ONE POT SYNTHESIS OF COUMARIN DERIVATIVES FORM SUBSTITUTED PHENOLS AND ITS ZONE OF INHIBITION ON GRAM NEGATIVE BACTERIA

Submitted in partial fulfilment of the requirements for the award of Master of Science Degree in Chemistry
By:

S. KUBENTHIRA

Reg.no:39910009

DEPARTMENT OF CHEMISTRY

SCHOOL OF SCIENCE & HUMANITIES

SATHYABAMA INSTITUTE OF SCIENCE AND TECHNOLOGY
(DEEMED TO BE UNIVERSITY)
Accredited with Grade "A" by NAAC I 12B Status by UGC I Approved by AICTE

JEPPIAAR NAGAR, RAJIV GANDHI SALAI, CHENNAI - 600 119

March – 2021

SATHYABAMA

INSTITUTE OF SCIENCE AND TECHNOLOGY (DEEMED TO BE UNIVERSITY)

Accredited with "A" grade by NAAC I 12B Status by UGC I Approved by AICTE

Jeppiaar Nagar, Rajiv Gandhi Salai, Chennai – 600 119

www.sathyabama.ac.in

DEPARTMENT OF CHEMISTRY

BONAFIDE CERTIFICATE

This is to certify that this Project Report is the bonafide work of **S. KUBENTHIRA (39910009)** who carried out the project entitled "**ONE POT SYNTHESIS OF COUMARIN DERIVATIVES FORM SUBSTITUTED PHENOLS AND ITS ZONE OF INHIBITION ON GRAM NEGATIVE BACTERIA**" under my supervision from December 2020 to March 2021.

Guide

Dr. T. KRITHIGA Ph.D.,

Associate Professor

Department of Chemistry

Head of the Department

Dr. J. KARTHIKEYAN Ph.D.,

Associate Professor

Department of Chemistry

Submitted for Viva voce Examination held on_____

Internal Examiner **External Examiner**

DECLARATION

I, S.KUBENTHIRA, hereby declare that the Project Report entitled "**ONE POT SYNTHESIS OF COUMARIN DERIVATIVES FORM SUBSTITUTED PHENOLS AND ITS ZONE OF INHIBITION ON GRAM NEGATIVE BACTERIA" done** by me under the guidance of **Dr. T. Krithiga M.Sc., M. Phil, Ph.D.,** Associate Professor, Department of Chemistry, Sathyabama Institute of Science and Technology is submitted in partial fulfilment of the requirements for the award of Master of Science degree in Chemistry.

DATE:

PLACE:

S.KUBENTHIRA

ACKNOWLEDGEMENT

I am pleased to acknowledge my sincere thanks to **Board of Management of SATHYABAMA** for their kind encouragement in doing this project and for completing it successfully. I am grateful to them.

I convey my thanks to **Dr. J. Karthikeyan,** Head of the Department, Department of Chemistry for providing me necessary support and details at the right time during the progressive reviews.

I would like to express my sincere and deep sense of gratitude to my Project Guide, **Dr. T. Krithiga** for her valuable guidance, suggestions and constant encouragement which paved way for the successful completion of my project work.

I wish to express my thanks to all Teaching and Non-teaching staff members of the Department of Chemistry who were helpful in many ways for the completion of the project.

S.KUBENTHIRA

ABSTRACT

The key goal of this project is to use oxalic acid as a catalyst to make 6-keto -8-methoxy -4-methyl -2-H-Chromen-2-one from Vanillin and Ethyl acetoacetate by Pechmann Condensation. It also aims to find antibacterial activity of same product by zone of inhibition method. The collected product's biological activity is investigated by evaluating its antibacterial activity. Substituted coumarin derivative was synthesized by the reaction of Vanillin and Ethyl acetoacetate using oxalic acid as a catalyst in Ethanol under reflux conditions. The obtained product was characterized by FTIR and NMR spectroscopic Techniques. The structure and the functional group present in the obtained product were found from spectral studies. The synthesized coumarin derivatives are tested for their antibacterial activity against a gram negative bacterium and found to have a good antibacterial activity against Escherichia Coli.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

MCR	-	Multicomponent Reactions
I-DOPA	-	l-3,4-dihydroxyphenylalanine
CGA	-	Chlorogenic acid
FTIR	-	Fourier Transform Infrared
NMR	-	Nuclear Magnetic Resonance
E. Coli	-	Escherichia Coli

CHAPTER 1

INTRODUCTION

1.1 MULTICOMPONENT REACTION

MCRs are convergent reactants, meaning they compane three or more commercially available or easily accessible starting materials to form a compound in which basically all or most of the atoms add to the newly formed product. Surprisingly, a name reaction is a chemical reaction that has achieved some status from various perspectives by being named after its discoverers. In the opinion of organic synthetic chemists, an optimal reaction pathway for the synthesis of structurally complex substances should include sequences that require the stereo controlled forming of several carbon–carbon bonds in a single step, beginning with simple commercially available or easily accessible composition. In this segment, we attempt to demonstrate the forming of various hetero cycles through MCRs by combining a name reaction such as the Michael reaction, Mannich reaction, Knovenagel reaction, Aldol reaction, and Wittig reaction with another name reaction (Majid heravi et al 2020).

Most methodological experiments on MCRs, which are mostly concerned with reactivity and environments, use readily available substrates to investigate the scope of the reaction, with benzaldehyde serving as the traditional testimonial substrate. The extension of MCRs to the valorization of bio sourced aldehydes would incorporate the characteristics of MCRs in terms of atom and energy economy, as well as the renewability of the starting platform molecules, in a more ecological perspective that would also include the preference for renewable resources. Furfural is likely the most widely found bio-based aldehyde in multicomponent reactions because it is readily available and has a stable reactivity, similar to simple aromatic aldehydes However, bio-based HMF and GMF behave differently in certain reactions than unsubstituted furfural due to the inclusion of additional hydroxy groups on the substrates, which raises solubility, reactivity. Furthermore, although the high appeal of such strategies, the limited availability of HMF prior to recent years has limited its use as starting materials for

complex molecules through MCRs. GMF is less often used due to its poor availability; however, its unique glycosylated structure provides useful possibilities and is hence an interesting analogue (Weigang Fan et al 2020). These techniques have been widely used to analyze medicines in mixtures, product formulations, and clinical samples. The primary aim of multicomponent spectrometric analysis is to create a calibration model that correlates multivariate spectrometer outputs to analyte compositions or properties observatory section (Iqbal Ahmad et al 2019). Hundreds of organic reactions have achieved such prominence among the tens of thousands of recognized organic reactions that they have been named after their discoverers or developers. The Biginelli reaction, Hantzsch reaction, Gewald reaction, Ugi reaction, and Ugi-azide reaction are all well-known examples. Since name reactions are important in the synthesis of heterocycles, we try to highlight synthesis of heterocycles using one-pot and multicomponent reactions through a name reaction in this devition (Majid Heravi et al 2020)

1.2 2-NAPTHOL

For hydroxycarboxylic acids, a sequence of BINOL-based molecules containing fluorescent quenching amino groups has been developed. The dimeric BINOL compound (S,S) is the first fluorescence enhancement sensor for mandelic acid (MA) chiral detection. The dynamic interaction of several hydrogen bonding interactions between the sensor and MA is depicted (S,S). (S)-MA stimulates (S,S) fluorescence rather than (R)-MA. G1 (R,R) and G2 (R,R) dendrimers with phenyl branches exhibit dramatically increased fluorescent responses and enhanced sensitivity (Yu et al 2017) .

Apart from its utility in converting 2-naphthol to 2-naphthylamine and then to other 2-substituted derivatives, the coupling of 2-naphthol with diazonium compounds is used in the industrial preparation of a variety of essential azo-dyes, such as Orange II. Substitution occurs primarily in the 1-position in all diazo-coupling reactions involving 2-naphthol. When 1-methyl-2-naphthol adjacent location is blocked the alternate position ortho to the initiating hydroxyl group (i.e) for coupling to occur, the three position is insufficiently reactive. This suggests that the negative charge on the 2-naphthoxide ion cannot be easily relayed to the 3-position, lending support to the possibility the C2-C3 bond has a lower double

bond-bond character than the C1-C3 bond (Smith et al 1969).

1.3 UGI REACTION

The Ugi reaction is a straightforward one-pot reaction that can be used to synthesise a wide variety of organic compounds with relatively good to excellent yields. Any of the materials can be used as intermediates in the synthesis of various nitrogen compounds, while others are effective synthetic targets (Ivar ugi et al 1991).

The four-component condensation which converts a mixture of substituted amine, isonitrile, aldehyde and carboxylic acid to acylaminocarboxylic acid amides, diacylamines , and aminocarboxylic acid amides. Furthermore, the reaction of aminocarboxylic acids with aldehydes and isocyanides produces a high yield of lactams (Gunter Benz et al 1991).

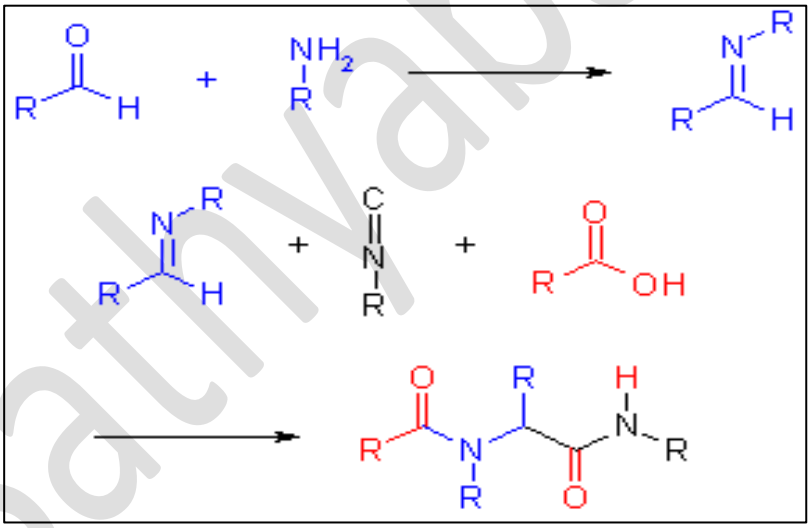

Fig. 1.1 ugi reaction

1.4 PECHMANN CONDENSATION

The Pechmann condensation is the most efficient method of producing coumarins by reacting activated phenols with ketoesters or unsaturated carboxylic acids. Traditional catalysts have used inorganic and organic acids, but these approaches

have many drawbacks, including heavy acid use, oxidation, toxicity, and difficult separation of chemicals (Sayed et al 1996). Transesterification, intramolecular hydroxyl alkylation, and dehydration are all steps in the Pechmann condensation of resorcinol and ethyl acetoacetate (EAA) to form 7-hydroxy-4-methyl chromen-2 one. The mechanism is based on proton transfer from the acid sites of the catalyst to the keto group of EAA through EAA-catalyst interaction. After that, a nucleophilic attack by a hydroxyl group of resorcinol produces an intermediate and ethanol. 7-hydroxy-4-methyl coumarin is formed when the intermediate undergoes rapid cyclization through intramolecular condensation (Shady et al 2020)

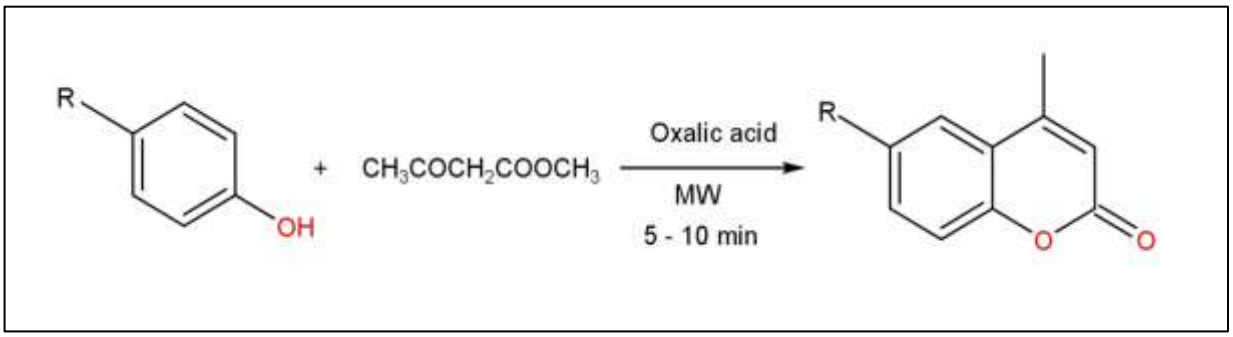

Fig. 1.2 Pechmann Condensation reaction

1.5 ANTIBACTERIAL ACTIVITY

Bacterial infections are now recognized as major public health threats, with increased morbidity and mortality. Pathogenic bacteria - multidrug resistant (MDR) bacterial strains resulting from cross resistances operative in natural bacterial consortia within the human body and in the environment - resist most modern antibacterial agents (Chita ranjan sahoo et al 2021).

The coumarin skeleton is found in biologically active natural products and is used as an intermediate in the synthesis of bioactive heterocyclic compounds, revealing antimicrobial, antifungal, anti-inflammatory, anti-cancer, anti-tubercular, antioxidant, and anticoagulant involvement. There have been a few synthetic compounds with a coumarin ring that have been shown to be effective against multi-drug resistant bacteria (Mohd. Shahnawaz khan et al 2019).

Coumarins are naturally occurring compounds derived from 1,2-benzopyrone.

They are not to be confused with Coumadin, a generic name for the vitamin K antagonist warfarin. It is a solid of white crystal. It is said to have a vanilla-like odour as well as a note of "freshly mowed hay" (Huai-li Qin et al 2020). The emergence of multidrug-resistant bacteria necessitates the development of a new generation of antibiotics, which may have a different inhibition or killing mechanism than current antibiotics. Yang et al have presented the design, synthesis and biological evaluation of 39 coumarin derivatives with the aim of combating antibacterial resistance by inhibiting the biosynthesis path (Yang Ku et al 2018). Coumarins (1-benzopyran-2-one) are organic compounds present in many plants that belong to the benzopyrone class. Coumarins have antimicrobial, antiviral, antiinflammatory, antidiabetic, antioxidant, and enzyme inhibitory activity, among other biological properties. Herve et al have provided a description of the isolation, structural characteristics, and pharmacological behaviour of a number of different compounds (Herve martial poumale poumale et al 2013).

CHAPTER 2

LITERATURE SURVEY

Multicomponent condensation reactions involving three or more reactants in one pot have recently been discovered to produce a structurally complex bioactive heterocyclic compound. It is seen as a method for increasing the efficiency of a chemical process in which a reactant is exposed to several chemical reactions in a single reactor rather than having to go through a lengthy isolation and purification steps to take. The synthetic schemes are built with the least amount of pollution to the atmosphere in mind. Some of such reactions which were previously reported are given below,

Huijun Zhang et al have synthesized 3,4-diaryl coumarins by an effective one-pot method involving visible-light-induced cyclization and Pd-catalyzed Suzuki cross-coupling processes is created. A sequence of alkynoates and aryl boronic acids were well suited for this catalytic method under light on-off optimized conditions, and were successfully converted into the corresponding products in moderate to high yielding.

Fang Ye et al have proposed a successful three-component cyclo condensation reaction in a single pot for the synthesis of coumarin derivatives. It defines how to synthesis 3-(5′-substituted-2′-benzoxazolyl)-7-diethylaminocoumarins from 4-diethylaminosalicylaldehyde, ethyl cyanoacetate and 4-substituted-2-aminophenol. The novel method has a fast reaction time, modest yields and an easy set-up.

Bahador karami et al proved the presence of a catalytic sum of K_2CO_3 as a simple catalyst, the reaction of 5,7-dihydroxy-4-substituted coumarin, malononitrile and aromatic aldehydes yields new pyrano-[2,3-h] coumarin derivatives in good to excellent yields. The reaction of malononitrile and 5,7-dihydroxy-4-substituted coumarin

Sitanshu Kumar et al have modified the substituents on two different starting materials and the synthetic compounds were also screened for anti-microbial activity and found to be moderate to excellent anti-bacterial agents.

Nadia Hanafy Metwally et al have shown a novel, one-pot synthesis of a series of N,N-bis(cyanoacetyl)hydrazine derivatives, bis-imino-2H-chromenes and bis-2-oxo-2H-chromene derivatives is formulated.

Chita Rajan sahoo et al have shown the bacterial infections epitomize significant health threats globally with an increased morbidity and mortality. Pathogenic bacteria-multidrug resistant bacterial strains resulting from cross resistances operative in natural bacterial consortia within the human body and in the environment-resist most modern anti-bacterial agents

As a result, the production of newer potential drug candidate(s) against the broad spectrum of MDR bacteria is expected. Coumarin and its derivatives, for example, have been related to a broad variety of biological inhibitory properties, including antibacterial activity.

Hao Lia et al designed and synthesized novel coumarin-thiazolyl ester derivatives with potent DNA gyrase inhibitory action.

CHAPTER 3

AIM AND SCOPE

3.1 AIM

The main goal of this project is to use oxalic acid as a catalyst to make 2 methyl 2H benzo coumarin from beta - naphthol and ethyl acetoacetate. FTIR and NMR Spectroscopy are used to determine the product's spectral analysis. The obtained product's biological activity is investigated by evaluating its antibacterial activity**.**

3.2 SCOPE

- Coumarin derivative prepared from beta-naphthol and ethyl acetoacetate by Pechmann reaction.
- Characterization experiments confirm the product (FTIR and 1H-NMR Spectroscopy).
- With Escherichia coli, the obtained sample was tested for antibacterial activity.

CHAPTER 4

MATERIALS AND METHODS

4.1 MATERIALS

The materials used in this reaction are beta-naphthol, ethyl acetoacetate, oxalic acid and ethanol, all of which are purchased from Merck chemicals and used as such without futher purification.

4.2 CHARACTERIZATION TECHNIQUES

4.2.1 *Fourier Transform Infrared Spectroscopy (FTIR)*

FTIR spectroscopy is the most insightful single tool for clay mineral composition and structure, as well as associations of clay minerals with inorganic or organic compounds. Following a short presentation of the technique's concepts, the chapter offers an outline of the potential of FTIR for mineralogical detection of clay mineral samples and research with clay minerals. Following a short explanation of the technique's principles, the chapter discusses the potential of FTIR for mineralogical identification of clay mineral samples, as well as exploring reactions with water and organic molecules. This section includes data from all three infrared regions: far, middle, and close (Petit et al 2013). FTIR will precisely determine the molecular composition of particular fluid inclusions. It is a nondestructive inclusion analysis technique, analogous to LRM. The LRM and FTIR methods share many similarities, including: (1) fundamental motions based on crystals and molecules; and (2) fixed-point microregion study of solid, gas and inclusions of liquid.

Identification of organic compounds, daughter crystals, and stable elements in inclusions; and (4) systematic analysis of the chemical properties of the consists substances. Neither method will tell you the composition of monoatomic compounds or rare gases. The following is an explanation of how FTIR functions.

The machine consists of an infrared optical table, a display and a printer (Shuming wen et al 2013)

Fig. 4.1 FTIR Spectrometer

In the study of peptide conformation, Fourier-transform infrared spectroscopy (FTIR) is extremely useful. The amide stretching vibrations of the backbone carbonyl groups are the most widely used spectral band (M.I aguilar et al 2005).

Fourier transform infrared (FTIR) spectroscopy is a type of vibrational spectroscopy that can be used to investigate a variety of soil chemical reaction. Many environmentally significant molecules, such as organic acids, soil organic matter, mineral phases and oxyanions, produce vibrations in the mid-infrared (mid-IR) range (D.P eak et al 2013).

4.2.2 Nulear Magnetic Resonance Spectroscopy (NMR)

The magnetic portion of electromagnetic radiation interacts with the very small magnetic moments possessed by atomic nuclei of isotopes with a nonzero spin

quantum number I, resulting in nuclear magnetic resonance spectroscopy. The energy separation, and thus the resonance frequency, of discrete nuclear magnetic moment orientation levels is proportional to the applied magnetic field B0

NMR spectroscopy, on the other hand, has an inherently poor sensitivity due to the limited separation between ground and ecstatic condition, as well as the long lifetimes of the excited states. High magnetic fields, time-averaging machines, and Fourier transform spectrometers can all be used to overcome this sensitivity limitation (Keith D.et al 1978).

Core plugs may also be examined using NMRS during fines invasion. Fordham et al., for example, used the NMRS imaging technique to investigate the invasion of clay particles within natural sedimentary rocks by injecting suspensions of clay particles. According to Faruk et al The proton spin-lattice relaxation time profiles calculated at different times do, in fact, indicate the effect of clay fines invasio (Faruk uvan et al 2016).

FIG 4.2 NMR SPECTROMETER

The structural analysis of polymers is well suited to NMR, especially 13C NMR. It provides knowledge on polymer chemical structure, branching, and cross-linking, as well as polymer tacticity. The sequence distribution in copolymers can be calculated using NMR data, such as the chemical shift of the olephinic carbons of vinyl monomers in vinyl copolymers (Pacakova et al 2005).

NMR methods are often used to determine the structure of polysaccharides isolated from various sources (von der Lieth, 2009). NMR can allocate all of the structural characteristics of carbohydrates, including stereochemistry and the form of linkages between saccharide units, without destroying them (Noham.sorour et al 2017).

Nuclear magnetic resonance (NMR) spectroscopy is one of the more advanced methods for analysing and validating the structural properties of polymers, nanomaterials, and composites made of nano materials. It relies on the population of magnetic nuclei in an external magnetic field to align the nuclei in a finite number of expected orientations (Ruqeya zazir et al 2019).

4.2.3 Mass Spectrometry

Mass spectrometry is an analytical technique that uses the mass-to-charge ratio (m/z) of ions manufactured form a perspective to receive and assess analytes. It can be used to analyze a variety of clinically important analytes, such as small molecules, proteins, and peptides. When mass spectrometry is combined with gas or liquid chromatographs, the resulting analyzers have extended analytical capabilities with a broad range of clinical applications, including the quantitation of analytes from a variety of body tissues and fluids. Furthermore, mass spectrometry is commonly used in the field of proteomics due to its ability to classify and quantify proteins.

Mass spectrometry necessitate an ionization phase, in which neutral atoms or molecules are converted into an ion. In gas chromatography–mass spectrometry, electron effect and chemical ionization are often used. Electrospray ionization (ESI) and atmospheric pressure are the most widely used techniques in liquid

chromatography–mass spectrometry (Alan L et al 2018)

FIG 4.3 Mass spectrometer

The analyzed compound's ions are produced and transformed to the gas phase; ions are separated and analyzed according to their mass-to-charge ratio; the ions are detected; and the resulting signals are captured, processed, and converted into a mass spectrum (D.zagorevskii et al 2003).

The aim of mass spectrometry is to identify unknown compounds in a sample. It can also be used to quantify materials that are already known. The process ionizes the chemical species' molecules and sorts them by charge-to-mass ratio and relative sufficiency. In a wide variety of samples, MS is used. The ioniser, analyzer, and detector are the three main components of a mass spectrometer (Pawel sengupta et al 2019).

Throughout the history of the sounding rocket programme, mass spectrometers have been used extensively to determine the composition or concentration of

different constituents in the stair. The basic instrument is a laboratory-based modification of particle accelerator techniques (M.F.Larsen et al 2003).

4.3 ONE POT SYNTHESIS

4.3.1 Synthesis of 4methyl 2H-benzo coumarin

In a round bottom flask, a mixture of beta-naphthol (10 mmol), ethyl acetoacetate (10 mmol), and oxalic acid (1 gramme) (Catalyst) was refluxed at 70oC for around 6 hours with sovent is ethanol (10 mL) . After the reaction was completed, the solvent was allowed to evaporate at room temperature, and the crude product was obtained

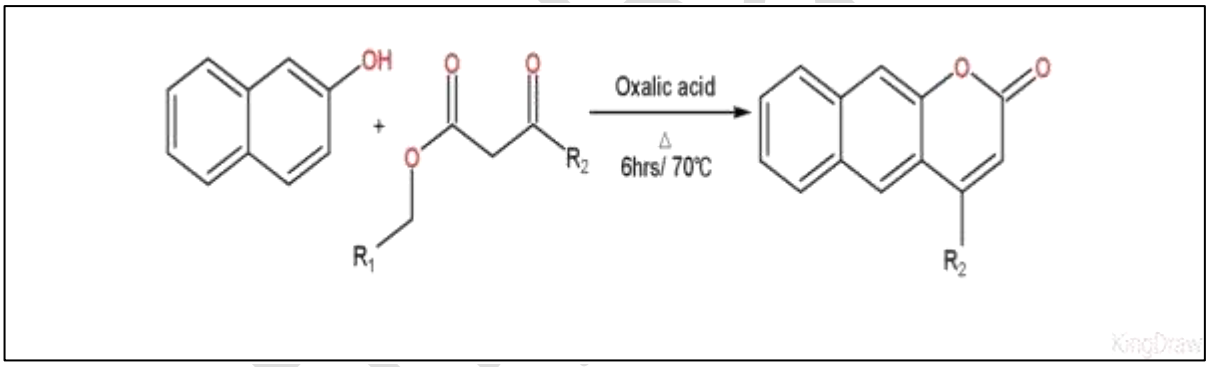

Fig.4.4 Reaction scheme of formation of substituted chromene derivation

CHAPTER 5

RESULT AND DISCUSSION

5.1 SYNTHESIS OF 4 METHYL 2H-BENZO COUMARIN

The simple Pechmann condensation reaction is carried out by reacting beta-naphthol and Ethyl acetoacetate in 1:1 ratio using oxalic acid as a catalyst. Ethanol is used as a solvent and the reaction is carried out for about 6 hours. The obtained product is subjected to spectral studies (FTIR, NMR Spectroscopy) to find the functional group and structural formula.

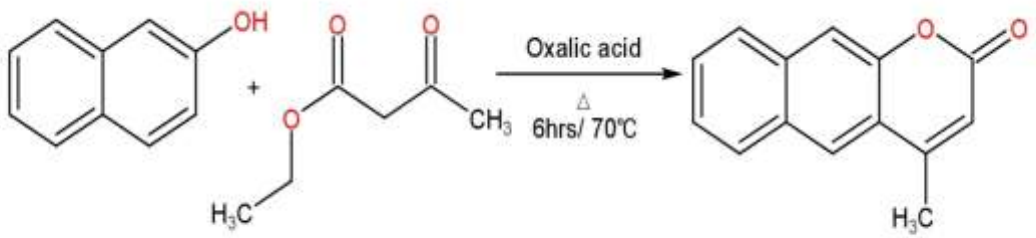

Fig. 5.1 Reaction scheme of formation of 4 Methyl-2H-benzo Coumarin

5.1.1 Spectral data of 4 methyl-2H-benzo Coumarin

FTIR Data: The FTIR Spectral data of the obtained product is shown in the below given Fig. 5.2. The obtained product peaks are 3114 cm^{-1} , 1313 cm^{-1} and 1096 cm^{-1} which corresponds to sp^3 -CH , C-O Stretch and C=O stretch.

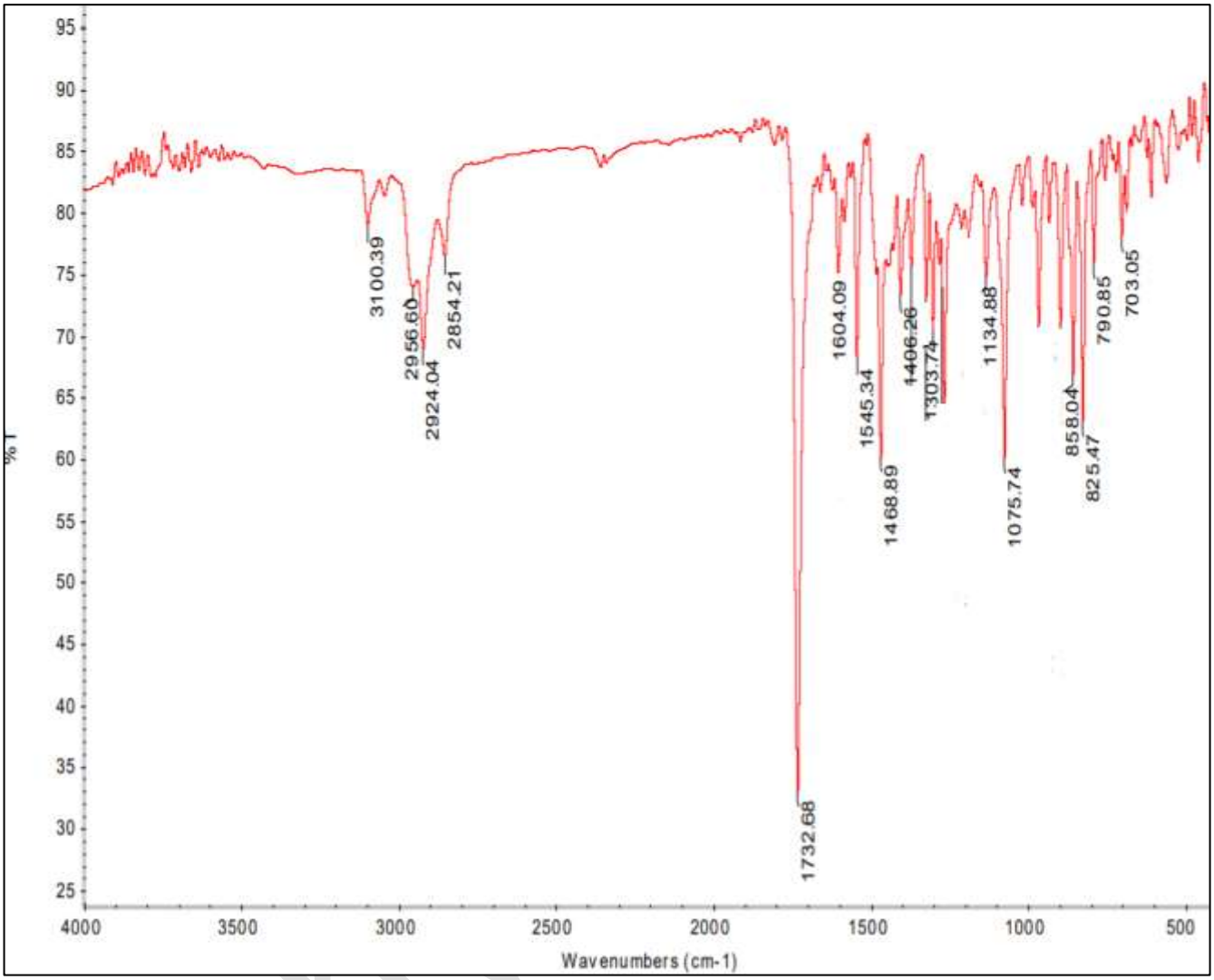

Fig. 5.2 FTIR Spectra of 4 methyl-2H-benzo coumarin

Table 5.1 FTIR Vibrational frequencies of 4 methyl-2H-benzo coumarin

Vibrational Frequency	Functional group identification
3100	C-H Stretching (Sp^2)
2956	C-H stretching (Sp^3)
1303	C-O Stretching
1545	Aromatic c=c bending
1732	C=O Stretching
1468	CH2 Bending

NMR Data: The ^{1}H NMR spectra of 4 methyl-2H-benzo coumarin are given in the figure 5.3 which will confirm its structure. The chemical shift of structural units from ^{1}H NMR Spectrum in 4 methyl-2H-benzo coumarin are shown in Table 5.2.

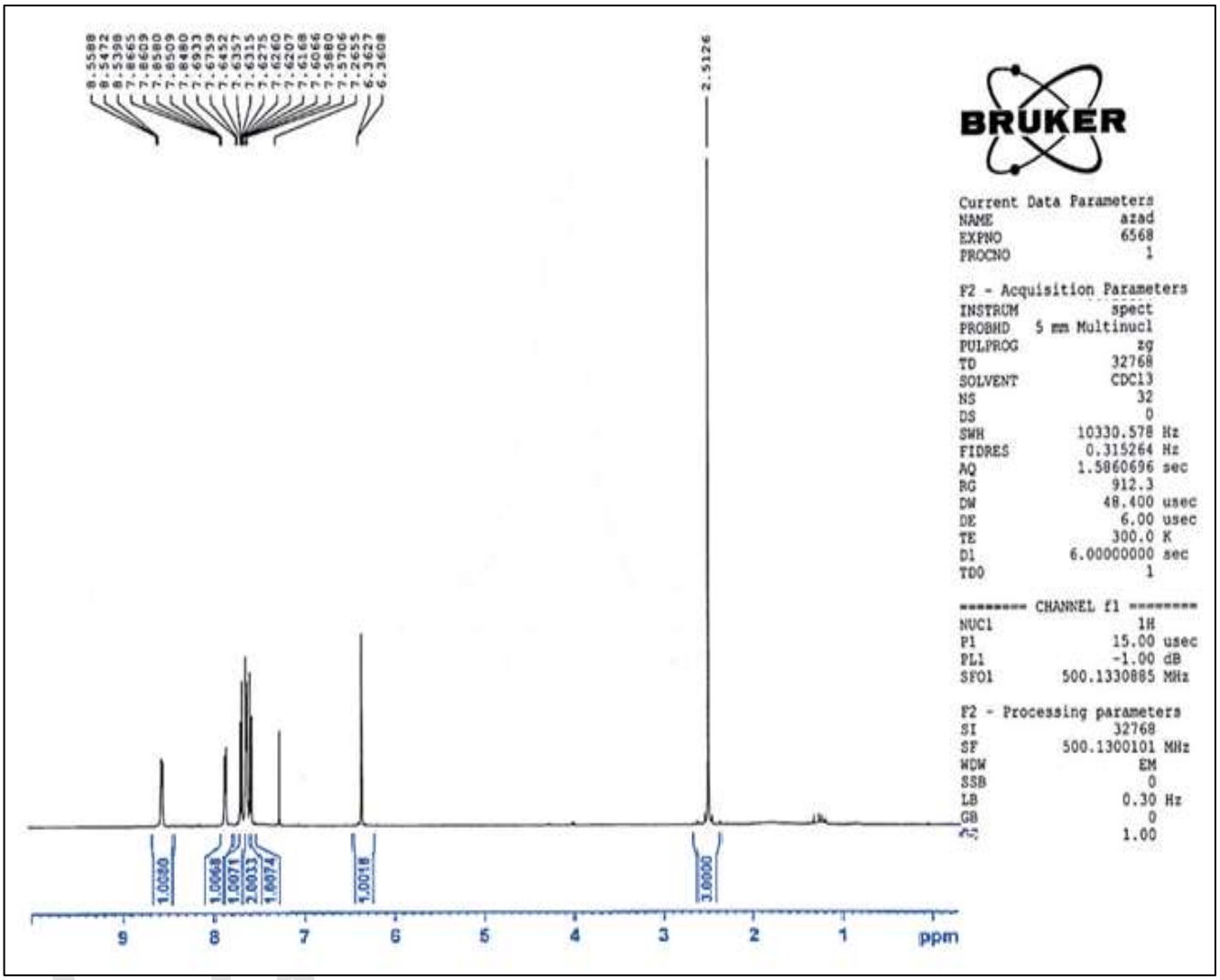

Fig. 5.3 NMR Spectra of 4 METHYL-2H-BENZO COUMARIN

Table 5.2 Chemical shift of structural units in from 4 methyl-2H- benzo coumarin from ^{1}H NMR Spectrum

Chemical shift(δ)	Structural unit
2.51	Ar-CH_3
6.36	Vinylic Proton
7.2-8.5	Aromatic Proton

5.2 MECHANISM OF FORMATION OF 4 METHYL-2H BENZO COUMARIN

A solid Bronsted acid, such as oxalic acid is used in this reaction. Transesterification reaction and keto-enol tautomerization reaction are all catalyzed by the acid.In the next step Coumarin skeleton is formed, when it undergoes a Michael Addition. Following this stage, rearomatization occurs. The compound is then formed by the acid-induced removal of water.

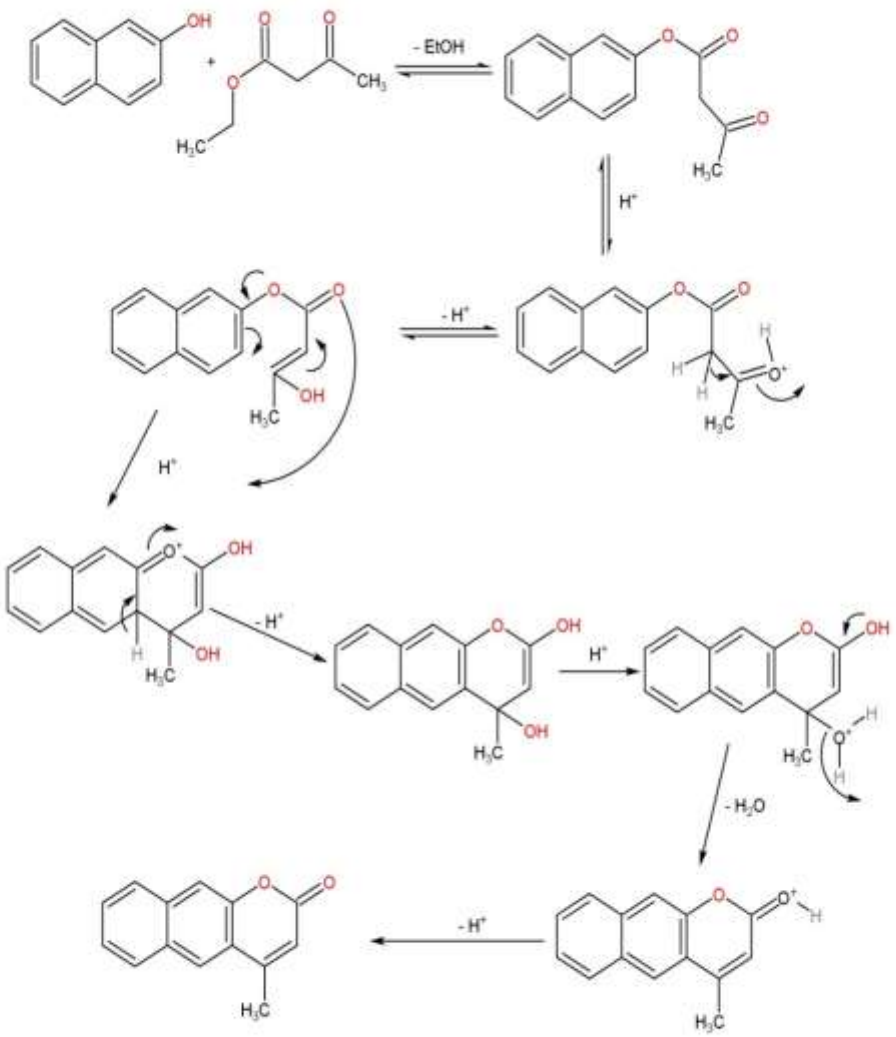

Fig. 5.4 mechanism of formation of 4 methyl-2H-benzo coumarin

5.3 ANTIBACTERIAL STUDIES

- Antibacterial behaviour may be measured using agar diffusion techniques.
- By scattering a volume of bacterial culture over the entire agar plate surface, the entire agar plate surface is injected.
- A 3 to 4 mm radius cavity is aseptically drilled with a sterile cork borer, and the extract solution or antimicrobial agent is pumped into the well at the desired concentration.
- Agar plates are incubated under suitable conditions based on the test microorganism.
- The zone of inhibition is the area around the discs that would be apparent if bacteria grew thickly around it.
- To determine antibacterial efficacy, the diameter of the region of inhibition is determined.

Table 5.3 zone of inhibition

MICRO-ORGANISM	ZONE OF INHIBITION IN mm
Pseudomonas aeuroginsa	15

5.3.1 Antibacterial Activity Result

- Antibacterial activity was discovered against the Pseudomonas aeuroginsa bacterium.

- RESULT: It shows good antibacterial activity.

FIG. 5.5 Zone of Inhibition **of Pseudomonas aeuroginsa**

CHAPTER 6

CONCLUSION

The present study reports the synthesis of substituted coumarin by Pechmann reaction. The reaction of the 2-naphthol with ethyl acetoacetate at ambient condition results in the successful formation of 4-methyl-2H-benzo coumarin by Pechmann reaction using MCR method. The mechanism of the formation of reaction product through one pot synthesis is proposed. The functional groups of the synthesized product were confirmed by FTIR spectroscopy. The structure of 4-methyl-2H-benzo coumarin was confirmed by the ^{1}H-NMR spectra. The biological activity of the synthesized 4-methyl benzo coumarin was tested against Pseudomonas aeruginosa. The synthesized 4-methyl-2H-benzo coumarin show good antibacterial activity against Pseudomonas aeruginosa.

REFERENCES

1. Alan L. Rockwood, Mark M. Kushnir, Nigel J. Clarke,2 - Mass Spectrometry,Editor(s): Nader Rifai, Andrea Rita Horvath, Carl T. Wittwer,Principles and Applications of Clinical Mass Spectrometry,Elsevier,2018,Pages 33-65.
2. Chita Ranjan Sahoo, Jyotirmaya Sahoo, Monalisa Mahapatra, Debananda Lenka, Pratap Kumar Sahu, Budheswar Dehury, Rabindra Nath Padhy, Sudhir Kumar Paidesetty,Coumarin derivatives as promising antibacterial agent(s),Arabian Journal of Chemistry,Volume 14, Issue 2,2021,102922,ISSN 1878-5352.
3. D. Peak,Fourier Transform Infrared Spectroscopic Methods of Soil Analysis☆Reference Module in Earth Systems and Environmental Sciences,Elsevier,2013
4. D. Zagorevskii,2.28 - Mass Spectrometry,Editor(s): Jon A. McCleverty, Thomas J. Meyer,Comprehensive Coordination Chemistry II,Pergamon,2003,Pages 367-380
5. El-Sayed H. El Ashry, Nagwa Rashed,7.16 - Bicyclic 6-6 Systems: Three Heteroatoms 1:2,Editor(s): Alan R. Katritzky, Charles W. Rees, Eric F.V. Scriven,Comprehensive Heterocyclic Chemistry II,Pergamon,1996,Pages 561-624,
6. Faruk Civan,Chapter 18 - Instrumental and Laboratory Techniques for Characterization of Reservoir Rock,Editor(s): Faruk Civan,Reservoir Formation Damage (Third Edition),Gulf Professional Publishing,2016,Pages 593-611
7. Günter Benz,2.3 - Synthesis of Amides and Related Compounds,Editor(s): Barry M. Trost, Ian Fleming,Comprehensive Organic Synthesis,Pergamon,1991,Pages 381-417,
8. Hervé Martial Poumale Poumale, Rebecca Hamm, Yanqing Zang, Yoshihito Shiono, Victor Kuete,8 - Coumarins and Related Compounds from the Medicinal Plants of Africa,Editor(s): Victor Kuete,Medicinal Plant Research in Africa,Elsevier,2013,Pages 261-300.

9. Hua-Li Qin, Zai-Wei Zhang, Lekkala Ravindar, K.P. Rakesh,Antibacterial activities with the structure-activity relationship of coumarin derivatives,European Journal of Medicinal Chemistry,Volume 207,2020,112832,ISSN 0223-5234.
10. Iqbal Ahmad, Muhammad Ali Sheraz, Sofia Ahmed, Zubair Anwar,Chapter Eight - Multicomponent spectrometric analysis of drugs and their preparations,Editor(s): Harry G. Brittain,Profiles of Drug Substances, Excipients and Related Methodology,Academic Press,Volume 44,2019,Pages 379-413,
11. Ivar Ugi, Severin Lohberger, Rosmarie Karl,4.6 - The Passerini and Ugi Reactions,Editor(s): Barry M. Trost, Ian Fleming,Comprehensive Organic Synthesis,Pergamon,1991,Pages 1083-1109,
12. Keith D. Bartle, Derry W. Jones,Chapter 23 - Nuclear Magnetic Resonance Spectroscopy,Editor(s): CLARENCE KARR,Analytical Methods for Coal and Coal Products,Academic Press,1978,Pages 103-160.
13. M.F. Larsen,OBSERVATION PLATFORMS | Rockets,Editor(s): James R. Holton,Encyclopedia of Atmospheric Sciences,Academic Press,2003,Pages 1449-1454,
14. M.-I. Aguilar, A.W. Purcell,PEPTIDES,Editor(s): Paul Worsfold, Alan Townshend, Colin Poole,Encyclopedia of Analytical Science (Second Edition),Elsevier,2005,Pages 29-36,
15. Majid Heravi, Vahideh Zadsirjan,2 - Direct synthesis of heterocycles via MCRs, using a name reaction,Editor(s): Majid Heravi, Vahideh Zadsirjan,Recent Advances in Applications of Name Reactions in Multicomponent Reactions,Elsevier,2020,Pages 15-138,
16. Majid Heravi, Vahideh Zadsirjan,3 - Synthesis of heterocycles via MCRs, using a name reaction in combination with another reaction ,Editor(s): Majid Heravi, Vahideh Zadsirjan ,Recent Advances in Applications of Name Reactions in Multicomponent Reactions,Elsevier,2020,Pages 139-268
17. Mohd. Shahnawaz Khan, Ranu Agrawal, Mohd Ubaidullah, Md. Imtaiyaz Hassan, Nazia Tarannum,Design, synthesis and validation of anti-microbial coumarin derivatives: An efficient green approach,Heliyon,Volume 5, Issue 10,2019,e02615,ISSN 2405-8440.
18. Noha M. Sorour, Ahmed A. Tayel, Rateb N. Abbas, Osama M.

Abonama,Chapter 3 - Microbial Biosynthesis of Health-Promoting Food Ingredients,Editor(s): Alexandru Mihai Grumezescu, Alina Maria Holban,In Handbook of Food Bioengineering,Food Biosynthesis,Academic Press,2017,Pages 55-93

19. P.W.G. SMITH, A.R. TATCHELL,CHAPTER IX - AROMATIC CONDENSED RING SYSTEMS,Editor(s): P.W.G. SMITH, A.R. TATCHELL,Aromatic Chemistry,Pergamon,1969,Pages 196-221,
20. Pavel Sengupta, Kalap Khanra, Amit Roy Chowdhury, Pallab Datta,4 - Lab-on-a-chip sensing devices for biomedical applications,Editor(s): Kunal Pal, Heinz-Bernhard Kraatz, Anwesha Khasnobish, Sandip Bag, Indranil Banerjee, Usha Kuruganti,In Woodhead Publishing Series in Electronic and Optical Materials,Bioelectronics and Medical Devices,Woodhead Publishing,2019,Pages 47-9.
21. Ruqeya Nazir, Mir Riasa Zaffar, Insha Amin,Chapter 8 - Bacterial biofilms: the remarkable heterogeneous biological communities and nitrogen fixing microorganisms in lakes,Editor(s): Suhaib A. Bandh, Sana Shafi, Nowsheen Shameem,Freshwater Microbiology,Academic Press,2019,Pages 307-340.
22. S. Petit, J. Madejova,Chapter 2.7 - Fourier Transform Infrared Spectroscopy,Editor(s): Faïza Bergaya, Gerhard Lagaly,Developments in Clay Science,Elsevier,Volume 5,2013,Pages 213-231
23. S. Yu, L. Pu,8.07 - Fluorescent Sensing of Chirality,Editor(s): Jerry L. Atwood,Comprehensive Supramolecular Chemistry II,Elsevier,2017,Pages 129-160,
24. Shady M. EL-Dafrawy, Shawky M. Hassan, Mervat Farag,Kinetics and mechanism of Pechmann condensation reaction over sulphated zirconia-supported zinc oxide,Journal of Materials Research and Technology,Volume 9, Issue 1,2020,Pages 13-21
25. Shuming Wen, Jian Liu, Jiushuai Deng,Chapter 3 - Methods for the detection and composition study of fluid inclusions,Editor(s): Shuming Wen, Jian Liu, Jiushuai Deng,Fluid Inclusion Effect in Flotation of Sulfide Minerals,Elsevier,2021,Pages 27-68.
26. V. Pacáková, J. Virt, PLASTICS,Editor(s): Paul Worsfold, Alan Townshend, Colin Poole,Encyclopedia of Analytical Science (Second Edition),Elsevier,2005,Pages 180-187.

27. Weigang Fan, Charlie Verrier, Lianjie Wang, Mohammed Ahmar, Jia-Neng Tan, Florence Popowycz, Yves Queneau,2 - 5-(Hydroxymethyl)furfural and 5-(glucosyloxymethyl)furfural in multicomponent reactions,Editor(s): Amélia Pilar Rauter, Bjørn E. Christensen, László Somsák, Paul Kosma, Roberto Adamo,Recent Trends in Carbohydrate Chemistry,Elsevier,2020,Pages 73-100
28. Yang Hu, Yufeng Shen, Xiaohu Wu, Xiao Tu, Gao-Xue Wang,Synthesis and biological evaluation of coumarin derivatives containing imidazole skeleton as potential antibacterial agents,European Journal of Medicinal Chemistry,Volume 143,2018,Pages 958-969,ISSN 0223-5234.