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Microwave assisted organic synthesis (MAOS): Green alternatives to existing laboratory methods involving toxic chemicals and solvents

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Abstract

Green chemistry approach emphasizes on designing synthetic methodologies to utilize and generate less toxic products and byproducts, generation of lesser waste materials with little or no toxicity to human health and environment. The goal is to utilize renewable feed-stocks and to minimize the energy requirements of chemical processes. Among the low energy consuming processes, chemical synthesis on microwave oven has shown remarkable results. The rapid heating from microwaves made the synthesis very fast and produces uniform materials. The fast and uniform heating capability of the microwave leads to considerable saving of energy and remarkable reduction in reaction time. Several classical methods prescribed in Chemistry laboratory courses, involve harmful chemicals and corrosive solvents, some of these are difficult to handle and generate hazardous waste affecting human health and ecosystem. To minimize their adverse impacts, such laboratory methods whenever possible should be replaced by alternative benign green methods, which also minimize the waste generation and energy requirements of the chemical process. This communication highlights 15 microwave assisted Organic synthesis (MAOS), that can be achieved even on consumer grade microwave oven and borosilicate glass beakers and flasks.

Keywords: Microwave heating, dipolar polarization, microwave assisted organic synthesis

Introduction

Green chemistry is a philosophy of chemical research and engineering that encourages the designing of better manufacturing processes for chemical products that minimize the use and generation of hazardous substances [1]. Worldwide, attempts are being made not only to quantify the greenness of a chemical process but also product yield, the price of reaction components, safety in handling chemicals, hardware demands, energy profile and ease of product workup and purification. In addition to protecting the environment, green chemistry has the potential to benefit the large and diverse group of people whose job or residence places are at risk for exposure to toxic chemicals produced by manufacturing [2]. Many recent advancements in Green Chemistry have been successful and with considerable advantages for energy consumption, less toxic products and minimum waste.

1. Microwaves in Organic Synthetic Chemistry

The potential of rapid microwave assisted synthetic methods are realized with lower energy requirements, lesser waste generation and economically sound chemical processes. Now, microwave-assisted eco-friendly organic syntheses have become a new trend with unlimited applications in synthetic organic Chemistry [2]. Microwave assisted reactions are cleaner and take only few minutes to complete, give higher yield, produce minimum waste and some of these may proceed even without solvent. Microwave assisted Organic Synthesis has gained popularity during last 2-3 decades as a powerful tool for rapid and efficient synthesis of a variety of compounds because of selective absorption of microwave energy by polar molecules [1-4]. Organic reactions under the microwave radiation have many advantages compared to the conventional reactions many of these need very high temperatures and long reaction time. One of the most valuable advantages is the dramatic reduction in reaction times from days and hours to minutes and seconds. Microwave heating also reduces side reactions and improves reproducibility. Thus, microwave assisted organic synthesis has become an expanding field that academia, R & D sector and chemical and pharmaceutical industry are taking much interest in MAOS for rapid optimization of reactions [3-6].

2. Microwave Radiation

Microwave radiation lie in the electromagnetic spectrum between infrared waves and radio waves, the wavelengths fall between 0.01 and 1 meter and operate in the frequency range between 0.3 and 300GHz [7]. The Worldwide legislation has allotted frequency band to scientific, industrial or domestic microwave ovens which corresponds to 2.45 GHz (2450MHz), having the wavelength of 12.24 cm [2]. The energy of the microwave photon in this frequency region is approximately 0.3 cal / mole, which is too low to break a chemical bond which needs energy around 100 Kcal/ mole and therefore microwaves cannot induce chemical reactions [8]. Thus, microwave radiation is non-ionizing and provides only thermal activation and unable to alter the molecular structure of the compound being heated. Heating of materials in microwave exposure can only result from material-wave interactions [9] that are caused due to the transformation of a fraction of energy of microwave radiation into heat.

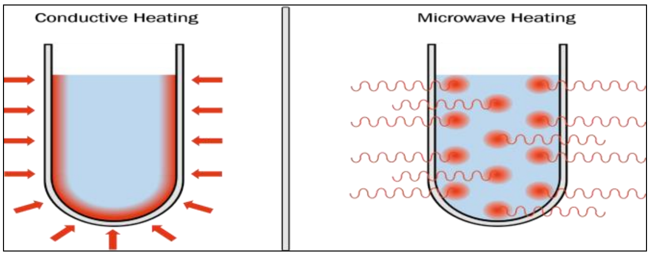


Fig 1: Conventional (conductive) heating vs Microwave heating [10].

3. Dielectric heating effects (Dipolar Polarization):

The electric component of an electromagnetic field causes heating by two main mechanisms, *dipolar polarization* and *ionic conduction*. Polar molecules can be oriented along an electric field, the dipolar polarization. The efficient heating of reaction materials by microwave dielectric heating effects depends on the ability of the solvent, catalyst or reagent to absorb microwave energy and convert it into heat [10]. However, in conventional heating [Fig.-1] the reactants are heated by ionic conduction and heat is transferred first from source to vessel and then from vessel to solution. This is a slow, non-uniform and inefficient method of heat transfer (Gedye *et al.*, 1986) [11], where the surfaces become much hotter than the inside of the material. In microwave assisted organic synthesis (MAOS), the heating effect is mainly due to dielectric polarization.

Under microwave irradiation the polar molecule is aligned with the applied field. In the fast changing electric field affects, the molecule continually attempts to align itself with the changing field and energy is absorbed [8]. In microwave radiation the dipoles of polar molecules align in the electric field. In dipolar rotation, a molecule rotates back and forth constantly, attempting to align its dipole with the ever-oscillating electric field [11]. The friction between each rotating molecule results in heat generation [12]. At very high frequency range inter-molecular forces may stop the motion of a polar molecule before it tries to follow the field, resulting in inadequate inter-particle interaction. However, under a low range microwave frequency, the polar molecule has sufficient time to align itself in phase with the field and no random interaction takes place between the particles [13]. Continually oscillating electric field component of microwave exerts a force to both dipoles of the molecule that causes it to rotate continually. And, the time taken by electric field component to oscillate is consistent with the time it takes for a water molecule to rotate 180°. Thus, when a water molecule is irradiated with microwaves, it aligns itself with the applied field and rotating as quickly as possible. The frequency of 2.45 GHz lies between these two extremes and gives the molecular dipole time to align in the field, but not to follow the alternating field precisely [12]. The rapidly changing electric field (at frequency of 2450 million times per second) affects the molecule and consequently the molecule continually attempts to align itself with the changing field and energy is absorbed [14]. In the presence of a continuous electric current, all the dipoles are lined up together in the same direction. If, submitted to an alternate current, the electric field is inversed at each alternate with a subsequent tendency for dipoles to move together to follow the field. Such a characteristic induces stirring and friction of molecules, which dissipates as internal homogenous heating [9]. The amount of heat generated by this process is directly related to the ability of the reactant materials to align itself with the frequency of the applied field. If the dipole does not have enough time to realign, or reorients too quickly with the applied field, no heating occurs. Thus, microwave can only heat dielectric materials due to material- wave interactions with a significant penetration deep into materials and close to a few centimeters, in wavelength. Here thermal phenomenon-conduction, convection, radiation only plays a minor part [14].

4. Microwave Solvents

The heating characteristics of a material under microwave irradiation are dependent on its dielectric properties. The larger the dielectric constant the greater is the coupling with microwaves. High dielectric solvents, such as water, methanol, ethanol, acetonitrile, DMF, ethyl acetate, chloroform, dichloroethane, acetone, ethylene glycol, acetic acid, etc. tend to heat rapidly under microwave radiation[2]. Less polar solvents such as aromatic and aliphatic hydrocarbons absorb poorly. On the other hand solvents without a permanent dipole moment such as benzene, dioxane, hexane, carbon tetrachloride etc. are transparent to microwave and not heated under microwaves [14]. Further, polar molecules in a non-polar solvent absorb energy, but not the solvent or the reaction vessel made of Teflon or ceramic or borosilicate or pyrex. It is also possible to use mixtures of microwave active reactants and microwave inactive solvents [15].

5. Advantages of Microwave irradiation:

Microwave radiation is non-ionizing and provides only thermal activation and unable to alter the molecular structure of the compound being heated. The notable advantages of microwave irradiation over the conventional heating are uniform heating throughout the material, enhancement in reaction speed sometimes many fold, highly efficient uniform heating throughout the reacting materials, lesser unwanted side reactions, high reproducibility, environmental heat loss avoided, eradicates the wastage of heat in heating reaction vessel and therefore low operational cost [2]. In addition to these, microwave heating dramatically reduces the reaction times, increases product yields and enhances purity of final product by reducing unwanted side reactions compared to conventional heating methods. The use of microwave has also exploited in the multistep total synthesis, medicinal chemistry, drug discovery, polymer synthesis, material sciences, and nanotechnology and biochemical processes [13]. Further, microwave assisted reactions take only few minutes to result higher yield and minimum waste.

6. Microwave Ovens and Microwave Digesters:

American Scientist Percy Lebaron Spencer discovered the use of microwaves for heating purposes and in 1947 he designed the commercial microwave oven for domestic use [16, 17]. Microwave ovens use radio waves set at a specific frequency, 2,450 MZH with a power ranging from 500 to 1500 watts [16]. The frequency of 2.45 GHz lies between these two extremes and gives the molecular dipole time to align in the field, but not to follow the alternating field precisely [12]. The microwave ovens, designed for domestic purpose have registered its expanding use in wide range of microwave assisted chemical reactions [10]. Some modifications in domestic microwave ovens are introduction of condensers by boring through the top of the oven or reaction flasks being fitted with condensers [2]. In microwave oven microwaves are generated by magnetron and the temperature is maintained by turning the on and off cycles of the magnetron. By inserting a reflux condenser in the domestic microwave ovens the safety factors are adjusted up to some extent [18]. As the domestic microwave ovens were not designed for laboratory purposes, the required safety controls were missing and the interior chamber of the oven was bound to attract the corrosive attack of acids, bases and solvents being used [10]. All the modern commercially available microwave reactors are with built -in magnetic stirrers, direct temperature control of the reaction mixture with the aid of fiber-optic probes and software that enables on-line temperature/pressure control. These days, advanced version of bench top microwave reactors are available in market [12].

Experimental

1. Reagent and Equipments

All the reagents and solvents used were AR grade from E.Merk or Loba-Chemie. Other chemicals, reagents and solvents used were also of AR grade.

Consumer Model L.G. Microwave oven (2.450 GH$_Z$, 1000W) and Perkin Elmer RX1 model FTIR were used for concerned purpose.

The products were identified by melting point and some by FTIR spectra.

2. Microwave Assisted Organic Synthesis (MAOS) on Microwave Oven

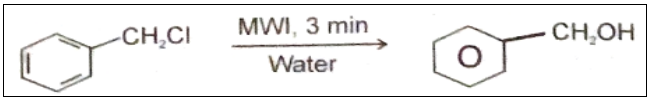
Several classical methods adopted over more than a century in chemical analysis prescribed in University Chemistry laboratory courses, involve harmful chemicals and solvents which generate hazardous waste that affect human health and ecosystem [2]. To minimize their adverse impacts, such laboratory methods whenever possible are being replaced by alternative Green methods, which are benign to humanity and environment [1]. Green Chemistry promotes and offers an education for sustainable development [20]. The inclusion of green chemistry education in university curriculum will promote the concepts of green chemistry among the Chemistry students. In west several international institutions, the American Chemical Society (ACS), RSC, and Polish Chemical Society promoted the concepts and achievements of green chemistry [19]. However, the developing countries are still far behind and need to emphasize more participation of masses in awareness programs specially the students, teachers from both undergraduate and graduate levels. In spite of the extensive efforts of Green Chemistry Net Work centre, New Delhi to popularize Green Chemistry concepts, most of the Indian Universities are reluctant to adopt the available green alternatives of the century old classical methods of analysis that involve toxic chemicals and reagents and halogenated solvents [1], except Central University of Rajasthan, few colleges of University of Delhi and other individual level efforts.

To follow the principles and applications of Green Chemistry and to minimize the use of hazardous chemicals and reagents in Chemistry laboratory courses, the introduction of Green practices in Green Chemistry experiments wherever possible is urgently needed [5]. The laboratory courses from undergr-aduate to post graduate semesters should eliminate the classical methods of synthesis, involving harmful chemicals, reagents and solvents and their wastes which have hazardous effects on students, teachers and supporting staff, as well as environment [19].

Fifteen important microwave assisted Organic Chemistry laboratory experiments are presented here with their working details. These experiments should be included in the Chemistry lab Courses of Indian Universities, by replacing the decades old experiments, which deals with harmful chemicals and solvents that generate nationwide huge hazardous waste affecting humanity and ecosystem. Doing this will create a workforce of the trained students to enter industry, academia and National Research laboratories, CSIR, DRDO etc, equipped with the tools to design more benign products and processes. Green chemistry experiments were included in the undergraduate and post graduate curriculum and lab courses of Pt. L. M. S. Govt. Post Graduate College, Rishikesh, Dehradun, on upgradation to Autonomous College by the UGC, New Delhi. These experiments were successfully carried out on consumer grade microwave oven under the guidance of Dr. S. K. Dabral and Dr. Dayadhar Dikshit.

3. MAOS Scheme-1: Microwave Assisted Hydrolysis of benzyl chloride with water

Desai [2] and Gedye *et al.*, 1991 [1, 21] reported microwave assisted hydrolysis of benzyl chloride with water is carried out in domestic microwave oven. This gives 97 % yield of benzyl alcohol in 3 min. The usual hydrolysis in normal way takes about 35 min.

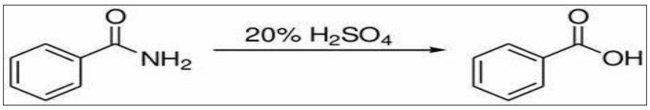


Green Aspects

This method is much superior than the conventional method which undergoes at higher temperature in the range of 100-180^{0}C and reaction times may be up to 3-4 hours **[1, 21]**.

4. MAOS Scheme-2: Microwave Assisted Hydrolysis of benzamide with water

The conventional hydrolysis of benzamide takes nearly 1 hr, however, under microwave conditions, the hydrolysis is achieved within 7 min with 99 % yield of benzoic acid [2, 22].

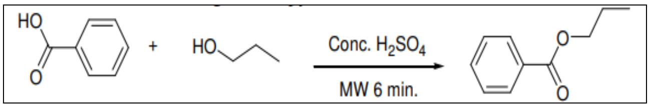


Green Aspects

In conventional method benzamide is first converted to sodium benzoate which is further acidified to benzoic acid. However, in microwave assisted process, hydrolysis of benzamide is done within 7 minutes with 99% yield [2, 22].

5. MAOS Scheme-3: Microwave Assisted Esterification of benzoic acid with n- propanol

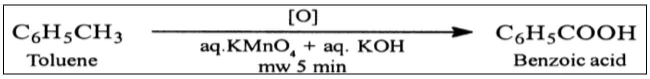
Microwave assisted esterification of benzoic acid with n-propanol to n-propyl benzoate is achieved on heating in a microwave oven for 6 min in presence of catalytic amount of conc. sulfuric acid [11,23].



Green Aspects

Traditional method of esterification of benzoic acid requires use of corrosive conc. Sulphuric acid that may cause moderate to serious chemical burns on skin or eyes. Further, the traditional method has limitations of lower yield and high reaction time.

6. MAOS Scheme-4: Microwave Assisted Oxidaion of Toluene with KMnO$_4$



$$\underset{\text{Toluene}}{C_6H_5CH_3} \xrightarrow[\text{aq.KMnO}_4\text{ + aq. KOH}\;\text{mw 5 min}]{[O]} \underset{\text{Benzoic acid}}{C_6H_5COOH}$$

The traditional method of oxidation of toluene needs refluxing for 10-12 hr as compared to microwave assisted oxidation that takes only 5 min, with 40% yield [2].

Green Aspects

The method avoids the corrosive hydrochloric acid that releases HCl gas.

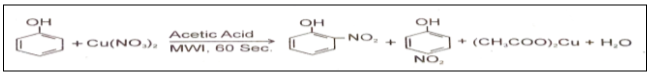
7. MAOS Scheme-5: Microwave-assisted Nitration of phenols using cupric nitrate.

In this experiment the microwave assisted nitration of phenol was done using cupric nitrate in acetic acid in a consumer model microwave oven, using borosilicate beaker [1, 24].

Requirements

1. AR grade phenol, 1.28 gm, copper nitrate, 3.6 gm, acetic acid,7 ml.
2. Borosilicate glass 100 mL beaker and consumer grade microwave oven, 320 W.

The reaction involves microwave-assisted, green electrophilic nitration of phenol using copper nitrate in acetic acid. The reaction takes only 60 seconds to complete.



Green Method

Phenol, 1.28 g and copper nitrate, 3.6g are taken in Borosilicate 100 ml capacity Beaker, to which 7 ml acetic acid are added. The contents are irradiated for 1 minute at 320 Watts. Beaker was taken out of oven and reaction mixture was allowed to cool and product thus obtained was recrystallised from ethanol: distilled water (1:1).

Green Aspect

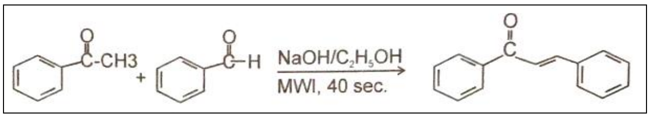
This experiment avoids the use of corrosive conc. nitric acid, which is difficult to handle.

8. MAOS Scheme-6: Microwave assisted synthesis of Chalcone from benzaldehyde and acetophenone

Microwave assisted synthesis of Chalcone from Benzaldehyde and Acetophenone can be achieved within 40 sec. [2, 25].

Requirements

1. Benzaldehyde, 2.2 ml, Acetophenone, 2.5 ml, NaOH, 2 Pellets and ethanol, 7 ml.
2. Microwave oven, 210 Watt, 30% MW power.



Green Method

A solution of acetophenone and benzaldehyde in 7 ml ethanol and 2 palettes of NaOH are taken in borosil beaker and irradiated for 40 seconds at 210 Watts with 30 % MW power. Reaction mixture is cooled and chalcone thus obtained is filtered and washed with ethanol.

Green aspects

The microwave assisted synthesis of Chalcone i.e. benzylidene acetophenone) can be achieved within only 40 seconds in contrast to traditional method that needs heating for several hours.

9. MAOS Scheme-7: Microwave Assisted Synthesis of Anthracene-Maleic anhydride adducts.

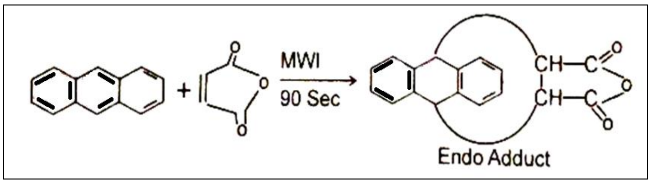
Microwave Assisted Synthesis of anthracene- maleic anhydride adduct (9, 10-dihydro anthracene – endo- α, β succinic anhydride) can be achieved in 90 seconds [1, 26].

Requirements

1. Anthracene, 1.8 g, Maleic anhydride, 0.98 g and Diglyme 5 ml.
2. Microwave oven, 210 Watt, medium power and Borosil Beaker 50 ml.

Green Method

Grind a mixture of 1.8g of anthracene and 0.98 g of maleic anhydride in a mortar and transfers it to a 50 ml borosilicate beaker. After adding 5 ml diglyme, shake the reaction mixture gently. Beaker is covered with watch glass and placed in a microwave oven to irradiate for 90 seconds at a medium power level. Beaker is taken out of the oven, allowed to cool to room temperature. The crystals of anthracene- maleic anhydride adduct appeared, which are filtered. The product is washed with methanol and dried. Melting point of the adduct 262^{0}C and 80% yield [1, 26].



Green aspects

The synthesis of anthracene- maleic anhydride adduct is achieved within 90 seconds under microwave heating, while the conventional method needs refluxing for 25 minutes in xylene.

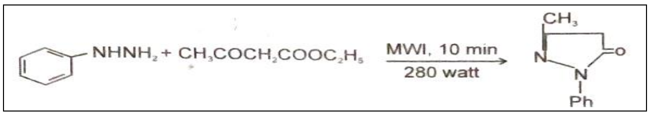
10. MAOS Scheme-8: Microwave assisted Synthesis of 3-methyl-1-phenyl-5-pyrazolone

Microwave assisted condensation between phenyl hydrazine and acetoacetic ester yields 3- methyl-1-phenyl-5-pyrazolone within 10 minutes [2].

Requirements

1. Ethyl acetoacetate, 2.9 gm and Phenyl hydrazine, 2.7 ml,
2. Microwave Oven, 280 Watts and Borosil beaker, 50 ml

Green Method: A solution of 2.9 ml of ethyl acetoacetate and 2.7 g of phenyl hydrazine are taken in Borosil beaker and kept in microwave oven and irradiated for 10 minutes at 280 Watts. The reaction mixture is cooled, product thus obtained is crystallised from ethanol: distilled water (1:1).



Green aspects

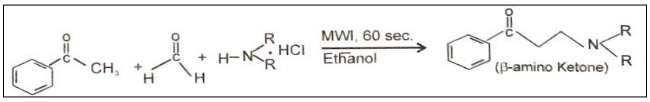
The solvent less synthesis of pyrazolone derivative is achieved on irradiation of microwave heating for 10 minutes.

11. MAOS Scheme-9: Microwave-assisted Synthesis of ß -amino ketone

Microwave assisted Mannich reaction between acetophenone, formaldehyde and secondary amine gives a ß-amino ketone with high yield [2,27].

Green Method

A Mannich condensation between acetophenone, formaldehyde and a secondary amine on microwave irradiation in presence of ethanol for 60 seconds produces a β-amino ketone, with 83 % yield.



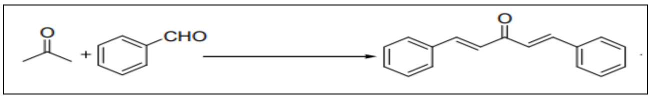
Green Aspects

This green method avoids the disadvantages of classical methods such as drastic reaction conditions and formation of undesired byproducts and low yields.

12. MAOS Scheme-10: Microwave assisted reaction between Benzaldehyde and acetone.

Microwave irradiation of benzaldehyde with acetone produces dibenzalacetone selectively without self-condensation product [1, 28].

Green Method



In a 10 ml microwave vessel, 50 mg of benzaldehyde and acetone were mixed and then aqueous solution of NaOH (containing 0.6g/liter) was added. The vessel was placed in microwave chamber for 10-15 minutes. Vessel was taken out. The product was crystallised with ethyl acetate by taking three installments of 25 ml each. The organic layer was dried over anhydrous $MgSO_4$, M. Pt. 112^0C [1, 28].

Green Aspects

The reaction is completed within 10-15 minutes with 79% yields.

13. MAOS Scheme-11: Microwave assisted synthesis of Indole derivative from Cyclohexanone and Phenyl hydrazine hydrochloride.

Microwave assisted Indole condensation between Cyclohexanone and Phenyl hydrazine hydrochlorid gives the desired product on irradiation of 3o seconds [1, 29].

Requirements

1. Cyclohexanone, 2 ml, Phenyl hydrazine hydrochloride, 2.9 ml, acetic acid, 7 ml,
2. Microwave oven, 210 Watt 30% MW power and Borosil beaker, 50 ml capacity.

Green Method

A solution of 2 ml cyclohexanone and 2.9 ml phenyl hydrazine hydrochloride and 7 ml acetic acid are taken in a Borosil beaker and kept in sample chamber of microwave oven and irradiated at 210 Watts, 30% power. The reaction is completed within 30 seconds with 385 fold rate acceleration with excellent yields. Reaction mixture is cooled and Indole derivative thus obtained is filtered and washed with distilled water [1, 29].

Green Aspects

The reaction is completed within 30 sec. with 385 fold rate acceleration and high yields.

14. MAOS Scheme-12: Microwave-assisted solvent less synthesis of *N*-phenylsuccinimide

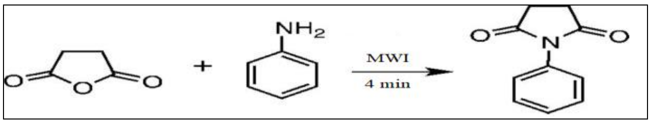
Thomas *et al* in 2011 [30] reported the microwave assisted solvent less synthesis of *N*-phenyl succinimide achieved by heating a mixture of aniline and succinic anhydride for 4 minutes in a microwave oven.

Requirements

Aniline, succinic anhydride, and domestic microwave oven, Borosilicate beaker

Green Method

In a borosil beaker, the mixture of aniline and succinic anhydride is irradiated for four minutes in a domestic microwave oven. The synthesis of the final product, *N*-phenyl succinimide was achieved within a single chemistry laboratory period [30].



Green Aspect

This microwave assisted method is achieved within 4-5 minutes as compared to the traditional synthesis taking 10 hours. This reaction is a solvent less method, energy efficient and atom efficient method than the traditional synthetic method. This method skips the use of halogenated solvent, dichloromethane [30].

15. MAOS Scheme-13: Microwave Assisted Synthesis of Aspirin from salicylic acid and acetic anhydride

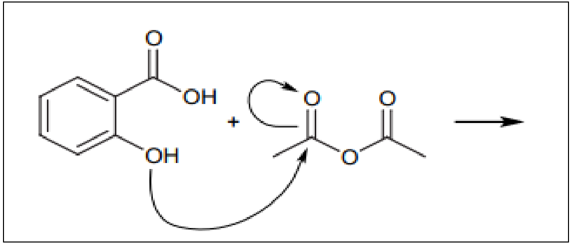
Microwave assisted solvent free synthesis of Acetyl salicylic acid is achieved on irradiating the micro wave radiation to a mixture of salicylic acid and acetic anhydride for 5 minutes, with 97% yield [31,32].

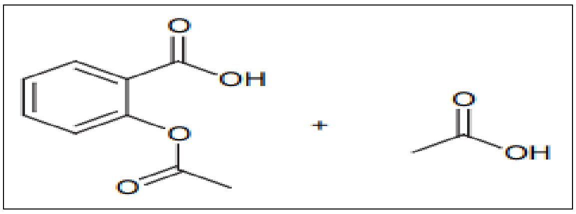
Requirements

1. Salicylic acid, 1.38 g, acetic anhydride 3.06 g, phosphoric acid, one drop.
2. Borosilicate beaker, 50 ml and Consumer microwave oven, 175 Watts.

Green Method

In a 50 ml borosilicate beaker 1.38g of salicylic acid, 3.06 g of acetic anhydride, and one drop of phosphoric acid were well mixed. The beaker was covered with a watch glass and was placed in microwave oven and irradiated at the power of 175 Watt for 5 minutes. Beaker was taken out of the microwave oven, allowed it to cool to room temperature and place in an ice bath for crystallization. Yield, 92%, melting point, 135^{0}C [31, 32].





Green Aspects

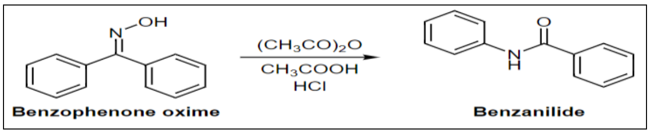
Microwave assisted solvent free synthesis of Aspirin was achieved within 5 minutes with 97% yield.

16. MAOS Scheme-14: Microwave assisted Beckmann rearrangement of benzophenone oxime

In this experiment Sugamoto *et al*, 2011 [33] demonstrated the microwave assisted Beckmann Rearran-gement of Benzophenone oxime to Benzanilide.

Green Method

Microwave assisted Beckmann rearrangement of benzophenone oxime to benzanilide can be achieved by irradiation of microwave energy of 350 Watt for 19 seconds [33].



Green Aspects

The reaction is carried out within 19 seconds, by using benign reagents.

17. MAOS Scheme-15: Microwave assisted Wolf Kishner Reduction Reaction

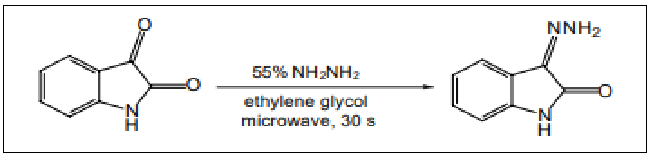
In the microwave assisted method Oxiindole is synthesized by irradiation of isatin, hydrazine and ethylene glycol for only 30 seconds to get isatin hydrazide, which with KOH in ethylene glycol is further irradiated to yield Oxi indole [34].

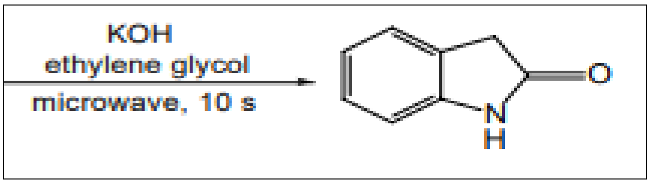
Requirements

1. Isatin 0.25g, hydrazine 0.30g, ethylene glycol, ethanol, KOH, Na_2SO_4, HCl and diethyl ether
2. Two Borosilicate beaker, 50 ml and Consumer microwave oven, 175 W.

Green Method

Isatin 0.25 g, hydrazine 0.30 g and ethylene glycol 1 ml are gently shaken in 50 ml borosil beaker till complete mixing. Beaker is then kept in microwave oven and irradiated at medium power for 30 sec. Beaker is taken out of oven and kept at room temperature for few minutes, then cooled in ice bath for 5 minutes. Filtered at suction to get isatin-3-hydrazone as yellow powder, washed twice with ethanol, 0.5 ml each time then air dried. Yield, 0.223g, 82 %.





In a clean 50 ml borosil beaker 0.5 ml of ethylene glycol and 62 mg KOH was irradiated for 10 seconds to dissolve the base. To this solution, Isatin-3-hydrazone 58.5 mg prepared above was added with 1 ml of ethylene glycol and irradiated for 10 seconds. The beaker was taken out of oven and cooled to room temperature. Brown solution thus obtained was diluted with 1 ml deionized water, acidified with 6M HCl till pH 2 and then extracted with diethyl ether thrice with 1.5 ml ether each time. The ether solution was dried with anhydrous Na_2SO_4 and evaporated to get yellow solid, which was crystallized from 0.7 ml of deionized water to get 15.5 mg of oxiindole as white needles, yield 35%, M. Pt., 125^{0}C [34].

Green Aspects

In instead of prolong heating at high temperature in conventional method; the synthesis of oxiindole is carried out within five minutes.

Result and discussion

The 15 microwave assisted organic synthesis (MAOS) Schemes (1-15) presented above utilize and adopt the principles, concepts and applications of Green Chemistry with a sincere goal to minimize the use of hazardous chemicals in Chemistry lab courses at secondary to University levels by introducing Green Chemistry experiments wherever possible. Out of the above reported green MAOS experiments, the hydrolysis of benzyl chloride (Scheme-1) needs heating at 100-180^{0}C for 3-4 hours, however, this reaction under microwave irradiation in domestic microwave oven gives 97 % yield of benzyl alcohol within 3 min [2, 21]. In contrast to the conventional hydrolysis of benzamide takes 1 hr, while under microwave conditions (Scheme-2), it takes only 7 min giving 99 % yield of benzoic acid [2, 22]. Traditional method of esterification of benzoic acid with n- propanol requires use of corrosive conc. sulphuric acid that may cause burns on skin or eyes, while under the microwave irradiation esterification of benzoic acid (Scheme-3) is carried out within 6 min [11, 23]. The oxidation of toluene in presence of conc. HCl needs refluxing for 10-12 hr, while microwave assisted oxidation with $KMnO_4$ (Scheme-4) takes only 5 minutes and it also avoids the use of corrosive HCl, which releases HCl gas [2]. The traditional nitration of phenol is carried out with Conc. HNO_3, but the microwave-assisted green nitration of phenol using copper nitrate in acetic acid (Scheme-5) is achieved within only 60 seconds and it also avoids use of corrosive HNO_3 [1, 24]. The microwave assisted synthesis of Chalcone is achieved within 40 seconds (Scheme-6), in contrast to traditional method that needs heating for several hours [2, 25]. The microwave assisted synthesis of anthracene- maleic anhydride adduct (Scheme-7) can be achieved in 90 seconds and avoids the use of corrosive conc. nitric acid [1, 26]. Microwave assisted condensation between phenyl hydrazine and acetoacetic ester (Scheme-8) produces pyrazolone derivative within 10 minutes [2].

Similarly, microwave assisted Mannich condensation between acetophenone, formaldehyde and a secondary amine (Scheme-9) is achieved in 60 sec., producing a ß-amino ketone with high yield, 83%, this also avoids the disadvantages of older methods, drastic reaction conditions, formation of undesired byproducts and low yields [2, 27]. The microwave assisted condensation between benzaldehyde and acetone (Scheme-10) within 10 minutes produces dibenzalacetone with 79% yield [1, 28]. The microwave assisted Indole condensation between cyclohexanone and phenyl hydrazine hydrochloride (Scheme-11) gives product within 3o seconds with 385 fold accelerated reaction rate and high yield [1, 29]. Similarly, microwave assisted synthesis of the N-phenyl Succinimide (Scheme-12) is achieved within 4-5 minutes [30], as compared to the traditional synthesis taking 10 hours, the preparation can be achieved in a single day laboratory period. This reaction is a solvent less, energy efficient and atom efficient method than the traditional synthetic method. This method skips the use of halogenated solvent, dichloromethane [30]. Microwave assisted solvent free synthesis of Aspirin from salicylic acid (Scheme 13), is achieved by the microwave irradiation to a mixture of salicylic acid and acetic anhydride for 5 minutes, with 97% yield [31, 32]. Microwave assisted Beckmann Rearr-angement of benzophenone oxime to benzanilide (Scheme 14), is achieved within 19 sec. [33]. Similarly, microwave assisted synthesis of Oxiindole by irradiation of isatin, hydrazine and ethylene glycol for only 30 seconds to get isatin hydra-zide, which with KOH in ethylene glycol is further irradiated to yield Oxi indole (Scheme 15). This green method totally avoids the prolong heating at high temperature in conventional method and the synthesis of oxiindole is carried out within few minutes [34]. Thus the microwave heating is a very convenient heating source in the chemical laboratories that many reactions precede much faster than with conventional heating means.

Conclusion

Now, *Green Chemistry* is at the frontiers of this evolving interdisciplinary science that attempts to reduce the environmental impact of the chemical industries hues waste by inventing new technology that is inherently non-toxic to living things and the environment. The notable advantages of microwave heating over the conventional heating includes, input of benign and renewable starting materials, highly efficient uniform heating throughout the reacting materials, lesser unwanted side reactions, taking only few minutes to complete, improved product yield, lesser waste generation, high reproducibility, increased purity of final product, reduced heat wastage and therefore low operational cost. These advantages have opened new opportunities, in the form of new reactions that are not possible by using conventional heating. Further, microwave-assisted organic synthesis has emerged as a sustainable technique with an environmentally friendly approach. The microwave heating is much cost effective due to energy and time savings, operational efficiencies, reduced manpower, reduced heat consumption and reduced maintenance costs. Therefore, to follow the principles of Green Chemistry, the laboratory courses in Chemistry from undergraduate to post graduate semesters, should eliminate the classical methods involving harmful chemical reagents and solvents. Thus, the need is to include the green Chemistry experiments in the Indian University curriculum of for Chemistry students, without further delay. These green chemistry experiments are bound to provide first hand learning experiences to the college and University students. Students through these experiments will become familiar to new approaches and thereby may develop new alternatives to several older methods of analysis involving hazardous reagents and chemicals and new green synthetic methodologies of newer dimensions. The green chemistry education in university curriculum will promote the concepts of green chemistry in the students, preparing them as young chemists to enter industry and academia equipped with the tools to design more environmentally benign products and processes for future generation.

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