International Journal of ChemTech Research
CODEN (USA): IJCRGG, ISSN: 0974-4290, ISSN(Online):2455-9555
Vol.10 No.6, pp 305-310, 2017

Microwave Assisted Synthesis an Approach to Green Chemistry

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Abstract : The interest in the microwave assisted organic synthesis hasbeen growing during the recent years. Drug companies areexploiting microwave in the area of organic/pharmaceuticalsynthesis for drug screening and discovery. Microwaveheating is also called as green chemistry and thedevelopment of cleaner technologies is a major emphasis ingreen chemistry. Among the several aspects of greenchemistry, using efficient and less hazardous energy sourcessuch as microwave energy is recommended. The aim of this review is to present microwave assisted synthesis withspecial emphasis on aspects that relevance to drug discovery.
Key words : Microwave assisted synthesis, Green chemistry, Drug Discovery.

Introduction:

Microwave assisted organic synthesis (MAOS) has emerged as a new "lead" inorganic synthesis. The technique offers simple, clean, fast, efficient, and economic forthe synthesis of a large number of organic molecules. In the recent year microwaveassisted organic reaction has emerged as new tool in organic synthesis.Importantadvantage of this technology include highly accelerated rate of the reaction,Reduction in reaction time with an improvement in the yield and quality of theproduct. Now day's technique is considered as an important approach toward greenchemistry, because this technique is more environmentally friendly. This technologyis still under-used in the laboratory and has the potential to have a large impact on thefields of screening, combinatorial chemistry, medicinal chemistry and drugdevelopment. Conventional method of organic synthesis usually need longer heatingtime, tedious apparatus setup, which result in higher cost of process and the excessiveuse of solvents/ reagents lead to environmental pollution. This growth of greenchemistry holds significant potential for a reduction of the by product, a reduction inwaste production and a lowering of the energy costs. Due to its ability to coupledirectly with the reaction molecule and by passing thermal conductivity leading to arapid rise in the temperature, microwave irradiation has been used to improve manyorganic syntheses.[1]

Microwaves are defined as electromagnetic waves with vacuum wavelength rangingbetween 0.1to 100cm or, equivalently, with frequenciesbetween 0.3 to 300GHz. Although the first reported bygroup of Gyedye and GigureMajetih in 1986, the use ofmicrowaves in organic synthesis was initially hampered by alack of understanding of the basic principal of MW heatingand the inability to obtain reproducible results with domesticmicrowave oven.With microwave heating energy canbe directly applied to the reaction not to the vessel where ittakes time for the reaction to be completed and also the timetaken is less and there is the consumption of time.Microwave heating is based on dielectric heating, i.e.,molecule exhibiting a permanent dipole moment will try toalign to the applied electromagnetic field resulting inrotation, friction and collision of

molecules and, thus in heatgeneration. Microwave irradiation in chemical reactionenhancement has been well recognized for increasingreaction rates and formation of clear.[2]

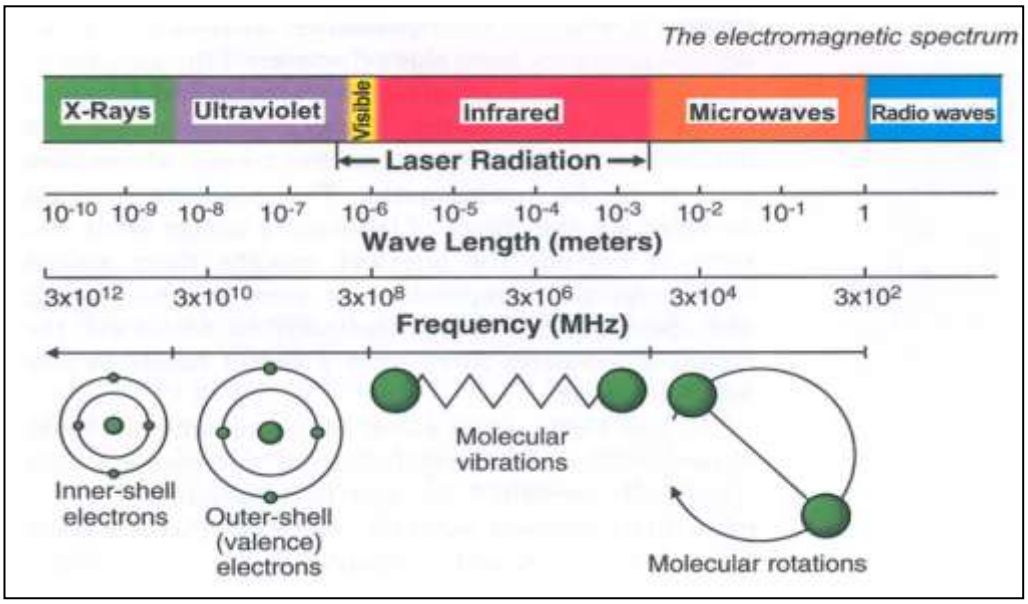


Figure no.1. Electromagnetic spectrum.

Principle of Microwave:

The basic principle behind the heating in microwave oven is due to the interaction ofcharged particle of the reaction material with electromagnetic wavelength ofparticular frequency. The phenomena of producing heat by electromagneticirradiation are ether by collision or by conduction, some time by both. All the wave energy changes its polarity from positive to negative with each cycle ofthe wave. This cause rapid orientation and reorientation of molecule, which causeheating by collision. If the charge particles of material are free to travel through thematerial (e.g. Electron in a sample of carbon), a current will induce which will travelin phase with the field. If charge particle are bound within regions of the material, theelectric field component will cause them to move until opposing force balancing theelectric force.[3-8]

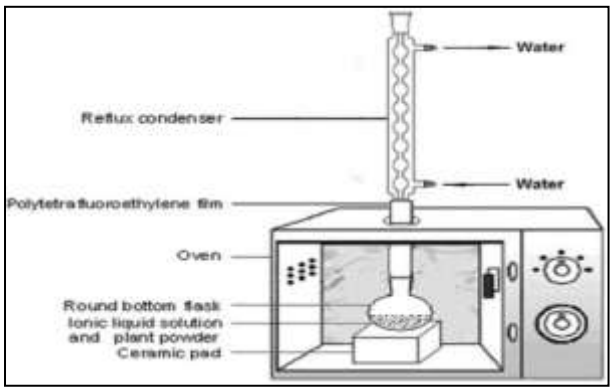


Figure no. 2. Schematic Diagram of Microwave.

Commonly Microwave Efficient Synthesis:

Following reactions have been performed through microwave heating:

Sr. no.	Reaction	Reference No.	Sr. no.	Reaction	Reference no.
1	Acetylation	1	18	Diel's-alder	18
2	Addition	2	19	Dimerization	19
3	Alkyaltion	3	20	Elimination	2
4	Alkyne metathesis	4	21	Esterification	20
5	Allylation	5	22	Enantioselective	21
6	Amination	6	23	Halogenation	22
7	Aromatic nucleophillic substitution reaction.	7	24	Hydrolysis	23
8	Arylation	8	25	Mannich	24
9	Carbonylation	9	26	Oxidation	25
10	Combinatorial	10	27	Phosphorylation	26
11	Condensation	11	28	Polymerization	27
12	Coupling	12	29	Reaarangment	28
13	Cynation	13	30	Reduction	29
14	Cylization	14	31	Ring-closing	30
15	Cyclo-addition	15	32	Solvent Free	31
16	Deacetylation	16	33	Transesterification	32
17	Dehalogenation	17	34	Transformation	33

Green Chemistry:

The term "green chemistry" is defined as "theinvention, design and application of chemical productsand processes to reduce or to eliminate the use andgeneration of hazardous substances". Green chemistrycan diminish the need for other approaches toenvironmental protection. Ideally, the application ofgreen chemistry principles and practice rendersregulation, control, clean-up, and remediationunnecessary, and the resultant environmental benefitcan be expressed in terms of economic impact. The concepts of atom economy and energy factor become a guiding principle of green chemistry which is given in 12 principles as below.

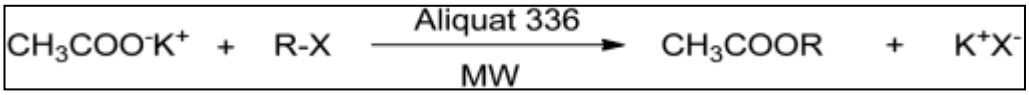
1. Prevention of waste.
2. Less hazardous chemical synthesis
3. Atom economy
4. Design safer chemical
5. Designs for energy efficiency
6. Safer solvent and auxiliaries
7. Use renewable feedstock
8. Reduced derivatives
9. Catalysis
10. Design for degradation.
11. Real time analysis for pollution prevention.
12. Inherently safer chemistry for accidental prevention.

Introduction of green technology in drug discovery can help streamline process improvement in the R & D field. Following table shows R & D philosophy in harmony with green chemistry principle.(10,11).

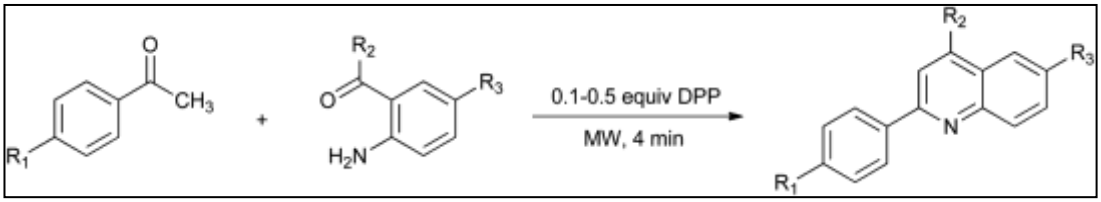
	Environmental thinking	**Economical Thinking**
Atom Economy	Minimal by-product formation	More from less-incorporate total value of material
Solvent reduction	Less solvent waste	Higher throughput- less energy
Reagent optimization Convergency	Catalytic, low stoichmetry, recyclable reagents minimize usage Due to increased process efficiency	Higher efficiency- Higher selectivity Higher efficiency- Fewer operations
Energy reduction	From power generation transport and use.	Reduced energy reflects increased efficiency, shorter process, and mild condition.
In-situ analysis	Reduce possibility for exposure to release to the environment	Real time data increases throughput and process efficiency , fewer reworks
Safety	Non-hazardous material reduce risk of exposure , release explosion and fires	Worker safety and reduced down time reduced time on special control measured

Some of the microawaveassited synthesis:

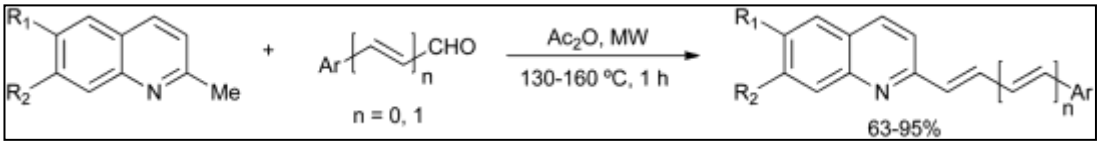
1. In 1993, Loupy reported that potassium acetate can be alkylated in the absence of solvent in a domestic oven using equivalent amounts of salt and alkylating agent in the presence of Aliquat 336 (10% mol) (34) Yields are practically quantitative within 1–2 min regardless of the chain length, the nature of the halide leaving group and the scale (up to 500 mmol).



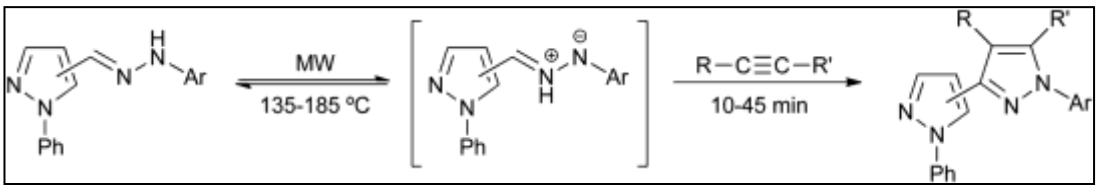
2. Quinolines are known not only for their important biological activities but also for the formation of conjugated molecules and polymers that combine enhanced electronic or nonlinear optical properties with good mechanical properties. Kwon described the preparation of a mini-library of 12 quinoline derivatives by Friedlander coupling condensation between an acetophenone and a 2-aminoacetophenone in the presence of diphenylphosphate (0.1–0.5 equiv.) within 4 min under microwave irradiation in the absence of solvent(35) This procedure afforded product yields of up to 85%, whereas the yield obtained with classical heating under similar conditions did not exceed 24%.



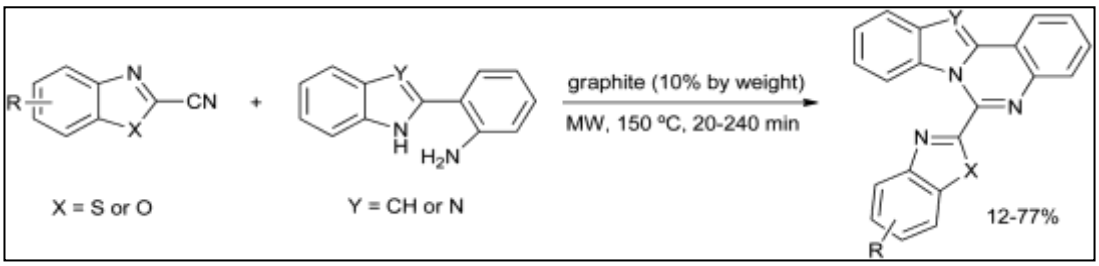
3. Styrylquinolines are valuable derivatives as imaging agents for β-amyloid plaques on human brain sections in Alzheimer patients. Menéndez reported a microwave-assisted solvent-free synthesis of 2-styrylquinolines by condensation of 2-methylquinolines with benzaldehydes or cinnamaldehydes in the presence of acetic anhydride.



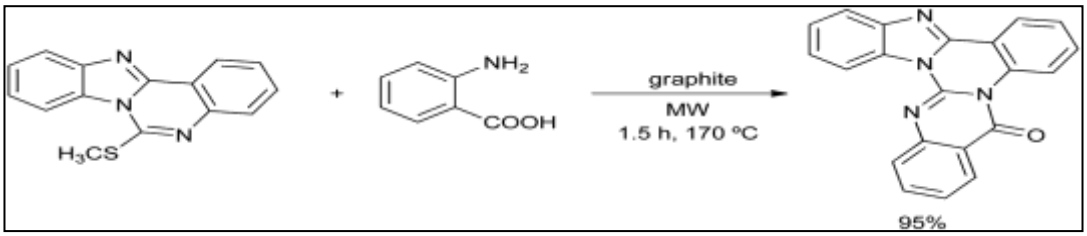
4. Thermal hydrazone/azomethine imine isomerization usually requires long reaction times (several hours or days) under reflux in high-boiling solvents (e.g. xylenes). However, this reaction can be easily promoted by microwave irradiation in the absence of solvent, as can the subsequent 1,3-dipolar cycloaddition with electron-deficient dipolarophiles. Thus, the use of pyrazolylhydrazones led to valuable products such as bipyrazoles within a few minutes in 30–84% yields (36) The application of classical heating led to considerably lower yields and, indeed, several dipolarophiles did not react at all



5. The thiazole and benzothiazole rings are present in various natural compounds. Likewise, indolo[1,2-c]quinazoline and benzimidazo[1,2-c]quinazoline skeletons are often present in potent cytotoxic agents. For these reasons, Besson described the fusion of these two systems under microwave irradiation in the presence of graphite as a sensitizer (10% by weight) and the expected products were obtained in good yields and in short reaction times (2)



6.Besson reported that a quinazolin-4-one ring can be fused onto a benzimidazo[1,2-c]quinazoline skeleton by a modified Niementowski reaction. Thermal heating of the two reagents at 120 °C or in refluxing butanol for 48 h gave only 50% of the target compound. The reaction time was reduced to 6 h in a microwave-assisted process, albeit without an improvement of the yield. However, irradiation of the quinazoline derivative and an excess of anthranilic acid (6 equiv.), absorbed on graphite, led to the desired product in 1.5 h with 95% yield (1)Furthermore, the fact that by-products were not detected allowed the easy purification of the product.



Acknowledgement

Author is thankful to Gokhale Education Society's Sir Dr. M. S. Gosavi College of Pharmaceutical Education and Research, Nashik-05. for providing necessary facilities.

Conflict of interest: No

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