CHAPTER 1
Study of Gel Entrapped Catalysts (GECs)

1.1 Introduction

Organic Synthesis

Organic synthesis is a special branch of chemical synthesis and is concerned with the construction of organic compounds which contain a higher level of complexity compared to purely inorganic compounds.

There are two main areas of organic research fields:

I. Total synthesis
II. Methodology

These areas have several uses in organic synthesis for commercial production and small scale production of compounds needed in research.

1.2 Catalysis

Catalysis is one of the most important technologies available, which play a crucial role in the research and development of chemical technology to carry out reactions efficiently and safely [1].

In 1836 the famous Swedish chemist Berzelius introduced the concept of catalysis. At the beginning of the 20th century, Ostwald presented the general definition of a catalyst as a species which increases the rate of chemical reaction through the formation of intermediate and which is restored at the end of the reaction. Thus catalysis is a cyclic process in which the reactants are bound to one form of the catalyst and the products are released from another, regenerating the initial state (Fig. 1.1). Ostwald was awarded the Nobel Prize in Chemistry in the year 1909 [2].

![Catalytic cycle](image-url)

**Fig. 1.1** Catalytic cycle
Catalysis involves the change in rate of a chemical reaction due to the participation of a substance called a catalyst. Unlike other reagents that participate in the chemical reaction, a catalyst is not consumed by the reaction itself. A catalyst may participate in multiple chemical transformations.

| a. | Catalysts that speed up the reaction | positive catalysts |
| b. | Catalysts that slow down the reaction | negative catalysts |
| c. | Catalysts that increase the activity of the reaction | promoter catalysts |
| d. | Catalysts that deactivate the reaction | poison catalysts |

Catalyst affects only the rate of the reaction i.e. Kinetics (Fig. 1.2) which changes neither of the reaction nor the equilibrium composition [3].

![Fig. 1.2](image.png)

This means the catalyst changes the reaction path by lowering its activation energy (Ea) and consequently increases the rate of reaction.

Catalysts (Fig. 1.3) can be roughly divided into two main groups. A heterogeneous catalyst is one in which the phase of the catalyst is different from that of the reactants. On the other hand a homogeneous catalyst is one which is in the same phase as that of the reactants. Presently, heterogeneous catalyst has greater world economic impact and is expected to be very important in the future.
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![Classification of catalysts](image)

Fig. 1.3 Classification of catalysts

a. Homogeneous Catalyst

When the catalyst and the reacting substances are present together in a single state of matter, usually a gas or a liquid, it is customary to classify the catalyst as a case of homogeneous catalyst.

Examples

- **Acid catalysis**
  - In an illustrative case, acids accelerate (catalyse) the hydrolysis of esters:
    \[
    \text{CH}_3\text{CO}_2\text{CH}_3 + \text{H}_2\text{O} \rightarrow \text{CH}_3\text{CO}_2\text{H} + \text{CH}_3\text{OH}
    \]

- **Organometallic chemistry**
  - Organometallic reactions like hydroformylation as well as certain kinds of Ziegler-Natta polymerization and hydrogenation [4].
  - Variety of industrial processes such as Wacker process, Monsanto process and Cativa process.

- **Other forms of homogeneous catalysis**
  - Enzymes are homogeneous catalysts that are essential for life. A well studied example is carbonic anhydrase, which catalyzes the release of CO$_2$ into the lungs from the blood stream.
**b. Heterogeneous Catalyst**

When the catalyst and the reactants are not present in the same phase i.e. state of matter, such catalyst is called as heterogeneous catalyst and processes are known as heterogeneous catalytic reactions. They include reactions between gases or liquids or both at the surface of a solid catalyst. Since the surface is the place at which the reaction occurs, it is prepared in various ways to produce large surface areas per unit of catalyst. The metals, metal gauzes, metals incorporated into supporting matrices and metallic films have been used in modern heterogeneous catalysis.

**Mechanism of heterogeneous catalyst**

Substrate has to be adsorbed on the active sites of the catalyst (Fig. 1.4).

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**Examples:**
- Sulfuric acid synthesis (Contact process)
- Ammonia synthesis (Haber-Bosch process)
- Nitric acid synthesis (Ostwald process)

**Advantages of heterogeneous catalyst:**
- Higher selectivity
- Easy establishment and control of the catalyst structure
- Easy heat transfer and diffusion
- Recyclability
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- More easy product separation and catalyst recovery
- Good resistance to high temperatures and temperature fluctuations
- High mechanical strength

Types of solid support used for catalyst immobilization (Fig. 1.5)

I. Organic support (mainly organic polymers and carbon material)
II. Inorganic support (silica, zeolites, metal oxides etc.)
III. Hybrid organic-inorganic support (mainly grafted silica, composites)

![Diagram of different solid supports](image)

Fig. 1.5

Development of efficient, cheap and recyclable catalysts for a reaction under green conditions is still a very attractive topic. Based on a wide range of renewable feedstock, we are searching the application of green chemical technologies with the aim of developing new, genuinely sustainable and low environmental impact support for catalyst immobilization to important chemical reactions. Aim of this study is to develop biopolymer supported catalyst for organic transformations.

1.3 Methods for Entrapment

Bead formation and its limitations include gel beads prepared from agar/agarose, \(\kappa\)-carrageenan, alginate and cellulose after special dissolution, chitosan
and to a lesser extent polyacrylamide and other synthetic polymers. Cells of microorganisms are entrapped by gel that permits the diffusion of small molecules, both substrate and product, at rates that are adequate for the cells’ viability and functioning. The methods of entrapment are given in Fig. 1.6.

![Methods for Entrapment](image)

**A] Single Step Method**

The major types of entrapment have been thoroughly reviewed (Cheetham 1980; Bucke 1983; Mattiasson 1983; Nussinovitch 1994, 1997). One of the most frequently used methods is single step entrapment. This involves the simple gelation of macromolecules by lowering or raising temperatures, using hydrocolloids such as agar, agarose, $\kappa$-carrageenan and chitosan, proteins such as gelatin and egg whites. Although quite simple to achieve, these preparations commonly suffer from heat damage and low mechanical strength.
a. Agar

![Fig. 1.7 Structural unit agar-agar](image)

Agar or agar-agar is a substance derived from a polysaccharide that accumulates in the cell walls of agarophyte red algae [5, 6]. The gelling agent is an unbranched polysaccharide (Fig. 1.7) obtained from the cell walls of some species of red algae, primarily from the genera *Gelidium* and *Gracilaria*, or seaweed (*Sphaerococcus euchema*). Agar (agar-agar) can be used as a laxative, a vegetarian gelatin substitute, a thickener for soups, in jellies, ice cream and other desserts, as a clarifying agent in brewing and for sizing paper and fabrics.

b. Agarose

![Fig. 1.8 Structural unit of agarose polymer](image)

Agarose is obtained from agar (Fig. 1.8) which is obtained from red algae and seaweed such as *Gracilaria* and *Gelidium*.

- Agarose is a purified form of agar.
- Agarose is more expensive than agar.
- Agar and agarose are extensively used in microbiological studies and for culturing bacteria.
- Agar is also used in the food industry for making jellies, ice cream and other culinary dishes while agarose is usually used in electrophoresis.
c. \(\kappa\)-Carrageenan

![Fig. 1.9 Structural unit of \(\kappa\)-carrageenan](image)

Carrageenans or carrageenins: a family of linear sulfated polysaccharides (Fig. 1.9) that are extracted from red seaweeds. There are several carrageenans, differing in their chemical structure and properties and therefore in their uses. Carrageenan consists of alternating 3-linked-\(\beta\)-D-galactopyranose and 4-linked-\(\alpha\)-D-galactopyranose units.

d. Alginate

![Fig. 1.10 Structural unit of alginate](image)

Alginate is a family of polysaccharides mainly produced by brown algae and composed of (1-4) linked \(\beta\)-D-mannuronic (M) and \(\alpha\)-L-guluronic (G) residues (Fig. 1.10). Alginites differ by their M/G ratio and are extensively used for the entrapment of biologically active materials. They are mostly applied in drug delivery systems and used as catalyst supports in many organic transformations [7].

e. Chitosan

Chitosan is a linear polysaccharide composed of randomly distributed \(\beta\)-(1-4)-linked D-glucosamine (deacetylated unit) and \(N\)-acetyl-D-glucosamine (acetylated unit) (Fig. 1.11).
It has a number of commercial and possible biomedical uses. Schiff base formation through the reaction of amine groups on the chitosan backbone with aldehydes is one of the most straightforward applications and the resulting Schiff bases have been used to promote metal catalyzed reactions such as oxidation, reduction and transition metal catalyzed C-C and C-X bond formation reactions [8].

Agricultural and Horticultural uses:
- Potential industrial use
- Possible health benefits
- Medical research

f. Cellulose

Cellulose is an organic compound with the formula \((C_6H_{10}O_5)_n\), a polysaccharide consisting of a linear chain of several hundred to over ten thousand \(\beta(1\rightarrow4)\) linked D-glucose units [9, 10] (Fig. 1.12). It has many synthetic applications such as cellulose-supported phase transfer catalysts,
lactase immobilization, cellulose grafted N-oxide reagent and development of the cellulose-bound peptide arrays [11].

g. Proteins

Protein is a group of naturally occurring compounds and found in animals, especially in the flesh and connective tissues of mammals [12]. It is the main component of connective tissue and is the most abundant protein in mammals [13] making up about 25 - 35 % of the whole-body protein content. Collagen has a wide variety of applications, from food to medical.

Medical uses:
- Cardiac applications
- Cosmetic surgery
- Reconstructive surgical uses

h. Gelatin

![Fig. 1.13 Structural unit of gelatin](image_url)

Gelatin (or gelatine) is a translucent, colorless, brittle (when dry), flavorless solid substance, derived from the collagen inside animals’ skin and bones. Gelatin is a mixture of peptides and proteins (Fig. 1.13) produced by partial hydrolysis of collagen extracted from the boiled crushed bones, connective tissues, organs and intestines of some animals. Gelatin forms a solution of high viscosity in water, which sets to a gel on cooling and its chemical composition is, in many respects, closely similar to that of its parent collagen [14].
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i. Synthetic Polymers

a] Polyacrylamide

![Structural unit of poly(2-prop-enamide)](image)

It can be synthesized as a simple linear-chain structure or cross-linked, typically using \(N,N'-\text{methylenebisacrylamide}\) (Fig. 1.14). Polyacrylamide is not toxic. However, unpolymerized acrylamide, which is a neurotoxin, can be present in very small amounts in the polymerized acrylamide [15], therefore it is recommended to handle it with caution.

Uses of polyacrylamide:

- One of the largest uses for polyacrylamide is to flocculate or coagulate solids in liquid.
- The ionic form of polyacrylamide has found an important role in the potable water treatment industry.

b] Polyvinyl Alcohol

![Structural unit of polyvinyl alcohol](image)

Uses of polyvinyl alcohol:

- Paper adhesive with boric acid in spiral tube winding and solid board production
- Thickener, modifier, in polyvinyl acetate glues
- Textile sizing agent
B] Two Step Method

Two-step methods may be used if they provide the manufacturer with improved processes or products or the possibility of overcoming evident problems. A procedure to create a more porous structure with desirable elastic behavior and mechanical stability throughout handling was reported by Klein and Eng (1979).

1.4 Study of Gel

Gel is defined as, “a substantially dilute cross-linked system, which exhibits no flow when in the steady-state” [16]. By weight, gels are mostly liquid, yet they behave like solids due to a three-dimensional cross-linked network within the liquid. It is the crosslink within the fluid that gives structure hardness and contributes to stickiness of a gel (Fig. 1.16). In this way gel is dispersion of molecules of liquid within solid in which the solid is the continuous phase and the liquid is the discontinuous phase.

![Fig. 1.16 Gel](image)

Gel consists of a solid three-dimensional network that spans the volume of a liquid medium and ensnares it through surface tension effects. This internal network structure may result from physical bonds (physical gel) or chemical bonds (chemical gel), as well as crystallites or other junctions that remain intact within the extending fluid. Virtually any fluid can be used as an extender including water (hydrogels), oil and air (aerogel). Both by weight and volume, gels are mostly fluid in composition and thus exhibit densities similar to those of their constituent liquids.
Types of gel (Fig. 1.17)

![Types of Gel Diagram](image)

**Fig. 1.17**

**a. Hydrogel**

Hydrogel (also called aquagel) is a network of polymer chains that are hydrophilic, sometimes found as a colloidal gel in which water is the dispersion medium (Fig. 1.18). Hydrogels are highly absorbent (they can contain over 99.9 % water) natural or synthetic polymers.

![Hydrogel Image](image)

**Fig. 1.18 Hydrogel**

Hydrogels also possess a degree of flexibility very similar to natural tissue, due to their significant water content. Common uses of hydrogels include as scaffolds in tissue engineering. When used as scaffolds, hydrogels may contain human cells to repair tissue. Environmentally sensitive hydrogels are also known as 'Smart Gels' or 'Intelligent Gels'. These hydrogels have the ability to change the pH, temperature, or the concentration of metabolite and release their load as result of such a change.
Classification of hydrogel:

- Based on the method of preparation, hydrogels are classified into:
  - Homopolymer hydrogels
  - Co-polymer hydrogels
  - Multi polymer hydrogels

- Based on the ionic charges, hydrogels can be classified into:
  - Neutral hydrogels
  - Cationic hydrogels
  - Anionic hydrogels
  - Ampholytic hydrogels

- Based on the structure, hydrogels can be classified into:
  - Amorphous hydrogels
  - Semi-crystalline hydrogels
  - Hydrogen bonded hydrogels

- Based on the mechanism controlling the drug release, they are classified into:
  - Diffusion controlled release systems
  - Swelling controlled release systems
  - Chemically controlled release systems
  - Environment responsive systems

Application:

- Ophthalmic use

b. Organogel

An organogel (Fig. 1.19) is a non-crystalline, non-glassy thermo-reversible (thermoplastic) solid material composed of a liquid organic phase entrapped in a three-dimensionally cross-linked network. The liquid can be, for example, an organic solvent, mineral oil or vegetable oil. The solubility and particle dimensions of the structurant are important characteristics for the elastic properties and firmness of the organogel. Often, these systems are based on self-assembly of the structurant molecules [17, 18].
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Photoactive Organogels

Photoactive organogels are networks in the swollen state (organic solvent) that contain photoactive molecules as crosslinkers. Thermally or by irradiation, the photoactive molecules start to relax and the original shape of the sample is recovered and molecules of solvent come back to the interior of the network (Fig. 1.20).

Organogels have potential for use in a number of applications:

- Pharmaceutical industries [19]
- Cosmetics, art conservation [20]
- Food industries [21]

C. Xerogel

A xerogel is a solid formed from a gel by drying with unhindered shrinkage (Fig. 1.21). Xerogels usually retain high porosity (25%) and enormous surface area (150–900 m²/g), along with very small pore size (1-10 nm). When solvent removal occurs under hypercritical (supercritical)
conditions, the network does not shrink and a highly porous, low-density material known as an aerogel is produced.

![Fig. 1.21 Xerogel](image)

**Green Chemistry**

The term Green Chemistry was coined in 1991 by Anastas [22]. “Green Chemistry is the design, manufacture and use of environmentally benign chemical products and process that prevents pollution and reduces environmental and human health risks.”

Green Chemistry protects the environment, not by cleaning up, but by inventing new chemical processes that do not pollute the environment. Chemists from all over the world are using their creativity and innovation to develop new synthetic methods, reaction conditions, analytical tools, catalysts and processes under the new paradigm of Green Chemistry due to their valuable contribution in research. Green Chemistry approach has received extensive attention [23-30] and involves many names including Green Chemistry, Environmentally Benign Chemistry, Clean Chemistry, Atom Economy and Benign by Design Chemistry.

**Twelve principles of Green Chemistry**

1. Waste prevention instead of remediation
2. Atom efficiency
3. Less hazardous/toxic chemicals
4. Safer products by design
5. Innocuous solvents and auxiliaries
6. Energy efficient by design
7. Preferably renewable raw materials
8. Shorter syntheses (avoid derivatization)
9. Catalytic rather than stoichiometric reagents
10. Design products for degradation
11. Analytical methodologies for pollution prevention
12. Inherently safer processes

1.5 Selection of Gel for Entrapment

Our investigations began with the selection of appropriate method of entrapment for the organic synthesis. Overall study shows agar–agar is suitable for entrapment. Agar gel also acts as Hydrogel.

Agar-agar

The word "agar" comes from agar-agar, the algae (Gigartina, Gracilaria) from which the jelly is produced [31]. Agar consists of a mixture of agarose and agarpectin. The predominant component, agarose, is a linear polymer, made up of the repeating monomeric units of agarobiose. Agarobiose is a disaccharide made up of D-galactose and 3,6-anhydro-L-galactopyranose (Fig. 1.22).

Fig. 1.22 Structure of agarose polymer
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- **Properties:**
  
  Agar exhibits hysteresis, melts at 85 °C (358 K, 185 °F) and solidifies from 32-40 °C (305-313 K, 90-104 °F) [32]. This property lends a suitable balance between easy melting and good gel stability at relatively high temperatures.

- **Applications:**
  
  - **Microbiology**
    
    Agar is used throughout the world to provide a solid surface containing medium for the growth of bacteria and fungi. Microbial growth does not destroy the gel structure because most microorganisms are unable to digest agar.

  - **Plant biology**
    
    Research grade agar is used extensively in plant biology as it is supplemented with a nutrient and vitamin mixture that allows for seedling germination in petri dishes under sterile conditions.

  - **To make salt bridges for use in electrochemistry.**

1.6 Present Work

Gel entrapment of the catalyst is one of the known immobilization techniques used in synthetic era. This catalyst provides mild reaction conditions and simple purification technique. The use of catch and release system provides time saving and allows greater creativity and increases levels of output. The gel entrapped catalyst is heterogeneous catalyst which can be regained from the reaction mixture and can be reused. These versatile features and renewed interests in immobilization of catalyst inspire us to use Gel Entrapped Catalyst in Organic Transformations. In this regard we have prepared base as well as acid-Gel Entrapped Catalysts.
Preparation of Gel Entrapped Base Catalysts (GEBCs)

To a boiling mixture of agar-agar (20 mL) in water (60 mL) was added a mixture of base KOH (10 g) in water (10 mL). The resultant solution was boiled with stirring for five minutes and cooled in ice bath to yield the desired KOH-GEBC [33]. The GEBCs are light yellow gelly like substances that can be cut into small cubic shaped pieces (Fig. 1.23).

The same procedure was used for preparation of piperidine-GEBC, Morpholine-GEBC and NaOH-GEBC. The nature and appearance of these GEBCs is just like as that of KOH-GEBC.

Preparation of Gel Entrapped DABCO

In a typical experiment, a mixture of agar-agar (5 g) in water (35 mL) was prepared and to this mixture, DABCO (2.5 g) in water (2.5 mL) was added. Then resultant solution was boiled with stirring for five minutes then transferred in petri dish. After cooling (5-10 min) it became hard. The Gel Entrapped DABCO is gelly-chocolate like substance that can be cut into blocks to yield the desired gel entrapped DABCO catalyst (Fig. 1.24).
Preparation of Gel Entrapped Lewis Acids (GELAs)

Agar-agar (20 g) in water (140 mL) was taken in beaker and after mild heating, solution of Lewis acid (ZnCl₂/AlCl₃) (10 g) in water (10 mL) was added. The resultant solution was boiled with stirring for few minutes and cooled in ice bath to yield the desired GELAs. This gives a milky-gelly like substance that can be cut into cubes (Fig. 1.25).

The prepared GECs are characterized by different techniques. TGA-DTA is the best technique for analysis of prepared GECs.
Characterization of Gel Entrapped Catalysts (GECs)

TGA-DTA analysis of KOH-GEBC, Morpholine-GEBC and Piperidine-GEBC

Thermal behaviour of GECs was studied by thermogravimetric analysis (TGA) and differential thermal analysis (DTA). The TGA curves of KOH-GEBC (Fig. 1.26) revealed that degradation of gel occurs with increase in temperature and completes at 151 °C as evident from strong endothermic peak observed in DTA. The thermal decomposition of agar polymer starts around 240 °C and is very slow up to 475 °C indicating that the polymer matrix may undergo some structural changes (which are slightly exothermic) leading to complete exothermic decomposition of polymer material around 500 °C leaving only anhydrous KOH which decomposes above 800 °C. However, in the case of GECs containing morpholine and piperidine (Fig. 1.27 and 1.28), the decomposition of bases is observed before the degradation of polymer. The process of base degradation is slow due to intercalation of morpholine and piperidine in polymer matrix.

![Fig. 1.26 TGA-DTA of KOH GEBC](image)
In the GEBCs, the reagent entrapped in the gel may leach into the solvent. To study the leaching of KOH in solvent, 1 g KOH-GEBC was stirred in 5 mL of ethanol at room temperature. The KOH-GEBC was filtered and
water (3 mL) was added to the filtrate. The KOH leached out was then determined by titrating against 0.1 N succinic acid solution using phenolphthalein as an indicator. It was observed that only 1.5 % KOH leached out from gel into ethanol.

**TGA-DTA analysis of DABCO-GEBC**

Thermal behavior of gel entrapped DABCO was studied by thermogravimetric analysis (TGA) and differential thermal analysis (DTA) (Fig. 1.29). The TGA curve revealed that the loss of water occurs initially upto ~150 °C and is accompanied with endothermic peak in DTA curve. The thermal decomposition of DABCO embedded polymer matrix occurs in two distinct steps giving approximately weight loss 11 % in each step. It is also revealed from the DTA curve that these processes are exothermic. The decomposition is completed at the temperature 510 °C.

![Fig. 1.29 TGA-DTA of DABCO-GEBC](image)

In the GEBCs, the reagent entrapped in the gel may leach into the solvent. To study the leaching of DABCO in solvent, 1 g gel entrapped DABCO was stirred in 5 mL of ethanol at room temperature. The catalyst was filtered and water (3 mL) was added to the filtrate. The
DABCO leached out was then determined by titrating against 0.1 N hydrochloric acid solution using methyl red as an indicator. It was observed that only 5 % DABCO leached out from gel into ethanol.

**TGA-DTA analysis of NaOH-GEBC (GENaOH)**

The TGA analyses of agar-agar and GENaOH are displayed in Fig. 1.30. The TGA profile shows three different weight losses at different temperatures. The first weight loss below 150 °C for GENaOH as well as agar could be due to removal of physisorbed or occluded water. The second step of decomposition which is initial above 240 °C in both agar-agar as well as GENaOH differed in their amount of respective weight losses (GENaOH ~8 %, agar-agar 63.5 %) could be assigned to thermal decomposition of agar polymer was agar-agar. The decomposition of remaining polymer matrix is accompanied with ~21 % weight loss. Third step is in the temperature range of 440-480 °C. On the other hand the additional exothermic weight loss centered at 710 °C is observed and could be assigned to the decomposition of carbonates frame if any. The entrapment of NaOH in gel matrix is evidenced by the comparatively large residual weight observed in the TGA profile of GENaOH than that of agar-agar (Fig. 1.31).

![Fig. 1.30 TGA-DTA of NaOH-GEBC](image-url)
It has been well established that in case of the GEBCs, the reagent trapped in the gel may leach into the solvent. To study the leaching of NaOH in solvent, 1 g GENaOH was stirred in 5 mL of ethanol at room temperature. The GENaOH was filtered and water (3 mL) was added to the filtrate. The NaOH leached out was determined by titration with 0.1 N succinic acid solution using phenolphthalein as an indicator. The study revealed that only 3.91 % NaOH leached out from gel into ethanol.

**TGA-DTA analysis of ZnCl$_2$-GELA**

Thermal behaviour of GELAs was investigated by thermogravimetric analysis (TGA) and differential thermal analysis (DTA) (**Fig.1.32**).

The thermograms displayed an initial weight loss upto 225 °C accompanied by an endotherm corresponding to loss of water molecules accumulated in the GELAs. A second weight loss which occurs between 225 °C to 520 °C can be attributed to thermal decomposition of polymeric matrix of agar-agar. This is followed by small weight loss (~4 %) which can be attributed to the decomposition of metal halide resulting in the formation of metallic species. These results revealed that the entrapment of Lewis acids into matrix of agar-agar does not affect the thermal stability of polymer.
Gravimetric analysis of GELAs

The gravimetric analysis is carried out by Loss on ignition method. Loss on ignition is a test used in the analysis of minerals. In this method, 100 mg of ZnCl$_2$-GELA was taken in crucible and kept in furnace for 8 h at 800 °C. After completion of the process weight of the ignited sample was taken. The gravimetric analysis of GELAs was performed to quantify the amount of Lewis acids (ZnCl$_2$) entrapped into gel. The results conceded the presence of approximately 8 % of metal chlorides in the GELAs and 0.13 % of Zn in ZnCl$_2$-GELA.

Atomic absorption spectroscopy of GELAs

It has been well established that in case of the gel entrapped catalysts, the reagent trapped in the gel may leach into the solvent. Atomic absorption spectroscopy was used for evaluation of stability of ZnCl$_2$-GELA towards leaching. The analysis revealed that only 65.5 mg/L Zn is leached from 1 g of ZnCl$_2$-GELA catalyst.
Shelf-Life of Gel Entrapped Catalysts

To study the shelf-life of Gel Entrapped Catalysts at room temperature, we selected KOH-GEBC (10 %) catalyzed Knoevenagel reaction of barbituric acid and benzaldehyde. The percentage yield of the product was same (92 %) in case of the freshly prepared catalyst as well as the catalyst prepared before 10 days, 20 days, 30 days, 40 days and so on. This observation supports that the Gel Entrapped Catalysts have good shelf-life i.e. catalytic activity remains intact for long time at room temperature (Fig. 1.33).

KOH-GEBC catalyzed Knoevenagel Condensation Reaction (Scheme 2.1.17)

Multi-Component Reactions (MCRs)

By using Base-GECs or Acid-GECs we have carried out several types of Multi-Component reactions.

Multi-component Reactions (MCRs) are convergent reactions [34], in which three or more starting materials react to form a product (Fig. 1.34) where basically all or most of the atoms contribute to the newly formed product. In MCR, a product is assembled according to a cascade of elementary chemical reactions. Thus, there is a network of reaction equilibria, which all finally flow into an irreversible step yielding the product. The challenge is to conduct MCR in such a way that the network of pre-equilibrated reactions channel into the
main product and do not yield side products. The result is clearly dependent on the reaction conditions: solvent, temperature, catalyst, concentration, the kind of starting materials and functional groups.

Multi-Component Reactions with Carbonyl Compounds

Some of the multi-component reactions which have been reported and are effective through derivatization of carbonyl compounds into more reactive intermediates, which can react further with a nucleophile. Carbonyl compounds played crucial role in the early discovery of multi-component reactions, as displayed by number of name reactions:

Examples:

- Mannich Reaction

\[
\text{RC}=\text{O} + \text{H}_2\text{C}=\text{O} + \text{R'NH}_2 \xrightarrow{\text{H}_2\text{O}} \text{RC}=\text{O} + \text{R'NH}=\text{CH}_2
\]

- Biginelli Reaction

\[
\text{EtO}_2\text{C}=\text{Me} + \text{H}_2\text{NCONH}_2 \xrightarrow{\text{H}^+ \text{ EtOH, } \Delta} \text{EtO}_2\text{C}=\text{MeNHCONH} + \text{Ph} \]

\[
\rightarrow \text{EtO}_2\text{C}=\text{MeNCONH} + \text{PhNH}
\]
• Gewald Reaction

\[
R\text{-CHO} + \text{N-acyl imine} + \text{H}_2\text{N-S} + \text{R}'' \rightarrow \text{R'}\text{-COOH}
\]

• Hantzsch Dihydropyridine (Pyridine) Synthesis

\[
R\text{-CHO} + 2\text{R'}\text{-COOH} + \text{NH}_3 \rightarrow \text{R'}\text{-COOR''}
\]

• Four component reaction of N-sulfonyl imines, (cyanomethylene) triphenyl phosphorane, nitromethane and formaldehyde for the synthesis of 3-substituted 2-methylene-4-nitro butanenitriles [39-41]

\[
\begin{array}{c}
\text{R} + \text{Ts} + \text{PPh}_3 + \text{MeNO}_2 + \text{HCHO} \rightarrow \text{R'}\text{-COOH}
\end{array}
\]

• One-pot, three-component synthesis of highly functionalized 1,3-oxazine derivatives via 1,4-dipolar cycloadditions [42-44]
• The efficient construction of several fused heterocyclic skeletons based on multi-component domino reactions has been shown in Fig. 1.35 [35-38].

Fig. 1.35 Multi-Component Domino Reactions (MDRs)
1.7 References


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