

Microwave Synthesis - A Potential Tool for Green Chemistry

S. Ravichandran* and E.Karthikeyan

Department of Chemistry , Saveetha School of Engineering, Saveetha University,
Thandalam, Chennai - 602 105, India.

*Corres.author: ravichanduru@yahoo.com

Abstract: Microwave radiation, an electromagnetic radiation, is widely use as a source of heating in organic synthesis. The basic mechanisms observed in microwave assisted synthesis are dipolar polarization and conduction. Microwave assisted organic synthesis (MAOS) has emerged as a new “lead” in organic synthesis. The technique offers simple, clean, fast, efficient, and economic for the synthesis of a large number of organic molecules, have provided the momentum for many chemists to switch from traditional heating method to microwave assisted chemistry. In the recent year microwave assisted organic reaction has emerged as new tool in organic synthesis. In the present article an attempt was made to focus on what is microwave, how is it generated and what importance may it have.

Keywords: Microwave radiation, electromagnetic spectrum, Green chemistry.

Introduction

Microwave assisted organic synthesis has revolutionized organic synthesis. Small molecules can be built in a fraction of the time required by classical thermal methods. As a result, this technique has rapidly gained acceptance as a valuable tool for accelerating drug discovery and development processes. A microwave is a form of electromagnetic energy, which falls at the lower end of the electromagnetic spectrum and is defined in a measurement of frequency as 300 to 300,000 Megahertz, corresponding to wavelengths of 1 cm to 1 m¹. The microwave region of the electromagnetic spectrum lies between infrared and radio frequencies^{2,3}. Wavelengths between 1 cm and 25 cm are extensively used for RADAR transmissions and remaining wavelength range is used for telecommunications. In order to avoid interference with radar and telecommunication activities, which also operate in this region, most commercial and domestic microwave ovens operate at 2450 MHz (12.25cm).

The difference between microwave energy and other forms of radiation, such as X- and γ -rays, is that microwave energy is non-ionizing and therefore does

not alter the molecular structure of the compounds being heated – it provides only thermal activation. The heating effect utilized in microwave assisted organic transformations is mainly due to dielectric polarization. When a molecule is irradiated with microwaves, it aligns itself with the applied field. The rapidly changing electric field (2.45×10^9 Hz) affects the molecule and consequently the molecule continually attempts to align itself with the changing field and energy is absorbed. The ability of a material to convert electromagnetic energy into thermal energy is dependent on the dielectric constant. The larger the dielectric constant the greater is the coupling with microwaves. Thus, solvents such as water, methanol, DMF, ethyl acetate, acetone, acetic acid, etc. are all heated rapidly when irradiated with microwaves. However, solvents with low dielectric constants such as hexane, toluene, carbon tetrachloride, etc. do not couple and therefore do not heat that rapidly under microwave irradiation. Microwave heating has thus been found to be a very convenient thermal source not only in the kitchen but also in a chemical laboratory. Chemists have explored the possibility of the application of a conventional microwave oven to carry out chemical reactions. It has been found that many reactions progress much faster upon microwave

irradiation than with traditional heating techniques. The application of microwave irradiation to activate and accelerate organic reactions has taken a new dimension and has experienced exponential growth in the last ten years. Microwave chemistry is becoming increasingly popular both in industry and in academia. We hope to demonstrate in this article the utility of this technique, and the potential that this methodology can give to the bench chemist.

Microwave Heating

Microwave dielectric heating uses the ability of some liquids and solids to transform electromagnetic radiation into heat to drive chemical reactions. However, the advantages of using microwave dielectric heating for performing organic transformations have only emerged since the mid-1980s. This technology opens up new opportunities to the synthetic chemist, in the form of new reactions that are not possible using conventional heating. Developments in this field have suggested that microwave-assisted chemistry could be used in most reactions that require heating.

Advantages

In the past, microwave chemistry was often used only when all other options to perform a particular reaction had failed, or when exceedingly long reaction times or high temperatures were required to complete a reaction. This practice is now slowly changing and, due to the growing availability of microwave reactors in many laboratories, routine synthetic transformations are now also being carried out by microwave heating. Microwave include following advantages, over the conventional heating.

- Uniform heating occurs throughout the material
- Process speed is increased
- High efficiency of heating
- Reduction in unwanted side reaction
- Purity in final product,
- Improve reproducibility
- Environmental heat loss can be avoided
- Reduce wastage of heating reaction vessel
- Low operating cost

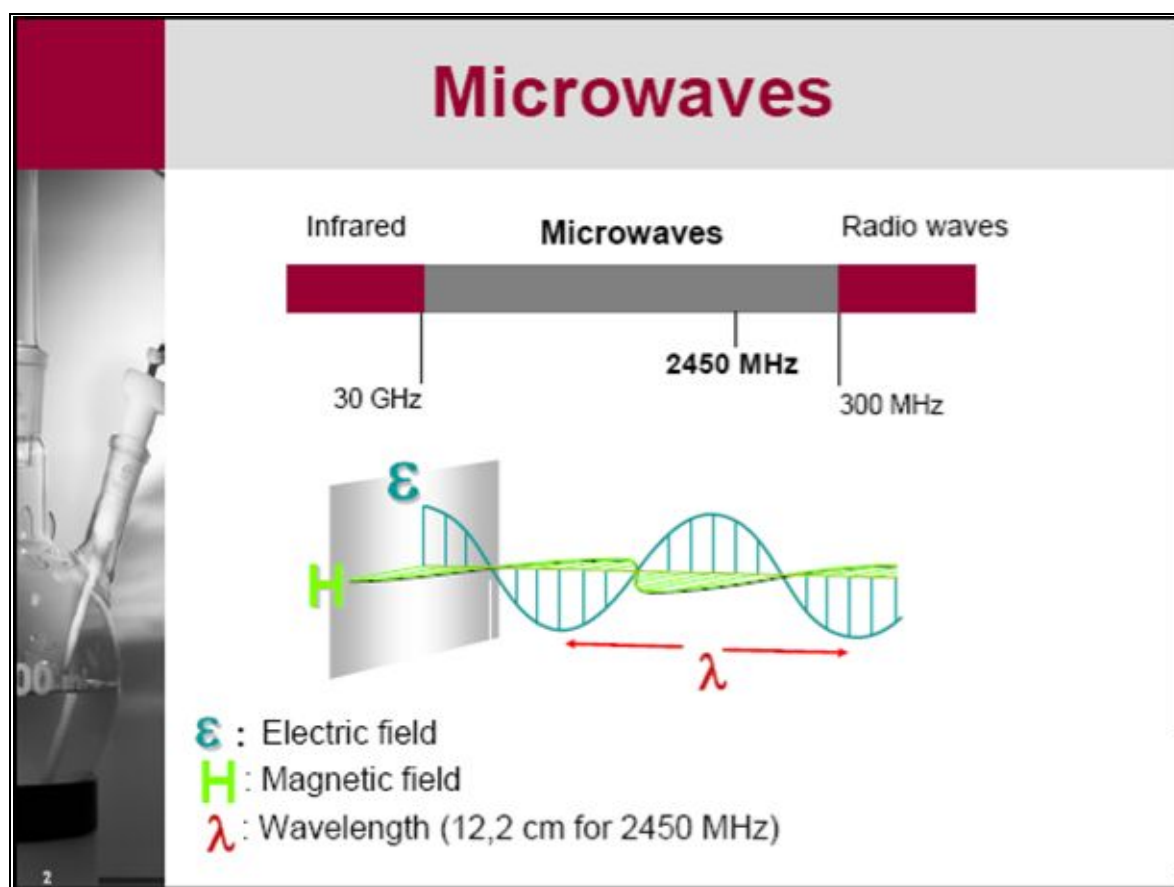


Fig.1. Range of frequencies of electromagnetic radiation

Green Technologies

The term “green chemistry” is defined as “the invention, design and application of chemical products and processes to reduce or to eliminate the use and generation of hazardous substances”. Green chemistry can diminish the need for other approaches to environmental protection. Ideally, the application of green chemistry principles and practice renders regulation, control, clean-up, and remediation unnecessary, and the resultant environmental benefit can be expressed in terms of economic impact.

Historically, chemists thought that compounds react only in the liquid state or if dissolved⁴. This has made solvents common in chemical syntheses, however, many compounds used as solvents were found to be environmentally unfriendly. The problem associated with waste disposal of solvents has been overcome by performing reactions without a solvent under microwave irradiation (MWI)⁵. Coupling of MWI with the use of mineral-supported catalyzed reactions, under solvent-free conditions, provides clean chemical processes with the advantage of enhanced reaction rates, higher yields, greater selectivity, and greater ease of manipulation. These expeditious and solvent-free approaches involve the exposure of neat reactants to MWI in conjunction with the use of supported reagents or catalysts⁶.

Dry media reactions

Avoiding organic solvents during the reactions in organic synthesis leads to a clean, efficient, and economical technology (green chemistry). There is an increasing interest in the use of environmentally benign reagents and procedures. Or, in other words, the absence of solvents coupled with the high yields and short reaction times often associated with reactions of this type make these procedures very attractive for synthesis. In the present discussion, we describe the advantages of dry reaction techniques coupled with microwave activation and their applications to organic synthesis using solid supports. The practical dimension to the microwave heating protocols has been added by accomplishing reactions on solid supports under solvent-free conditions⁷. These solvent-free microwave-assisted reactions⁸ provide an opportunity to work with open vessels, thus avoiding the risk of high-pressure development and increasing the potential of such reactions to upscale. The practical feasibility of microwave-assisted solvent-free synthesis has been demonstrated in various useful transformations^{9,10} and in synthesis of heterocyclic systems^{11,12}.

Microwave for Synthesis

While fire is now rarely used in synthetic chemistry, it was not until Robert Bunsen invented the burner in 1855 that the energy from this heat source could be applied to a reaction vessel in a focused manner. The Bunsen burner was later superseded by the isomantle, oil bath or hot plate as a source of applying heat to a chemical reaction. In the past few years, heating chemical reactions by microwave energy has been an increasingly popular theme in the scientific community. Since the first published reports on the use of microwave irradiation to carry out organic chemical transformations by the groups of Gedye¹³, more than 5000 articles have been published in this fast moving and exciting field, today generally referred to as microwave-assisted organic synthesis¹⁴⁻¹⁸.

In the early days of microwave synthesis, experiments were typically carried out in sealed Teflon or glass vessels in a domestic household microwave oven without any temperature or pressure measurements. Kitchen microwave ovens are not designed for the rigors of laboratory usage: acids and solvents corrode the interiors quickly and there are no safety controls. The results were often violent explosions due to the rapid uncontrolled heating of organic solvents under closed vessel conditions.

In the 1990s several groups started to experiment with solvent-free microwave chemistry (so-called dry-media reactions), which eliminated the danger of explosions¹⁹. Here, the reagents were pre-adsorbed onto either a more or less microwave transparent inorganic support (i.e., silica, alumina or clay) or a strongly absorbing one (i.e., graphite), that additionally may have been doped with a catalyst or reagent.

In many of the published examples, microwave heating has been shown to dramatically reduce reaction times, increase product yields and enhance product purities by reducing unwanted side reactions compared to conventional heating methods. The advantages of this enabling technology have, more recently, also been exploited in the context of multistep total synthesis²⁰ and medicinal chemistry/drug discovery²¹, and have additionally penetrated related fields such as polymer synthesis²², material sciences²³, nanotechnology²⁴ and biochemical processes²⁵. The use of microwave irradiation in chemistry has thus become such a popular technique in the scientific community that it might be assumed that, in a few years, most chemists will probably use microwave energy to heat chemical reactions on a laboratory scale. The statement that, in principle, any chemical reaction that requires heat can be performed under microwave conditions has today been generally accepted as a fact by the scientific community.



Microwave-assisted heating has been shown to be an invaluable technology in synthesis, since it can often dramatically reduce reaction times, typically from days or hours to minutes or even seconds. It can also provide pure products in quantitative yield and selectivity.

Microwave Synthesis on Solid Supports

Microwave heating for carrying out reactions on solids has also attracted considerable attention in recent years. For such 'dry media' reactions, solid supports such as alumina, silica, montmorillonite clay and zeolites have been investigated. The practical feasibility of microwave assisted solvent-free protocols has been demonstrated in useful transformations like protection, deprotection, condensation, oxidation, reduction, rearrangement reactions and in the synthesis of various heterocyclic systems on solid supports. A wide variety of industrially important compounds and intermediates such as enones, imines, enamines and nitroalkenes have been prepared by this environmentally friendly solvent-free approach. In these reactions, the organic compounds adsorbed on the surface of inorganic oxides, such as alumina, silica and clay or 'doped' supports absorb microwaves whereas the solid support does not absorb or restrict their transmission. The bulk temperature is relatively low in such solvent free reactions.

Other Applications

The rapid heating effect has also been exploited to create better crystallinity in intercalation

compounds such as ceramics and synthetic zeolites. Polymer curing too has benefited from microwave heating. Certain organometallic compounds of second row transition metals which are often impossible to produce by conventional means can be quickly made with microwave heating. The major industrial applications of microwave includes the preparation of hydrogen cyanide, a chlorination plant, drying of pharmaceutical powders and pasteurization of food products.

Conclusions

The entry of microwave ovens in the chemistry laboratory has made it possible to carry out many transformations with greater efficiency and ease of workup. In recent years, the use of microwave has becomes very attractive in the field of pharmaceutical science. In today's competitive era microwave is one of the major tools for the rapid lead generation and optimization through which medicinal chemist will able to deliver critically need new chemical entities and candidate drug. Microwave also used in pharmaceutical drying that can change the drug release properties by polymeric cross linkages and drug interaction improves drug dissolution. We believe that in the future many more microwave-assisted reactions will be developed which will simplify time consuming conventional procedures. It is also hoped that appropriate technology will develop so that some of these fascinating microwave-assisted transformations could be done on industrial scales thereby increasing the overall efficiency of the

processes and reducing pollution of the environment through the use of solvent free reaction protocols. The exploitation of microwaves for assisting different organic reactions has blossomed into an important tool in synthetic organic chemistry. The future for the application of microwave technology looks bright because of its efficiency and its potential to contribute to clean products.

References

1. P. T. Anastas, J. C. Warner. Green Chemistry, Theory and Practice, Oxford University Press, Oxford (1998).
2. M. Lancaster. Green Chemistry: An Introductory Text, The Royal Society of Chemistry, London (2002).
3. A. K. Nagariya, A. K. Meena, Kiran, A. K. Yadav, U. S. Niranjan, A. K. Pathak, B. Singh and M. M. Rao, J. Pharm. Res., 3 (3), 575 (2010).
4. F. Toda. Acc. Chem. Res. 28, 480 (1995).
5. M. Kidwai, R. Venkataraman, B. Dave. Green Chem., 3, 278 (2001).
6. D. Stuerge, P. Gaillard. Tetrahedron, 52, 5505 (1996).
7. M. Kidwai, P. Sapra. Synthesis 10, 1509 (2001).
8. M. Kidwai. Pure Appl. Chem. 73, 147 (2001).
9. M. Csiba, J. Cleophax, A. Loupy, J. Malthete, S. D. Gero. Tetrahedron Lett.34, 1787 (1993).
10. R. S. Varma, R. K. Saini, R. Dahiya. Tetrahedron Lett. 38, 7823 (1997).
11. M. Kidwai, P. Sapra. Org. Prep. Proced. Int. 33, 381 (2001).
12. M. Kidwai, R. K. Garg, K. R. Bhushan. J. Chem. Res.(S), 586 (2000).
13. R. Gedye, F. Smith, K. Westaway, H. Ali, Tetrahedron Lett., 27, 279 (1986).
14. A. Loupy, Microwaves in Organic Synthesis, Wiley-VCH, Weinheim (2002).
15. P. Lidstrom, J. Tierney, B. Wathey, Tetrahedron, 57, 7764 (2001).
16. M. Kidwai, Pure Appl. Chem., 78 (11), 1983 (2006).
17. Rashmi Sanghi, Resonance, March,77 (2000).
18. S. Ravichandran, N. Jeyachandramani, Int. J. Chem. Sci., 5(3), 1258 (2008).
19. R.S. Varma, Tetrahedron, 58, 1235 (2002).
20. D.D. Artman, R.M. Williams, J.Amer. Chem. Soc., 129, 6336 (2007).
21. S.Ravichandran, K.Subramani, R.Arun Kumar, Int. J.Chem.Sci., 6, 1800,(2008).
22. C. Zhang, L. Liao, S. Gong, Green Chemistry, 9, 303 (2007).
23. S. Sinwell, H. Ritter, Aus. J. Chem., 60, 729 (2007).
24. M. Tsuji, M. Hashimoto, Y. Nishizawa, M. Kubokawa, T. Tsuji, Chemistry – A European Journal, 11, 440 (2005).
25. J.M. Collins, N. E. Leadbeater, Organic and Biomolecular Chemistry, 5,1141 (2007).

Acknowledgements

Dr. SR and Dr. EK thank the President, Director, Principal, Dean and Head (S&H) of Saveetha School of Engineering, Saveetha University, Chennai for their constant support, blessing and encouragements.
