

**Development of Green Methodologies for Synthesis of
Azomethine and Benzoxanthone Analogues via Multi
Component Condensations of Aromatic Aldehydes**

A

Thesis

Submitted to



For the award of

DOCTOR OF PHILOSOPHY (Ph.D)

in

Chemistry

By

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LOVELY PROFESSIONAL UNIVERSITY
PUNJAB
2020**

DECLARATION

I declare that the thesis entitled “**Development of Green Methodologies for Synthesis of Azomethine and Benzoxanthone Analogues via Multi Component Condensations of Aromatic Aldehydes**” has been prepared by me under the guidance of **DR. TANAY PRAMANIK, Associate Professor**, Department of Chemistry, School of Chemical Engineering and Physical Sciences, Lovely Professional University, Punjab. It is further certified that the results incorporated in this thesis have not been submitted, in part or full, to any other university or institution for the award of any degree or diploma.

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CERTIFICATE

It is hereby certified that thesis entitled, “**Development of Green Methodologies for Synthesis of Azomethine and Benzoxanthone Analogues via Multi Component Condensations of Aromatic Aldehydes**” being submitted by **POOJA BEDI**, in department of Chemistry, School of Chemical Engineering and Physical Sciences, Lovely Professional University, Punjab, for the award degree of **Doctor of Philosophy** in chemistry is a record of bonafied research work carried out by her. **POOJA BEDI** has worked under my supervision and guidance and has fulfilled all the requirements for the submission of the thesis. It is further certified that the results incorporated in this thesis have not been submitted, in part or full, to any other university or institution for the award of any degree or diploma.

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Abstract

Green Chemistry is the branch of chemistry which comprises a group of principles by implementation of which we minimize or eliminate the use and production of dangerous substances in the creation and utilization of chemical products. The ethics of green chemistry demands for the invention of new processes which are beneficial in the formation of chemical products and are absolutely safe for health and environment. The developments of more environmentally benign and efficient products have significant economic effects. So, by applying Green Chemistry researchers develop latest techniques of synthesizing organic molecules and designing products which are safe for mankind as well as for environment. Recently, it has been proven in a number of organic synthesis and chemical transformations that applications of green chemistry techniques minimize chemical wastes and reaction times. Several ecofriendly protocols which involve greener alternatives have been studied to illustrate the advantages of green chemistry in synthetic organic chemistry.

The aim of the present research work is to develop new eco-friendly methodologies for carrying out two components and three components Condensations of aromatic aldehydes. Azomethine is taken as model molecule for two component condensation where as benzoxanthone is taken as model molecule for three component condensation product of aromatic aldehydes. Various ecofriendly catalysts and green solvents will be employed for development of new green methodologies for synthesis of azomethines and benzoxanthone analogues.

Synthesis of azomethine and benzoxanthone has been performed by using various green acid catalysts like lemon juice, glucose, garlic, oxalic acid and polyacrylic acid and various ecofriendly source of energy such as microwave, ultrasound irradiations. Reactions were also performed via frictional activated driving force. Most of the reactions in the present investigation were carried out either in solvent free condition or in water medium.

Various spectroscopic techniques like IR, $^1\text{H-NMR}$, $^{13}\text{C-NMR}$, HRMS-ESI and melting point are used to characterize synthesized compounds. Compared to

conventional methods, these methods are more convenient, provide products in good yield, show more efficiency, and take lesser time without causing pollution.

Dedicated to
Satguru Baba Hardex Singh Ji
Maharaj For His Countless
Blessings

ACKNOWLEDGEMENTS

At the very outset my everlasting bow (in reverence and humble gratitude) is to “The Almighty” whose gracious blessing enabled me to complete my thesis in time. I feel indebted to my teacher and Supervisor Dr. Tanay Pramanik for his consistent guidance, constructive criticism, cool attitude and whose dynamic magnanimous and, invaluable suggestions, directive criticism, constant encouragement and above all punctuality and creative guidance paved the way for successful completion of this work.

I would like to express my deep gratitude and heartfelt thanks to Prof. R.C, Thakur, Head Department of Chemistry who despite their tight schedule kept all the facilities at my disposal for carrying out my work properly and in time. I am also indebted to Dr. Richa Gupta whose lovable attitude, and painstaking efforts are gratefully acknowledged. I am indebted to entire lab staff members Manoj, Manish, Varun, Bhawneet Singh, Sandeep, Suraj Sir and Rinky Mam who helped to accomplish my work without any hurdle and their cooperative behaviour throughout my work is really appreciable. Their lovable attitude and painstaking efforts are gratefully acknowledged.

I have spent more time in lab than anywhere else for past two years. I recall with gratitude the selfless help and involvement of my lab mates Diksha, Gurpreet Kaur, Ravi, Dharminder, Rajesh, Vivek, Tanu and Rinku at different stages of my work. I am also heavily indebted to all my friends in the department of Chemistry; they made my time here an enjoyable and positive one.

Above all, the credit of completion of this work goes to my family and in laws for their constant support and encouragement, unfailing love and blessings. My Father is the one who sincerely raised me with his caring and gentle love. None of this would be possible without my family. I will never fail to remember the cooperation and time to time assistance of respondents. I am sincerely thankful to them.

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acid

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Scheme-3.12 Synthesis of benzoxanthenes with Polyacrylic acid under
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LIST OF ABBREVIATIONS AND SYMBOLS

AcOH	Acetic acid
AR	Analytical reagent
CAN	Ceric Ammonium Nitrate
CDCl ₃	Deuteriochloroform- <i>d</i>
¹³ C NMR	Carbon Nuclear Magnetic Resonance
Conc.	Concentration
CSA	Camphor Sulphonic Acid
d	Doublet.
D	Dextrorotatory
DCM	Dichloromethane
DMSO	Dimethylsulfoxide
E _a	Activation energy
EI -MS	Electron Impact Mass Spectrum
ESI -MS	Electron Spray Ionization Mass Spectrum
EtOH	Ethyl alcohol
FT-IR	Infrared Fourier Transform
GS	Grindstone
¹ H NMR	Proton Nuclear Magnetic Resonance
H	Hour(s)
H-bond	Hydrogen Bond
HRMS	High Resolution Mass Spectrum
Hz	Hertz
i.e.	That is (Latin <i>id est</i>)
<i>J</i>	Coupling Constant
LR	Laboratory Reagent
M	Molar
m	Multiplate
MCR	Multicomponent Condensation Reactions
MeOH	Methanol
mL	Milliliter(s)

Mmol	Millimol
<i>m/z</i>	Mass/Charge
MW	Microwave
NMR	Nuclear Magnetic Resonance
NUS	Nonultrasonic
PAA	Polyacrylic acid
PCL	Polycaprolactum
PEG	Polyethylene glycol
PLA	Polylactic acid
PGA	Polyglycolic acid
Ppm	Parts per Million
pTSA	Para toluene sulphonic acid
Q	Quartet
S	Singlet
SB	Schiff base
SSA	Silica Sulphuric Acid
US	Ultrasound
UV	Ultraviolet
T	Triplet
TBAF	Tetrabutylammonium Fluoride
TCT	TichloroTriazine
TLC	Thin Layer Chromatography
TTAB	Tetra decyltrimethylammonium bromide
W	Watt

CHAPTER-1

INTRODUCTION

Along with the development of chemistry and technology, as new compounds and processes have been flourished by the researchers in one hand, enough demolition of environment has also been done for last few decades on the other hand. Thus, to conserve the environment the researchers have no other option but to adopt the concept of sustainable development and green chemistry so that advancement of chemistry and protection of environment can go on parallel to each other. Due to our thriving interest for the environment and the need of advancement of chemical science at the same time, the concept of sustainable development and green chemistry has drawn much attention from the researchers for last few decades.

Green chemistry is that class of chemistry which demands techniques, tools and technologies which are beneficial for chemists, chemical engineers in establishment of more green and effective products and processes which may also have remarkable economical assets.

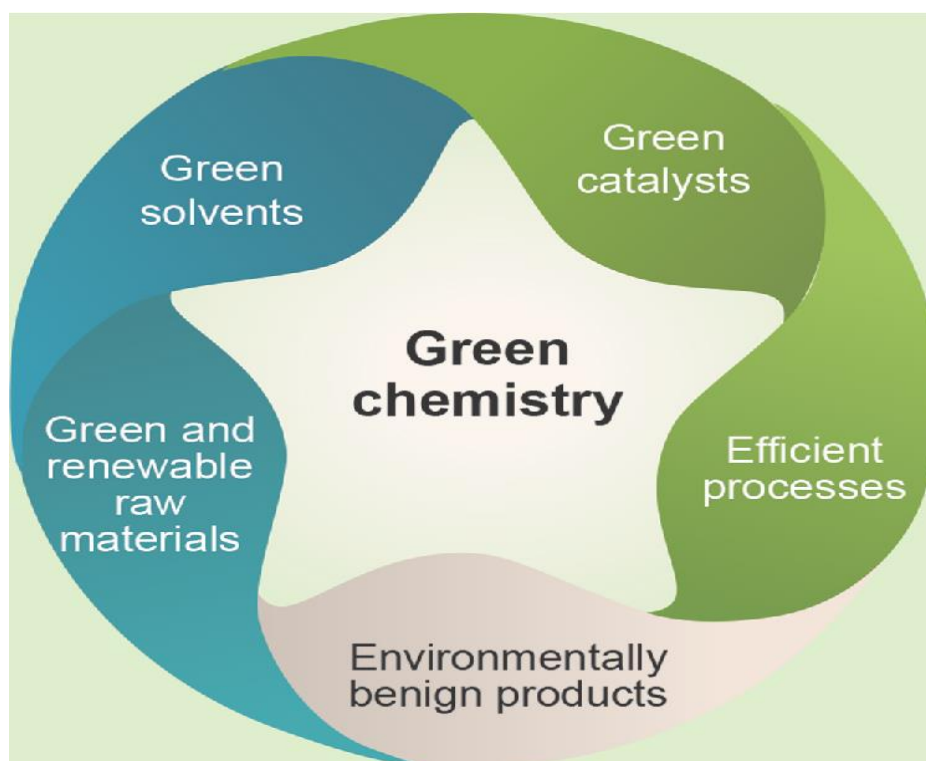


Figure-1.1: Main Topics in green chemistry

In modern era, green chemistry has become an indispensable aid in the synthetic chemistry¹. By applying green chemistry techniques, designing of drug molecules and synthesis of organic compounds can be done in latest way. It offers numerous

valuable economic and environmental advantages over conventional synthetic processes². The current progress in green chemistry has opened the doors of new opportunities and possibilities for the organic chemists to develop new reaction conditions which can minimize the application of harmful poisonous chemicals and minimize the release of organic solvents which are volatile³. The implementation of green chemistry simplifies the isolation/purification process, boosts selectivity and shortens reaction time.

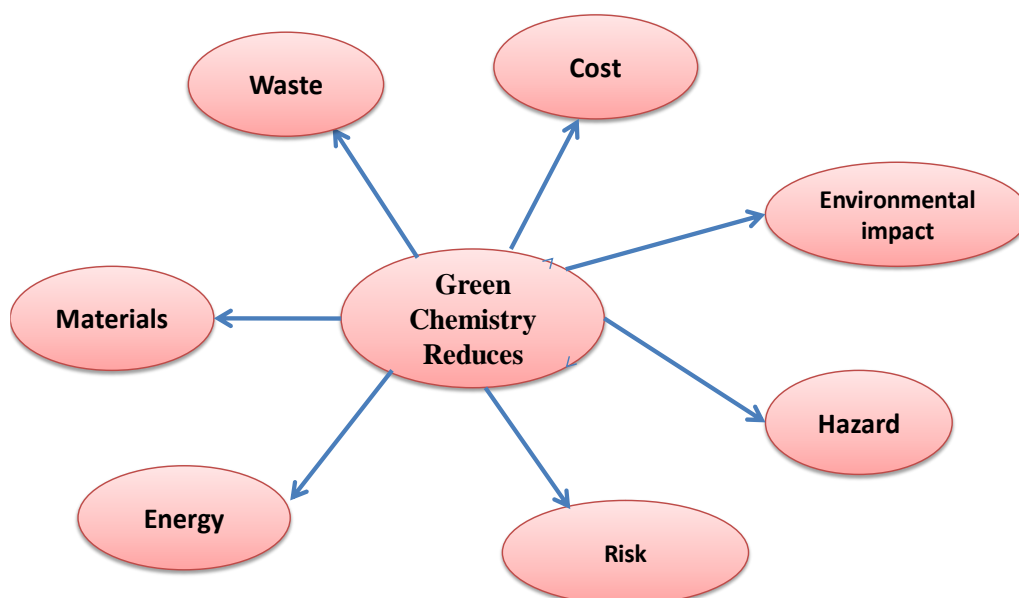


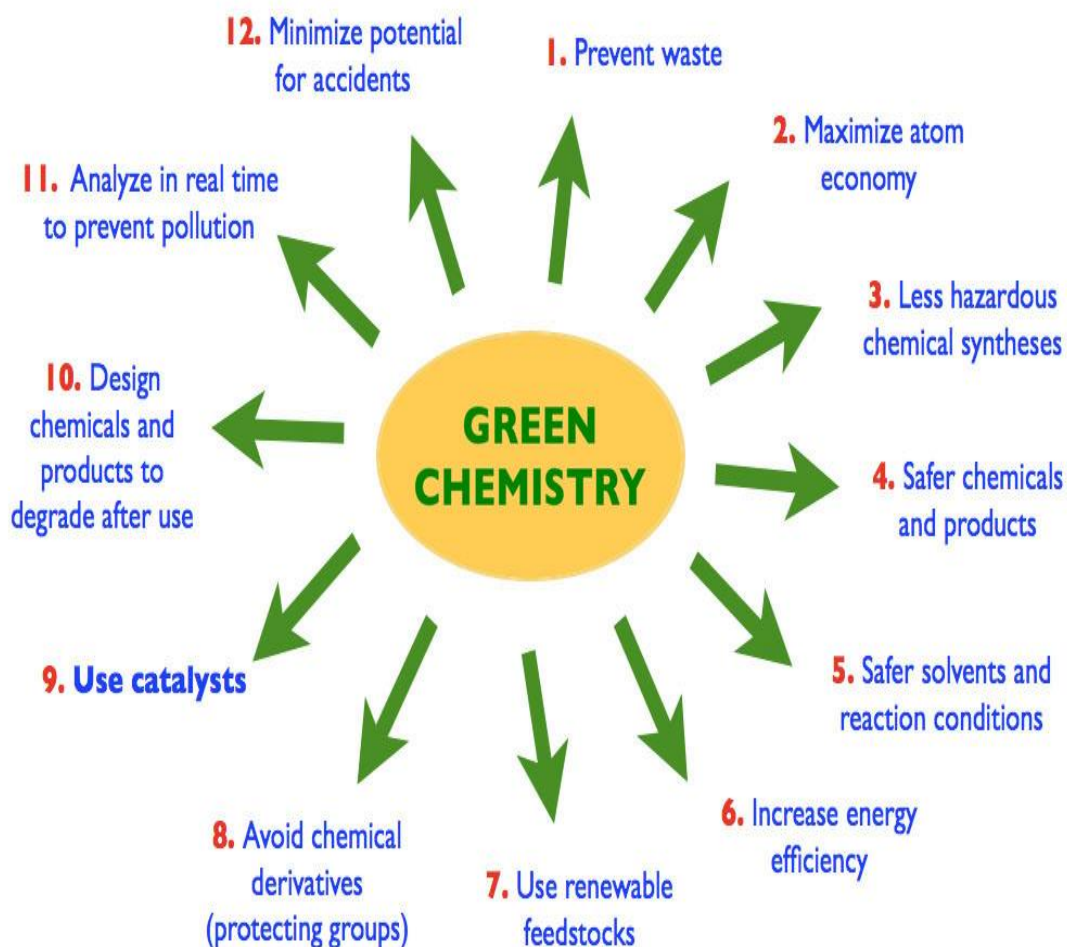
Figure-1.2: Advantages of Green Chemistry

To achieve these targets, a group of principles was published by Paul Anastas and John C. Warner in 1998 to guide the implementation of green chemistry. These principles are:

- **Prevention of Waste:** It is better to check the generation of waste rather than to smash deal with it after it is formed.

Atom Economy: Design new techniques of formation in such a way that final product which is formed should contain maximum part of all the materials used in the process.

- **More safe chemical synthesis:** Chemical Synthesis wherever possible should be carried out in such a way that it should be completely safe for mankind as well as for environment. It will be possible only if production and use of harmful or toxic substances should be minimized.
- **Making Safer Chemicals:** The synthesized chemicals should be made as nontoxic as possible.
- **Avoid use of unsafe solvents and supplements:** If possible stop the utilization of supplementary substances such as solvents, isolating agents, etc.
- **Efficient energy designing:** Minimize the use of energy requirements and if possible make use of ecofriendly source of energy like microwave, ultrasound.
- **Avoid use of exhaustible Feedstock:** Instead of using nonrenewable sources make use of viable feedstock and raw material which are renewable.
- **Avoid protecting groups:** Avoid using protective group as far as possible.
- **Catalysis:** It's recommended to use catalyst wherever possible because catalyst can speed up the reaction by reducing energy of activation.
- **Design chemicals and products to degrade after use:** Design products of chemical processes in such a way that after the completion of their working they disintegrate into non dangerous crumbles and do not exist in the environment.
- **Checking real time pollution:** Real time systematic strategies desired to be evolved to check the release of pollutants and harmful vapors.
- **Accidental free Safer Chemistry:** Choice of materials used in a chemical process should be done in such a way that it lessens potential for chemical mishaps such as fires, explosions and releases.



Anastas and Warner (1998)

Figure-1.3: Principles of Green Chemistry

One pot multi component condensation reactions are very popular from the green chemistry point of view because green chemistry demands usage of lesser number of synthetic steps. Multicomponent condensation reactions (MCRs), defined as the reactions which involve joining of at least three dissimilar reactants through covalent bonds in same container. In synthetic organic chemistry these reactions have progressively gained importance. MCRs enable the construction of number of bonds in a single action and offer marvelous benefits over conventional multistep reactions. These reactions are very successful in making simple molecules bearing variety of functional groups from easily accessible starting substances in one operation with characteristic variability for designing diversity and complexity of molecules along

with reduction of time, hard work, price and unwanted materials. Various large molecules and complicated heterocyclic compounds of extreme medical importance can be synthesized easily via single step one pot multi component condensation instead of going through multi-step synthesis. Thus the need of purification of products in every single step and hassles of multi-step synthesis can be eliminated by performing one pot multi component condensation. One pot multi component condensation reaction also gives higher atom economy and getting a higher percentage of atom economy is very much desired in green chemistry.

A large number of multi component condensation reactions of aromatic aldehydes are well known in literature. A few of the name reactions of aromatic aldehydes are depicted below:

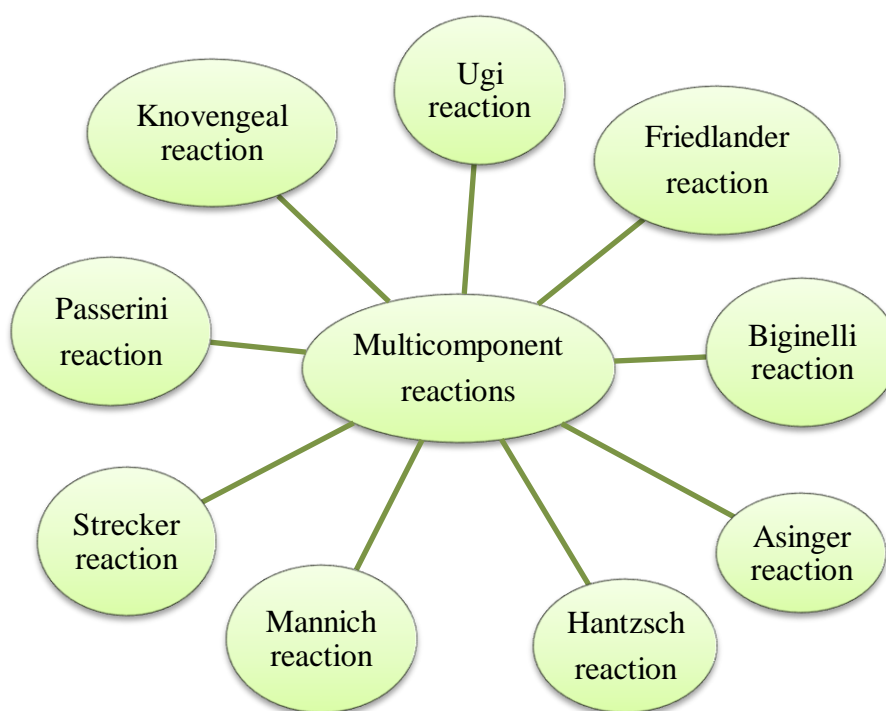


Figure-1.4: Name of some Multicomponent condensation Reactions of aromatic aldehydes

Out of such immense number of reaction of aromatic aldehyde, synthesis of Azomethine and benzoxanthenes is under keen observation of researchers for last few decades due to the multipurpose importance of these compounds in medicinal chemistry and material science

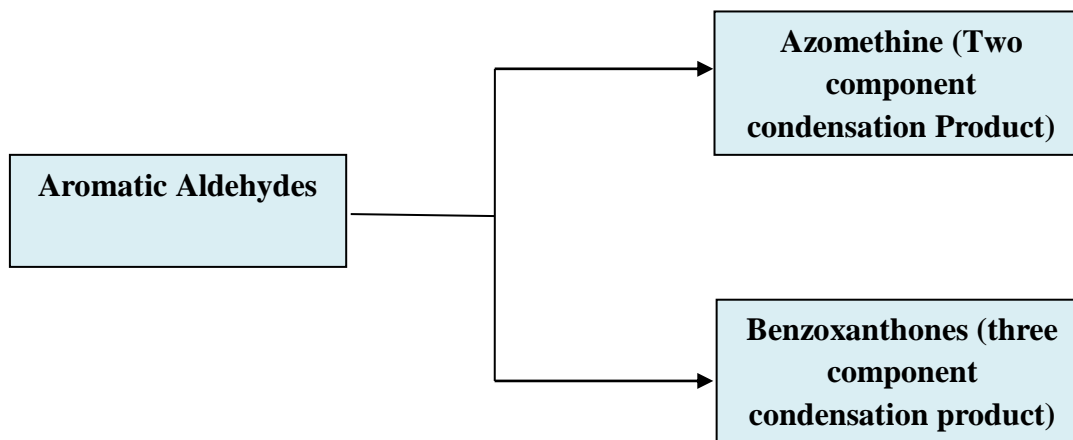


Figure-1.5: Target compounds to be synthesized

Azomethines one of the major groups of bioactive molecules commonly known by the name Schiff bases were first discovered by Hugo Schiff, a German Chemist in 1864 hence named so after the name of the inventor. Azomethines are compounds containing imine or azomethine functional group. Azomethines are also known as **Anils**. Generally they are shown by following structural formula:

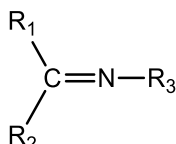
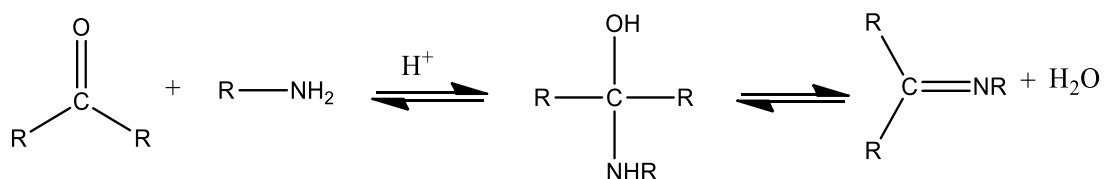


Figure-1.6: General Structural Formula of azomethines

Where R_1 and R_2 represents hydrogen, an alkyl or an aryl and R_3 an alkyl or aryl group

Azomethines are crystalline or oily substances. These are soluble in organic solvents and insoluble in water. They are generally weak bases. Being basic they react with acids in anhydrous medium to form salts. In aqueous solutions they undergo hydrolysis to form aldehydes and amine. They are very readily reduced by addition of hydrogen providing secondary amines ($R_1R_2CH-NHR_3$). Mostly azomethines are stable in alkaline medium.

Generally Azomethines are formed by condensation of primary amines and carbonyl compounds. In modern scenario, they are acquiring significance day by day because of their versatility as pharmacophore for designing and developing various bioactive compounds.



Scheme-1.1: One pot synthesis of Azomethine derivatives

Mechanism of the reaction:

The reaction is catalyzed by acidic medium. In the presence of acidic medium reaction becomes facile because acid catalyst makes the carbonyl carbon more electrons deficient hence makes the attack of nucleophile that is primary amine on carbonyl carbon easy. The addition product carbonyl amine formed in first step being unstable readily undergoes dehydration to form azomethine.

Factors affecting the synthesis of Azomethines:

Several factors affect the synthesis of azomethines:

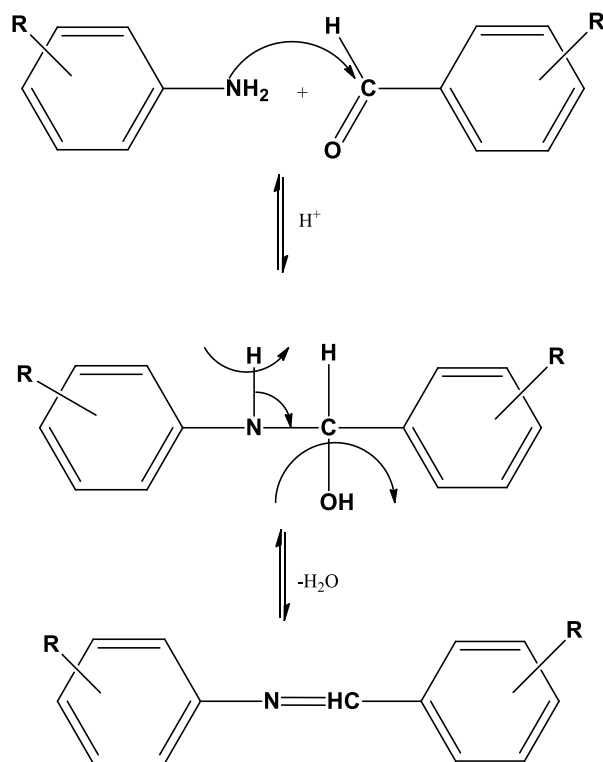
(a) p^H of the solution:

p^H of the reaction should be carefully controlled because if the medium is too acidic then amine will get protonated and no longer will act as nucleophile and reaction cannot proceed and if the medium is too alkaline then dehydration of carbonyl amine becomes difficult due to lack of proton which attacks on OH group.

(b) Steric and electronic factors of carbonyl compound and amine:

Aldehydes being less sterically hindered react faster than ketones. Secondly extra carbon of ketones increases electron density on carbonyl carbon and so makes ketones less electrophilic than aldehydes.⁴

All the steps in reaction are reversible.



Scheme-1.2: Mechanism of azomethine formation

Due to wide range of biological applications of azomethines great attention is paid to them by organic chemists. Biologically, they are used as antimicrobial⁵, antibacterial⁶, anti-inflammatory⁷, antituberculosis⁸, antihelminthic⁹, anticancer¹⁰, antitumor¹¹, antidepressant¹², anticonvulsant¹³, anti-dyslipidemia¹⁴, anti-HIV¹⁵, antihypertensive¹⁶ agents. In addition to above mentioned biological activities, they also make their important place in co-ordination chemistry as they are excellent complexing agents¹⁷⁻²³. Azomethines are known as useful intermediates²⁴ in organic chemistry. Azomethines are also applied as corrosion inhibitors as they suppress corrosion by quickly forming a single layer on the surface to be protected²⁵. A large number of Azomethines has also found their uses in magnetochemistry and photophysical processes²⁶.

Benzoxanthenes are well known oxygen containing heterocycles. These form an important class of biologically active heterocycles. Benzoxanthone was first discovered by W. Knapp in 1913. Among xanthene based compounds 12-aryl-9,9-dimethyl-8,9,10,12-tetrahydrobenzo[a]-xanthene-11-ones because of their peculiar

framework and great prospective for more transformations occupy important place.²⁷

General structure of benzoxanthone is shown as:

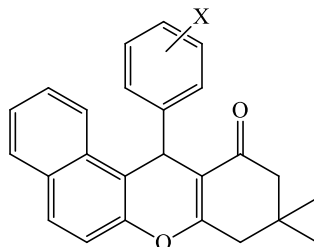
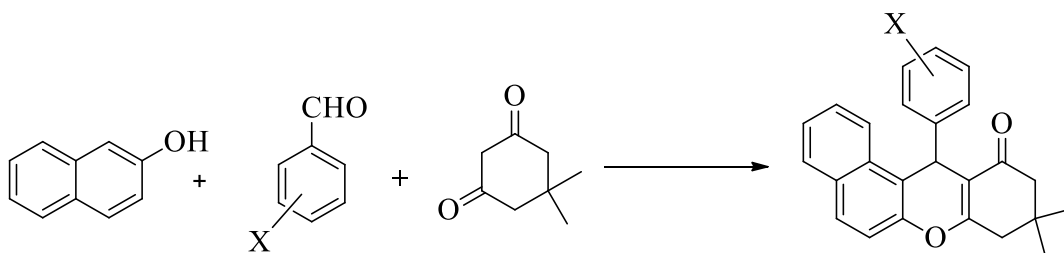


Figure-1.7: Structure of Benzoxanthone

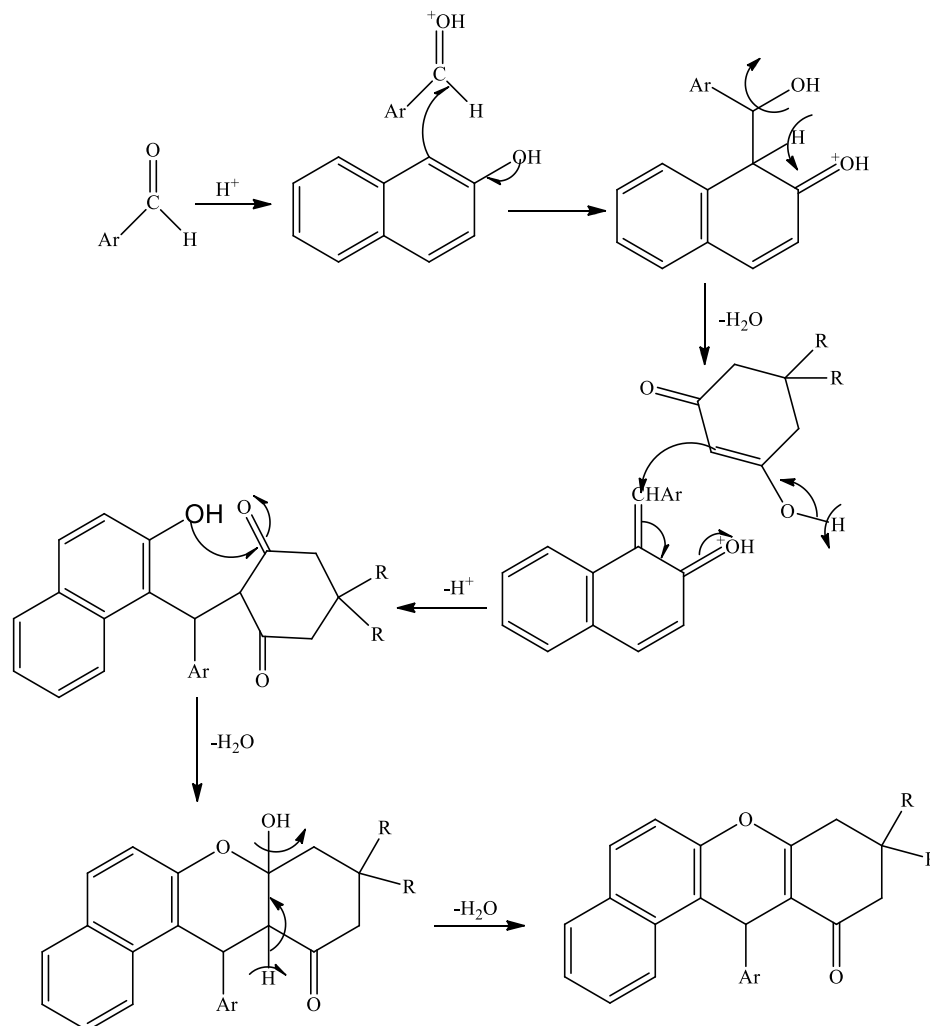
Broad spectrum applications of benzoxanthenes and their analogues in biological and material science have made their study interesting. This class of compounds not only possesses antibacterial²⁸, antiviral²⁹, anti-inflammatory³⁰, antimicrobial³¹, antimalarial³², anti- HIV³³, antioxidant³⁴, anticarcinogenic³⁵, antitumour³⁶, antidiabetics³⁷, antiallergic³⁸ activities but also they have found their usages in Photodynamic therapy³⁹ and laser technology⁴⁰. These are also employed as antagonist for zoxazolamine produced paralysis in young rats⁴¹. Moreover, these compounds can also be applied as dyes⁴² and fluorescent materials which are sensitive to pH can also be employed for visualization of biomolecules⁴³.

Due to such wide range of applications, the synthesis of Benzoxanthenes has become subject of great interest and scientists have already found efficient, economic, convenient method to synthesize this Benzoxanthone via single pot multi component condensation reaction [Scheme-2] of aromatic aldehyde, 2-naphthol and cyclic 1,3 dicarbonyl compounds⁴⁴. One pot single step multi component condensation reaction has remarkable advantages over multi step chemical synthesis, like rapid automation, easy workup, extrication, purification processes and hence there is minimization in the unwanted products. One-pot MCRs are superior to multi-step syntheses in terms of time, cost, yield and safety measures.



Scheme-1.3: One pot Synthesis of Benzoxanthone derivatives

Mechanism of Reaction:



Scheme-1.4: Mechanism of benzoxanthone formation

Recent Applications of Azomethines and benzoxanthenes:

In Present days, azomethines have been used as a linker in Donor –Linker- Acceptor based photo induced electron transfer molecule which has been frequently applied for the designing of versatile chemo/biosensors⁴⁵. Fluorescent boron schiff bases produced by condensation of azomethines with diphenylborinic acid show their application as cytoplasm staining dyes⁴⁶⁻⁴⁷. These dyes which are used for staining cytoplasm showed very low Cytotoxicity, simple synthesis, high photo-stability, and

specific staining for cytoplasm structure. They are also used as activators of carbonic anhydrase which might have found applications in the neurodegenerative disorder of memory and cognitive function (Alzheimer's disease)⁴⁸. They also serve as photostabilizer for polymer PVC⁴⁹. Though azomethines have been working as very good complexing agent since long time but even in current scenario a variety of azomethine has been prepared to synthesize a huge variety of complexes with different metals and the new complexes so formed possesses antimicrobial properties and can also be applied for purification of water as they kill or inhibit the growth of water borne bacteria. Hence metal complexes of azomethines could find potential applications in designing new therapeutic agents⁵⁰⁻⁵⁹. Recently researchers have prepared biopolymeric schiff bases and their complexes and used them as anticancer and antimicrobial agent⁶⁰.

Nowadays benzoxanthone and its derivatives are well known for their biological applications⁶¹. They are frequently used for formation of fluorescent dyes. Yellow fluorescent dyes prepared from them are used in remote phosphor LED systems as colour converters⁶²⁻⁶⁴.

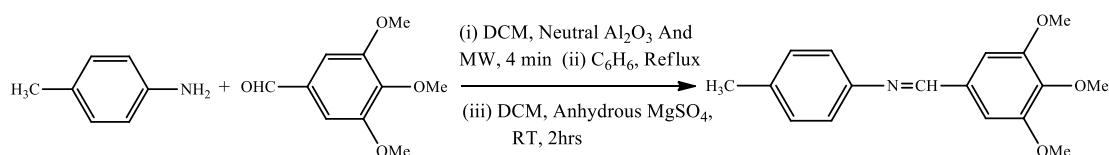
CHAPTER-2
LITERATURE REVIEW AND
OBJECTIVES

In the chapter-1 several applications of azomethines and benzoxanthenes in various fields of chemistry are mentioned. By considering these diverse applications, researchers have done a lot of research on the synthesis of these two compounds even now new methodologies for synthesis of these compounds have been developed by them. Data reported in literature for synthesis of these compounds are summarized below:

2.1 Literature Review: Azomethines

Azomethines which were discovered by Hugo Schiff in the year 1864 have also been formed by reaction of 1° amines with carbonyl compounds⁶⁵.

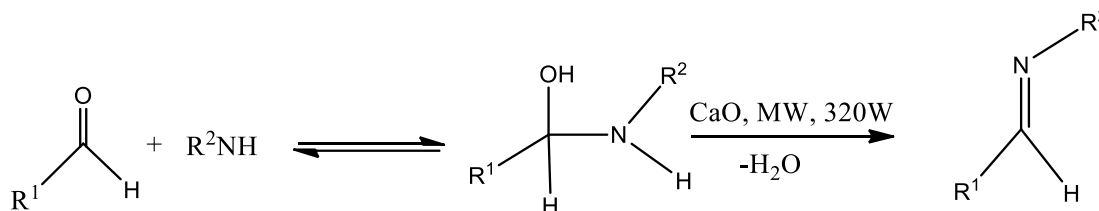
In the year 2006, azomethine synthesis from 3,4,5-trimethoxybenzaldehyde and p-toluidine (a) under MW conditions using neutral alumina and dichloromethane (b) by refluxing with benzene (c) by stirring at RT with DCM, anhydrous MgSO₄ was described by Zhaoqi Y, Pinhua S⁶⁶. All the three methods were compared by them. By comparing these methods they found that microwave assisted method the best one as maximum yield was provided by this method. In this method time taken was only 4 min as compared to several hours in other two techniques.



Scheme-2.1: Synthesis of azomethines by Zhaoqi Y et al⁶⁶

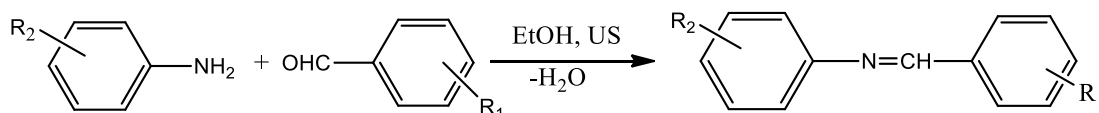
In the year 2007, Microwave assisted synthesis of azomethines catalysed by CaO has been revealed by Gopalakrishnan et al⁶⁷. Variety of aromatic aldehydes and aromatic amines were employed by them to perform the reactions. To prove the efficiency of catalyst the reactions were also performed in presence as well as in absence of catalyst by them. The reactions were also conducted at different temperatures in the presence of catalyst by Gopalakrishnan et al and finally it was concluded by them that with

CaO under MW irradiations highest amount of azomethines were obtained in very short duration of time.



Scheme-2.2: Synthesis of azomethines by Gopalakrishnan et al⁶⁷

In the year 2007, Synthesis of schiff bases under ultrasound irradiations in the presence of ethanol solvent was reported by Yu Yuye⁶⁸. Several azomethines with both electron rich and electron deficient aldehydes and also with electron poor and electron rich anilines were prepared by the researcher to determine the effect of substituents. It was observed by them that reaction rate increased when the reaction was performed with electron deficient aldehydes and electron rich anilines. All the reactions carried out by them completed in 10- 20 min.

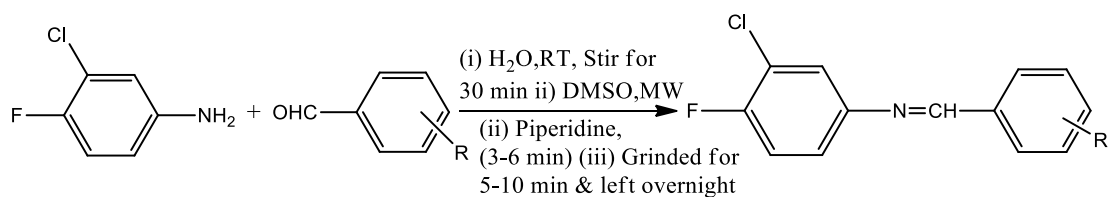


Scheme-2.3: US assisted synthesis of azomethines by Yu Yuye et al⁶⁸

In the year 2008, A number of azomethines were synthesized from 2-amino thiazolyl bromocoumarin and variety of aldehydes by conventional heating as well as refluxing and also by mw irradiation in ethanol solvent by Venugopala KN, Jayashree BS⁶. It was noticed by them that MWI method is excellent one than conventional heating as well as refluxing because products were obtained in 1-2 min in MWI method in comparison to very long time taken (1-2 hrs) for getting the same product in other two methods. Antibacterial screening of formed compounds was also carried out by Venugopala et al.

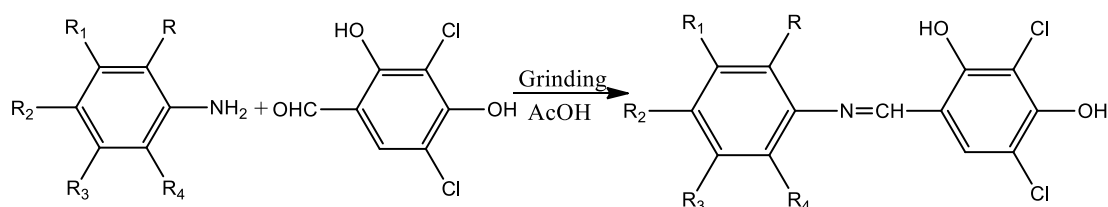
In the year 2009, Preparation of azomethines from 3-chloro-4-fluoroaniline and several benzaldehydes at room temperature in water medium, MW assisted synthesis of SBs in DMSO solvent and also by grindstone technique was reported by Naqvi A.

et al⁶⁹. All of these methodologies developed by them were green but out of these water based formation of azomethines was best one on the basis of yield followed by MW assisted method which in turn was considered better than friction activated method. On the basis of time MW assisted method was considered best by Naqvi A et al.



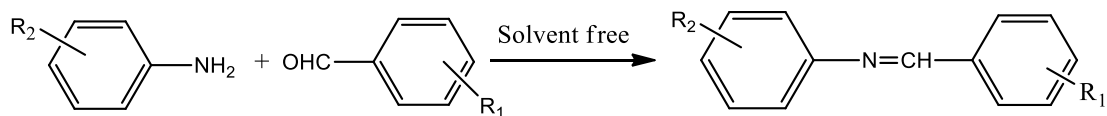
Scheme-2.4: Synthesis of azomethines by Naqvi A et al⁶⁹

In the year 2009, A simple & efficient synthesis of some new azomethines with 3,5-dichloro-2,4-dihydroxy benzaldehyde and substituted aniline in the solvent ethanol containing traces of glacial acetic acid by applying grindstone technique was documented by Vibhute AY et al⁷⁰. All the compounds were got by the researchers in duration of 15-20 min. Same compounds were also produced in low yield by heating the same components for 3 hours by the researchers.



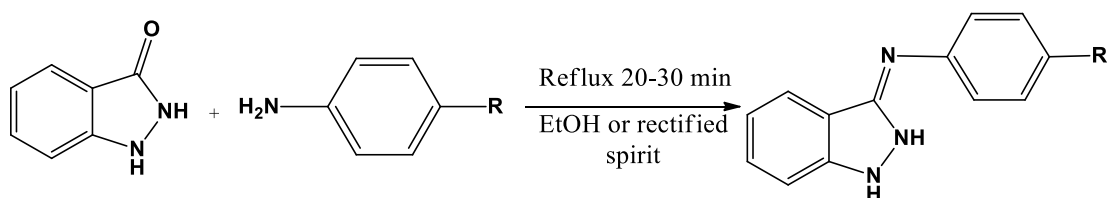
Scheme-2.5: Grindstone assisted synthesis of azomethines by Vibhute AY et al⁷⁰

In the year 2010, Preparation of azomethines by condensation of primary aromatic amines with aryl aldehydes catalyzed by cerium chloride heptahydrate without using solvent was registered by Ravishankara L. et al⁷¹. First reactions were carried out by them in the absence of catalyst. Further it was noted by the researchers that in the absence of catalyst the deactivated amines either did not give any reaction or provide very poor yield of product, similarly deactivated aldehydes i.e. aldehydes bearing electron releasing groups provide product at faster rate in presence of catalyst than in the absence of catalyst.



Scheme-2.6: Cerium chloride heptahydrate catalyzed synthesis of azomethines by Ravishankara L. et al⁷¹

In the year 2010, A series of azomethines from 3-indazolone on reaction with 4 substituted aniline by heating the solution in water bath by using reflux condenser was revealed by Muthumani P, Meera R. et al⁷². The biological activities like antibacterial, anti-inflammatory and analgesic activities of the formed compounds were also screened by the scientists.

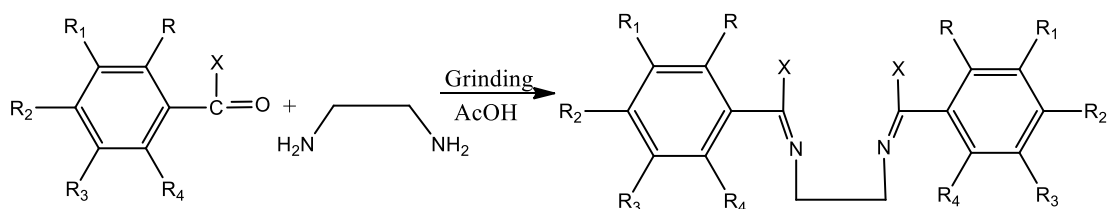


Scheme-2.7: Synthesis of azomethines by Muthumani P et al⁷²

In the year 2010, A library of azomethines was synthesized by Satyanarayana VSV et al⁷³ using different aldehydes and highly substituted acetohydrazide at position-2 in $CHCl_3$, CH_3OH , $AcOH$ medium by refluxing and in acetic acid medium under ultrasonic conditions. It was noticed by them that ultrasound method was far better than refluxing because under US irradiations reactions progressed at faster rate and took only 6-12 min whereas under reflux reactions were progressed at slower pace and took 180-240 min. So ultrasound is much effective and energy conservative method.

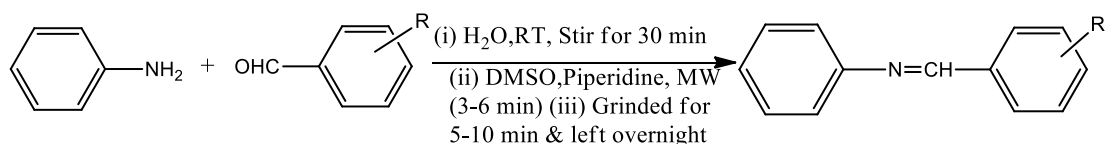
In the year 2010, The synthesis of novel bis-azomethines from aromatic aldehydes/ketones and ethane-1,2-diamine (a) by Grind stone technique using acetic acid (b) by refluxing with ethanol in Acetic acid catalyst was reported by Chavan SB et al⁷⁴. It was seen by them that in grindstone technique product was generated in 1-10 min whereas under refluxing 2-15 min were taken. Secondly, It was also noticed by them that in refluxing method lot of wastage of solvent occurred. So friction activated

method was considered superior to conventional method by the researchers as no solvent was used in this technique hence it was in agreement with protocols of green chemistry.



Scheme-2.8: Synthesis of azomethines by Chavan SB et al⁷⁴

In the year 2010, An ecofriendly and energy efficient greener methodologies for the formation of azomethines by stirring aniline bearing different substituents along with benzaldehyde and water at room temperature; by irradiating mixture in MW in presence of piperidine catalyst and DMSO solvent; by grinding mixture in the absence of catalyst and solvent was developed by Khadsan RE, et al⁷⁵. It was concluded by researchers that water based formation of azomethines at RT was best although time taken was more than MWI method because in MWI technique catalyst and solvent used were non green and also the yield was not as good as in the former method despite of ecofriendly source of energy. Formation of azomethines via grindstone way took longer time and provides poor yield though no solvent or catalyst was applied.



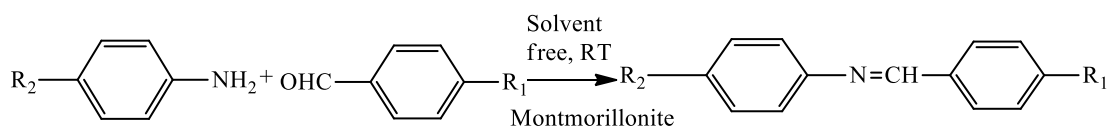
Scheme-2.9: Synthesis of azomethines by Khadsan RE, et al⁷⁵

In the year 2011, The synthesis of azomethines in UV chamber, sonicator as well as by grindstone method have been reported by Bendale AR. et al⁷⁶. First azomethines were prepared by them with the use of UV chamber without solvent and catalyst and then they made the use of sonicator with acetic acid as catalyst. Reactions were also conducted by them without application of catalyst in methanol solvent. Same azomethines were also prepared by the researchers by grindstone method without solvent and catalyst. It was further noted by them that time taken to produce same

azomethine varies in all the methods and minimum time was taken when reaction was carried with catalyst in sonicator.

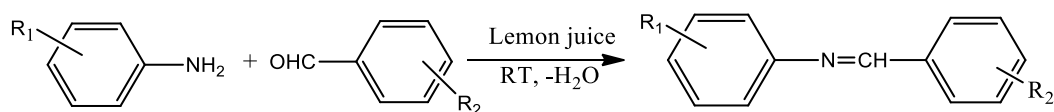
In the year 2011, Three new series of azomethines were prepared by condensing variety of aldehydes and amines in 25 ml ethanol by refluxing for 2 hrs by Muhammad AA, et al⁷⁷. The obtained azomethines were screened for antibacterial and antifungal activities by the researchers. Antibacterial activities were tested on *E. coli*, *S. aureus* and *B. subtilis* and antifungal activities were tested on *Asperigillus niger* and *Chalara Corda* by Muhammad AA, et al.

In the year 2011, Solvent-Free Synthesis of Schiff Bases by using Montmorillonite as a Heterogeneous Catalyst was given by Hossein Net al⁷⁸. For the preparation of azomethines first grinding of the reactants along with catalytic amount montmorillonite was performed by them and then they transferred the reaction mixture to flask and stirred it mechanically for suitable time. Addition of chloroform to reaction concoction was done by Hossein Net al after the reaction gets completed. It was seen by them that with aldehydes reactions were much faster than with ketones.



Scheme-2.10: Synthesis of azomethines by Hossein Net al⁷⁸

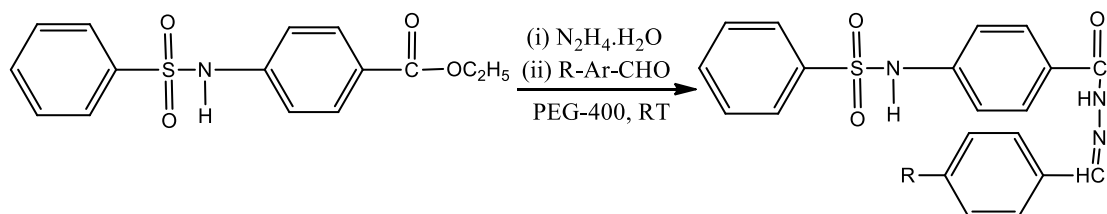
In the year 2012, Solventless synthesis of azomethines catalyzed by lemon juice as natural acid at room temperature by the reaction between primary aromatic amines and aryl aldehydes is in good yields was revealed Patil et al⁷⁹. A long series of azomethines was prepared by taking different aldehydes and amines by the researchers. It was noticed by Patil et al that most of the reactions took 15-300 min for completion and in few cases no product was obtained even after quite long time. No doubt their approach for synthesis of azomethines was green but time taken was long.



Scheme-2.11: Lemon juice catalyzed synthesis of azomethines by Patil et al⁷⁹

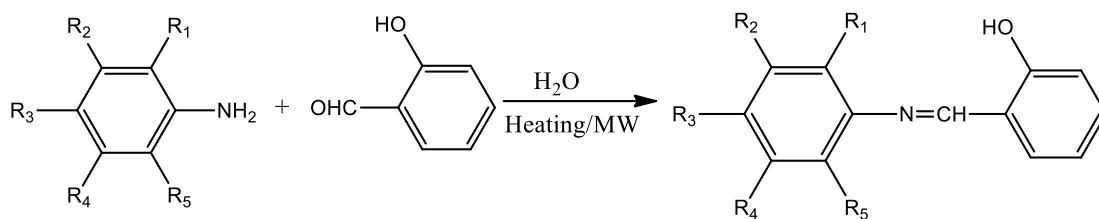
In the year 2012, Azomethines synthesis by grinding together indole-3-aldehyde with substituted aryl amines at room temperature along with minute quantity of acetic acid without using solvent was reported by Subhash BJ et al⁸⁰. A series of imines by using heterocyclic aldehydes and highly substituted aromatic amines was prepared by them and then comparison of this method was done with conventional method. In the end it was concluded by Subhash BJ et al that products were synthesized at faster speed (6-12 min) and in better yield (83-91%) in grinding method than in conventional method (60-210 min and 63-73% yield)

In the year 2012, The efficient and ecofriendly synthesis of azomethines was conducted in presence of PEG-400 as green reaction medium without catalyst by Jagrut VB et al⁸¹. For the formation of azomethine the reactants were dissolved in PEG-400 and stirred for 10 hrs by Jagrut VB et al. PEG was recovered and used again and again without losing its activity by them. It was seen that though PEG served as green reaction medium yet time duration of the reactions was too long.



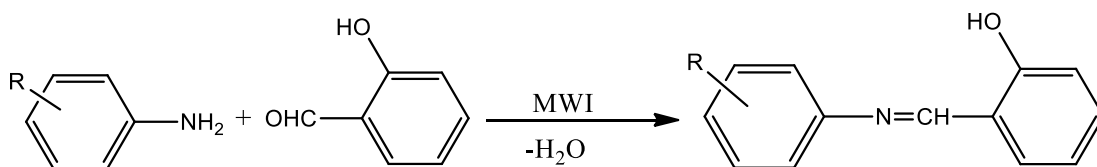
Scheme-2.12: PEG-400 catalyzed synthesis of azomethines by Jagrut VB et al⁸¹

In the year 2013, The preparation of azomethines was described under microwave] irradiation by reaction of 2-hydroxybenzaldehyde with several aryl amines in water by Bhagat S, Sharma, N⁸². Reactions were carried out at different temperatures by them by keeping the power of MW reactor constant. 70⁰ C was detected as most suitable temperature by them as maximum yield was obtained at this temperature so they performed other reactions at this temperature. Comparison of yield and reaction time with conventional methods was also done by them. In the end it was concluded by researchers that MWI method was much efficient than conventional method.



Scheme-2.13: Synthesis of azomethines by Bhagat S, Sharma, N⁸²

In the year 2014, Schiff Base Synthesis by applying microwave irradiations as ecofriendly energy source without Solvent was documented by Abirami M et al⁸³. A long chain of azomethines was prepared in excellent yield with 2-Hydroxyaldehyde and variety of aromatic amines in 3-5 min by Abirami M et al. The approach was made absolutely green by using nonpolluting and non toxic materials by the researchers.

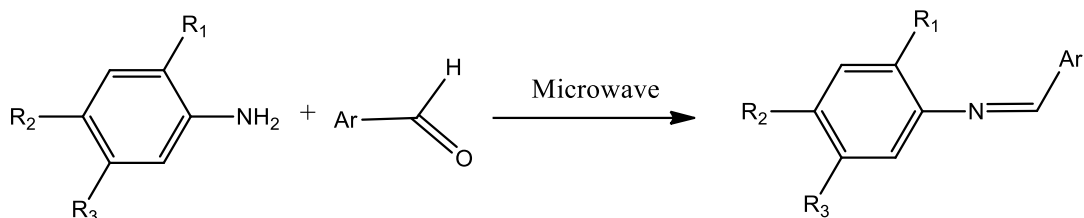


Scheme-2.14: MW assisted synthesis of azomethines by Abirami M et al⁸³

In the year 2014, An ecofriendly synthesis of some substituted azomethines by microwave irradiation was reported by Bodale VP et al⁸⁴. It was considered absolutely green approach by them as here MW irradiations were applied as ecofriendly source of energy but at the same time toxic non green solvent DMSO in excessive amount was also applied. No doubt it was seen by them that yield of azomethines was excellent.

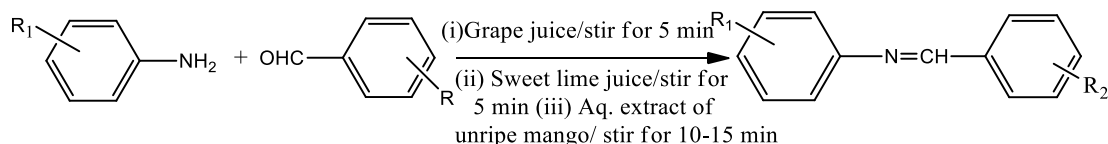
In the year 2014, Solvent free synthesis of some imine derivatives assisted by microwave irradiations was given by Bekdemir Y et al⁸⁵. Reactions were performed at different powers of MW with and without wetting agent β -ethoxyethanol by them and finally inference was drawn by them that at 360 W power of MW reactor in presence of wetting agent β -EE the amount of azomethine obtained was maximum in short duration of time. All the other reactions were then carried out by them under these conditions with different aldehydes and amines and as result long chain of

azomethines was synthesized. In the end it was inferred that MWI method was much more efficient than conventional method.



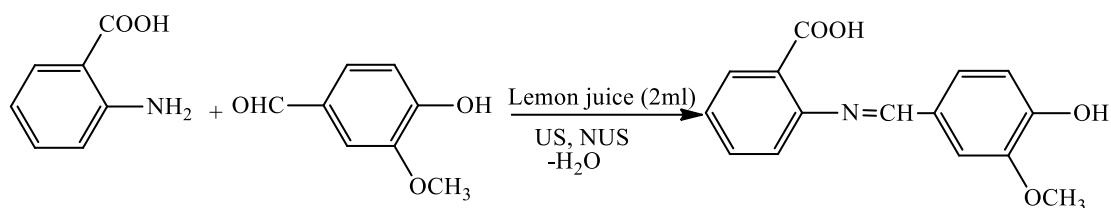
Scheme-2.15: MW assisted synthesis of azomethines by Bekdemir Y et al⁸⁵

In the year 2015, The synthesis of Azomethines was carried out by using natural acid catalysts like fruit juice of grapes, unripe mango and sweet lemon under solvent free conditions by researchers Yadav G, Mani JV⁸⁶. The influence of amount of catalyst on the yield of azomethines was studied by them and found that by increasing the amount of catalyst the yield of product decreased. In the end conclusion was drawn by Yadav G et al that out of these catalysts grape juice provided maximum yield and sweet lime juice provided minimum yield.



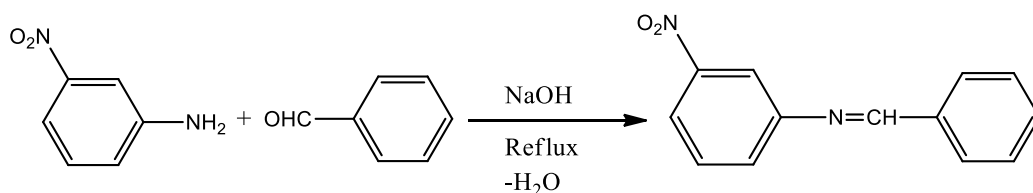
Scheme-2.16: Synthesis of azomethines by Yadav G, Mani JV⁸⁶

In the year 2015, The classical azomethines were synthesized from 4- hydroxy-3-methoxybenzaldehyde and 2-amino benzoic acid (Anthranilic acid) under conventional/nonultrasonic (NUS) by refluxing and ultrasonic conditions with catalytic amount of lemon juice as a green acid was documented by Mohammed A et al⁸⁷. It was seen by them that reactions under ultrasonic conditions were accomplished fastly (10 min) than under NUS conditions (1 hr). Comparison of % yield, morphological data and stability of azomethines formed in two methods was also done by Mohammed A. et al. It was inferred that compounds formed under ultrasonic conditions were relatively more stable and crystalline in nature.



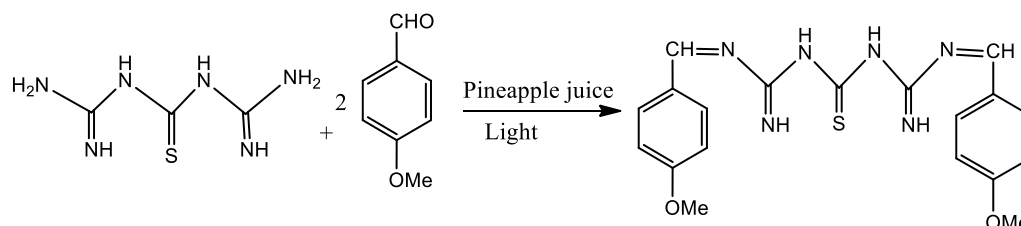
Scheme-2.17: Lemon juice catalyzed synthesis of azomethines by Mohammed A et al⁸⁷

In the year 2015, Azomethines were synthesized by refluxing alcoholic solution of m-nitroaniline and benzaldehyde along with 2-3 drops of NaOH by Muzammil K et al⁸⁸. These azomethines were used as ligands by them for forming complexes with metals copper and cobalt. Screening of these complexes for antimicrobial activities was also done by Muzammil K et al. It was further inferred by them that copper complexes possesses more antimicrobial activity than cobalt complexes.



Scheme-2.18: Synthesis of azomethines by Muzammil K et al⁸⁸

In the year 2016, The synthesis of azomethines in presence of pineapple juice with the aid of visible light was derived by using 1,3-diformamidothiocarbamide and various aldehydes was documented by Tayade DT, Ingole SP⁸⁹. For this purpose reactants along with 20 ml fresh pineapple juice was taken by them in round bottom flask. Product was obtained in good yield after exposure of reaction mixture to sunlight for 52 hrs. Some other azomethines were also prepared by them in the same way but by adding a drop of sulphuric acid.



Scheme-2.19: Synthesis of N'(p-methoxy)benzylene-N''-(p-methoxy)benzylene-iminothiobiurate

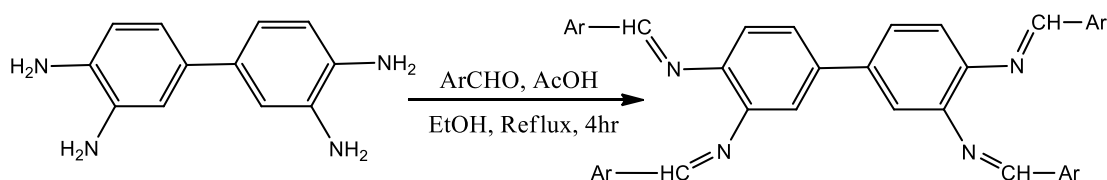
In the year 2016, The synthesis of some azomethines derived from some aldehydes with amino acids such as glycine and alanine in EtOH solvent and KOH catalyst was reported by Mohana, ER⁹⁰. *In silico* studies of formed compounds were also studied by them. Biological properties of obtained azomethines were predicted by the researchers by the application of PASS software.



Scheme-2.20: Synthesis of azomethines from amino acids by Mohana, ER⁹⁰

In the year 2017, A long series of histamine schiff bases were prepared by Akocak S et al⁴⁸ by the reaction of histamine with variety of aldehydes in the presence dry MeOH as solvent and KOH as catalyst at RT. It was investigated by the researchers that these azomethines act as activators for five selected human (h) CA isozymes, the cytosolic hCA I, hCA II, and hCA VII, the membrane-anchored hCA IV and transmembrane hCA IX. It was further documented by them that activity of histamine schiff bases depend upon structure of aldehyde used for the preparation of schiff base.

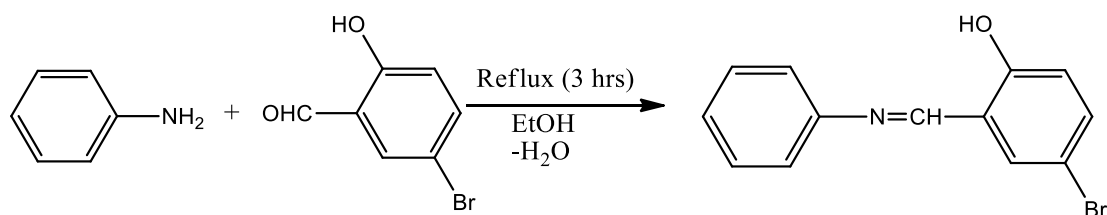
In the year 2017, The formation of three new tetra schiff bases by condensation of biphenyl-3,3',4,4'-tetraamine and three different aromatic aldehydes (in excess 4 mol equivalent) dissolved in ethanol solvent under reflux (4 hrs) in the presence of acetic acid as catalyst was reported by Ahmed DS et al⁴⁹. These synthesized azomethines were applied by them as photostabilizer for PVC. It was further noted by them that photostabilization activity for PVC films was maximum when azomethine formed from salicylaldehyde was used and minimum when 4-nitrobenzaldehyde was used for the synthesis of azomethine.



Scheme-2.21: Synthesis of azomethines by Ahmed DS et al⁴⁹

In the year 2017, The preparation of biopolymeric Azomethines was carried out with the aid of Chitosan and Salicylaldehydes by Barbosa HFG et al⁶⁰. The azomethines prepared by Barbosa et al were used as ligands to form complexes with Pt(II) and Pd(II). Screening of complexes was done by researchers for antimicrobial and antitumour activities. They found that antitumour activity of these complexes of Chitosan based biopolymeric azomethines was very good against the breast cancer cell line MCF-7.

In the year 2018, The synthesis of azomethine by refluxing a mixture of 5-Bromo-2-hydroxybenzaldehyde and aniline in super dry ethanol for 3 hours was given by Dave RH et al⁵⁷. This ligand was then used by them for the formation of complexes with Cu(II), Ni(II),Co(II), Mn(II), V(II) and Fe(II). Both complexes as well as ligand were screened by the researchers for antibacterial activity against several bacteria like *E. coli*, *B. subtilis*. They found that complexes possess good antibacterial activity as compare to azomethines.

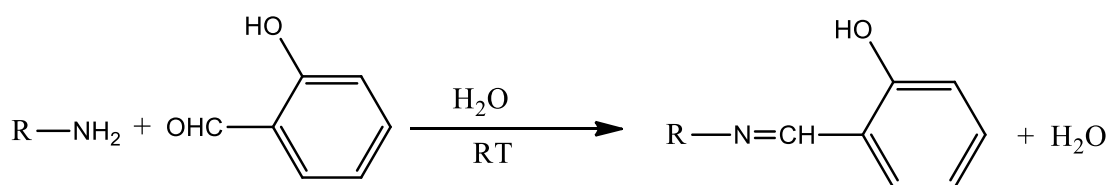


Scheme-2.22: Catalyst free synthesis of azomethines by Dave RH et al⁵⁷

In the year 2018, The preparation of azomethine by refluxing 5-hydroxy methylfuran-2-carbaldehyde and 1-aminoquinolin-2(1H)-one in ethanol solvent was reported by Alturiqi et al⁵⁸. The azomethine was then used by them as ligand to form complexes with several different metal ions like Cr(III), Ru(III), Mn(II), Co(II), Ni(II), Cu(II), and Zn(II). Cytotoxic activities of all the synthesized compounds towards human breast (MCF-7) and lung cancer (A549) cell lines were also studied by Alturiqi et al.

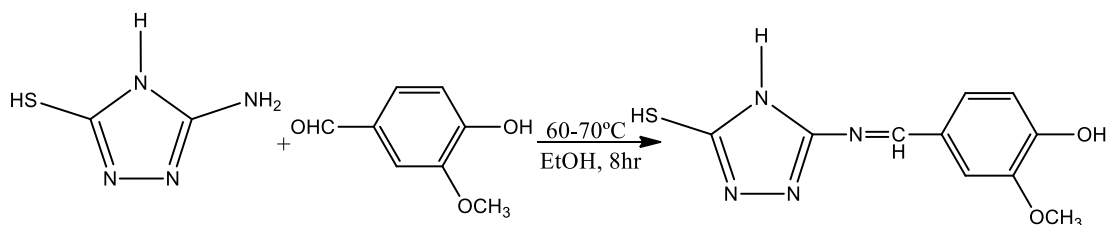
In the year 2018, A new synthetic approach for the formation of salicylaldimines in aqueous medium was given by Shamly P et al⁵⁰. Three different azomethines were prepared by the researchers by the reaction of 2-hydroxybenzaldehyde with aniline, ethylenediamine and aminobenzoic acid. The complexes of these azomethines with

metal Ni and Mg were prepared and examined for the antimicrobial properties by the scientists. Comparison of antimicrobial properties among these complexes as well as with azomethines was also executed by Shamly P et al. In the end they found that metal complexes show better antimicrobial properties than azomethines and among metal complexes antimicrobial activity was higher for Mg metal complexes. These complexes were also used by them for purification of water as these kill microorganisms.



Scheme-2.23: Water based synthesis of azomethines by Shamly P et al⁵⁰

In the year 2019, Formation of azomethine by refluxing an ethanolic solution of 5-amino-4*H*-1,2,4-triazole-3-thiol and 3-hydroxy-4-methoxybenzaldehyde in acidic medium for 6 hours was documented by Vinusha HM et al⁵². The azomethines synthesized by them were utilized as ligand to form complexes with Cu(II), Co(II), Mn(II), Ni(II) and Zn(II) metal ions. *In vitro* antibacterial activity of azomethine and their complexes were checked by them against nine food pathogens. They found that complexes exhibited higher antibacterial effects than the corresponding ligand. Antioxidant activities and *in vitro* Inhibitory effects on yeast α -glucosidase were also studied by the Vinusha et al. It was noticed by them that potentiality of Zn complex was highest among the complexes tested for antibacterial, antioxidant and inhibitory activity.

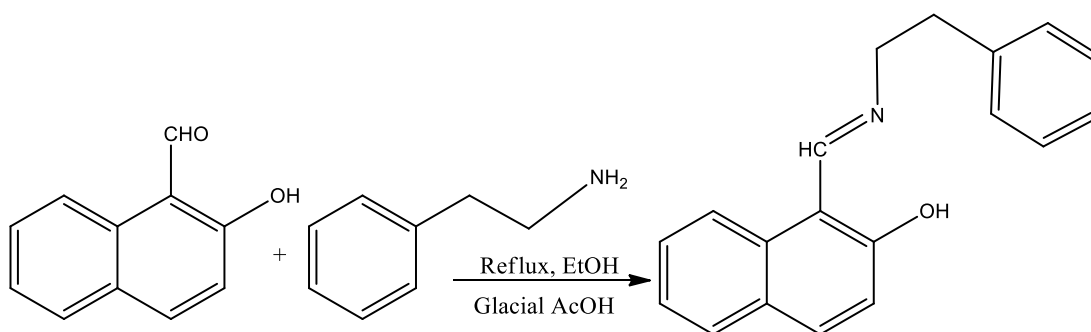


Scheme-2.24: Synthesis of azomethines by Vinusha HM et al⁵²

In the year 2019, MW assisted preparation of an azomethine from 2,4-dimethoxybenzaldehyde and 4-Amino-1,5-dimethyl-2-phenyl-1,2-dihydropyrazol-3-

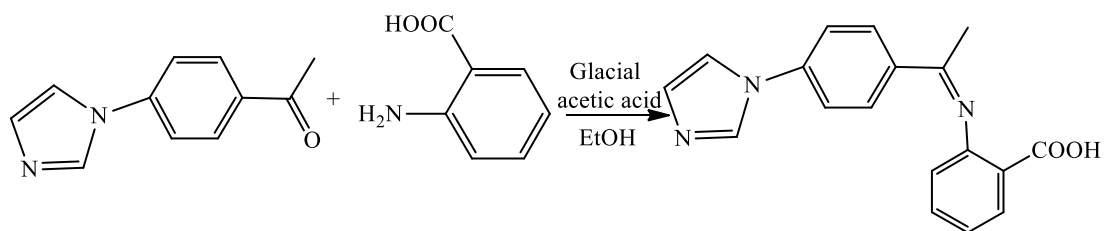
one was reported by A-Zoubi W et al⁵³. The synthesized azomethine was utilized by them to form complexes with Ni(II), Pd(II), Pt(IV), Zn(II), Cd(II) and Hg(II). Screening of both azomethine as well as its complexes was done by the scientists for antibacterial and antifungal activities against *S. aureus*, *E. coli*, *C. albicans* and *C. tropicalis*.

In the year 2019, A new Schiff base was synthesized by Hatim IH et al⁵⁶ by carrying out reaction of ethanolic solution of phenylethylamine with hot ethanolic solution of 2-hydroxynaphthaldehyde in presence of glacial acetic acid. Then toxicity of the synthesized compounds were checked by the scientists. They found that the compounds were almost safe for environment as well for mankind.



Scheme-2.25: Synthesis of 1-((phenethylimido)methyl)naphthalen-2-ol by Hatim IH et al⁵⁶

In the year 2020, The formation of azomethine by condensation of Anthranilic acid (dissolved in ethanol) and Imidazoleacetophenone (dissolved in hot absolute ethanol) catalysed by glacial acetic acid was reported by Hussein TI et al⁵¹. The reactions of synthesized azomethine with Ni(II), Cd(II) and Co(II) metal ions were performed by them to obtain the requisite complexes. Both the azomethine as well as its metal complexes were assessed for *in vitro* antimicrobial activities by the researchers. It was noticed by them that antimicrobial activity of complexes was much higher than azomethine.



Scheme-2.26: Synthesis of azomethines by Hussein TI et al⁵¹

In the year 2020, An easy and systematic synthetic route for the construction of azomethine from 4-fluoroaniline and 5-chlorosalicylaldehyde at room temperature in EtOH solvent was documented by Ommenya FK et al⁵⁹. The reaction was carried out by them by adding two drops (0.2 mL) of glacial acetic acid. The metal complexes were prepared by the scientists then by the application of this azomethine. Both azomethine and its metal complexes were tested for their bactericidal activity against no. of gram positive and gram negative bacteria by Ommenya FK et al. It was found by them that metal complexes possess higher antibacterial activity than free ligand.

Table- 2.1: Various Reaction conditions, catalysts and solvents for the synthesis of Azomethines

S.NO.	Reference	Catalyst	Solvent	Reaction conditions
1	65	-----	EtOH	Reflux (2 Hrs)
2	66	Neutral Al ₂ O ₃	DCM	MW (4 min)
		-----	C ₆ H ₆	Reflux (over 7 Hrs)
		Anhydrous MgSO ₄	DCM	RT (Stir 2 Hrs)
3	67	CaO	-----	MW(70 sec)
4	68		EtOH	US (10-20 min)
5	6	-----	EtOH	Reflux (2 Hrs)
		-----	-----	Heat (in oil bath at 180°C)

			EtOH	MW(65-113 sec)
6	69	-----	Water	RT (Stir 30 min)
		Piperidine	DMSO	MW(3-6 min)
		-----	-----	GS(overnight)
7	70	CH ₃ COOH	-----	GS (15-20 min)
8	71	CeCl ₃ .7H ₂ O	-----	Reflux(5-50min)
9	72	-----	Rectified spirit or EtOH	Reflux(20-30min)
10	73	Glacial CH ₃ COOH	CHCl ₃ - MeOH	Reflux(3-4Hrs)
			DMSO	US(6-12 min)
11	74	CH ₃ COOH	-----	GS(1-10 min)
			EtOH	Reflux (2-15min)
12	75	-----	Water	RT(stir 30 min)
		Piperidine	DMSO	MW(3-6 min)
		-----	-----	GS(overnight)
13	76	-----	-----	UV Chamber (15min)
		-----	MeOH	US (45°C, 13- 15min)
		CH ₃ COOH	MeOH	US (45°C, 9- 10min)
		-----	-----	GS (Overnight)
14	77		EtOH	Reflux (2 Hrs)
15	78	Montmorillonite	-----	Grind(RT 3-120 min)
16	79	Lemon juice	Lemon juice	RT(15-300min)
17	80	CH ₃ COOH	-----	Grind (2-3 min)
18	81		PEG-400	RT(stir 10 Hrs)
19	82	-----	Water	RT (Stir 1-2 Hrs)
			Water	MW (0.5-2 min)

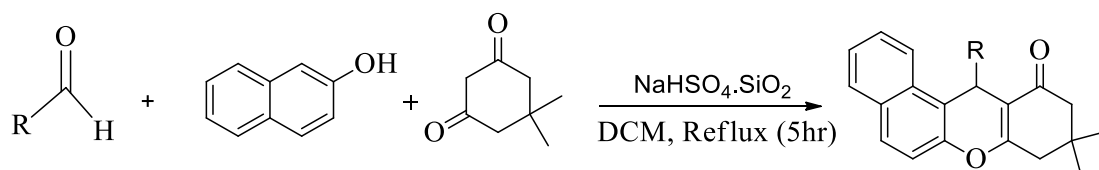
20	83	-----	-----	MW (3-5 min)
21	84	-----	DMSO	MW(40-62 sec)
22	85	β -ethoxyethanol	-----	MW (1-3min)
		-----	EtOH	Reflux (120min)
23	86	Grape juice ^a , sweet lime juice ^b , unripe mango ^c	----- ^{a,b} Water ^c	RT (stir 5-10 min) ^{a,b} RT(stir10-15 min) ^c
24	87	Lemon juice	Lemon juice	Reflux (1Hr)
				US(10 min)
25	88	NaOH	EtOH	Reflux (4 Hrs)
26	89	Pineapple juice	Pineapple juice	Sunlight (52 Hrs)
27	90	KOH	EtOH	Heat (60-180 min)
28	48	KOH	MeOH	RT
29	49	CH ₃ COOH	EtOH	Reflux (4Hrs)
30	60	-----	EtOH+ Glacial acetic acid	Thermostated bath (55°C), stir 18 Hrs
31	57	-----	EtOH	Reflux (3Hrs)
32	58	-----	EtOH	Reflux (3Hrs)
	50	-----	Water	Stir at RT (10 min)
33	52	Acidic medium	EtOH	Reflux (6Hrs)
34	53	-----	-----	MW(15 min)
35	56	Glacial acetic acid	EtOH	Reflux (3Hrs)
36	51	Glacial acetic acid	EtOH	Reflux (2Hrs)
37	59	Glacial acetic acid	EtOH	RT

2.2 Literature review: Benzoxanthone

In the year 2007, Solvent free synthesis of benzoxanthenes by conventional heating method in presence of ZnCl₂, POCl₃ as catalyst was reported by Liu Yet al⁹¹.

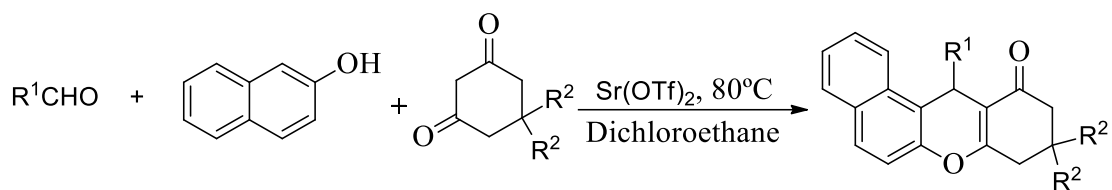
Structural activity relationship was studied by evaluating their inhibitory activities towards yeast α -glucosidase by the researchers. It was concluded by them that inhibitory activity of benzoxanthone towards yeast α -glucosidase was many times more than that of xanthenes.

In the year 2007, Novel formation of benzofused analogues of xanthenes by refluxing with $\text{NaHSO}_4\text{-SiO}_2$ catalyst and DCM solvent was developed by Das B, Laxminarayan K et al⁹². Several reactions were performed by them for the selectivity and efficiency of catalysts. First the reaction was conducted by Das B. et al by taking 4-chlorobenzaldehyde as representative aldehyde individually with catalysts $\text{NaHSO}_4\text{-SiO}_2$, Amberlyst-15 and montmorillonite K-10 clay in DCM under reflux for five hrs. Maximum yield was obtained by the application of $\text{NaHSO}_4\text{-SiO}_2$ catalyst. Then reactions were carried out by them first without solvent and then with different solvents like DCM, chloroform and acetonitrile by taking catalyst $\text{NaHSO}_4\text{-SiO}_2$ and achieved highest yield with DCM.



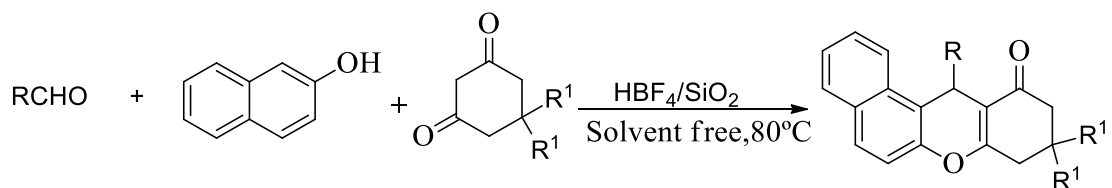
Scheme-2.27: Synthesis of benzoxanthenes by Das B et al⁹²

In the year 2008, benzoxanthone derivatives were prepared with the help of strontium triflate catalyst and 1, 2-dichloroethane solvent by conventional heating by researchers Li J, Tang W et al⁹³. To check selectivity and efficiency of catalysts and solvents, reactions were conducted with variety of catalysts and also with different amounts of catalysts and finally inferred that better catalytic activity was shown by 10 mol% strontium triflate and DCM was selected as best solvent by the researchers as maximum yield of product was procured under these conditions. Further the recyclability of catalyst was also examined by them. It was also found by Li J et al that no loss of catalytic activity occurred even after reusing it 5 times.



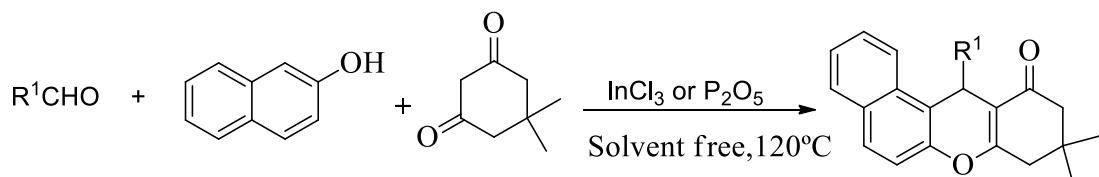
Scheme-2.28: Sr(OTf)₂ catalysed synthesis of benzoxanthenes by Li J et al⁹³

In the year 2009, Xanthone derivatives were synthesized efficiently without using solvent with HBF₄/SiO₂ catalyst by heating was documented by Zhang ZH et al⁹⁴. Reactions were done with different amounts of HBF₄/SiO₂, different solvents and at different temperatures by them and finally it was inferred by them that most appropriate reaction conditions for formation of benzoxanthone are 10 mol% HBF₄/SiO₂, solvent free and 80 °C temperature.



Scheme-2.29: Synthesis of benzoxanthenes by Zhang ZH et al⁹⁴

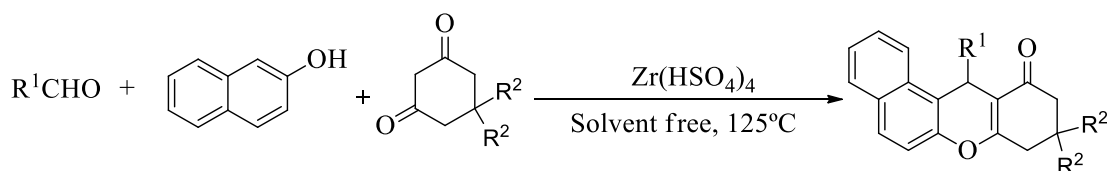
In the year 2009, Solventless preparation of benzoxanthone derivatives by using catalytic amount of InCl₃ or P₂O₅ by conventional heating was reported by Nandi GC et al⁹⁵. To perform reaction first the reactants were grounded then catalyst InCl₃ (30 mol %) or P₂O₅ (20 mol%) was added and again grounded for more 15 min by them. Then reaction mixture was heated in oil bath at 120 °C. Efficiency of both the catalysts were also compared by Nandi et al and inferred that InCl₃ was better catalyst than P₂O₅ in terms of yield as well as time.



Scheme-2.30: InCl₃ or P₂O₅ catalysed synthesis of benzoxanthenes by Nandi GC et al⁹⁵

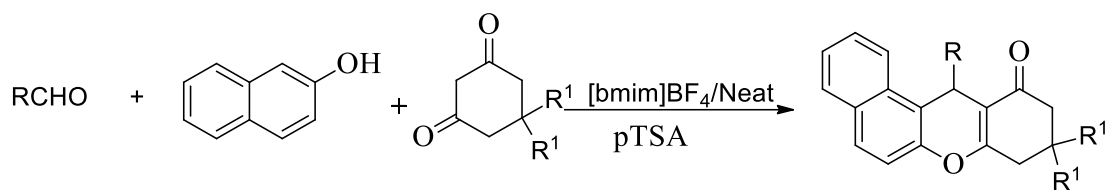
In the year 2009, Ecofriendly formation of benzofused derivative of xanthenes by using TBAF as PTC in Water as a Green medium was developed by Gao S et al⁹⁶. To set up reaction conditions, first model reactions were carried out with different catalysts in different amount and in different solvents by taking 4-fluorobenzaldehyde by Gao S et al. 10 mol % TBAF in water solvent was proved to be best catalyst as with it provided maximum yield. Further the recyclability of catalyst was determined by them and it was seen by them that TBAF can be recovered and reused 4 times without much lost in its effectiveness.

In the year 2009, A Green procedure for the formation of derivatives of xanthen-11-one without application of Solvent in presence of $Zr(HSO_4)_2$ was described by Foroughifar et al⁹⁷. Reactions were conducted by the researchers with different amount of catalyst under solvent free conditions at 125⁰C with one representative aldehyde and noticed that 2 mol% of catalyst gave maximum yield. These conditions were applied for reactions with other aldehydes. Catalyst was also reused by recovering it and seen that no significant decrease in activity of catalyst occurred even after using it 5 times.



Scheme-2.31: $Zr(HSO_4)_2$ catalysed synthesis of benzoxanthenes by Foroughifar et al⁹⁷

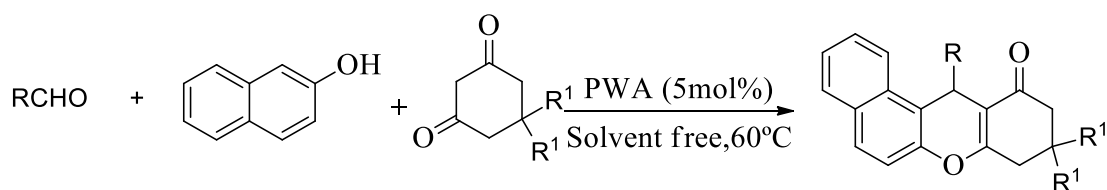
In the year 2009, Preparation of highly substituted derivatives of xanthen-11-ones catalyzed pTSA in ionic liquid and under Solventless conditions was developed by Khurana JM, Magoo D⁹⁸. By using paratoluenesulphonic acid as catalyst, they reactions were conducted without solvent by heating at 120 °C in oil bath and also with ionic liquid at 80 °C separately. It was noticed by them that without the application of ionic liquid reactions progressed at faster rate.



Scheme-2.32: Synthesis of benzoxanthenes by Khurana JM, Magoo D⁹⁸

In the year 2009, Benzofused derivatives of xanthenes were synthesized by utilizing Iodine-catalyst by researchers Wang RZ et al⁹⁹. To set up efficient conditions for conducting reactions, model reaction was carried out by Wang RZ et al by selecting one representative aldehyde with as well as without solvent and also with different amount of catalyst and it was found that 10 mol% of catalyst under Solventless conditions increased the rate as well as yield of reactions.

In the year 2009, Dodecatungstophosphoric acid catalyzed preparation of benzoxanthone analogues was reported by Wang HJ et al¹⁰⁰. A long chain of benzoxanthenes was prepared by using wide range of aromatic aldehydes by the researchers. It was found by scientists that reactions took 40-95 min for completion and products were obtained in excellent yield. It was further claimed by them that catalyst can be used again and again without losing its activity and influencing the yield of product.

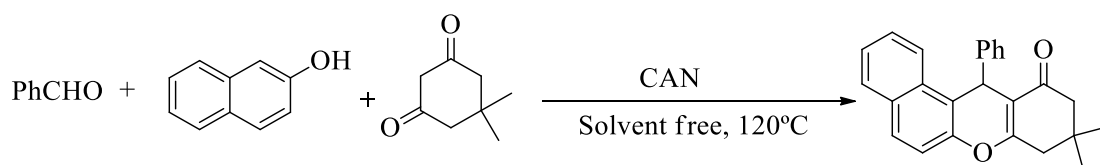


Scheme-2.33: PWA catalyzed synthesis of benzoxanthenes by Wang HJ et al¹⁰⁰

In the year 2010, A library of benzoxanthone derivatives under Solventless conditions with the aid of silica- perchloric acid catalyst by heating was synthesized by Mo LP et al¹⁰¹. By carrying out model reaction with 4-chlorobenzaldehyde as representative aldehyde the appropriate conditions for the reactions was set up by the researchers. For this purpose reactions were conducted at different temperatures with different

amount of catalysts and also with same amount of different catalysts. Finally it was sum up by them that among all the solid catalysts silica- perchloric acid in 0.01g was most effective at 80 °C as it provided maximum yield under these conditions.

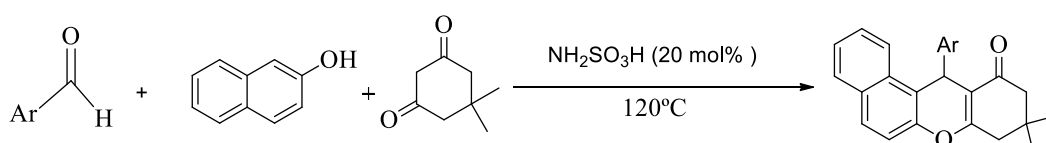
In the year 2010, Solventless synthesis of benzoxanthone derivatives using CAN by heating was carried out by Kumar A, Sharma S et al¹⁰². Reactions were performed first without catalyst and then with variety of catalysts by varying amount of catalyst by them and found 5 mol % the best amount as it provided highest yield, the yield did not vary significantly even after reusing catalyst five times. Then reactions were conducted by them with this catalyst by applying different solvents as well as in the absence of solvent and considered Solventless conditions best for all the reactions.



Scheme-2.34: Synthesis of benzoxanthenes by Kumar A, Sharma S et al¹⁰²

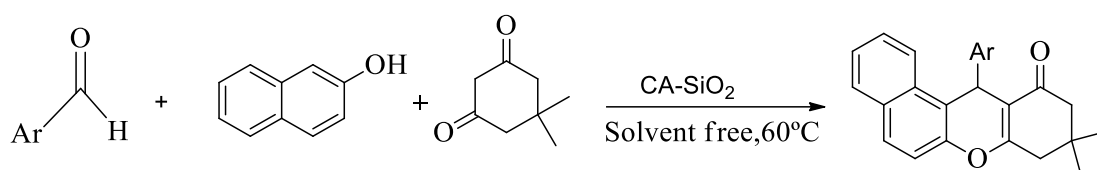
In the year 2010, Proline triflate catalyzed synthesis of benzoxanthenes in green solvent water was reported by Li JJ et al¹⁰³. Reactions were carried out with different catalysts along with different solvents by the researchers and detected 10 mol % proline triflate as best catalyst and water as suitable solvent. Reactions with different aldehydes were performed by Li JJ et al and observed that the products were formed in 2.5 to 4 hrs under reflux conditions.

In the year 2010, A series of benzofused derivatives of xanthen-11-ones and xanthen-9-ones with fused heterocyclic ring was assembled by catalyst Sulfamic acid without solvent, documented by Heravi M, Alinejhad H et al¹⁰⁴. They performed reactions with 20 mol% of Sulfamic acid at 120 °C and found that reactions took 1.5 to 2.16 hrs for completion and provided products in excellent amount.



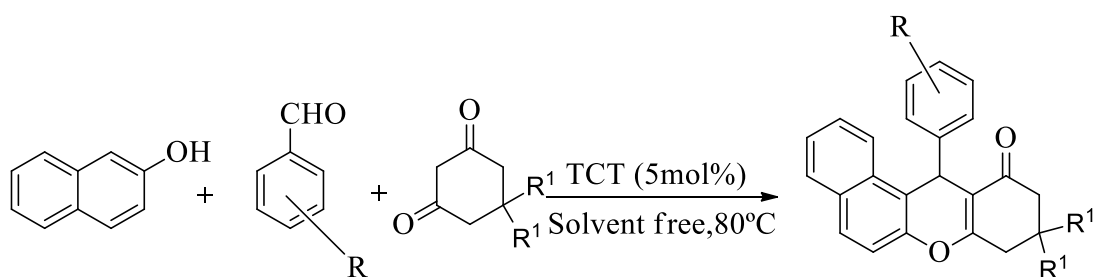
Scheme-2.35: Synthesis of benzoxanthenes by Heravi M, Alinejhad H et al¹⁰⁴

In the year 2010, A new approach for the preparation of benzoxanthone in existence of Caro's Acid–Silica Gel was reported by Karimi N et al¹⁰⁵. To set the optimum reaction conditions model reaction was first carried them by taking benzaldehyde as representative aldehyde at different temperatures and then with different amount of catalyst and noticed that optimum temperature and amount of catalyst was 60 °C and 0.1g respectively. By applying these conditions reactions were conducted by them with various aldehydes and very good yield of products was attained.



Scheme-2.36: Synthesis of benzoxanthenes by Karimi N et al¹⁰⁵

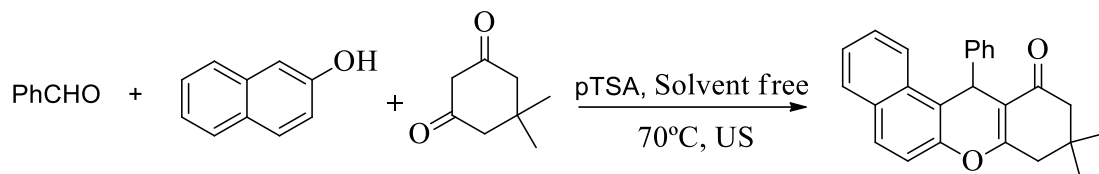
In the year 2010, Solventless condensation of dimidone, 2-naphthol and different aldehydes of 12-along with catalytic amount of cyanuric chloride was given by Zhang ZH et al¹⁰⁶. Optimization of reaction conditions was brought about by Zhang ZH et al by performing model reaction of 4-chlorobenzaldehyde with variety of catalysts, for varying period of time and catalyst amount. Finally it was concluded by them that optimum conditions for conducting reactions were 5 mol % of TCT at 80 °C under solvent free conditions.



Scheme-2.37: Synthesis of benzoxanthenes by Zhang ZH et al¹⁰⁶

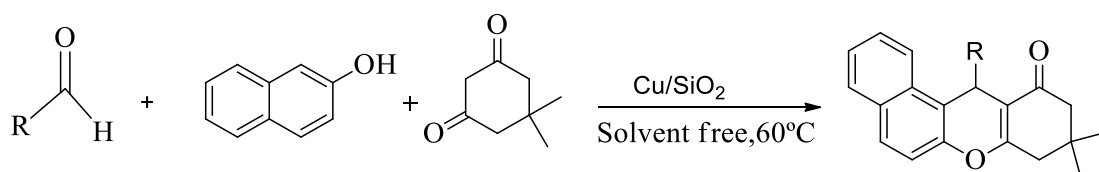
In the year 2010, Ultrasound assisted and Solvent-Free Aldehydes, 2- Naphthol and 5, 5-dimethylcyclohexan-1,3-dione in a single container catalysed by p-TSA was documented by Li, J et al¹⁰⁷. Reactions were carried out by Li J et al by using catalytic amount of p-TSA (10 mol%) in a number of solvents for proper solvent

selection and noticed that in the absence of solvent highest yield of products was obtained.



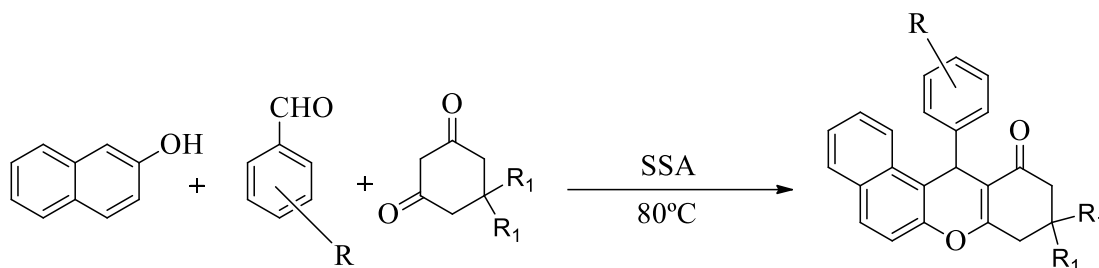
Scheme-2.38: pTSA catalysed synthesis of benzoxanthenes by Li, J et al¹⁰⁷

In the year 2011, Solventless Synthesis of benzoxanthone analogues in the presence of catalyst Cu/SiO₂ was given by Oskooie HA, Heravi MM et al¹⁰⁸. To check the selectivity and efficiency of catalyst reactions were conducted with variety of catalysts and by varying the amount of catalyst by them and noted that Cu/SiO₂ in 0.05g was most fit catalyst. It was further seen by them that catalyst can be reused two three times without significant changes in its catalytic activity.



Scheme-2.39: Synthesis of benzoxanthenes by Heravi MM et al¹⁰⁸

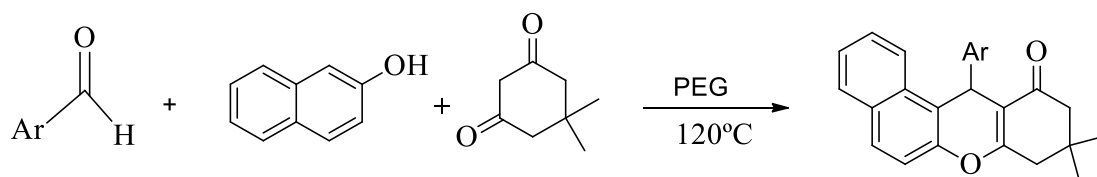
In the year 2011, A library of 9, 10-dihydro-12 aryl-8*H*-benzo[α]xanthene-11(12*H*)-one was synthesized by Silica sulphuric acid catalyst in the absence of solvent was described by Nazeruddin GM, Pandharpatte MS, Mulane KB¹⁰⁹. Reactions were conducted by Nazeruddin et al first without catalyst and then in presence of catalysts like SiO₂, H₂SO₄ and silica sulphuric acid and found that the later one was best on the basis of yield. Then with this catalyst the reactions were performed with different amount of catalyst at different temperatures and finally it was concluded by them that 0.08g of SSA and 80 °C the optimum conditions for formation of various benzoxanthone analogues.



Scheme-2.40: Synthesis of benzoxanthenes by Nazeruddin GM et al¹⁰⁹

In the year 2011, Microwave Promoted Single Pot Synthesis of Xanthene Derivatives by Perchloric Acid catalyst under Solventless conditions was documented by Nazeruddin GM, Pandharpatte MS¹¹⁰. By using 0.3mmol of perchloric acid and 420 w power of MW all the reactions were performed by them. Within a time span of 2-3 min products were obtained in excellent yield by the researchers. Although their approach was quite green but use of perchloric acid was not safe.

In the year 2011, PEG-400 employed as environmental friendly reaction medium for the preparation of benzoxanthone was developed by Shitole NV et al¹¹¹. By applying PEG-400 as reaction medium reactions were carried out by Shitole et al at various temperatures with 4-chlorobenzaldehyde and came to conclusion that 120 °C temperatures is efficient for the formation of benzoxanthone analogues as at this temperature maximum yield was obtained. Yield was also checked by researchers by reusing the catalyst and noticed that the yield did not change appreciably.

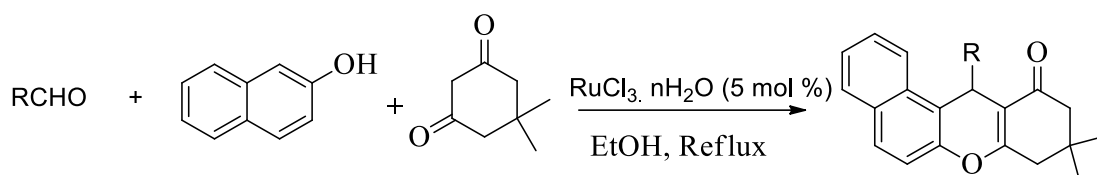


Scheme-2.41: PEG-400 catalysed synthesis of benzoxanthenes by Shitole NV et al¹¹¹

In the year 2011, A series of xanthen-11-one with fused benzene rings was prepared by applying Ultrasound irradiations as ecofriendly source of energy, with Catalyst ClSO₃H without the use of Solvent was reported by Nazeruddin GM, Al-Kadasi AMA¹¹². Reactions were conducted with several aldehydes by them and in short duration of time (15-40 min) they got products in excellent amounts (83-98 %). It was

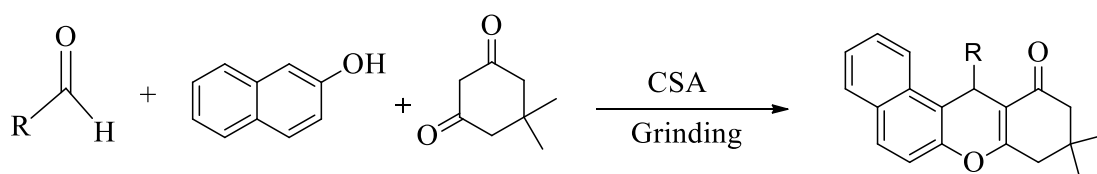
claimed by Nazeruddin GM et al that applications of US irradiations and solvent free conditions were in accordance with protocols of green chemistry but the use of ClSO_3H was against the ethics of green chemistry.

In the year 2011, A series of derivatives of xanthen-11-one was prepared by applying homogeneous catalyst $\text{RuCl}_3 \cdot n\text{H}_2\text{O}$ (5 mol %) by refluxing (80 °C) by Tabatabaeian K, Khorshidi A et al ¹¹³. Reactions were carried out by Tabatabaeian K et al with the application of wide variety of aldehydes and products were obtained in quite high yield. The influence of reusability of catalyst on amount of product was also determined by the researchers and noticed no appreciable change in amount. The some reactions were also performed under MW irradiations by using same catalyst. In the end it was concluded by them that MW assisted reactions proceed at much faster rate than by refluxing method.



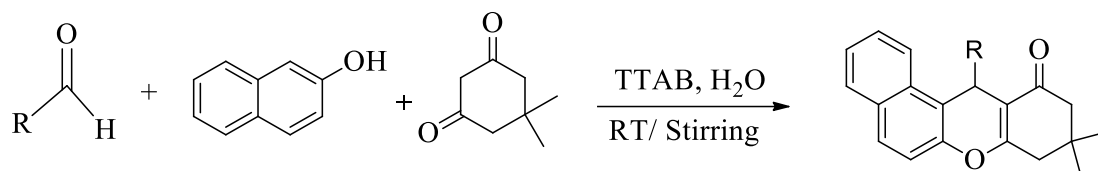
Scheme-2.42: Synthesis of benzoxanthenes by Tabatabaeian K, Khorshidi A et al ¹¹³

In the year 2011, A novel synthetic Route for the synthesis of Tetrahydrobenzo[a]xanthen-11-ones *via* Grinding Technique using Camphor sulphonic acid catalyst was developed by Pravin VS et al¹¹⁴. First of all screening of catalysts was done under grinding technique by the researchers and found camphor sulphonic acid as best catalyst. After screening of catalyst the reactions were conducted with CSA by heating as well as by stirring with water at room temperature. It was decided by researchers that grinding method was better than other as it took lesser time and provided higher yield.



Scheme-2.43: Grindstone assisted and CSA catalysed synthesis of benzoxanthenes by Pravin VS et al¹¹⁴

In the year 2011, A chain of benzofused analogues of xanthen-11-ones was composed by using a surfactant catalyst Tetradecyltrimethylammoniumbromide in water at ambient temperature by Shingare MS et al¹¹⁵. After initial screening of surfactants tetradecyltrimethylammonium bromide was selected as perfect one for performing reactions by Shingare et al. Then the reactions were performed by them with different concentrations of TTAB and finally 15 mol % was selected as efficient conc. Further the effect of temperature on the rate of reactions was observed by them and they noticed that with increasing temperature, yield of products decreased. So the reactions were carried out at Room temperature by them.

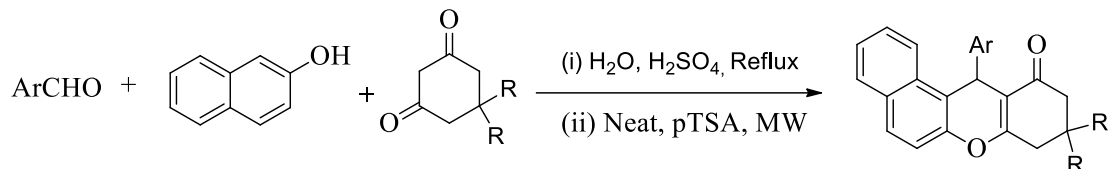


Scheme-2.44: TTAB catalysed synthesis of benzoxanthenes by Shingare MS et al¹¹⁵

In the year 2011, A simple and systematic method for the preparation of benzoxanthenes involving use of Ammonium chloride catalyst under solvent free conditions was stated by Foroughifar N et al¹¹⁶. First of all a model reaction was performed by them by taking benzaldehyde, 2-naphthol and dimecane without solvent and with number of solvents (EtOH, DCM, CH₃CN, THF and Toluene). It was noticed by them that solventless condition was best to carry out all the reactions. After judicious choice of solvent a model reaction was carried by the scientists by changing the amount of catalyst and temperature. It was cited by them that 10 mol % of catalyst at 120 °C most favorable to conduct all the reactions.

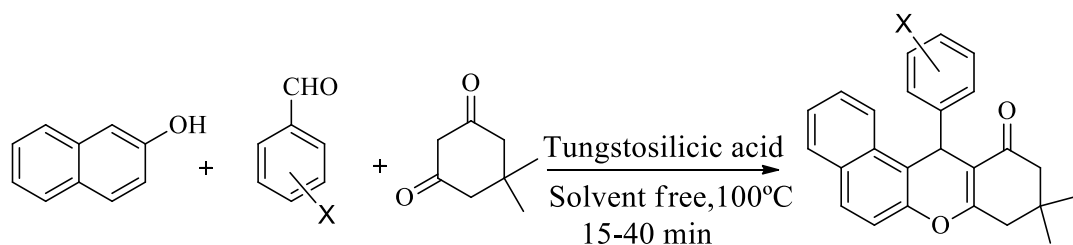
In the year 2012, The formation of chain of benzoxanthenes (a) by refluxing with sulphuric acid in water (b) solvent free, MW assisted and pTSA catalysts were explained by Khurana JM, Lumb A et al⁴⁴. Two set of conditions for the formation of benzoxanthenes were applied by Khurana et al. Comparison of these set of conditions against one another was also done by them. They noticed that yield of benzoxanthone

analogues was higher under former set of conditions where as speed of reactions was faster under MWI method.



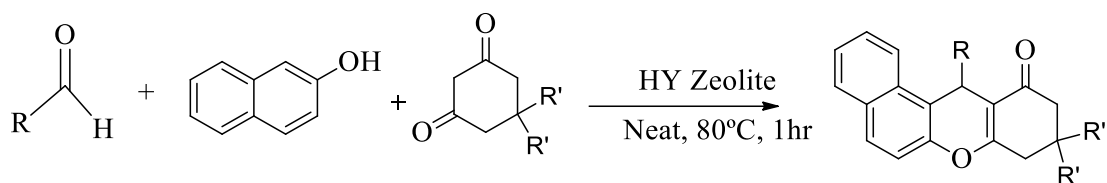
Scheme-2.45: Synthesis of benzoxanthenes by Khurana JM, Lumb A et al⁴⁴.

In the year 2012, Solvent-Free, $\text{H}_4\text{SiW}_{12}\text{O}_{40}$ Catalyzed formulation of benzoxanthenes was reported by Hassankhani A et al¹¹⁷. Reactions were run by them with and without catalyst. It was observed by them that without catalyst product was obtained in trace amount after long period of time whereas in presence of catalyst products were formed quickly in excellent amount. Another important feature of the catalyst was also mentioned by them that it can be recycled and used again and again. By using this catalyst a long series of benzoxanthone analogues in very efficient way was prepared by the researchers.



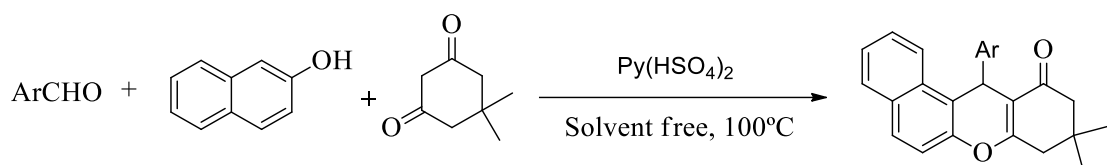
Scheme-2.46: Solvent free synthesis of benzoxanthenes by Hassankhani A et al¹¹⁷

In the year 2012, Solvent free multicomponent single pot construction of benzoxanthenes catalysed by HY zeolite was reported by Rama V et al¹¹⁸. A chain of reactions were performed by them under various conditions like without solvent and without catalyst; with catalyst and variety of solvents; with catalyst and without solvent. Finally it was inferred by the researchers that 20 mg of HY zeolite under solvent free conditions provided highest yield of products. Further with this amount of catalyst the effect of increase in temperature was determined by them and observed that 80°C was most suitable for the formation of benzoxanthone analogues.



Scheme-2.47: Synthesis of benzoxanthenes by Rama V et al¹¹⁸

In the year 2012, A long series of benzoxanthone analogues was prepared by Zare A et al¹¹⁹ in the presence of protic acidic ionic liquid pyrazinium di(hydrogen sulfate) {Py(HSO₄)₂} under solvent free conditions at 100 °C. A model reaction was first performed with no. of catalysts by the researchers and they noticed that {Py(HSO₄)₂} gave excellent yield of product in short duration of time. After this assessment of suitable amount of catalyst by conducting model reaction with varying amount of catalyst at different temperatures was executed by them and it was observed by them that 10 mol% amount of catalyst at 100 °C the most relevant one to perform all the reactions..



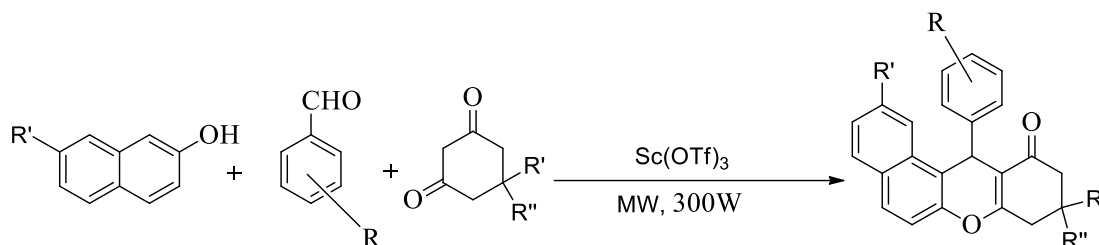
Scheme-2.48: Synthesis of benzoxanthenes by Zare A et al¹¹⁹

In the year 2012, Triethylamine -bonded sulfonic acid {[Et₃N -SO₃H]Cl} catalysed formation of benzoxanthone under solventless condition was described by Zare A et al¹²⁰. The evaluation of various parameters like catalyst quantity and temperature was done by the scientists carrying out model reactions with 4-nitrobenzaldehyde dimedone and 2-naphthol. It was investigated by them that 25 mol% catalyst at 120 °C were most appropriate for performing series of reactions with other aldehydes.

In the year 2012, An easy and systematic green procedure for the synthesis of benzofused analogues of xanthenes was depicted by Rajitha B et al¹²¹. For this purpose reaction mixture along with 10 mol% of Ionic liquid (4-sulfobutyl)tris(4-sulfophenyl)phosphonium hydrogen sulphate was heated (80 °C) by them. A long series of benzoxanthenes in very short duration of time (0.5 to 1 Hr) was prepared by

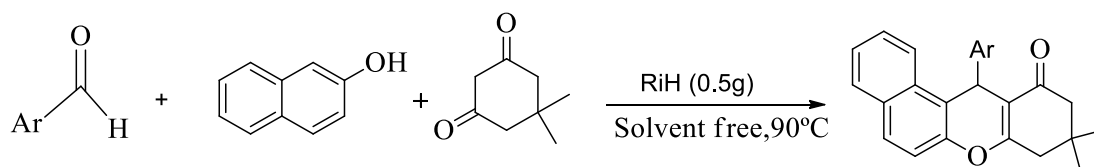
Rajitha et al. It was seen by researchers that yield of product was unchanged even after using the catalyst five times.

In the year 2012, Microwave assisted formation of benzoxanthenes catalysed by scandium triflate was given by Rao MS et al¹²². Screening of different parameters like quantity of catalyst, solvent, time and power of MW reactor was also done by them by performing model reaction. In the end it was found by them that 20 mol % of catalyst under neat conditions for 5 min exposure to MW irradiations at 300W were most efficient conditions for synthesizing variety of benzoxanthenes.



Scheme-2.49: MW assisted synthesis of benzoxanthenes by Rao MS et al¹²²

In the year 2013, The synthesis of a chain of benzofused analogues of xanthen-11-ones catalysed by husk of Rice as green, moderate and reusable catalyst was reported by Shirini F et al¹²³. The various benzoxanthone analogues were obtained in time duration of 30-75 min in excellent amount by Shirini F et al. Reactions were carried out with different amount of rice husk (RiH) at different temperatures by them and best results were achieved with 0.5 g of RiH in the absence of solvent at 90 °C.

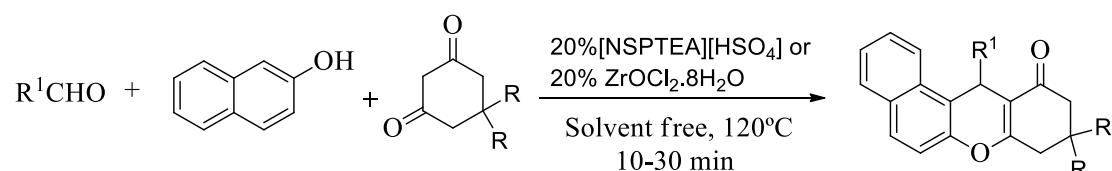


Scheme-2.50: Rice husk catalysed synthesis of benzoxanthenes by Shirini F et al¹²³

In the year 2013, A new method for the synthesis of benzoxanthenes by the use of vitamin B₁ i.e. thiamine hydrochloride as a green catalyst in aqueous micellar system was described by Fatma S et al¹²⁴. Testing of parameters such as type of surfactant and amount of catalyst was done by the researchers by conducting model reaction

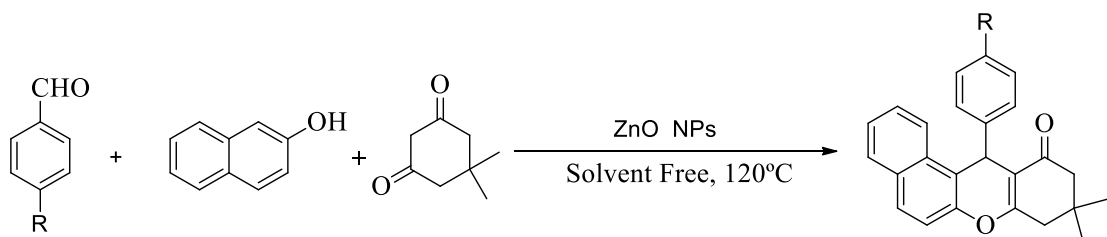
with 4-chlorobenzaldehyde. After testing it was mentioned by them that 5 mol% of Vitamin B₁ with CTAB at RT were perfect conditions to perform all the reactions. By applying these conditions a very long series of benzoxanthenes was made by them.

In the year 2013, A systematic method for the formation of benzoxanthenes was given by Xu-dong JIA et al¹²⁵. Ionic liquid [NSPTEA][HSO₄] and ZrOCl₂·8H₂O were individually applied as catalyst under solvent-free conditions by them. To accomplish the task the reaction mixture was heated in oil bath at 120 °C for suitable time by the researchers. Optimization of the reaction conditions by running model reaction with different quantity of catalyst and also with number of solvents was also done by the scientists. In the end it was found by them that 20% of catalyst under solventless conditions was the most relevant one.



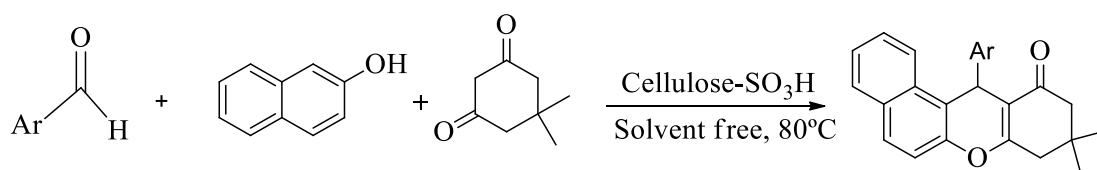
Scheme-2.51: Synthesis of benzoxanthenes by Xu-dong JIA et al¹²⁵

In the year 2014, A Systematic and easy construction of xanthen-11-ones derivatives catalysed by Nanoparticles of Zinc Oxide was done by Safaei-Ghomi J et al¹²⁶. To choose optimum catalyst the model reaction were carried out with different catalysts and ZnO nanoparticles were chosen as best catalyst. The optimization of the amount of ZnO NP was done by researchers and found 10mol% amount as most suitable one as it gave maximum yield. Further the selection of optimum solvent was also done by conducting model reaction with varying solvents and also without solvent by the researchers and noticed that solvent free conditions at 120 °C best suited for reactions.



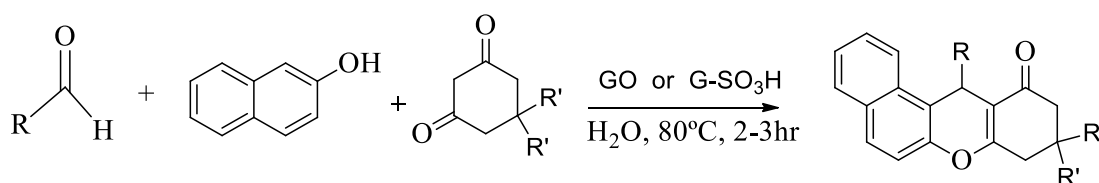
Scheme-2.52: Synthesis of benzoxanthenes by Safaei-Ghomi J et al¹²⁶

In the year 2014, A green procedure for the designing of benzofused derivatives of xanthone by making use of cellulose-SO₃H as biodegradable, reusable catalyst was developed by Shaterian HR et al¹²⁷. A series of benzoxanthenes was obtained by them by conducting reactions with 0.1g of catalyst at 80 °C. All the derivatives were obtained in good to excellent yield in short duration of 10 to 19 min by the Shaterian HR et al.



Scheme-2.53: Synthesis of benzoxanthenes by Shaterian HR et al¹²⁷

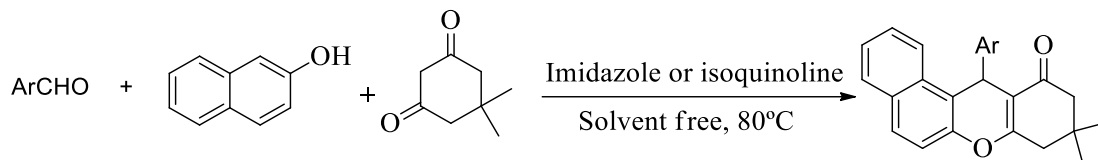
In the year 2014, Preparation of benzofused derivatives of xanthone-11-one catalysed by Graphene oxide and sulphated grapheme nanosheets was given by Shaabani A et al¹²⁸. The reactions were performed by them at 80 °C with 0.03g GO and 0.02g GO-SO₃H in aqueous medium. Reaction conditions were assessed by running model reaction first with different quantity of catalyst and then with varying solvents by the scientists. In the end comparison of the efficacy of GO and GO-SO₃H was done by them and it was investigated by them that GO-SO₃H was more efficient than GO in terms of yield.



Scheme-2.54: Synthesis of benzoxanthenes by Shaabani A et al¹²⁸

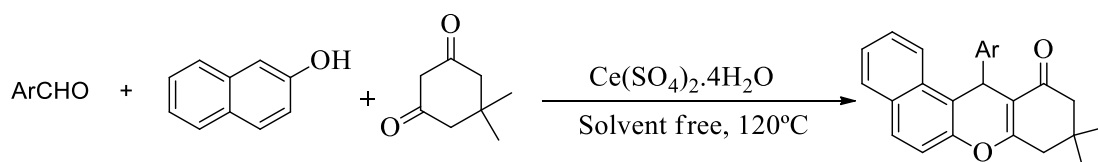
In the year 2015, Neutral and efficient organo-catalysts i.e. imidazole and isoquinoline were employed for formation of benzoxanthenes in single vessel without using solvent was developed by Heydari R et al¹²⁹. To optimize reaction conditions, the model reactions were performed by taking different quantity of catalyst under different temperature conditions by Heydari R et al and found 10 mol % of imidazole and 15 mol % of isoquinoline the suitable amount of catalyst at temperature of 80 °C under solvent free conditions. Comparison of the efficiency of catalysts was also

executed and noticed that imidazole worked as better catalyst than isoquinoline because it provided products in short duration of time as compared to isoquinoline.



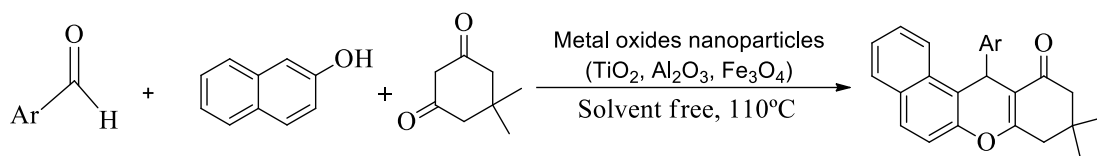
Scheme-2.55: Synthesis of benzoxanthenes by Heydari R et al¹²⁹

In the year 2015, A Fast and green method for the formulation of series of benzofused derivatives of Xanthenes catalysed by cerium (IV) sulphate tetrahydrate as a novel, heterogeneous, reusable catalyst was developed by Taghavi-Khorasani F et al¹³⁰. To set suitable reaction conditions model reaction was run with different solvents as well as without solvent by Taghavi-Khorasani F et al and detected solvent free conditions best suited. Further model reaction was performed with different quantity of catalyst at different temperatures by them and seen that 0.1g of catalyst at 120 °C as best set of conditions as under this set of reaction conditions maximum yield was obtained by Taghavi-Khorasani F et al.



Scheme-2.56: Ce(SO₄)₂.4H₂O catalysed synthesis of benzoxanthenes by Taghavi-Khorasani F et al¹³⁰.

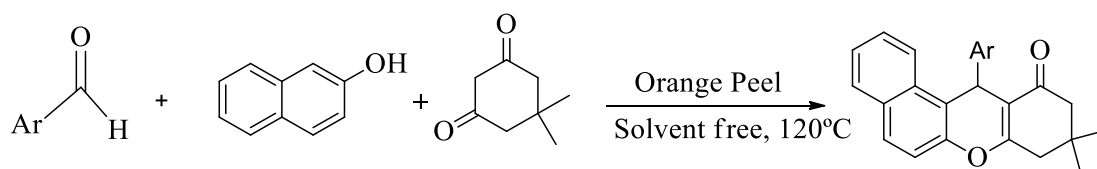
In the year 2016, A comparative study of oxides of Ti, Al and Fe nanoparticles as a reusable heterogeneous catalysts for the preparation of benzoxanthenes analogues was given by Davoodnia A et al¹³¹. By conducting model reaction with nanoparticles of oxides of Ti, Al And Fe under different conditions like with varying amount of catalyst and at different temperatures, optimization of reaction conditions was done. In the end conclusion was drawn by them that with 20 mol % without using solvent at 110 °C were most favorable conditions for formation of benzoxanthone. The properties of recyclability and reusability of catalyst was also mentioned in their work was obtained.



Scheme-2.57: Synthesis of benzoxanthenes by Davoodnia A et al¹³¹

In the year 2016, An extremely simple and highly systematic construction of benzofused derivatives of xanthenes by organo-catalyst-Guanidine Hydrochloride was done by Sadeghpour M et al¹³². First of all model reaction was run with salicylaldehyde at various temperatures and noticed that 80 °C was most effective temperature in terms of time as well as yield. Then the reactions were conducted with various concentrations of catalyst by them and found 10 mol % as most suitable concentration. By applying this set of reaction conditions products were obtained within 15-60 min in good to excellent yield by Sadeghpour M et al.

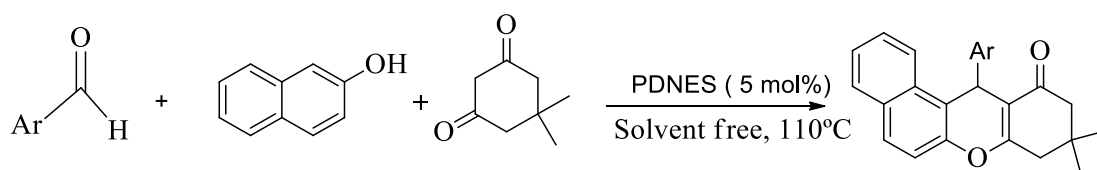
In the year 2016, A green procedure for the preparation of benzoxanthone derivatives catalysed by orange peel as natural green catalyst was described Taghavi F et al¹³³. A model reaction by taking benzaldehyde as representative aldehyde with varying amount of catalyst at various temperatures was performed by Taghavi F et al to fix suitable reaction conditions. A model reaction was also carried out by the investigators without solvent as well as with solvents. In the end most appropriate reaction conditions chosen by them were 0.05g of catalyst at 120 °C under solvent free condition. A number of reactions with wide variety of aldehydes were run by them by applying these conditions.



Scheme-2.58: Orange peel catalysed synthesis of benzoxanthenes by Taghavi F et al¹³³

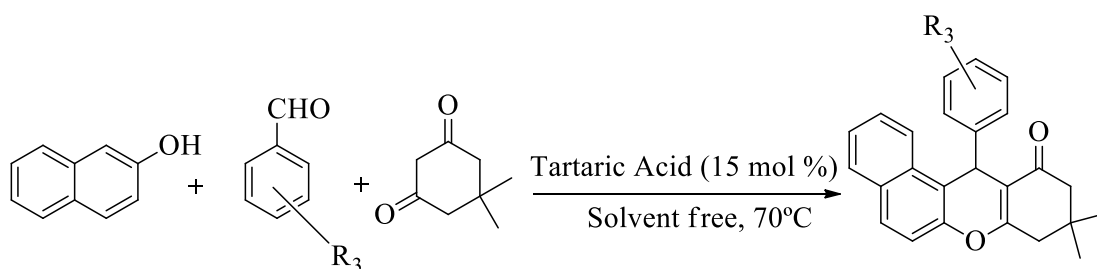
In the year 2017, Solvent free synthesis of benzofused analogues of xanthene-11-one by applying of poly(N,N'-dibromo-N-ethyl-naphthyl-2,7-sulfonamide) i.e PDNES was

described by Khazaei A et al¹³⁴. A reaction of benzaldehyde, dimedone and β -naphthol was selected by them as model reaction to assess suitable reaction conditions. The effect of amount of catalyst, temperature and solvent was studied by them by performing the model reaction. In the end it was described by them that 5 mol% catalyst at 110 °C without using solvent was most appropriate to conduct series of reactions.



Scheme-2.59: PDNES catalysed synthesis of benzoxanthenes by Khazaei A et al¹³⁴

In the year 2018, A series of Xanthen-11-ones fused with benzene rings with catalytic amount of tartaric acid without Solvent- was reported by Maghsoodlou MT et al¹³⁵. First model reactions without tartaric acid and also with various amounts of tartaric acid at different temperatures with and without solvent were performed by researchers. Best result was achieved with 15 mol % of tartaric acid at 70 °C under Solventless conditions.

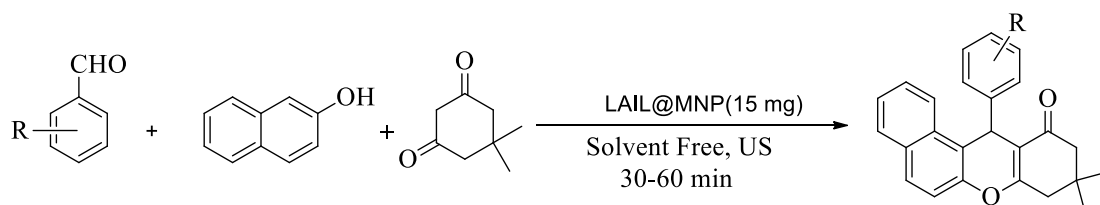


Scheme-2.60: Tartaric acid catalysed synthesis of benzoxanthenes by Maghsoodlou MT et al¹³⁵

In the year 2018, The formation of benzoxanthenes by using altered magnetic nanoparticles was done by Taghavi F et al¹³⁶. First of all representative reactions were run with varying quantity of Cu (II) nanoparticles with wide range of solvents at different temperatures to optimize reaction conditions by the researchers. At the end it

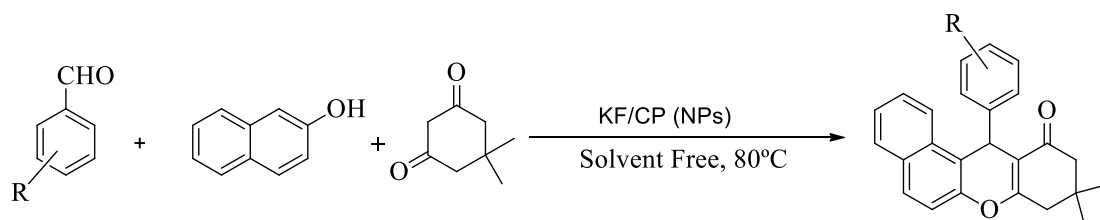
was sum up by them that 0.02 g of catalyst at 120 °C under Solventless conditions was most appropriate one.

In the year 2018, An ultrasound assisted synthesis of benzofused derivatives of xanthenes by the use of magnetic nanomaterial-immobilized Lewis acidic ionic liquid (LAIL@MNP) was reported by Nguyen HT et al¹³⁷. It was seen by them that the catalyst applied was quite efficient having good recyclability and ability to catalyse reactions under mild conditions. The efficiency of catalyst was examined by the researchers by using similar type of nanocatalysts. It was investigated by them that 15 mg of LAIL@MNP at 80 °C under solvent free sonication conditions was best to carry out reactions.



Scheme-2.61: US assisted synthesis of benzoxanthenes by Nguyen HT et al¹³⁷

In the year 2019, A series of benzoxanthenes was synthesized by Khalilzadeh MA et al¹³⁸ by using KF impregnated on clinoptilolite nanoparticles as catalyst. It was noticed by them that reaction proceeds smoothly in solvent free conditions. Then screening of other parameters such as temperature, amount and influence of catalyst was done by them to optimize reaction conditions. It was observed by them that no product was formed in the absence of catalyst. In the end it was concluded by the researchers that excellent yield of benzoxanthenes was obtained with 0.03g KF impregnated on clinoptilolite under solvent free conditions at 80 °C.



Scheme-2.62: Synthesis of benzoxanthenes by Khalilzadeh MA et al¹³⁸

Table-2.2: Various Reaction conditions, catalysts and solvents for the synthesis of Benzoxanthenes

S.NO.	Reference	Catalyst	Solvent	Reaction conditions
1	91	ZnCl ₂ -POCl ₃	-----	Heat(70-80 °C)
2	92	NaHSO ₄ -SiO ₂	1,2-Dichloroethane	Reflux(4-7Hrs)
3	93	Sr(OTf) ₂	1,2-Dichloroethane	Heat(80°C for 5- 7Hrs)
4	94	HBF ₄ /SiO ₂	-----	Heat(80°C, 55-90 min)
5	95	InCl ₃	-----	Heat(120°C, 25-75 min)
		P ₂ O ₅	-----	Heat(120°C, 30-80 min)
6	96	TBAF	Water	Reflux(2 Hrs)
7	97	Zr(HSO ₄) ₂	-----	Heat (125°C, 20 min)
8	98	pTSA	[bmim]BF ₄	Heat (80°C, 2-3 Hrs)
			-----	Heat (80°C, 35-45 min)
9	99	Iodine	-----	Heat (60°C, 45-95 min)
10	100	Dodecatungstophosphoric acid	-----	Heat (60°C, 40-95 min)
11	101	HClO ₄ -SiO ₂	-----	Heat (80°C, 0.8-1.5Hrs)
12	102	CAN	-----	Heat (120°C)
13	103	Proline triflate	Water	Reflux(4.5-15 Hrs)
14	104	Sulfamic acid	-----	Heat (120°C,1.5-2.16Hrs)
15	105	Caro acid	-----	Heat (60°C, 30-55min)
16	106	TCT	-----	Heat (80°C, 30-70min)
17	107	pTSA	-----	US(70°C)
18	108	Cu/SiO ₂	-----	Heat (60°C, 20-35min)
19	109	SSA	-----	Heat (80°C, 15-210min)
20	110	HClO ₄	-----	MW(2-120min)
21	111	PEG-400	-----	Heat (120°C, 5.5-7.5 Hrs)
22	112	ClSO ₃ H	-----	US(15-40 min)
23	113	RuCl ₃ .nH ₂ O	EtOH	Heat (80°C, 30-70 min)

24	114	CSA	-----	RT(15-50 min)
25	115	TTAB	Water	Heat(RT, 2-8Hrs)
26	116	NH ₄ Cl	-----	Heat (120°C, 8-60 min)
27	44	H ₂ SO ₄	Water	Reflux(2-3Hrs)
		pTSA	-----	MW(4-6 min)
28	117	H ₄ W ₁₂ SiO ₄₀	-----	Heat (100°C, 15-40 min)
29	118	HY-Zeolite	-----	Heat (100°C, 5 Hrs)
30	119	{Py(HSO ₄) ₂ }	-----	Heat (100°C, 15-45 min)
31	120	{[Et ₃ N –SO ₃ H]Cl}	-----	Magnetically stir (100°C, 30-60 min)
32	121	[P(PhSO ₃ H) ₃ C ₄ H ₈ SO ₃ H] HSO ₄	-----	Heat (80°C, 15-45 min)
33	122	Sc(OTf) ₃	-----	MW(300W, 5 min)
34	123	Rice husk	-----	Heat (90°C, 30-75 min)
35	124	Thiamine hydrochloride	water/CTAB micelle	RT(45°C, 20-40 min)
36	125	[NSPTEA][HSO ₄]	-----	Heat (oil bath 120°C, 10-30 min)
		ZrOCl ₂ ·8H ₂ O		
37	126	ZnO nanoparticles	-----	Heat (120°C, 10-30 min)
38	127	Cellulose-SO ₃ H	-----	Heat (80°C, 10-19 min)
39	128	GO	Water	Heat (stir, 80°C, 3 Hrs)
		G-SO ₃ H		
40	129	Imidazole	-----	Heat (80°C, 9-180 min)
		isoquinoline		
41	130	Ce(SO ₄) ₂ ·4H ₂ O	-----	Heat (120°C, 8-30 min)
42	131	Nanosized metal oxides TiO ₂ , Al ₂ O ₃ , Fe ₃ O ₄	-----	Heat (110°C, 18-60 min)
43	132	Guanidine Hydrochloride	-----	Heat (80°C, 25-60 min)

44	133	Orange peel	-----	Heat (120°C, 60 min)
45	134	PDNES	-----	Heat (110°C, 0.5-2min)
46	135	Tartaric acid	-----	Heat (70°C, 10-20 min)
47	136	Cu(II)/ Fe ₃ O ₄	-----	Heat (120°C, 20-90 min)
48	137	LAIL@MNP	-----	Sonication (80°C, 30 min)
49	138	KF/CP NP	-----	Heat (oil bath at 80°C, 60-120 min)

RESEARCH GAP

It is quite evident from the literature survey that most of the synthetic strategies described in chapter-2 have some shortcomings. In most of these synthetic methods, either the reactions are carried at high temperature by conventional heating or have taken prolonged time to go for completion. Some of them have even used toxic, non-biodegradable and expensive catalysts/solvents which are unsafe for the environment. In addition to these conventional methods, a large no. of green approaches are also cited in the literature for Azomethine and fewer one for benzoxanthone but they too either uses hazardous solvent or toxic, non-biodegradable catalyst. So in other words they are not completely benign for environment or safer for analyst. Therefore, our need for the expansion of more ecofriendly and greener methodologies for the generation of Azomethines, Benzoxanthone and their analogues is there to keep the surroundings safe and clean.

OBJECTIVES OF THE RESEARCH PROPOSAL

After literature review it was noticed that lot of efforts have not been made by the researchers for green synthesis of Benzoxanthone derivative till date. To the best of our knowledge, till date not even one literature is there regarding the utility of glucose to carry out synthesis of azomethine and their analogues. Although some researchers

have taken some attempts to explore the green synthesis of Azomethines, synthesis of azomethine via grindstone chemistry using garlic or biodegradable polymer as catalyst is not reported in literature till date.

The possibilities of using glucose and oxalic acid as green catalyst for ecofriendly preparation of Azomethines and Benzoxanthenes are also not at all explored by the researchers.

Keeping this in view, the main broad objectives of our research work are listed here:

1. Microwave assisted green synthesis of azomethines and benzoxanthenes by using ecofriendly reaction medium
2. Ultrasound assisted green synthesis of azomethines and benzoxanthenes in biodegradable reaction medium.
3. Grindstone synthesis of azomethines and benzoxanthenes by using suitable green catalyst.
4. Exploring the utility of biodegradable polymers as green catalyst for the synthesis of azomethines and benzoxanthenes from aromatic aldehydes.

CHAPTER-3

RESULTS AND DISCUSSION

As per the objectives of thesis, this chapter has been divided into following sections:

3.1. Chemical and their specifications

3.2. Preparation of Azomethines and Benzoxanthenes

3.2.1 Microwave assisted green synthesis of azomethines and benzoxanthenes by using ecofriendly reaction medium

3.2.2 Ultrasound assisted green synthesis of azomethines and benzoxanthenes in biodegradable reaction medium.

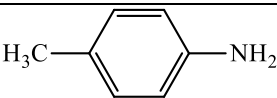
3.2.3 Grindstone synthesis of azomethines and benzoxanthenes by using suitable green catalyst.

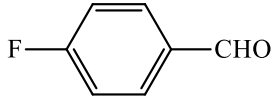
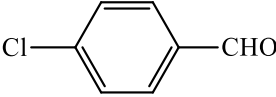
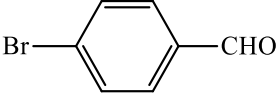

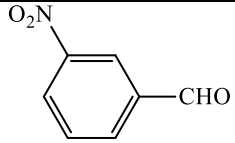
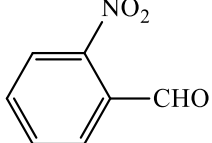
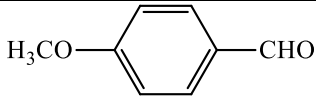
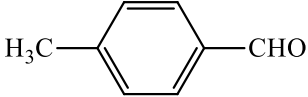
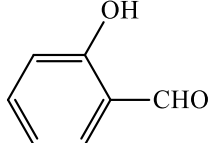
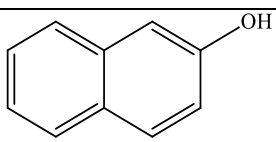
3.2.4 Exploring the utility of biodegradable polymers as green catalyst for the synthesis of azomethines and benzoxanthenes from aromatic aldehydes.

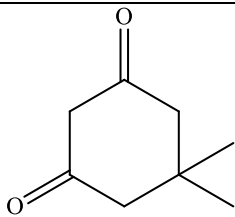
3.1 Chemical and their specifications

All the chemicals i.e. 4-toluidine, 2-naphthol, dimedone, oxalic acid, Polyacrylic acid and aromatic aldehyde like salicylaldehyde, 2-, 3-,4-nitrobenzaldehyde,4-chlorobenzaldehyde, 4-bromobenzaldehyde, 4-methoxybenzaldehyde, 4-methylbenzaldehyde, 4-fluorobenzaldehyde were used for synthesis. The source and structure of the chemicals used in the study are given in **table- 3.1**. All the chemicals were used as such without any further purification.

Table-3.1: Chemical and their specification

S.No.	Chemical Name	source	Structure
1	p-toluidine	Loba Chemie AR	

2	Oxalic acid	Loba Chemie AR	$\begin{array}{c} \text{COOH} \\ \\ \text{COOH} \end{array} \cdot 2\text{H}_2\text{O}$
3	Polyacrylic acid	Central Drug House LR	$\left[\text{CH}_2 - \underset{\text{COOH}}{\text{CH}} \right]_n$
4	Glucose	Loba Chemie AR	$\text{C}_6\text{H}_{12}\text{O}_6$
5	p-fluorobenzaldehyde	Alpha Chemika	
6	p-chlorobenzaldehyde	Alpha Chemika	
7	p-bromobenzaldehyde	Central Drug House LR	
8	p-nitrobenzaldehyde	Loba Chemie AR	
9	m-nitrobenzaldehyde	Alpha Chemika	
10	o-nitrobenzaldehyde	Loba Chemie AR	
11	p-methoxybenzaldehyde	Alpha Chemika	
12	p-methylbenzaldehyde	Alpha chemika	
13	o-hydroxybenzaldehyde	Alpha Chemika	
14	2-Naphthol	Central Drug House LR	

15	Dimedone	Alpha chemika	
----	----------	---------------	---

3.2. Preparation of azomethines and Benzoxanthenes

3.2.1 Microwave assisted green synthesis of azomethines and benzoxanthenes by using ecofriendly reaction medium

Organic reactions assisted by microwave irradiations are gaining popularity day by day as a nonconventional method for fast organic synthesis¹³⁹⁻¹⁴². Synthetic organic chemistry especially medicinal/combinatorial is greatly influenced by microwave assisted synthesis.

In most of the organic reactions heat is provided by conventional heat transfer appliances like heating jackets, sand/ water /oil baths. These heating modes have several disadvantages like it takes long time for completion of reaction and temperature gradient is created within the sample.

In comparison to conventional heating, microwave is considered as clean and efficient source of energy because it reduces the reaction time from many hours to few minutes hence conserve energy and minimize waste. Another major benefit of this technology is that it boosted the rate of reaction as well as amount and yield of product¹⁴³⁻¹⁴⁸.

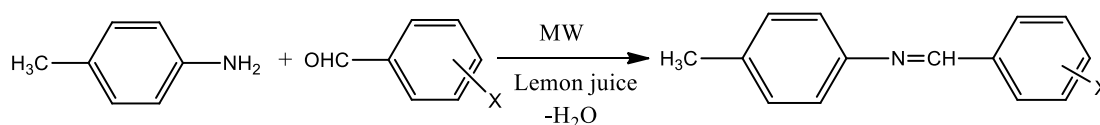
In present days, there is great demand of green and inexpensive acid catalysts as compare to conventional mineral acids such as HF, HCl and H₂SO₄ in chemical operations. Mineral acids are abrasive and hazardous catalysts¹⁴⁹ whereas biodegradable catalysts are safe for human beings as well as for the environment. Most of these are easily available, inexpensive and nontoxic. In present section we have made use of lemon juice and glucose as ecofriendly catalyst for the preparation of azomethines. Aqueous solution of oxalic acid is also used as a green catalyst for the production of benzoxanthenes.

M.W assisted synthesis of azomethines in lemon juice

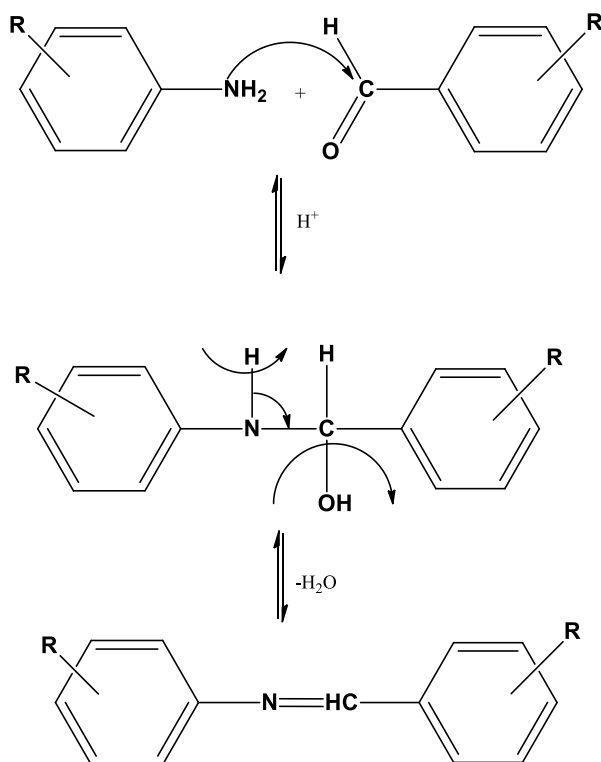
Lemon juice being acidic is used by many researchers for the synthesis of many compounds^{79, 150-155} but it is used for the synthesis of azomethines for the very first time by us. The lemon juice contains 85% moisture, 11.2% carbohydrates, 5-7% citric acid, 1% protein, 0.9% fats and 0.5% ascorbic acid. With variation in geographic and cultural pattern and also harvesting and processing in different seasons, the composition of the lemon juice varies. So, the presence of citric acid and ascorbic acid is responsible for acidic nature ($p^H=2-3$) of lemon juice hence it serves as effective acid catalyst for condensation of aromatic aldehydes and p-toluidine.

General procedure for synthesis of azomethines in lemon juice:

0.01 mole of p-toluidine and 0.01 mole of required aromatic aldehyde were taken in 100 ml borosilicate conical flask. 2-10 ml of lemon juice was added into this reaction mixture. The reaction mixture was exposed to microwave (power 240W) irradiations for suitable time in microwave synthesizer (of Ragatech Company having 10 power levels, stirrer with selectable speed, timer, temperature meter with flexible probe and fitted with reflux condenser. Both timer and speed are adjustable during running). After every half min exposure to MW irradiations, the concoction of reaction was cooled by stirring to bring it to room temperature. The progress of the reaction was continuously monitored by means of TLC. After completion of the reaction (which was shown by TLC) the reaction mixture was put into ice cold water. Immediately precipitation of the solid crude product from the reaction mixture was observed. The crude product was filtered and desiccated properly. To obtain neat product the crude product was recrystallized from hot ethanol to obtain pure azomethines which physically appear as creamish white/ yellowish solid powder. The obtained azomethines were characterized by melting point, IR and NMR and mass spectroscopy. The melting point, IR and NMR spectra, molecular mass, HRMS of the synthesized compounds were identical to those of reported ones.



Scheme-3.1: Synthesis of azomethines in lemon juice under MW irradiations



Scheme-3.2: Mechanism of Schiff base formation under acid catalyst

Results and discussion:

The series of reaction were carried out employing an equimolar mixture of p-toluidine with various derivatives of benzaldehyde bearing varying functional groups showing -I and +I effect. The reactions used to take 0.5-3 minutes duration for completion.

From the above table it is evident that the electronic nature of aromatic aldehydes, -I-effect of 'X' and its vicinity to carbonyl group greatly affect the yield.

It's very interesting to note that reactions are usually faster with electron deficient aromatic aldehydes than the reactions with electron rich aromatic aldehydes. Along with increase in electron withdrawing effect of "X" the electrophilic nature of the carbonyl center of aromatic aldehyde increases as a result of which the nucleophilic attack of aromatic amine on aromatic aldehyde becomes easier.

Considering the dual effect namely -electron withdrawing factors of “X” and vicinity of the substituents “X” to the aldehyde group, the reaction takes minimum time with 2- NO₂-benzaldehyde and maximum time with 4-Br-benzaldehyde, to go for completion.

It is worthy to note that reactions in which aromatic aldehydes bearing group with -I-effect provides more yield than with those bearing group with +I-effect. The obtained outcomes are shown in **Table-3.2**

Table-3.2: MW assisted preparation of azomethines with different aldehydes in lemon juice

Entry	X	Time (Min)	% Yield	Observed M. P of product (°C)
1	4-Cl	0.5	93	123-125
2	4-Br	1	88	136-138
3	4-NO ₂	0.5	91	124-128
4	3-NO ₂	0.5	93	80-82
5	2-NO ₂	0.5	92	70-72
6	4-OCH ₃	3	81	94-96
7	4-CH ₃	1	78	78-80
8	2-OH	0.5	95	103-104

Characterization of Synthesized azomethines

Spectroscopic techniques are very useful tool for elucidating the structure of compound. Various Spectroscopic techniques which we have used for determining the structure of synthesized molecules is Infrared, Proton nuclear magnetic resonance, Carbon-13 nuclear magnetic resonance and mass spectrometry.

IR spectroscopy mainly tells us about nature of functional groups present in the compound. Instrumentation which we have used for recording the IR spectrum is FT-IR 8400 S. It is of SHIMADZU brand.

Proton nuclear magnetic resonance tells about different type of hydrogen nuclei present in the molecules and also about their neighboring environment and Carbon-13 describes the different carbon nuclei Instrument used for recording the proton and ^{13}C -NMR is NMR spectrometer of 400 MHz and 100 MHz JEOL JNM ECS 400. CDCl_3 is used as solvent for recording NMR.

Mass spectrometry is used to determine the molecular mass and formula of the sample. Name of instruments used for recording HRMS is XEVO G2-XS QTOF.

1. 4-methyl-N-[(4-chlorophenyl)methylidene]aniline: White solid; 93% Yield; m.p. 123-125°C; IR (KBr): ν_{max} (cm^{-1}) =3087, 3029, 2914, 1621, 1587, 681. ^1H -NMR (CDCl_3 , 400MHz): δ (ppm) 2.36 (3H, s), 7.13 (2H, d, $J=8.6\text{Hz}$), 7.20 (2H, d, $J=8.0\text{Hz}$), 7.41(2H, d, $J=8.0\text{Hz}$), 7.83(2H, d, $J=8.6\text{Hz}$), 8.42(1H, s). ^{13}C -NMR (CDCl_3 , 100MHz): δ (ppm) 21.1, 120.9, 129.1, 129.9, 131.0, 134.9, 136.2, 137.2, 149.1, 158.1. HRMS-ESI: calculated for $\text{C}_{14}\text{H}_{13}\text{NCl}$ $[\text{M}+\text{H}]^+$: 230.0737, Found: 230.0729

2. 4-methyl-N-[(4-bromophenyl)methylidene]aniline: White solid; 88% Yield; m.p. 136-138°C; IR (KBr): ν_{max} (cm^{-1}) =3084, 3027, 2875, 1671, 1478, 657. ^1H -NMR (CDCl_3 , 400MHz): δ (ppm) 2.36 (3H, s), 7.12 (2H, d, $J= 8.4\text{Hz}$), 7.18 (2H, d, $J=8.4\text{Hz}$), 7.60(2H, d, $J=8.6\text{Hz}$), 7.76(2H, d, $J= 8.6\text{Hz}$), 8.41(1H, s). ^{13}C -NMR (CDCl_3 , 100MHz): δ (ppm) 21.15, 120.91, 125.75, 129.93, 130.15, 131.08, 135.33, 136.27, 149.09, 158.15. HRMS-ESI: calculated for $\text{C}_{14}\text{H}_{13}\text{NBr}$ $[\text{M}+\text{H}]^+$: 274.0231, Found: 274.0218.

3. 4-methyl-N-[(4-nitrophenyl)methylidene]aniline: Yellow solid; 91% Yield; m.p. 124-128°C; IR (KBr): ν_{max} (cm^{-1}) =3078, 2987, 2887, 1594, 1516, 1443 and 1338. ^1H -NMR (CDCl_3 , 400MHz): δ (ppm) 2.38 (3H, s), 7.21 (4H, m), 8.06 (2H, t), 8.31 (2H, d, $J=8.4\text{Hz}$), 8.55 (1H, s). ^{13}C -NMR (CDCl_3 , 100MHz): δ (ppm) 21.17, 121.29, 124.59, 129.77, 131.08, 133.61, 137.09, 148.55, 149.38, 154.89. HRMS-ESI: calculated for $\text{C}_{14}\text{H}_{13}\text{N}_2\text{O}_2$ $[\text{M}+\text{H}]^+$:241.0977, Found: 241.0981

4. 4-methyl-N-[(3-nitrophenyl)methylidene]aniline: Light Yellow solid; 93% Yield; m.p. 80-82°C; IR (KBr): ν_{max} (cm^{-1}) =3096, 3035, 2948, 1623, 1528, 1445, 1347, 673. ^1H -NMR (CDCl_3 , 400MHz): δ (ppm) 2.37 (3H, s), 7.22 (4H, m), 7.63 (1H, t), 8.23 (1H, d, $J=8.00\text{Hz}$), 8.30 (1H, dd, $J=7.92$ and 1.20Hz), 8.54 (1H, s), 8.71 (1H,

t). ^{13}C -NMR (CDCl_3 , 100MHz): δ (ppm) 21.17, 121.03, 123.48, 125.47, 129.85, 130.03, 134.07, 137.06, 138.10, 148.28, 148.75, 156.33. HRMS-ESI: calculated for $\text{C}_{14}\text{H}_{13}\text{N}_2\text{O}_2$ $[\text{M}+\text{H}]^+$: 241.0977, Found: 241.0970.

5. 4-methyl-N-[(2-nitrophenyl)methylidene]aniline: Light Yellow solid; 92% Yield; m.p. 70-72°C; IR (KBr): ν_{max} (cm^{-1}) = 3077, 3014, 2875, 1609, 1566, 1512, 1335, 701. ^1H -NMR (CDCl_3 , 400MHz): δ (ppm) 2.38 (3H, s), 7.21 (4H, m), 8.06 (2H, d, $J=8.0\text{Hz}$), 8.30 (2H, dd, $J=7.32$ and $J=1.84\text{Hz}$), 8.55 (1H, s). ^{13}C -NMR (CDCl_3 , 100MHz): δ (ppm) 21.20, 121.10, 124.08, 129.36, 129.83, 130.53, 130.08, 137.34, 141.85, 148.32, 149.21, 156.43. HRMS-ESI: calculated for $\text{C}_{14}\text{H}_{13}\text{N}_2\text{O}_2$ $[\text{M}+\text{H}]^+$: 241.0977, Found: 241.0967

6. 4-methyl-N-[(4-methoxyphenyl)methylidene]aniline: White solid; 81% Yield; m.p. 94-96°C; IR (KBr): ν_{max} (cm^{-1}) = 3000, 2976, 2874, 1598, 1565, 1505, 1453, 1247, 1165, 1105. ^1H -NMR (CDCl_3 , 400MHz): δ (ppm) 2.35 (3H, s), 3.86 (3H, s), 6.97 (2H, d, $J=8.8\text{Hz}$), 7.11 (2H, d, $J=8.8\text{Hz}$), 7.18 (2H, d, $J=8.0\text{Hz}$), 7.83 (2H, d, $J=7.2\text{Hz}$), 8.38 (1H, s). ^{13}C -NMR (CDCl_3 , 100MHz): δ (ppm) 21.12, 55.51, 114.25, 120.91, 129.47, 129.85, 130.51, 135.56, 149.83, 159.08, 162.20. HRMS-ESI: calculated for $\text{C}_{15}\text{H}_{16}\text{NO}$ $[\text{M}+\text{H}]^+$: 226.1232, Found: 226.1223

7. 4-methyl-N-[(4-methylphenyl)methylidene]aniline: Creamish white solid; 78% Yield; m.p. 78-80°C; IR (KBr): ν_{max} (cm^{-1}) = 3026, 2991, 1665, 1598, 1565, 1504, 1443, 1413. ^1H -NMR (CDCl_3 , 400MHz): δ (ppm) 2.36 (3H, s), 2.41 (3H, s), 7.11 (2H, d, $J=8.8\text{Hz}$), 7.17 (2H, d, $J=8.4\text{Hz}$), 7.27 (2H, d, $J=8.8\text{Hz}$), 7.79 (2H, d, $J=8.0\text{Hz}$), 8.42 (1H, s). ^{13}C -NMR (CDCl_3 , 100MHz): δ (ppm) 21.14, 21.75, 120.95, 128.85, 129.62, 129.87, 133.91, 135.68, 141.77, 149.74, 159.71. HRMS-ESI: calculated for $\text{C}_{15}\text{H}_{16}\text{N}$ $[\text{M}+\text{H}]^+$: 210.1283, Found: 210.1282

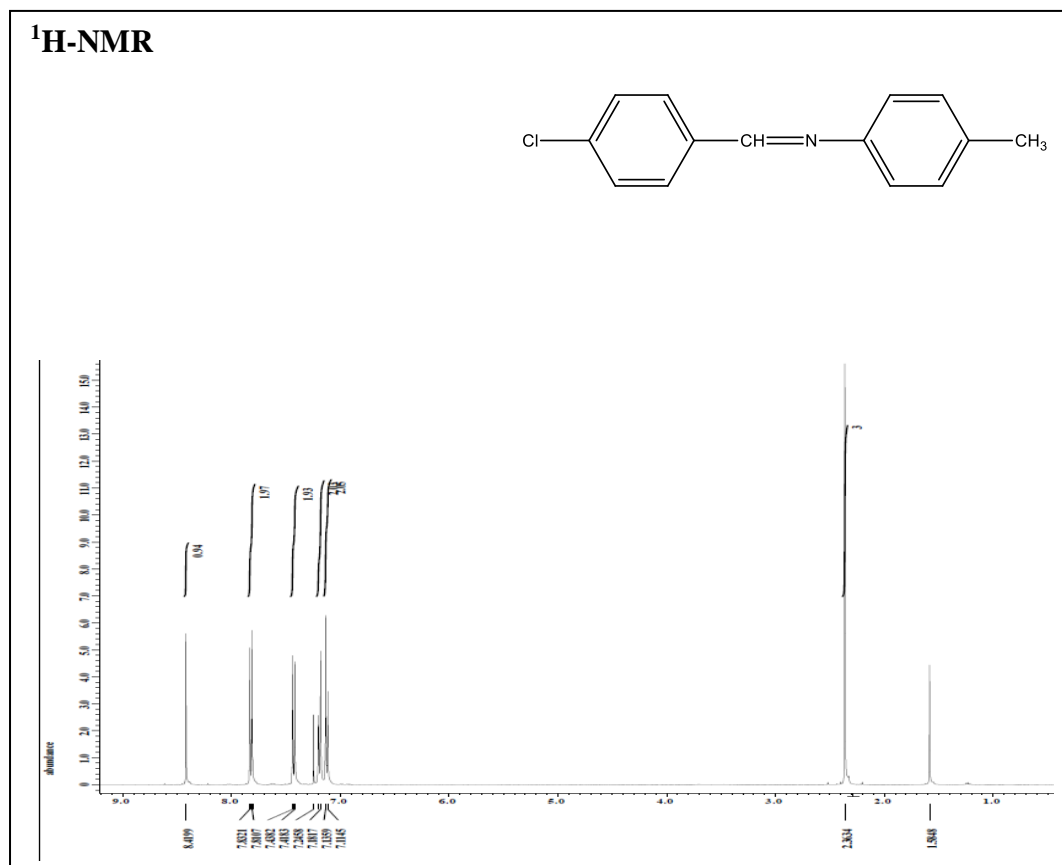
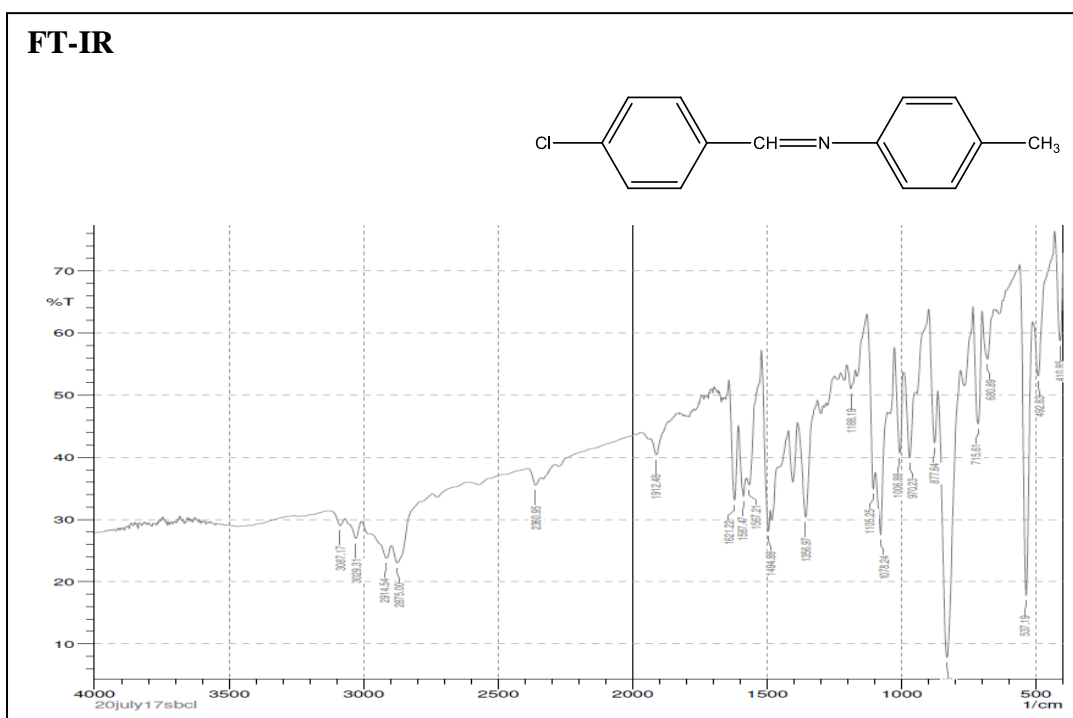
8. 4-methyl-N-[(2-hydroxyphenyl)methylidene]aniline: Yellow solid; 95% Yield; m.p. 103-104°C; IR (KBr): ν_{max} (cm^{-1}) = 3637, 3022, 1613, 1565, 1498, 1413, 1182, 1031. ^1H -NMR (CDCl_3 , 400MHz): δ (ppm) 2.37 (3H, s), 6.94 (1H, m), 7.01 (1H, d, $J=8.4\text{Hz}$), 7.24 (4H, m), 7.38 (2H, m), 8.61 (1H, s), 13.38 (1H, s). ^{13}C -NMR (CDCl_3 , 100MHz): δ (ppm) 21.18, 117.29, 119.09, 119.39, 121.11, 130.11, 132.23, 133.01, 137.01, 145.93, 161.19, 161.79. HRMS-ESI: calculated for $\text{C}_{14}\text{H}_{14}\text{NO}$ $[\text{M}+\text{H}]^+$: 212.1075, Found: 212.1074

Conclusion:

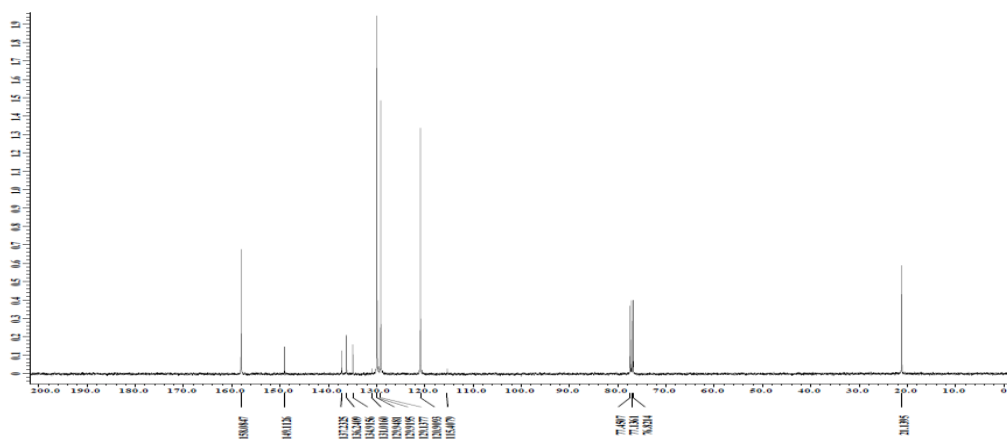
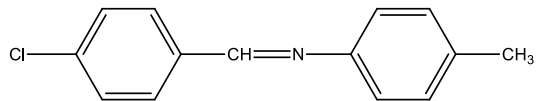
In nutshell a cost-effective, efficient, eco-friendly and easy method for synthesis azomethine has been evolved by our group. Our present study has successfully demonstrated the green synthesis of pharmaceutically important azomethines in lemon juice medium using MW radiations as ecofriendly energy resource. This is the first of its kind study where MW radiations have been applied for the very first time to execute azomethines in the fruit juice medium. It is concluded that salicylaldehyde, 2-, 3-, 4-nitrobenzaldehyde, 4-chlorobenzaldehyde have taken minimum time and 4-meyhoxybenzaldehyde have taken maximum time to provide product. Yield of the product is excellent in each case but maximum yield is obtained with the use of salicylaldehyde and minimum with 4-methylaldehyde.

So our current effort may motivate the scientists to carry out more of MW induced green multi component condensation reactions in fruit juice medium, in near future.

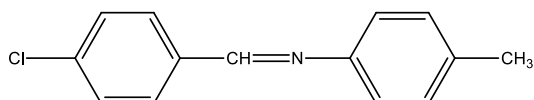
Representative FT-IR, NMR and HRMS



¹³C- NMR



HRMS-ESI



Elemental Composition Report

Single Mass Analysis

Tolerance = 50.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for I-FIT = 3

Monoisotopic Mass, Even Electron Ions

4 formula(s) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 10-15 H: 11-15 N: 0-2 Cl: 0-1

IIITRFR

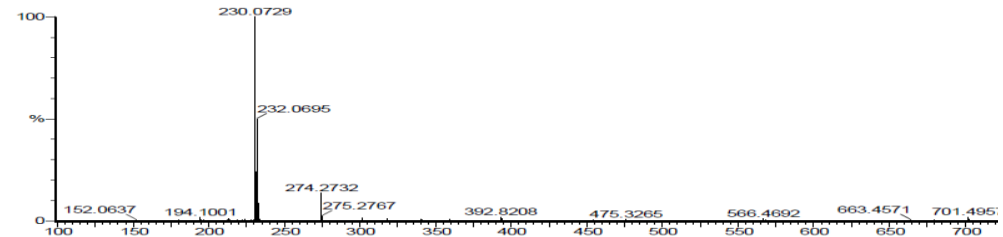
XEVO G

Sample Name : SBPCI

Test Name : HRMS-1

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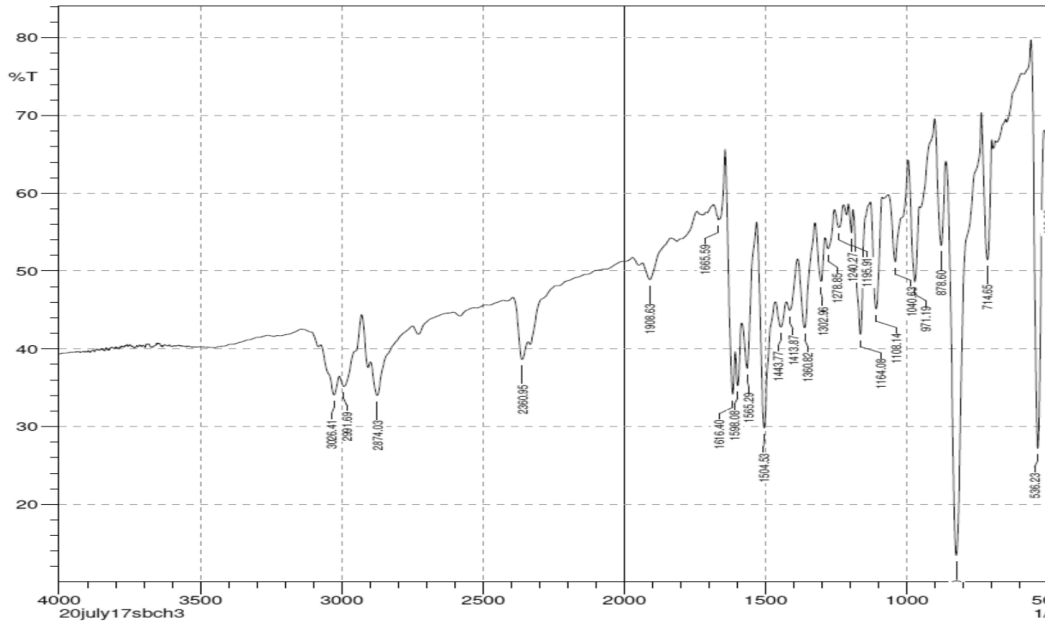
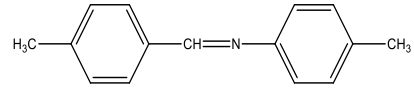
1: TO



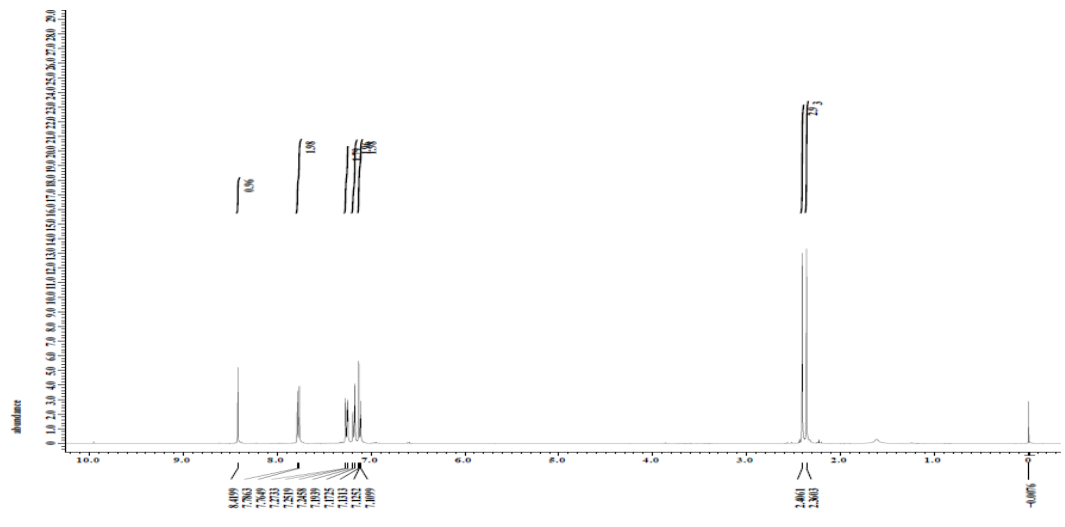
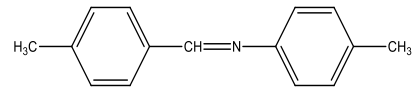
Minimum: Maximum: 5.0 50.0 50.0

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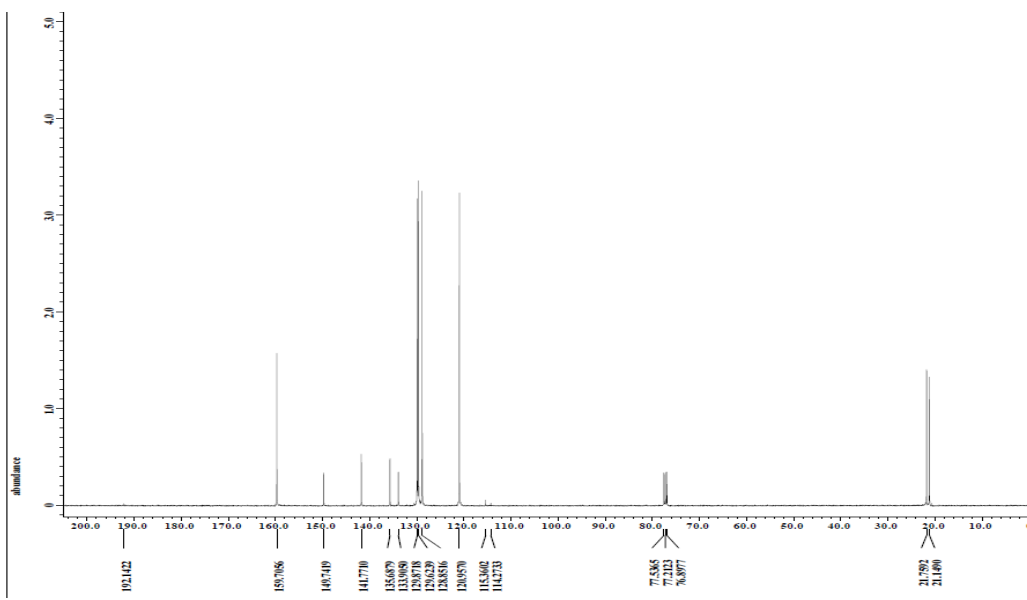
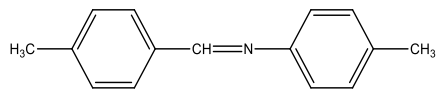
FT-IR



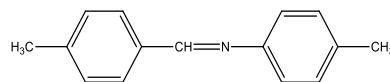
¹H-NMR:



¹³C-NMR



HRMS-ESI



Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 50.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

2 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 10-15 H: 11-20 N: 0-2

Sample Name : SBPMe IITRPR

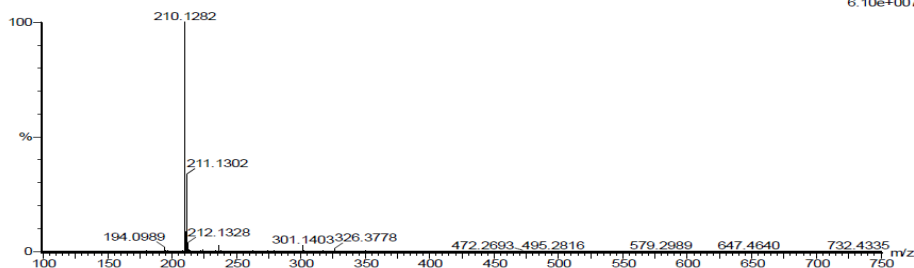
XEVO G2-XS QTOF

Test Name : HRMS-1

1: TOF MS ES+

210119-SBPMe 15 (0.157) AM2 (Ar,19000.0,0.00,0.00); Cm (15:18)

6.10e+007

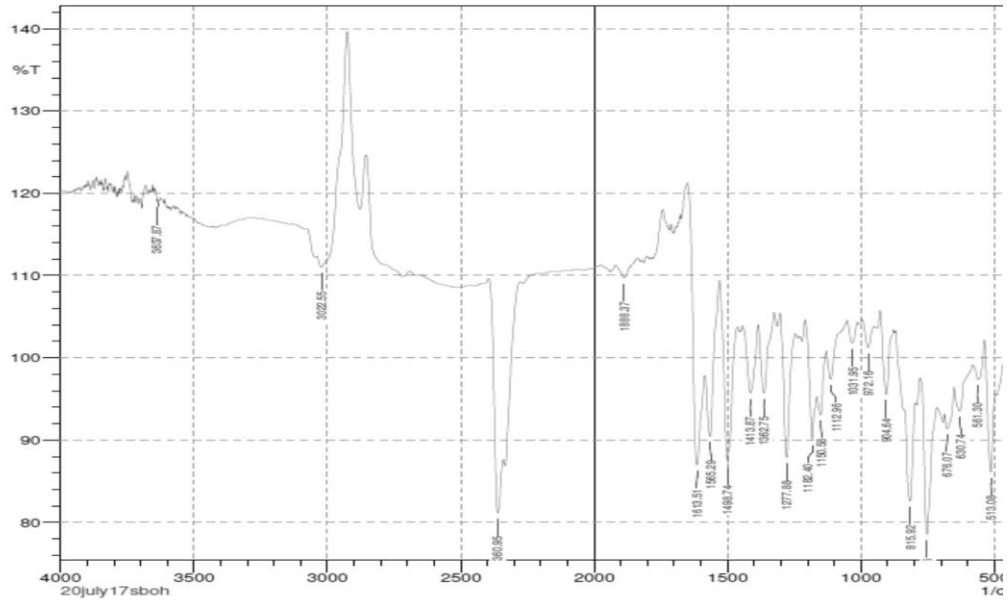
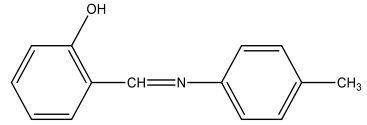


Minimum:
Maximum:

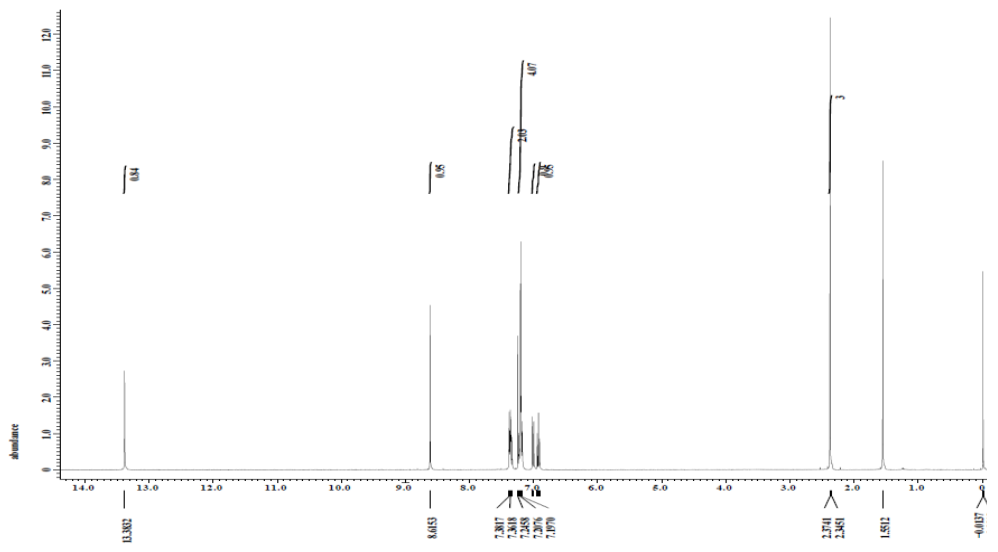
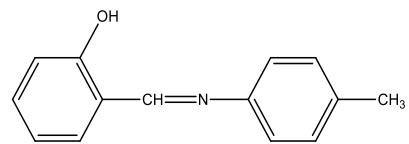
5.0 50.0 -1.5
50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
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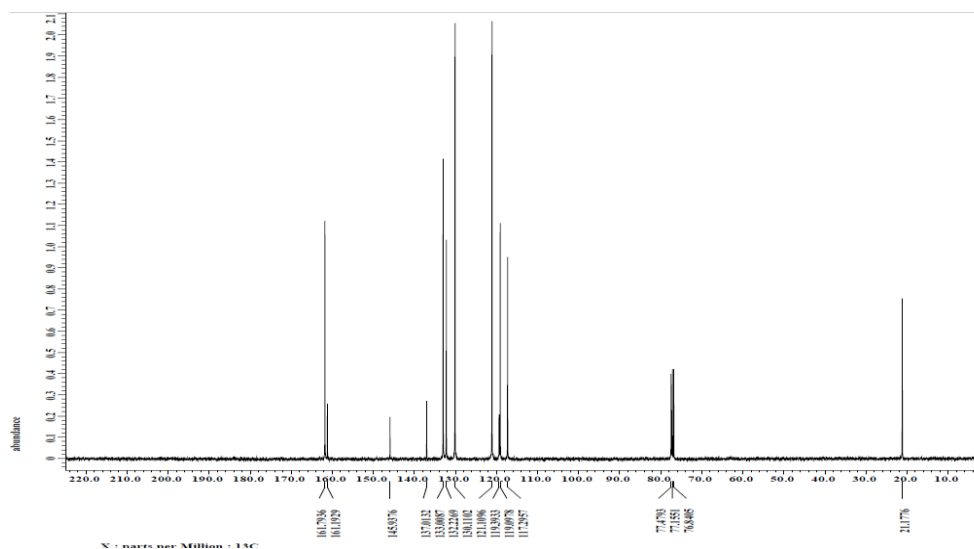
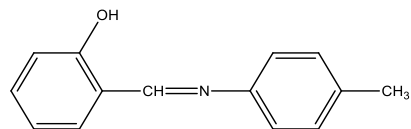
FT-IR



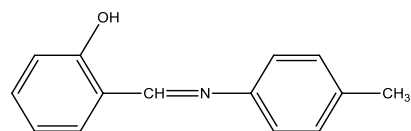
¹H-NMR



¹³C-NMR



HRMS-ESI



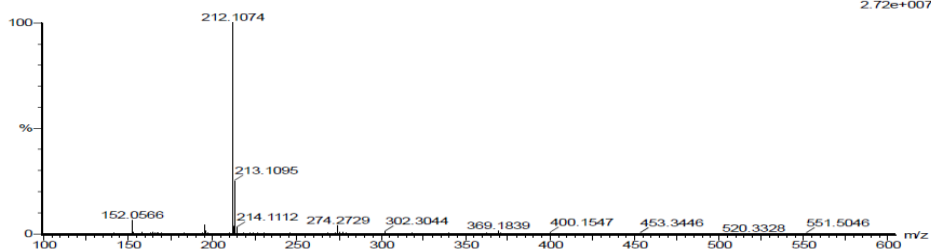
Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
25 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:
C: 11-20 H: 5-35 N: 0-3 O: 1-4
Sample Name : FOH IITRPR
Test Name : HRMS-1 XEVO G2-XS QTOF
090919-FOH 23 (0.237) AM2 (Ar,22000.0,0.00,0.00); Cm (23:24) 1: TOF MS ES+ 2.72e+007



Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
212.1074	212.1075	-0.1	-0.5	8.5	1143.6	n/a	n/a	C14 H14 N O

MW assisted Synthesis of azomethines in aqueous solution of Glucose

The use of glucose as a natural and biodegradable catalyst is absolutely new concept which is first time developed by our group. The idea of using glucose as natural ecofriendly catalyst came to our mind from the fact that PEG was used as a catalyst for the synthesis of azomethines and benzoxanthone^{81, 111} in literature. Like PEG, glucose OH group can also make intermolecular H-bonding with O-atom of carbonyl group of aldehydes, thereby decreasing electron density on the carbonyl carbon and making attack of nucleophile on the carbonyl carbon to be more facile.

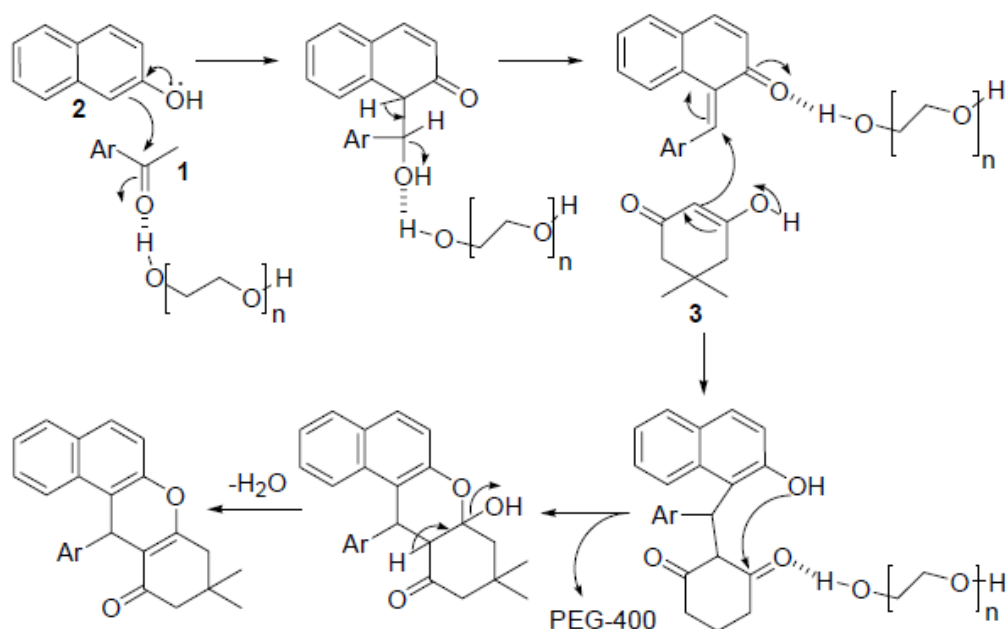


Figure-3.1: The intermolecular H-bonding between oxygen atom of the reactants with the -OH of the PEG-400 as reported in literature.

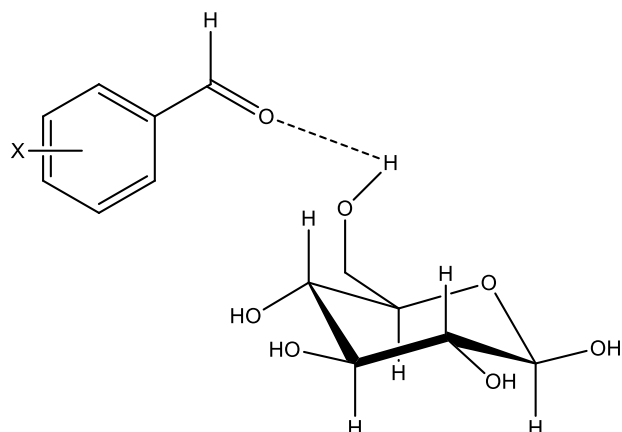
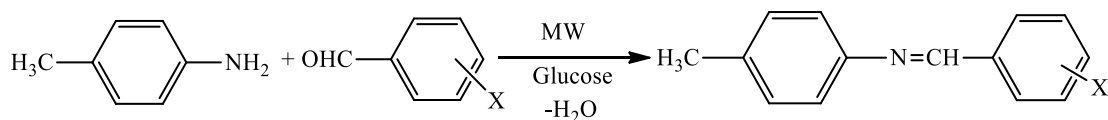


Figure-3.2: Intermolecular H-bonding between D-glucose and aromatic aldehyde



Scheme-3.3: Synthesis of azomethines in aq. solution of glucose under MW irradiations

The efficiency of catalysts is evaluated by performing the reactions in presence as well as in absence of glucose catalyst where 4-chloro benzaldehyde was made to react with p-toluidine under MW irradiation for making azomethines. It is worthy to note that the reaction took 5.5 min time duration to go for completion in water medium in absence of glucose catalyst. The same reactions with the same reactants were completed successfully in comparatively lesser time duration when the reactions were performed with glucose catalyst and water solvent. To analyze the effect of concentration of catalyst on the rate of reaction; the reactions were performed in different concentration of aqueous glucose solution. The consequences obtained are shown in **Table-3.3**.

Table-3.3: Comparison of reaction in presence and absence of catalyst

Reaction medium	H₂O without glucose catalyst	0.5 M aqueous glucose solution	1 M aqueous glucose solution	2 M aqueous glucose solution
Time in min	5.5 min	4.5 min	1 min	0.5 min

It was observed from the results depicted in **table-3.3** that the reaction took minimum time to go for completion in 2M aqueous solution of D-glucose. Thus remaining all the reactions were carried out in 2M aqueous solution of D-glucose.

General procedure for synthesis of azomethines in aqueous solution of glucose

100 ml borosilicate conical flask was charged with 0.0025 mole of p-toluidine and 0.0025 mole of desired aldehyde. Then 10 ml of desired glucose solution was added to this reaction mixture. The reaction mixture was irradiated with MW (240 W) for specified time in microwave synthesizer. The reaction mixture was taken out of microwave and was cooled, stirred successively at room temperature after every half min of exposure under microwave irradiation. By checking TLC, the advancement of the reaction was continuously recorded. The concoction of reaction mixture was put into chilled water after the reaction is finished (which was indicated by TLC). To get pure product, the solid crude product which came out of the reaction concoction was first filtered, dried and recrystallized from hot ethyl alcohol. Pure azomethines are obtained as white/yellowish solid powder. The synthesized azomethines were then characterized by melting point, IR and NMR and mass spectroscopy. The melting point, IR, NMR spectra and molecular mass of the prepared compounds were identical to those of reported ones.

Table-3.4: MW assisted synthesis of Azomethines with different aldehydes in 2M- glucose solution

Entry	X	Time (Min)	% Yield	Observed M. P of product (°C)
1	4-Cl	0.5	94	122-124
2	4-Br	2	78	136-138
3	4-NO ₂	1	84	120-122
4	3-NO ₂	2.5	81	80-82
5	2-NO ₂	0.5	88	71-73
6	4-OCH ₃	1	77	93-95
7	4-CH ₃	4	72	78-80
8	2-OH	0.5	96	102-104

The structure of all the derivatives of synthesized azomethines is shown in **figure-3.3**. It was interesting to note that while a series of azomethine were synthesized using different derivatives of benzaldehyde; all the reactions were completed successfully within time duration of 0.5 min to 4 min. The obtained results were summarized in **table-3.4**.

The reactions have exhibited significant dependence on the electronic nature of aromatic aldehydes, -I-effect of 'X' and its vicinity to carbonyl group greatly affects the yield and reaction time.

From above table it is clear that ortho and para substituted aldehydes provides more yield than meta-substituted aldehydes. Further it is worth to observe that the process takes minimum time when the X is electron withdrawing group whereas the reaction completes at comparatively longer time when X is electron donating group. 2-OH and 4-Cl-benzaldehyde took lesser time because of electronegativity of oxygen and chlorine. 3-NO₂-benzaldehyde took more time than its ortho and para derivatives because of lack of conjugation at meta position.

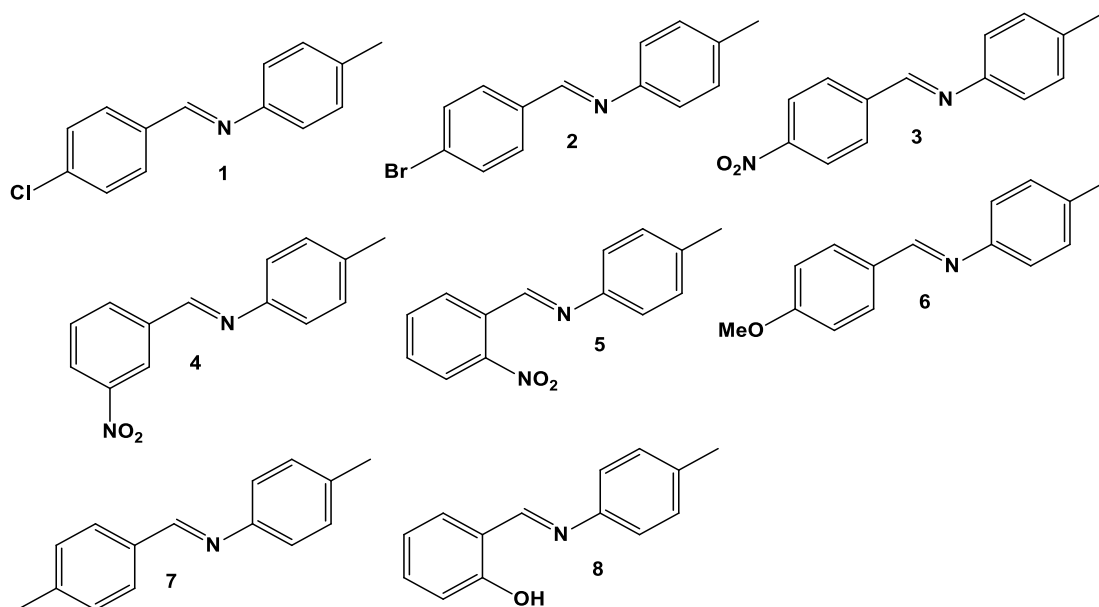


Figure-3.3: Various derivatives of azomethines synthesized

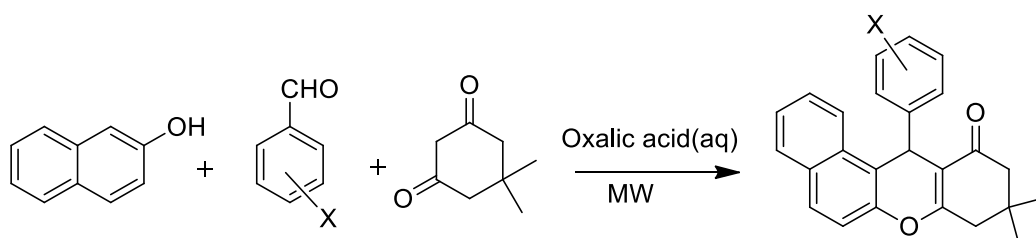
Conclusion:

So it is concluded that by using aqueous solution of glucose as a catalyst reactions are carried out efficiently with excellent yield of products. Further it has been noted reactions have taken minimum time with 4-Cl, 2-NO₂ and 2-OH benzaldehydes and maximum time with 4-CH₃-benzaldehyde for providing azomethines. Maximum yield of azomethine is obtained with salicylaldehyde and minimum with 4-CH₃-benzaldehyde. Hence a green, simple, eco-friendly, efficient and economic process is developed for the very first time ever for glucose catalyzed green synthesis of azomethines via microwave irradiation. The approach is completely green as it avoids depletion of natural resources and avoids the usages of hazardous materials.

So our current effort may motivate the scientists to carry out more of MW induced green multi component condensation reactions in glucose medium, in near future.

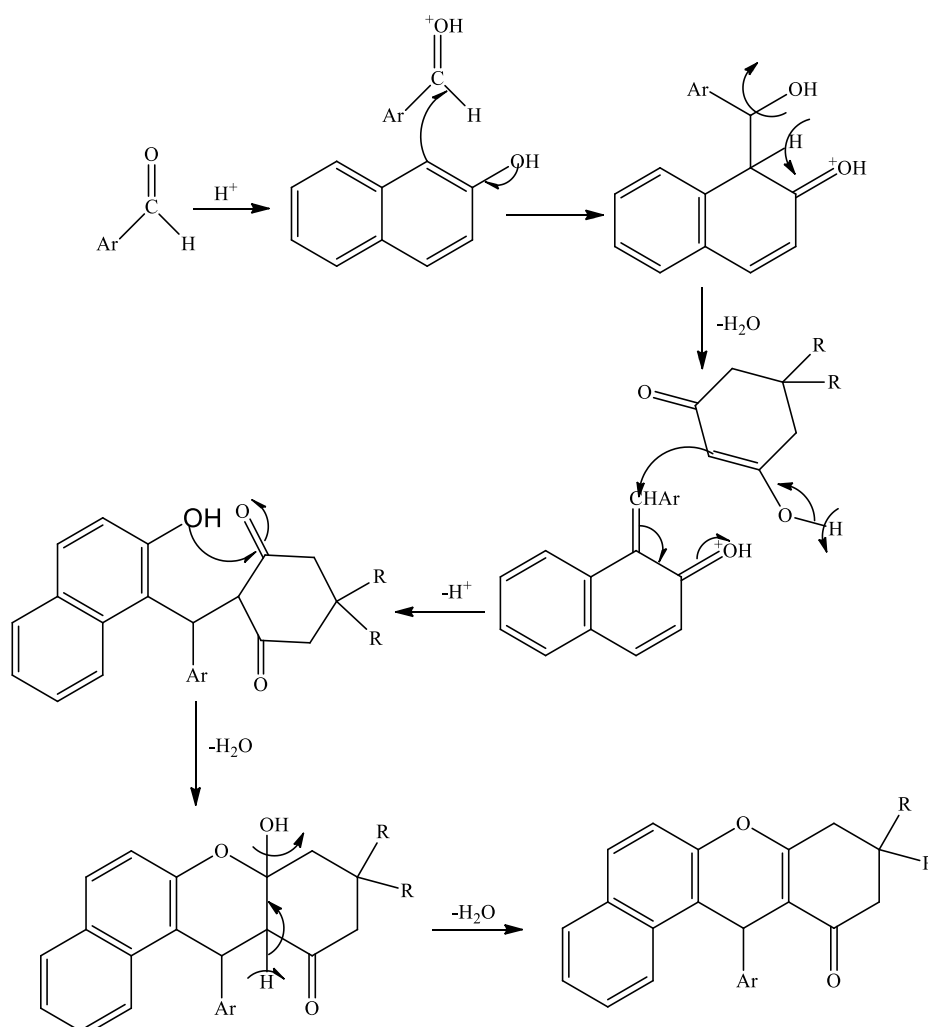
MW assisted Synthesis of benzoxanthenes in aqueous solution of oxalic acid

Oxalic acid is one of the most important green catalysts. It is strongly acidic due to presence of two carboxyl groups which are joined directly. It is biodegradable, non toxic, economical, environmental friendly catalyst and that's why making use of it for the last few years for organic transformation is gaining great significance. It has been applied as catalyst for formulation of some heterocyclic compounds but never for synthesis of Benzoxanthenes. At the same time water works as green and ecofriendly solvent. The utilization of aqueous medium is not only economical but also ecologically benign¹⁵⁶. It has been proposed that cause of occurrence of organic reaction is high interior pressure put by aqueous solution resulting from powerful coherent energy¹⁵⁷. So both oxalic acid and water are working as green catalyst and solvent respectively. Hence we used aqueous solution of oxalic acid for the synthesis of benzoxanthenes. Moreover, the insoluble impurities can be isolated by filtration when water soluble catalyst is used. So there is strong need of that catalytic system which is stable in water and also entirely dissolves in it.



Scheme-3.4: Synthesis of benzoxanthenes in aqueous solution of oxalic acid under MW irradiations

Mechanism:



Scheme-3.5: Mechanism of the reaction catalysed by aqueous solution of oxalic acid under MW irradiations

General Procedure for Synthesis of benzoxanthenes in aqueous solution of oxalic acid

0.015 moles of each of β-naphthol, dimedone and desired aldehyde were taken in a conical flask. Then 10 ml of aqueous solution of 2M oxalic acid was added to the flask. Microwave irradiations were allowed to pass through reaction mixture for specific time at 560 W in microwave reactor. After every 1 min of the exposure under MW the reaction mixture was cooled down to room temperature. By checking thin-

layer chromatography (TLC) the advancement of reaction was continuously tracked. The reaction was quenched by pouring the reaction mixture into crushed ice after the accomplishment of reaction (indicated by TLC). The unpurified solid product that was precipitated in water medium was isolated by filtration. The recrystallization of crude product was done with hot ethyl alcohol (two times) to get authentic pure benzoxanthone and then finally the product was washed with hexane to remove any non-polar impurities. The obtained pure product was specified by melting point, FT-IR, NMR and mass spectra.

Results and Discussion:

Here in a systematic and easy preparation of benzoxanthone derivative in single container by condensation of dimedone, 2-naphthol and different aryl aldehydes using ethane-1, 2-dioic acid as bio degradable catalyst under microwave irradiation was reported. After various attempts of synthesis of our target compound with various amounts of solvents and catalysts, it was found that 10mL aqueous solution of 2M oxalic acid was the most suitable one for carrying out our reactions.

Table-3.5: MW assisted synthesis of benzoxanthenes with different aldehydes in aqueous solution of oxalic acid

Entry	X	Time (Min)	% Yield	Observed M. P of product (°C)
1	4-Cl	33	81	180-182
2	4-Br	30	72	185-186
3	4-F	27	84	176-178
4	2-NO ₂	30	78	216-218
5	3-NO ₂	44	71	167-168
6	4- NO ₂	25	81	174-176
7	4-CH ₃	30	73	172-174

After carrying out a series of same reactions under various different power of microwave reactor,

560 W powers was found to be the most optimized and effective power of MW irradiation which was allowing the reaction to be completed within stipulated time duration and giving considerably good percentage of yield of the desired product. The purification of the compound was a challenging job. As all the crude products were obtained in solid form and we wanted to minimize the usage of solvent by keeping the principle of green chemistry in mind for the purpose of purification, the purification of the crude compounds were carried out via recrystallization instead of doing the same via column chromatography. The purity of the compound was not up to the mark after first time recrystallization from hot ethanol. Thus a 2nd time recrystallization was carried out from hot ethanol to obtain compound with enough purity. Finally a hexane wash was given to remove the non-polar impurities from the compound. The compound was pure enough only after giving the final round of hexane wash, as seen from their spectroscopic data analysis.

The obtained outcomes are compiled in table -3.5. As observed from table-3.5, different aryl aldehydes underwent the reaction evenly and all of them have given the products with good to excellent percentage of yields. It was worthy to note that all the reactions were completed within time duration of 25 to 44 minutes. It was interesting to note that 3-NO₂benzaldehyde took maximum time to go for completion of reaction when it was made to react with β -naphthol and dimedone whereas the reaction took minimum time to go for completion with 4-NO₂benzaldehyde. Thus the position of the functional group of aromatic aldehyde plays an important role while the rate of reaction is considered. In general, it was an electron withdrawing group of aldehyde which makes the reaction more feasible. The mechanism of the reaction also justifies the same observation as an electron withdrawing group increases the electrophilicity of aromatic aldehyde.

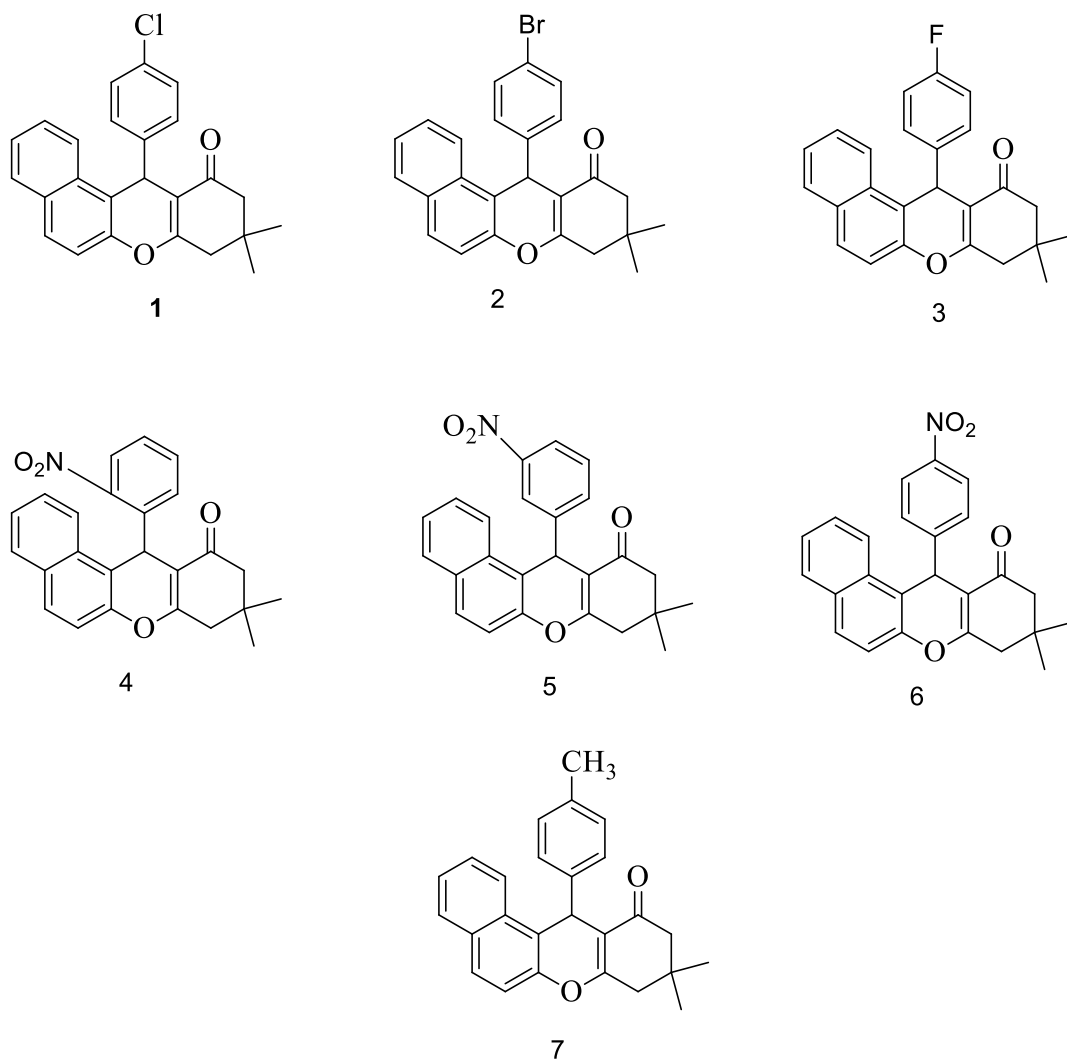


Figure-3.4: Various derivatives of benzoxanthone synthesized

Characterization of Synthesized benzoxanthenes:

Spectroscopic techniques are very useful tool for elucidating the structure of compound. Various Spectroscopic techniques which we have used for determining the structure of synthesized molecules is Infrared, Proton nuclear magnetic resonance, Carbon-13 nuclear magnetic resonance and mass spectrometry.

IR spectroscopy mainly tells us about nature of functional groups present in the compound. Instrumentation which we have used for recording the IR spectrum is FT-IR 8400 S. It is of SHIMADZU brand.

Proton nuclear magnetic resonance tells about different type of hydrogen nuclei present in the molecules and also about their neighboring environment and Carbon-13 describes the different carbon nuclei Instrument used for recording the proton and ¹³C-NMR is NMR spectrometer of 400 MHz and 100 MHz JEOL JNM ECS 400. CDCl₃ is used as solvent for recording NMR.

Mass spectrometry is used to determine the molecular mass and formula of the sample. Name of instruments used for recording mass and HRMS are XEVO G2-XS QTOF.

1.12-(4-Chlorophenyl)-9,9-dimethyl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-

one: White solid; 82% Yield; m.p. 180-182°C; IR (KBr): ν_{\max} (cm⁻¹) = 2956, 2879, 1629, 1593, 1515, 1485, 1443, 1367, 1182, 776. ¹H NMR (CDCl₃, 400 MHz): δ ppm: 7.88 (1H, d, *J*=8.0Hz), 7.77–7.75(2H, m), 7.27– 7.10 (7H, m), 5.67(1H, s), 2.56(2H, s), 2.32(1H, d, *J*=16.5 Hz), 2.25(1H, d, *J*=16.5 Hz), 1.11 (3H, s), 0.95 (3H, s). ¹³C-NMR (CDCl₃, 100 MHz): δ ppm: 196.96, 164.15, 147.84, 143.43, 132.04, 131.62, 131.32, 129.96, 129.25, 128.64, 128.54, 127.26, 125.16, 123.57, 117.20, 113.89, 50.94, 41.44, 34.33, 32.33, 29.47 and 27.18. HRMS-ESI: calculated for C₂₅H₂₂O₂Cl [M+H]⁺:389.1308, Found: 389.1324

2.12-(4-Bromophenyl)-9,9-dimethyl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-

one: White solid; 72% Yield; m.p. 185-186°C; IR (KBr): ν_{\max} (cm⁻¹) = 3064, 2959, 1649, 1595, 1527, 1483, 1468, 1277, 1224, 1170, 662. ¹H- NMR (CDCl₃, 400 MHz): δ ppm: 7.90 (1H, d, *J*=8.0 Hz), 7.79–7.75 (2H, m), 7.43–7.20 (7H, m), 5.66 (1H, s), 2.55 (2H, s), 2.32 (1H, d, *J*=15.9Hz), 2.25 (1H, d, *J*=16.5Hz), 1.11 (s, 3H), 0.95 (s, 3H). ¹³C-NMR (CDCl₃, 100 MHz): δ ppm: 197.00, 164.19, 147.79, 143.85, 131.43, 131.27, 130.30, 129.22, 128.59, 127.24, 125.13, 123.54, 120.20, 117.14, 117.05, 113.80, 50.94, 41.47, 34.35, 32.36, 29.41 and 27.24. HRMS-ESI: calculated for C₂₅H₂₂O₂Br [M+H]⁺: 433.0803, Found: 433.0805

3.12-(4-Fluorophenyl)-9,9-dimethyl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-

one: White solid; 84% Yield; m.p. 176-178°C; IR (KBr): ν_{\max} (cm⁻¹) = 2956, 2878, 1653, 1596, 1507, 1466, 1226, 1162, 1145, 1070. ¹H NMR (CDCl₃, 400 MHz): δ ppm: 7.94 (1H, d, *J*= 8.0 Hz), 7.77 (2H, t, *J*= 8.0 Hz), 7.43-7.29 (5H, m), 6.85 (2H, t, *J*=

8.0 Hz), 5.70 (1H, s), 2.55(2H, s), 2.33 (1H, d, $J=15.9\text{Hz}$), 2.26 (1H, d, $J=16.5\text{Hz}$), 1.11 (3H, s), 0.95 (3H, s). $^{13}\text{C-NMR}$ (CDCl_3 , 100 MHz): δ ppm: 197.06, 164.05, 162.49, 160.06, 147.81, 140.67, 140.65, 131.60, 131.33, 129.12, 128.58, 127.17, 125.09, 123.62, 117.46, 117.17, 115.26, 115.04, 114.17, 50.95, 41.48, 34.09, 32.35, 29.43, 27.16. HRMS-ESI: calculated for $\text{C}_{25}\text{H}_{22}\text{O}_2\text{F}$ $[\text{M}+\text{H}]^+$: 373.1604, Found: 373.1601

4.12-(2-Nitrophenyl)-9,9-dimethyl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one:

Pale Yellow solid; 78% Yield; m.p. 216-218°C; IR (KBr): ν_{max} (cm^{-1}) = 3065, 2960, 1771, 1737, 1656, 1597, 1173. $^1\text{H NMR}$ (CDCl_3 , 400 MHz): δ ppm: 8.56 (1H, d, $J=8.4\text{Hz}$), 7.84–7.80 (3H, m), 7.39–7.17 (5H, m), 7.05-7.03(1H, m), 6.57 (1H, s), 2.54 (2H, s), 2.23 (1H, d, $J=16.5\text{Hz}$), 2.18 (1H, d, $J=15.9\text{Hz}$), 1.08 (3H, s), 0.86(3H, s). $^{13}\text{C-NMR}$ (CDCl_3 , 100 MHz): δ ppm: 196.97, 163.86, 148.31, 139.24, 132.87, 131.89, 131.63, 131.18, 129.82, 128.33, 127.71, 127.17, 125.37, 124.78, 124.57, 117.03, 116.28, 113.48, 50.55, 41.52, 32.27, 30.36, 29.23, 27.15. HRMS-ESI: calculated for $\text{C}_{25}\text{H}_{22}\text{NO}_4$ $[\text{M}+\text{H}]^+$: 400.1549, Found: 400.1544

5.12-(3-Nitrophenyl)-9,9-dimethyl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one:

White solid; 71% Yield; m.p. 167-168°C; IR (KBr): ν_{max} (cm^{-1}) = 3055, 2956, 1899, 1818, 1649, 1595, 1529, 1467, 1444, 1348, 1223, 1171. $^1\text{H NMR}$ (CDCl_3 , 400 MHz): δ ppm: 8.11–7.78 (6H, m), 7.44–7.33 (4H, m), 5.80 (1H, s), 2.59 (2H, s), 2.34(1H, d, $J=15.9\text{Hz}$), 2.25(1H, d, $J=16.5\text{Hz}$), 1.12 (3H, s), 0.94(3H, s). $^{13}\text{C-NMR}$ (CDCl_3 , 100 MHz): δ ppm: 196.92, 164.65, 148.45, 147.90, 146.87, 134.94, 131.67, 129.75, 129.17, 128.79, 127.46, 125.29, 123.33, 123.21, 121.69, 117.32, 116.08, 113.21, 50.84, 41.44, 34.84, 32.42, 29.35, 27.24. HRMS-ESI: calculated for $\text{C}_{25}\text{H}_{22}\text{NO}_4$ $[\text{M}+\text{H}]^+$: 400.1549, Found: 400.1555

6.12-(4-Nitrophenyl)-9,9-dimethyl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one:

White solid; 81% Yield; m.p. 174-176°C; IR (KBr): ν_{max} (cm^{-1}) = 3073, 2957, 1647, 1619, 1594, 1518, 1467, 1223, 1182. $^1\text{H NMR}$ (CDCl_3 , 400 MHz): δ ppm: 8.04 (1H, d, $J=8.0\text{Hz}$), 7.81–7.80 (3H, m), 7.52–7.34 (5H, m), 5.80 (1H, s), 2.59 (2H, s), 2.35(1H, d, $J=16.4\text{Hz}$), 2.25(1H, d, $J=15.9\text{ Hz}$), 1.12 (3H, s), 0.94(3H, s). $^{13}\text{C-NMR}$ (CDCl_3 , 100 MHz): δ ppm: 196.89, 164.74, 151.97, 147.84, 146.39, 131.64, 131.09,

129.73, 129.46, 128.76, 127.49, 125.34, 123.74, 123.20, 117.19, 113.05, 50.85, 41.49, 34.95, 32.37, 29.41 and 27.17. HRMS-ESI: calculated for C₂₅H₂₂NO₄ [M+H]⁺ : 400.1549, Found: 400.1552

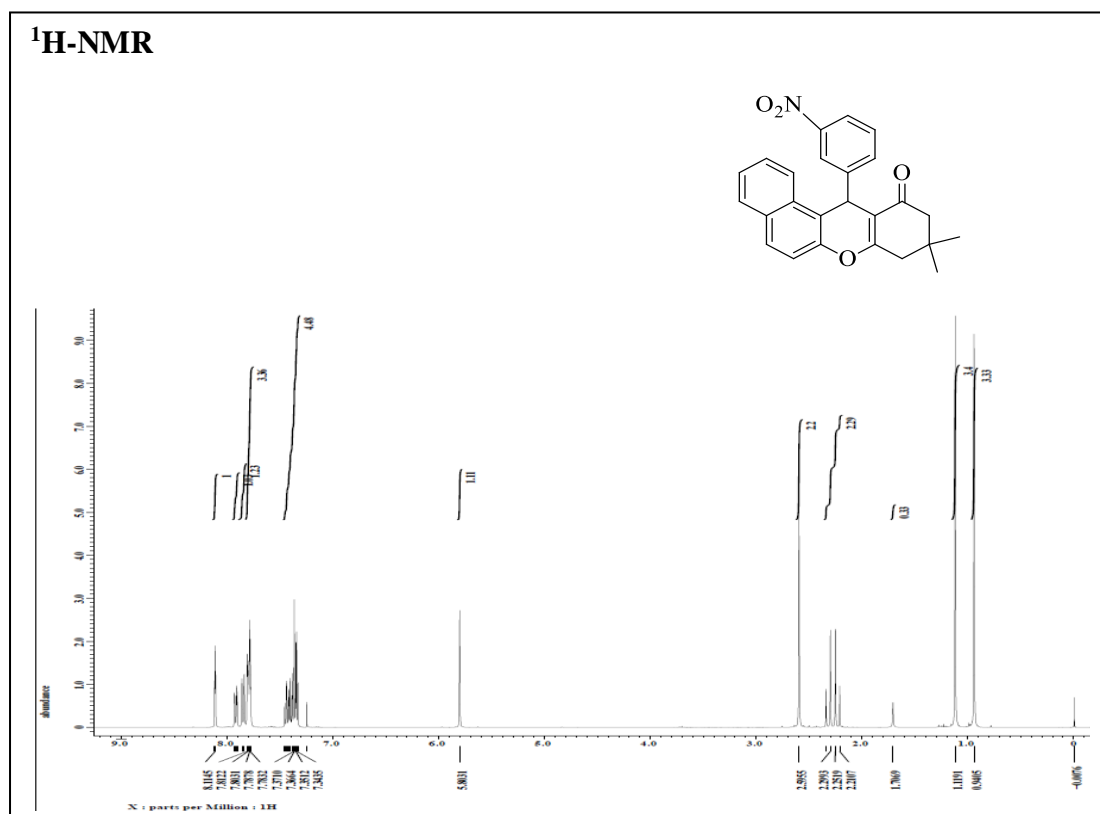
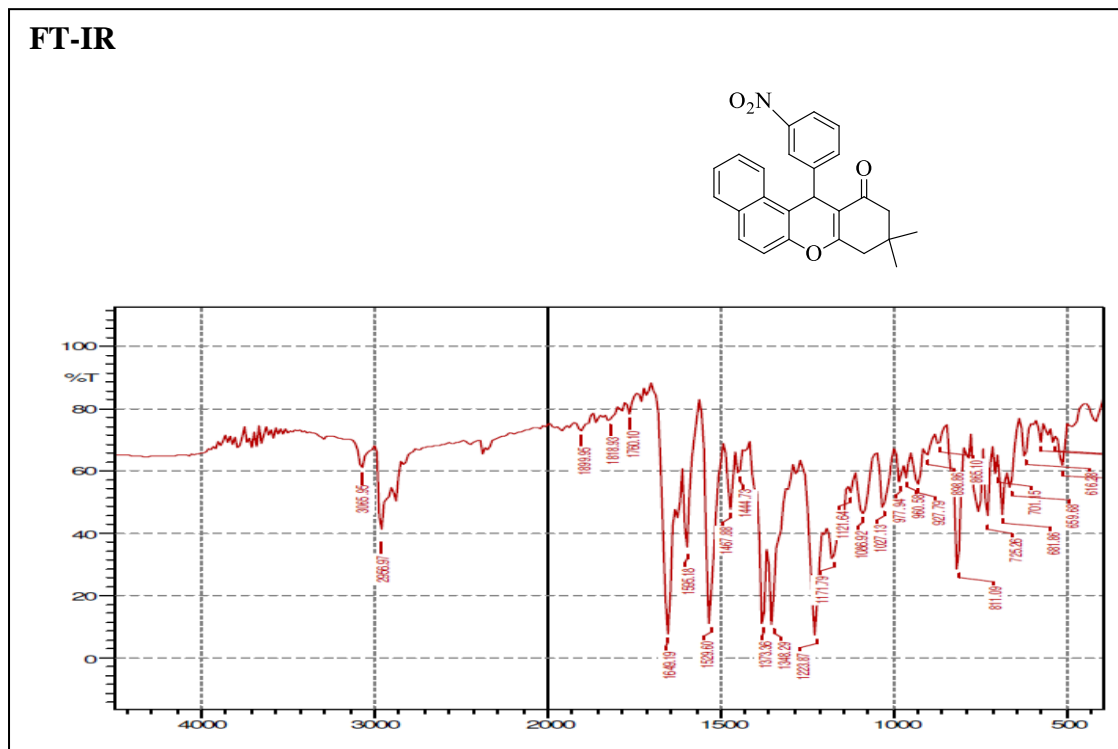
7.12-(4-Methylphenyl)-9,9-dimethyl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-

one: White solid; 73% Yield; m.p. 172-174°C; IR (KBr): ν_{\max} (cm⁻¹) =2952, 2868, 1648, 1619, 1596, 1511, 1463, 1184. ¹H NMR (CDCl₃, 400 MHz): δ ppm: 8.01 (1H, d, *J*=8.0 Hz), 7.77–7.73 (2H, m), 7.44–7.21 (5H, m), 6.97(2H, d), 5.66 (1H, s), 2.56 (2H, s), 2.31(1H, d, *J*=16.5Hz), 2.22(1H,d, *J*=16.5Hz) 2.15(3H, s), 1.11 (3H, s), 0.96(3H, s). ¹³C-NMR (CDCl₃, 100 MHz): δ ppm: 197.09, 163.89, 141.94, 135.75, 131.56, 129.02, 128.79, 128.46, 128.36, 127.06, 124.94, 123.77, 117.13, 114.45, 51.00, 41.49, 34.36, 32.40, 29.36, 27.38 and 21.09. HRMS-ESI: calculated for C₂₆H₂₅O₂ [M+H]⁺ :369.1855, Found: 369.1857

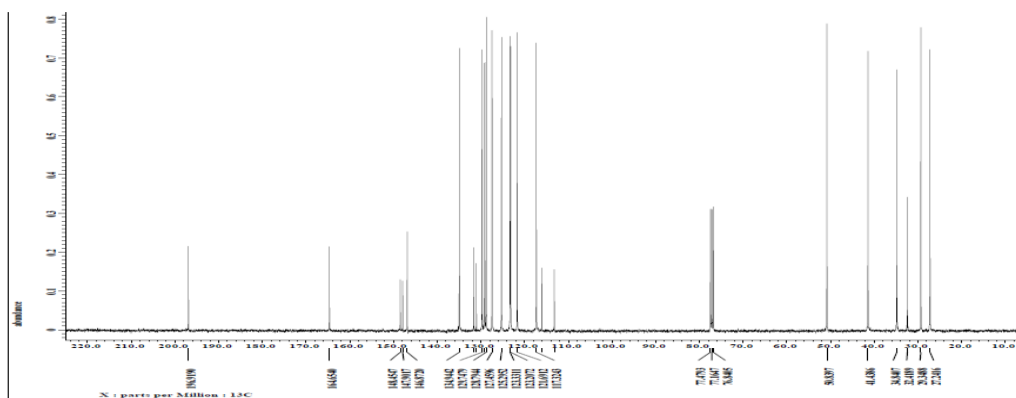
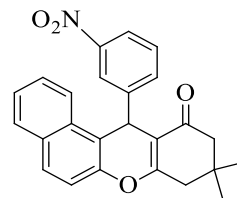
Conclusion:

It was first of its kind study where a completely new ecofriendly methodology was developed for the synthesis of benzoxanthenes by making aromatic aldehydes react with dimedone and β -naphthol in aqueous oxalic acid solution. All the reactions were performed in water medium and bio degradable oxalic acid was applied as green ecofriendly catalyst for formation of this class of compound for the very first time ever. All the reactions were completed within 25-44 minutes time duration under microwave irradiation. Various aromatic aldehydes with various electronic natures have given considerably good percentage of yield. It was 4-nitro derivatives which has made the reaction to be most feasible. Thus an easy, economic, ecofriendly, simple, new methodology is developed for the very first time ever for synthesis of benzoxanthenes in water medium employing biodegradable acid as catalyst. It has opened a new door of opportunity for the chemist to employ oxalic or such biodegradable acid as green catalyst instead of using toxic catalyst for synthesis of pharmaceutically potent heterocyclic compounds in water medium.

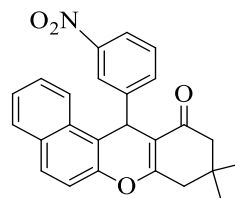
Representative FT-IR, NMR and HRMS



¹³C-NMR



HRMS-ESI



Elemental Composition Report

Page 1

Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for I-FIT = 3

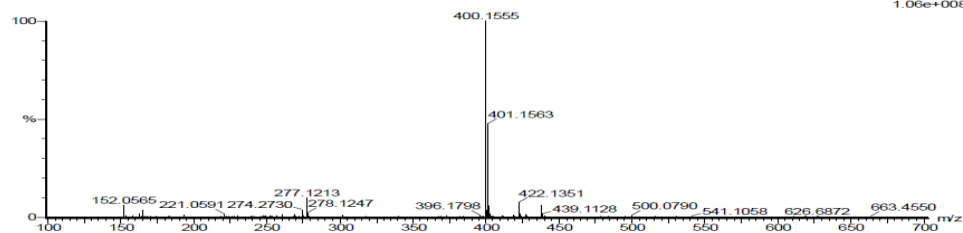
Monoisotopic Mass, Even Electron Ions
27 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:
C: 15-27 H: 5-35 N: 0-3 O: 1-4
Sample Name : BXOUS-3NO2
Test Name : HRMS-1
090919-BXOUS-3NO2-31 (0.305) AM2 (Ar,22000.0,0.00,0.00); Cm (31:37)

IITRPR

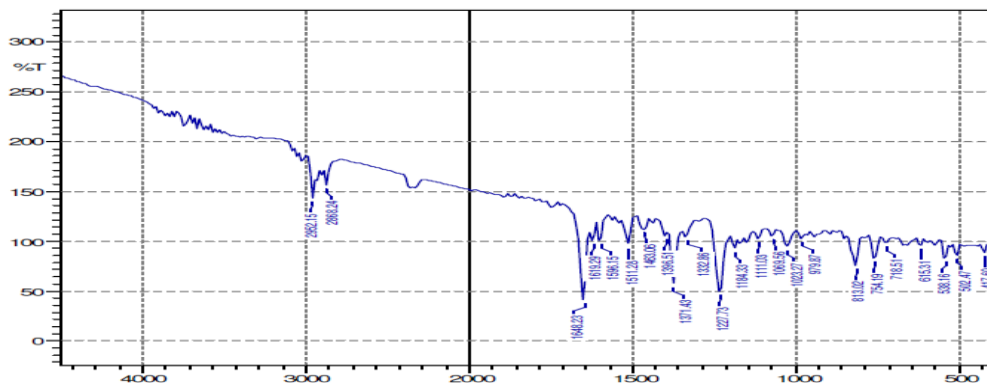
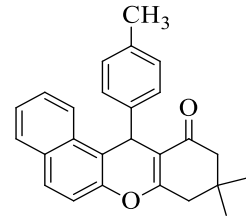
XEVO G2-XS QTOF

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1.06e+008

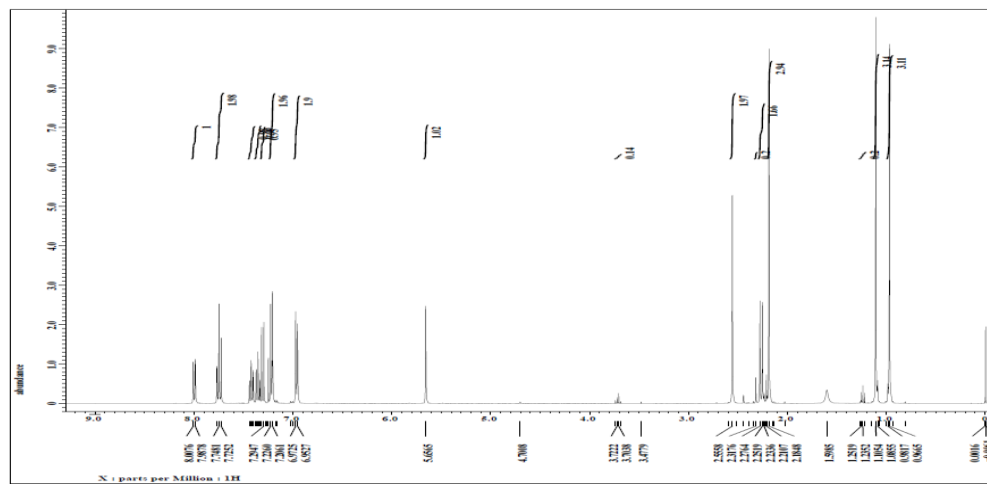
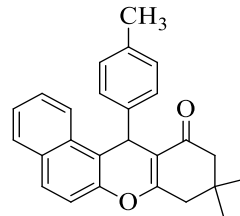


Minimum:	Maximum:								
		5.0	5.0	-1.5					
				50.0					
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula	
400.1555	400.1549	0.6	1.5	15.5	968.8	n/a	n/a	C25 H22 N O4	

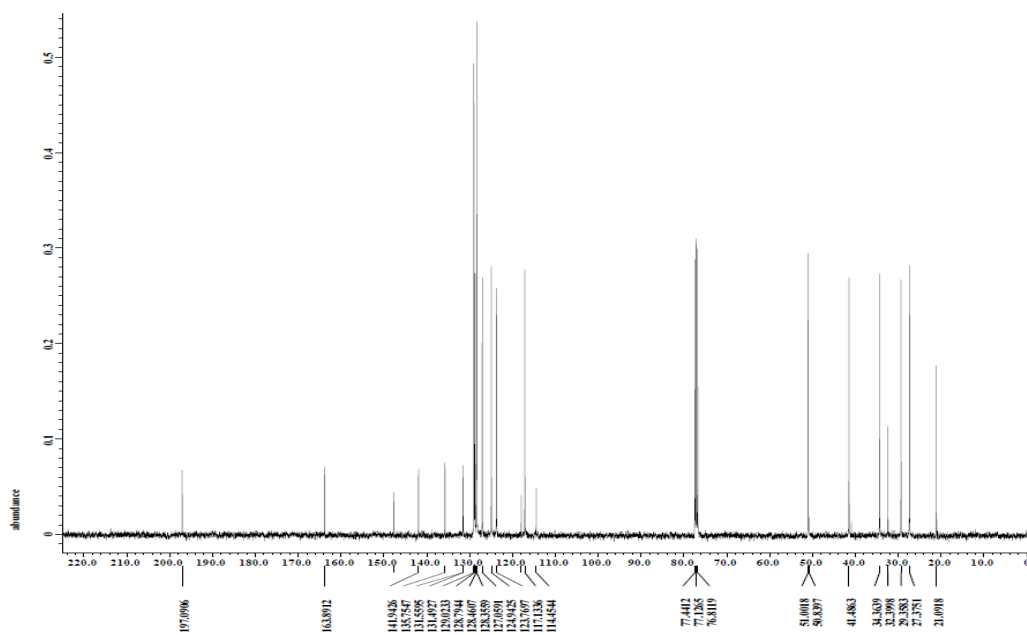
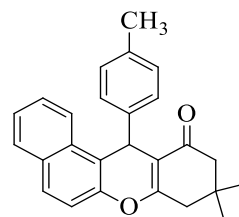
FT-IR



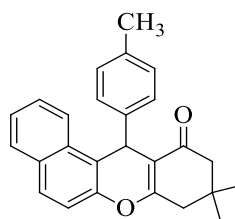
¹H-NMR



¹³C-NMR



HRMS-ESI



Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for I-FIT = 3

Monoisotopic Mass, Even Electron Ions
40 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 15-27 H: 5-35 N: 0-3 O: 1-4

ITRFR

XEVO G2-XS QTOF

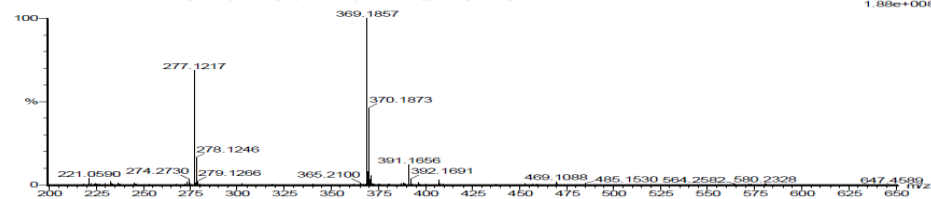
Sample Name : BXC0MW-4ME

Test Name : HRMS-1

090919-BXC0MW-4ME 33 (0.323) AM2 (Ar,22000.0,0.00,0.00); Cm (33:45)

1: TOP MS ES+

1.88e+008



Minimum:	Maximum:	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
369.1857	369.1855	0.2	0.5	14.5	1063.0	n/a	n/a	n/a	C26 H25 O2

3.2.2 Ultrasound assisted green synthesis of azomethines and benzoxanthenes in biodegradable reaction medium

In the last three decades ultrasound irradiation has been considered as a useful tool in organic synthesis¹⁵⁸. A number of organic reactions can be carried out under ultrasound irradiations¹⁵⁹⁻¹⁶². Prominent features of ultrasound approach are formation of purer products in higher yield under milder conditions¹⁶³. Compared with traditional method ultrasound technique is convenient, easily controllable, conserve energy, and reduces production of waste¹⁶⁴⁻¹⁶⁵. In ultrasonication, condensation proceeded at 40 \pm 5 °C temperature.

A huge quantity of cavitation bubbles which swells up swiftly are produced by application of ultrasonic irradiations on reaction mixture. Afterwards, these bubbles collapse resulting in the formation of micro jets which produce emulsion between the reactants¹⁶⁶. Due to great disintegration of cavitation bubbles the internal temperature within the reaction concoction rises and this finally helps to surpass the E_a barrier¹⁶⁷. These valuable aspects have prompted organic scientists to allow the utilization of ultrasound irradiations in great extent and because of this, in the latest past, the synthesis of wide variety of bioactive heterocycles has been done by applying ultrasound irradiations.¹⁶⁸⁻¹⁷⁴

From the last few years, synthesis of organic molecules by using easily accessible, biodegradable, green catalysts is attaining vast significance due to their simple mode of working, lack of toxicity. In this section we have reported the applications of two different green reaction medium- aqueous solution of glucose for preparing azomethines and aqueous solution of oxalic for the synthesis of benzoxanthenes.

US assisted Synthesis of azomethines in aqueous solution of glucose

Glucose has great potentiality to be used as ecofriendly catalyst for synthesis of azomethines because it is completely biodegradable, cost effective, innocuous and safe for the environment. In literature no synthesis of azomethines has ever been reported employing glucose as green catalyst in water medium. Thus hereby we are

reporting glucose catalyzed green synthesis of azomethine in aqueous medium under ultrasonic irradiation, for the very first time ever.

The affluent application of PEG-400 as the reaction medium for benzoxanthone synthesis^{81, 111} has made us think to use similar type of harmless and easily degradable material as catalyst for our reaction.

As observed from the mode of action of PEG-400, the interaction of oxygen atom of the aromatic aldehyde (reactants) with the –OH of the PEG-400 via intermolecular H-bonding is the actual driving force for this reaction to occur successfully. It's expected that the similar type of H-bonding formation between OH groups of D-glucose molecule and oxygen atom of aldehyde functional group is also possible. This type of H-bonding decreases the electron density on the carbonyl carbon thereby making carbonyl carbon to be more electron deficient for easy attack by nucleophilic amino group.

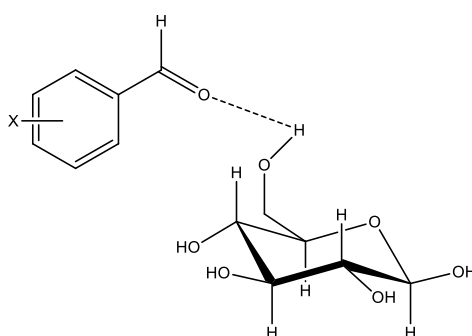
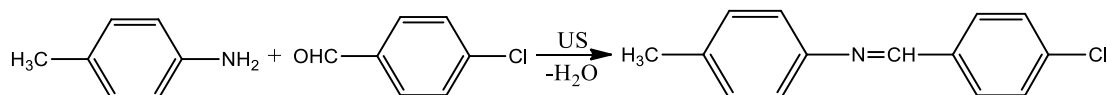


Figure-3.5: Intermolecular H-bonding between D-glucose and aromatic aldehyde

To assess the efficiency of catalysts, first the reactions were performed in presence as well as in absence of glucose catalyst where 4-chloro benzaldehyde was made to react with p-toluidine under ultrasonic irradiation in water medium [Scheme-3.6]. It is worthy to note that in water medium and in absence of glucose catalyst, the reaction completed in 10 min duration. The same reactions with the same reactants were completed effectively in comparatively shorter time of duration when the reactions were conducted in presence of glucose catalyst in water solvent. To examine the influence of catalyst concentration on the rate of reaction; the reactions were

performed in different concentration of aqueous glucose solution. The results obtained are shown in **table-3.6**.



Scheme-3.6: Representative reaction with 4-chlorobenzaldehyde and p-toluidine.

Reaction medium	Water	Aqueous Glucose solution			
Conc.		0.25 M	0.5 M	1 M	2 M
Time in min	10	12	2	4	5

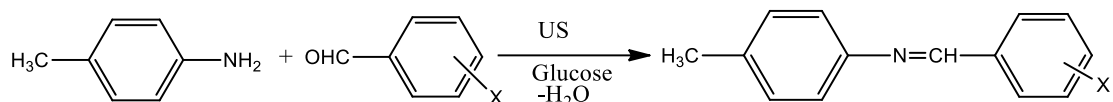
Table-3.6: Comparison of reaction in presence and absence of catalyst under US

From the results depicted in **table-3.6** it was noticed that the reaction took minimum time to go for completion in 0.5M aqueous solution of D-glucose. Thus remaining all the reactions was carried out in 0.5M aqueous solution of D-glucose. The reaction with 0.25M glucose solution has taken significantly longer time.

General procedure for synthesis of azomethines aqueous solution of glucose:

For synthesis of azomethines, 100 ml borosilicate conical flask was charged with 0.00125 mole of p-toluidine and 0.00125 mole of desired aldehyde in 2.5 ml of desired glucose solution. The reaction mixture was exposed to ultrasonic irradiations for specific time (in ultrasonic bath of Lab tech Company having timer and temperature meter). The progress of the reaction was continuously monitored by checking TLC after every 0.5 mins of time interval. When the reaction gets completed as revealed by TLC the reaction concoction was added into chilled water. The solid crude product precipitated out of the reaction concoction was filtered and dried. To get pure product, the crude product was recrystallized from hot ethanol. Pure azomethines are obtained as white/yellowish solid powder. The synthesized azomethines were then characterized by melting point, IR, NMR and mass

spectroscopy. The melting point, IR and NMR spectra of the prepared compounds were identical to those of reported ones.



Scheme-3.7: Synthesis of azomethines in aq. solution of glucose under ultrasound irradiations

Table-3.7: US assisted synthesis of azomethines with different aldehydes in glucose solution

Entry	X	Time (Min)	% Yield	Observed M. P of product (°C)
1	4-Cl	2	92	122-124
2	4-Br	23	81	136-138
3	4-NO ₂	4	84	120-124
4	3-NO ₂	1	78	81-83
5	2-NO ₂	1	86	68-70
6	4-OCH ₃	3	80	95-97
7	4-CH ₃	14	76	80-82
8	2-OH	0.5	94	104-106

It was interesting to note that while a series of Schiff base were synthesized using different derivatives of benzaldehyde; all the reactions were completed successfully within time duration of 0.5 mins to 23 mins. The obtained results were summarized in **table-3.7**.

The reactions have exhibited significant dependence on the electronic nature of aromatic aldehydes, -I-effect of 'R' and its vicinity to carbonyl group greatly influences the yield and reaction time.

From above table it is evident that ortho and para substituted aldehydes provides more yield than meta substituted aldehydes. Further it is good to observe that the reaction takes minimum time when the R is electron withdrawing group whereas the reaction completes at comparatively longer time when R is electron donating group. NO₂ being electron withdrawing has reduced the reaction time significantly.

It was quite surprising and interesting to note that the reaction took quite a longtime to go for completion when 4-bromobenzaldehyde was used. The reaction was performed for several times to verify the surprising result and the same result was obtained in every time while repeating the reaction. The reason for such a huge difference in reaction time on changing 4-Cl to 4-Br is still now not very clear to us.

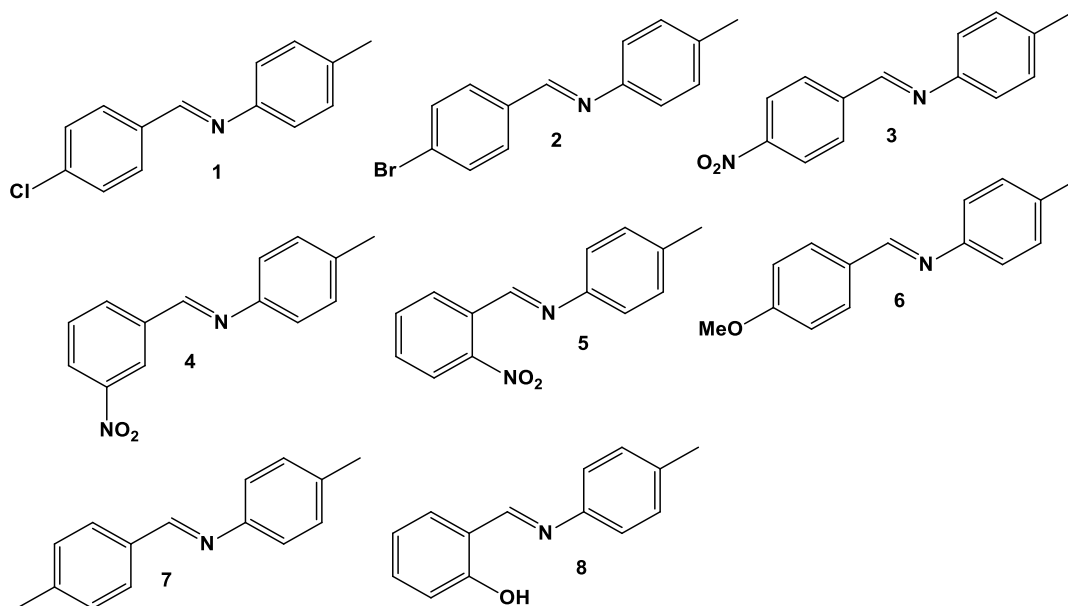


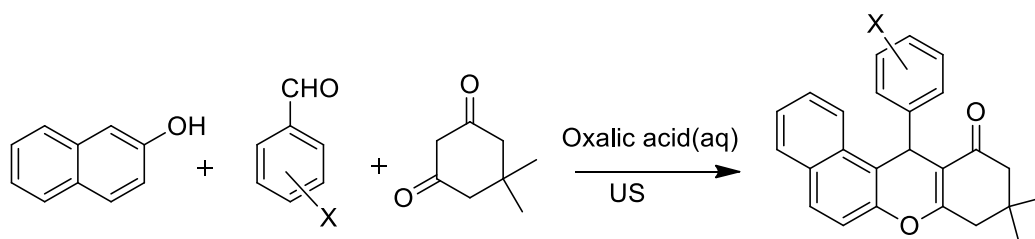
Figure-3.6: Structure of various derivatives of synthesized azomethines by using aqueous solution of glucose

Conclusion:

Hereby an efficient methodology have been developed for one pot synthesis of azomethine by condensation of various substituted benzaldehydes with p-toluidine by using glucose as green catalyst in aqueous medium under ultrasonic irradiation. This methodology has numerous benefits such as inexpensive green solvent, ecofriendly catalyst, shorter reaction time and the excellent yield of the products. All the reactions took 0.5 to 23 min for completion. The reaction with 4-bromobenzaldehyde took maximum time for completion. 2-hydroxybenzaldehyde took minimum time and gave maximum yield while minimum yield is obtained with 4-methylbenzaldehyde which have +I effect showing methyl group.

US assisted Synthesis of benzoxanthenes in aqueous solution of oxalic acid

Oxalic acid ($C_2H_2O_4 \cdot 2H_2O$) is quite strong organic acid having $p^H=3$. This is due to presence of two carboxylic groups which are joined directly to each other. It is completely biodegradable, non toxic, cost effective and efficient catalyst which is used for organic conversions¹⁷⁵⁻¹⁷⁶. We have used it by forming its aqueous solution because water also works as green and universal solvent.



Scheme- 3.8: Synthesis of benzoxanthenes in aq. solution of oxalic acid under ultrasound irradiations

General Procedure for Synthesis of benzoxanthenes in aq. solution of oxalic acid:

0.015 moles of each of β -naphthol, dimedone and desired aldehyde were taken in a conical flask. Then the flask was charged with aqueous solution of 2M oxalic acid (10 ml). The reaction mixture was exposed to ultrasound irradiation for specific time. The reaction progress was tracked continuously by checking thin-layer

chromatography (TLC). The reaction was quenched by pouring the reaction mixture into crushed ice after the reaction gets completed (shown by TLC). The unpurified solid crude product that was precipitated in water medium was removed out by filtration. Recrystallization of the unrefined product was done from hot ethyl alcohol (two times) to get impurity free benzoxanthone and then it was washed with hexane to remove any non-polar impurities. The obtained pure product was specified by melting point, FT-IR, NMR and mass spectra.

Results and Discussion:

Related to our ongoing research work for synthesis of various non carbocyclic compounds by green methods, herein we report preparation of benzoxanthone analogues by condensation of 2-naphthol, different substituted benzaldehydes and dimedone in one vessel by using oxalic acid as bio degradable, nontoxic catalyst in an easy and well organized way. All the reactions were carried out by employing ultrasound irradiations. A chain of reactions were conducted by employing various derivatives of benzaldehyde with varying functional groups.

It was seen that all the reactions were completed successfully within a time duration of 30 min to 120 mins while employing ultrasound irradiation as ecofriendly source of energy. Moreover it was worthy note that reaction was fastest with 4-Me benzaldehyde whereas slowest with 4-Br benzaldehyde derivatives. All the reactions have given a considerably good percentage of yields with 4-F derivatives giving the maximum one. The obtained results are sum up in table-3.8

Table-3.8: US assisted synthesis of benzoxanthenes with different aldehydes in aqueous Solution of oxalic acid

Entry	X	Time (Min)	% Yield	Observed M. P of product (°C)
1	4-Cl	86	81	178-180
2	4-Br	120	70	183-185
3	4-F	74	88	178-179

4	2-NO ₂	60	71	218-220
5	3-NO ₂	100	87	167-168
6	4- NO ₂	44	78	173-175
7	4-CH ₃	30	81	170-172

The compounds synthesized are not entirely new ones, instead they are the compounds which are already reported in the literature, the prepared compounds are identified by melting point, IR, ¹H and ¹³C and by HRMS. The obtained results are verified by comparing the same with literature reported characterizations. The spectroscopic data and melting point prepared molecules were comparable to those of published ones.

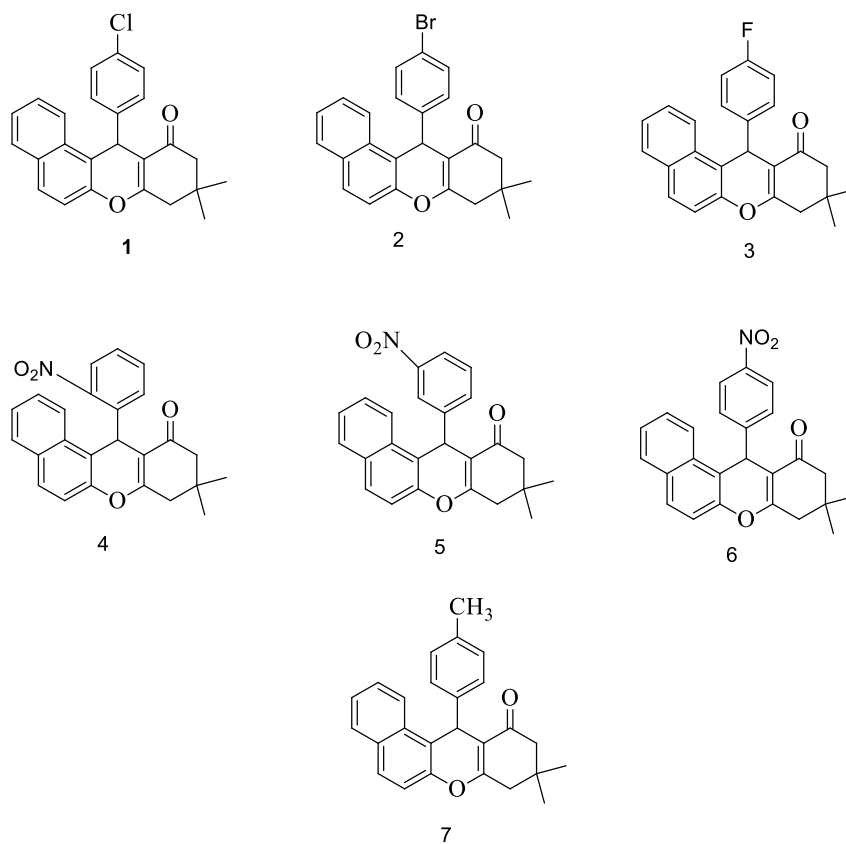


Figure-3.7: Structure of various derivatives of benzoxanthone synthesized by using oxalic acid

Conclusion:

In brief, we have established new method for the formation of benzoxanthone derivatives under ultrasonic irradiations. Especially important aspects of this practice comprise excellent yield and straight ward procedure which expand the application of ultrasonic irradiations in the production of heterocyclic molecules. The reaction with 4-bromobenzaldehyde took maximum time and provide minimum yield while with 4-Fluorobenzaldehyde maximum yield of benzoxanthone is obtained. The reaction proceeded at fastest pace with 4-methylbenzaldehyde.

3.2.3 Grindstone synthesis of azomethines and benzoxanthenes by using suitable green catalyst.

In the past two decades, new approaches had been applied in classical organic chemistry which explores molecules and techniques in the chemical industry that are ecologically sustainable¹⁷⁷. Therefore, there is urgent requirement of “greener technologies” to check depletion of natural resources¹⁷⁸.

A remarkable field in organic synthesis involves Solventless “grinding reactions” which provide very striking route of flourishing environmentally benign techniques for the formulation of biodynamic heterocycles. Actually the grinding of two or more components together in solid state allows the reaction to proceed¹⁷⁹. This concept of grinding was developed by Toda and others¹⁸⁰. Driving force for these reactions to happen is that when we grind two or more constituent together it brings about the interaction of collision and frictional forces due to which large amount of energy is evolved which perform an important part in facile transformation of reactants to products¹⁸¹⁻¹⁸². A large number of reactions are carried out by grinding technique under solvent free conditions^{69, 75, 80, 183-185}. This protocol has several benefits like decreasing the requirement of traditional cooling and heating hence leads to conservation of energy. It also reduces the use of harmful organic solvents which are volatile in nature. This technique prevents the use of conventional and mechanochemical grinding¹⁸⁶.

In literature, a wide variety of organic reactions are documented which involves the use of natural catalysts like animal bone, natural phosphates, clay and numerous fruit juices. Aqueous fruit juice like lemon, pomegranate, pineapple, coconut, grapes, unripe mango, star fruit and Tamarindus indica fruit are found to be acidic hence works as suitable substitute in comparison to toxic, expensive and non biodegradable acid catalysts^{86, 153, 187-193}. So the use of such natural green acid catalysts gives us idea to use garlic as green catalyst for the synthesis of azomethines and benzoxanthenes.

Grindstone assisted Synthesis of azomethines by using Garlic

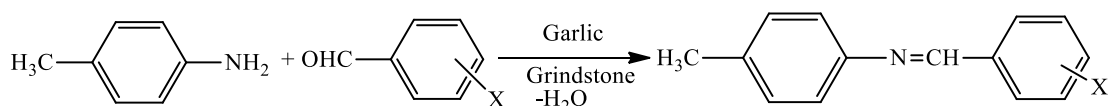
Garlic is natural acidic catalyst having $p^H= 5.61$. Garlic possesses many ingredients in rich amounts including vitamin B₆, C and dietary minerals manganese and phosphorus. It also contains large number of sulphur compounds. Its acidic nature is mainly due to presence of amino acid allin which is modified form of cysteine. It is used for the very first time ever by our group as catalyst for organic reactions.

General procedure for synthesis of azomethines by using garlic as biocatalyst:

2.5 mmol of p-toluidine, 2.5 mmol of substituted benzaldehyde along with a piece of garlic were grinded together in a mortar with a pestle in a completely solvent free condition for particular time duration. The reaction mixture changes to pasty material after few minutes of grinding. The speed of the process was successively scanned by examining the thin layer chromatography. After accomplishment of the reaction, recrystallization of solid unrefined product was carried out from absolute ethyl alcohol as a result of which we get pure azomethines as white/yellowish solid. The azomethines so obtained were identified by melting point, IR, NMR and HRMS. The melting point, IR and NMR spectra and HRMS data of the obtained products were almost similar to those of reported ones.

Results and discussion:

It is observed that formation of azomethines takes place by condensation between carbonyl compounds and primary amines. The reaction is facile owing to the good electrophilic nature of carbonyl compounds and nucleophilic nature of amines.



Scheme-3.9: Synthesis of azomethines by using garlic as natural acid biocatalyst via grindstone technique

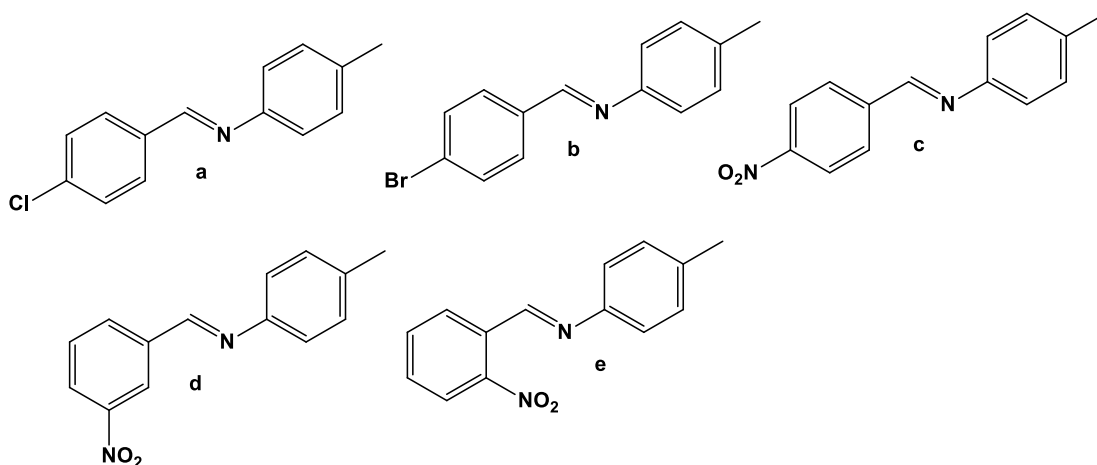


Figure-3.8: Structure of various derivatives of synthesized azomethines by using garlic

All the products were obtained successfully simply by grinding an equimolar mixture of aromatic aldehyde and aromatic amine with the help of mortar and pestle. All the reactions were carried out in completely solvent free condition, employing garlic as a green catalyst (As shown in scheme-3.11).

Table-3.9: Grindstone assisted, garlic catalyzed synthesis of azomethines with different aldehydes

Entry	X	Time (Min)	% Yield	Observed. M.P(°C)
A	4-Cl	7	73.8	120-122
B	4-Br	12	63	136-138
C	4- NO ₂	5.5	81	120-122
D	3-NO ₂	7.5	53.3	84-86
E	2-NO ₂	6	62.5	70-72

The obtained results are outlined in table-3.9. From table-3.9 it is clear that the reactions have taken 5-12 minutes time duration for completion.

The reactions have exhibited significant dependence on the electronic nature of aromatic aldehyde. Inductive effect of 'X' and its vicinity to carbonyl group greatly influence the amount of product as well as time duration of the process.

It is good to note that the reactions with electron deficient aromatic aldehydes produce more percentage of yield and the percentage yield of the products decreases with decrease in electron withdrawing effect of the functional group **X**. So the reaction with 4- NO₂benzaldehyde gives maximum percentage of yield whereas the reaction with 4-Br benzaldehyde gives comparatively lower percentage of yield.

The reaction time also varies depending on the electron withdrawing effect of **X**. Thus the reaction takes minimum time with 4- NO₂-benzaldehyde and maximum time with 4-Br-benzaldehyde. It was also worthy to note that only 5 selective derivatives (which are solid at room temperate) of Benzaldehyde were used as reactant for carrying out grindstone assisted reaction. It was done so just to make sure that all grindstones assisted reactions were performed in a completely solvent free & solid state condition

Conclusion:

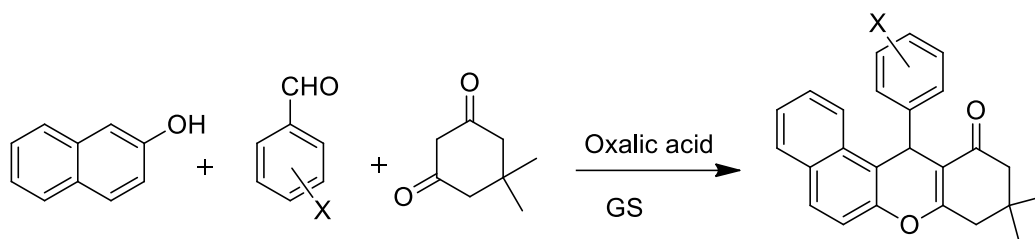
In this work, we have demonstrated a too straightforward, easy, energy saving, cost effective, ecofriendly and new methodology for grindstone assisted synthesis of azomethines, using garlic as natural biocatalyst in a completely solvent free condition. This method has a number of benefits like simple experimental set up, relatively short duration of reaction, low cost and at last but not the least it is in agreement with the protocols of green chemistry. This is the first of its kind study where garlic is successfully explored as green bio catalyst for solvent free green synthesis of azomethines for the very first time ever in literature. This work will motivate the researcher to use garlic/ other such bio catalysts instead of toxic catalyst/ solvents for ecofriendly synthesis of azomethines or other such organic molecules of biological importance. From this work we noticed that the reactions with different aldehydes took 5.5 to 12 minutes for completion and it is seen that the reaction is fastest with 4-nitrobenzaldehyde and slowest with 4-bromobenzaldehyde. It is also observed that product is obtained in maximum yield with 4-nitrobenzaldehyde and in minimum yield with 3-nitrobenzaldehyde.

Grindstone Assisted Synthesis of benzoxanthenes with oxalic acid

A number of heterocyclic compounds are constructed by employing oxalic acid as green catalyst but to the best of our knowledge this catalyst has never been employed successfully by any researchers till date for grindstone assisted synthesis of Benzoxanthenes. Thus keeping in mind this research gap, hereby one pot green synthesis of Benzoxanthenes via grindstone technique employing oxalic acid as an ecofriendly catalyst is reported.

General procedure for synthesis of benzoxanthenes by using oxalic acid:

0.015 moles of each of β -naphthol, dimedone and desired aldehyde were put in mortar along with catalytic amount of oxalic acid. The mixture was grounded with the help of pestle for suitable time until the reaction mixture turns pasty and indication of accomplishment of reaction was shown by TLC. The solid crude reaction material was added into chilled H₂O to quench the reaction, after accomplishment of the reaction. The crude product which was precipitated in water medium was isolated by filtration. To get pure benzoxanthone the crude product was recrystallized from hot ethanol (two times) and then it was washed with hexane to remove any non-polar impurities. The obtained pure product was characterized by melting point, FT-IR, NMR and mass spectra.



Scheme-3.10: Synthesis of benzoxanthenes with oxalic acid by grindstone technique

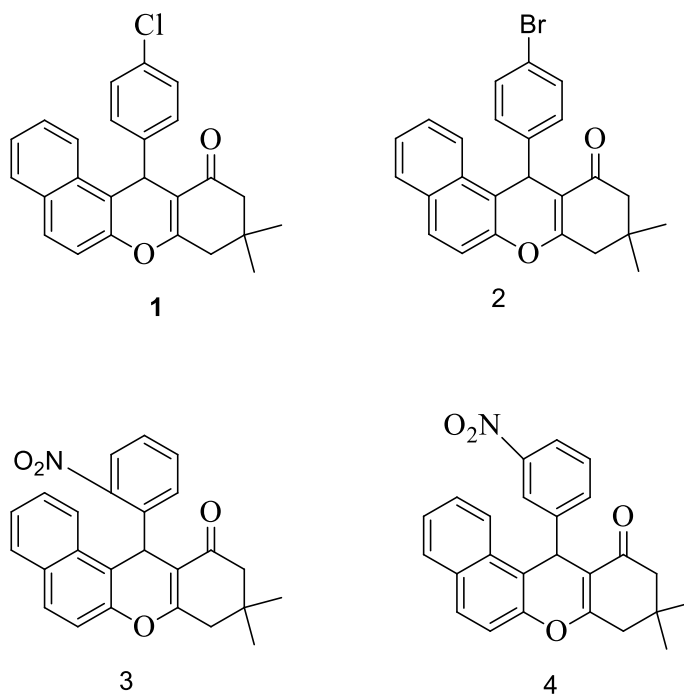


Figure-3.9: Structure of various derivatives of synthesized benzoxanthenes by using oxalic acid

Results and Discussion:

Linked with our continuing research work for formulation of different heterocycles by green methods, herein we report single vessel synthesis of benzoxanthone analogues by combination of different aryl aldehydes, 2-naphthol and dimedone applying oxalic acid as bio degradable, nontoxic catalyst by a very simple and effective way. All the reactions were carried out by grinding techniques. A series of reactions were carried out by employing various aldehydes bearing different substituents having +I and -I effect.

The results of grindstone synthesis as shown in table-3.10 have revealed that 2 nitro benzaldehyde has taken minimum time for grindstone assisted reaction whereas 4-Br derivative has taken maximum time to go for completion. The yield of the product was also minimum for 4-Br derivative. It was also worthy to note that only 4 selective derivatives (which are solid at room temperature) of Benzaldehyde were used as reactant for carrying out grindstone assisted reaction. It was done so just to make sure that all grindstone assisted reactions were performed in a completely solvent free & solid state condition.

Table-3.10: Grindstone assisted synthesis of benzoxanthenes with different Aldehydes in Oxalic acid

Entry	X	Time (Min)	% Yield	Observed M. P of product (°C)
1	4-Cl	95	73	176-178
2	4-Br	130	63	182-184
3	2-NO ₂	73	71	218-220
4	3-NO ₂	100	68	168-170

Conclusion:

Oxalic acid promotes the condensation of 2-naphthol, dimedone and aldehydes by grindstone technique under solvent-free conditions. The notable advantages of this procedure are: (a) reasonably good yield; (b) moderate conditions; (c) in line with green synthesis preventing toxic reagents; It is believed that this procedure will play an important role in the preparation of oxygen containing heterocyclic derivatives. Reactions with various aromatic aldehydes took different time for completion i.e. 73 to 130 min and proceed fastly with 2-nitrobenzaldehyde and is slowest with 4-bromobenzaldehyde. Yield of product with all the aldehydes is quite good but 4-chlorobenzaldehyde gave maximum yield and 4-bromobenzaldehyde gave lowest yield.

3.2.4 Exploring the utility of biodegradable polymers as green catalyst for the synthesis of azomethines and benzoxanthenes from aromatic aldehydes.

In organic chemistry, microwave promoted formation of organic molecules has come out as a new “lead” because of its numerous benefits like easier manipulation, prevention of energy, decreasing reaction time, generation of purer products, high yields, more effective and milder conditions and reduction of waste. So, organic chemists are worried in the evolution of ecofriendly procedures under solvent less condition or in H₂O as a green solvent by applying microwave irradiations.

One of the well-known challenges is the application of microwave irradiation chemistry to boost the efficiency and/or selectivity of organic reactions¹⁹⁴. It is well known fact that formation of diversity of compounds is promoted by microwave irradiation^{138, 195-198}. Actually under MW chemical reactions are accelerated because of specific absorption of microwave by polar molecules.

Nowadays, significant attention has been received by interaction of microwave irradiation with organic molecules having some value of dipole moment under solvent less conditions¹⁹⁹. There are some particular reactions which could be feasible only by microwave irradiation but do not occur under traditional conditional heating as revealed by the literature survey²⁰⁰.

Since the last few years making the use of easily accessible, non hazardous and biodegradable catalyst for organic conversion are in great demand because of their stability, environmentally benign nature, nontoxicity, functional simplicity and comparatively lower price. Moreover, to cope with the qualities of familiar organic processes, these reagents are highly selective and proficient. Biodegradable polymers are one of such type of catalysts which satisfy all the above mentioned requirements. The major advantage of biodegradable polymers is that they can be composted with organic matter and returned to enrich the soil, their use not only lessen the cost of labor for removal of plastic wastes in the environment but will also reduce injuries to wild animals as they are decomposed naturally. Their decomposition will help to

increase longevity and stability of landfills by decreasing the amount of waste. There are large no of biodegradable polymers which are acidic in nature. Among these the most common are starch, cellulose, PEG, PAA, PLA, PGA, PCL etc. Some researchers have employed PEG, a biodegradable polymer for the synthesis of variety of organic compounds^{81, 111, 201-202}. In this section we are making use of aqueous solution of PAA as a biodegradable green catalyst.

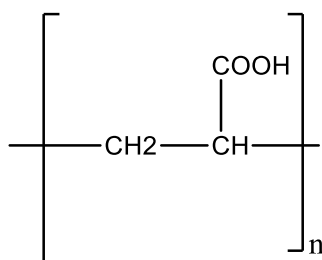
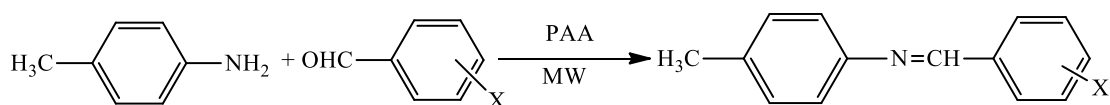


Figure- 3.10: Structure of polyacrylic acid

Synthesis of azomethines in aqueous solution of Polyacrylic acid

Polyacrylic acid is non toxic, safe and completely biodegradable. It is polymer of acrylic acid. Our extensive literature search has revealed that Polyacrylic acid has not at all been employed as environmental friendly catalyst for the formation of azomethines. So we are the first to report the synthesis of azomethines in aqueous solution of PAA.



Scheme-3.11: Synthesis of azomethines by using Polyacrylic acid as natural catalyst under microwave irradiations

General procedure for synthesis of azomethines by using aqueous solution of Polyacrylic acid:

The 100 ml conical flask was charged with 1.25 mmol of each of p-toluidine and desired aldehyde along with 10 ml aqueous solution of Polyacrylic acid (50% v/v). The reaction mixture was exposed to microwave irradiation at 350W power for

specific time in microwave synthesizer. The progress of reaction was continuously monitored by checking TLC. After the completion of reaction (indicated by TLC), the reaction mixture was poured into crushed ice. The solid crude product that was precipitated in water medium was isolated by filtration. To obtain the pure product; there crystallization of unpurified product was done with hot ethanol to get pure azomethine. The obtained pure product was identified by spectroscopic techniques and melting point determination.

Results and Discussion:

Table-3.11: MW assisted synthesis of azomethines with different aldehydes in aqueous solution of Polyacrylic acid

Entry	X	Time (Min)	% Yield	Observed M. P of product (°C)
A	4-Cl	0.5	94	120-122
B	4-Br	1	90	136-138
C	4-NO ₂	1.5	87	123-125
D	3-NO ₂	0.5	84	84-86
E	2-NO ₂	1	83	70-72
F	4-OCH ₃	0.5	81	93-95
G	4-CH ₃	1	79	78-80
H	2-OH	0.5	96	102-104

The obtained results are summarized in table-3.11. From table-3.11 it is clear that the reactions have taken 0.5-1.5 minutes time duration for completion.

From the table it is also evident that the reaction time does not depend on the electronic nature of aldehyde.

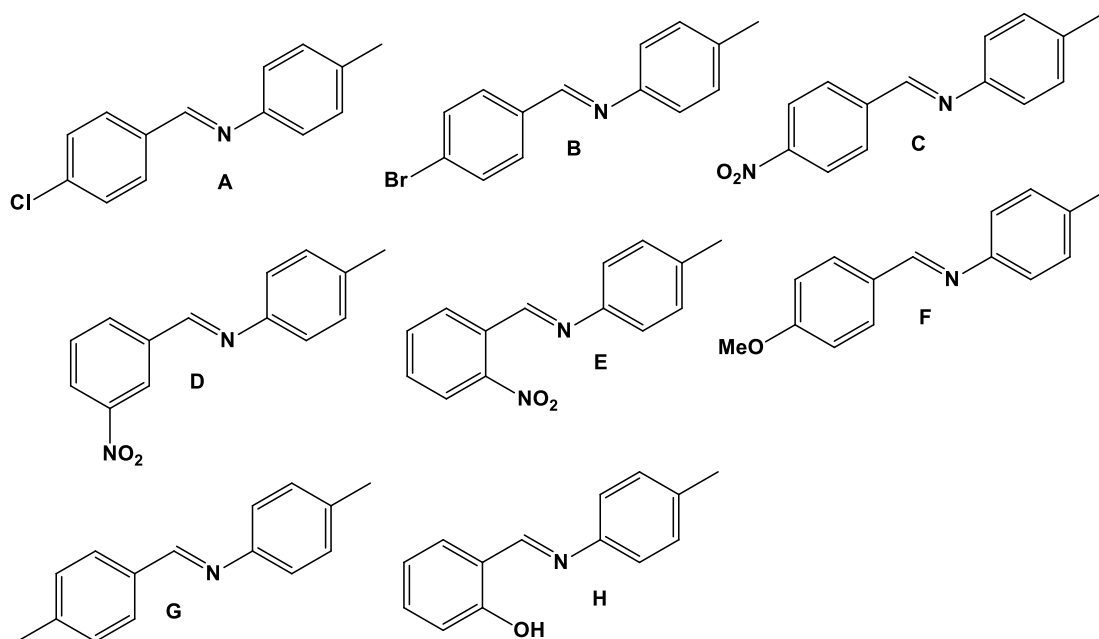


Figure-3.11: Structure of various derivatives of synthesized azomethines by using aqueous solution of Polyacrylic Acid

Conclusion:

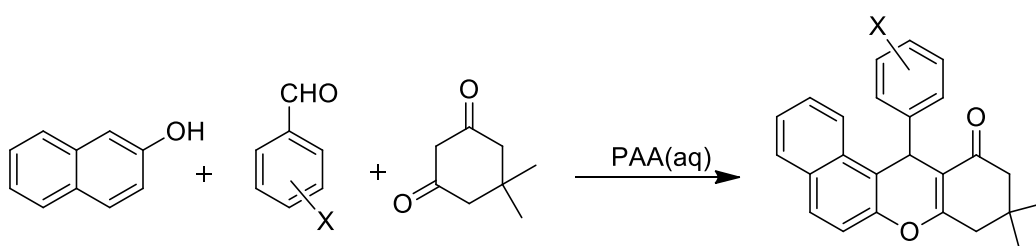
From the above work, it is concluded that reactions with variety of aromatic aldehydes by applying polyacrylic acid as catalyst completed in 0.5 to 1.5 min. Reaction is slowest when we made the use of 4-nitrobenzaldehyde. In most of the cases reactions have taken only half minute for completion which is the minimum time required as presented in above table. Although the percentage yield of compound synthesized is quite good in all the cases yet salicylaldehyde is best one on the basis of providing yield as it provided maximum yield and 4-methylbenzaldehyde provided minimum yield.

So, through this research work, new methodology for microwave assisted synthesis of azomethine, using Polyacrylic acid as completely biodegradable polymer has been established in easy, cost effective, ecofriendly, systematic and simple way. This method has a number of advantages like simple experimental set up, relatively short duration of reaction, low cost and at last but not the least it is in tune with the protocols of green chemistry. This is the first of its kind study where we have

successfully explored biodegradable polymer as an efficient catalyst for microwave assisted green synthesis of azomethine in water medium for the very first time ever in literature. This work will motivate the researcher to use polyacrylic acid/ other such biodegradable polymer as catalysts instead of toxic, non-biodegradable catalyst for ecofriendly synthesis of azomethines and other such organic molecules of biological significance.

Synthesis of benzoxanthenes in aqueous solution of Polyacrylic acid

In literature very few methods for the synthesis of benzoxanthenes are reported which involves the use of green catalysts or reaction medium⁷⁵⁻⁷⁷. So our research group has made the use of Polyacrylic acid as completely ecofriendly and green catalyst for synthesis of benzoxanthenes by applying ecofriendly source of energy in the form of microwave irradiations for the very first time ever. Till now no one has applied Polyacrylic acid as catalyst for the formation of benzoxanthenes in literature.



Scheme-3.12: Synthesis of benzoxanthenes with Polyacrylic acid under microwave irradiations

General procedure for synthesis benzoxanthenes by using aqueous solution of Polyacrylic acid:

Equimolar mixture of 2-naphthol, dimedone and suitable aldehyde along with 10 ml aqueous solution of Polyacrylic acid (50% v/v) in 100 ml conical flask was exposed to microwave irradiation at power 560W for specific time in microwave synthesizer. The progress of reaction was continuously monitored by checking TLC. When reaction gets completed (as indicated by TLC), the reaction mixture was poured into crushed ice as a result of which the solid crude product was precipitated in water medium. The crude product so obtained was separated out by filtration, recrystallized two times

from hot ethanol and finally washed with hexane to remove non polar impurities to purify benzoxanthone up to the mark. The obtained pure product was specified by melting point, FTIR, ¹H-NMR, ¹³C-NMR spectroscopy and by HRMS.

Results and Discussion:

Here we have mentioned single vessel formation of benzofused analogues of xanthen-11-one derivatives by condensation of 2-naphthol, dimedone and various substituted benzaldehydes employing Polyacrylic acid as bio degradable catalyst under microwave irradiations in an eco-friendly and very simple way.

Table-3.12: MW assisted synthesis of benzoxanthenes with different aldehydes in aqueous Solution of Polyacrylic acid

Entry	X	Time (Min)	% Yield	Observed M. P of product (°C)
A	4-F	35	73	180-182
B	4-Cl	43	71	180-182
C	4-Br	57	65	185-186
D	4-NO ₂	41	68	174-175
E	3-NO ₂	33	77	165-166
F	2- NO ₂	31	70	218-220
G	4- CH ₃	50	68	174-175

From the above table-3.12 it is clear that the reaction is faster with aldehydes bearing both type of substituents having +I and -I effect. Also the vicinity of the groups effects the reaction rate for example reaction with 2-nitrobenzaldehyde is faster than 3- nitrobenzaldehyde which in turn is faster than 4- nitrobenzaldehyde. The yield of product is too influenced by nature of aldehydes participating in the reaction as the aldehydes bearing electron withdrawing groups give better yield.

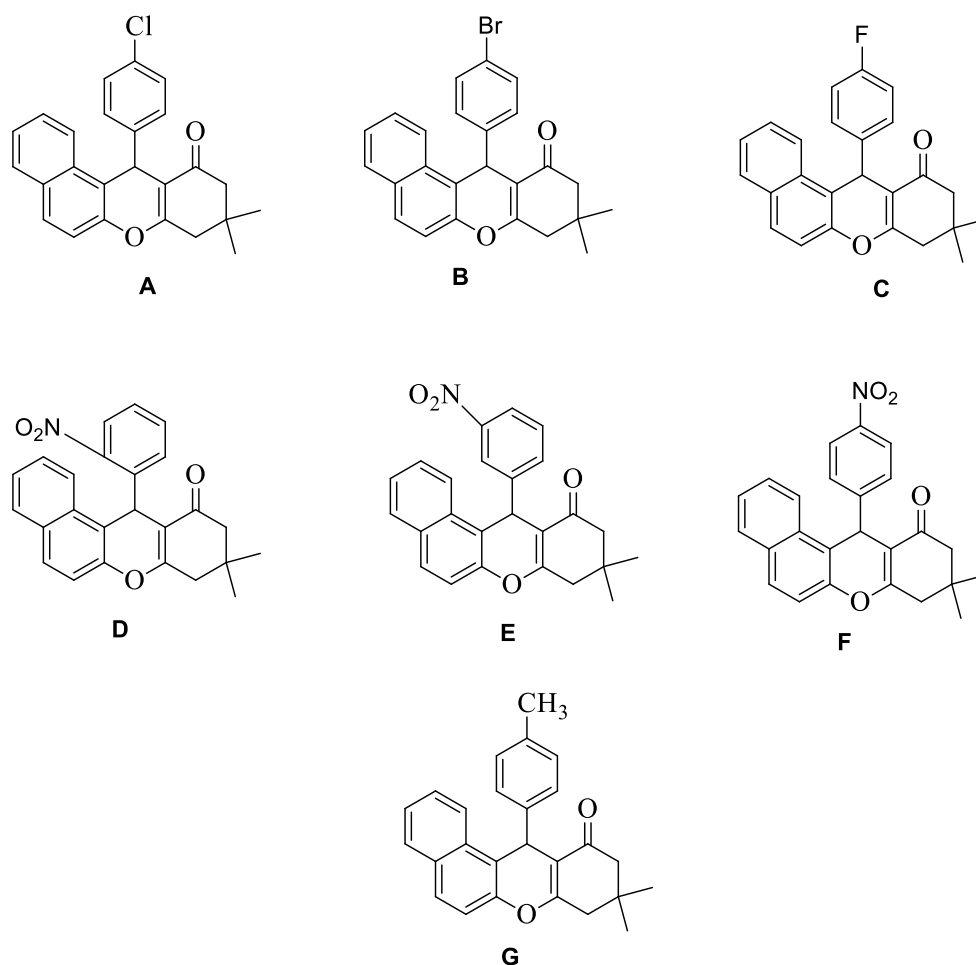


Figure-3.12: Structure of various derivatives of benzoxanthone synthesized by using aqueous solution of Polyacrylic acid

Conclusion:

So, from above work it is seen that among all the reactions, reaction with 4-fluorobenzaldehyde is completed in minimum duration of time while with 4-bromobenzaldehyde reaction took maximum time. Although yield of reaction is quite good in all the cases yet 3-nitrobenzaldehyde gave maximum yield and 4-bromobenzaldehyde gave minimum yield.

In nutshell, a new method for the formation of series of benzoxanthone analogues by applying Polyacrylic acid as bio degradable catalyst under microwave irradiation has been put forward by three component reaction of 2-naphthol, dimedone and different

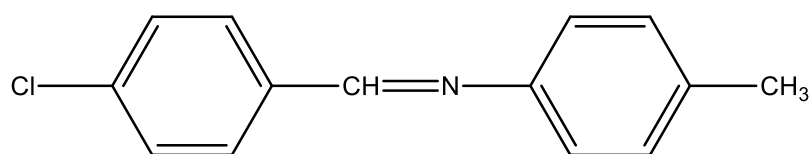
aryl aldehydes in a single container. Important features of the reaction are easy work up and use of non toxic, biodegradable catalyst which makes it valuable and interesting process for the formation of these indispensable compounds.

CHAPTER-4
CONCLUSION AND FUTURE
PROSPECTIVE

Conclusion

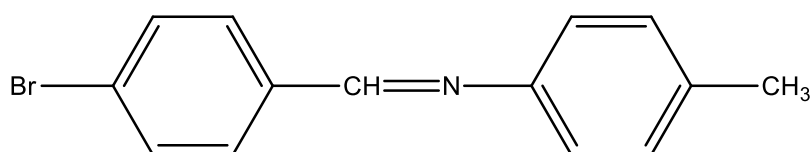
In conclusion, we have developed new, simple, efficient, clean and green synthetic protocols for the synthesis of azomethines and benzoxanthone analogues with the aid of natural, biodegradable catalysts, by applying ecofriendly source of energy in green reaction media.

4-methyl-N-[(4-chlorophenyl)methylidene]aniline



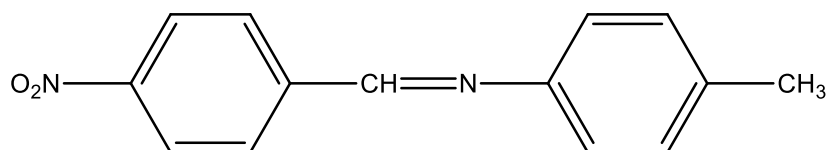
4-chlorobenzaldehyde under microwave irradiations by using either lemon juice or PAA or Glucose as catalyst has taken same time for providing azomethine. Time taken for the formation of product with all these catalysts are same and that is the minimum time required for formation of the product whereas reaction of 4-chlorobenzaldehyde via garlic catalyst reaction under grindstone conditions has taken maximum time to go for completion. The yield of product is very good with all the catalysts and under all conditions. The maximum yield of 4-methyl-N-[(4-chlorophenyl) methylidene] aniline is obtained by using glucose and polyacrylic acid as catalyst under microwave irradiations and the minimum yield of the product was obtained when reaction was performed under grindstone technology using garlic as biodegradable green catalyst.

4-methyl-N-[(4-bromophenyl)methylidene]aniline:



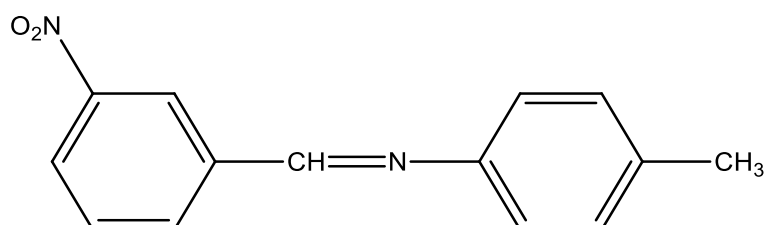
4-bromobenzaldehyde by using either lemon juice or PAA or Glucose as catalyst under microwave irradiations has taken same time for providing 4-methyl-N-[(4-bromophenyl)methylidene]aniline. Maximum time for providing this product is taken under ultrasound irradiations by using glucose as catalyst. Maximum yield of 4-methyl-N-[(4-bromophenyl)methylidene] is obtained with polyacrylic acid and minimum with garlic. So PAA was proved to be the best catalyst for synthesis of 4-methyl-N-[(4-bromophenyl)methylidene] as it has given the product with maximum percentage of yield at minimum time.

4-methyl-N-[(4-nitrophenyl)methylidene]aniline



4-nitrobenzaldehyde has taken least time and gave maximum yield of 4-methyl-N-[(4-nitrophenyl)methylidene]aniline with lemon juice as catalyst and MW as ecofriendly source of energy while maximum time to provide this product is taken by garlic catalyst under grindstone technique.

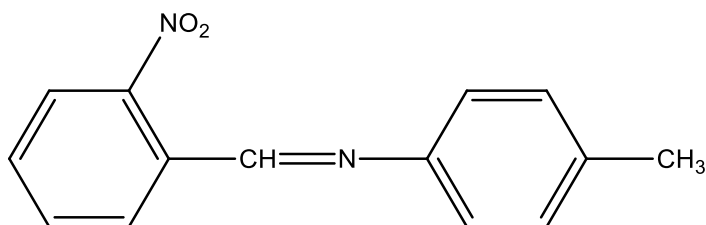
4-methyl-N-[(3-nitrophenyl)methylidene]aniline:



4-methyl-N-[(3-nitrophenyl)methylidene] aniline is synthesized in shortest duration of time under MW irradiations using lemon juice and polyacrylic acid as catalysts. The

time of reaction with 3-nitrobenzaldehyde is maximum when garlic was used as catalyst under frictional activated method. The yield of product is maximum with lemon juice catalyst under microwave irradiations and minimum with garlic catalyst under grindstone method. Out of these two catalysts namely -lemon juice and polyacrylic acid, lemon juice was proven to be better catalyst because it provides higher yield than PAA catalyst though both have taken same time to form this product.

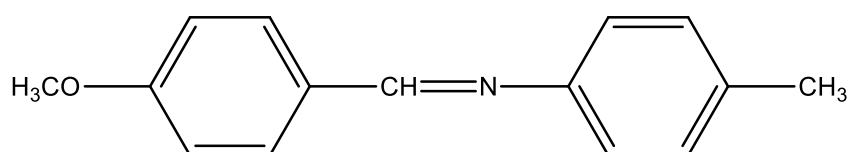
4-methyl-N-[(2-nitrophenyl)methylidene]aniline:



4-methyl-N-[(2-nitrophenyl)methylidene]aniline is prepared in shortest duration of time with maximum yield using lemon juice as catalyzed under MW assisted method. This product has taken long duration of time to form under grindstone technique by using garlic as natural green catalyst.

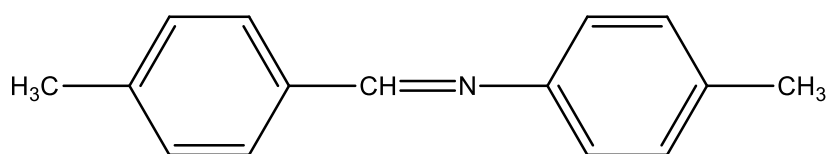
So, it is concluded that for the synthesis of requisite azomethine from aldehyde, lemon juice is best catalyst as it has taken least time (under all circumstances- MW, US, grindstone technique) to give the product. The yield is also maximum with this catalyst (lemon juice) under microwave irradiations compared to all other methods.

4-methyl-N-[(4-methoxyphenyl)methylidene]aniline:



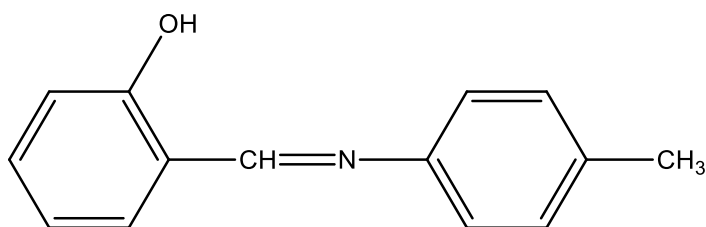
4-Anisaldehyde took least time and provided maximum yield to generate 4-methyl-N-[(4-methoxyphenyl)methylidene]aniline by making use of PAA as catalyst under microwave irradiations whereas microwave assisted lemon juice catalysed method and US assisted Glucose catalysed method took maximum time to cater the same product. The minimum yield of the same product is obtained under microwave assisted Glucose catalysed method. So the best method for the synthesis of 4-methyl-N-[(4-methoxyphenyl)methylidene]aniline is microwave assisted PAA catalysed method.

4-methyl-N-[(4-methylphenyl)methylidene]aniline:



4-methyl-N-[(4-methylphenyl)methylidene]aniline prepared in highest percentage of yield and in least time with polyacrylic acid under microwave irradiations. Lowest amount of yield of the product was produced with glucose catalyst under MW irradiations. The longest time to furnish this product was taken by US assisted glucose catalysed method.

4-methyl-N-[(2-hydroxyphenyl)methylidene]aniline:



Salicylaldehyde took same time to deliver 4-methyl-N-[(2-hydroxyphenyl)methylidene]aniline with any of the catalysts under US as well as under MW irradiations. Although yield did not vary much yet it gave highest yield

with PAA and glucose under MW irradiations and minimum yield in US assisted glucose catalysed method.

Lemon juice was proved to be the best catalyst followed by PAA which in turn is better than glucose for azomethine synthesis.

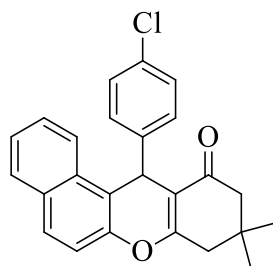
From the tables-3.4 and 3.7 it is evident that microwave assisted reactions are faster and provide better yield than ultrasound assisted reactions. Although in grindstone technique use of garlic a natural, biodegradable catalyst is done but the yield of products is less than all other methodologies.

So overall we concluded that microwave irradiated reaction with lemon juice is the most efficient method for synthesis of azomethine.

Table-4.1: Best reaction conditions for formation of azomethines from each aldehyde

S.No.	Name of Aldehyde	Best reaction conditions
1	p-Chlorobenzaldehyde	MW, Glucose solution and MW, PAA
2	p-Bromobenzaldehyde	MW, PAA
3	p-Nitrobenzaldehyde	MW, lemon juice
4	m-Nitrobenzaldehyde	MW, lemon juice
5	o-Nitrobenzaldehyde	MW, lemon juice
6	p-Methoxybenzaldehyde	MW, PAA
7	p-Methylbenzaldehyde	MW, PAA
8	o-Hydroxybenzaldehyde	MW, Glucose solution and MW, PAA

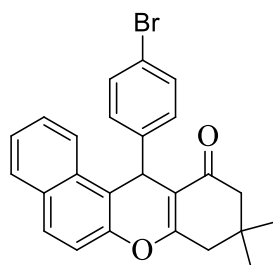
12-(4-Chlorophenyl)-9,9-dimethyl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one



4-chlorobenzaldehyde took least time to provide 12-(4-Chlorophenyl)-9,9-dimethyl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one with oxalic acid as catalyst under MW irradiations whereas with same catalyst it took maximum time in grindstone

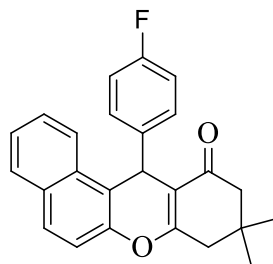
methodology. The yield of product is also highest with oxalic acid as catalyst under MW.

12-(4-Bromophenyl)-9,9-dimethyl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one



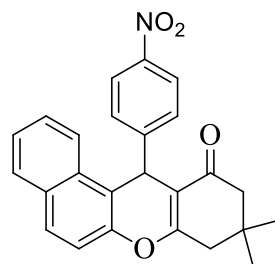
The synthesis of 12-(4-Bromophenyl)-9,9-dimethyl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one is slowest under grindstone technique with oxalic acid as catalyst and fastest with MW irradiations by using oxalic acid as catalyst. The yield of product was poorest in grindstone method and best with oxalic acid under MW irradiations.

12-(4-Fluorophenyl)-9,9-dimethyl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one



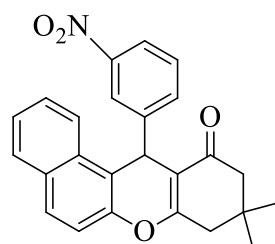
12-(4-Fluorophenyl)-9,9-dimethyl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one was synthesized in minimum time with oxalic acid catalyst under MW irradiations and it took maximum time for its preparation under US method by the use of oxalic acid catalyst. The yield of product is highest with oxalic acid catalyst under US irradiations and minimum with polyacrylic acid catalyst under MW irradiations.

12-(4-Nitrophenyl)-9,9-dimethyl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one



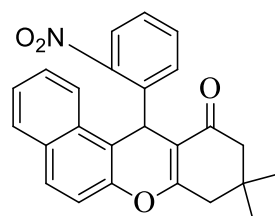
The product 12-(4-Nitrophenyl)-9,9-dimethyl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one was obtained with maximum yield in minimum time under MW irradiations by using oxalic acid as catalyst while yield of product is lowest under MW irradiations by using polyacrylic acid as catalyst.

12-(3-Nitrophenyl)-9,9-dimethyl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one



The reaction of 3-nitrobenzaldehyde with dimidone and 2-naphthol completed in short duration of time by using polyacrylic acid as catalyst under MW irradiations whereas the reaction took longest time using oxalic acid as catalyst under US. The yield of product was excellent under US technique and lowest under grindstone technique.

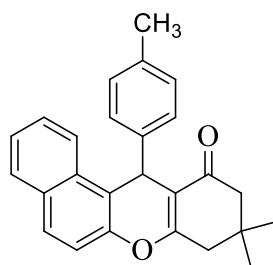
12-(2-Nitrophenyl)-9,9-dimethyl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one



2-nitrobenzaldehyde furnished product in great percentage of yield with oxalic acid catalyst under MW irradiations whereas the least percentage of yield of 12-(2-

Nitrophenyl)-9,9-dimethyl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one was attained with PAA under MW irradiations. The reaction with 2-nitrobenzaldehyde is fastest under MW source of energy and slowest under grindstone technique by using same catalyst (oxalic acid). So oxalic acid is the best catalyst and MW is the best source of energy for formation of 12-(2-Nitrophenyl)-9,9-dimethyl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one.

12-(4-Methylphenyl)-9,9-dimethyl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one



The formation of 12-(4-Methylphenyl)-9,9-dimethyl-8,9,10,12-tetrahydrobenzo[a]xanthen-11-one took maximum time under MW source of energy with PAA as catalyst whereas it took the minimum time with oxalic acid as catalyst under MW/US irradiation. On the basis of yield, oxalic acid catalyst reaction under US irradiations was proven to be best. The minimum yield of product is obtained with PAA under MW irradiations.

Similarly, through this research work new ecofriendly methodologies for the synthesis of tetrahydrobenzo[a]xanthene-11-ones have been developed by using natural green solvent like water and non toxic biodegradable catalyst like oxalic acid/PAA. Oxalic acid has been employed as catalyst under MW, US and grindstone techniques.

Table-4.2: Best reaction conditions for formation of benzoxanthenes from each aldehyde

S.No.	Name of Aldehyde	Best suited reaction conditions
1	p-Chlorobenzaldehyde	MW, Oxalic Acid solution
2	p-Bromobenzaldehyde	MW, Oxalic Acid solution

3	p-Fluorobenzaldehyde	MW, Oxalic Acid solution
4	o-Nitrobenzaldehyde	MW, Oxalic Acid solution
5	m-Nitrobenzaldehyde	MW, PAA
6	p-Nitrobenzaldehyde	MW, Oxalic Acid solution
7	p-Methylbenzaldehyde	US, Oxalic Acid solution

Among all these techniques the best one is the MW irradiations and the best catalyst is oxalic acid for synthesis of benzoxanthenes.

This work has opened several doors of new opportunities in front of researchers for green synthesis of azomethine and benzoxanthenes employing green solvent, green catalyst under green energy sources.

Future prospective

In near future more of heterocyclic molecules of medicinal importance can be synthesized via green methodologies like MW, US instead of using conventional heating. More of green catalysts and green solvents (as explored in this thesis) will be employed instead of toxic non ecofriendly solvents and catalysts for synthesis of those molecules of immense medicinal importance. So this work may motivate the researchers to find out more of green methodologies for synthesis of small organic molecule which may help our tomorrow to be a better one.

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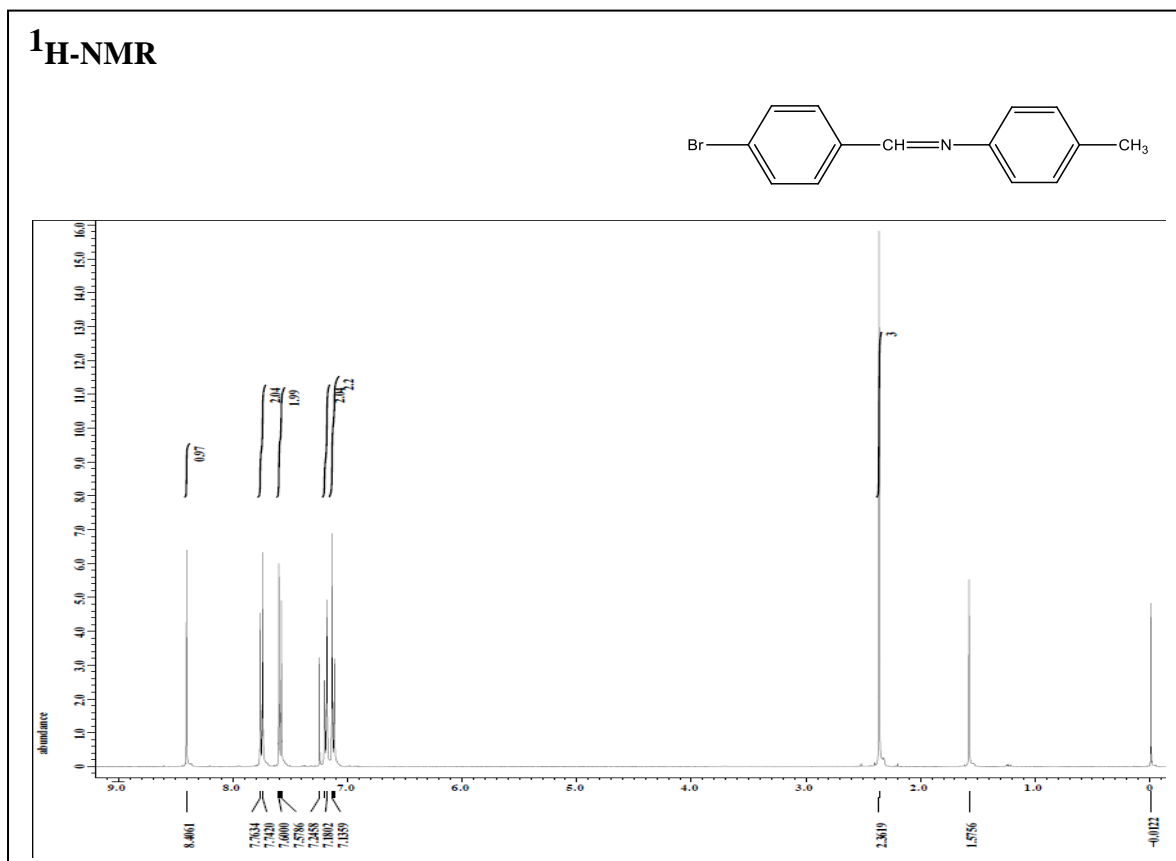
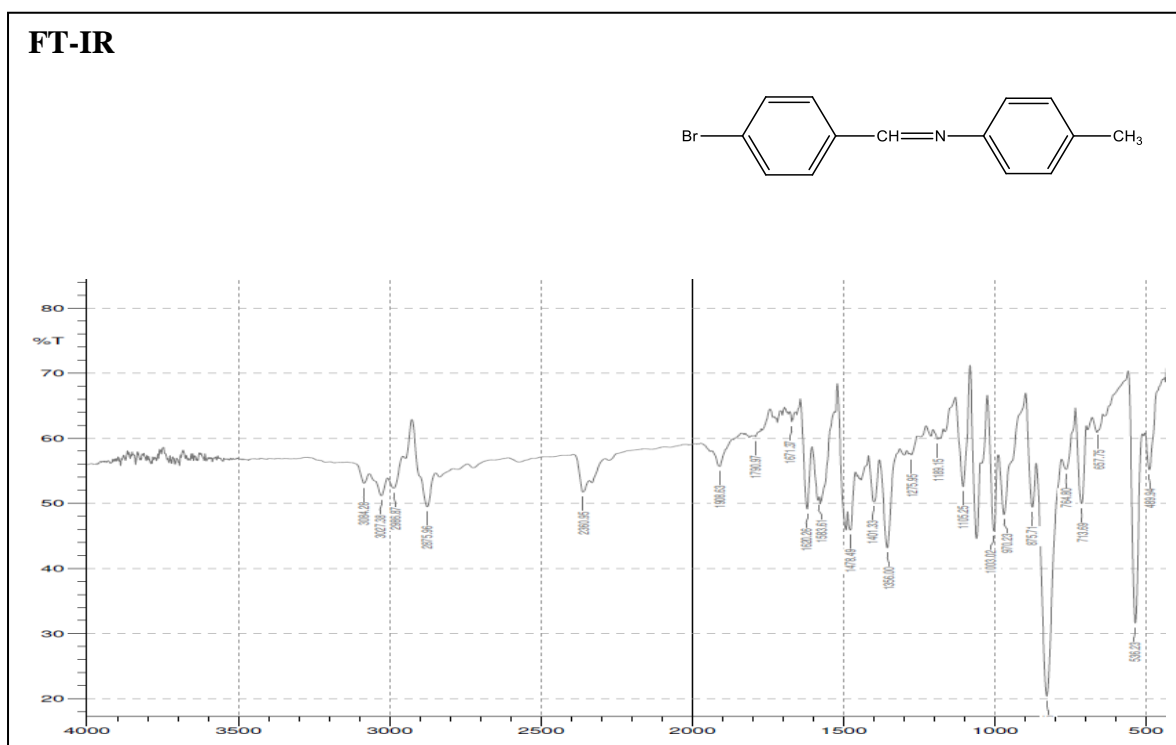
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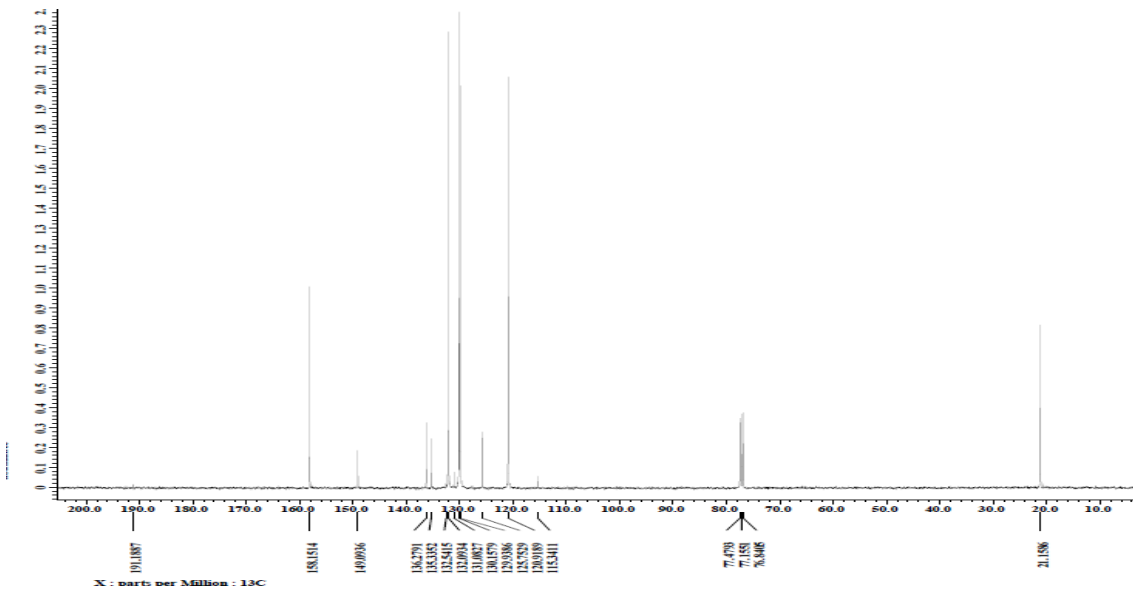
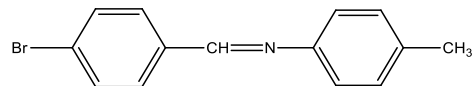
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APPENDIX

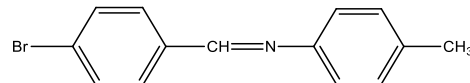
Representative FT-IR, NMR and HRMS



¹³C-NMR



HRMS-ESI



Elemental Composition Report

Page

Single Mass Analysis

Tolerance = 50.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

6 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 10-15 H: 11-15 N: 0-2 Br: 0-1

Sample Name : SBPBr

IITRPR

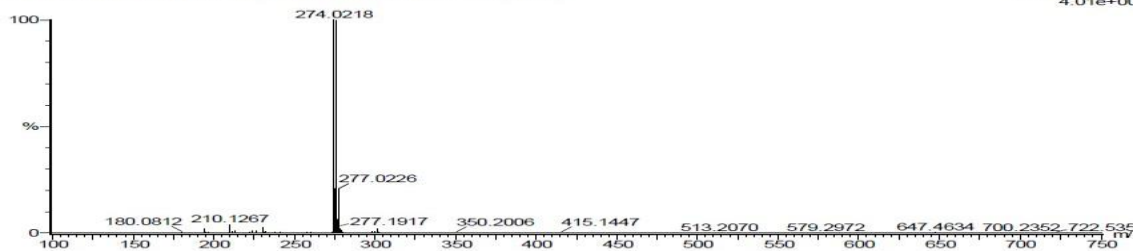
XEVO G2-XS QTC

Test Name : HRMS-1

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1: TOF MS ES

4.01e+00



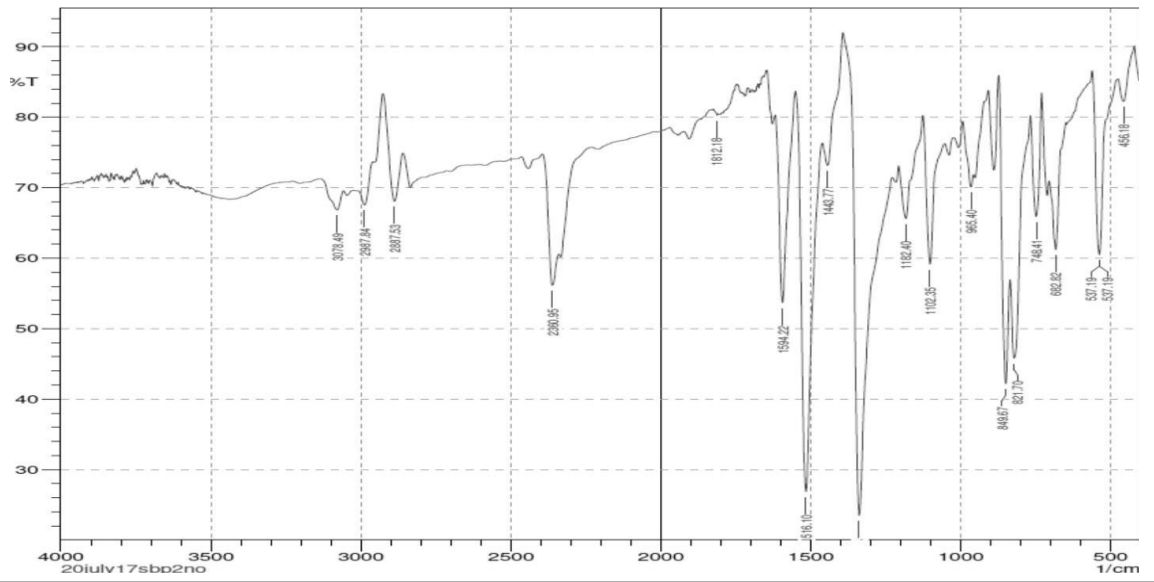
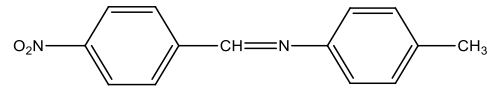
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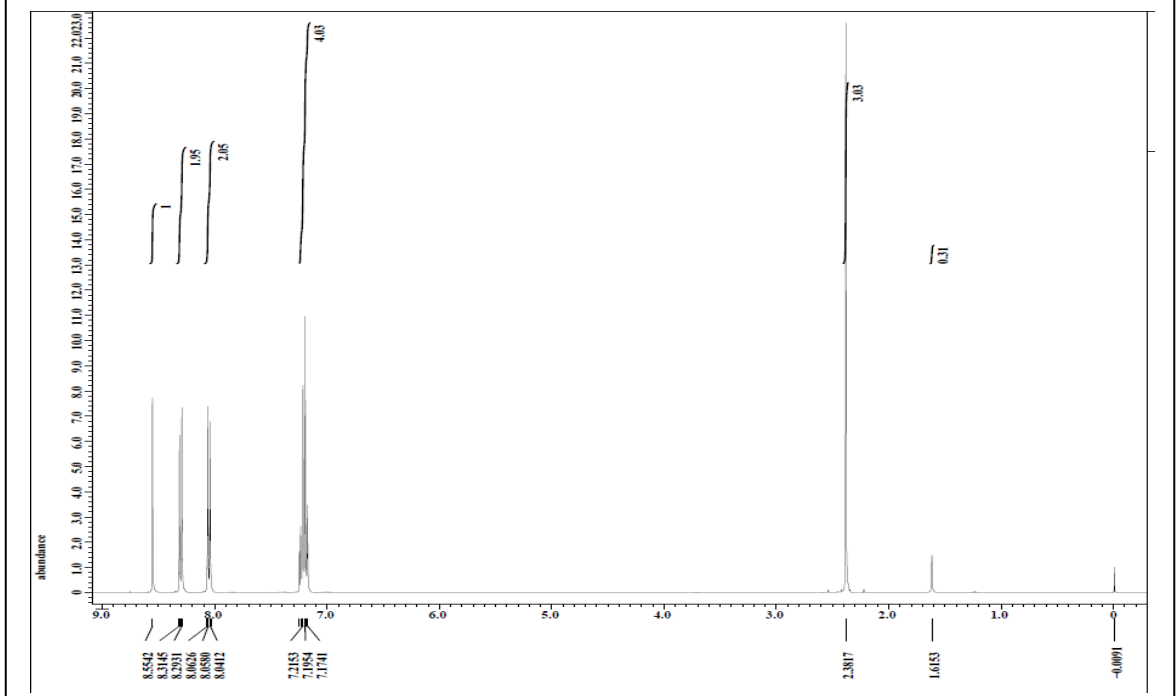
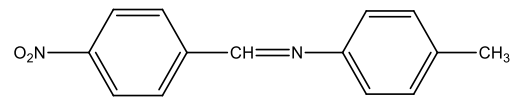
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
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274.0218	274.0231	-1.3	-4.7	8.5	906.9	n/a	n/a	C14 H13 N Br
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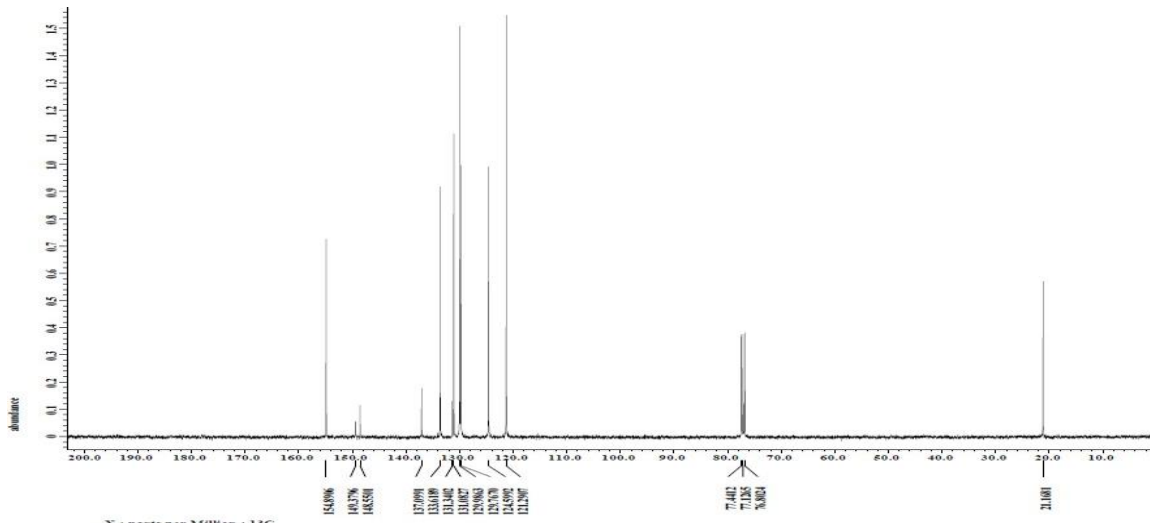
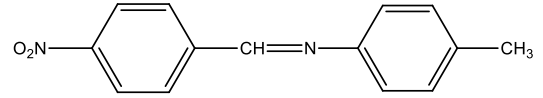
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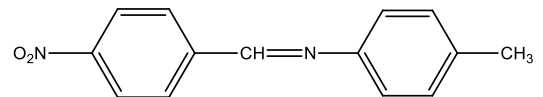
¹H-NMR



¹³C-NMR



HRMS-ESI



Elemental Composition Report

Page

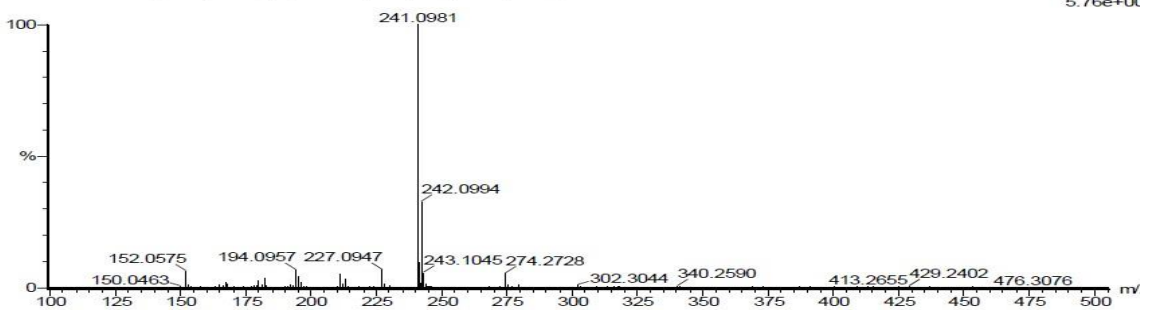
Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
 Element prediction: Off
 Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
 39 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

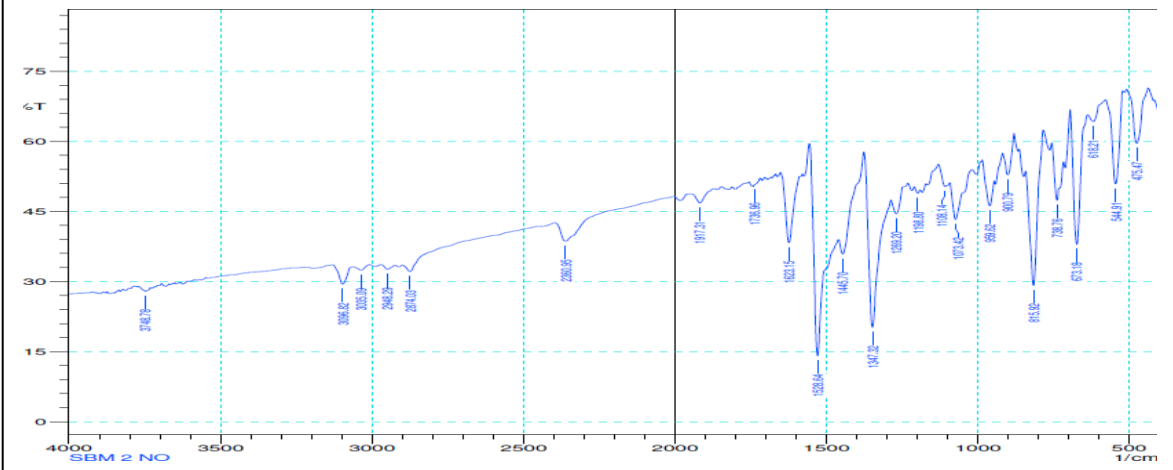
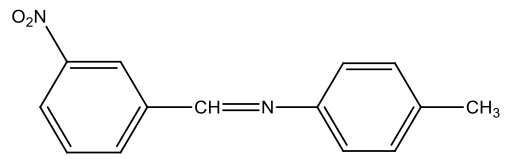
Elements Used:
 C: 11-20 H: 5-35 N: 0-3 O: 1-4
 Sample Name : FPNO IITRPR
 Test Name : HRMS-1 XEVO G2-XS QTC
 090919-FPNO 15 (0.157) AM2 (Ar,22000.0,0.00,0.00); Cm (15:19)

1: TOF MS ES
 5.76e+00

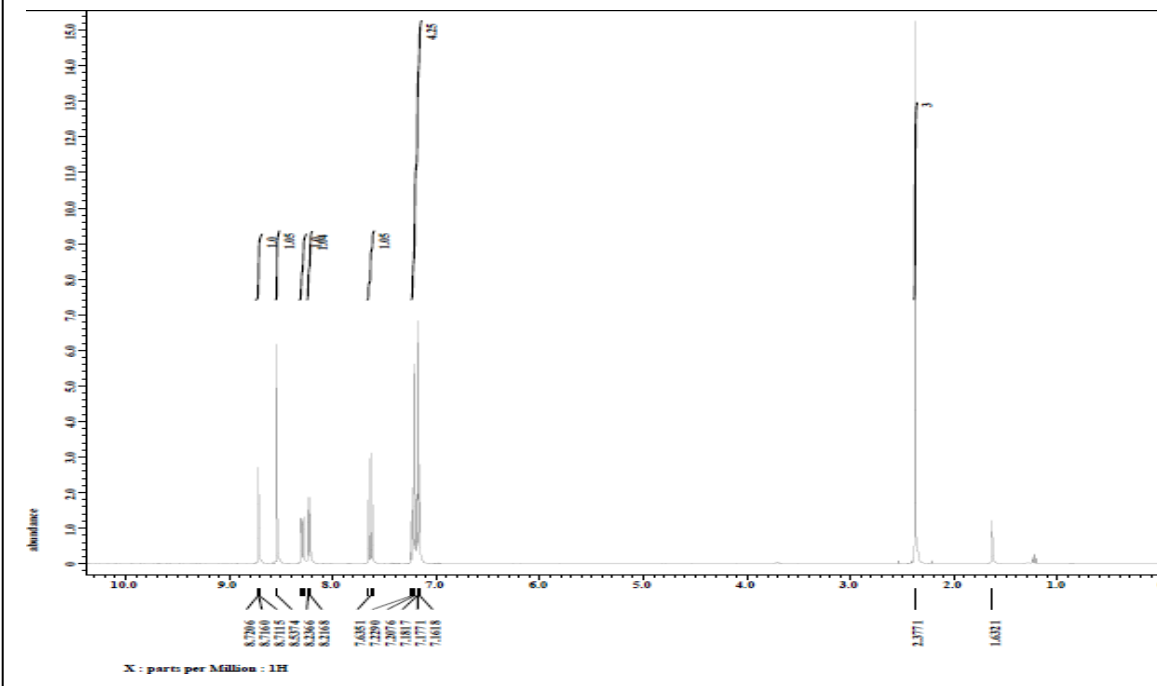
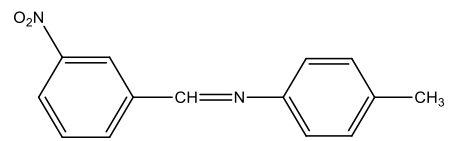


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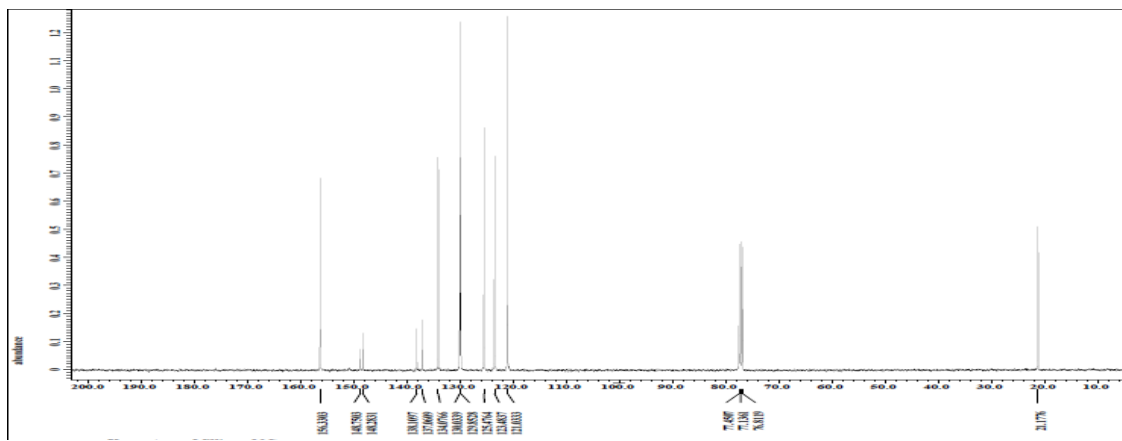
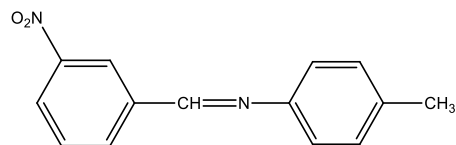
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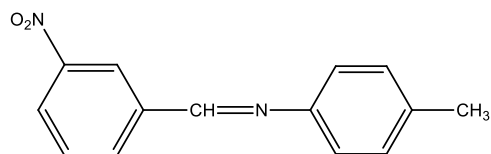
¹H-NMR



¹³C-NMR



HRMS-ESI



Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

39 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 11-20 H: 5-35 N: 0-3 O: 1-4

Sample Name : FMNO

IITRPR

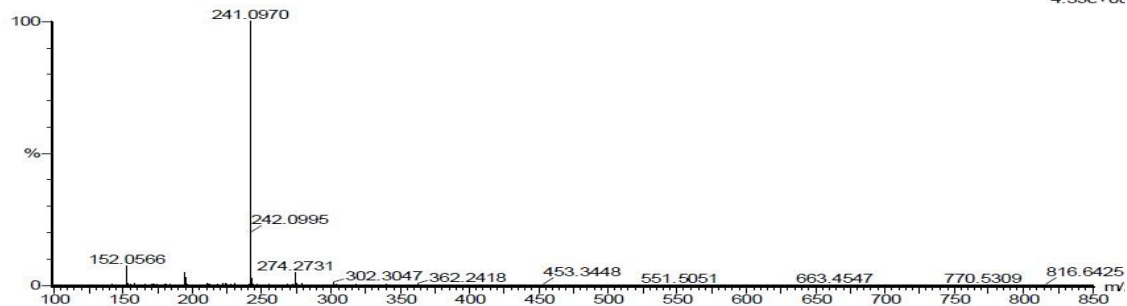
XEVO G2-XS QTC

Test Name : HRMS-1

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4.39e+06

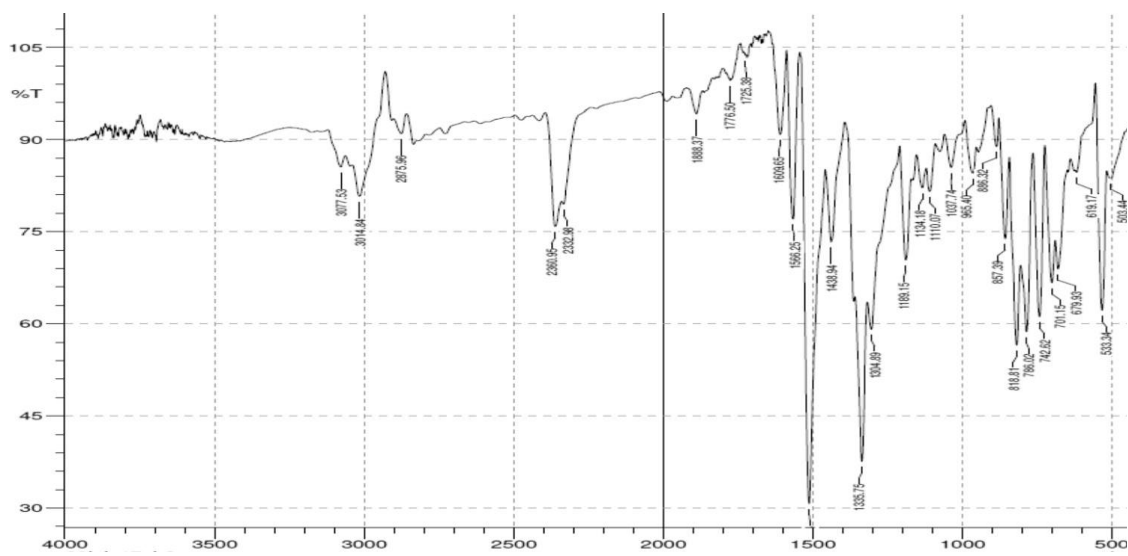
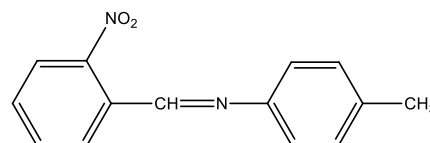


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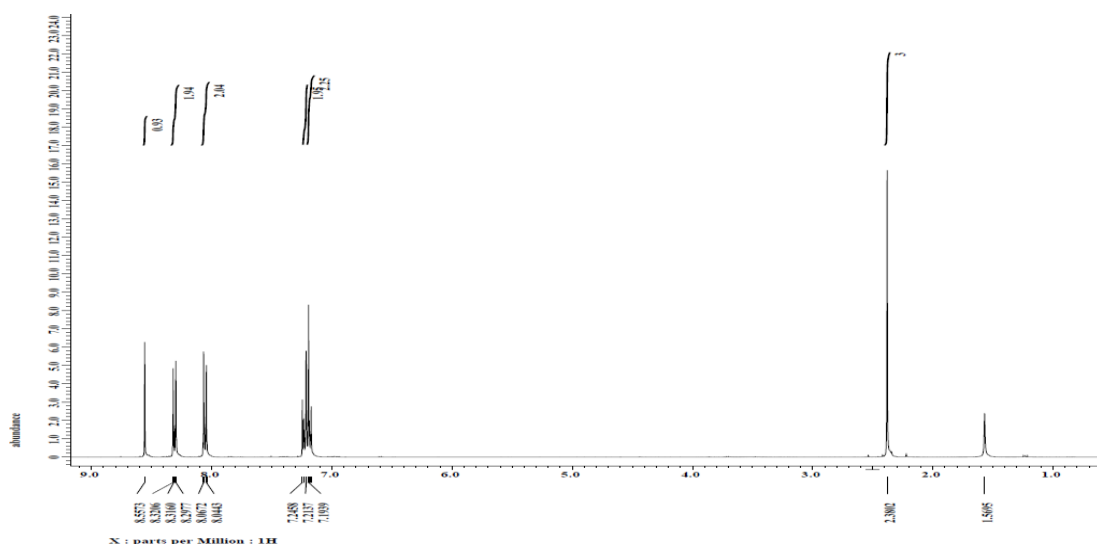
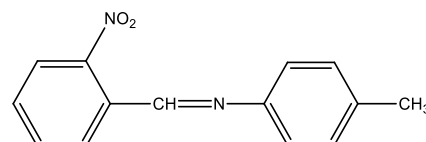
Maximum: 5.0 5.0 -1.5

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
241.0970	241.0977	-0.7	-2.9	9.5	1063.5	n/a	n/a	C14 H13 N2 O2

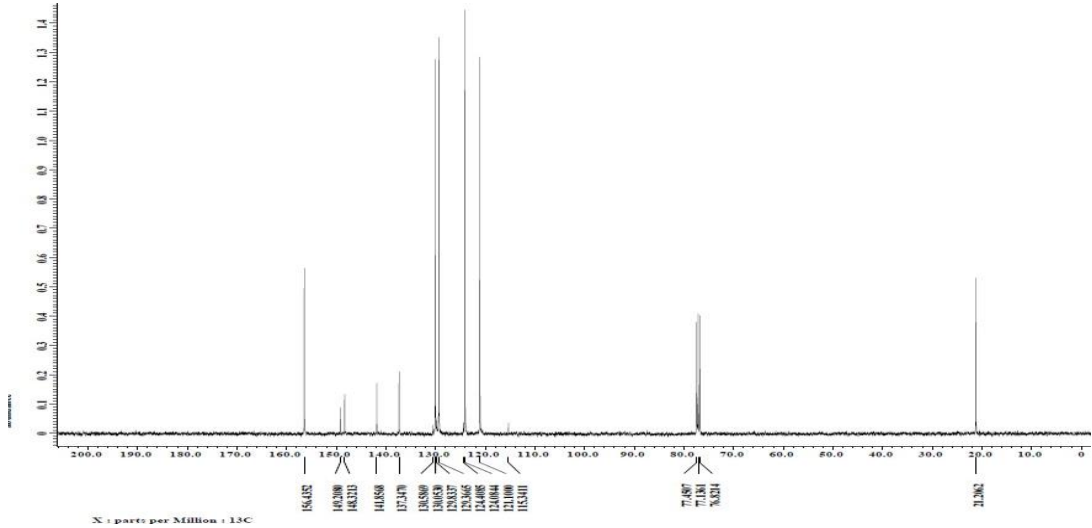
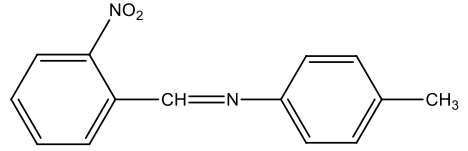
FT-IR



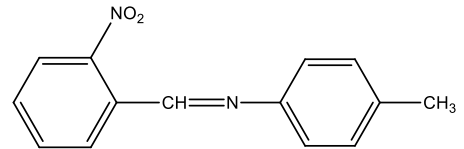
¹H-NMR



¹³C-NMR



HRMS-ESI



Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 50.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

1 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

Z: 10-15 H: 11-20 N: 0-2 O: 1-2

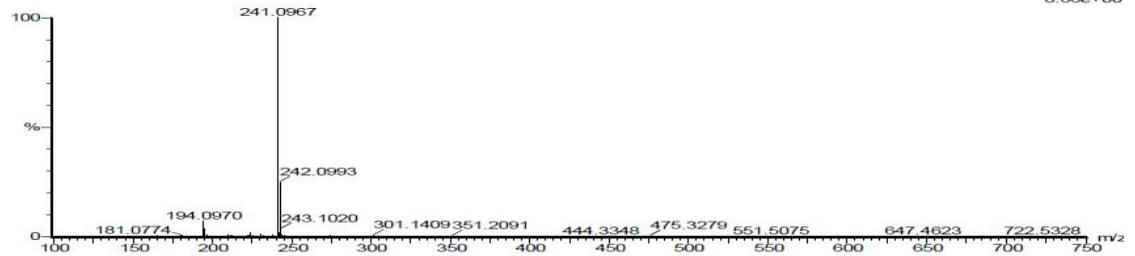
Sample Name : SBONO2 IITRPR

Test Name : HRMS-1

210119-SBONO2 18 (0.183) AM2 (Ar, 19000.0,0.00,0.00); Cm (18:23)

XEVO G2-XS QTOF

1: TOF MS ES+
8.66e+00



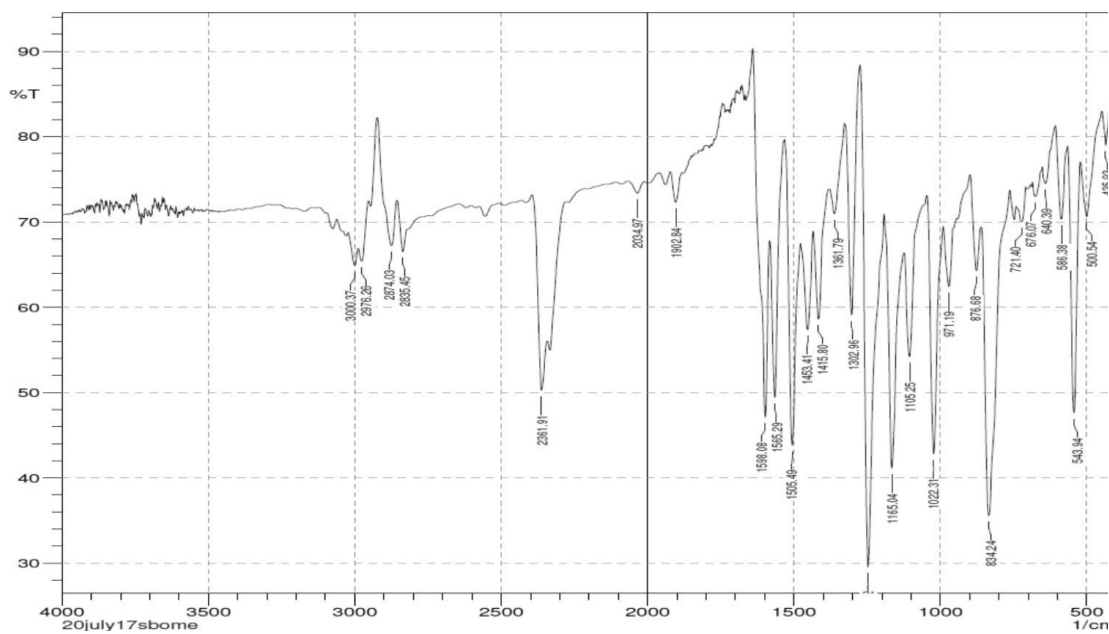
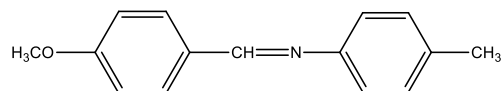
Minimum:

Maximum: 5.0 50.0 -1.5

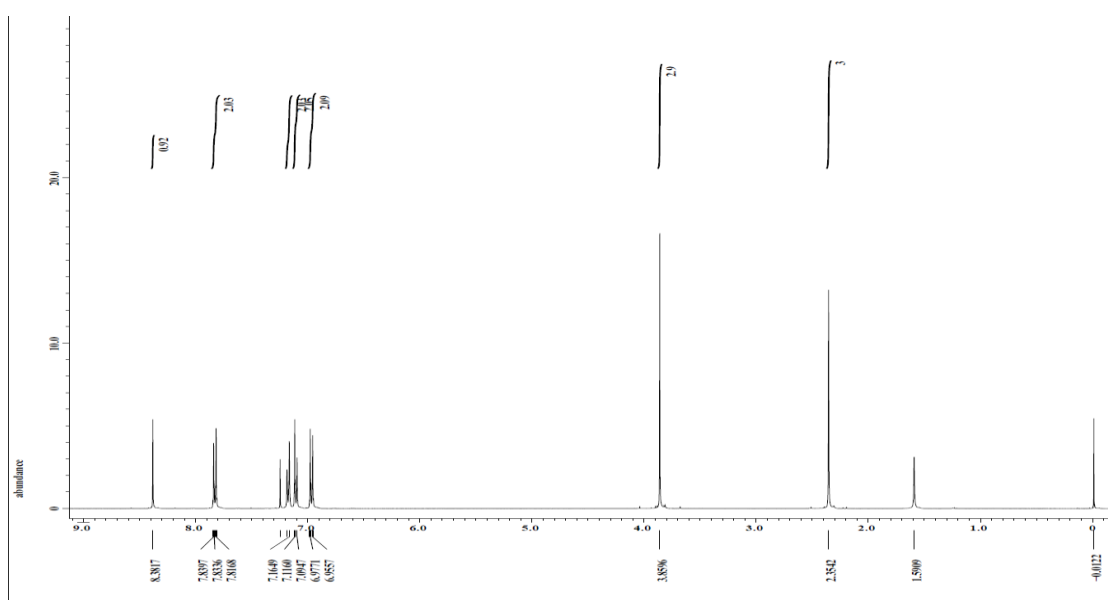
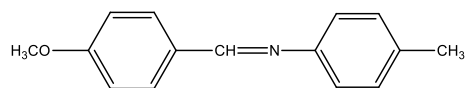
Mass Calc. Mass mDa PPM DBE i-FIT Norm Conf (%) Formula

:41.0967 241.0977 -1.0 -4.1 9.5 996.0 n/a n/a C14 H13 N2 O2

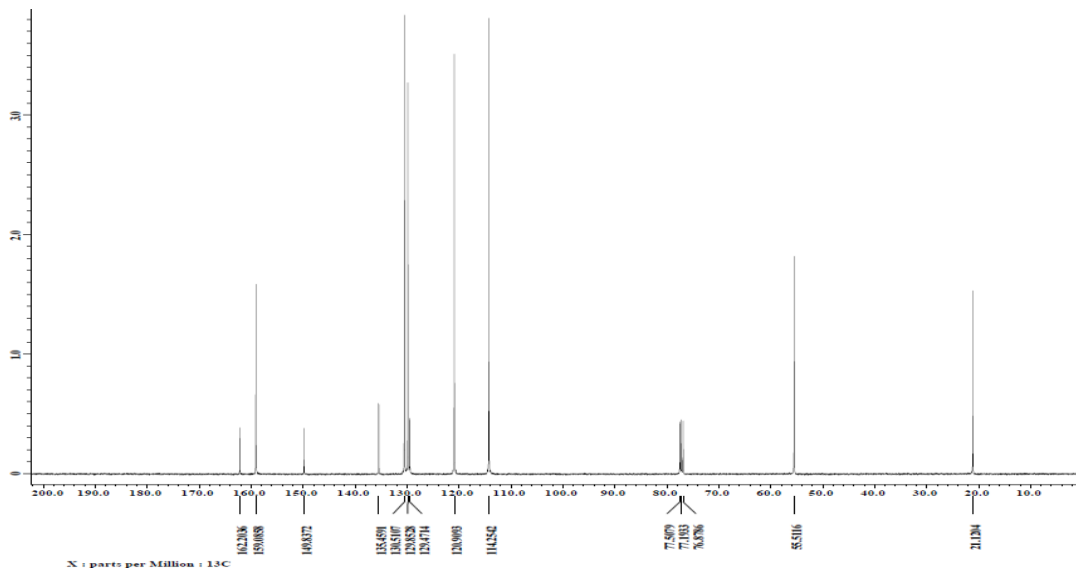
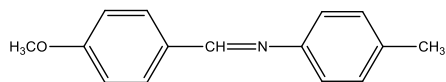
FT-IR



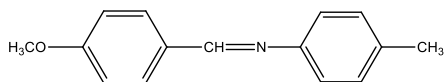
¹H-NMR



¹³C-NMR



HRMS-ESI



Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 50.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

Formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

>: 10-15 H: 11-20 N: 0-2 O: 1-2

IITRPR

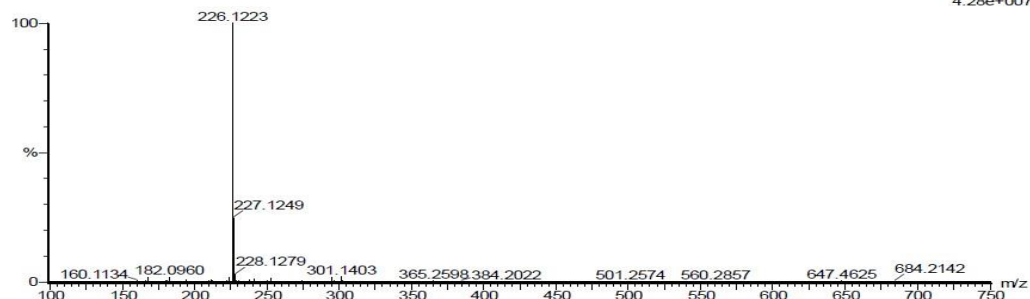
XEVO G2-XS QTOF

Sample Name : SBPOMe

Test Name : HRMS-1

?10119-SBPOMe 17 (0.174) AM2 (Ar,19000.0,0.00,0.00); Cm (17:20)

1: TOF MS ES+
4.28e+007

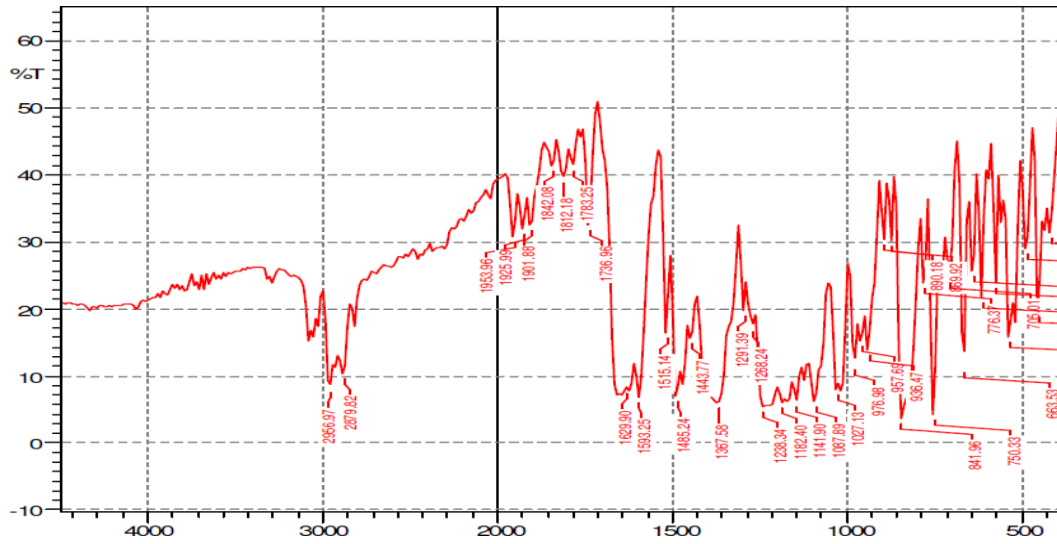
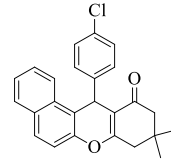


Minimum: 5.0 -1.5

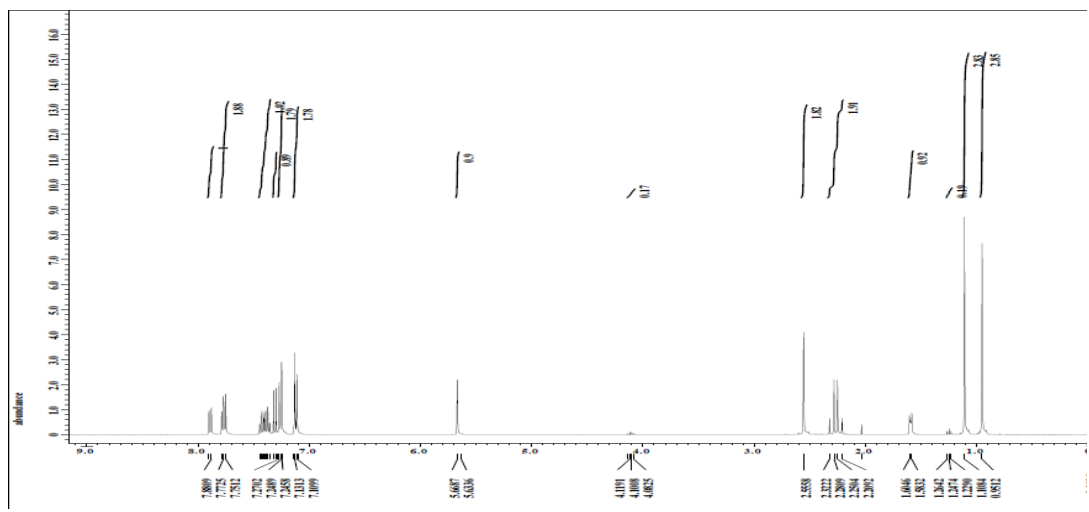
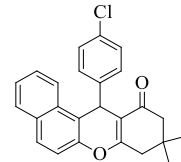
Maximum: 50.0 50.0

Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
226.1223	226.1232	-0.9	-4.0	8.5	961.0	n/a	n/a	C15 H16 N O

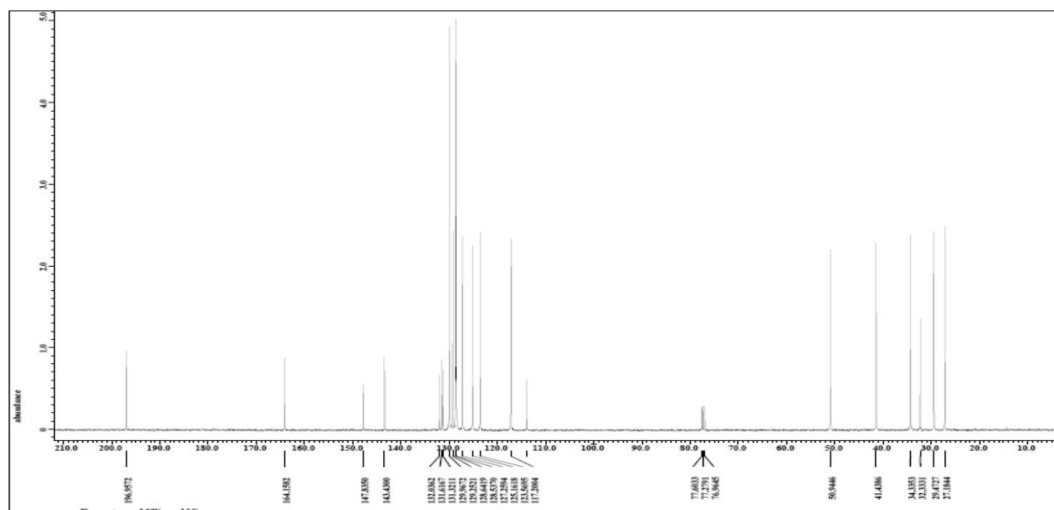
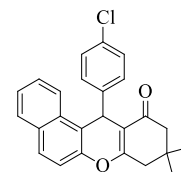
FT-IR



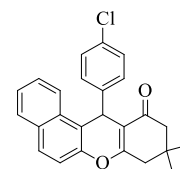
¹H-NMR



¹³C-NMR



HRMS-ESI



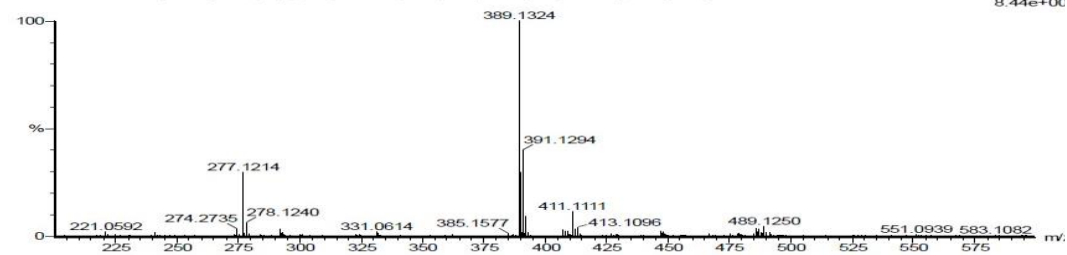
Elemental Composition Report

Page 1

Single Mass Analysis

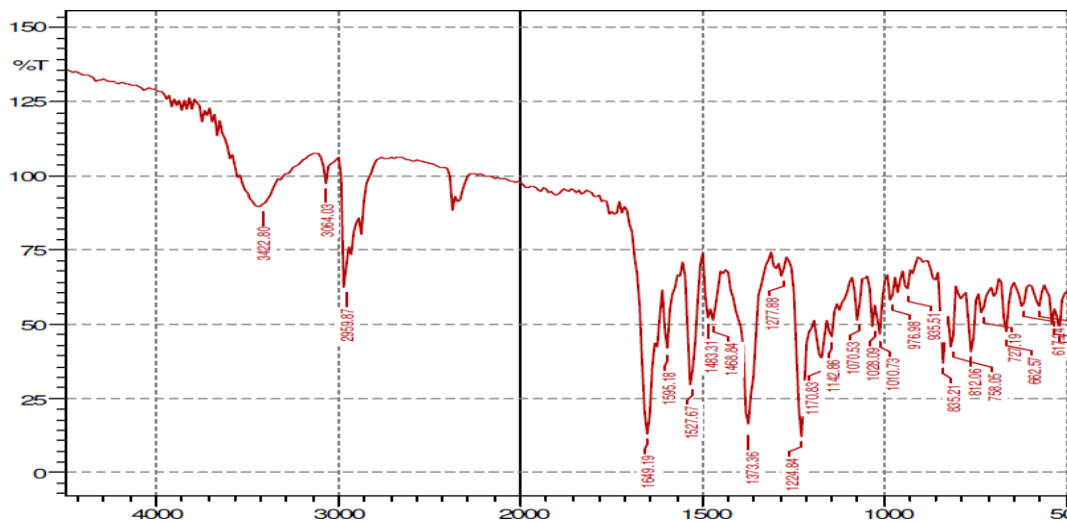
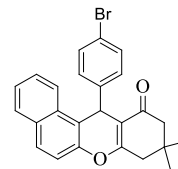
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
 Element prediction: Off
 Number of isotope peaks used for I-FIT = 3

Monoisotopic Mass, Even Electron Ions
 4 formula(s) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
 Elements Used:
 C: 20-25 H: 20-25 O: 0-4 Cl: 0-2
 Sample Name : BXU-3
 Test Name : HRMS-1
 281117-BXU-3- 10 (0.125) AM (Top,4, Ar,10000.0,0.00,0.00); Sm (SG, 1x3.00); Cm (9:13)
 INDIAN INSTITUTE OF TECHNOLOGY ROYAPAL
 XEVO G2-XS QTC
 1: TOF MS ES-
 8.44e+00

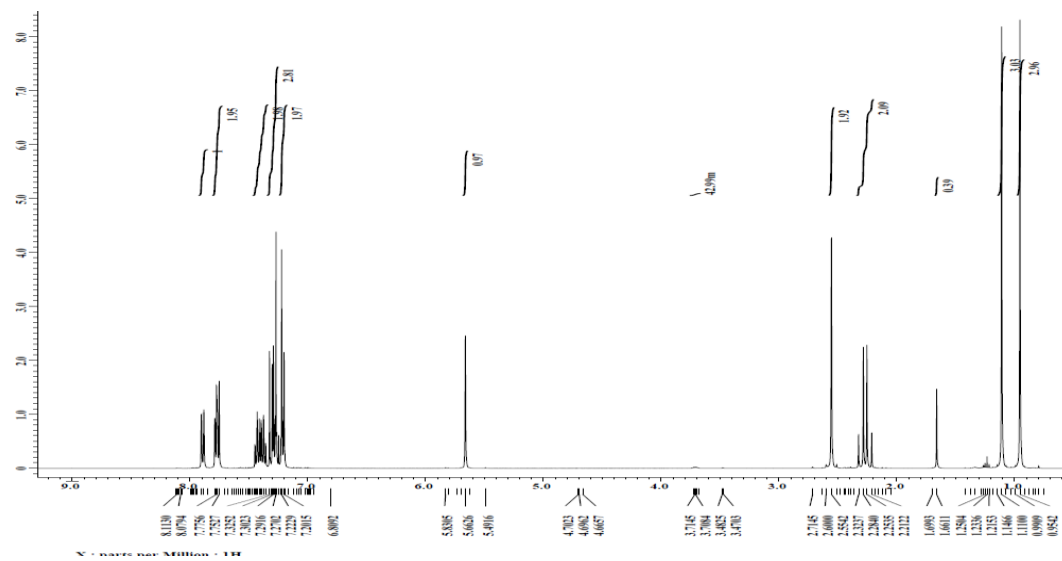
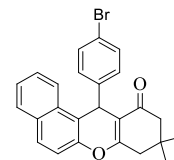


Minimum:	5.0	5.0	-1.5					
Maximum:	50.0	50.0	50.0					
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
389.1324	389.1308	1.6	4.1	14.5	832.9	n/a	n/a	C ₂₅ H ₂₂ O ₂ Cl

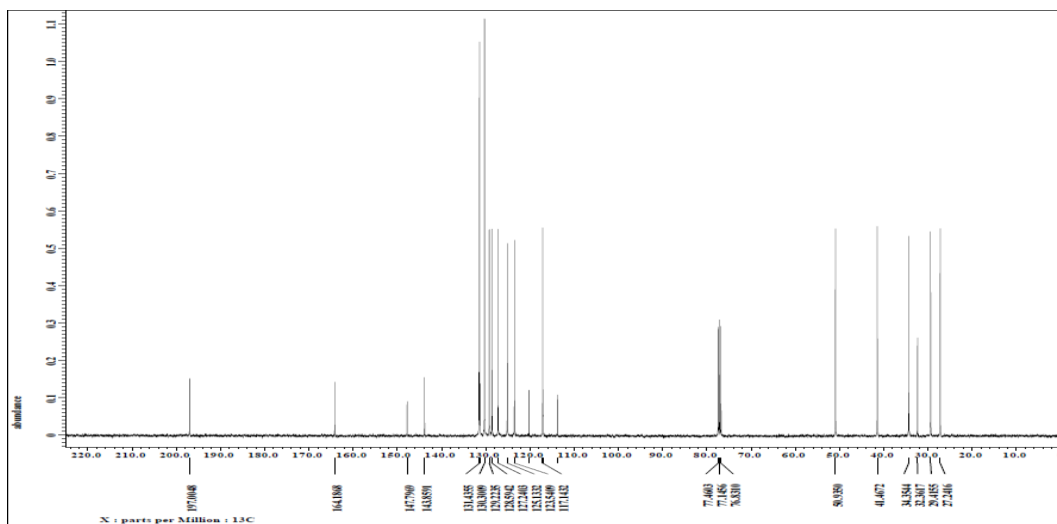
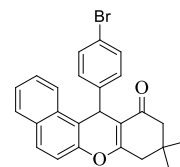
FT-IR



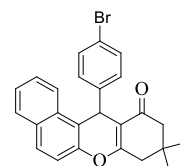
¹H-NMR



¹³C-NMR



HRMS-ESI



Elemental Composition Report

Page 1

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

12 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 15-27 H: 5-35 O: 1-4 Br: 0-1

Sample Name : BXOUS-BR

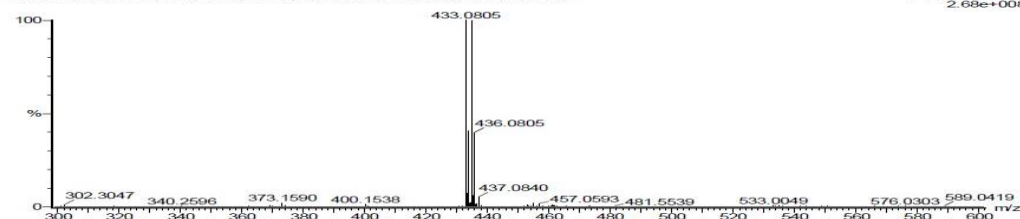
Test Name : HRMS-1

060919-BXOUS-BR 111 (1.049) AM2 (Ar,22000.0,0.00,0.00); Cm (110:128)

IITRPR

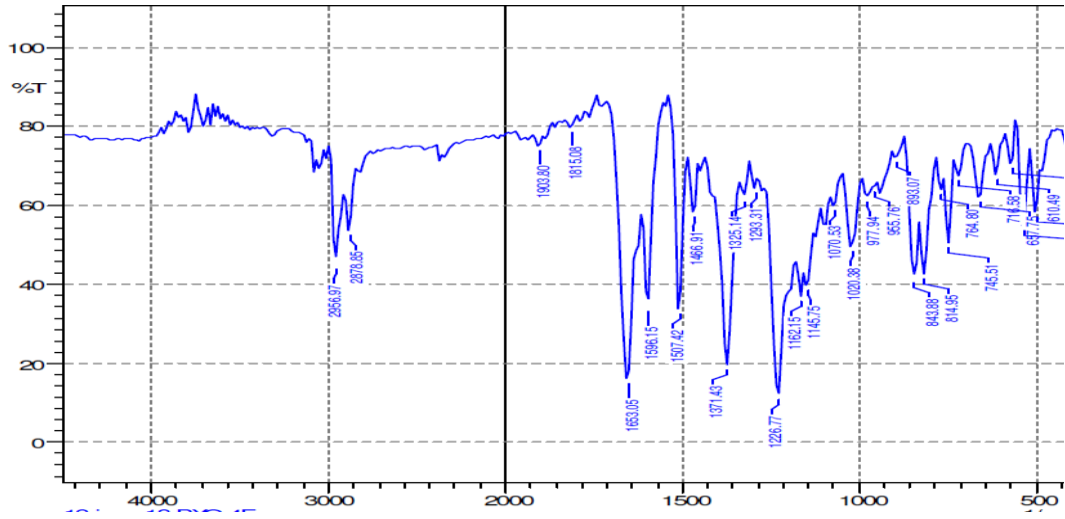
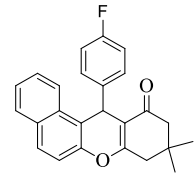
XEVO G2-XS QTOF

1: TOF MS ES+
2.68e+008

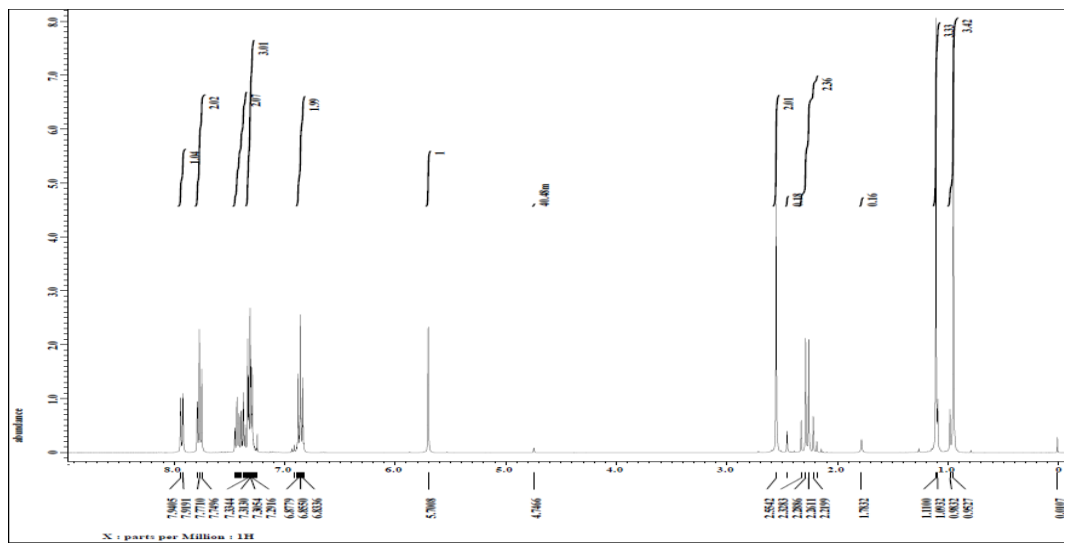
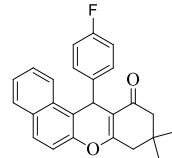


Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
433.0805	433.0803	0.2	0.5	14.5	1123.4	n/a	n/a	C25 H22 O2 Br

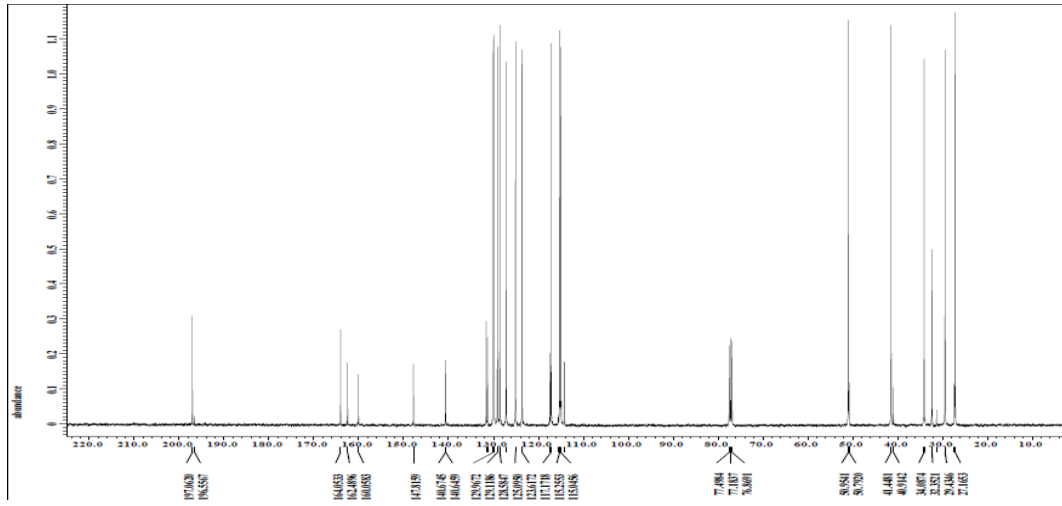
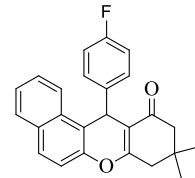
FT-IR



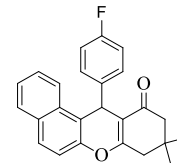
¹H-NMR



¹³C-NMR



HRMS-ESI



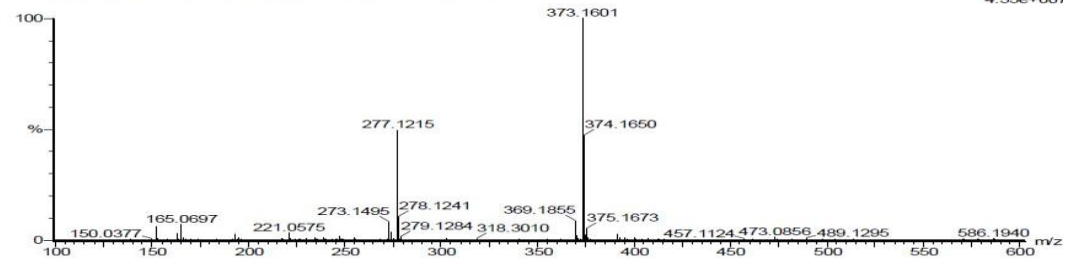
Elemental Composition Report

Page 1

Single Mass Analysis

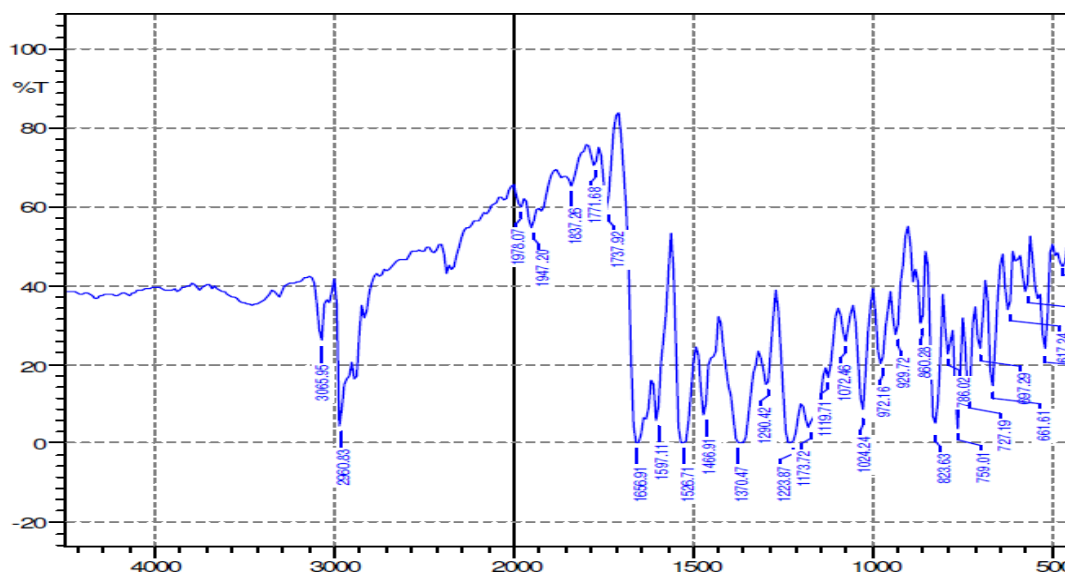
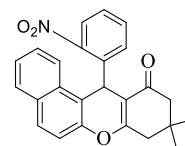
Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
 Element prediction: Off
 Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
 18 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)
 Elements Used:
 C: 15-27 H: 5-35 O: 1-4 F: 0-1
 Sample Name : BXOUS-F IITRPR
 Test Name : HRMS-1 XEVO G2-XS QTOF
 090919-BXOUS-F 34 (0.331) AM (Top,4, Ar,10000.0,0,00,0,00); Cm (34:36) 1: TOF MS ES+
 4.55e+007

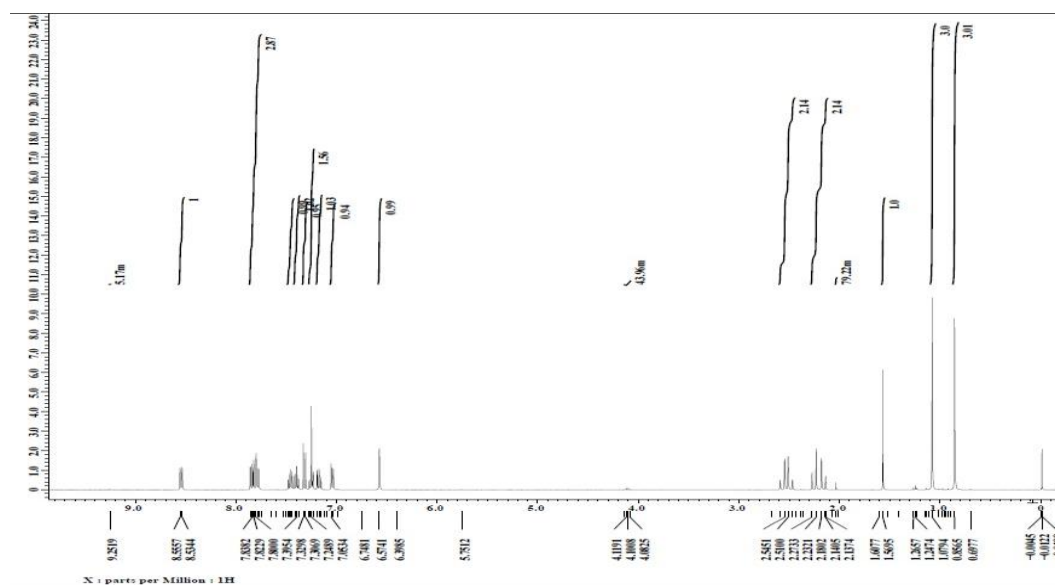
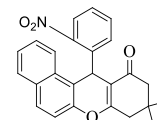


Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
373.1601	373.1604	-0.3	-0.8	14.5	1237.1	n/a	n/a	C25 H22 O2 F

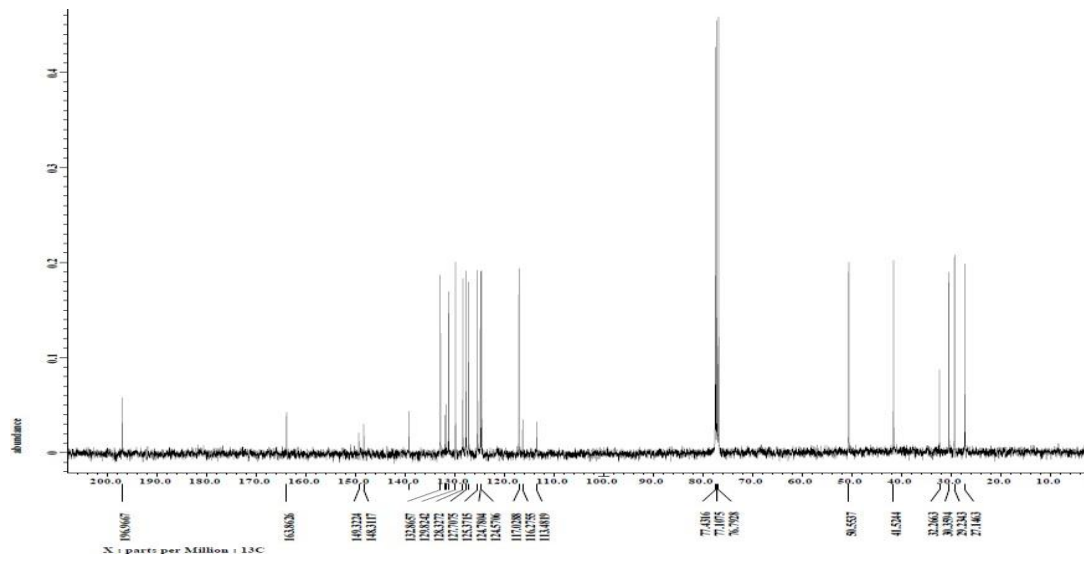
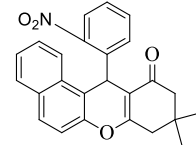
FT-IR



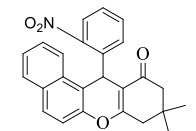
¹H-NMR



¹³C-NMR



HRMS-ESI



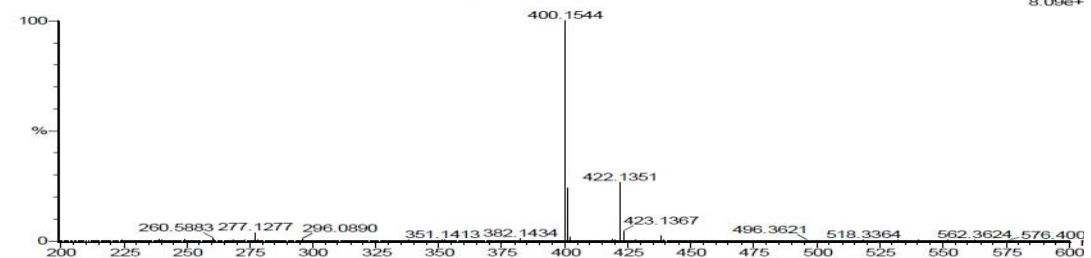
Elemental Composition Report

Page

Single Mass Analysis
 Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
 Element prediction: Off
 Number of isotope peaks used for i-FIT = 3

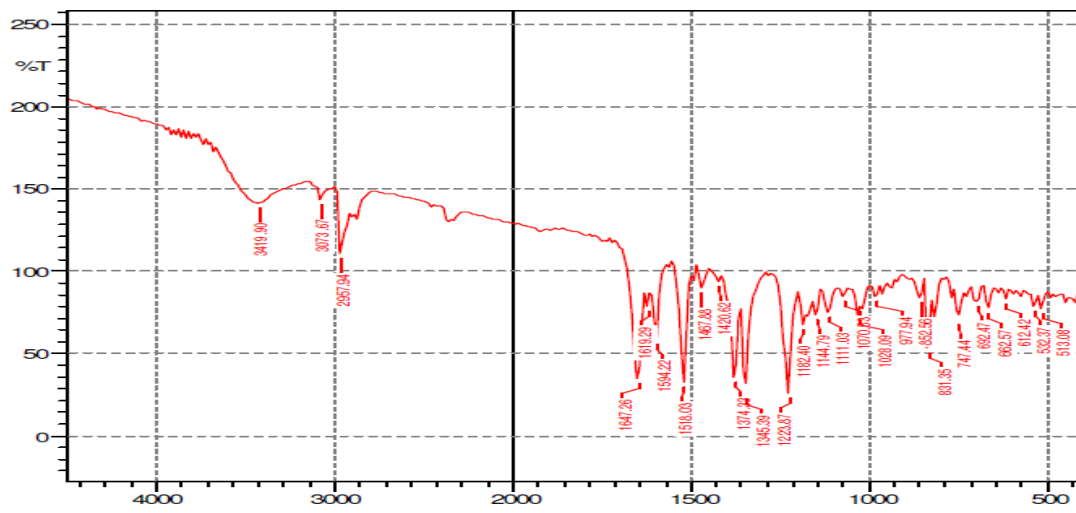
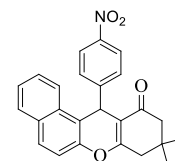
Monoisotopic Mass, Even Electron Ions
 4 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
 Elements Used:
 C: 20-25 H: 15-25 N: 0-1 O: 0-4
 Sample Name : BXO-2NO2 INDIAN INSTITUTE OF TECHNOLOGY
 Test Name : HRMS-1 ROFAR
 300118-BXO-2NO2- 18 (0.183) AM (Top,4, Ar,10000,0,0,0,0,0); Cm (18:22)

XEVO G2-XS G
 1: TOF MS E
 8.09e+

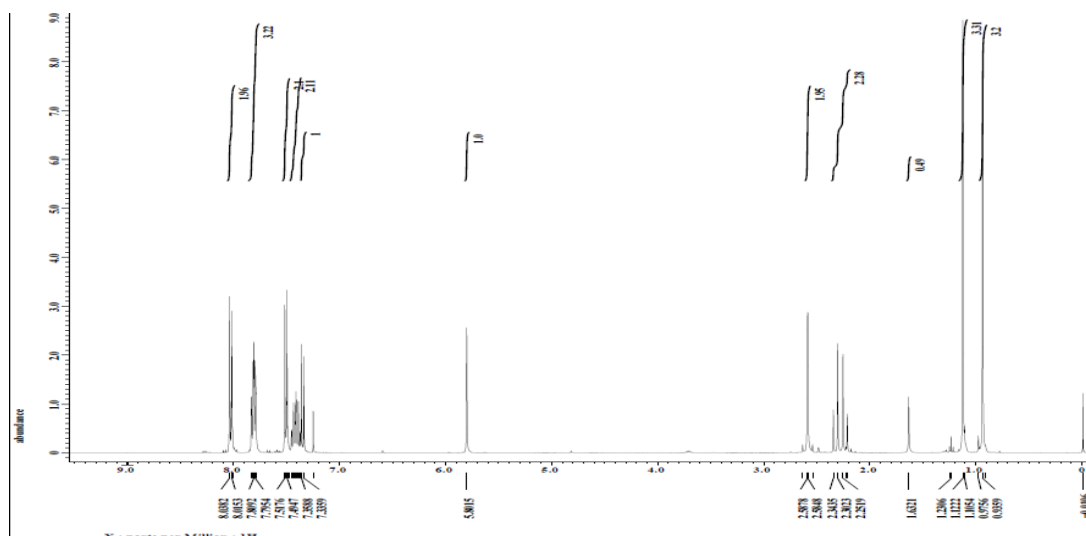
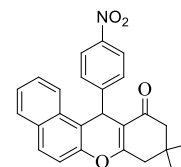


Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
400.1544	400.1549	-0.5	-1.2	15.5	311.3	n/a	n/a	C25 H22 N O4

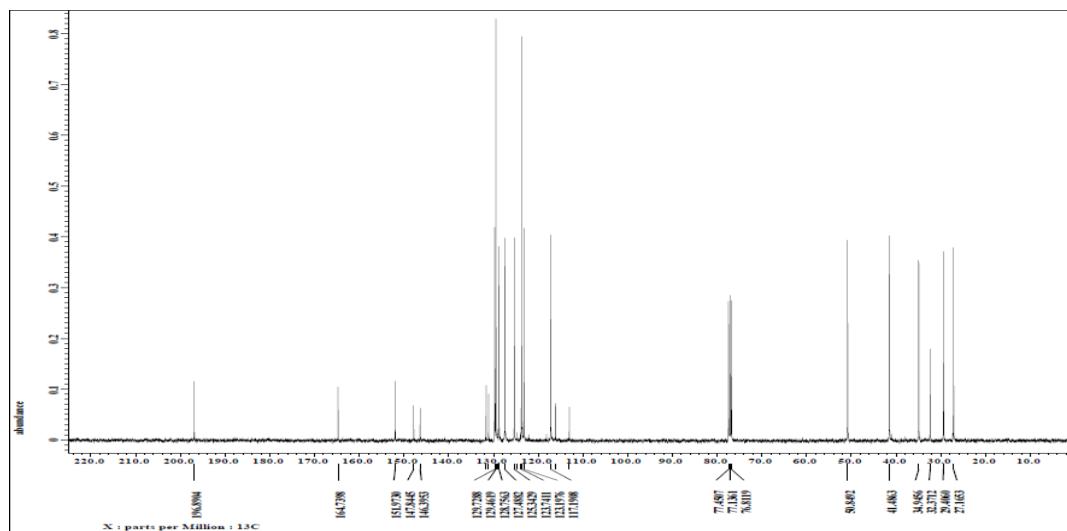
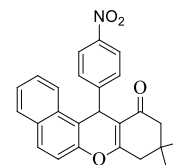
FT-IR



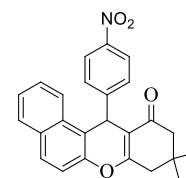
¹H-NMR



¹³C-NMR



HRMS-ESI



Elemental Composition Report

Page

Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -1.5, max = 50.0
 Element prediction: Off
 Number of isotope peaks used for I-FIT = 3

Monoisotopic Mass, Even Electron Ions
 27 formula(e) evaluated with 1 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

C: 15-27 H: 5-35 N: 0-3 O: 1-4

Sample Name : BXOMW-4NC2

IITRPR

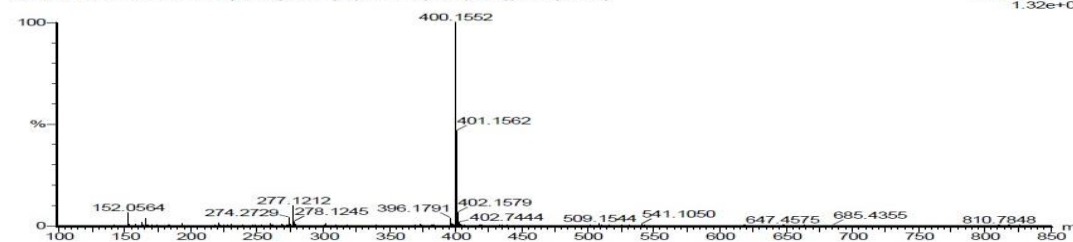
XEVO G2-XS QTR

Test Name : HRMS-1

050919-BXOMW-4NC2_19 (0.203) AM2 (Ar,22000.0,0.00,0.00); Cm (19:27)

1: TOF MS ES

1.32e+0



Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf (%)	Formula
400.1552	400.1549	0.3	0.7	15.5	994.7	n/a	n/a	C25 H22 N O4

LIST OF PUBLICATIONS

1. **“Comparative efficacy of microwave, visible light and ultrasound irradiation for green synthesis of Dihydropyrimidinones in fruit juice medium”**-Tanay Pramanik, Simarjit Kaur Padan, Richa Gupta, Pooja Bedi and Gurinderpal Singh. *AIP Conference Proceedings*, **2017**, 1860, 020059.
2. **“Synthesis and Properties of Pharmaceutically Important Xanthenes and Benzoxanthone Analogs: A Brief Review”**-Pooja Bedi, Richa Gupta and Tanay Pramanik. *Asian Journal of Pharmaceutical and Clinical Research*, **2018**, 11 (2), 12-20.
3. **“Microwave Assisted Green Synthesis of Schiff Bases in Lemon Juice Medium”**- Pooja Bedi, Lalit Malkania, Richa Gupta and Tanay Pramanik-*Research Journal of Chemistry and Environment*, **2018**, 22(8) 19-23.
4. **“Lactic acid catalyzed and microwave-assisted green synthesis of pharmaceutically important bis(indolyl) methane analogs in aqueous medium”** Lalit Malkania, Pooja Bedi and Tanay Pramanik-*Drug Invention Today*, **2018**, 10 (9), 1740-44.
5. **“Exploring the utility of glucose as ecofriendly catalyst for microwave assisted green synthesis of Schiff base”**- Pooja Bedi and Tanay Pramanik-*Research Journal of Chemistry and Environment*, **2019**, 23(2) 99-104.
6. **“Glucose Catalysed and Ultrasound Assisted Synthesis of Pharmaceutically Potent Azomethine Analogues in Water Medium: A Complete Green Approach”**- Pooja Bedi, Goutam Pramanik and Tanay Pramanik-*International Journal of Pharmaceutical Research*, **2019**, 11(2), 433-436.
7. **“Ultrasound irradiated one pot green synthesis of pharmaceutically potent Bis (Indolyl) methane in water medium employing bio degradable lactic acid as ecofriendly catalyst”**- Pooja Bedi, Lalit Malkania, Shubham Sharma, Goutam Pramanik, Tanay Pramanik- *Drug Invention Today*, **2019**, 11 (6), 1282-1286.

8. **“Microwave assisted ecofriendly synthesis of pharmaceutically important azomethine analogues employing bio degradable polyacrylic acid as catalyst and water as solvent”**-Pooja Bedi and Tanay Pramanik—*International Journal of Pharmaceutical Research*, **2019**, 11(2), 584-590.
9. **“Microwave assisted green synthesis of pharmaceutically potent benzoxanthone analogues employing biodegradable oxalic acid as ecofriendly catalyst”** Pooja Bedi, Goutam Pramanik and Tanay Pramanik- *Biointerface research in applied chemistry*, **2019**, 9(5), 4311-4316.
10. **“ Garlic Catalysed and Grindstone Assisted Solvent Free Green Synthesis of Pharmaceutically Important Schiff Bases: ”**-Pooja Bedi, Goutam Pramanik and Tanay Pramanik-*Research journal of pharmacy and technology*, **2020**, 13(1), 152-156.