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MICROWAVE ASSISTED SYNTHESIS A GREEN APPROACH FOR SYNTHESIS OF BENZOFUSED NITROGEN CONTAINING HETEROCYCLIC DERIVATIVES

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ABSTRACT

This paper aims to review on the detail information about most routinely used greener approach such as microwave assisted synthesis including their mechanism and it is also highlights significant examples where microwave heating provided key advantages over a conventional thermal method. Various advantages of microwave assisted synthesis includes, Rapid reactions, High purity of products, Less side-products, Improved yields, Simplified and improved synthetic procedure, Wider usable range of temperature, Higher energy efficiency, Sophisticated measurement and safety technology, Modular systems enable changing from mg to kg scale. Disadvantages of microwave assisted synthesis includes Heat force control is difficult, Water evaporation, Closed container is dangerous because it could be burst. Various examples are of microwave assisted synthesis as greener approach for synthesis of nitrogen containing benzofused heterocyclic derivatives are given.

KEYWORD: Microwave assisted synthesis, heterocyclic, quinazoline.

INTRODUCTION

The organic synthesis is one of the major role of research in chemistry, from plastics to medication it participates in the improvements of everyone life. Over the past few decades, many significant advances in practical aspects of organic chemistry have included novel synthetic strategies and methods as well as advent of a vast array of analytical techniques. In these environmentally conscious days, the developments in the technology are directed towards environmentally sound and cleaner procedures. Chemist have restored to using wide variety of techniques such as photochemical, electrochemical, sonochemical, microwave and enzymatic methods. First microwave oven was introduced by Tappan in 1955 but the widespread use of domestic microwave ovens occurred during the 1970s and 1980s. The first application of microwaves irradiation in chemical synthesis was published in 1986. Microwave irradiation has gained popularity in the past decade as a powerful tool for rapid and efficient synthesis of a variety of compounds because of selective absorption of microwave energy by polar molecules. The application of Microwave irradiation to provide enhanced reaction rate and improved product field in chemical synthesis and it is providing quite successful in the formation of a variety of carbon-heteroatom bonds. Conventional method of organic synthesis usually need longer heating time, tedious apparatus setup, which result in higher cost of process and the excessive use of solvents/ reagents lead to environmental pollution.[1,2]

Principle

The basic principle behind the heating in microwave oven is due to the interaction of charged particle of the reaction material with electromagnetic wavelength of particular frequency. The phenomena of producing heat by electromagnetic irradiation are ether by collision or by conduction, sometimes by both.

In the electromagnetic spectrum the microwave radiation region is located between infrared radiation and radio-waves. Telecommunication and microwave radar equipment occupy many of the band frequencies in this region. In order to avoid interference with these systems, the household and industrial microwave ovens operate at a fixed frequency of 2.45 GHz. The energy of the quantum involved can be calculated by the Planck's law $E = h\nu$ and it is found to be 0.3 calmol–1.[3,4]

Presently, organic transformations take place by either of the two ways

Conventional heating

In this method of heating, reactants are slowly activated by a conventional external heat source. Heat is driven into the substance, passing first through the walls of the vessel in order to reach the solvent and the reactants. This is a slow and inefficient method for transferring energy into the reacting system.

Microwave heating

In the microwave couple directly with the molecule of the entire reaction mixture, leading to a rapid rise in the temperature. Since the process is not limited by the thermal conductivity of the vessel, the result is an instantaneous localized superheating of any substance that will respond to either dipole rotation or ionic conductivity. Only the reaction vessel contents are heated and not the vessel itself; better homogeneity and selective heating of polar molecules might to be achieved.

The acceleration of chemical reactions by microwave exposure results from the interactions between the material and electromagnetic field leading to the thermal and specific (non-thermal) effects. For microwave heating, the substance must possess a dipole moment. A dipole is sensitive to external electric field and tries to align itself with the field by rotation. If submitted to an alternating current, the electric field is inversed at each alternate and therefore dipoles tend to move together to follow the inversed electric field. Such a characteristic induces rotation and friction of the molecules, which dissipates as internal homogeneous heating. The electric field of commonly used irradiation frequency (2450 MHz) oscillates 4.9 × 109 times per second.

Thus, microwave heating is directly dependent on dielectric properties of a substance, dielectric constant (ε') and dielectric loss (ε"). The ability of a material to convert electromagnetic energy into heat energy at a given frequency and temperature, is calculated using $\boldsymbol{\varepsilon'' / \varepsilon' = \tan \delta}$.

where δ is the dissipation factor of the sample, ε" is the dielectric loss, which measures the efficiency with which heat is generated from the electromagnetic radiation and ε' is the dielectric constant which gives the ability of a molecule to be polarized by an electric field. The high value of dissipation factor δ indicates large susceptibility to microwave energy.[4-6]

Mechanism

Dipolar Polarisation

Dipolar polarisation is a process by which heat is generated in polar molecules. On exposure to an oscillating electromagnetic field of appropriate frequency, polar molecules try to follow the field and align themselves in phase with the field. However, owing to inter-molecular forces, polar molecules experience inertia and are unable to follow the field. This results in the random motion of particles, and this random interaction generates heat.

Dipolar polarisation can generate heat by either one or both the following mechanisms

1. Interaction between polar solvent molecules such as water, methanol and ethanol.
2. Interaction between polar solute molecules such as ammonia and formic acid.

Conduction mechanism

The conduction mechanism generates heat through resistance to an electric current. The oscillating electromagnetic field generates an oscillation of electrons or ions in a conductor, resulting in an electric current. This current faces internal resistance, which heats the conductor.

The main limitation of this method is that it is not applicable for materials that have high conductivity, since such materials reflect most of the energy that falls on them.[7]

Various Types of Microwave assisted Organic Reactions

- Microwave Assisted Reactions using Solvents
- Microwave Assisted solvent free reaction

Instrument of Microwave Reactor

- Multimode Microwave Reactors
- Monomode Microwave Reactors

Multimode Microwave Reactor Vs Monomode Microwave Reactor

- Same: chemical performances
- Same: field homogeneity
- Different: reaction scale
- Different: application versatility[8]

Working of the Microwave Oven

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. Thevariable power available in domestic ovens is produced by switching the magnetron on and offaccording 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. 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.[8,9]

Microwave assisted synthesis techniques

- Domestic household oven- solvent free open vessel reaction.
- Reflux system.
- Pressurized system
- Continuous flow system[10]

Conventional vs Microwave Heating

Microwave heating is different from conventional heating in many respects. The mechanism behind microwave Synthesis is quite different from conventional synthesis. Points enlisted in Tablediffer the microwave heating from conventional heating.[11-14]

Conventional heating	Microwave heating
Reaction mixture heating proceeds from a surface usually inside surface of reaction vessels	Reaction mixture heating proceeds directly inside mixture
The vessel should be in physical contact with surface source that is at a higher temperature source (e.g. metal, oil bath, steam bath.	No need of physical contact of reaction with the higher temperature source. While vessel is kept in microwave cavities
By thermal or electric source heating takes place	By electromagnetic wave heating takes place.
Heating mechanism involve conduction.	Heating mechanism involve dielectric polarization and conduction
Transfer of energy occur from the wall, surface of vessel, to the mixture and eventually to reacting species.	The core mixture is heated directly while surface (vessel wall) is source loss of heat.
In conventional heating, the highest temperature (for a open vessels) that can be achieved is limited by boiling point of particular mixture.	In microwave, the temperature of mixture can be raised more than its boiling point i.e. superheating take place.

In the conventional heating the entire compound in mixture are heated equally.	In microwave, specific component can be heated specifically.

Advantages

- Rapid reactions
- High purity of products
- Less side-products
- Improved yields
- Simplified and improved synthetic procedure
- Wider usable range of temperature
- Higher energy efficiency
- Sophisticated measurement and safety technology
- Modular systems enable changing from mg to kg scale.

Disadvantages

- Heat force control is difficult
- Water evaporation
- Closed container is dangerous because it could be burst

Application of Microwave

1. Application of Microwave in material Chemistry.
2. Preparation of catalyst under microwave irradiation.
3. Application of Microwave Technology for Nanotechnology.
4. Application of Microwave in polymer synthesis.
5. Analytical Chemistry.
6. Digestion.
7. Microwave irradiation in waste management.
8. Application of microwave in organic synthesis.[15-16]

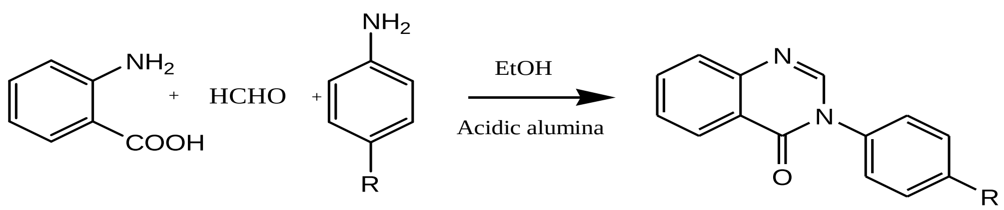
Following reactions have been performed through microwave heating.[16]

Sr. No.	Reaction Name	Reaction Name
1	Acetylation Reaction	Diels's-Alder reaction
2	Addition Reaction	Dimerization Reaction
3	Alkylation Reaction	Elimination Reaction
4	Alkynes Metathesis	Estrification Reaction
5	Alkylation Reaction	Enantioselective Reaction
6	Amination Reaction	Halogenation Reaction

7	Aromatic Nucleophillic Substitution Reaction	Hydrolysis Reaction
8	Arylation Reaction	Mannich Reaction
9	Carbonylation Reaction	Oxidation Reaction
10	Combinatorial Reaction	Phosphorylation Synthesis
11	Condensation Reaction	Polymerization Reaction
12	Coupling Reaction	Rearrangement Reaction
13	Cyanation Reaction	Reduction Reaction
14	Cyclization Reaction	Solvent Free Reaction
15	Cyclo-Addition Reaction	Transformation Reaction
16	Deacetylation Reaction	Transestrification Reaction

Some examples of Microwave assisted synthesis

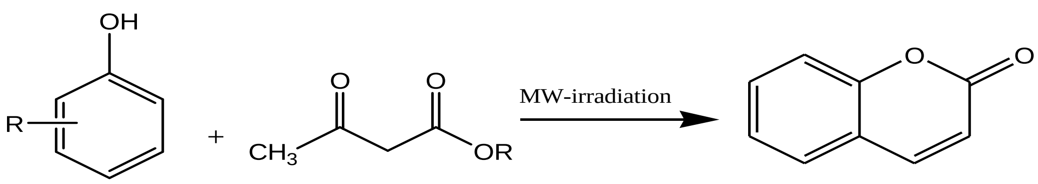
1. A .D. Mishra developed a 3-substituted 4-(2H)-quinazolinones derivatives in presence of anthranilic acid, Formaldehyde and primary aromatic amines by using microwave assisted synthesis.[5]



Anthranillic acid **Substituted aniline** **3- substituted -4-(2H)-quinazolinone**

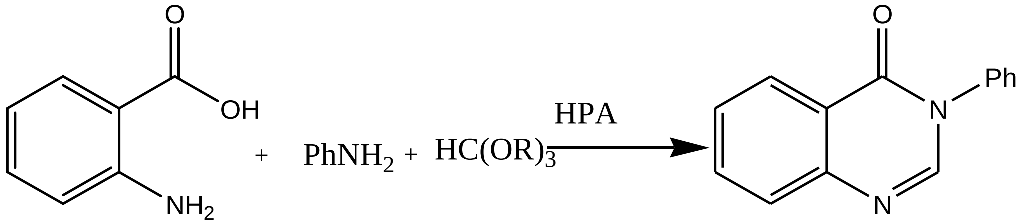
General procedure for the synthesis of 3- substituted -4-(2H)-quinazolinones derivatives.
R=H**,** CH, CH2CH3, OCH_3, Cl, Br.

2. Pawar T.B. synthesized one pot two component Pechmann Condensation using FeF_3 as a catalyst under solvent – free microwave irradiation.[6]



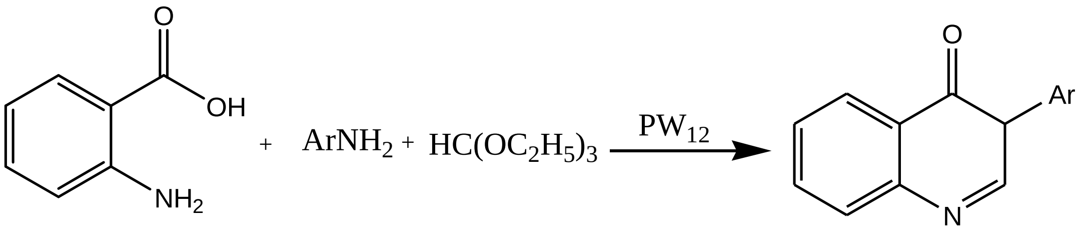
Substituted phenols **ethyl acetoacetate** **Coumarin**

3. Karima Ighilahriz *et al.* synthesized 4-(3H)-quinazolinones by cyclo-condensation of anthranilic acid, Aniline, orthoester or Formic acid in presence of HPA as a catalyst and by using microwave irradiation.[7]



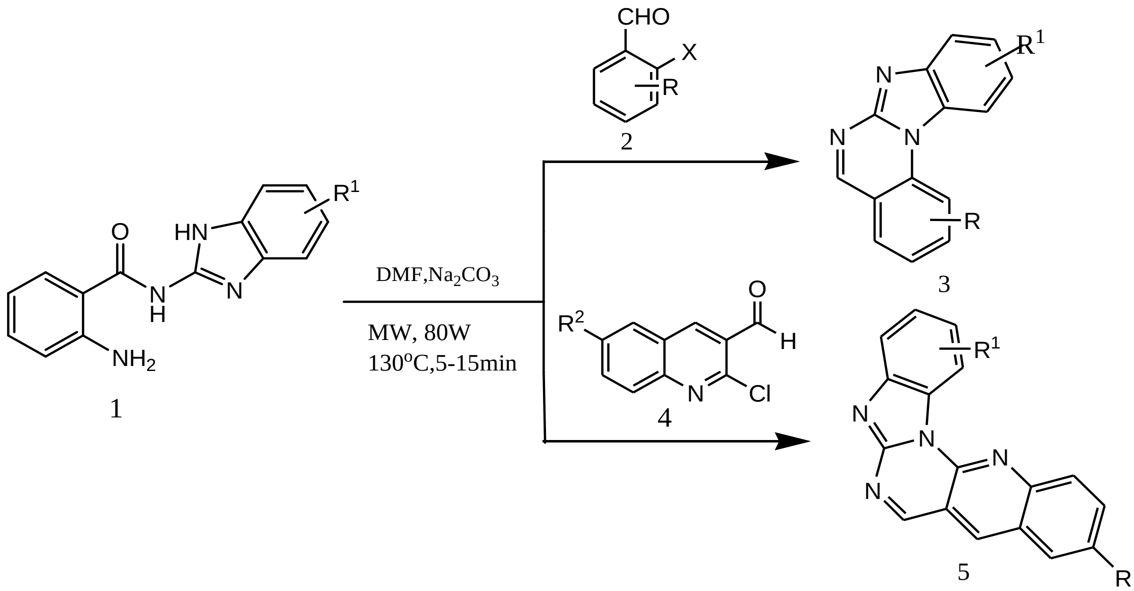
Anthranilic acid Aniline orthoester substituted 4-(3H)-quinazolinones

4. **Karima Ighilahriz *et al.*** synthesized one pot synthesis of 4(3H)quinazolinones under the solvent free conditions, microwave irradiation and PW_{12} mediated catalysis with anthranillic acid, various substituted anilines and triethyl Orthoformate.[7]



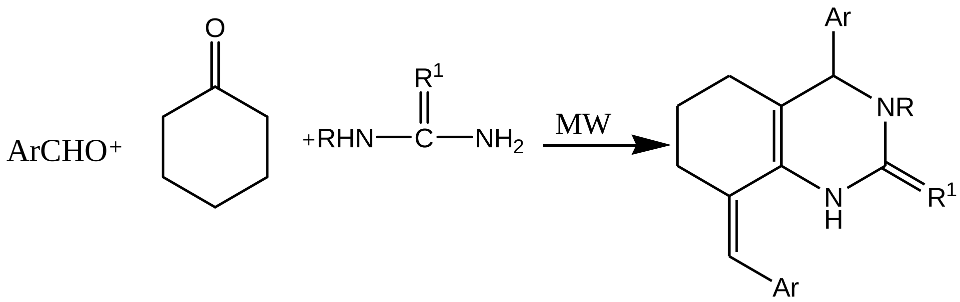
Anthranillicacid Aniline Triethylorthoformate substituted 4(3H) quinazolinones

5. Prashant Kumar et al. synthesized a benzimidazo [1,2a] quinazoline derivatives by using metal free microwave assisted synthesis.[9]

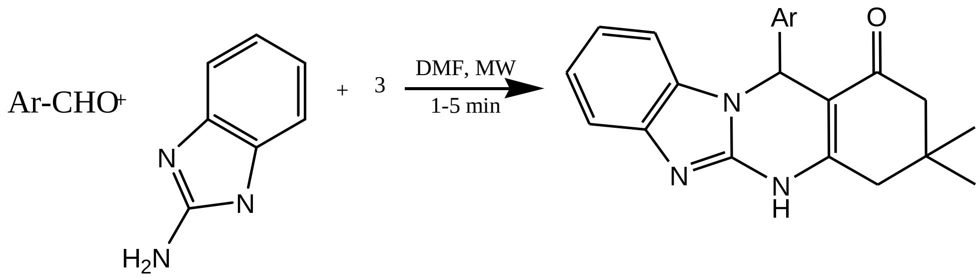


substitutedbenzimidazo[1,2-a]quinazoline

6. T.A Nadiaa Biginelli one pot three component reaction involving cyclohexanone, aromatic or heterocyclic aldehydes, and urea thiourea or HCl was used for the preparation of quinazolin-2(1H)one derivatives under solvent free and microwave irradiation.[10]

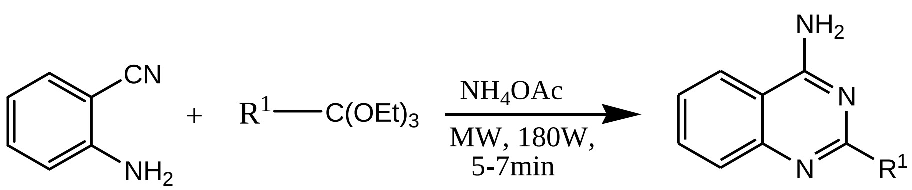


7. Aboul Fetouh E. *et al.* microwave irradiation can be used to induce the synthesis of fused quinazolinones mainly benzimidazoquinazolinones by using aromatic aldehydes and dimedone in DMF.[12]

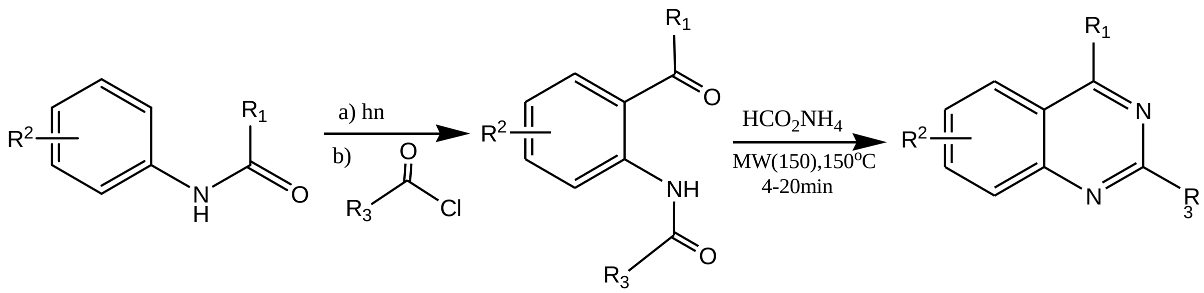


Dimedone **substituted benzimidazoquinazolinones**

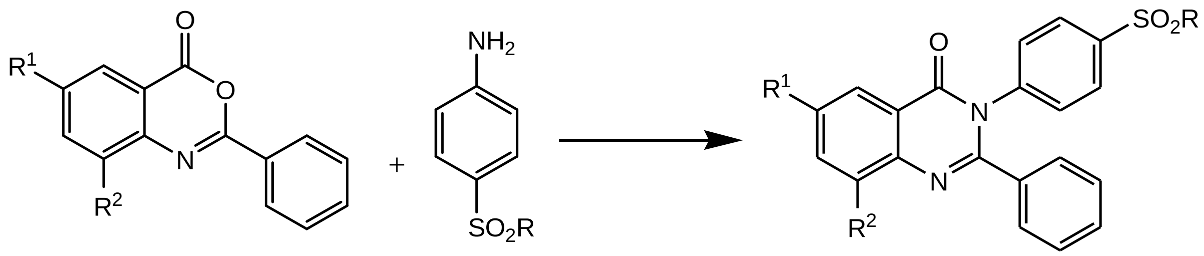
8. **Arpi Majumder** synthesized various quinazolines by using microwave assisted synthesis from 2-aminobenzonitrile, orthoester and ammonium acetate under a solvent freeconditions.[13]



9. Mahajan and co-workers developed a solvent free and catalyst free approach towards the selective synthesis of quinazolines and benzo quinazolines by using N-arylamidines with various aldehydes in presence of Lewis acid catalyst.[15]



10. Periya samselvam *et al.* synthesized substituted 2- sulphonamido-quinazolin-(3H)-ones derivatives by using microwave assisted synthesis in presence of benzoxazine sulphonamides and glacial acetic acid.[17]



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