SOME ORGANIC REACTIONS INDUCED BY ULTRASONIC AND MICROWAVE IRRADIATION

One of the challenges to research workers during the recent years has been to develop green procedures that are both environmentally desirable and economically acceptable. “Green chemistry” is considered an integral part of a comprehensive program to protect human health and the environment. Most of organic solvents used in industry are toxic, costly and problematic to use. Carrying out reactions with lesser amount or no solvent would lead to clean, efficient and economical processes. With the increasing environmental concerns and the regulatory constraints faced by the chemical and pharmaceutical industries, development of environmentally benign organic reactions has become a crucial and demanding research area in modern organic chemical research\(^1\). Therefore more and more chemists are devoted to the researching “Green Synthesis” which means the reagent, solvent and catalyst are environmentally friendly in the organic chemical reactions.

New strategies have recently been developed which contributes to Green Synthesis. Some of the methods, which are used in organic synthesis, are mentioned below:

- Use of Microwaves
- Use of Ultrasound waves
- Water mediated organic reaction
- Use of reusable catalyst in organic synthesis
Among the non-conventional methods in organic synthesis\textsuperscript{2}, microwave irradiation takes a particular place being an emerging technique that provides an alternative to conventional heating for introducing energy into chemical reactions by using the ability of some liquids and solids to transform electromagnetic energy into heat. With microwaves, the heating is created in the interior of the sample and is then radiated outward. This is contrast with conventional heating, where the heat is generated in the outer region and directed towards the center.

In the electromagnetic spectrum, the microwave radiation region is located between infrared radiation and radio waves. Microwaves have wavelength of 1mm-1m corresponding to frequencies between 0.3-300 GHz.

Main benefits of MW heating are\textsuperscript{3-4}:

1. Very fast heating
2. Absence of inertia. Only the reaction contents are heated, not the reaction vessel.
3. Easy to use. Power regulator is easy with instantaneous on and off.
4. Better homogeneity in temperature with quick transfer of energy in the whole mass without superficial heating.
5. The selective heating of polar molecules.

In a MW oven, microwaves are generated by a magnetron\textsuperscript{5}, was designed by Randall and Booth at the University of Birmingham as part of the development of RADAR during the Second World War. A magnetron is a thermionic diode having an anode and a directly heated cathode. As the
cathode is heated, electrons are released and are attracted towards anode. The anode is made up of an even no. 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 its overtones. A very strong magnetic field is induced axially through the anode assembly and has the affect 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 cavity. Alternative 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 the anode via an antenna. The variable power available in domestic oven is produced by switching the magnetron on and off according to duty cycle. Even in early days, it was recognized that microwaves could heat water in dramatic fashion and domestic and commercial applications for heating and cooking foodstuffs began to appear in 1950’s. In 1955 Tappan introduced first kitchen microwave oven but its widespread domestic use occurred during the 1970’s and 1980’s. The first application of microwave energy in organic synthesis is the aqueous emulsion polymerization of butyl acrylate, acrylic acid and methacrylic acid using pulsed electromagnetic radiation. After that, several groups, have demonstrated that chemical synthesis may be dramatically accelerated using MW irradiation. The superheating conditions caused by this kind of heating, lead directly to acceleration in the reaction times compared with conventional reflux conditions. The first application of MW in
chemical synthesis was published in 1986 by Gedye et al. using domestic microwave oven. Giguere et al. in 1989 appeared the first review dealing with microwave heating in organic synthesis. Since then an increasing number of articles has been published\textsuperscript{9-33}.

Sonochemistry: chemical reaction under the influence of ultrasonic energy field is one of the promising experimental techniques recently introduced into the tools of chemical synthesis\textsuperscript{34-37}.

The first report about the effect of ultrasound to chemical reactions is from 1927, by Richards and Looms involving rate studies on the hydrolysis of dimethyl sulfate and the iodine “clock” reaction (the reduction of potassium iodate by sulfurous acid)\textsuperscript{38}.

In 1938, Porter and Young reported that ultrasound increased the rate of the Curtius rearrangement\textsuperscript{39}. In 1950, Renaud prepared an organometallic compound using ultrasound\textsuperscript{40}. Since 1982 when Han and Boudjouk significantly increased the yields and rates of Reformatsky reactions\textsuperscript{41}, ultrasound has been investigated intensively in organic synthesis.

The driving force for ultrasound developments in organic synthesis has many advantages. The increasing requirement for environmentally clean technology that minimizes the production of waste at source\textsuperscript{42}. Ultrasound may offer cleaner reactions by improving product yields and selectivities, enhancing product recovery and quality through application to crystallization and other product recovery and purification processes. Ultrasound enhances the rates of reactions\textsuperscript{43}. Sonication allows the use of
non-activated and crude reagents as well as an aqueous solvent system; therefore it is friendly and non-toxic. Ultrasound is widely used for improving the traditional reactions that use expensive reagents, strongly acidic conditions, long reaction times, high temperatures, unsatisfactory yields and incompatibility with other functional groups\textsuperscript{44}.

During the last few years a large number of short communications have appeared on the use of this versatile technique and excellent reviews are also available\textsuperscript{45-48}. Ultrasounds are waves at frequencies above those within the hearing range of the average person, i.e., at frequencies above 16 KHz. Many sonicators are useful for the production of ultrasound. The important one are ultrasonic cleaning bath, ultrasonic probe systems, the cuphorn system, the flow cell system etc.

When ultrasonic energy at high power is applied to a liquid, a phenomenon called ‘cavitation’ occurs. Cavitation is the formation, growth and collapse of bubbles in the liquid. this results in ‘cold boiling’ of liquid. Ultrasonic vibration reduces the thickness of liquid films. Ultrasonic energy (high energy sound waves) produces an alternating adiabatic compression and rarefaction of the liquid media being irradiated. In the rarefaction part of the ultrasonic wave (when liquid is unduly stretched or “torn apart”), microbubbles form because of reduced pressure. These microbubbles contain vaporized liquid or gas that was previously dissolved in the liquid. The microbubbles can be either stable about their average size for many cycles(stable cavitation) or transient when they grow to certain size and violently collapse or implode during the compression part of the wave.
(transition cavitation). The critical size depends on liquid and the frequency of the sound (Fig. 1).

Fig. 1: Generation of an acoustic bubble
With the increasing environmental concerns and the regulatory constraints faced by the chemical and pharmaceutical industries, development of environmentally benign organic reactions has become a crucial and demanding research area in modern chemical research\textsuperscript{49}. Therefore more and more chemists are devoted to the researching “Green Synthesis,” which means the reagent, solvent and catalyst are environmentally friendly in the organic chemical reactions. Recently organic reactions in water without use of harmful organic solvents have attracted much attention, because water is a cheap, safe and environmentally benign solvent\textsuperscript{50-52}.

Some of organic reactions in water have been reported, such as, Diels-Alder reaction\textsuperscript{53-55}, Michael reaction\textsuperscript{56}, Claisen rearrangement\textsuperscript{57-58}, Aldol condensation\textsuperscript{59}, Radical addition reactions\textsuperscript{60}, Darzens condensation\textsuperscript{61}, applied for the synthesis of 3-carboxycoumarins\textsuperscript{62}, synthesis of ylidenenitriles of 4-Oxo-(4H)-1-benzopyran-3-carbaldehyde\textsuperscript{63}, Novel synthesis of anilines\textsuperscript{64}, the clean and efficient condensation reactions of anilines with aldehyeds\textsuperscript{65}, the Knoevenagel condensation reaction\textsuperscript{66}, tetrahydropyranylation of alcohols\textsuperscript{67}, Synthesis of 4H-Pyran derivatives\textsuperscript{68}, Suzuki cross coupling reaction\textsuperscript{69} and Synthesis of 2-carboxy substituted diphenylethers\textsuperscript{70}. We focus our attention on the new way of organic synthesis using water as a solvent in lieu of organic solvent.

4-Oxo-(4H)-1-benzopyran-3-carbaldehyde\textsuperscript{71} is a versatile synthone and can be converted into large number of heterocyclic compounds upon condensation with different nucleophiles.
The effective and facile method for the synthesis of 3-formylchromones was developed by Nohara\textsuperscript{72} et al. They have synthesized a number of 3-formylchromones by formylating various 2-hydroxy acetophenones by the application of Vilsmeier-Haack reaction. The most suitable formylating reagent was a complex of dimethylformamide and phoshorousoxychloride. The reaction can be represented as follows:

\[ \text{R1} \text{R2} \text{R3} \text{R4} \xrightarrow{\text{DMF/POCl}_3} \text{R1} \text{R2} \text{R3} \text{R4} \]

In the present work the various 3-formylchromones (4-Oxo-(4H)-1-benzopyran-3-carbaldehydes) are prepared by the above method.

The 4-Oxo-(4H)-1-benzopyran-3-carbaldehyde has three reactive centers Viz. carbon-carbon double bond, \( \alpha \), \( \beta \)-unsaturated carbonyl group i.e. pyrone ring and formyl group. Of these three reactive centers, the reaction is chemoselctively occurs at formyl group.

4-Oxo-(4H)-1-benzopyran-3-carbaldehydes when condensed with 3-methyl-1-phenylpyrazolin-5-(4H)-one gives 3-methyl-4-\{chromon-3-yl\}methylene]-1-phenylpyrazolin-5-(4H)-ones. This title compound was found to be associated with significant bactericidal\textsuperscript{73} and antihistaminic\textsuperscript{74} activities.

3-aryl-1-phenyl-1H-pyrazol-4-carbaldehydes are associated with biological activities\textsuperscript{75-78} such as bactericidal, anti-inflammatory and
hepatoprotective activities. In the present work the required 3-aryl-1-phenyl-1H-pyrazol-4-carbaldehydes have been prepared by Vilsmeier-Haack reaction on substituted acetophenone phenylhydrazones\textsuperscript{79-81}.

The present work is described into four parts:

**Part I**

The first part describes the general introduction and literature survey.

**Part II**

This part describes the different reactions carried out under microwave irradiation. It is divided into four sections.

**Section A**

This section describes an efficient, solventfree and chemoselective procedure for the synthesis of acylals and its deprotection to 4-Oxo-(4H)-1-benzopyran-3-carbaldehydes catalyzed by reusable Envirocat EPZ10\textsuperscript{R} under microwave irradiation.

**Section B**

This section deals with solventfree transesterification of methyl/ethyl ketoesters with various alcohols in good yield under microwave irradiation using borate zirconia (B\textsubscript{2}O\textsubscript{3}/ZrO\textsubscript{2}) as solid acid catalyst.

**Section C**

This section deals with the use of MoO\textsubscript{3}/SiO\textsubscript{2} as most efficient solid acid catalyst for Transesterification of methyl/ethyl ketoesters with various alcohols under microwave irradiation.
Section D

In this section a rapid, solvent free and environmentally friendly Knoevenagel condensation reaction of 4-Oxo-(4H)-1-benzopyran-3-carbaldehyde with Meldrum’s acid has been described under microwave irradiation.

Part III

This part deals with the Knoevenagel condensation reaction of 4-Oxo-(4H)-1-benzopyran-3-carbaldehyde with different nucleophiles by the application of ultrasonic waves. It is divided into three sections.

Section A

This section describes a newer route for the condensation of 4-Oxo-(4H)-1-benzopyran-3-carbaldehyde with 3-methyl-1-phenylpyrazolin-5-(4H)-one under ultrasonic irradiation at room temperature in distilled water as solvent, catalyzed by borate zirconia.

Section B

This section describes a simple procedure for the preparation of acylals from 4-Oxo-(4H)-1-benzopyran-3-carbaldehyde using EPZ10 \textsuperscript{R} catalyst under ultrasonic irradiation.

Section C

This section deals with the synthesis of 3-methyl-4-[(chromon-3-yl)-methylene]-1-phenyl pyrazolin-5(4H)-ones by the condensation reaction of 4-Oxo-(4H)-1-benzopyran-3-carbaldehyde with 3-methyl-1-phenylpyrazolin-5(4H)-one under ultrasonic irradiation at room temperature without use of catalyst.
Part IV

This part describes the synthesis of different heterocyclic compounds such as 5-(4-oxo-4H-chromen-3-yl)-2,2-dimethyl-[1,3]dioxane-4,6-dione, 3-methyl-4-[(chromon-3-yl)methylene]-1-phenylpyrazolin-5-(4H)-ones by using different conditions. It is divided into four sections.

Section A

In this section a simple, environmental friendly, economical viable and cleaner route has been developed for the Knoevenagel condensation of 4-Oxo-(4H)-1-benzopyran-3-carbaldehyde with Meldrum’s acid (2,2-dimethyl-1,3-dioxan-4,6-dione) in distilled water at 90°C for 1-2 hr, in absence of any catalyst.

Section B

In this section ceric ammonium nitrate catalyzed efficient and chemoselective method for protection and deprotection of 4-Oxo-(4H)-1-benzopyran-3-carbaldehyde is described.

Section C

In this section we have developed efficient synthesis of 5-(4-oxo-4H-chromen-3-yl)-2,2-dimethyl-[1,3]dioxane-4,6-dione by using basic hydrotalcite at room temperature in very short time.

Section D

This section describes Borate zirconia mediated Knoevenagel condensation reaction in water.
References:


