MICROWAVE ASSISTED REACTIONS UNDER BENIGN CONDITIONS

A
Thesis submitted

in partial fulfillment of the requirements
for the degree of
Master of Science in Chemistry

Submitted by:
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Rajni Singla

Candidate's Declaration

I hereby declare that the work presented in the thesis entitled, **"Microwave assisted reactions under benign conditions"**, in partial fulfillment of the requirements for the award of the degree of Master of Science in Chemistry and being submitted to School of Chemistry and Biochemistry, Thapar University, Patiala, is my own work during the period of Jan 2009 to May 2009, under the supervision of Dr. Satnam Singh, Assistant Professor, School of Chemistry and Biochemistry, Thapar University, Patiala. I have not submitted the contents embodied in this thesis for the award of any other degree.

Rajni Singla.

Patiala
Date: 9/6/09

Rajni Singla

This is to certify that the above statement made by the candidate is correct and true to the best of our knowledge.

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Certificate

This is to certify that the thesis entitled **"Microwave assisted reactions under benign conditions"**, being submitted by **Ms. Rajni Singla** to School of Chemistry and Biochemistry, Thapar University, Patiala, in partial fulfillment of the requirements for the award of degree of Master of Science in Chemistry, is a bonafide work carried out under my supervision, and that no part of this thesis has been submitted for the award of any other degree.

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Abstract

Microwave chemistry has an edge over conventional heating methods for conducting chemical reactions, and is emerging as the preferred technology for performing chemical reactions. Microwave technology enable chemists to achieve cleaner and more efficient chemical reactions with higher yields, compared to conventional heating methods. The possibility of performing reactions in a very short time period by direct interaction of microwave energy with the reaction mixture as opposed to the indirect transfer of energy by utilizing an oil bath certainly can be considered "green", not only because of the reduced energy consumption, but also it enable us to do the reaction using water as solvent or even under neat conditions. Water behaves as pseudo organic solvent at high temperature.

During the present study, Mannich base, benzyl alcohol, Diels-Alder adduct, alkyl thiocyanates have been synthesized by the use of domestic microwave oven and the reactions were complete in very short interval as compared to thermal conditions. These reactions were studied by the use of microwave irradiations under solvent-less condition or by the use of water as benign solvent.

Mannich base has been synthesized by using secondary amine and hydrogen chloride in water instead of using hydrochloride salt of secondary amine (which requires anhydrous conditions) in the domestic microwave oven, followed by amine exchange with another amine using ethanol as solvent. Another reaction viz., Diels Alder adduct was studied under microwave radiation and was complete within 3 minute as compared to conventional heating method, which required 2 hour of refluxing.

Cross Cannizzaro reaction of aldehyde leads to two products, one is alcohol and other as acid. Reaction of benzaldehyde, paraformaldehyde and barium hydroxide octahydrate in microwave leads to benzyl alcohol. Reaction has been done in solvent less condition. Other substitution reactions studied are by the use of alkyl halides (bromooctane and benzyl chloride) and potassium thiocyanate in aqueous media without the use of phase transfer catalyst and were complete within 15- 20 minutes under microwave irradiation.

CHAPTER 1

INTRODUCTION AND LITERATURE SURVEY

Nonclassical heating technique using microwaves, termed “Bunsen burner of the 21st century”, is rapidly becoming popular and is dramatically reducing reaction times. The use of emerging microwave-assisted chemistry techniques in conjunction with greener reaction media is dramatically reducing chemical waste and reaction times in several organic syntheses and chemical transformations. The possibility of performing reactions in a very short time period by direct interaction of microwave energy with the reaction mixture as opposed to the indirect transfer of energy by utilizing an oil bath or similar device certainly can be considered “green”, not only because of the reduced energy consumption, but also because of the associated time savings, thereby increasing efficiency. There is a variety of approaches for the development of sustainable methods, which reflects the enormity and complexity of this field. Twelve Principles of Green Chemistry[1] has been given by Paul Anastas and John Warner in 1998. Fifth principal state that, “The use of auxiliary substances (solvent etc) should be made unnecessary wherever possible and, innocuous when used”. Sixth principal states that, “Energy requirements should be recognized for their environmental and economic impacts and should be minimized. Synthetic methods should be conducted at ambient temperatures and pressure”. Among the 12 principles of green chemistry, the desire for utilizing “safer solvents” and to “design for energy efficiency” can be considered two important key principles of relevance to synthetic chemists.

1.1 Microwave chemistry

Microwaves lie in the electromagnetic spectrum between infrared waves and radio waves. They have wavelengths between 0.01 and 1 meter, and operate in a frequency range between 0.3 and 30 GHz. However, for their use in laboratory reactions, a frequency of 2.45 GHz is preferred, since this frequency has the right penetration depth for laboratory reaction conditions. All domestic microwave ovens, microwave reactors and other laboratory and industrial systems usually work at 2.45 GHz.

1.1.1 Interaction of Microwave Irradiation with material

The mechanism of energy transfer in a microwave is significantly different from a hotplate or heating mantle. Microwave energy heats the sample through direct activation. In the microwave, energy is transferred to the reaction components within the solution. There are two components of a microwave: an electric field and a magnetic field.

The electric field will interact with any molecule that has a dipole or that is ionic. The electric component causes heating by two main mechanisms viz.,

(i) Dipolar polarization (Fig. 1.1) and (ii) Ionic conduction (Fig. 1.2)

The interaction of electric field component with the polar molecules is called the dipolar polarization mechanism.

Fig. 1.1 : Dipolar interaction

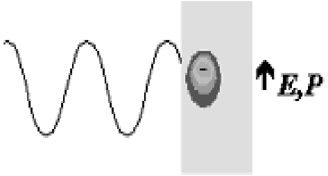


Fig. 1.2 : Ionic conduction

When exposed to microwave frequencies, the molecular dipoles align in the applied electric field. As the applied field oscillates, the dipole field attempts to follow these oscillations and the energy is lost in the form of heat through molecular friction and dielectric loss. The amount of heat generated by this process is directly related to the ability of the molecules to align itself with the frequency of the applied field[2].

The second major heating mechanism is the ionic conduction.

During the ionic conduction, the dissolved charged particles in a sample (usually ions) oscillate back and forth under the influence of the electric component of microwave irradiation. They collide with their neighboring molecules or atoms. These collisions cause agitation or motion, creating heat.

1.1.2 Microwave apparatus

Most pioneering experiments in chemical synthesis using microwaves were carried out in domestic microwave ovens. However, developments in microwave equipment technology have enabled researchers to use dedicated apparatus for organic reactions[3]. The following are the two categories of apparatus.

(i) Single-mode apparatus (ii) Multi-mode apparatus

(i) Single-mode Apparatus

The differentiating feature of a single-mode apparatus is its ability to create a standing wave pattern, which is generated by the interference of fields. This interface generates an array of nodes where microwave energy intensity is zero, and an array of antinodes where the magnitude of microwave energy is at its highest.

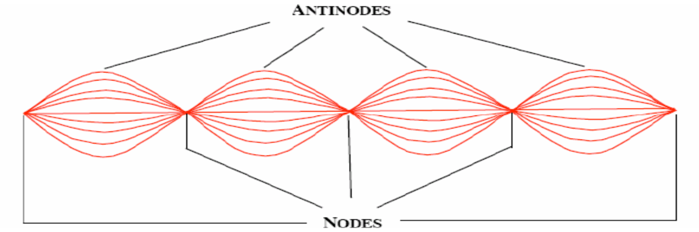


Fig. 1.3 : Generation of standing wave pattern

The factor that governs the design of a single-mode apparatus is the distance of the sample from the magnetron. This distance should be appropriate to ensure that the sample is placed at the antinodes of the standing electromagnetic wave pattern.

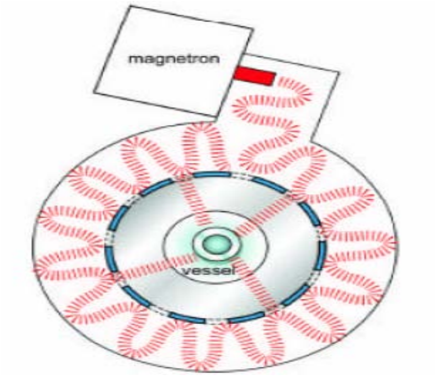


Fig. 1.4 : Single-mode Heating Apparatus

(ii) Multi-mode Apparatus

An essential feature of a multi-mode apparatus is the deliberate avoidance of generating a standing wave pattern inside it .The goal is to generate as much chaos as possible inside the apparatus. The greater the chaos, the higher is the dispersion of radiation, which increases the area that can cause effective heating inside the apparatus. As a result, a multi-mode microwave heating apparatus can accommodate a number of samples simultaneously for heating, unlike single-mode apparatus where only one sample can be irradiated at a time. A major limitation of multi-mode apparatus is that even with radiation distributed around them, heating samples cannot be controlled efficiently[4].

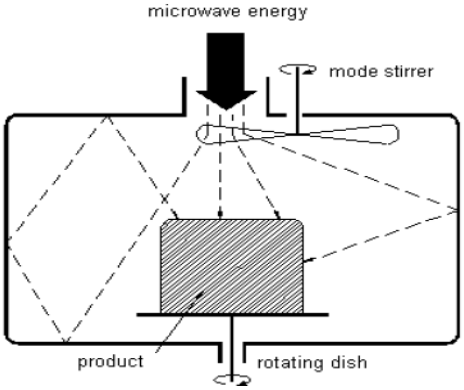


Fig. 1.5 : Multimode heating apparatus

1.1.3 Microwave effect

There are three possibilities for rationalizing the rate-enhancements observed in microwave-assisted process: thermal effect (kinetics), specific thermal microwave effect and specific non-thermal microwave effect.

1.1.3.1 Thermal (kinetic) effect

In the majority of cases the reason for the observed rate enhancement of chemical reaction is a purely thermal (kinetic) effect. It means that high reaction temperature achieved rapidly under microwave irradiation of polar materials cause increase in the chemical reaction rate.

1.1.3.2 Specific thermal microwave effect

In addition to thermal effect, there is microwave effect that is caused by the unique nature of the microwave dielectric heating but essentially is still thermal effect.

Wall effect: With microwave heating, the surface of the wall of the reactor is generally not heated since the energy is dissipated inside the whole volume of the reaction mixture.

Volumetric heating: Another phenomenon characteristic of microwave dielectric heating is rapid and even heating of the whole reaction mixture by microwaves, almost without any temperature gradient.

Uniform heating

Microwave radiation, unlike conventional heating methods, provides uniform heating throughout a reaction mixture (Fig. 1.6). In conventional heating, the walls of the oil bath get heated first, and then the solvent result in temperature difference between the walls and the solvent. In the case of microwave heating, only the solvent and the solute particles are excited which results in uniform heating of the solvent.[5]

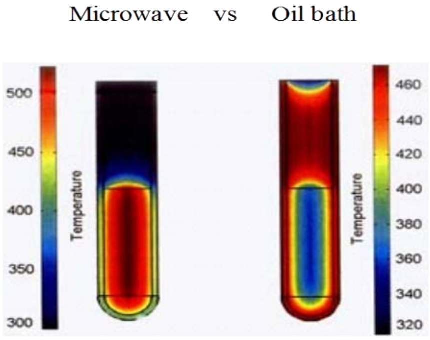


Fig. 1.6 : Inverted temperature gradients in microwave versus oil-bath heating: Difference in the temperature profiles (finite element modeling) after 1 min of microwave irradiation (left) and treatment in an oil-bath (right)

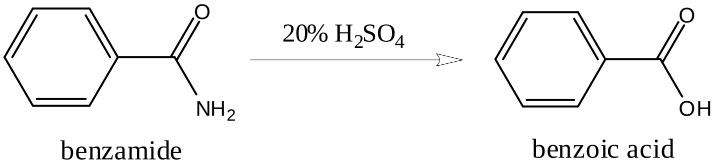
1.1.3.3 Specific non-thermal microwave effect

In contrast to specific thermal microwave effect an existing of specific non-thermal microwave effect is also studied. These can be classified as acceleration of chemical processes in a microwave field that cannot be rationalized in terms of either purely thermal/kinetic or specific thermal microwave effect. Essentially, most non-thermal effects result from a proposed direct interaction of the electric field with specific molecules in the reaction medium and electrostatic polar effect.

1.2 LITERATURE SURVEY

MICROWAVE ASSISTED ORGANIC SYNTHESIS

Use of Microwave Ovens for Rapid Organic Synthesis was demonstrated for the first time in 1986 by Gedye et al. [6]. They studied the utilization and advantages of microwave irradiation for organic synthesis involving hydrolysis of benzamide to benzoic acid under acidic conditions. Rate of reaction increases considerably (5 - 1000 fold) for the transformations compared to classical thermal reflux conditions.



conventional heating: 1h 90%
microwave heating: 10 min 99%

The advantages of using microwave dielectric heating for performing organic reactions were realized thereafter by many different groups and as a consequence the amount of articles describing high-speed chemical synthesis promoted by microwave irradiation has grown quickly from ~200 in 1995 to ~1000 in 2001[7].

Recent reviews available in the literature on the subject are: Microwave-Assisted synthesis in water as solvent by Dallinger et al.[8] , controlled microwave heating in modern organic synthesis by Kappe et al. [2], aqueous microwave chemistry: a clean and green synthetic tool for rapid drug discovery by Polshettiwar et al. [18] and microwaves in organic synthesis - thermal and non-thermal microwave effects by Hoz et al[5].

In the present work, some organic reactions were studied by the use of domestic microwave oven. The literature concerning nucleophilic substitution reaction, Mannich base preparation using acetophenone, paraformaldehyde, morpholine and hydrogen chloride, preparation of Diels Alder adduct, Cross Cannizzaro reaction is being presented.

Microwave Chemistry in Water

Not only is water nontoxic and readily available at low cost, it is also nonflammable and environmentally benign, providing opportunities for clean processing and pollution prevention. Apart from performing reactions in aqueous solutions in a moderate temperature range (0-100°C), chemical processing in water is also possible and of considerable interest under “superheated conditions” (>100°C) in sealed vessels because of the favorable changes that occur in the chemical and physical properties of water at high temperatures and pressures. Water around its critical point (374°C, 221 bar) possesses properties very different from those of ambient liquid water and is attracting increased attention as a medium for organic chemistry[8].

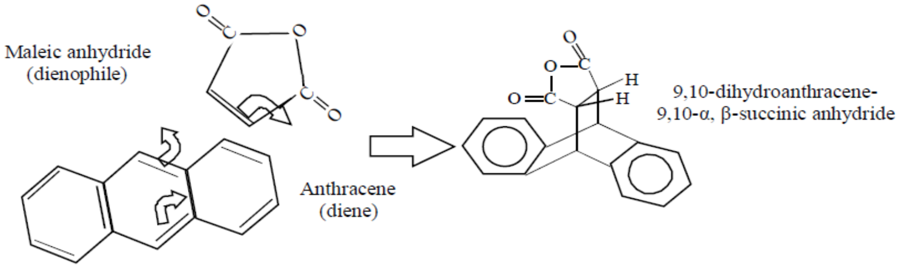
Fluid	Ordinary water(T<150°C, p< 4 bar)	Near-critical water (T=150-350°C, p<4-200 bar)	Supercritical water(T>374°C, p> 221 bar)
Temp(°C)	25	250	400
Pressure (bar)	1	50	250
Density (g cm^{-3})	1	0.8	0.17
Dielectric constant (ϵ’)	78.5	27.1	5.9
pKw	14	11.2	19.4

In contrast, the so-called near-critical (also termed subcritical) region of water at temperatures between 150 and 300 °C is of greater importance to organic synthesis. High temperature near-critical water under autogenic pressure provides a more favorable reaction medium for organic synthesis than does water under supercritical condition (>374°C). At 250°C, water exhibits a density and polarity similar to those of acetonitrile at room temperature[9]. The dielectric constant of water drops rapidly with temperature, and at 250°C it falls from 78.5 (at 25°C) to 27.5. This means that as the water temperature is increased, the solubility of organic compounds increases much more than expected for the natural effect of temperature. In addition to the environmental advantages of using water as pseudo-organic solvent in place of organic solvents, isolation of products becomes easier[10]. Once cooled, the organic products are no longer soluble in water at ambient temperatures, and this result in easy separation of product.

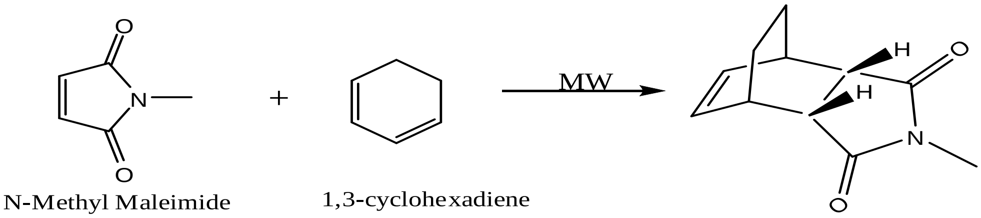
1.2.1 Diels-Alder Reaction

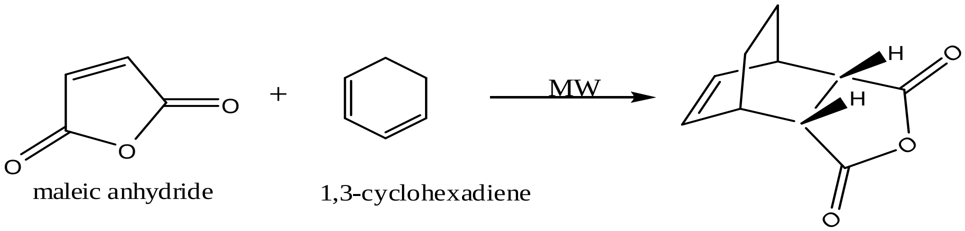
One important reaction that has transitioned into the microwave environment is that of the Diels-Alder reaction. Diels-Alder reactions are some of the most used reactions in organic chemistry due to their easy setups and high yields[11]. Specifically, the Diels-Alder reactions take place between 5 and 10 minutes and 125^{o}C to 150^{o}C in the CEM microwave. This can be used as a baseline when an unknown Diels-Alder reaction is attempted. This involved the reaction between anthracene and maleic anhydride via

Diels-Alder reaction to yield 9,10-dihydroanthracene-9,10-α,β-succinic anhydride. Anthracene is the diene and maleic anhydride is the dienophile.

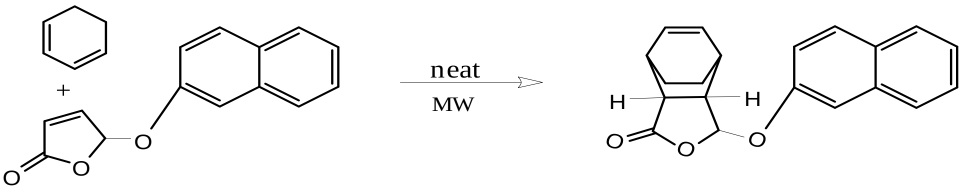


Others Diels-Alder adduct are of maleic anhydride and 1,3-cyclohexadiene, n-methyl meleimide and 1,3-cyclohexadiene.



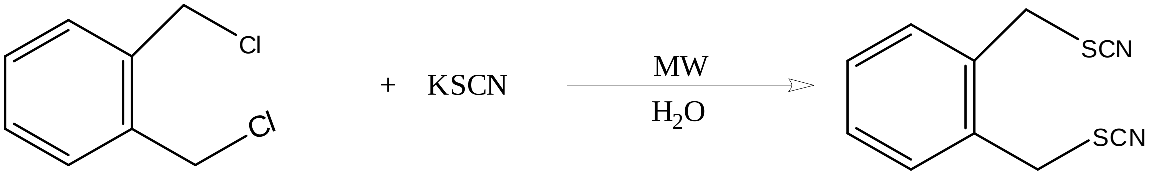


The recent examples of Diels-Alder cycloaddition performed by microwave dielectric heating are diene and dienophile reacted neat without the addition of solvent. For this transformation irradiation for 20 minutes at 165°C (or for 60 min at 150°C) gave the cycloadduct in near quantitative yield[2].

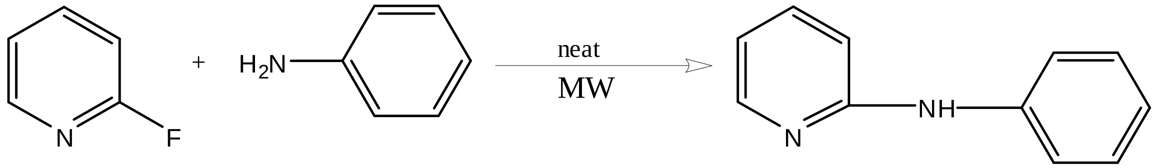


1.2.2 Nucleophilic Substitution Reactions

Reactions in aqueous media are of paramount importance in organic syntheses. The use of many toxic and volatile organic solvents contributes pollution to the environment. Utilization of water as reaction media in conjunction with microwave irradiation is one of the emerging nonconventional methods being recognized as viable environmentally benign alternatives[12]. In the continuation of studies on microwave-assisted organic synthesis in an aqueous medium, the nucleophilic substitution reaction of alkyl halides or tosylates using readily available alkali azides, thiocyanates, and sulfonates under microwave irradiation that proceed safely and efficiently in aqueous media[13]. Thiocyanates are well-known in the area of organosulfur chemistry and widely used as key intermediates in various organic transformations[14] and as biocides. Thiocyanates are also considered to be an important class of compounds found in some anticancer natural products formed by deglycosylation of glucosinolates derived from cruciferous vegetables. Further, R-thiocyanato carbonyl compounds are the preferred substrates for the synthesis of thiazoles of various herbicidal and related biological activities. In this, reaction mixture using water as solvent were placed in a 10 ml crimp-sealed thick-walled glass tube equipped with a pressure sensor and a magnetic stirrer[13]. The reaction tube was placed inside the cavity of a CEM Discover focused microwave synthesis system, operated at 120°C (temperature monitored by a built-in infrared sensor), power of 70-100 W, and a pressure of 60-100 psi for 30 min.

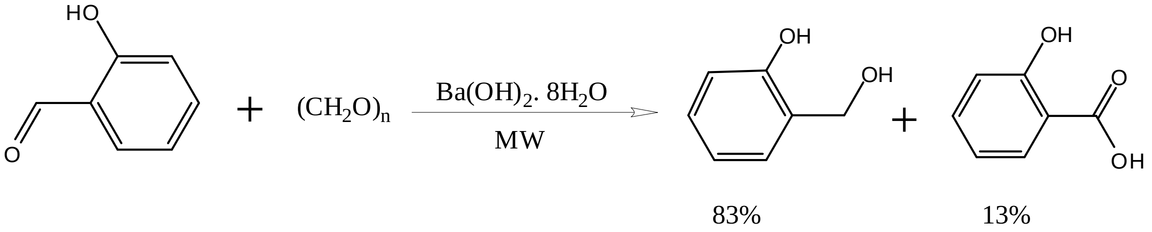


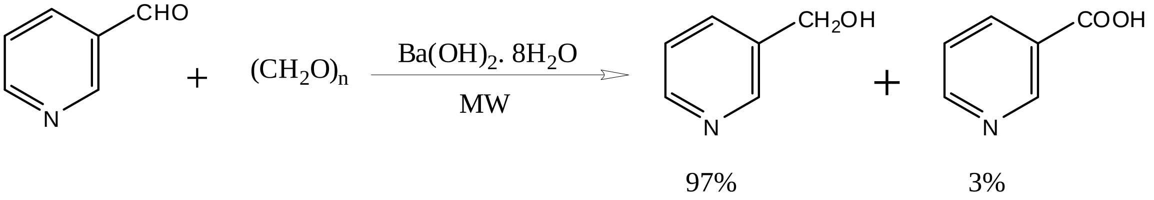
A benzene derivative substituted by a leaving group may be treated, for example, with an amine, but here the benzene derivative must generally also contain an electron-withdrawing group. Efficient nucleophilic aromatic substitutions driven by microwave heating involving either halogen-substituted aromatic or heteroaromatic systems[2].



1.2.3 Cross Cannizzaro reaction

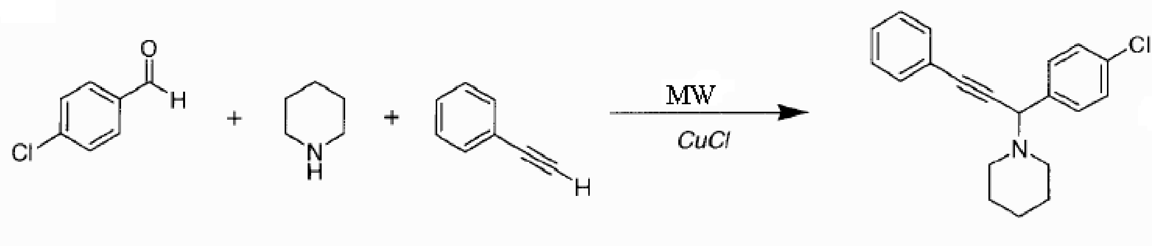
The Cannizzaro reaction is the disproportionation of an aldehyde to an equimolar mixture of primary alcohol and carboxylic salt and is restricted to aldehydes that lack the alpha hydrogens and therefore can not undergo aldol condensation. The crossed Cannizzaro reaction, using a scavenger and inexpensive formaldehyde to yield alcohol in higher yields, however, had been a method of choice prior to the introduction of hydride reducing agents[15]. Interestingly, the reaction occurred readily on barium hydroxide, $Ba(OH)_2.8H_20$, in a relatively short period of time. Microwave-mediated reaction with barium hydroxide as catalyst in a solventless condition in a number of organic syntheses. Reduction of aldehydes to alcohols using a formaldehyde equivalent, paraformaldehyde; under neat conditions in the absence of solvent has been studied[16].



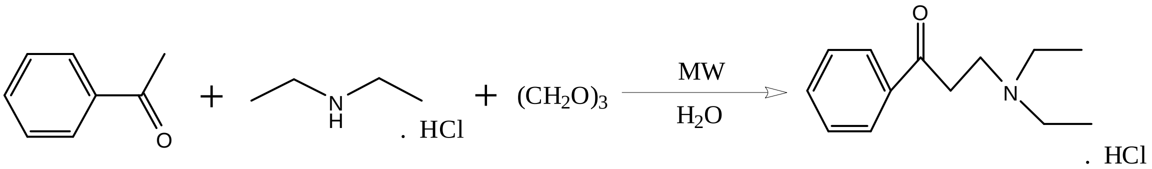


1.2.4 Mannich-type three-component reactions

The Mannich reaction, a classic example of a three-component condensation, is one of the most important reactions in organic chemistry. Multi-component reactions are highly valued as synthetic methodologies because several elements of diversity can be introduced into a molecule in a single step. These reactions play an increasingly important role in combinatorial chemistry and drug discovery. There are well over 300 multi-component reactions in the literature and although this offers an excellent toolbox for synthetic chemists, one of the problems with many of these reactions is that the conditions are not optimised[17]. This represents a significant challenge since the conditions required for the sequential steps may, in fact, be very different and so some compromise has to be reached. Many multicomponent reactions are performed at room temperature and reaction times can be very long. The use of microwave promotion in multi-component reactions offers a fast way into the generation of large numbers of compounds.



Over recent years, one of the most imperative issues for chemists is the search for cleaner chemical transformations. One of the aims of green chemistry is to replace volatile organic solvents with clean solvents as water as the reaction Media[18]. Continuing studies in this area, synthesis of β-aminoketones via Mannich reaction in water promoted by microwave irradiation. Initially, studied the reaction of acetophenone with trioxymethylene and diethylamine hydrochloride in water[19].



Mannich reactions could be run in a domestic multimode microwave oven using nitroacetophenone, paraformaldehyde, and dimethylamine with EtOH as solvent[20].

1.3 OBJECTIVES

1) To study the greenness of some organic reactions by the use of domestic microwave oven and to compare the greenness of microwave induced reactions with thermal reactions.
2) To study some organic reactions under water/solventless condition.

CHAPTER 2

MATERIALS, METHODS AND EXPERIMENTAL PROCEDURE

2.1 MATERIALS AND METHODS

This chapter lists various sources from which the reagents were obtained. Maleic anhydride, anthracene, benzaldehyde, potassium thiocyanate were obtained from MERK (INDIA), barium hydroxide octahydrate, paraformaldehyde, bromooctane, benzyl chloride were obtained from SD Fine Chemicals (INDIA), acetophenone, morpholine, diethylammine were obtained from Loba cem(India). All the chemicals and solvents were used as received without any purification or recrystallization.

Melting points was determined on melting point apparatus and are uncorrected.

FT-IR spectra

IR spectrum in the range of 4500-500 cm^{-1} was recorded on “Perkin Elmer” horizontal attenuated total reflectance mode FTIR Spectrometer, from School of Physics and Material Science, Thapar University, Patiala. Software Origin Pro 7.5 was used to draw the curves and was fitted using the protocols available with the software.

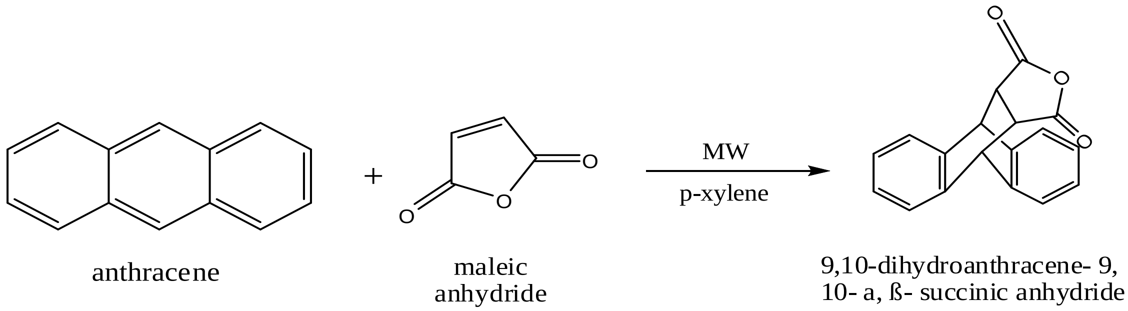
^{1}H NMR Spectra

^{1}H NMR Spectra were recorded on 400 MHz FT-NMR Cryo-magnet Spectrometer (Bruker), from SAIF department of Punjab University, Chandigarh.

2.2 EXPERIMENTAL PROCEDURE

This chapter describes the experimental detail of methodology by which various organic reactions has been carrying out under microwave irradiation and thermal condition. The Cross Cannizzaro reaction has been done in neat condition i.e. without solvent[21]. The thiocyanates and Mannich base preparation has been done in aqueous media.

2.2.1 Synthesis of 9,10-dihydroanthracene-9,10-α,β-succinic anhydride



a. Under Microwave irradiation

Grinded 1.8 gm (0.01 mole) of anthracene and 0.98 gm (0.01 mole) of maleic anhydride to fine powder in pestle and mortar. Transferred the powder to conical flask and added 10 ml of p-xylene. Swirled the mixture for 30 sec, covered the flask with watch glass. Placed the flask to domestic microwave oven and subjected to MWI for 3 min (turn of 1 min) at its full power. On completion of reaction as indicated by TLC (hexane: ethyl acetate 6:4), reaction mixture was allowed to cool and crude product was collected under suction, recrystallised in xylene, collected the product by vacuum filtration, rinse with cold xylene and then collected the product. The product was cream white crystalline solid.

m.pt : 262°C (lit. m.pt.: 262- 264°C)

b. By Conventional method

Grinded 1.8 gm (0.01 mole) of anthracene and 0.98 gm (0.01 mole) of maleic anhydride to fine powder in pestle and mortar. Transferred the powder to round bottom flask and added 20 ml of p-xylene. Then refluxed it for 2 hours. On completion of reaction as indicated by TLC (hexane: ethyl acetate 6:4), reaction mixture was allowed to cool and crude product was collected under suction, recrystallised in xylene, collected the product by vacuum filtration, rinse it with cold xylene and then collected the product. The product was cream white crystalline solid. m.pt.: 262°C (lit. m.pt.: 262- 264°C)

2.2.2 Synthesis of Octyl thiocyanate by substitution reaction

Bromooctane Potassium thiocyanate Octyl thiocyanate

2.2.2.1 Under Microwave irradiation

In a conical flask added 8.7 ml (0.05 mole) of bromooctane and 9.7 gm (0.1 mole) of potassium thiocyanate. To the above mixture added 15 ml of water and covered the conical flask with watch glass and placed it in domestic microwave oven, also placed another beaker of ice in microwave oven to avoid hot spot formation. The reaction mixture were subjected to MWI for 15 min. (turn of 30 sec) at its full power. On completion of reaction as indicated by TLC (hexane: ethyl acetate 8:2), the reaction mixture was allowed to cool. Then diethylether used for extraction, added to reaction mixture to extract the product, after that solvent was removed under reduced pressure, leaving the solid product behind. The product was light yellow colored solid.

m.pt. : 22°C (lit. m.pt.: 21°C)

2.2.2.2 By Conventional method

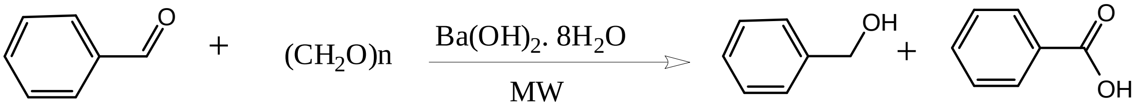
In a round bottom flask added 17.3 ml (0.1 mole) of bromooctane and 19.4 gm (0.2 mole) of potassium thiocyanate. To the above mixture added 30 ml of water and refluxed the reaction mixture. The completion of reaction were checked after every hour, and done the refluxing for 6 hours, but TLC indicated the incompletion of reaction, and it not completed even after the 6 hour refluxing. So the conventional reaction using water as solvent not completed but occurred in microwave with in 15 min.

2.2.3 Synthesis of Benzyl thiocyanate by substitution reaction under microwave irradiations

Benzyl chloride Potassium thiocyanate Benzyl thiocyanate

In a conical flask added 5.2 ml (0.05 mole) of benzyl chloride and 7.2 gm (0.075 mole) of potassium thiocyanate. To the above mixture added 15 ml of water and covered the conical flask with watch glass and placed it in domestic microwave oven. Also placed another beaker of ice in microwave oven to avoid hot spot formation. The reaction mixture were subjected to MWI for 15 min (turn of 30 sec) at its full power. On completion of reaction as indicated by TLC (hexane: ethyl acetate 9:2), the reaction mixture was allowed to cool. Then diethylether was used for extraction, added to reaction mixture to extract the product, after that solvent was removed under reduced pressure, giving the solid light yellow colored product. m.pt.: 40°C (lit. m.pt. : 38- 43°C)

2.2.4 Synthesis of benzyl alcohol via microwave irradiation



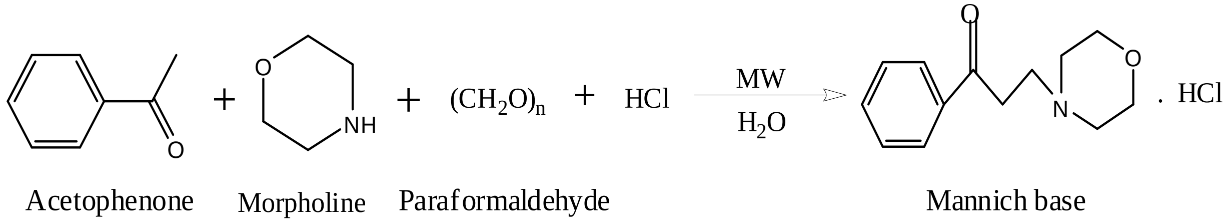
Benzaldehyde Paraformaldehyde Benzyl alcohal 99% Benzoic acid 1%

In a small beaker 4.75 gm (0.05 mole) of benzaldehyde was added in to finally powdered of 3gm (0.1 mole) paraformaldehyde. To the above mixture, 31.5 gm (0.1 mole) powdered barium hydroxide octahydrate was added. Initially reaction were done by placing the reaction mixture beaker in other beaker having neutral alumina, so that alumina can provide heating to reaction vessel as we used solid state condition and neutral alumina is polar, so absorb microwave irradiation, reaction showed change in just 30 sec, and by doing more heating, the reaction mixture solidify to hard mass. Then reaction were performed by adding around 20 gm of neutral silica to the reaction mixture, covered the beaker with watch glass and also placed another beaker of ice in microwave oven to avoid hot spot formation. Then after placing the beaker in the microwave oven, irradiated the sample with microwave irradiation for 6 min. (turn of 20 sec) at its full power. On completion of reaction as indicated by TLC (hexane: ethyl acetate 4:1), extraction of product has been done using ethyl acetate, and then neutralized the above extracted product in ethyl acetate with dilute HCl. The organic extract was dried over anhydrous sodium sulphate, and solvent removed under reduced pressure and the liquid product was collected.

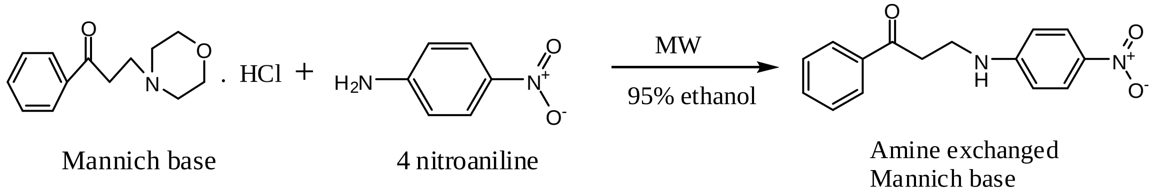
2.2.5 Synthesis of Mannich base under microwave irradiation

Mannich base was prepared by 2 step reaction

a. Preparation of substituted β-aminopropiophenone through Mannich reaction



b. Preparation of secondary Mannich base through amine exchange reaction of the above synthesized ketone with p-nitroaniline.



2.2.5.1 Synthesis of 3-morpholino-1-oxo-1-phenylpropane hydrochloride under microwave irradiation

Reaction has been done using morpholine and hydrogen chloride in 1:1 ratio instead of morpholine hydrochloride as described in literature method and using paraformaldehyde instead of trioxymethylene, in domestic microwave oven. Firstly 4.35 ml (0.05 mole) of morpholine was placed in a beaker and 10 ml of HCl was added to it slowly. Then this mixture was placed in 100ml conical flask. After that added 0.9 gm (0.03 mole) of paraformaldehyde, 6.5 ml (0.06 mole) of acetophenone and 5 ml of water as a solvent to above reaction mixture. Covered the conical flask with watch glass and placed it in a domestic microwave oven at full power of 1000 watt for 7 min (30 sec run). Also placed 1 beaker of ice so that hot spot formation was avoided and reaction take place completely. After completion of reaction, the reaction mixture was allowed to cool at room temperature. Then added 30 ml of acetone to reaction mixture and finally chilled in refrigerator for overnight. The separated crude product was collected under suction and was recrystallised from ethanol: acetone (1:4) mixture yielding shining white colored crystals, m.pt.: 166°C (lit. m.pt. : 174°C)

2.2.5.2 Synthesis of 3-morpholino-1-oxo-1-phenylpropane hydrochloride by conventional method

The reaction was performed using same reactant but conventionally by doing refluxing. Firstly 4.35 ml (0.05 mole) of morpholine was placed in a beaker and 10 ml of HCl was added to it slowly. Then this mixture was placed in 100ml round bottom flask. After that added 0.9 gm (0.03 mole) of paraformaldehyde, 6.5 ml (0.06 mole) of acetophenone and 5 ml of water as a solvent to above reaction mixture. Then refluxed the reaction mixture for 4 hours. But after long refluxing no result came. Then added 30 ml of acetone to it and placed the RB in refrigerator for overnight. No crystal appear, so reaction failed conventionally.

2.2.5.3 Synthesis of 3-(4-nitroanilino)-1-oxo-1-phenylpropane by amine exchange under microwave irradiation

Amine exchanged reaction of synthesized Mannich base with 4-nitroaniline in MW condition took place in 30 min but conventionally, this reaction take 15 hour. In a conical flask 2.56 gm (0.01 mole) of 3-morpholino-1-oxo-1-phenylpropane hydrochloride and 1.38 gm (0.01 mole) of 4-nitroaniline was mixed in 30 ml of absolute ethanol. Covered the conical flask with watch glass and subjected to MWI for 30 min. (1 min run). Also placed one beaker of ice so that hot spot formation was avoided and reaction takes place completely as done in previous experiment. The reaction mixture was kept for overnight at room temperature. Solid product that separated was collected under suction and recrystallised from (30: 70) benzene: petroleum ether to give yellow crystalline product. m.pt : 162°C (lit. m.pt. : 170°C)

2.2.5.4 Synthesis of 3-(4-nitroanilino)-1-oxo-1-phenylpropane by amine exchange by conventional method

In the round bottom flask added 2.56 gm (0.01 mole) of 3-morpholino-1-oxo-1-phenylpropane hydrochloride and 1.38 gm (0.01 mole) of 4-nitroaniline were mixed in 30 ml of absolute ethanol. The reaction mixture was then refluxed for 15 hours. The reaction mixture was kept overnight at room temperature. Solid product that separated was collected under suction and recrystallised from (30:70) benzene: petroleum ether to give yellow crystalline product. m.pt.: 163 °C

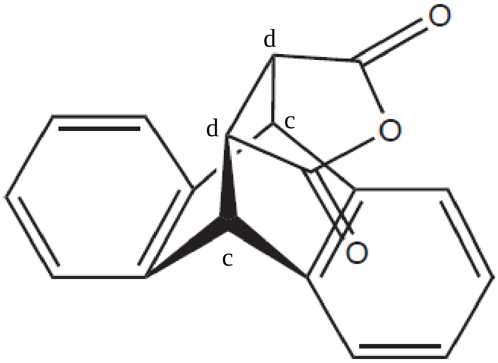
CHAPTER 3

RESULTS AND DISCUSSION

The reactions were characterized by ^{1}H NMR and FT-IR spectral studies. From the ^{1}H NMR spectra we can find out the number of proton(s), type of proton, splitting of peak give information about the number of protons on the adjacent carbon. From the IR spectra we can find out the type of functional group present in compound.

3.1 Characterization of 9,10-dihydroanthracene-9,10-α,β-succinic anhydride

The structure analysis has been done by ^{1}H NMR spectra and by FT-IR spectra.



^{1}H NMR (CDCl$_3$) δ (ppm) : 3.51 (2Hd), 4.82 (2Hc),
7.17–7.25 (4H, m), 7.30-7.39 (4H, m).

^{1}H NMR spectrum showed the presence of multiplet of eight aromatic protons at δ 7.17 – 7.25 (4H, m) and 7.30-7.39 (4H, m). Two signals at δ 3.51 (2H), 4.82 (2H) are assigned to d and c protons. In the maleic anhydride the protons appear at δ 7.3 and in anthracene proton signal appear at δ 7.4-8.3. The appearance of two additional signals in the product at δ 3.51 (2Hd), 4.82 (2Hc) showed the formation of adduct.

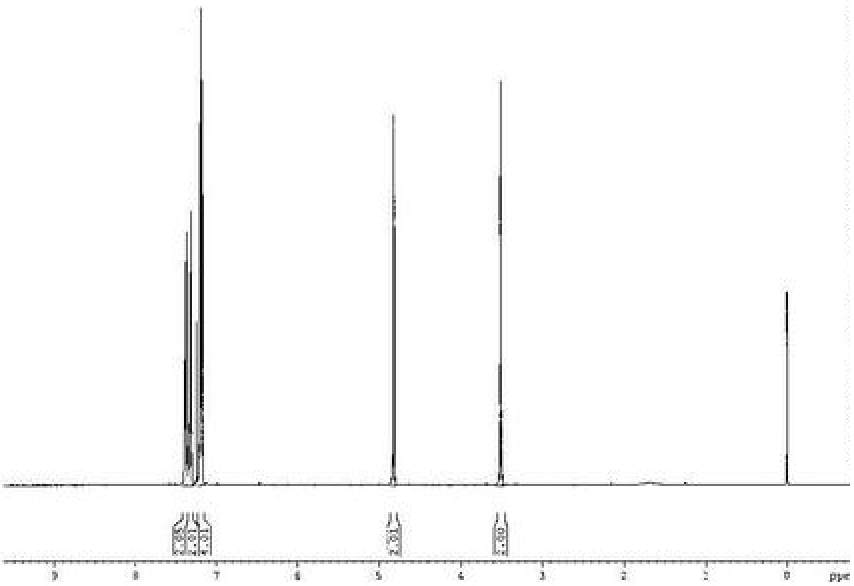


Fig. 3.1: ^{1}H NMR spectra of 9,10-dihydroanthracene-9,10-α,β-succinic anhydride

FT-IR Analysis

On the product spectrum there is a peak located at 3026 cm^{-1} represents aromatic carbon-hydrogen bonds. The peak at 2970 cm^{-1} indicates the presence of alkane C-H bonds. The product spectrum also yields two distinctive peaks at 1860 cm^{-1} and 1766 cm^{-1}. These peaks represent the carbonyl groups of the anhydride, and together indicate anhydride functional group. They can be compared with the peaks located at 1850.43 cm^{-1} and 1778.98 cm^{-1} on the maleic anhydride spectrum. The peak at 1224 cm^{-1} indicates C—O stretching vibration.

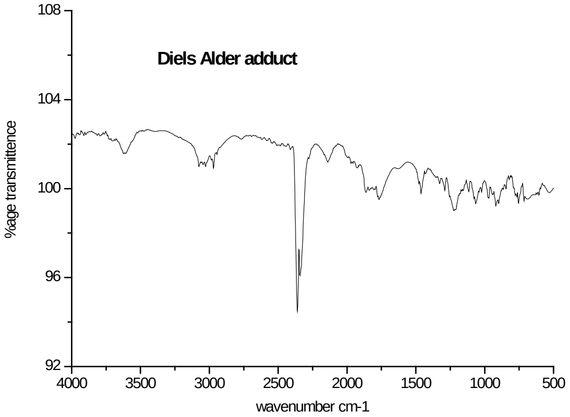
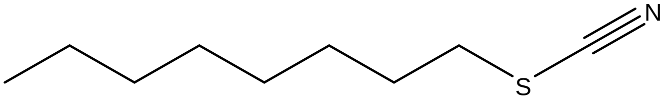


Fig. 3.2: IR spectra of 9,10-dihydroanthracene-9,10-α,β-succinic anhydride

With conventional heating, reaction has been completed in 2 hours and under microwave irradiation it has been completed in 3 min.

3.2 Characterization of Octyl thiocyanate

The completion of reaction as indicated by the TLC, and from the melting point value, and change in the physical appearance showed the formation of product. The structure of benzyl thiocyanate is predicted by FT-IR spectra.



FT-IR Analysis

The strong peak at 2170-2220 cm^{-1} represents $C\equiv N$ stretching. This suggest that substitution reaction occurred and bromine of bromooctane i.e. reactant is replaced or substituted by thiocyanate group. Another peak at 2870-2900 cm^{-1} represents C-H (stretch) vibration of alkanes.

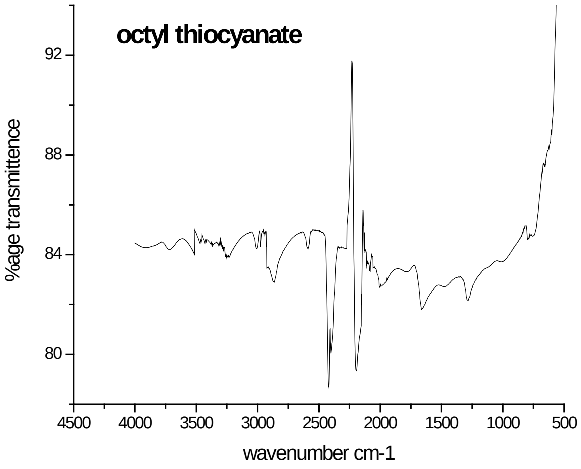


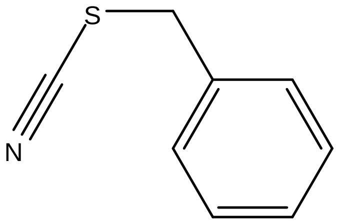
Fig. 3.3 : IR spectra of Octyl thiocyanate

Under conventional conditions using water as solvent reaction has not been completed in 6 hour of refluxing but with microwave irradiation, the reaction was complete with in 15 min.

3.3 Characterization of Benzyl thiocyanate

The structure of benzyl thiocyanate is predicted by ^{1}H NMR spectra.

^{1}H NMR ($CDCl_3$) δ (ppm) : 4.15 (2H, s), 7.25 – 7.38 (5H, m)



The reactant used for its preparation is benzyl chloride. From the literature the ^{1}H NMR spectrum of benzyl chloride showed two benzylic protons at δ 4.59 ppm, and this peak shift to 4.16 ppm for benzylic proton of benzyl thiocyanate. The product showed benzylic proton is at 4.15, which is agreement with the literature value[22]. One multiplet at δ 7.25–7.38 (5H, m) show the presence of benzene proton.

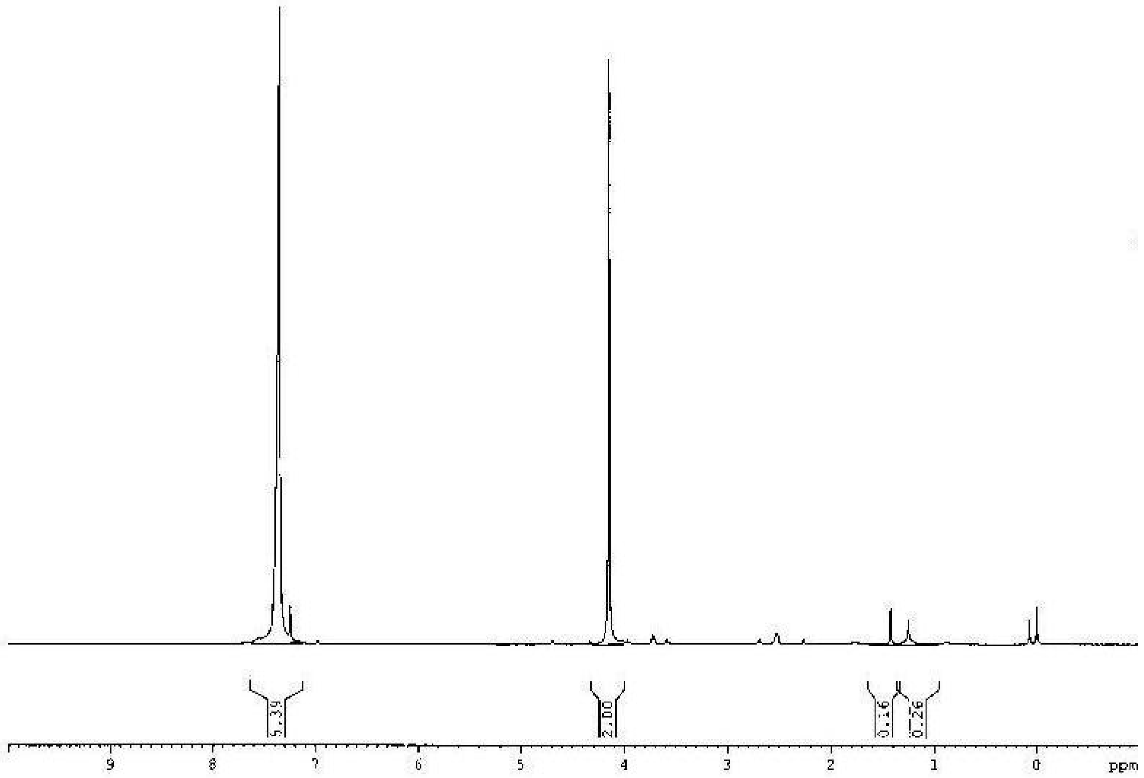
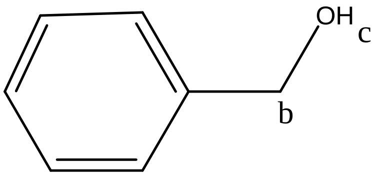


Fig. 3.4 : ^{1}H NMR spectra of Benzyl thiocyanate

3.4 Characterization of Benzyl alcohol

The structure of benzyl alcohol is studied on the basis of ^{1}H NMR spectra and FT-IR spectra. The ^{1}H NMR spectra provide information about the number of proton in the product and FT-IR spectra studied the presence of hydroxyl group in the product.

^{1}H NMR ($CDCl_3$) δ (ppm) : 3.43 (1Hc, broad s,), 4.47 (2Hb, s) , 7.19- 7.31 (5H, m).



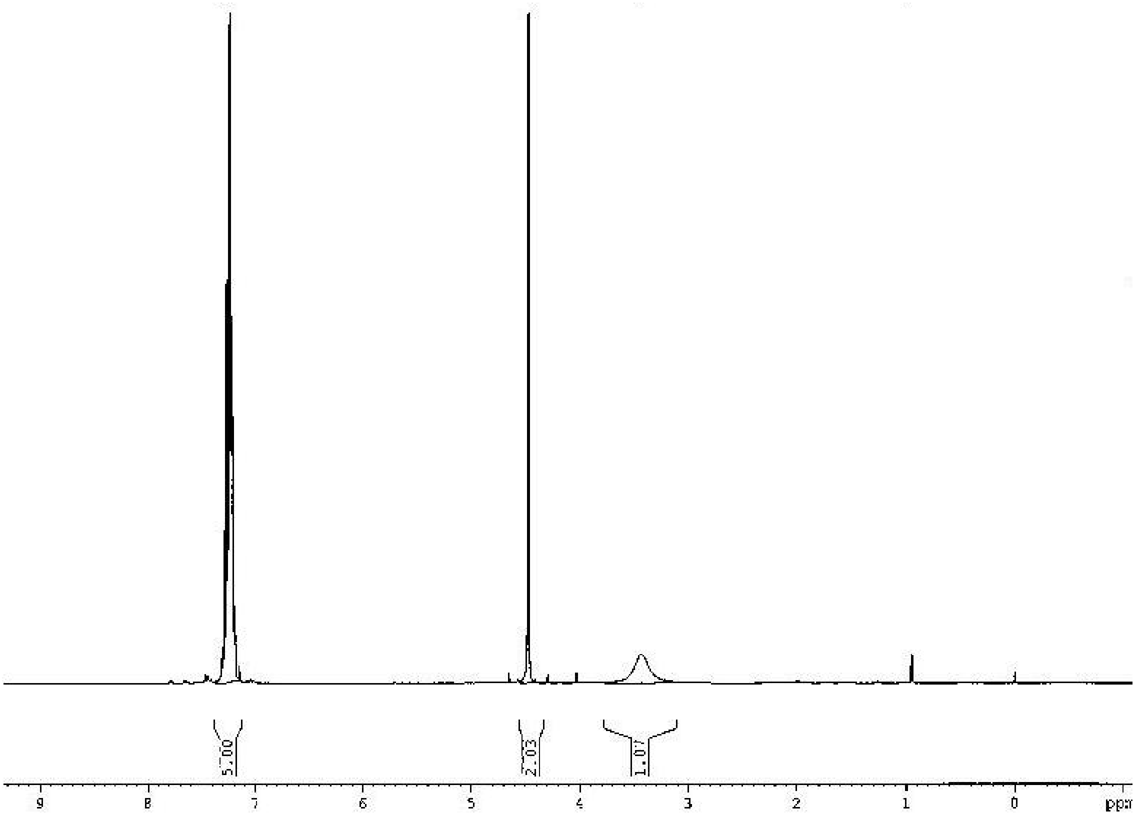


Fig. 3.5 : ^{1}H NMR spectra of Benzyl alcohol

The reactant used for its preparation is benzaldehyde, which have 6 proton and the product spectra shows 8 protons. The appearance of signal at δ 4.47 due to benzylic proton and absence of signal at δ 10 showed the conversion of aldehyde in to alcohol and the signal due to hydroxyl group appear broad at δ 3.43. There is signal due to aromatic proton appear at δ 7.19-7.31 (5H, m).This chemical shift values signify product formation.

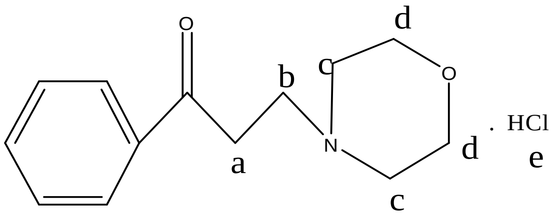
FT-IR Analysis

The broad peak at 3400- 3200 cm^{-1} suggests the presence of —OH functional group. Another peak is at 3040-3020 cm^{-1} represent C—H (stretch) aromatic bond. No peak at 1800 cm^{-1} suggests the benzaldehyde in to benzyl alcohol as showing peak at 3200-3400 cm^{-1}.

3.5 Characterization of 3-morpholino-1-oxo-1-phenylpropane hydrochloride

Structural analysis of this compound is on the basis of ^{1}H NMR. There are total 18 protons in the product and their assignment is as under:

^{1}H NMR ($CDCl_3$), δ (ppm) : 3.25 (4Hc, t), 3.56 (2Hb, t), 3.83 (2Ha, t)
4.15 (4Hd. t), 7.46-7.50 (2H, m), 7.59-7.63
(1H, m), 7.99-8.02 (2H, m), 12.90 (1He, s)



Due to presence of ketonic group with benzene ring , the single multiplet of benzene split to ortho, meta and para protons, as each class of aromatic proton feel different field, having Chemical shift δ 7.46-7.50 (2H, m), 7.59-7.63 (1H, m) ,7.99-8.02 (2H, m). The product is hydrochloride salt of Mannich base, the peak at 12.90 represent the peak for HCl proton. Chemical shift value of δ 3.25 (4Hc, t), is of 4 equivalent methylene protons of morpholine ring having carbon attach to nitrogen, showing triplet, and the another peak is again triplet of four methylene proton having δ 4.15 (4Hd, t) of morpholine ring having carbon attached to oxygen.

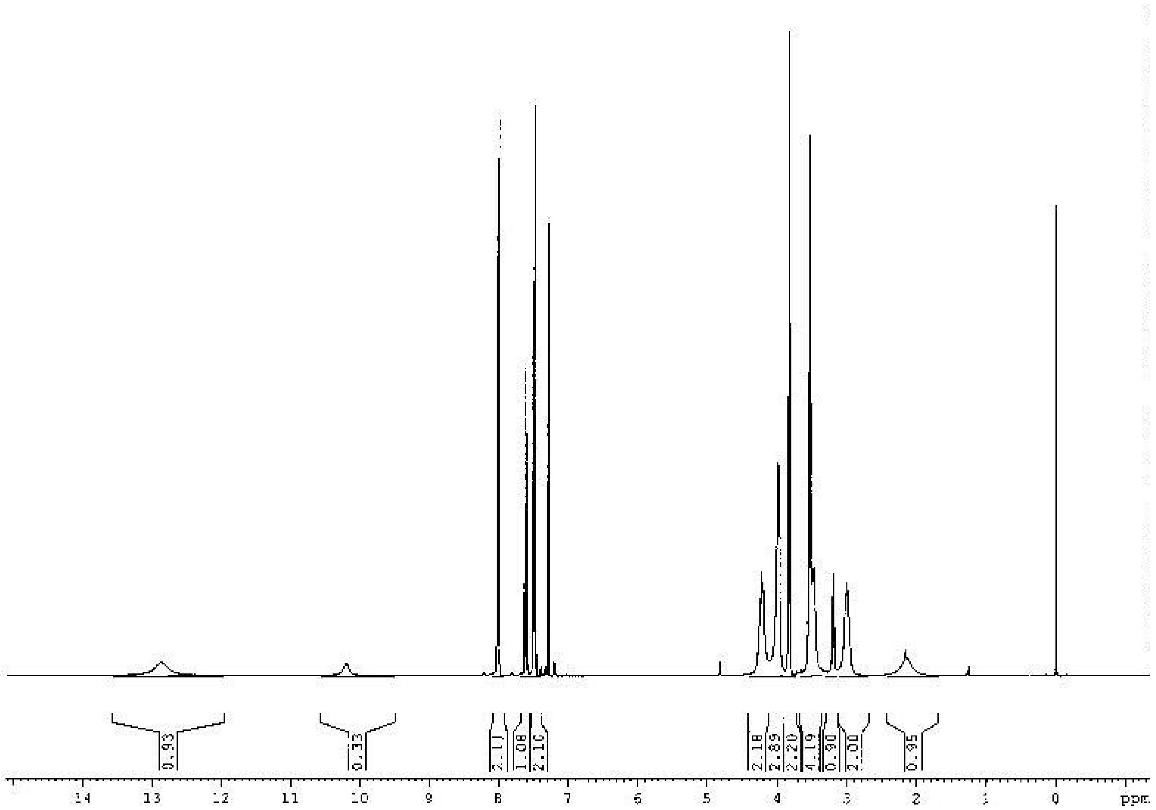


Fig. 3.6 : ^{1}H NMR spectra of 3-morpholino-1-oxo-1-phenylpropane hydrochloride

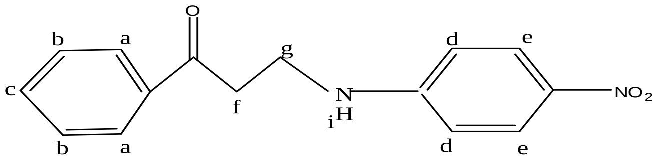
This peak is estimated from the peak of tetrahydro-1,4-oxazine. There are two more methylene group of propane moiety, one showing δ 3.83 (2Ha, t) attached to -C(=O) and the other attach to –N have δ 3.56 (2Hb, t)[23]. Both of the peak split to triplet due to presence of two protons on their adjacent carbon.

The reaction has been done in aqueous conditions. Reaction failed conventionally but under the microwave irradiations it was complete in 7 min

3.6 Characterization of 3-(4–nitroanilino)-1-oxo-1-phenylpropane

Structure of amine exchanged Mannich base is analyzed using by ^{1}H NMR and FT-IR spectral studies.

^{1}H NMR ($CDCl_3$) δ (ppm) : 3.32 (2Hf, t), 3.72 (2Hg, t), 6.54-6.60 (2Hd, m)
6.54-6.60 (2Hd, m), 7.46-7.50 (2Hb, m), 7.58-7.62
(1Hc, m), 7.94-7.97 (2Ha, m), 8.06-8.10 (2He, m).



These ^{1}H NMR spectra shows the amine exchange. The morpholine proton peaks shifted to aromatic proton peaks. The product showed 9 aromatic protons and these are present in product and peak of the methylene group of propane chain are also observed in the spectra. Of the aromatic peaks, the proton at position 'e' show chemical shift of maximum value, as this proton is in close vicinity of nitro group. The aromatic proton of 'a' position has δ 7.94-7.97 due to the withdrawing effect of carbonyl carbon, δ value increase. There are two triplet of two methylene protons, one is attached to -C(=O) have δ 3.32 and the other attach to –N have δ 3.72

FT-IR Analysis

The broad peak at 3600- 3200 cm^{-1} suggests the presence of –NH functional group. Another peak is at 3050-3020 cm^{-1} represent C–H (stretch) aromatic bond. The presence of carbonyl group is analyzed by the presence of peak at 1710 cm^{-1}. The two small peaks at 1580 cm^{-1} and 1460 cm^{-1} represents the presence of nitro group in the compound. The peak at 1250-1200 is due to C–N stretching vibrations.

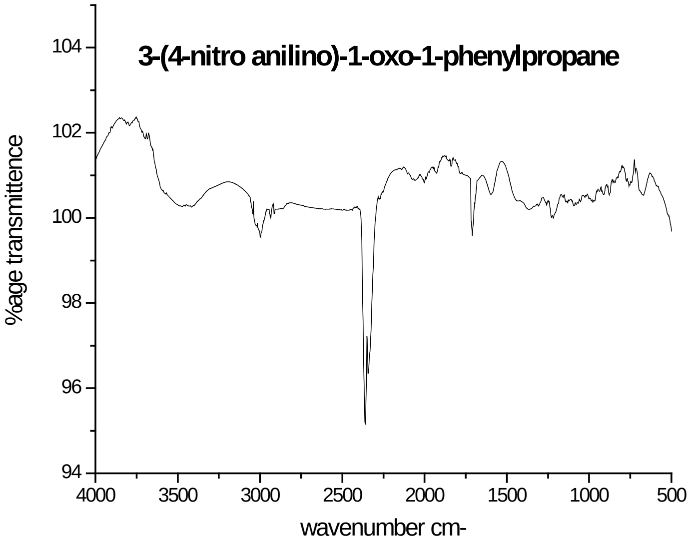


Fig. 3.7 : IR spectra of 3-(4–nitroanilino)-1-oxo-1-phenylpropane

CHAPTER 4

CONCLUSIONS AND FUTURE SCOPE

CONCLUSION

Objective of greener reaction can be achieved by development of wide variety of synthetic protocols using various techniques, such as selective microwave heating of neat reactant using solvent less condition, use of benign solvent as water. In the present work, some organic reactions were studied by the use of domestic microwave oven. Benzyl thiocyanate and octyl thiocyanate has been synthesized by nucleophilic substitution reaction, Mannich base, 3-morpholino-1-oxo-1-phenylpropane hydrochloride has been synthesized by using acetophenone, paraformaldehyde, morpholine and hydrogen chloride in aqueous conditions, benzyl alcohol has been synthesized by Cross Cannizzaro reaction and 9,10-dihydroanthracene-9,10-α,β-succinic anhydride, a Diels-Alder adduct is synthesized by Diels-Alder reaction. Diels Alder adduct formation was completed within 3 minute as compared to conventional heating method, which required long time of refluxing. Mannich base and alkyl thiocyanates were synthesized in aqueous media. The benzyl alcohol has been syntheised in solvent less condition. In order to study greenness reactions were performed by the use of microwave irradiations, by solvent less condition and by the use of water as benign solvent. These compounds have been synthesized by the use of domestic microwave oven and the reactions were complete in very short interval as compared to thermal conditions.

Thus microwave technology enables chemists to achieve cleaner and more efficient chemical reactions, compared to conventional heating methods.

FUTURE SCOPE

This thesis study key developments in the field of microwave chemistry. Microwave chemistry has an edge over conventional heating methods for conducting chemical reactions, and it may soon emerge as the preferred technology for performing chemical synthesis relating to lead development in pharmaceutical and biotechnology companies.

The possibility of performing reactions in a very short time period by direct interaction of microwave energy with the reaction mixture as opposed to the indirect transfer of energy by utilizing an oil bath certainly can be considered “green”, not only because of the reduced energy consumption, but also it enable us to do the reaction using water as solvent or under neat conditions.

In the future, microwave chemistry is likely to become a preferred method for conducting synthetic reactions in laboratories. This is validated by the increasing number of publications in the field, from about 500 in 1997, to over 2000 up to 2004. As microwave chemical synthesis has advanced, its applications have been extended to include the synthesis of fine chemicals.

Based upon work performed, it can be said that there is a great scope for performing reactions in water or solventless condition and enhancement of rate enhancement microwave irradiation.

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