ONE POT SYNTHESIS OF 4-H PYRANS VIA KNOEVENAGEL CONDENSATION REACTION

Submitted in partial fulfilment of the requirements for the award of Bachelor of Science Degree in Chemistry

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BONAFIDE CERTIFICATE

This is to certify that this Project Report is the bonafide work of ARUNKUMAR R(39030003),DHARUNKUMAR R(39030007),MOHAMMED ALI M (39030013), who carried out the project entitled **"ONE POT SYNTHESIS OF 4-H PYRANS VIAKNOEVENAGEL CONDENSATION REACTION"** under my supervision from December 2021 to April 2022.

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We **ARUNKUMAR R, DHARUNKUMAR R, MOHAMMED ALI M**, hereby declare that the Project Report entitled **"ONE POT SYNTHESIS OF 4-H PYRANS VIA KNOEVENAGEL CONDENSATION REACTION"** done by us under the guidance of **Dr. T. Krithiga MSc., 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 Bachelor of Science degree in Chemistry.

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ABSTRACT

Magnesium oxide nanoparticles were green synthesized by using magnesium nitrate and sodium hydroxide at room temperature in presence of henna leaves extract which is very simple and cost effective method. The characterization of synthesized magnesium oxide nanoparticles was done using X-ray diffraction, scanning electron microscopy (SEM) and Fourier transform infra-red (FTIR) spectroscopy.

X-ray diffraction pattern indicates that the nanoparticles are crystalline in nature. The crystalline size of magnesium oxide nanoparticle was calculated by Debye-Scherer formula and the crystallite size was found to be 40 nm. The surface morphology of nanoparticles was observed and investigated using SEM. The material at room temperature, shows crystallite of cubical shape with strong agglomeration of particles. The presence of Magnesium – Oxygen bond (Mg– O) bond in the synthesized sample was confirmed by the peak at 811.62 cm^{-1} in the FTIR spectrum of magnesium oxide nanoparticles.

The catalytic activity of the synthesized Magnesium oxide nanoparticles was tested by the one-pot synthesis of 5-acetyl-2-amino-4-(4-hydroxy-3-methoxyphenyl)-6-methyl-4H-pyran-3-carbonitrile. The product formation was confirmed by the FTIR and Mass Spectrometry.

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LIST OF ABBREVIATIONS

MCR	-	Multicomponent Reaction
FTIR	-	Fourier Transform Infrared Spectroscopy
SEM	-	Scanning Electron Microscope
XRD	-	X-RAY Diffraction
MgO	-	Magnesium Oxide
NM	-	Nano Meter

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CHAPTER 1

INTRODUCTION

1.1 *M*ETAL OXIDE CATALYST

Metal oxide catalysts are related to most manufacturers Catalytic process. They include simple oxides, such as silica, Alumina, Clays, , Titan, Zirconia, ZnO and foam and Oxide of metal mesopious, or complex oxide, such as Kegin or type of polyoxometate type Dawson, phosphates, perovinskites, and hexaaluminate. These metal oxides have specific characteristics such as Acidity, basic, oxidative characteristics, resulting in specific Catalytic characteristics.

They also form the basis of metal catalysts, to irrigation Catalysts, for Denox and Desox reactions, such as perofin or doped oxide in Ceribasé. The main catalytic areas include oxidation, Catalytic acid and basic, fertilizer, criticism and Convert biomass. Metal oxides are sometimes used simple As a support period of operation, such as Silica, Alumina, Silicatumina, mesopious oxide, MOF,can Effect of catalytic characteristics by synergy, electrons Conductive In fully oxidised $CaMnO_{3-\delta}$ and $CaFeO_{3-\delta}$ perovskites, Mn and Fe are at +4 oxidation state and $\delta = 0$, the material can accommodate up to 17% oxygen vacancies without loosing its structure.

The $Sr_{1-x}La_xCo_{1-y}Fe_yO_{3-\delta}$ series, with brownmillerite-type oxygen defects, exhibit high electronic/oxygen ion mobilities. In some perovskites a small oxygen excess can be accommodated by the formation of cation vacancies at A- or B-sites, leaving the oxygen sub-lattice intact. Effects or / and heat, hold Interactive oxidizing metals. Metal oxide surface. Ending with Oxygen O2-anion, who is bigger than that Cation MN. It obeys symmetry, coordination, and The accessibility of reactive molecules of Mn cations is lost at surface. Furthermore, the surface of an oxide can contain error types and environments, example may play some role in catalysis leads to the sensitivity of the metal oxide structure to the catalyst react. full oxidized $CaMnO_{3\delta}$ and $CaFeO_{3\delta}$

perovskites, Mn and Fe at 4 oxidation states and =, the material can hold up to 17% oxygen vacancy without losing its structure. the Sr1 – xLaxCo1 – yFeyO3 – series, with brownmillerite oxygen defects, exhibiting high ion/oxygen mobility. Sure perovskites, a small amount of excess oxygen can be form cation sites on sites A or B, leaving intact oxygen subnet. [J. L. G. Fierro et al,2006]

1.2 METAL OXIDE NANOPARTICLES

Nano particles consist of a functionalized surface, a shell of various layered materials and a central/major nano particle. The properties of bulk materials differ from those of nanoparticles due to their large surface-to-volume ratio, surface layer, solvent affinity, coating type, quantum mechanical effect, diffusion rate, and specificity. mechanical and ferromagnetic properties. The large surface-to-volume ratio makes the nanoparticles highly reactive and capable of penetrating membranes. The chemical nature of the nanoparticles needs to be studied to improve their ability to attach molecules to the surface.

Oxide nanoparticles can exhibit physical and chemical properties due to limited dimensions and high angular or edge surface density websites. Particle size is expected to affect three basic groups of properties in any material. The first includes the structural features, namely the network symmetry and mobility parameters. Mass oxides are usually robust and stable systems with the crystal structure is clearly defined. However, the increasing importance of the surface free energy and stress with decreasing particle size must be taken into account: changes in size-related thermodynamic stability can induce changes in cell parameters and/or structural transformations and in extreme cases, nanoparticles can disappears due to interaction with the surrounding environment and a large free zone energy.To show mechanical or structural stability, a nanoparticle must low surface free energy. Due to this requirement, the phases have Stability in bulk materials can become very stable in nanostructures. This structure the phenomenon has been detected in TiO2, VOx, Al2O3 or MoOx oxides.

Metal oxide nanoparticles has received a lot of attention around the world because it can be specifically synthesized to be highly toxic to bacteria. The importance of their application as an antibacterial agent takes into account the limited range and efficacy of antibiotics on the one hand, the abundance of metal oxides on the other hand, and the much lower tendency of nanoparticles to induce resistance to antibiotics. Then it becomes clear. Effective suppression of broad-spectrum bacteria against bacteria is known for several monometal nanooxides (Fe_3O_4, TiO_2, CuO, ZnO), but further research into multimetal oxides is needed. This is understandable because the relationship between physicochemical properties and bioactivity is complex and seems difficult to generalize even with metal oxide nanoparticles composed of only one metal component. Despite the widespread use of metal oxide nanoparticles as antibacterial agents, there are problems in their practical use given their cytotoxic effects. In this respect, the consideration of polymetal oxides for biological applications is even greater. Because they provide a synergistic effect and can combine the best physicochemical properties of their constituents. [Hernández-Alonso,Corondo et al,2007]

1.3 CHEMICAL SYNTHESIS OF METAL OXIDE NANOPARTICLES

Nanotechnology is an important modern research area concerned with the synthesis, strategy and structure control of particles ranging in size from about 1 to 100 nm. Nanoparticles have new or improved satisfactory properties compared to larger partners of the same material. Unique properties are adjusted by the size and shape of nanoparticles. Therefore, control Size and shape allows designing nanoparticles with specific attributes desired in their Applications.

Due to these unique properties of nanoparticles and their recent development Synthesis methods, current and potential applications of nanoparticles are developing rapidly. Among the many types of nanoparticles, metal oxide nanoparticles are extremely widely used many industries including integrated circuit manufacturing, biomedical and cancer treatment, renewable energy, environmental protection, pharmaceuticals, personal care, coatings, plastics, textiles, food, building materials, electronics and automobiles.

Material choice affects the solubility of the by-product phase and granules matrix volume ratio. As a source of metal ions in metal oxides nanomedicine, metal salts such as chloride are commonly used due to their availability.

Alkaline earth oxide is considered as a suitable reactant for metal chloride because they are converted to water-soluble alkaline earth chlorides during the reaction with metal chloride, this allows and remove the green color of the by-product phase. However, alkaline earth oxides such as CaO are generally inactive during the ammo process crushing, even if the Gibbs free energy change of the reaction is mostly negative

. For the synthesis of nano materials, there are a large number of techniques to produce nano materials in the form of colloids, aggregates, powders, tubes, rods, wires, thin films, etc. All techniques are generally based on two approaches. One approach is summarized under so-called "top-down" technology and refers to the manufacture of very small structures from building blocks of materials by grinding, engraving, or other mechanical processing. The manufactured millionaire microchips fall into this category. The desired paths are predefined by lithography.

The current distance and path width is less than 100 nm. On the other hand, nanomaterials can also be produced using what is known as "bottom-up" technology. In this case, the structures are built atom by atom or molecule by molecule. In general, metal nanoparticles can be prepared by various methods such as chemical reduction in the solution phase, UV photolysis, metal vapor deposition thermal decomposition, electrochemical engineering, laser cutting, sputtering and ball milling/mechanical milling. [A.Yoko,G.Seong, T.Tomai,et al,2020]

1.4 GREEN SYNTHESIS OF METAL OXIDE NANOPARTICLES

Green synthesis is a modern method for synthesizing organic compounds and designing different drugs under easy protocols, efficient conditions, environmentally friendly and high yield molecular methods. with outstanding advantages compared to traditional organic synthesis methods. It often reduces by-products, costs and develops environmentally friendly processes.

This includes a wide range of modern techniques for the synthesis of bioactive compounds, such as microwave assisted synthesis, solid phase solvent-assisted synthesis, reaction with organic catalyst, single-pot multicomponent reaction and chemical synthesis, using ionic liquid technique. Pharmaceutical companies are also improving chemicals to reduce environmental risks and reduce ecological risks. green synthesis methods for synthesizing metal oxide nanoparticles.

Green nanoparticles are Widely used as anti-bacterial agent, photocatalyst and adsorbent. green metal oxide nanoparticles exhibit low toxicity and high biocompatibility, allowing them to biomedical applications, especially for targeted drug delivery.

Green synthesis is a modern method for synthesizing organic compounds and designing different drugs under easy protocols, efficient conditions, environmentally friendly and high yield molecular methods. with outstanding advantages compared to traditional organic synthesis methods. It often reduces by-products, costs and develops environmentally friendly processes. This includes a wide range of modern techniques for the synthesis of bioactive compounds, such as microwave assisted synthesis, solid phase solvent-assisted synthesis, reaction with organic catalyst, single-pot multicomponent reaction and chemical synthesis, using ionic liquid technique. Pharmaceutical companies are also improving chemicals to reduce environmental risks and reduce ecological risks.

Metal nanoparticles (MNPs) and metal oxide nanoparticles (MONPs) are used in many fields. New nano-based entities are being created in abundance and integrated into daily personal care products, cosmetics, drugs, drug delivery and clothing to impact the manufacturing and industrial sectors., which means that the commercialization of nanomaterials and nano-assisted devices will continue to grow. They can be prepared by many methods such as green synthesis and classical chemical synthesis. Green synthesis includes infinite binding capacity to produce MNPs and MONPs with demanding properties. The structure-function relationship between nanomaterials and information is important for life cycle assessment leading to the production of high-performance, soft and environmentally friendly nanomaterials.

In this study, we focus on biosynthetic processes for the synthesis of MNPs and MONPs, including a comparison between green synthesis and classical chemical methods as well as some new directions of green synthesis of MNPs. nanoparticles from different plant parts, namely plant leaf extracts. Plants with reducing compounds are the preferred choice for synthesizing precious metals - metal ions can be reduced to the corresponding metals in the absence of any other chemicals under irradiation Microwave using water as a mild solvent.

Green nanotechnology gives us the ability to prevent negative effects. Green nanotechnology has a business effect on nanomaterials or product design by eliminating or reducing pollution, which means it solves existing environmental problems.

Recently, green synthesis of metal nanoparticles has attracted attention due to its feasibility and very low environmental impact.As such, green synthesis is considered an important tool for reducing the destructive effects associated with traditional nanoparticle synthesis methods commonly used in the laboratory and in industry. In this review, we have summarized the basic processes and mechanisms of "green" synthesis, especially for metals and metal oxides from natural extracts. [Malik P, Shankar R,et al 2014]

1.5 CATALYST INTRODUCTION

Magnesium oxide is an inorganic salt of magnesium formed with ions of magnesium and oxygen. Magnesium is an element your body needs to function normally. Magnesium oxide may be used for different reasons. Some people use it as an antacid to relieve heartburn, sour stomach, or acid indigestion. Magnesium oxide, also known as Magnesia, is an ionic compound formed by the metal (Magnesium) and nonmetal (Oxygen) by transfer of electrons between Mg2 and O2–. The chemical formula of Magnesium oxide is MgO. Magnesium oxide is a type of magnesium mineral supplement that is mostly made of magnesium—it actually contains more magnesium than other magnesium supplements. Magnesium oxide is acquired by burning magnesium with pure oxygen, but this method is quite costly. The cheapest method is to expose oxygen to magnesium salts using soil sediments, seawater, or salt bottoms. With this method, the source of

magnesium salts determines the quality of the magnesium oxide produced. Magnesium is an important mineral for normal bone structure in the body. Magnesium is a naturally formed alkali metal that is important for our organs and systems, especially muscles and nerves. Magnesium oxide is a compound containing magnesium combined with oxide ions. It is chemically basic and has a pH between 8 to 10.

1.6 MAGNESIUM OXIDE STRUCTURE

The chemical and molecular formula of magnesium oxide is MgO. Its molecular mass or molar mass is 4.34 g/mol. Furthermore, it has the empirical formula MgO and consists of a network of magnesium cations Mg2 and the oxygen anion O2− linked by ionic bonds. Magnesium oxide is an odorless white powder. Its density is 3.6 g/cm^3. Furthermore, its boiling point is 3600^{o}C and its melting point is 2852^{o}C). It is soluble in acids, ammonia and very soluble in water, where it forms magnesium hydroxide. However, it is insoluble in alcohol. Its refractive index is 1.7355 and its thermal conductivity is 45−60W·m $^{-1}$·K $^{-1}$ and its heat capacity is 37.2 J/mol K. Magnesium oxide (MgO) is a compound Ionicsubstances are formed by transferring valence electrons from Magnesium and Oxygen. Magnesium is electropositive in nature and has two valence electrons, and since oxygen is more electronegative, it tends to attract valence electrons towards itself, while magnesium atom tends to donate two electrons. its valence electron to form its stable electronic configuration. As a result, strong electrostatic attraction holds the cation (Mg2+) and anion (O2–) together to form an ionic bond in MgO. The crystal lattice of magnesium oxide has an octahedral geometry; it is in Halit form, which has a lattice constant of a = 4.212A^o. In which Mg2 and O2– ions are tightly bound together, increasing their melting point.

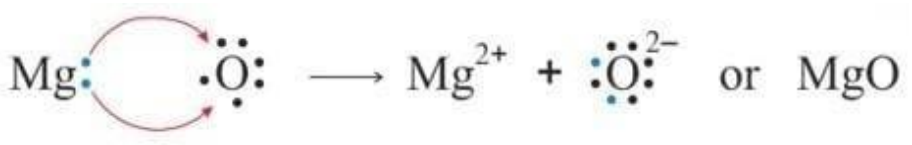


Fig 1.1Formation of MgO

Source: https://www.embibe.com/exams/magnesium

1.7 HENNA LEAVES

Henna leaves is a well-known ethno botanical species that has been used in cosmetics and medicine for over 9, years. Its use in traditional Indian folk medicines is well documented. Lawsonia inert Linn (Lythraceae) is a perennial plant commonly known as henna. One of the most notable uses of henna is its ability to protect the skin from infection and eliminate inflammation. In the southern regions of India it has been used as a folk medicine to treat ringworm infections and skin diseases. Henna is a well-known ethnobotanical species that has been used in cosmetics and medicine for over 9, years. It is native to North Africa and Southeast Asia, and is commonly grown as an ornamental throughout India, Persia, and along the Mediterranean coast of Africa. Henna grows best in tropical savanna and arid tropical regions, at latitudes between 15° and 25°N and S, producing the highest dye content at temperatures between 3455°C. Range. The optimum soil temperature for germination is 253°C. Henna leaves are a very popular natural dye for coloring hands, fingers, nails and hair. The color molecule, lawsone, ismain component of the plant; Its highest concentration was detected at thepetiole.51.5% [Abulyazid Elsayed,M.E., Ragaa,M. et al,2013]

Fig 1.2 HENNA LEAVES

Source : https://www.moolihai.com/benefits-of-henna/

1.7.1 BOTANICAL DESCRIPTION

Henna is a much branched glabrous shrub or small tree 2 to 6 m in height, which may be spiny. Bark greyish brown, unarmed when young, older plants with spine tipped branchlets. Young branches quadrangular, green but turn red with age. Flowers small, white, numerous; in large pyramidal terminal cymes, fragrant, 1 cm across, 4 petals crumpled in the bud. Calyx with 2mm tube and 3mm spread lobes; petals orbicular to obovate, white or red; stamens 8, inserted in pairs on the rim of the calyx tube; ovary 4 celled, style up to 5 mm long, erect. Fruit small, brown, globose, 48 mm. diameter diameter, many seeds, uneven opening, sawn into 4 parts, yes enduring style. Seeds 3 mm diameter, angular, thick seed coat. Leaves small, opposite, entire margin elliptic to broad lanceolate, stalkless, about 1.5-5 cm long, .5-2 cm wide, green-brown to gray-green, petiolate short and glossy to ap pointed or obtuse with tapered ends. base. New branches are green and quadrangular, turning red with age. The seeds have a characteristic, pyramidal, hard and thick seed coat with a slightly brown color.

1.7.2 ANTIBACTERIAL ACTIVITY

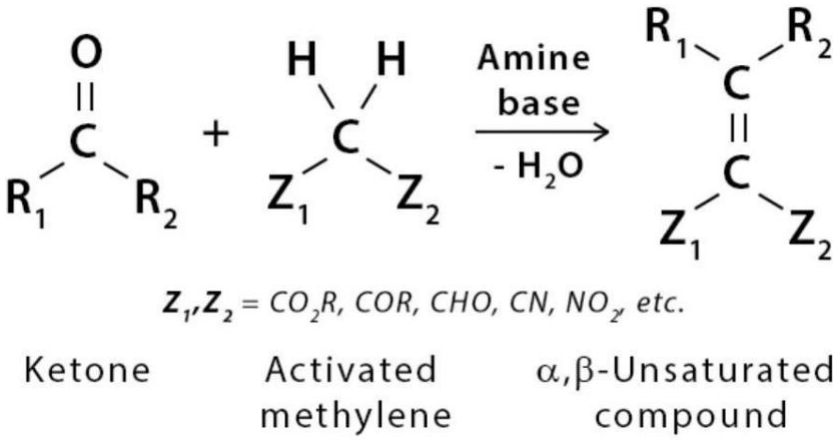
The antibacterial properties of medicinal plants are more and more being mentioned from one-of-a-kind parts of the world. the world fitness employer estimates that plant extracts or their active components are used as folk remedies in conventional remedies by way of 80% of the sector's populace. harmful microorganisms can be controlled with pills, ensuing in the emergence of several drug-resistant microorganism, creating alarming medical situations in the remedy of infectious illnesses. The pharmaceutical enterprise has created many new antibiotics. Microbial resistance to these tablets is growing. In widespread, microorganism have the genetic capacity to transfer and collect resistance to artificial tablets used as healing sellers.

Henna has been widely used for centuries in medicine and cosmetics in several parts of the world. Henna leaves and seeds are known to relieve a number of skin ailments including fungal infections and cracked feet. Plant parts were extracted by maceration method. Phytochemical examination revealed the presence of saponins, flavonoids and steroids in all extracts. All tested isolates were sensitive to all 1µg/ml. The highest

activities were observed in the aqueous extract of the plant against Staphylococcus aureus and Epidermophyton floccosum(19mm). While the standard drugs have similar activity against isolates at 20µg/ml with an area of 28 mm and the results of this study suggest that Henna may act as a potential antibacterial agent. and provides the basis for the isolation and identification of the bioactive components in these extracts. The alcohol extracts had the highest antibacterial activity with a MIC of .125.15 g/mL against ßhemolytic streptococci and against coagulase-negative staphylococci of .125175 µg/mL. Henna leaf extract has antibacterial activity against bacteria that cause common skin infections. Alcohol and oil extracts of henna have effects similar to some antibiotics commonly used in clinical practice. Antibacterial activity of henna shows absolute toxicity against quinonoid compounds, especially those isolated from ringworm species such as Microsporum natural source, has not yet been explained. Gypsum and Trichophyton mentagrophytess. antibacterial activity of natural naphthoquinone Alcannin and shikonin products and their derivatives with antiviral activity: Ethanolic extracts of Lawsone, an antibacterial agent in henna has an inhibitory effect on common nosocomial pathogens such as Escherichia coli, Proteus mirabilis, Klebsiella pneumoniae, Pseudomonas aeroginosa and Staphylococcus aureus at certain concentrations**.** [Abdelraouf, A., Elmanama,et al,2011]

1.7.3 KNOEVENAGEL CONDENSATION

Knoevenagel condensation is the nucleophilic addition of an activated methylene compound to an aldehyde or a ketone using an amino base (e.g. pyridine or piperidin) as a catalyst, followed by a dehydration reaction in which the molecule is broken down. water molecules are removed (condensation). The product is usually an α, β-unsaturated carbonyl compound (enone). The Knoevenagel reaction is a special variant of the aldol reaction with the subsequent removal of water. It is widely used in organic chemistry to form C=C bonds. The activated methylene compound must have the form ZCH2Z, where Z is the electron withdrawing group**.** [Bhuiyan, M.M.H.; Hossain, M.I.,et al,2021]



1.8 MULTICOMPONENT REACTION

Multicomponent reactions (MCRs) are synthetic processes, where three or more compounds react to form a single product. The popularity of MCRs lies in the simplicity and versatility of the experimental procedures that unlock the access to a wide range of products through the manifold possibilities of reagent combinations.

This is where multicomponent reactions (MCRs) come into play. Multicomponent reactions combine at least three reactants in the same pot to generate a product containing most (preferably all) atoms of the starting materials.8 Their atom economy, efficiency, mild conditions, high convergence and concomitant step economy in combination with their general compatibility with green solvents would justify a central place in the toolbox of 5 sustainable synthetic methodologies.Thus, despite the general understanding and dissemination of the chemical benefits of MCRs (convergence/divergence, diversityoriented synthesis, library generation), the sustainability aspect of this chemistry is marginally acknowledged and reviewed in literature.

This review thus aims to point out the opportunities and challenges that the utilization of MCRs brings for green synthesis and process design.Multicomponent reactions (MCRs) provide a new approach towards the efficient synthesis of diverse compounds and compound libraries.

MCRs are evolving from being purely a chemistry curiosity to being recognized as having increasing relevance for drug discovery in terms of lead discovery and optimization.

Recent needs in drug discovery for more diverse small molecules and their efficient synthesis have now shifted chemists' attention to the still largely unexplored field of chemistry. this.

In recent years, many new types of MCR have been discovered and applied to synthesize bioactive molecules. Similarly, many biotech companies and large pharmaceutical companies are now trying to exploit MCR chemistry to create chemical diversity. Organic chemists are stepping up their efforts to better control the results of RCM by introducing new catalysts and reaction conditions. Thus, the original MCR-derivative product can be considered as a fusion center for a variety of new cyclic or alternating scaffolds using different secondary transformations. Normally, only 13 synthesis steps are required to synthesize a drug-like advanced compound library.

MCRs have been recognized by the synthetic community in industry and academia as the preferred method for the design and discovery of bioactive compounds. MCRs also allow for easy access to a library of important and structurally complex molecules in a one pot fashion by simply varying the starting materials. The result is clearly dependent on the reaction conditions: solvent, temperature, catalyst, concentration, the kind of starting materials and functional groups. Such considerations are of particular importance in connection with the design and discovery of novel MCRs. Multi-component reactions thus address the requirements for efficient high-throughput synthesis of compounds in a cost- and time-effective manner. The characteristic aspect of MCR is that the final products contain almost all portions of substrates, generating almost no by-products. That makes MCRs an extremely ideal and eco-friendly reaction system. [Brauch. S,et al,2013]

CHAPTER 2

LITERATURE SURVEY

One-Pot synthesis of Knoevenagel–Michael–Cyclization Cascade Reaction for the Synthesis of Functionalized Novel 4H-pyrans by Using ZnCl2 as a Catalyst.

An expedient and cost-effective protocol has been developed for the synthesis of novel 2-methyl-6-(methylamino)-5-nitro-4-(4-aryl)-4*H*-pyran-3-carboxylate derivatives. This domino, one-pot, three-component reaction was carried out between β-ketoesters, aromatic aldehydes, and *(E)*-N-methyl-1-(methylthio)-2-nitroethenamine (NMSM) in the presence of 30 mol% anhydrous $ZnCl_2$ under the neat condition at 120°C. The synthesized 4*H*-pyran derivatives were characterized by spectroscopic techniques such as IR, ^{1}H NMR, ^{13}C NMR, CHNS, and HRMS. The molecular structure of compound methyl-2-methyl-6-(methylamino)-5-nitro-4-(4-nitrophenyl)-4*H*-pyran-3-carboxylate **4a** was confirmed by the single crystal X-ray analysis. This solvent-free protocol has several advantages such as shorter reaction time, an inexpensive catalyst, good yields, simple workup, and column-free purification.

One-pot efficient green synthesis of spirooxindole-annulated thiopyran derivatives via Knoevenagel condensation followed by Michael addition.

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A green, operationally simple and highly efficient one-pot three-component approach for the synthesis of spiro[indoline-3,4′-thiopyrano[2,3-*b*]indole] derivatives has been developed by the domino reaction of indoline-2-thione, isatin and ethyl cyanoacetate or malononitrile in ethanol at 80 °C for just 20 min. The significant advantages of this protocol are short reaction time, excellent yields, operational simplicity and formation of three new bonds in one operation from easily available starting materials

One-pot green synthesis of magnesium oxide nanoparticles using Penicillium chrysogenum melanin pigment and gamma rays with antimicrobial activity against multidrug-resistant microbes

Author links open overlay panelGharieb S.El-SayyadFarag M.MosallamAhmed I.El-Batal

the green synthesis of melanin after optimizing the media compositions. A method has been designed that included one-step synthesis of magnesium oxide nanoparticles (MgO NPs) by fungal melanin under the influence of different doses of gamma rays.

Synthesis and Characterization of Mgo Nanoparticles by Neem Leaves through Green Method

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Metal oxide nanoparticles can be used in electronics, catalysis, ceramics, petrochemical products, coatings and many other fields such as sound-proof, light-weight, heat-insulating and refractory fibre board and metallic ceramics. Synthesis of metal oxide nanoparticles can be done through three methods like physical, chemical, and green

methods. Present work focus on synthesis of MgO nanoparticles by Neem leaves through Green method. This method is non-toxic and eco-friendly. In this work, the precursor materials was $Mg(NO3)_2$ and fresh Neem leaves extract. The Neem leaves extract acting as a reducing agent in the reaction. The particles thereby obtained were characterized by different analytical techniques. X-Ray Diffractometer (XRD) for to calculate the average crystalline size, Particle Size Analyser for average particle size, Field Emission Scanning Electron Microscope (FESEM) for morphological studies, UV-Visible spectroscopy (UV-Vis) for to analyse the absorption patterns, Fourier Transform Infrared (FTIR) spectroscopy is used for analysing the functional groups which is involved in the reaction

CHAPTER 3

AIM AND SCOPE

3.1 AIM

The main aim of the project is to synthesize magnesium oxide nanoparticles by green synthesis method using henna leaves extract. The green synthesis of magnesium oxide nanoparticles was carried out using magnesium nitrate and sodium hydroxide at room temperature in presence of henna leaves extract as reducing agent. This method is cost effective and simple and environmentally safe. MgO Nanoparticles were characterized with the help of FTIR, SEM, XRD spectroscopy techniques. The synthesized MgO nanoparticles were tested for its catalytic activity by the one pot synthesis of 5-acetyl-2-amino-4-(4-hydroxy-3-methoxyphenyl)-6-methyl-4H-pyran-3-carbonitrile and the product was confirmed by FTIR and Mass spectroscopy.

3.2 Scope

- Synthesizing magnesium oxide nanoparticles using henna leaf extract.
- Characterization of magnesium oxide nanoparticles by FTIR Spectroscopy, XRD, SEM-EDX.
- To test its catalytic application of magnesium oxide by one pot Synthesis of substituted 4-H Pyrans using synthesized magnesium oxide nanoparticle.
- Product confirmation by FTIR and Mass spectrometry.

CHAPTER 4

MATERIALS AND METHODOLOGY

4.1 MATERIALS

Materials used in this process is, Magnesium nitrate, Malononitrile, Vanillin, Acetyl Acetone, Sodium hydroxide and ethanol were purchased from Merck chemicals and use it is. Henna leaves extract was taken from dried henna leaves were collected from Harith Tharang botanical plant nursery.

4.2 CHARACTERIZATION TECHNIQUES

4.2.1FTIR (Fourier Transform Infrared Spectroscopy)

FTIR (Fourier Transform Infrared Spectroscopy) is a very versatile tool for assessing the surface properties of nanoparticles. Under certain conditions, the chemical composition of the NP surface can be determined, and the reactive surface sites responsible for surface reactivity can be identified by the conjugation between the nanomaterial and the adsorbed biomolecule. increase. The FTIR spectrum consists of absorption peaks that correspond to the vibrational frequencies between the atomic bonds of the nanoparticles. FTIR is an excellent technique for qualitative analysis; Peak intensity is a direct indication of the properties of the material present. The big advantage is the lack of sample preparation for liquid and solid samples. When light is reflected at a critical angle on a particular material, it is totally reflected and a small amount of light is absorbed by the material in contact with the crystal surface. Penetration depth depends on the index of refraction of both the sample and the material of the crystal itself. Since the index of refraction is wavelength dependent, the spectra recorded by the ATR have slightly different intensity ratios throughout the spectrum and need to be corrected for comparison Transmission spectrum.

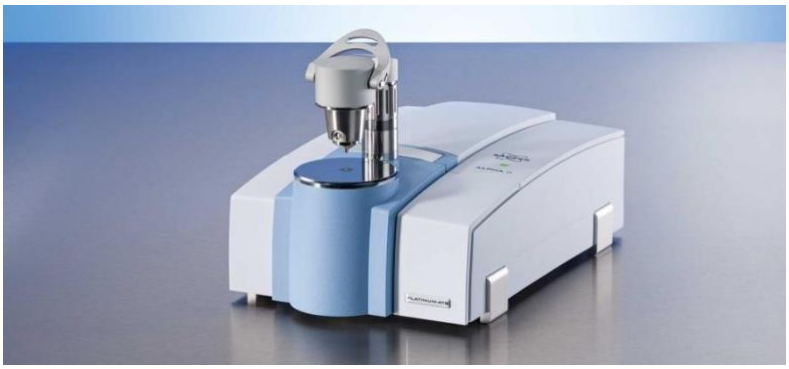


Fig 4.1 FTIR (Fourier Transform Infrared Spectroscopy)

Source:https://www.bruker.com/en/products-and-solutions/infrared-and-raman/ft-ir-routine-spectrometer/alpha-ii-compact-ft-ir-spectrometer.html

4.2.2SEM (Scanning Electron Microscopy)

SEM (Scanning Electron Microscopy) generates images from a sample by scanning the surface with a focused electron beam to visualize individual cells in detail. excite secondary electrons drifting away from the sample surface, or 2) they can be directly reflected(backscatter) from the sample. The detector collects secondary electrons and is backscattered to create an image. SEM also provides information on microstructures, such as bone, for implantation studies (measurement and pathophysiology) to analyze tissue response to different types of implanted biomaterials. . Inorganic crystals and a wide variety of synthetic and natural materials can be easily imaged using our SEM, which can be further characterized using EDX. EDX Our SEM system is equipped with an energydispersive Xray spectroscopy which detects Xray produced by the interaction of the electrons with the sample. Analysis of the Xray signals are used to map the distribution and estimate the abundance of specific elements in the analyzed sample. SEM provides detailed high resolution images of the sample by rastering a focussed electron beam across the surface and detecting secondary or backscattered electron signal. An Energy Dispersive XRay Analyzer (EDX or EDA) is also used to provide elemental identification and quantitative compositional information.SEM analysis is a powerful investigative tool which uses a focused beam of electrons to produce complex, high magnification images of a sample's surface topography. Once an area of interest has been identified on the sample and evaluated using SEM, our experts can dive deeper into the detail of the

material using energydispersive xray spectroscopy, or EDX analysis. Scanning electron microscopy (SEM) coupled with EDS (Energy Dispersive XRays spectroscopy) is based on sample excitation by a high energy electron current and the subsequent use of appropriate detectors that recover the signal emitted by the sample (when it looses the excitation stage) and convert it into images (when secondary or retrodispersed electrons are used) or in a semiquantitative analysis (when X ray are used). The microscope available in the ICB can be used with different electron acceleration voltages, emitting in a range from 1 to 3kV. SEMEDX can be used to provide surface elemental composition information of areas as small as nanometers in diameter. A finely tuned electron beam scans the sample and monitors the reflected electrons from the sample surface. The impact of the electron beam produces xrays that are characteristic of the elements in the sample. SEMEDX is also capable of analyzing multiple spots to create elemental maps of the surface of a sample, which can indicate materials present in either broad phases, or as small localized impurities. SEMEDX detects all the elements from B to U, with detection limits of 1 – 3 ppm, depth resolution of .53um, and a probe size of 1545 Å. SEM analysis is utilized for particle characterization, such as wear debris generated during mechanical wear testing. The high magnification, highresolution imaging of our SEM analysis supports the determination of the number, size, and morphology of small particles, allowing clients to understand the wear properties of their material. Energy dispersive xray spectroscopy, also referred to as EDX, EDS or EDAX, provides additional understanding of the surface material during the SEM analysis process. EDX analysis is used to obtain the elemental composition of the sample and provides more quantitative results than those provided by SEM analysis alone. The combination of SEM and EDX analysis provides chemical composition and elemental investigation - providing a comprehensive review of metallurgy.

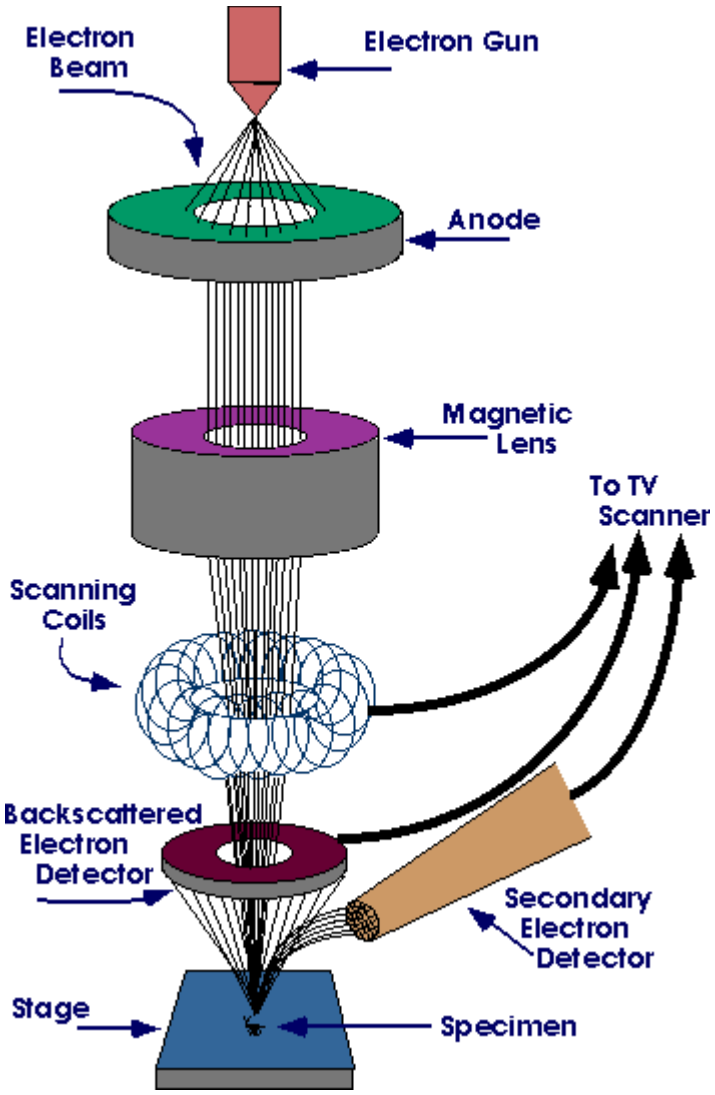


Fig 4.2* SEM (Scanning Electron Microscopy*)

Source:https://www.purdue.edu/ehps/rem/laboratory/equipment%20safety/Research%20Equipment/sem.html

4.2.3 XRD (X-Ray Diffraction)

When a beam of Xrays illuminates a single crystal, many “spots” are generated. The positions of the spots are determined by the size and shape of the unit cell and the symmetry. The intensities of the spots are determined by the arrangement of the atoms

within the crystal. After measuring the intensities of all of the diffraction spots (reflections), it is generally possible to determine the positions of the atoms in the unit cell (the structure) in a straightforward manner. Sometimes, however, the sample is more complex (twinning, aperiodic structure, diffuse scattering), and the structural analysis becomes a challenge for even the most skilled crystallographers. Most solids are actually not monocrystalline (that's why we love monocrystalline gems so much!), but are made up of lots of tiny crystals, so they described as polycrystalline. In diffraction imaging, the effect is that each point is spread out in a ring. If the crystals are oriented randomly, the rings are uniform and no information is lost when measured along the vector ray of the full three-dimensional diffraction image. The result is a histogram of the diffraction intensity relative to the angle of a powder sample

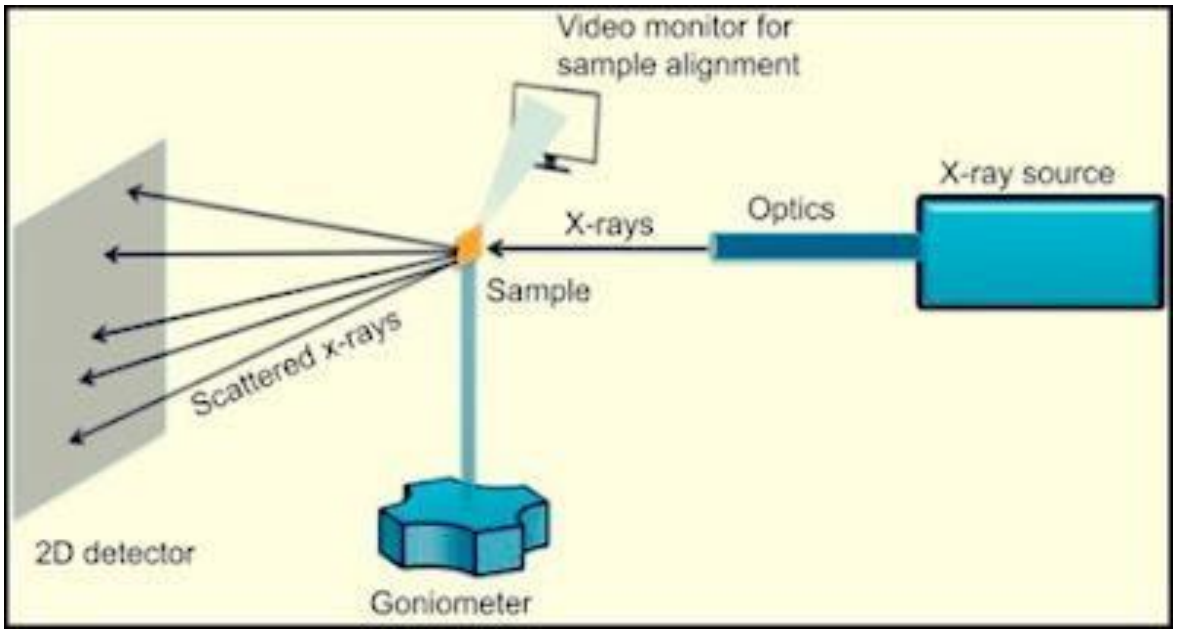


Fig 4.3 X-Ray Diffractrometer

Source https://www.14impressions.in/2020/09/principle-instrumentation-types-and.html

4.2.4 Nuclear Magnetic Resonance (NMR)

Nuclear Magnetic Resonance (NMR) is a spectroscopic method that characterizes the nucleus (Nuclear) that has wide applications in the physical sciences and industries. Nuclei in which there is at least one unpaired proton or neutron behave like small magnets, and the strong magnetic field exerts a force that causes them to precede them in the same way that the axis of the spinning tops outlines shaped surfaces. cones as they move. transitions in the Earth's gravitational field. The nucleus of an atom with an even number of protons and neutrons has zero spin, and all other atoms with an odd number have non-zero spin. If an external magnetic field is applied, it is possible to transfer energy between the fundamental energy to a higher energy level. Energy transfer takes place at a wavelength corresponding to the radio frequency, and when the spin returns to the ground level, energy is emitted at the same frequency. NMR spectroscopy is a non-destructive and non-invasive technique used to determine molecular structure and dynamics. Similarly, biochemists use NMR to identify proteins and other complex molecules. Besides identification, NMR spectroscopy provides detailed information about the structure, dynamics, reaction state and chemical environment of molecules. The nuclear spins of some active nuclei in NMR are likely to apply two different directions as they align to the external magnetic field (B). One direction corresponds to the lowest energy level of the nucleus and the other direction corresponds to the highest energy level of the nucleus.

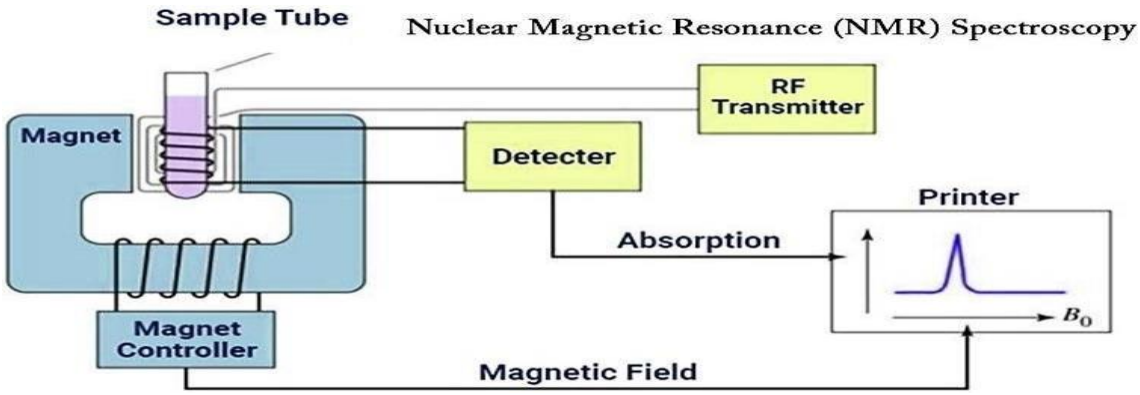


Fig 4.4 Nuclear Magnetic Resonance (NMR)

Source:https://www.researchgate.net/figure/NMR-spectroscopy-instrumentation_fig2_357242343

4.3 METHODOLOGY

4.3.1 SYNTHESIS OF HENNA LEAF EXTRACT

In this preparation, fresh leaves of henna are washed with distilled water and sun-dried for 4 to 5 days. 5 g of dried leaves were heated to 80 °C. in 100 ml of double-chambered water and stirred with a magnetic stirrer. After cooling the boiled solution, centrifugation was carried out to obtain the leaf extract.

4.3.2SYNTHESIS OF MAGNESIUM OXIDE NANOPARTICLES

To 100ml of Magnesium nitrate solution 30 ml of leaf extract is mixed and heated at 80℃ for 30 minutes. The pH of the solution is adjusted to 2M and NaOH is added while stirring and heated at 70℃ for about 30 minutes. A Reddish Brown precipitate of magnesium nitrate is obtained which is washed using water, filtered and kept to dry in hot air oven at 70℃ and the MnO nanoparticles are obtaine, which is used as a green catalyst**.**

4.3.3ONE POT SYNTHESIS

A mixture of vanillin (1.0 mmol, 0.106g), malononitrile (1.0 mmol, 0.066g), Acetyl acetone (1.0 mmol, 0.13g) and SBA-15 (10 mol %) was added and refluxed at 80^{o}C for 2hr using Ethanol (10ml) as a solvent. After completion of the reaction, as indicated by TLC, the solvent was evaporated and the crud product was extracted from ethyl acetate and water. The organic layer was dried with Na2SO4 and the solvent was evaporated to obtain the crude product. Yield: 73%

CHAPTER 5

RESULTS AND DISCUSSION

5.1 Characterization of Magnesium Oxide Nanoparticles

5.1.1 FTIR Spectrum Magnesium Oxide Nanoparticles

FTIR spectrum of magnesium oxide nanoparticle fig 5.1 shows the peak at 811.62 cm^{-1} which is due to Mg – O bond. A sharp peak at 1043.10cm^{-1},1325.56cm-1,1534.30cm^{-1},1789.52cm^{-1} and 2356.97cm^{-1} was because of H-O-H bending. The peak at 3000- 3500 cm^{-1} region represents the –OH group and interstitial water molecule.

Vibrational Frequency	Functional group identification
3338.65 cm-1	O-H Stretching of absorbale water molecule on Magnesium oxide.
2356.97	O-H-O Stretching
1769.52	
1634.30	
1325.56	
1043.10	
811.62	MgO Stritching

Table 5.1 FTIR Spectro of MgO

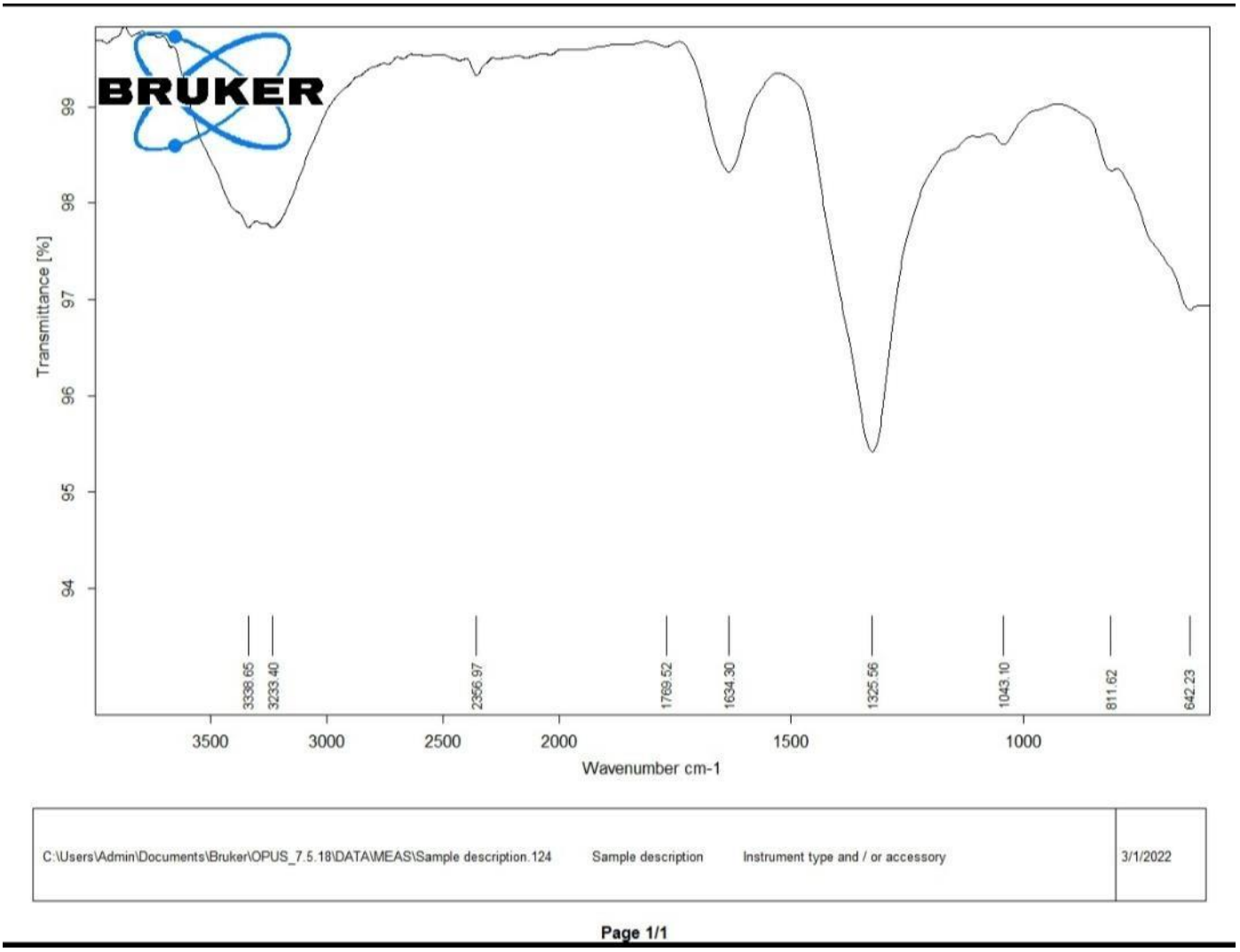


Fig 5.1 FTIR spectrum of Magnesium oxide nanoparticle

5.1.2 SEM and EDAX image of Magnesium oxide nanoparticle

The SEM image of magnesium oxide nanoparticle is shown in the Fig. 5.2. the image explains that magnesium oxide nanoparticle obtained have spherical shape. The SEM

image also shows the presence of agglomeration of MgO nanoparticles. The EDAX spectra shows the presence of Mg and O in the MgO catalyst**.**

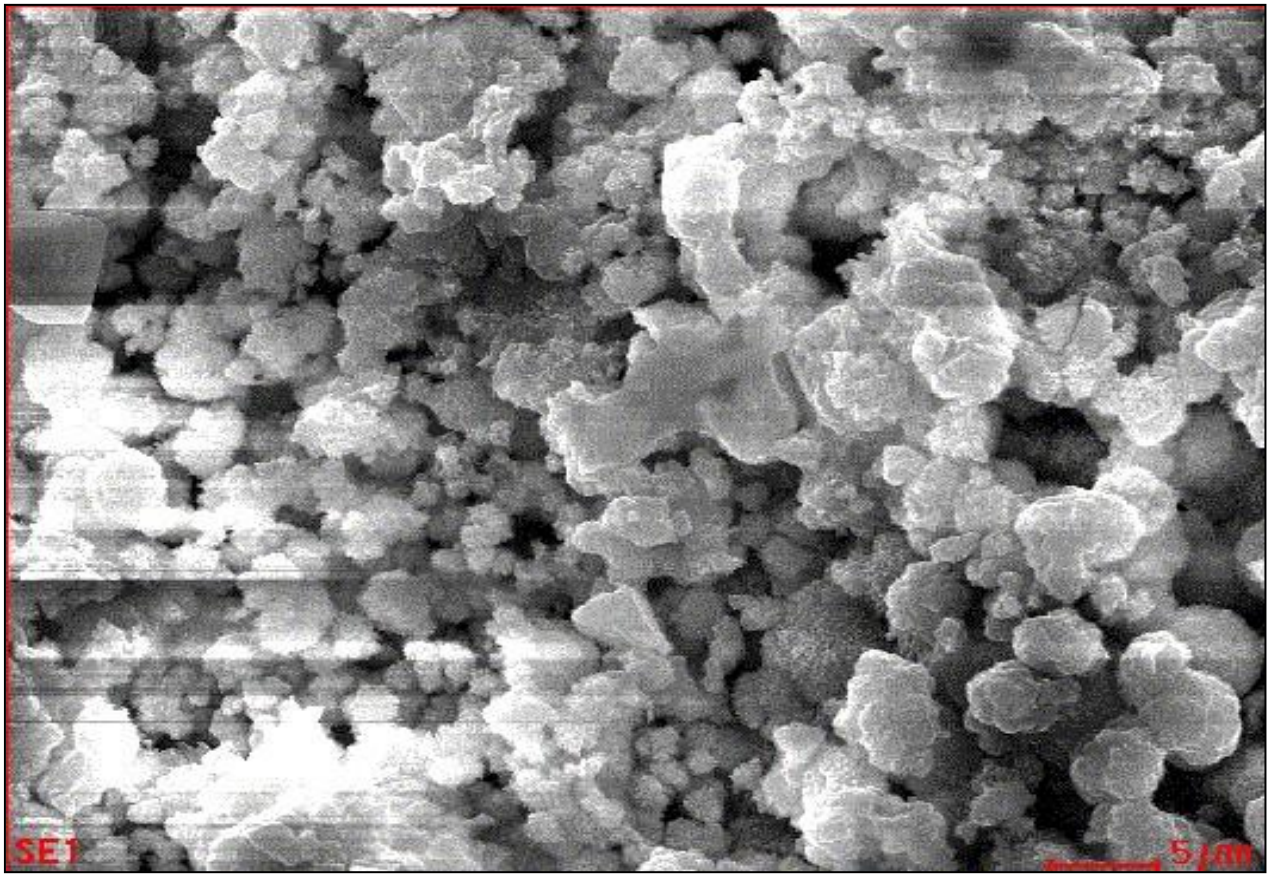
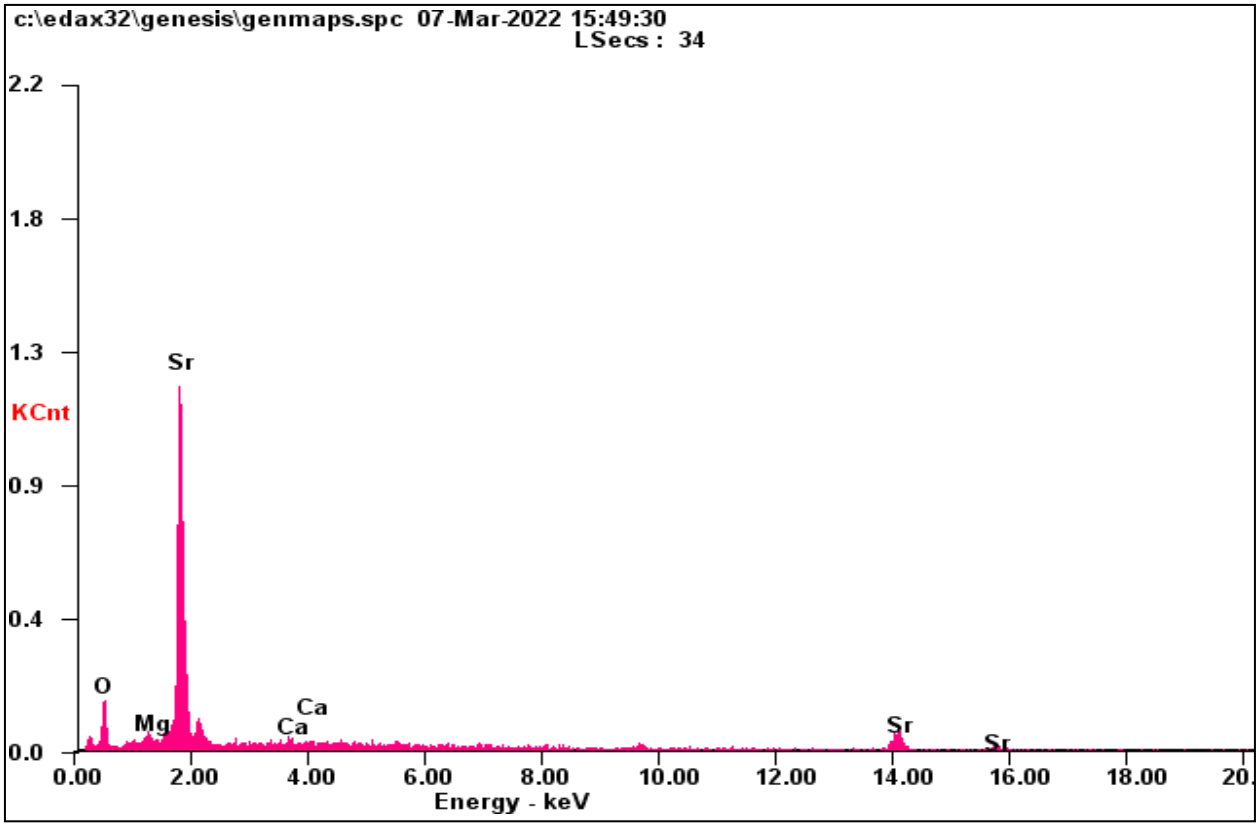


Fig 5.2 SEM image of Magnesium oxide nanoparticles

Element	Wt%	At%
CK	26.44	47.26
OK	30.73	41.23
MgK	01.17	01.03
CaK	00.92	00.49
SrK	40.74	09.98
Matrix	Correction	ZAF

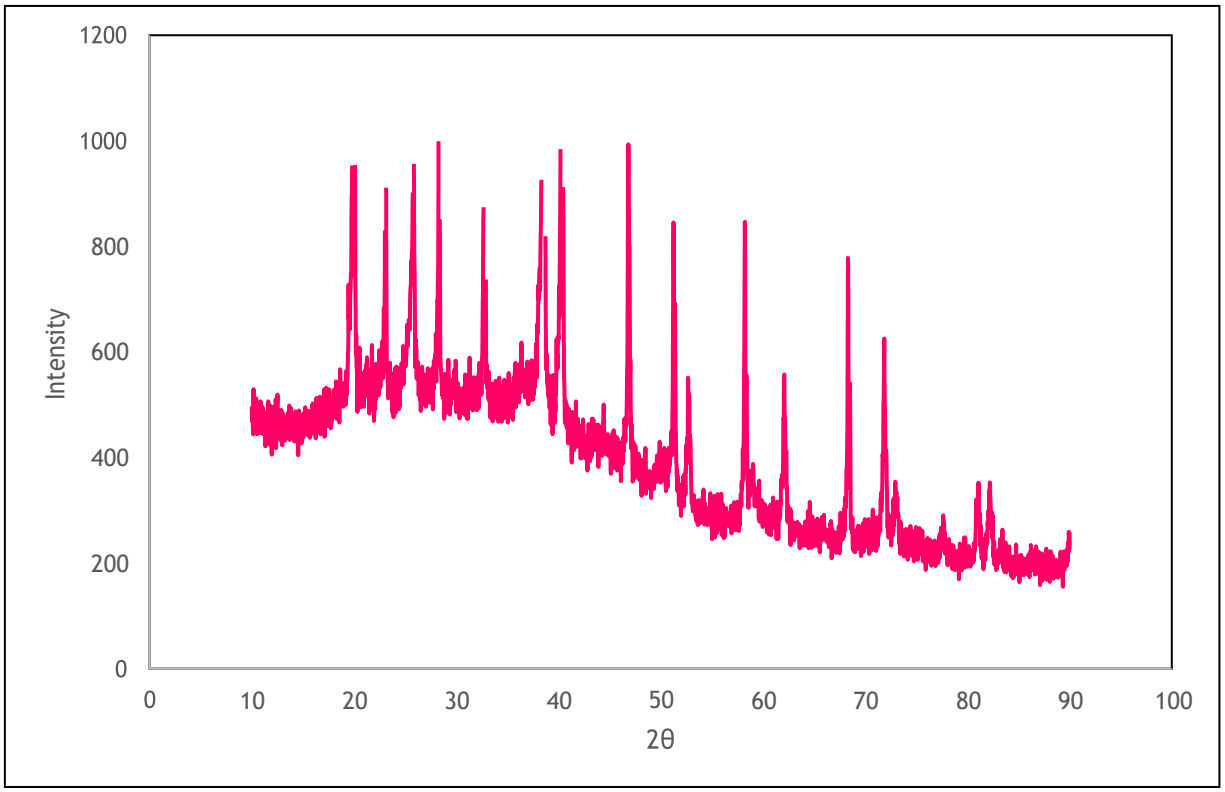
Table 5.2 Elementals analysis of MgO nanoparticles



5.3 EDAX Spectrum of MgO

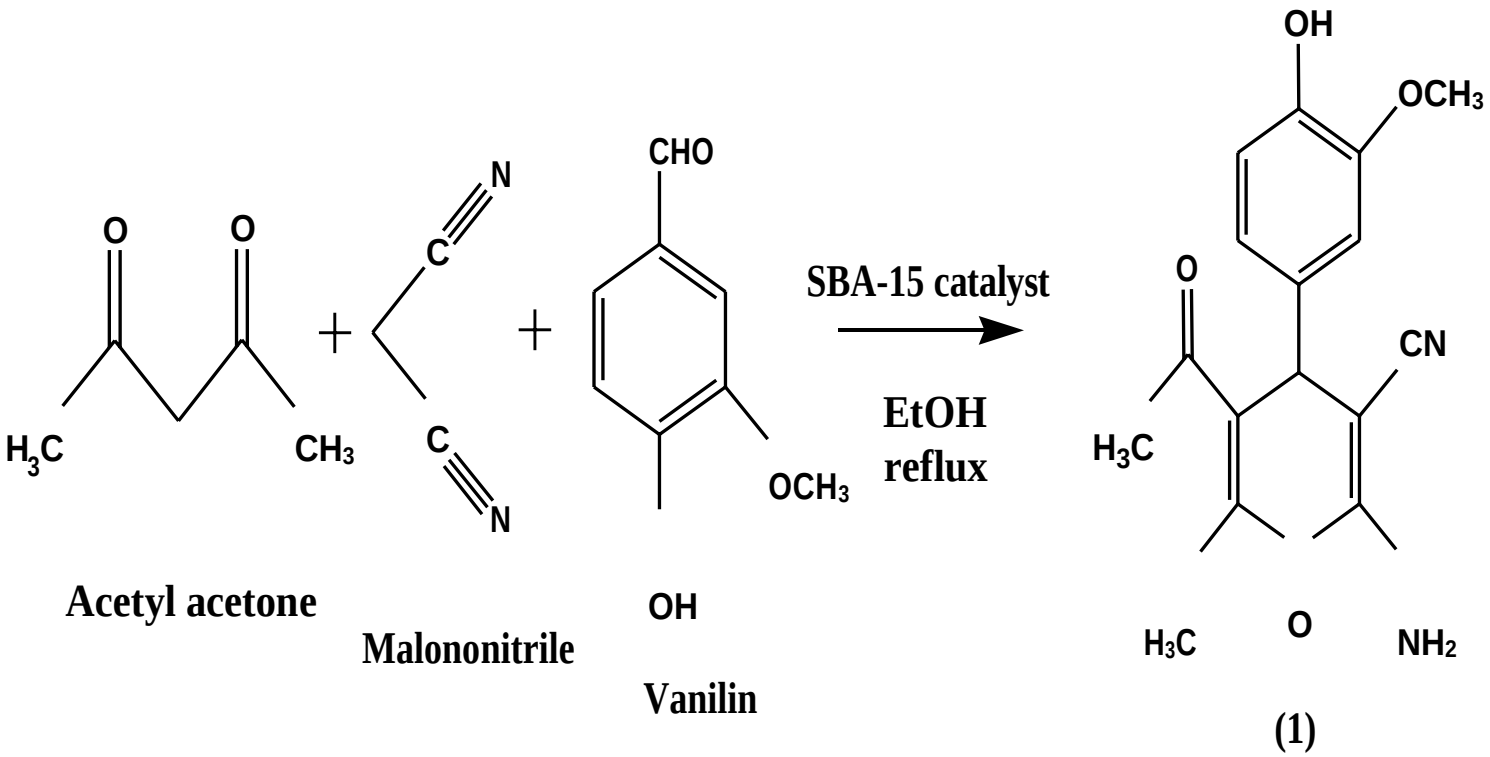
5.1.3 XRD pattern of magnesium oxide nanoparticle

X- ray diffraction pattern shows crystalline nature of nanoparticle. Diffraction peaks matches with the database (JCDS file #75-1525) which expressed the cubic structure. The Debye-Scherrer equation D = 0.94λ / bcosq was used to calculate the crystalline size.where β is the full width at half maximum of peak. λ represent the X-ray wavelength and q referred as Bragg diffraction angle. The crystalline size is about 40nm. The X ray diffraction pattern is shown in Fig. 5.3.



5.4 XRD pattern of magnesium oxide nanoparticle

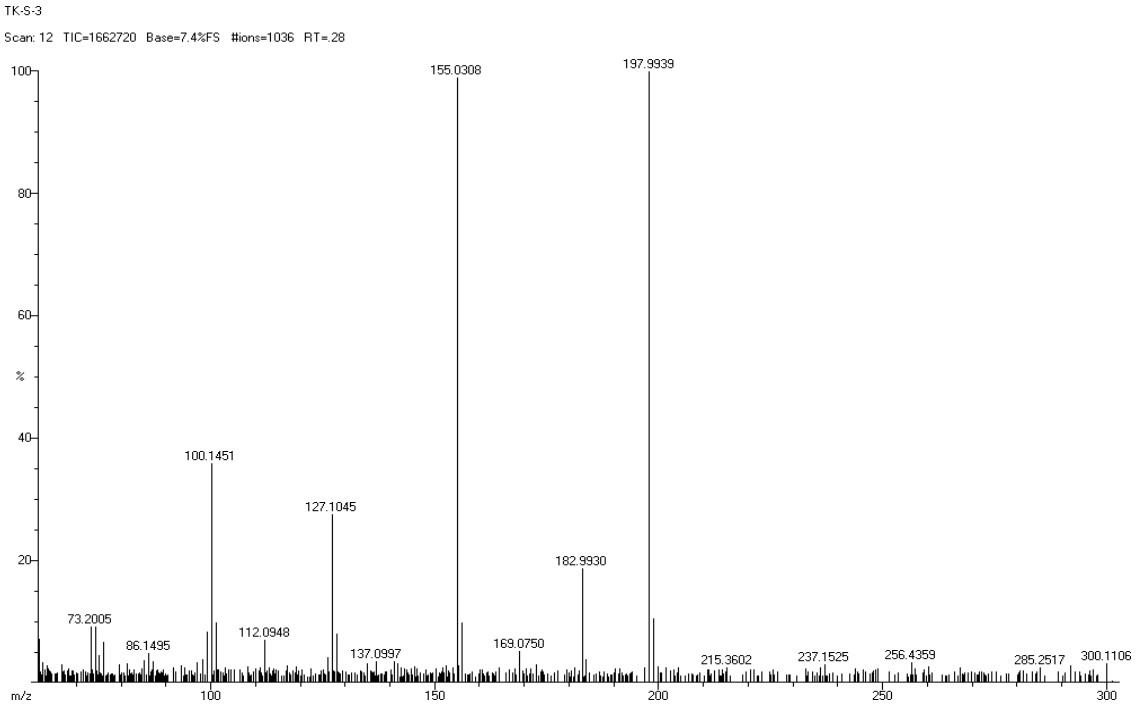
5.1.4 Spectral Data of Synthesis of 5-acetyl-2-amino-4-(4-hydroxy-3-methoxyphenyl)-6-methyl-4H-pyran-3-carbonitrile (1):



Yield: 73%

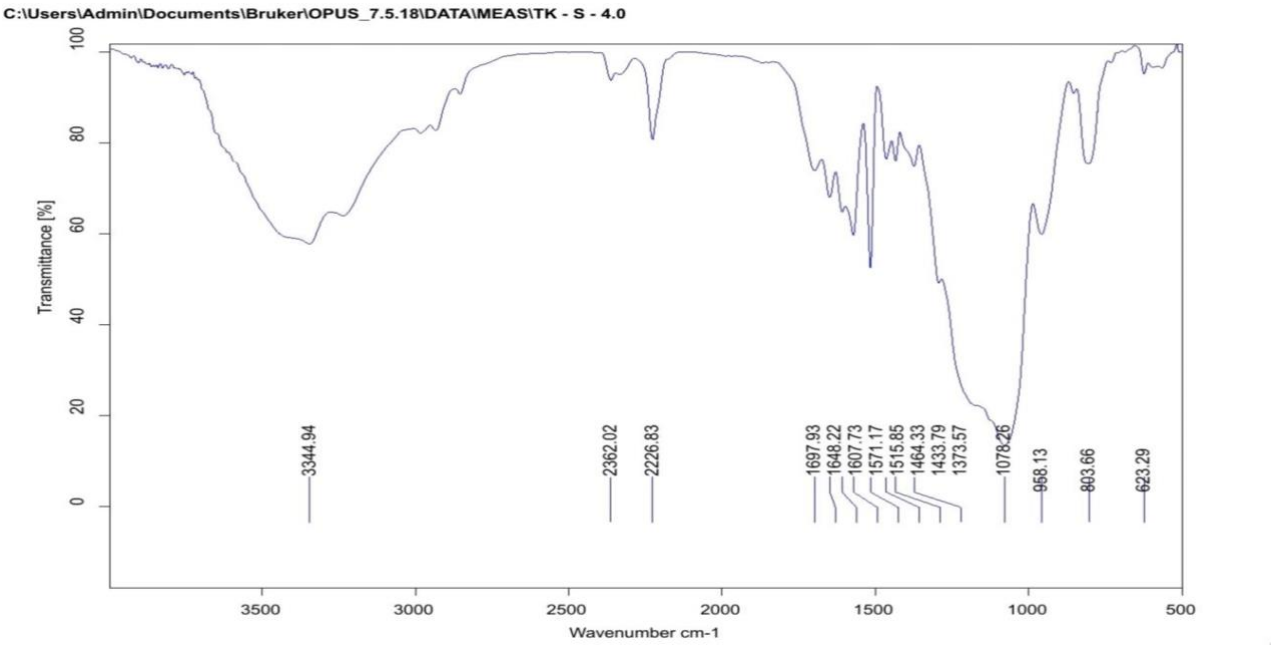
Mass Data:

GCMS Data Exact mass 300.11 Observed mass 300.11 (M^+), 300.31 (M+ H^+)



FTIR Data:

(KBr / cm-1): 1611 (NH), 2221 (CN), 1668 (C=O), 1188 (C-O), 3388(OH).

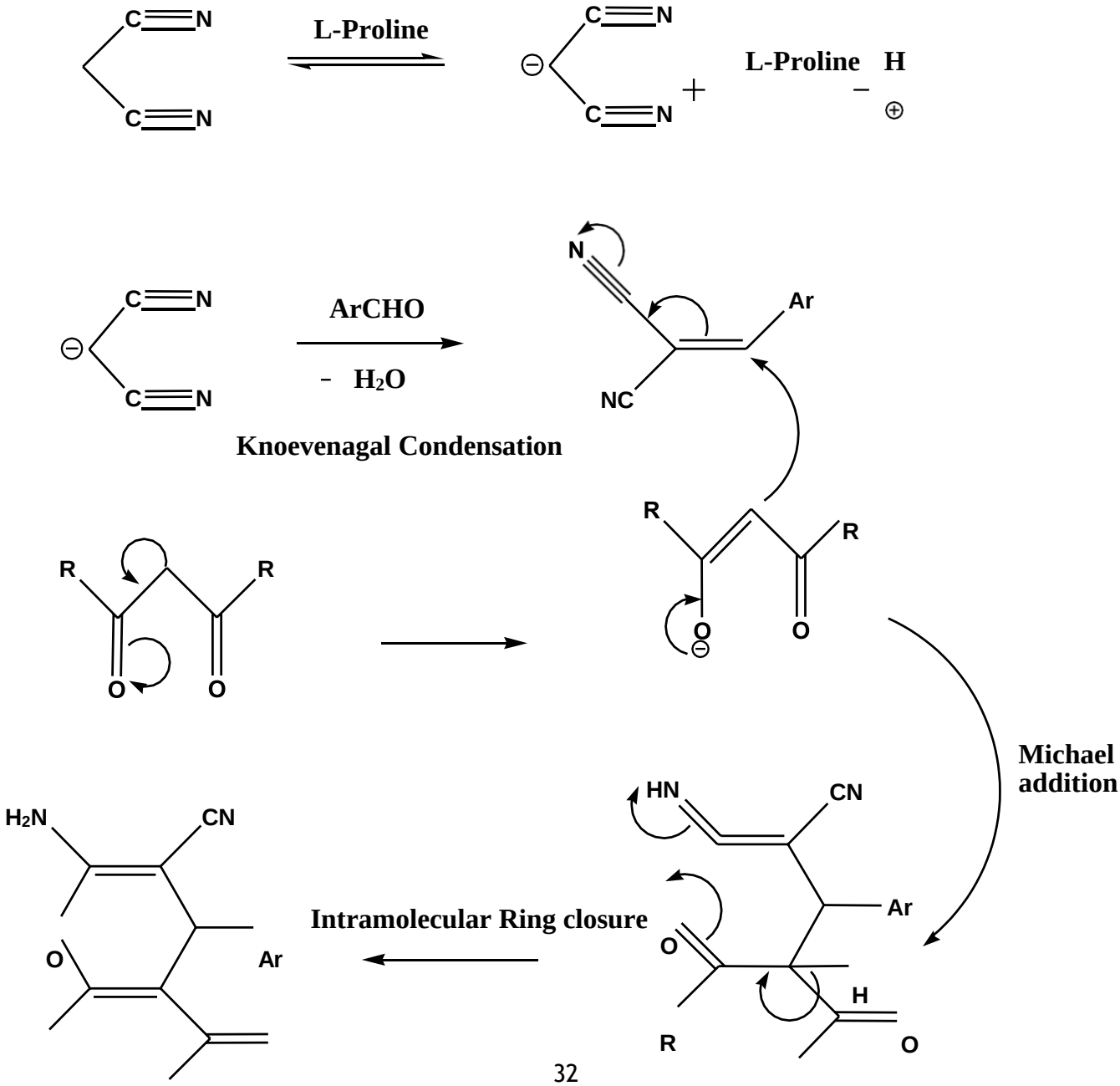


5.1. MECHANISM OF THE THREE COMPONENTS COUPLING OF 4-H-PYRAN:

The mechanism of the formation of 4H-pyran via a three-component coupling strategy is generally accepted to begin with a Knoevenagel condensation between the active methylene compound and the aldehyde, followed by Michael addition with the less reactive active methylene compound, and finally an intramolecular ring closure.

This mechanism is highly probable in the case of the traditional approach for synthesizing those compounds. Initial condensation of aromatic aldehyde with malononitrile in the presence of L-proline leads to the formation of arylidenemalononitrile with the loss of a water molecule. The nucleophilic addition of the enolizable ethylacetoacetate to arylidene malononitrile followed by intramolecular cyclization of the resulting species produce the 2-amino-4H-pyrans. In addition, a reduction in yields have been observed in this study when combining the three components simultaneous in comparison with combining the malononirtile and aldehyde, then adding the nucleophile after five minutes. With two active methylene compounds present along with the aldehyde, the initial condensation reaction could occur first with malononitrile or dimedone, each would afford different intermediate. Malononitrile is the more reactive active methylene compound and thus the

arylidenemalononitriles intermediate should dominate. With these intermediates formed, condensations can then result in at least 4 products.



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CHAPTER 6
CONCLUSION AND REFERENCES

6.1 CONCLUSION

Due to the rich biodiversity of plants, the green world has potential for the synthesis of noble metal nanoparticles Green synthesis technology is a clean, non-toxic and environmentally friendly technology for synthesizing metal nanoparticles and is of great interest due to its commercial perspective and feasibility. However, to make these methods cost-effective and comparable to traditional methods for large-scale production of nanoparticles, improving reliable and environmentally friendly methods for synthesizing metal nanoparticles. In addition, most of these strategies are still in development and there are challenges to overcome. Metal nanoparticles produced by plants and / or plant extracts are more stable than those produced by other organisms and are required for the biosynthesis and stabilization of nanoparticles in large quantities of proteins, enzymes, and biomolecules. It has an amazing ability to be optimized for the formation of molecules. Production of metal nanoparticles by applying "green synthesis". Magnesium oxide nanoparticle Synthesized using the green synthesis method. Characterization Analysis of MgO nanoparticles was performed by X-ray Diffraction, SEM and Fourier transform infrared (FTIR). This shows the X-ray diffraction pattern Nanoparticles are crystalline in nature. The crystalline size of magnesium oxide nanoparticle was calculated by Debye-Scherer formula and the crystallite size was found to be 40 nm. The surface morphology of nanoparticles was observed and investigated using SEM. The material at room temperature, shows crystallite of cubical shape with strong agglomeration of particles. The presence of Magnesium – Oxygen bond (Mg – O) bond in the synthesized sample was confirmed by the peak at 811.62 cm-1 in the FTIR spectrum of magnesium oxide nanoparticles.

The catalytic activity of the synthesized Magnesium oxide nanoparticles was tested by the one-pot synthesis of 5-acetyl-2-amino-4-(4-hydroxy-3-methoxyphenyl)-6-methyl-4H-pyran-3-carbonitrile. The product formation was confirmed by the FTIR and Mass Spectrometry.

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