: low, medium, or high absorber, as shown in Figure 6. The low absorbers are generally hydrocarbons while the high absorbers are more polar compounds, such as most alcohols.

Eventually lead to improved treatments for stroke, Alzheimer’s disease, and muscular dystrophy. Following an earlier protocol from the 1960s, the authors coupled acyl chlorides with various isonitriles. α-Keto imidoyl chloride intermediates were formed, which were then converted to the α- veto amides upon hydrolysis (Scheme 1).

	Acetonitrile, HMPA, Methy Ethyl Ketone, Acetone, Nitromethane, Dichlorobenzene, 1,2- Dichloroethane, Acetic Acid, trifluoroacetic Acid
Low	Chloroform, DCM, Carbon tetrachloride, 1,4-Dioxane, Ethy Acetate, Pyridine, Triethyamine, Toluene, Benzene, Chlorobenzene, Pentane, Nexane and other hydrocarbons

Absorbance level	Solvents
High	DMSO, EtOH, MeOH, Propanols, Nitobenzen, Formic Acid, Ethylene Glycol
Medium	Water, DMF, NMP, Butanol,

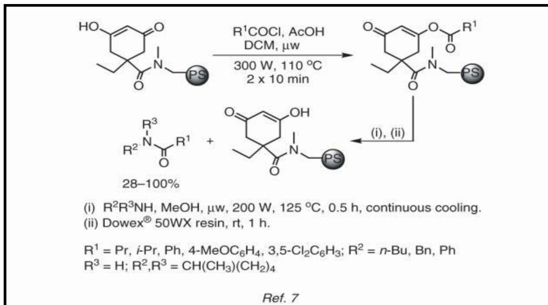


Scheme 1. Improved Synthesis of α-Keto Amides by Enhanced Microwave Synthesis (EMS).

RECENT ADVANCES IN MICROWAVE ASSISTED SYNTHESIS

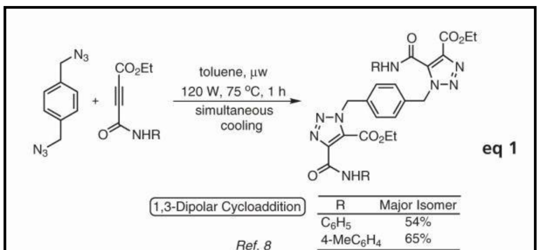
Enhanced Microwave Synthesis (EMS) Recently, an alternative method for performing microwave assisted organic reactions, termed “Enhanced Microwave Synthesis” (EMS), has been examined. By externally cooling the reaction vessel with compressed air, while simultaneously administering microwave irradiation, more energy can be directly applied to the reaction mixture. In “Conventional Microwave Synthesis” (CMS), the initial microwave power is high, increasing the bulk temperature (TB) to the desired set point very quickly. However, upon reaching this temperature, the microwave power decreases or shuts off completely in order to maintain the desired bulk temperature without exceeding it. When microwave irradiation is off, classical thermal chemistry takes over, losing the full advantage of microwave- accelerated synthesis. With CMS, microwave irradiation is predominantly used to reach TB faster. Microwave enhancement of chemical reactions will only take place during application of microwave energy. This source of energy will directly activate the molecules in a chemical reaction; therefore, it is not desirable to suppress its application. EMS ensures that a high, constant level of microwave energy is applied.

Research published very recently in leading organic synthesis journals supports the use of simultaneous cooling of reactions being heated by microwave energy. Simultaneous cooling enables a greater amount of microwave energy to be introduced into a reaction, while keeping the reaction temperature low. This results in significantly greater yields and cleaner chemistries. EMS was employed in the synthesis of a variety of α-keto amides to support a protease inhibitor discovery project. This may Under conventional heating conditions, this took between 2 to 6 hours for completion; whereas under optimized EMS conditions, the two steps were completed in 2 min and in 21–74% yields. EMS has also been beneficial in producing higher release levels of the desired amides from the solid- phase resin, as compared with microwave heating alone (Scheme 2).



Scheme 2. Improved Release Levels of Amides from Resin by EMS.

More recently, Katritzky et al. illustrated the advantages of EMS in preparing bistriazoles by the 1,3-dipolar cycloaddition reactions of 1,4- bis(azidomethyl)benzene with monoacetylenes. When reacting the diazide with a carbamoylpropiolate at 120 W and 55 °C for 30 minutes, cycloaddition only occurred at one of the azido moieties. Higher temperatures and irradiation powers resulted in decomposition. By using EMS for the reaction between the diazide and butynoate at 120 W and 75 °C for 1 hour, the Katritzky group successfully synthesized the bistriazole (eq 1).

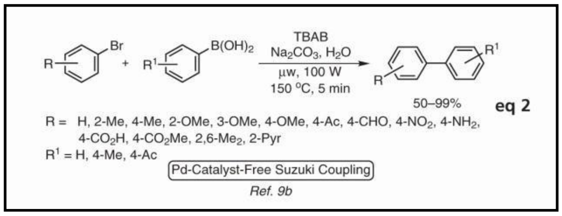


The major isomer was isolated in 54–65% yields.

It is well documented that microwave irradiation is applicable to solid-phase synthesis. The majority of peptide synthesis is performed on a solid phase, and it has been shown that microwave irradiation can enhance deprotection, coupling, and cleavage reactions.

NEW SYNTHETIC APPLICATIONS

The recent publication of several major reviews on microwave-assisted organic synthesis not with standing,l a plethora of very recent articles describing a variety of new chemistries performed with microwave irradiation have appeared. This section will document many of these synthetic applications. at the end of this section, provides an in-depth summary of the wide range of microwave- assisted applications that are not discussed here in detail. In organometallic chemistry, two of the most phenomenal recent discoveries are transition-metal- free Suzuki and Sonogashira couplings. Lead beater and coworkers have shown that reacting an activated aryl bromide with an arylboronic acid in water, using tetrabutylammonium bromide (TBAB) as a phase-transfer catalyst, results in a successfully coupled biaryl Suzuki product without the aid of a palladium catalyst (eq 2).



USE OF MICROWAVE IRRADIATION IN BIOCHEMICAL APPLICATIONS

Microwave irradiation is fast becoming a source of energy for biochemical applications. The hesitancy of its onset, compared to organic synthesis, is most likely due to the high temperatures associated with microwave-assisted transformations. Many of the biochemical molecules are temperature-sensitive. Now, with current technology, temperatures as low as 35–40 °C can be maintained by precise power input (additional accessories allow temperatures as low as –100 °C247), which permits a much wider range of chemistries to be explored. At present, there have been relevant studies published on carbohydrates, nucleosides peptides, proteins, peptoids, the polymerase chain reaction (PCR), and trypsin digestion.

CONCLUSION

Microwave technology is emerging as an alternative energy source powerful enough to accomplish chemical transformations in minutes, instead of hours or even days. For this reason, microwave irradiation is presently seeing an exponential increase in acceptance as a technique for enhancing chemical synthesis. A growing number of investigators are adopting microwave- assisted synthesis as a means to increase their productivity.

Enhanced Microwave Synthesis (EMS) provides the ability to cool a reaction vessel externally while simultaneously administering microwave irradiation, allowing more energy to be directly applied to a chemical reaction. A higher microwave power input results in substantially enhanced chemistry while maintaining a desired bulk temperature (TB). Reactions with large activation energies will benefit greatly from this new technology.

In addition, as seen in the previous section, a whole new arena of biochemical applications can now be explored.

The obvious next step in microwave technology is scale-up for chemical development. Scaling up syntheses from gram quantities to kilograms is essential for drug development, as this is a discouraging bottleneck for present-day process chemists. Many milligram- and gram-scale syntheses cannot be replicated, or even attempted for safety reasons, on larger scales. Development chemists often must start from the beginning. Microwave technology provides the possibility that the same chemistries used in the initial route can be safely scaled up, enabling chemists to spend their valuable time creating novel synthetic methods, not recreating them.

Clearly, microwave irradiation has emerged as a powerful tool for organic synthesis. In concert with a rapidly expanding applications base, microwave synthesis can be effectively applied to any type of chemistry, resulting in faster reaction times and improved product yields. In addition, microwave synthesis creates new possibilities in performing chemical reactions. Because microwaves can transfer energy directly to the reactive species, they can promote transformations that are currently not possible using conventional heat, creating a new realm in synthetic organic chemistry.

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