

Since the 60s, with natural resources dwindling, the focus turned heavily to the search of effective and efficient energy sources and efficient methods of heating. That waves are a carrier of energy has been known for a long time now. Hence, it was thought that the use of electromagnetic radiations for heating purposes could be a highly effective method of heating.

Of all the electromagnetic radiations, microwaves were among the first to be used as a method of heating for domestic purposes. Microwave ovens (MWO) are now widely accepted as a safe and convenient cooking device in the kitchen. In such an oven, microwaves generated in a magnetron are guided into an open cavity where they are absorbed by the food items.

Since dramatic reduction in the heating time was observed for cooking purposes, it was thought that microwaves could also be used for rapid heating in chemical reactions. Since 1986, interest in this field has led to more than 220 papers including several reviews. Pioneering work in the applications of microwaves in accelerating chemical reactions was carried out by Gedye et al in 1986¹.

Applications of Microwaves in Organic Chemistry

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Table.1 : Summary of the work carried out by Gedye et al.

Product	Classical		Microwave		Ratio of rates (Classical/Microwave)
	Time	Yield (%)	Time	Yield (%)	
1. Hydrolysis of benzamide to benzoic acid.	1hr	90	10 min	99	6
2. Oxidation of toluene to benzoic acid.	25min	40	5 min	40	5
3. Esterification of benzoic acid with					
a. Methanol	8hr	74	5 min	76	96
b. Propanol	7.5hr	89	18 min	86	25
c. n-butanol	1hr	82	7.5 min	79	8
4. S _N ² reaction of 4-cyano phenoxide ion with benzyl chloride	12hr	72	3min	74	240

Physical Nature of Microwaves

Microwaves are electromagnetic radiations whose frequencies range from 300 MHz to 300 GHz (i.e., $\lambda = 1\text{ m} - 1\text{ mm}$). The frequencies correspond to vary small quantum energy ($1.2\text{ eV} < W < 1.2\text{ meV}$) as compared to the ionisation potentials of the elements. Hence, the absorption of microwaves does not cause any electron transition in the atoms.

Microwave heating

A molecule of water within the cavity experiences an electric field analogous to that experienced by a dielectric within a capacitor. Because of its dipole moment, the water molecule tries to align itself in the direction of the field of the radiation.

However, as the microwaves pass by the molecule, the electric field changes 2.45×10^9 times per second. Thus, just as the molecule gets partially aligned with the field, the magnetic field direction reverses, forcing the molecule to realign. This aligning and realigning of the water molecule produces heating through frictional effects. The rotational freedom of water molecules in the liquid state is perhaps the reason why water gets heated easily in MWO, while ice does not; since in the latter case the molecules are fixed by hydrogen bonding. Similarly, a cup filled with water is heated

very rapidly, whereas the cup itself is not heated because of insufficient rotational motion possible in the crystal lattice and long chain polymers.

The frequencies of microwaves allow a coupling between the oscillating magnetic field and the molecular rotation provided the molecule has a permanent dipole moment. The average time taken to rotate a molecule through one radian (correlation time) is about 10^{-12} to 10^{-9} seconds (for water at 10°C it is 2.7×10^{-12} secs). This is the average time, but, in actual distribution, the correlation time can be as large as 10^{-4} seconds. Thus, effective heating is possible with microwaves which may not be the case with other types of radiations for e.g., IR, UV, etc.

Factors affecting the heating: Polar solvents show a rapid rise in temperature, whereas nonpolar solvents don't show rapid rise in the temperature. The difference between the rates of rise of the temperature in polar solvents is essentially due to the difference in their heat capacities. Also the volatility and pressure generated in the reactions are also major factors affecting rate enhancements similar to the observations made in some conventional heating methods. The high pressure is generated primarily due to the vapours of the solvents in which the reaction are

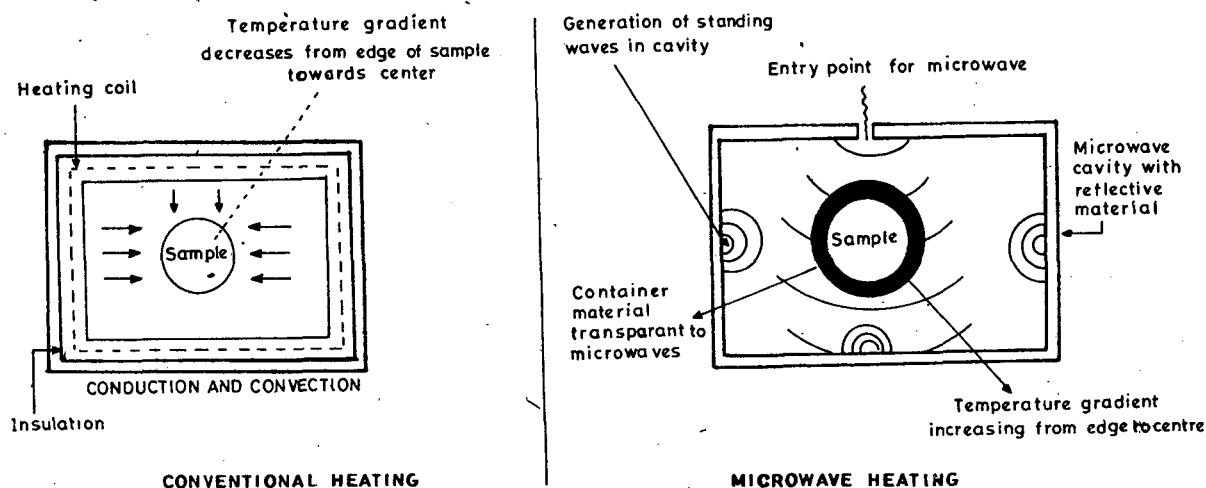


Fig.1. Conventional heating v/s Microwave heating

carried out. The high pressures generated lead to the super heating of the reaction mixture similar to that in a pressure cooker. Similarly, the volatility of the solvent control the ability to generate the pressure as explained above. A more volatile solvent will generate greater pressure in a shorter time than a less volatile solvent.

Thus, we have seen that the key to microwave-induced organic reaction enhancement technique is the proper choice of microwave energy transfer medium and a non-traditional approach to the set-up of the organic reactions. Hydrocarbon solvents such as benzene or toluene, which are commonly used as reaction media in organic laboratory are not suitable, as they absorb microwave irradiation poorly. On the contrary, polar solvents like glycols, alcohols, THF, etc., are used for the purpose.

Chemical Reactions in the Presence of Microwaves

Some reactions whose rates are enhanced using microwave heating techniques are given below :

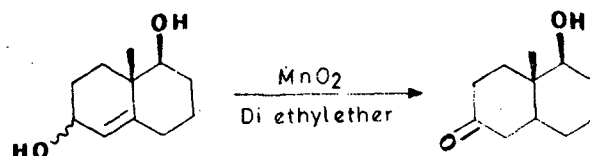
(1) Synthesis of chalcones and related enones⁵: We apply MORE chemistry techniques to the synthesis of chalcones and related enones by the condensation of aldehydes and ketones (aromatic) in the presence of NaOH, in open borosil beakers, under microwave irradiation using ethanol as solvent. The reaction displays 120-600 fold increase in microwave oven. For example, The reaction between acetone and benzaldehyde shows a 400 fold rise in reaction rate (Yield 100% -MWO, 80% conventional).

(2) Diels-Alder reaction⁶: The reaction between anthracene and maleic anhydride

in open systems in MWO was studied employing chlorobenzene, o-dichlorobenzene and diglyme as energy transfer media by Bose et al⁶. The yield was about 40% in chlorobenzene (b.p. 130°C) (2-3 min). In o-dichlorobenzene, it was 80-85% (b.p. 178°C) (2 min). About the same yield was obtained when diglyme was used as a solvent (b.p. 162°C) (90%, 1 min).

The reaction between anthracene and dimethyl fumarate proceeds in low yield (5%, 5 min) in o-dichlorobenzene and diglyme (15-20%, 5 min). When 1,2,4-trichlorobenzene was used as an energy transfer medium, higher yield was obtained (70 %, 10 min)

(3) Oxidation⁷: Most oxidation would not benefit from MW heating. However, manganese dioxide oxidations are amenable to this techniques.



In indispensable cases, where solvent used does not absorb MW radiation, like diethyl ether, the reactions are carried out in a special reaction vessel⁶ as shown

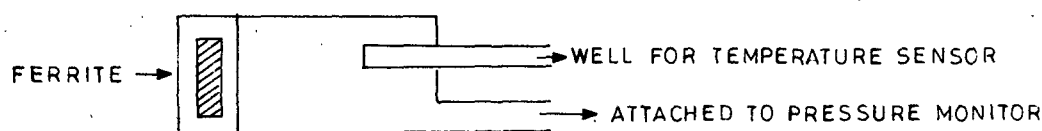


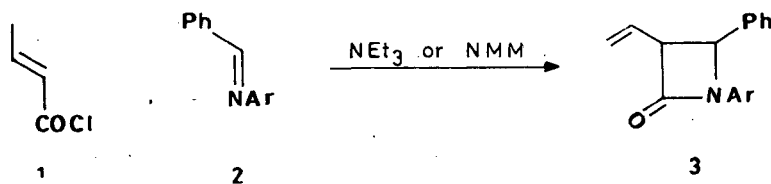
Fig. 2.

below. (fig.2.).

A special quartz vessel is used to contain the nonmicrowave absorbing solvent. A piece of ferrite which readily absorbs microwaves is used inside to heat the reaction mixture through conduction.

(4) Hydrolysis⁷: Esters, amides, and nitriles may be hydrolysed either by aqueous

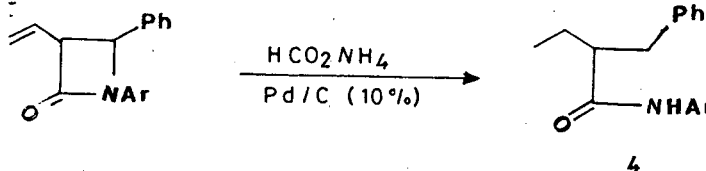
acids or bases. For example, glycyl-d-leucine on hydrolysis with 1M HCl gives glycine.HCl and leucine.HCl with 98% yield (160°C, 30 mins). Also, 2-methylbenzonitrile gives improved selectivity in the following reaction.



benzene was replaced by chlorobenzene (b.p. 131°C) to obtain more yield (65-70%, 5 min) of 3.

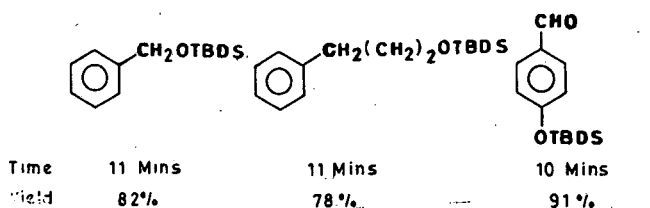
(7) Catalytic hydrogenation ⁶:

α -Vinyl- β -lactam can be hydrogenated in the presence of ammonium formate and Pd/C (10%) catalyst with ethylene glycol as a solvent in a MWO to give the corresponding amide (45 sec, 110°C). Such rapid hydrogenation should be of great value in the manufacture of short lived radio pharmaceuticals.

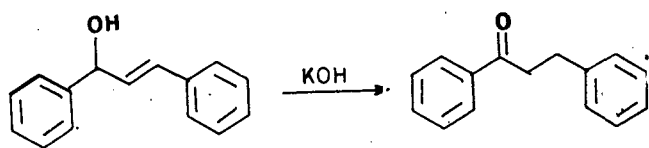
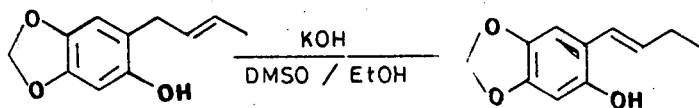


NMM = N-methylmorpholine
Ar = 4-methoxyphenyl

The deprotection involving the cleavage of t-butyl dimethyl silyl ethers was studied on alumina surface without any solvent and using microwave heating.



(5) Isomerisation ⁷: The isomerisation of double bonds using either an acid or a base is a useful transformation. The first example shows migration into a more stable position and the second example shows tautomerisation.

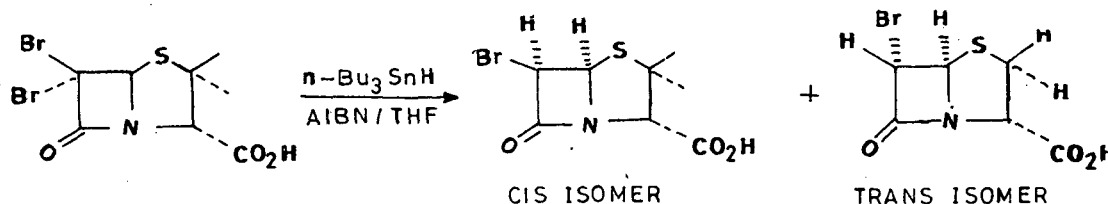


(6) α -vinyl- β -lactam synthesis ⁶: In the synthesis of α -vinyl- β -lactams (3) by the

(8) Free radical reactions: ⁶ α -Halo- β -lactams undergo stereoselective dehalogenation by free radical reaction in dry THF with tri-butyltin hydride in the presence of 2,2-azobisisobutyronitrile. 6,6-dibromo penicillanic acid can be converted to the *cis*-6 β -isomer with minor amounts of *trans*-6 β -isomer (3 mins, low energy).

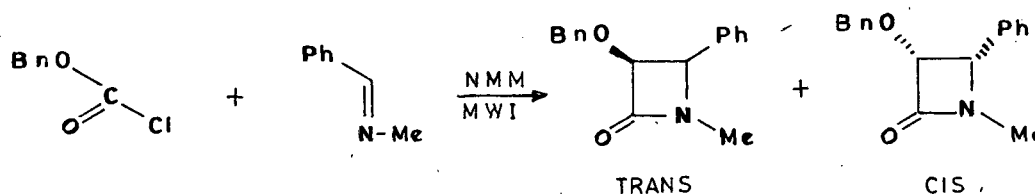
(9) Stereocontrol of β -lactam formation: ⁸

The synthesis of α -hydroxy β -lactams is now in attention, because the side chain of an anti-tumor drug TAXOL can be derived from the compounds of this type. Preliminary observations on the preparation of α -benzyloxy β -lactams from benzyloxyacetyl chloride showed varying amounts of *cis* and *trans* β -lactams. At a lower level of radiation, the *cis* β -lactam was favoured (69°C, 84:16), while at about 112°C (final reaction

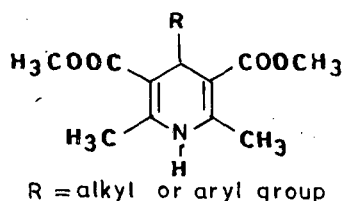


temp.), there was more of trans product (55:45, high power).

reaction time permits the use of microwave heating in the production of radio-



(10) Hantzsch reaction : ⁹ The reaction between methyl 3-aminocrotonate, alkyl acetoacetate and aromatic or aliphatic aldehydes in ethanol to give 4-aryl-1,4-dihydropyridines was 145-180 times faster in microwave process with considerable yields (65-80%).



Recently, this reaction was carried out in aqueous medium using hydrotropic agents ¹² which increase solubility of a normally insoluble substance. Since aqueous solutions are used, fire hazards are quelled.

(11) Conversion of alcohols to alkyl bromides : The simplest method for preparing alkyl halide is to treat alcohol with mineral acid. For example : Cyclohexanol in presence of NaBr and sulphuric acid gives cyclobromohexane in 10 minutes in microwave conditions at 49% yield.

Advantages of the MORE chemistry Techniques

The main advantage of the use of microwave heating in organic synthesis is the reduction in the energy losses. This is because, as compared to conventional methods, no energy is used up to heat the reaction vessel and the surroundings. Short

pharmaceuticals and other short lived pharmaceuticals. Also, probably due to quick reactions, there is reduction in the side products and unwanted polymeric products. In some reactions stereochemical control of the product is possible.

Limitations

The major limitation in the microwave heating applications is the difficulties in the scaling up of the reactions for commercial purposes. Also, some researchers feel that due to the high cost of the microwave sources, it could be unsuitable for reactions on a large scale in near future. There is also a problem concerning the uniform distribution of heat energy in the reaction mixture. There is a limited choice of solvents for microwave heating, essentially because commonly available hydrocarbon solvents, like benzene, toluene, etc., are unsuitable as energy transfer media. The limited choice of solvents is also due to fire hazards evolving due to the high pressures and temperatures developed in the reaction. This problem can be solved to some extent by developing safe solvent systems and by modifying the microwave ovens.

Recent Technological Advances

For the potential applications of microwave technology to be fully exploited, specifically designed reactors are required which are safe and can operate reliably on a routine basis. They should also have the

potential for scaling up in chemical process applications. Recently two such laboratory scale reactors have been developed.

(1) Continuous microwave reactor (CMR) ¹⁰:

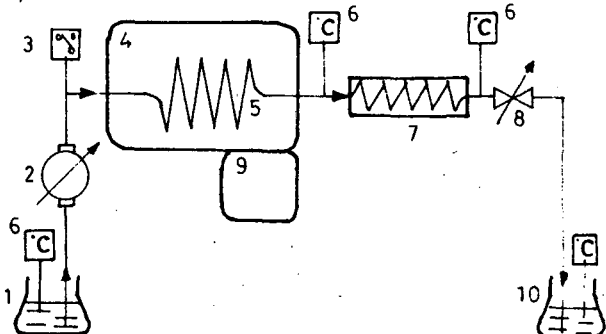


Fig.3. A schematic diagram of CMR.

1. reaction mixture 2. pump 3. pressure sensor 4. microwave cavity 5. Reaction coil 6. temperature sensor 7. heat exchanger 8. Pressure control valve 9. Electronic key pad & display 10. Product mixture.

In the CMR (See fig.3.), the reaction mixture is passed through a tubing which is coiled in the microwave cavity. The time of flow of the reaction mixture through the cavity is equal to the reaction time. The tubing is made of perfluoroalkoxy (PFA) teflon or quartz since they are chemically inert and microwave transparent. The reaction mixture is cooled rapidly under pressure in a heat exchanger after it has exited the microwave cavity. Thermosensors allow the monitoring of the temperature of the reaction mixture before it entered the microwave zone, after it exits and after it is cooled. Feed back microprocessor control is introduced to allow the operator to preset the pump rate and temperatures for heating and cooling of reactions. Safety provisions are made in the software so that the unit would shut down if temperature exceeds the maximum allowable temperature.

Advantages: The continuous flow allows unstable products to be quickly removed from the reaction zone and cooled. Also, the reactants can be sampled and analysed while the material is being processed.

(2) Microwave Batch Reactor (MBR) ¹¹:

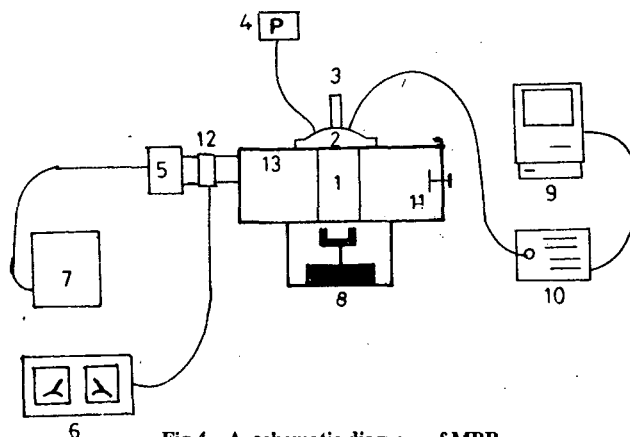


Fig.4. A schematic diagram of MBR.

1. Reaction vessel 2. Top flange 3. cold finger 4. Pressure meter 5. Magnetron 6. Forward/Reverse power supply 7. Magnetron power supply 8. Magnetic stirrer 9. Computer 10. Optical Fibre thermometer 11. load matching device 12. wave guide 13. multi modal cavity

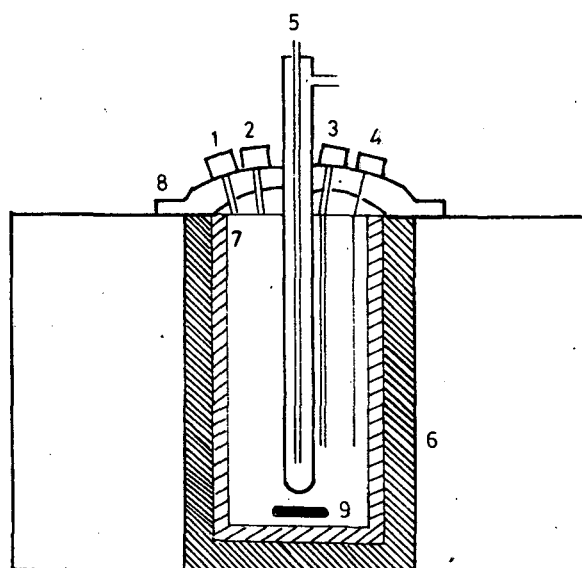


Fig.5. A schematic diagram of the reaction vessel.

1. pressure transducer 2. pressure relief valve 3. sample addition/removal port 4. retaining cylinder.

In the MBR, the reaction is carried out in batches. Microwave power is generated in a magnetron and regulated by a variable power supply. The microwaves are directed into the cavity via the waveguide. The reaction vessel is equipped with a magnetic stirrer bar for mixing and uniform heating purposes. The cold finger cooling system provides rapid quenching if necessary for thermally labile products which can decompose during gradual cooling.

Advantages: The unit can be operated

at temperatures upto 260°C and pressure upto 10 mega Pascals and in presence of organic solvents. Additionally, there are minimal temperature gradients within samples and wall effects are eliminated.

Conclusion

The use of microwave heating in chemical synthesis is still in its infancy as far as the commercial applications are concerned. Perhaps, in future, with more research and development in this field and a greater insight into the mechanism and control of microwave heating it may be successfully applied in the commercial production.

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