Unit-V

Combinatorial Chemistry

Presented By,

Mr. Samarpan Mishra (Assistant Professor)

Specialization – Pharmaceutical Chemistry

Combinatorial Chemistry

- **Combinatorial chemistry** is a technique used in chemistry to rapidly synthesize and test a large number of different but structurally related compounds simultaneously.
- It is widely used in **drug discovery**, **materials science**, and **catalysis** to speed up the identification of new molecules with desirable properties.

Methods of Combinatorial Chemistry

1. Solid-Phase Synthesis (SPS)

Compounds are synthesized on a solid support, like polymer beads.

Example: **Peptide synthesis** using resin beads.

2. Solution-Phase Synthesis

Traditional chemical reactions are carried out in solution.

More flexible than solid-phase methods but harder to automate.

3. Split and Pool Synthesis (Mix and Split Method)

A method to create large compound libraries.

Compounds are divided into portions, reacted with different reagents, and then recombined.

4. Microarray and DNA-Encoded Libraries

DNA tags are used to track chemical reactions.

Used for drug discovery and molecular screening

Applications of Combinatorial Chemistry

1. Pharmaceutical Industry

Drug discovery (e.g., new antibiotics, cancer drugs)

Identifying lead compounds for further optimization.

2. Material Science

Development of new polymers and catalysts.

3. Agrochemicals

Design of new pesticides and herbicides.

4. Nanotechnology

Creation of nanoparticles with specific chemical functionalities.

1. Solid Phase Synthesis In Combinatorial Chemistry

- **Solid-phase synthesis (SPS)** is a widely used method in **combinatorial chemistry**, where molecules are synthesized while attached to an **insoluble solid support** (such as polymer beads or resin).
- This technique allows for the efficient creation of large libraries of compounds with minimal purification steps.

Key Steps in Solid-Phase Synthesis

1. Attachment to a Solid Support

A starting material (e.g., an amino acid or small organic molecule) is covalently bound to an insoluble resin (e.g., polystyrene beads).

2. Stepwise Synthesis

Chemical reactions (e.g., coupling, deprotection, modification) occur while the molecule remains attached to the solid support.

Excess reagents and byproducts are easily removed by washing.

3. Cleavage from the Support

Once the desired compound is synthesized, it is **cleaved** from the solid support using specific reagents.

4. Purification & Analysis

Since the product remains bound to the resin during synthesis, impurities are removed through washing, reducing the need for extensive purification.

Advantages of Solid-Phase Synthesis

1. Simplifies purification

Unreacted reagents and byproducts are washed away.

2. Efficient automation

Easily adaptable for robotic synthesis, making it ideal for combinatorial chemistry.

3. High-throughput synthesis

Thousands of compounds can be generated simultaneously.

4. Scalability

Can be used for both small-scale research and large-scale drug discovery.

Applications of Solid-Phase Synthesis in Combinatorial Chemistry

1. **Peptide Synthesis** – Used in drug discovery and protein research. Example: Merrifield Peptide Synthesis (developed by Robert Merrifield in 1963).
2. **Oligonucleotide Synthesis** – Essential for DNA and RNA-based research.
3. **Small Molecule Drug Discovery** – Creating large libraries of potential drug candidates.
4. **Catalyst Development** – Designing novel catalysts for chemical reactions.

2. Solution-Phase Synthesis in Combinatorial Chemistry

- **Solution-phase synthesis** is a method in **combinatorial chemistry** where chemical reactions are performed in a liquid (solution) phase rather than on a solid support.
- This approach is similar to traditional organic synthesis but optimized for high-throughput generation of diverse chemical libraries.

Steps in Solution-Phase Synthesis

1. **Starting Materials** – Selection of diverse reactants (building blocks).
2. **Reaction Setup** – Multiple reaction vessels are used, each containing different reagents.
3. **Reaction Execution** – Chemical transformations occur under optimized conditions.
4. **Purification** – Since products remain in solution, purification (e.g., chromatography, extraction) is required.
5. **Analysis & Screening** – The synthesized compounds are tested for desired properties.

Applications of Solution-Phase Synthesis in Combinatorial Chemistry

Small Molecule Drug Discovery – Used to generate diverse drug-like molecules.

Natural Product Synthesis – Modifying bioactive compounds for medicinal chemistry.

Agrochemical Development – Creating new pesticides and herbicides.

Materials Science – Designing novel polymers and catalysts.

Thank You

www.pharmrecord.com