SRINIVASAN COLLEGE OF ARTS AND SCIENCE

PERAMBALUR - 621 212

(Affiliated to Bharathidasan University, Tiruchirappalli)

COURSE MATERIAL

DEPARTMENT OF CHEMISTRY
M. Sc. Chemistry
Supramolecular Chemistry

SYLLABUS

UNIT I: Concepts of Supramolecular Chemistry

Concepts and languages of supramolecular chemistry – various types of noncovalent interactions – hydrogen bonds, C-H…X interactions, halogen bonds – π-π interactions, non–bonded interactions – various types of molecular recognition. Crystal engineering of organic solids – hydrogen bonded supramolecular patterns involving water / carboxyl / halide motifs – concepts of different types of synthons based on non-covalent interactions – principles of crystal engineering and non-covalent synthesis – polymorphism and pseudopolymorphism – supramolecular isomorphism / polymorphism – crystal engineering of pharmaceutical phases.

UNIT II: Metallo Organic Frameworks

M.O.F (Metallo Organic Frameworks) – organometallic systems – combinations of different interactions to design molecular rods, triangles, ladders, networks, etc. – design of nanoporous solids – interligand hydrogen bonds in metal complexes – implications for drug design – crystal engineering of NLO materials, OLED.

UNIT III: Co-receptor Molecules and Multiple Recognition

Dinuclear and polynulclear metal ion cryptates – linear recognition of molecular length by ditopic co-receptors – heterotopic co-receptors – cyclophane receptors, amphiphilic receptors and large molecular cages – multiple recognition in metalloreceptors – supramolecular dynamics.

UNIT IV: Supramolecular Reactivity and Catalysis

Catalysis by reactive macrocyclic cation receptor molecules – catalysis by reactive anion receptor molecules – catalysis with cyclophane type receptors – supramolecular metallocatalysis – cocatalysis – catalysis of synthetic reactions – biomolecular and abiotic catalysis. Supramolecular chemistry in solution – cyclodextrin, micelles, dendrimers, gelators – classification and typical reactions – applications.

UNIT V: Supramolecular Devices

Supramolecular devices and sensors – various types of supramolecular devices– an overview – supramolecular photochemistry – molecular and supramolecular photonic devices – light conversion and energy transfer devices – molecular and supramolecular electronic devices – electronic conducting devices – molecular wires, modified and switchable molecular wires – molecular and supramolecular ionic devices – tubular mesophases, molecular protonics – switching devices – electro-photo switch – ion and molecule sensors – role of supramolecular chemistry in the development of nanoscience and technology.

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UNIT-1

Concepts of supramolecular chemistry

Supra means huge moieties – means complex molecules. It consist of crystal engineering.

Father of crystal engg "Desiraju".

Weak inter molecular interaction

Strong inter molecular interaction

Hydrogen bonding

Electrostatic interaction – Weak dipale

Vander Walls interaction

Halogen bonding

π …π interaction (Stacking)

Hydrostatic interaction

Hydrostatic interaction

Concepts in supramolecular chemistry

Molecular self-assembly:

Molecular self-assembly is the construction of systems without guidance or management from an outside source (other than to provide a suitable environment). The molecules are directed to assemble through noncovalent interactions. Self-assembly may be subdivided into intermolecular self-assembly (to form a supramolecular assembly), and intermolecular self-assembly (or folding as demonstrated by foldamers and polypeptides). Molecular self-assembly also allows the construction of larger structures such as micelles, membranes, vesicles,liquid crystals, and is important to crystal engineering.

Molecular recognition and complexation :

Molecular recognition is the specific binding of a gust molecule to a complementary host molecule to form a host-gust complex. Often, the definition of which speciesthe "host" and which is the "gust" is arbitrary. The molecules are able to identify each other using noncovalentinteractions. Key applications of this field are the construction of molecular sensors and catalysis.

Mechanically-interlocked molecular architectures :

Mechanically – interlocked molecular architectures consist of molecules that are linked only as a consequence of their topology. Some noncovalent interactions may exist between the different concepts (Often those that were utilized in the construction of the system), but covalent bonds do not. Supramolecularchemistry, and template-directed synthesis in particular, is key to the efficient synthesis of the compounds. Example of mechanically-interlocked molecular architectures include catenaries, rotaxanes, molecular knots, and molecular Borromeanrings.

Dynamic covalent chemistry :

In dynamic covalent chemistry covalent bonds are broken and formed in a reversible under thermodynamics control. While covalent bonds are key to the process, the system is directed by noncovalent forces to form the lower energy structures.

Biomimetics :

Many synthetic supramoleculessystems are designed to copy functions of biological systems. These biomimetics architectures can be used to learn about both the biological model and the synthetic implementation. Examples include photodectrochemical systems, protein design and self-replication.

Imprinting :

Molecular imprinting describes a process by which a host is constructed from small molecules using a suitable molecular species as a template. After construction, the template is removed leaving only the host. The template for host constructions may be subtly different from the guest that the finished host bind. In its simplest form, imprinting utilities only steric interactions, but more complex systems also incorporate hydrogen bonding and other interactions to improve binding strength and specificity.

Molecular machinery :

Molecular machinery are molecules or molecular assemblies that can perform functions such as linear or rotational movement switching, and entrapment. These devices exist at the boundary between supramolecular chemistry and nanotechnology, and prototypes have been demonstrated using supramolecular concepts.

Building blocks of supramolecularchemistry :

Supramolecular systems are rarely designed from first principles. Rather, chemists have a range of well-studied structural and functional building blocks that they are able to use to build up larger functional architectures. Many of these exist as whole families of similar units, from which the analogwhich the analog with the exact desired properties can be chosen.

Halogen bonding :

Halogen bonding is the noncovalent interaction where halogen atoms functions as electrophilic species. The energetic and geometrical features of the interaction are described along with the atomic characteristics that confer molecules with the specific ability to interact through this interaction.

Comparison between hydrogen and halogen bonding :

Hydrogen bonding
A•••H-D
Halogen bonding
A•••X-D

In both cases, A (the hydrogen/halogen bond acceptor) is the atom, group, or molecule that donates electrons to the electron poor species H-D or X-D (the hydrogen or halogen bond donors respectively). H is the hydrogen atom involved in hydrogen bonding, and X is the halogen atom involved in halogen bonding. Note the halogen bond donor accepts electrons while the halogen bond acceptor donates electrons.

A parallel relationship can easily be drawn between halogen bonding and hydrogen bonding (HB). In both types of bonding, an electron donor/electron acceptor relationship exists. The difference between the two is what species can act as electron donor/electron acceptor. In hydrogen bonding, a hydrogen atom acts as the electron acceptor and forms a non-covalent interaction by accepting electron density from an electron rich site (electron donor). In halogen bonding, a halogen atom is the electron acceptor. Simultaneously, the normal covalent bond between H or X and D weakens, so the electron density on H or D appears to be reduced. Electron density transfers results in a penetration of the van der Waals volumes.

π- Interactions

Unlike hydrogen bonding, other intramolecularinteractions are much harder to control and predict for crystal-engineering purposes. This difficulty generally arises from lack of strength and directionality. The most commonly observed interaction other than hydrogen bonding is $\pi - \pi$ stracking. Interactions between π-systems are most common when there are few other possible interactions that may take precedence within the structure, so allowing the structures of fused aromatic rings to display stacking between the molecules. As we saw in Chapter 1, Section 1.3.3, there are two major ways in which π-systems are able to arrange themselves, i.e. face-to-face and edge-to-face. Although these remain relatively unexploited in deliberately engineered systems, owing to their tendency to be over-ridden by other, stronger interactions, there are many examples of these motifs frequently recurring. Aside from the relatively simple layered structure of graphite and the herringbone structure of benzene, one well-studied synthon is the *phenyl embrace*. These motifs are commonly found between pairs of tetrahedrally disposed EAr_3 units (E=P, As, B) or the related EAr_4cations and involve three phenyl rings from each group. The two EAr_3 groups are staggered with respect to each other with each of the phenyl rings, both donating and receiving in edge-to-face $\pi \ldots \pi$ interactions (Figure 4.20), with the opposing groups appearing to embrace each other. As there are a total of six phenyl rings involved, this motif is commonly referred to as the 'six-fold' phenyl embrace.[10]The large number of interactions act in a summative manner, being weak when regarding individually, and yet the phenyl embrace is a relatively strong synthon. Similar embrace motifs are seen with other aryl containing species, such as $M(2,2' - bipy)_3{}^{n+}$ complexes, where the strength of the embrace overcomes the repulsive cation-cationinteractions.

Polymorphism :

- Polymorphism is the solid state material exists as one and more than structural forms.
- Polymorphism found in any crystalline material such as polymers, minerals and metals and related to allotropy.
- The complete morphology of a material is described by polymorphism and other various types such as crystal habit, amorphous fraction or crystallographic defects.
- Polymorphism is relevant field of Pharmaceutical, agrochemicals, pigments, dyestuffs, food and explosives.
- When polymorphism exists as a result of a different crystal packing .It is called 'packing polymorphism.'
- Glycine can form monocyclic and hexagonal crystals.
- Silica known as alpha-quartz, beta-quartz, trydymite, moganite.
- Calcite and aragonite born form calcium carbonate.
- Paracetamol powder has poor compression properties, this poses difficulty in making tablets, so new polymorph of paracetamol was found which is more compressible.

Pseudo polymorphism :

- It is the phenomenon wherein a compound is obtained in crystalline forms that differ in nature or stoichiometry of include solvent molecules.
- This subject has not been treated systematically through it is perceived to be general importance , for example, In pharma industry.
- Presence of solvates or false polymorphs.
- Typical solvents including polymorphic change are water, methanol, ethanol, acetone, chloroform, n-propanol, isopropanol, n-butanol, n-pentanol, toluene and benzene.
- Distinct of false and true polymorphs can be obtain by the melting behaviour of the compound dispersed in silicone oil using hot stage microscopy.
- Pseudo polymorphs will evolve a gas (steam or solvent vapour) causing oil to bubble.
- True polymorphs merely met, forming a second globular phase.
- The temperature at which solvent volatilizes will be close to the boiling point of the solvent.

UNIT – II

Metallo Organic Frameworks

Metal Organic Frameworks are classes of compounds consisting of metal ions or clusters coordinated to Organic ligand to form one, two, or three dimensional structure. They are subclass of coordination polymers with the special feature that these are often porous. The organic ligand include are sometimes r4ffered to as “struts.” For example, 1,4-benzediene carboxylic acid. It is called as hybrid of Organic and Inorganic.

Organometallic systems:

Organometallic chemistry is the study of organometallic compounds, chemical compound containing at least one chemical bond between a carbon atom of an organic molecule and a metal, including alkaline, alkaline earth, and transition metals, and sometimes broadened to include metalloids like Boron, Silicon, and Tin

Zeolite:

- Na2Al2SiO3.H2O – a poly nuclear compound or complex.
- Alumino silicate minerals commonly used as adsorbent and catalyst.
- It have a wide variety of metal ion such as Na+, K+, Al2+, Ca2+, Mg2+ etc.
- Naturally zeolite is obtained by reacting volcanoic rocks / ash on with alkaline water of earth crust.

- Zeolites are Alumino silicates (AlO_4 and SiO_4) and it is come under the family of micro process material and it is also called as "Molecular sieves."

Molecular Ladder:

Supramolecular pattern involving strong hydrogen bonding between two bulkier system paralelly.

Molecular networks:

Supramolecular pattern involving strong and weak intermolecular interaction in a bulkier cage like structure. It is located and arranged as branch like structure.

Molecular rods:

- Nano rods or tubes of carbon about 10,000 times thinner than human hair.
- These consists of rolled up sheets of multilayer carbon atom in hexagon shape.
- They conduct electricity better than Copper and more stronger than steel wire.
- It can store huge volume of gas.
- It can be used as tips in probe microscope that is edge of microscope

Non-linear optic(NLO):

- Frequency doubling is carried out by placing a nonlinear medium in a laser beam. While there are many types of nonlinear media, the most common used crystals are BBO(beta-barium borate), KDP(potassium dihydrogen phosphate), KTP(potassium titanyl phosphate), and lithium niobate.
- An NLO material is a compound which a non linear polarization is invoked on. Application of intense electric field. This electric field results from the external application of an intense laser-source.
- It have centro symmetry and the inversion centre is possible. It is optically active.
- Another one is non centro symmetry and here the conversion centre is not poasible. It is optically inactive.

Organic Light Emitting Diode(OLED):

- Organic light emitting diode devices have received much attention, because they are expected to be a next generation display and light sources, thanks to lightweight and flexible materials.
- The OLED was focused on practicals use, after tang et al. First observed the OLED device by use of a two layered organic thin film.

- An amorphous material is useful for an OLED device , because it is transparent , homogeneous, isotropic and easily processible. A practical OLED device further requires excellent heat-resistance and durability.
- Many hole transport materials based on triphenylamine derivatives (TPD) are widely usable, because they are heat-resistance and amorphous.
- In addition to the TPDs, oxidazole derivatives(PBD) having an electron transport property , Alq3 as a host material, and blue emmisive distylyl derivatives are fundamental materials for amorphous OLED devices.

UNIT-3 : Co-receptor Molecule and Multiple Recognition

Dinuclear and Polynuclear Metal Ion Cryptates:

- Mcarocyclic ligands of coreceptor type incorporating two or more binding subunits for metal ions, form dinuclear or polynuclear cryptates in which the distance and arrangement of the cations held inside the molecular cavity may be controlled through ligand design.
- They allow the study of cation-cation interactions as well as the inclusion of bridging substrates to yield cascade complexes, which are of interested for bioinorganic modelling and multicentre-multi electron catalysis.
- Dissymmetric ligands that contains subunits with hard and soft binding sites yield complexes in which the bound ions act as either Lewis acid and redox centres.
- Numerous dinucleating macrocyclic ligands have been synthesised, in particular by the versatile amine + carbonyl gives imine reaction; they form dinuclear metal complexes as well as cascade complexes with bridging gropus, for instance in dicobalt complexes that are oxygen carriers.
- Polynuclear receptors have the ability to assemble metal ions and bridging species within their molecular cavity to form” Cluster Cryptates.”
- Modelling of biological iron-sulphur clusters sites may employ acyclic assembling ligands or inclusion into appropriate macrocyclic cavities. These few examples may at least have shown how rich the field of polynuclear metal cryptates is , both in structures anfd properties.

Linear Recognition of Molecular length by Ditopic Coreceptors:

- Receptor molecule possessing two binding subunits located at the two poles of the structure will complex preferentially substrates bearing two appropriate functional group at a distance compatible with the separation of the subunits.
- This distance complemetarity amounts to a recognition of molecular length of the substrate by the receptor. Such linear recognition by ditopic coreceptors has been achieved for both dicationic and dianaionic susbstrates, diammonium and dicarboxylate ions respectively;its corresponds to the binding modes.
- Both the terminal diammonium and dicarboxylate substrates, selective binding by the appropriate receptors describes a linear recognition process based on length complemetarity in a ditopic binding mode.
- Important biological species, such as polyamines, amino acid and peptide diamines, and dicarboxylates may also be bound selectively.
- Recognition is achieved by multiple coordination to metal ions in dinuclear bis-macrocyclic coreceptors that complex selectively complementary bis-imisdazole substrates of compatible length.
- Numerous variations in the nature of the binding subunits or of the bridges linking them are conceivable and may be tailored to specific complexation properties.

Heterotopic Coreceptors :

- The combination of binding subunits of different nature yields heterotopic receptor that may complex substrate by interacting simultaneously with cationic, anionic and neutrsl sites, making uyse of electrostatic and vander waals forces as well as of donor-acceptor and solvophobic effects.
- Whereas homotopic coreceptors complex dicationic or dianionic substrates, heterotropic ccoreceptors may allow the binding of two different substrate, of ion pairs or of zwitterionic species.
- Enantioselective and diastereoselective molecular recognition is achieved by chiral coreceptors. A particularly interesting example of the latter is the bonding of aromatic amino acids with high enantioselective recognitipon by an acyclic tritropic receptor that contains a guadinium, a macrocyclic and a naphthalenic unit for simultaneous interaction with, respectively, the carboxylate, the ammonium and the aromatic groups of the substrate.
- Although much work has already been performed and many interesting results have been obtained, there is still a very open future for the design of receptor molecules

especially tailored towards the recognition of more or less complex organic molecule, such as the C60 fullerene which forms a supramolecular association gamma-cyclodextrin, with calixarenes and in the solid state.

- Combination of structural units whose features have already been defined and constructionof novel architectures offer wide perspectives.

Amphiphilic Coreceptors :

- It having both hydrophilic and hydrophobic components with them. It is also called as “Surfactants” which have both Polar and Non-polar compounds in it.
- The head have greater affinity on polar molecules and tail have affinity against non-polar molecules that is vise verza.
- Polar copmpound said to be ‘head’ and Non polar is said to be ‘tail.’
- It have wide application in biological system in human lives, Bile salt is act as a surfactant for the various metabolism in lives i.e absorbing vitamins etc,.

Cyclophane receptors:

- Cyclophanes have aliphatic and aromatic compounds in it.
- Cyclic molecule act as host and it can sense hydrophobic molecules that is guest.
- It having tails, walls and caps.
- Aromatic ring in the cyclophane can be substituted with heteroatoms and it is classified into two types, that is Heterocyclic and Heteracyclic.
- If a hetero atom present in the aromatic ring, it is called heterophane. If it is present in an aliphatic chain it is called as Hetraphane.
- If a heteroatom present both cyclohexane and alkyl chain is called “Hetero heteraphane”.
- If monomeric cyclophanes moderate guest binding ability. The polytopic cyclophanes the guest can bind with target effectively.

Supramolecular Dynamics :

- Dynamics means its a active one should rounded the system for chose the recognised place.
- Physical moment of an atom or molecules.
- The atom or molecule are allowed to interact for a fixed period of time then giving a viewn of the dynamic evalution of the system.
- Newton’s law of motion is applied for the system.

- Finding out the conformational space.
- During site selectivity, the molecule may collaid with each other.
- The stability of the system uis decreased during thus increasing the temperature.

UNIT-4 : Supramolecular Reactivity and Catalysis

Catalysis by Reactive Macrocyclic Cation Receptor Molecules:

- The ability of [18]-O6 macrocyclic polyetheras to bind primary ammonium ions opens the possibility to induce chemical transformation on such substrates.
- Activation and orientation by binding was observed for the hydrolysis of O-acetylhydroxylamine, which forms such a stable complex with the macrocyclic tetracarboxylate receptor that it remains protonated and bound even at neutral pH, despite of low pKa of the free species.
- As a consequence, its hydrolysis is accelerated and exclusively gives acetate and hydroxylamine, whereas in the presence of K+ ions, which displays the substrate, it yield also acetylhydroxamic acid, CH3CONH-OH.
- Thus, strong binding may sufficient for markedly accelerating a reaction and affecting its course a result that also bears enzyme-catalysed reaction.
- The terta-L-cysteinyl macrocycle binds p-nitrophenyl esters of amino acids and peptides, and reacts with the bound species, releasing p-nitrophenol.
- The reaction displays, Substrate selectivity in favoue of dipeptide ester substrates, with
- Marked rate enhancements,
- Inhibition by complexable metal cations that displace the bound substrate,
- High chiral recognition between enantiomeric dipeptide esters, and
- Slow but definite catalytic turn over.
- Hydrogen transfer has been induced with macrocyclic receptor bearing 1,4-dihydropyridal groups. Bound pyridinium substartes are reduced by hydrogen transfer from DHP chains within the supramolecular species.
- The first order intracomplex reaction is inhibited and becomes biomolecular on displacement of the bound substrate by complexable cations.
- Reactions with carbonyl or sulphonium substrates have been performed with other DHP containing macrocycles.

Catalysis by Reactive Anion Receptor Molecules :

- The development of anion coordination chemistry and anion receptor molecules has opened up the possibility to perform molecular catalysis on anionic substrates of chemical and biochemical interest, such as adenosine triphophate.
- The catalysis of Phosphoryl transfer is of particular interest, namely in view of the crucial role of such processes in biology and of the numerous enzymes that catalyse them.
- ATP hydrolysis was found to be catalysed by a number of protonated macrocyclic polyamines.
- In particular, [24]-N6O2, strongly bind ATP and markedly accelerates its hydrolysis to ADP and inorganic phosphate over side pH range.
- The reaction presents first-order kinetics and is catalytic with turnover. It proceeds via initial formation of a complex between and ATP and protonated followed by an intracomplex reaction that may involve a combination of acid, electrostatic, and nucleophilic catalysis.
- Structure of the compound represents a possible binding mode in the ATP-X complex and indicates how cleavage of the terminal phosphoryl groups might take place.
- A transient intermediate, identified as phosphoramidate 81, is formed by phosphorylation of the macrocycle by ATP and is subsequently hydrolysed.

Catalysis with Cyclophane Type Receptors:

- A number of studies have made us of functionalized cyclophanes for developing supramolecular catalysts and enzyme models.
- Their catalytic behaviour is based on the implementation of electrostatic, hydrophobic and metal coordination features for effecting various reactions in aqueous media.
- Hydrophobic species bearing bearing hydrocarbon chains present vitamin B12 or vitamin B6 type activity. Such systems lend themselves to inclusion in membrane or micellar media.
- Thus they provide a link with catalysis in more or less organized media such as membranes, vesicles, micelles, polymers.
- Water soluble cyclophanes showing, for example, transminase, acetyl transfer, pyruvate oxidase or nucleophilic substitution activity.

- Cyclophane catalysts offer a rich playground for developing novel reaction and enzyme models in view of the variety of their structural types, the large cavities they contain and the possibility to attach several functional groups.

Supramolecular Metallocatalysis:

- Supramolecular metallocatalysis consist in principle of the combination of recognition subunit that selects the substrate and of a metal ion, bound to another subunit, that is the reactive site.
- Complexed metal ions presenting free coordination positions may present a variety of substrate activation and functionalization properties.
- Heterotropic coreceptors bind simultaneous a substrate and metal ion bridging them into proximity, thus potentially, allowing reaction between them.
- Approaches towards the development of artificial metalloenzymes have been made, based on cyclodextrins or macrocycles and involving various metal ion as, Zn, Cu, Co for facilitating hydrolysis, epoxidation , hydrogen transfer, etc.
- Metallophorpyrins have been used for epoxidation and hydroxylation and phosphine –rhodium complex for isomerisation and hydrogenation.
- Cytochrome P-450 model systems are represented by a porphyrin-bridged cyclophane , macrobicyclic transition metal cyclidenes or beta-cyclodextrin-linked porphyrin complexes that may bind substrate and perform oxygenation reactions on them.
- Supramolecular metallocatalysts, by combining a substrate recognition unit with a catalytic metallic site, offer powerful entries to catalystspresenting shape, region and stereoselectivity.

Cocatalysis :

- Either a pair of the cooperative catalyst that improves each others catalytic activity. In cooperative catalysis, there is two catalyst forms a cycle to create single new bond .
- It activity proceed by two ways .Those are nucleophilic and electrophilic .
- For example, 2moles of $KClO3$ gives in the presence of $MnO2$ gives 2KCl and 3 moles of water.

Synthetic Reaction:

- Multiple reaction combine single product.
- It release its energy as ‘light and heat’ with the help of exothermic process.
- Rewlease of the product and the free catalyst of a new cycle.
- For example, Phosphoryl transfer.

- Bond-making such as those described above extend supramolecular reactivity to catalysis, mediating 'synthetic reactions' within the supramolecular entities formed by coreceptor molecules.

Biomolecular and Abiotic Catalysis:

- Supramolecular catalysts may make use if biological materials and processes for tailoring appropriate recognition sites and achieving high rates and selectivities of reactions.
- Modified enzymes obtained by chemical mutation or by protein engineering represent biochemical approaches to artificial catalysts.
- This is also the case for the generation of catalytic proteins by induction of antibodies. Antibodies to reactive haptens are able to facilitate the transformation of the bound species.
- Generating antibodies against analogues of transition states should lead transition state stabilization and facilitate the process.
- Such 'catalytic antibodies or abzymes' have been produced for a variety of reaction and an active field of research has developed along such lines.It represents an approach to substrate specific, efficient and selective catalysis of supramolecular types, that is of much basic and applied interest.
- The strong affinity TS of the reaction of a given substrate leads it along the way and thus facilitate the process.
- The biomolecular and abiotic catalysts step to three ways to induct the antibodies.
    1. Modified enzyme
    2. Chemical mutayion
    3. Protein engineering
    4. Approach the artificial catalysts
    5. Induction antibodies that is 'Abiotic catalysts.'
- For example, Protein or nuclei.

Supramolecular Chemistry in Solutions:

Cyclodextrins:

- Cyclodextrins are obtained form starch via certain enzymes. Starch is a polysaccharide with an alpha 1-4 linkage of glucose, and it has a left- handed spiral structure.

- The enzyme changes this polysaccharides into a cyclic oligomer with an appropriate number of glycopyranoside units. The cyclic structure oligomers with six, seven, eight glycopyranoside units are the most called alpha, beta, gamma- cyclodextrin, respectively.
- Cyclodextrins dissolved in an aqueous phase can accommodate hydrophobic guests such as aromatic hydrocarbons in their cavities. However, the inorganic ions and gas molecules can also be included.
- The number of saccharide units that the cyclodextrin contains. Therefore, the guests selected dependon the size of the cavity.
- The hydroxyl group on the cyclodextrin can be modified using an appropriate organic reaction, and various types of functionalized cyclodextrins have been proposed.
- Cyclodextrins provide a hydrophobic micromeddium in an aqueous phase. This characteristic is analogous to the reaction pockets of enzymes. Enzymes provide size-selective hydrophobic cavities and catalyze the reaction of bound substrates.
- A phosphodiester is hydrolyzed through cooperative interactions with two imidazolyl groups. The relative positions of the imidazolyl groups and the inclusion geometry of the hydrophobic substrate are structurally well matched. This artificial enzyme can be regarded as a model of ribonuclease A.

Micelle:

- An aggregate of molecules in a colloidal solutions, such as those formed by detergents. A typical micelle in aqueous solution forms an aggregate with the hydrophilic “head” regions in contact with surrounding solvent, sequestering the hydrophobic single-tail regions in the micelle center.
- The tail of the surfactant attached to water. The head that is a hydrocarbon also attract by attractive force to the head of surfactant.
- The surfactant drag the dirt to upward with the formation bubbles.
- In concentrated solutions of surfactants, micelles can form various phases, such as lamellar, cubic and hexagonal phases. These phases can be moved and placed on to solid materials.
- Under selected conditions, surfactant form rod like micelles that further assemble into hexagonal arrangements.
- Solidifying the surroundings of the hexagonally packed micellar rods using a sol-gel reaction with an appropriate silica reagent results in hexagonally arranged solid

silicates. The organic micelles are subsequently removed by calcinations, and porous material is obtained. This is called as "Mesoporous silica."

- Selective removal of the alkyl tail by acid hydrolysis leaves open pores densely populated with functional groups. Since the surfactant bites the silica wall and removes its tail, this method is called "Lizard Templating."

Dendrimers :

- Fullerenes and carbon nanotubes are formed spontaneously based on the restricted rules of carbon linkage. Therefore, their fundamental frameworks are not easily redesigned.
- Super structures where we are free to design their sizes and shapes are sometimes moer attractive prospects.
- In this section, the 'dendrimer' family is introduced, as examples of artificially controllable superstructures. The word "dendrimers" contain the root "dendr"-which means tree, an accurate reflection of the structure of dendrimers- molecular trees.
- The first dendrimer was proposed by Tomalia. Deendrimers are also called as "Drug vehicle."
- Outer surface affect the solubility and chelation ability.
- Dendrimers are nothing but symmetrical bulkier molecules with well defined homogenous mono dispose structure.
- The three major portion were generate polydispose. Product with different molecular weight.
- Dendrimers have gained broad range of application in supramolecular chemistry,especially in "Host-Guest and Sellf assembly."
- Dendrimers can be prepared by two ways . That is Divergent and Convergent.

Gelators :

- In 1926, Gel found by Dorothy Jordon Coyd. That is any substrate can forming gel with the capable of 'soft and solid' in colloidal state.
- Physical gel are non-covalent gel. Chemical gels are covalent gel.
- Classification of gels are source and medium . Source have sub classification as natural and artificial. Then medium classified as organo, hydro, aaero and xero.

- Organo gelators it have two classification like one component and two component. The one component have solvent+solute. The two component system having solution + gel.
- Gels are used in Sensor application and Organic electronic image.
- 2,3-bis-n-decyloxy anthracene gel helps in the thermo sensors.

Subject	Chemistry
Paper No and Title	14: Organic Chemistry- IV (Advanced Organic Synthesis, supramolecular chemistry and carbocyclic rings)
Module No and Title	34: CAGED MOLECULES
Module Tag	CHE_P14_M34

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Table of Contents

1. Learning outcomes

After studying this module, you shall be able to understand:

- Basics of caged molecules
- Synthetic methodology of caged molecules
- Applications of caged molecules

2. Introduction

The dictionary meaning of the word "cage" says that it is a closed pattern having space in the middle where something can be located. In the similar pattern of definition, caged molecule in chemistry is a polycyclic compound that contains atoms connected with one another in such a way that an enclosed space is created where other atom or molecules can be located.

According to the definition of IUPAC, a cage compound is a ‘polycyclic compound with the shape of a cage’. An organic cage molecule is as an organic molecule where the backbone consists of carbon–carbon (C-C) bonds and/or other functional groups which are found in organic molecules. There are also inorganic or coordination caged molecules. In general, a caged molecule is a shape-persistent macrocycles that have a defined interior space, large enough to host other molecules, and do not crumple to a more dense or twisted structure (Figure 1).

During 1960’s to 1980’s period, three platonic shaped hydrocarbon molecules such as tetrahedrane, cubane and dodecahedrane (Figure 1) had been targeted for several multistep syntheses. The caged polycyclic compounds had drawn the interest of synthetic chemists due to their strained nature and unusual reactivity patterns. The caged molecules were found to be useful in different drugs, supramolecules and high-energy materials.

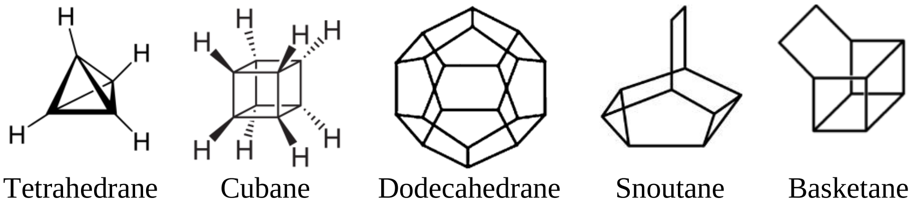


Figure 1. Chemical structure of some caged molecules

On the basis of types of atoms involved, caged molecules are classified as homoatomic rings and heteroatomic rings. The caged molecule having same atoms are homoatomic rings like the white phosphorus (P) which exists in perfect tetrahedra of P_4.

The caged molecule having more than one type of atoms involved are called heteroatomic cages which includes polymetal clusters, iron-molybdenum-sulfur clusters (Fe_3MoS_4) having the cubane-like framework, adamantane-like P_4O_6, carbosilanes etc. The metal–organic frameworks (MOFs) are also an example of heteroatomic caged molecules. They are crystalline polymeric coordination networks which have metal centers and ligands that form a three dimensional architectures with potential inner porosity. A variety of metal–organic caged molecules are known that encapsulate appropriate guests on the basis of non-covalent interactions like Coulomb, van der Waals, ion-association forces, hydrogen bonding and steric interactions.

Another important caged molecule is cyclodextrins (CDs) (Figure 2). They are synthetic substances obtained from the enzymatic degradation of polysaccharides. The core of their structure is consists of a stable hydrophobic cavity that can encapsulate other molecules. The applications of CDs are found in all sectors of industry such as food, pharmaceutical, chemistry, chromatography, biotechnology, agriculture, cosmetics, hygiene, medicine, textiles, and the environment. Other specialized applications include the formulation of detergents, glues and adhesives, the industry of fibers and paper and the sector of plastics.

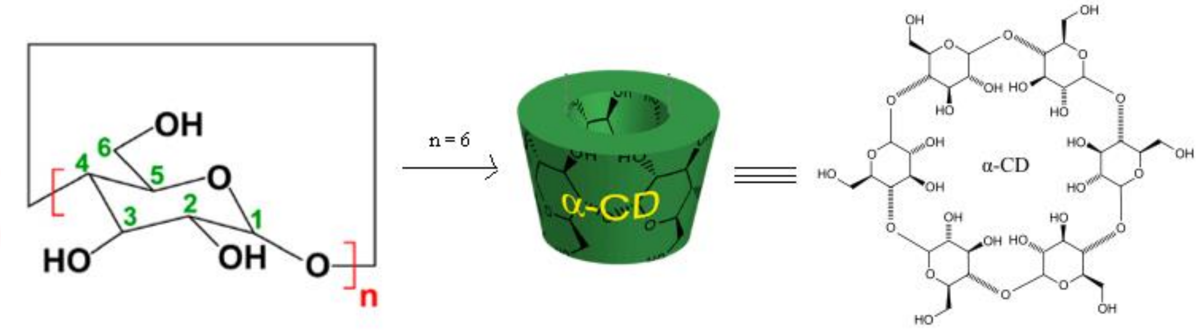


Figure 2a. Chemical structure of α-Cyclodextrin

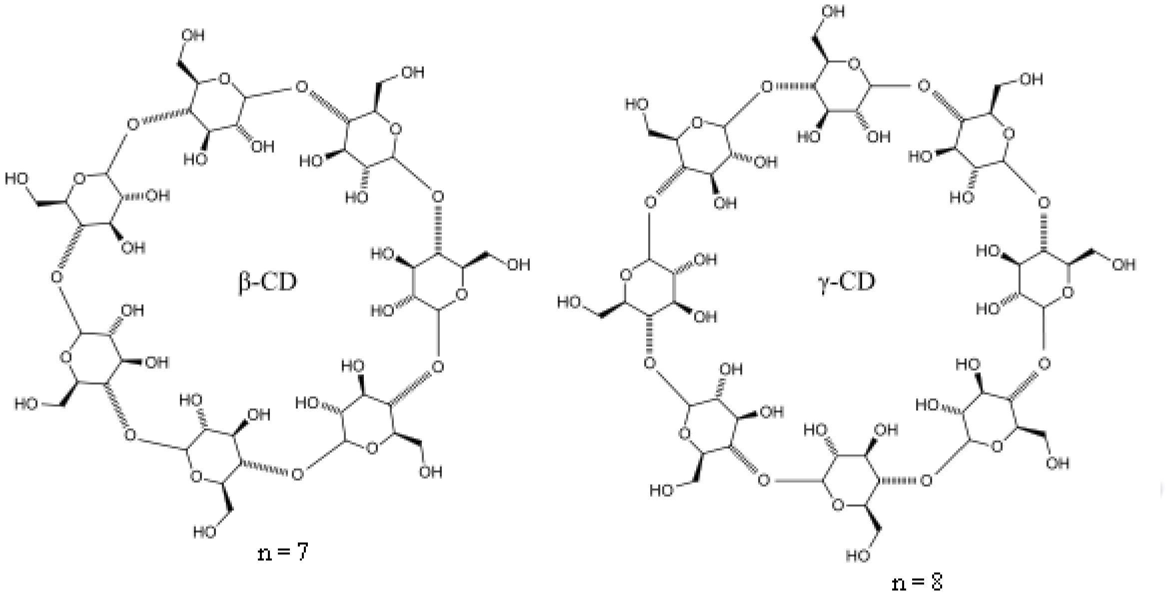


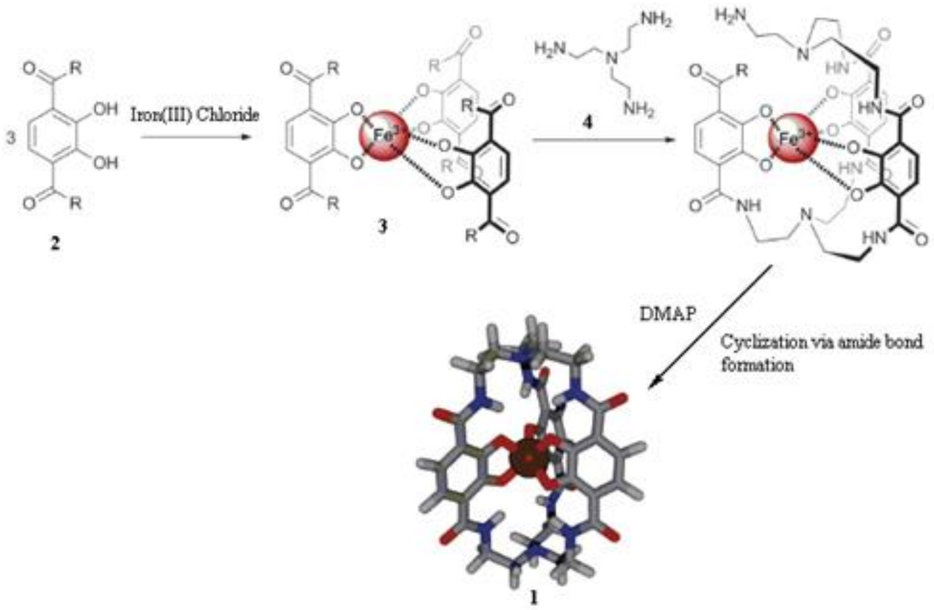
Figure 2b. Chemical structures of β-Cyclodextrin and γ-Cyclodextrin

3. Synthesis of selected cage compounds

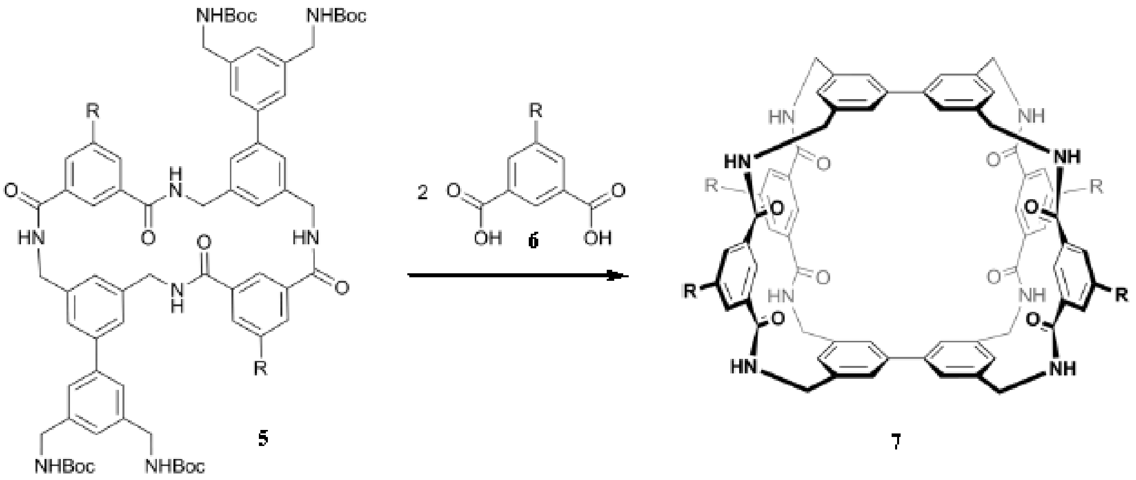
The caged compounds possessing organic molecules can be synthesized by two popular methods.
(i) Irreversible bond formation method like cross-coupling reactions or amidation, and
(ii) Reversible bond formation method.

3.1 Irreversible bond formation method:

Using amide-bond formation: In this method of synthesis, the final cyclization step leading to the cage compound synthesis is due to the formation of one or more amide bonds. The Raymond group have synthesized caged molecule (**1**) using iron(III) cations as a template to pre-organize three catechol (**2**) units that further reacts with tris(2-aminoethyl)amine (TREN, **4**) in remarkable 70% yields (Scheme 1). Davis group has synthesized another monosaccharide receptor caged molecule by cyclization of compounds **5** and **6** (Scheme 2).



Scheme 1. Synthesis of caged molecule by Raymond group



Scheme 2. Synthesis of caged molecule by Davis group

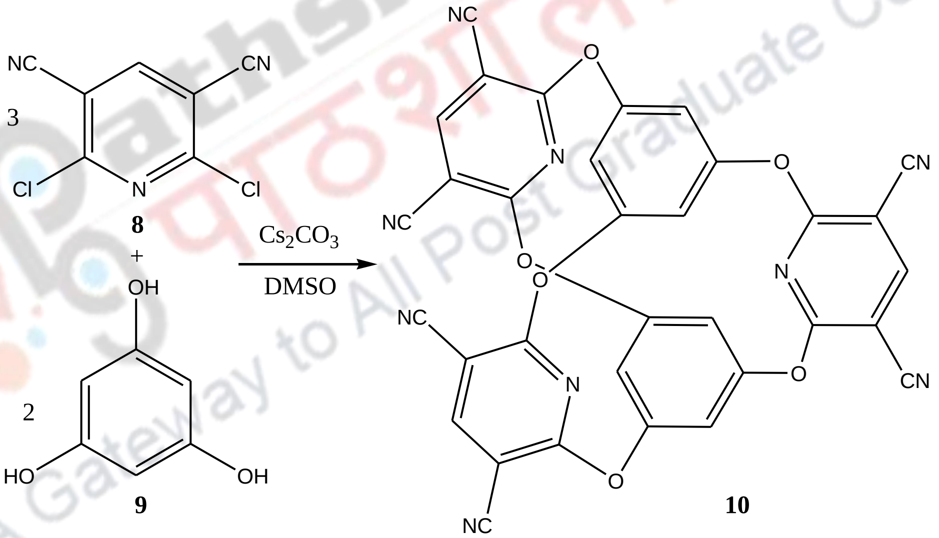
Using nucleophilic aromatic substitutions: The nucleophilic substitution reactions form stable covalent bond to give smaller [2+3] caged molecules (Scheme 3). The caesium cation might have a template effect and it preorganizes the 2,6-dichloropyridine-3,5-dicarbonitrile (**8**) which further reacts with benzene-1,3,5-triol (**9**) to give the caged molecule **10** (Scheme 3).

Using the formation of carbon–carbon bonds: Using this method, caged compounds with a fully carbon–carbon bonded backbone can be prepared. They are very important synthetic targets due to their chemical and thermal stability and photophysical properties. The major problem with this method is the overall yields which is quite low. An important macrobicycle **11** was synthesized by Moore and co-workers in a multistep Sonogashira–Hagihara approach.

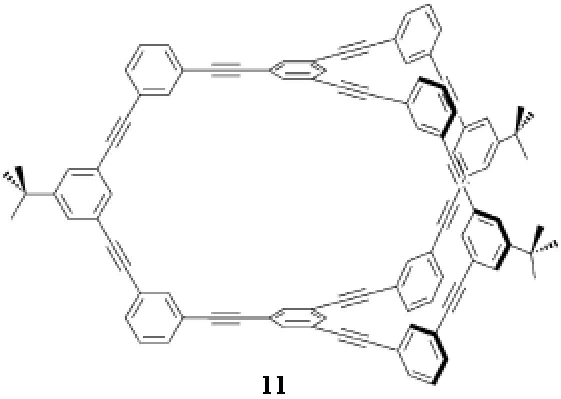
3.2 Reversible bond formation method:

Another method to prepare caged compounds is the use of reversible covalent bond formation. This is a type of self-healing processes of bond making and breaking to achieve a thermodynamic stable product.

Using imine bond formation: The imine bond (>C=N-) formation takes place by the condensation of amines and aldehydes/ketones. This bond formation is very frequently used in the synthesis of large caged molecules. A large [4+4] cage was synthesized by linking a bowl-shaped ruthenium complex possessing three aldehyde groups with an extended adamantane-cored triamine (Scheme 4). Another large caged molecule [12+8] was synthesized by the reaction of 4-*tert*-butyl-2,6-diformylphenol and 1,3,5-triaminocyclohexane by Skowronek et al (Scheme 5). It has been observed that the entropy of the caged molecules contributes in the cage formation process. The higher symmetrical cages are entropically more favoured in comparison to lower symmetric caged molecule.



Scheme 3. Synthesis of small cage molecule using nucleophilic substitution reaction



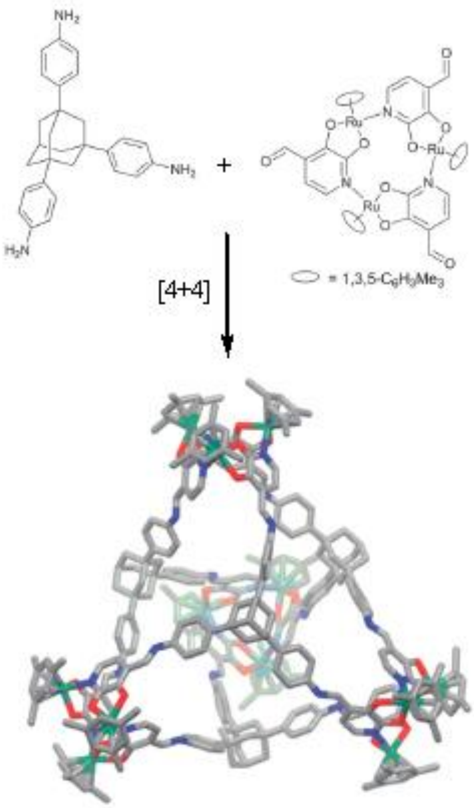
11

Using imine and olefin metathesis: The imine bond formation is a condensation reaction. The condensation and metathesis reactions are orthogonal to each other. With this concept, Zhang and co-workers gave the synthesis of caged molecule having imine bonds and olefin bonds in one pot (Scheme 6). The first step is the condensation of amine with aldehyde, in which the evolved water was removed under vacuum. The resulting product without purification used for the olefin metathesis to give the caged compound by dimerization.

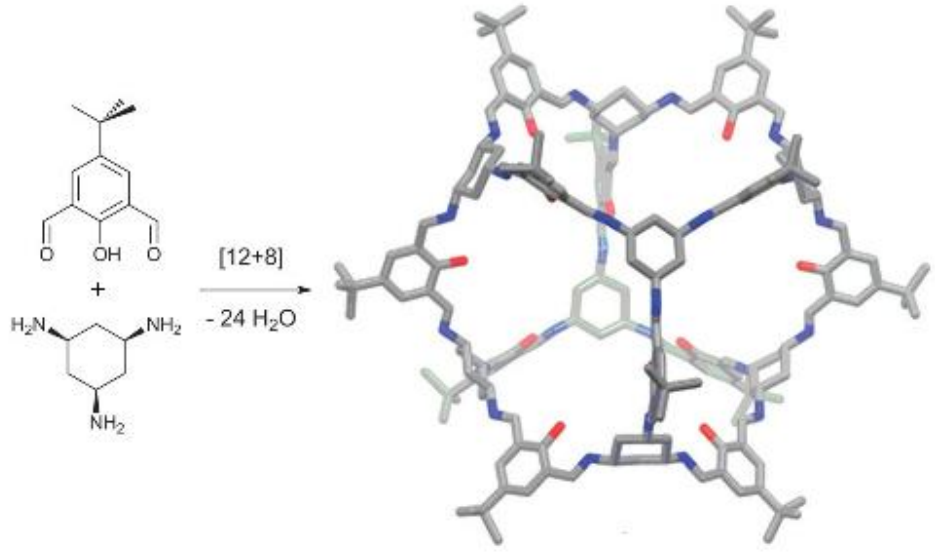
For the synthesis of metal-organic caged molecules, transition metal ions are commonly used to make the metal–organic caged molecules. In theses cage assemblies, the metals usually occupy the vertices. The metal ions such as Pd(II), Rh(II), Ru(II), Mo(II), Fe(II), Co(II), Ni(II), Cu(II), Zn(II) etc. have been used for the synthesis of metal-organic caged molecules. The required properties and shape has been achieved on the basis of metal ion and ligands employed and interaction taking place between them. The multidentate ligands bearing different types of functionalities like carboxylic, hydroxyl, Schiff base donor groups usually employed for the construction of metal-organic caged molecules. The proper conditions of a suitable solvent system, temperature and pressure lead to the self-organization of linked metal ions and donor ligands to achieve a suitable caged molecule.

4. Applications of caged compounds

The caged molecules have been utilized in variety of fields. There have been several studies on the investigation of their properties, especially their specific interaction with other guest molecules binding inside the cavity. Caged compounds are biologically useful because illumination can be so easily controlled in timing, location and amplitude.



Scheme 4. Synthesis of a [4+4] cage by connection of metallamacrocycles *via* imine bonds.



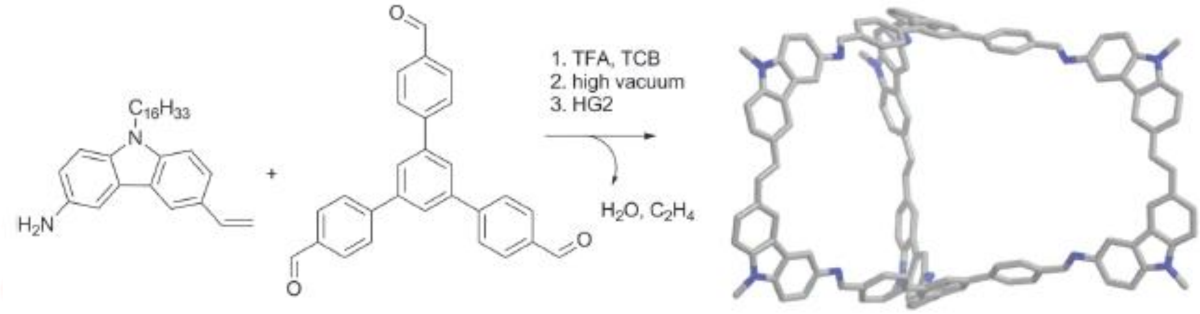
Scheme 5. Synthesis of an octahedral [12+8] cage

4.1 Stability of reactive compounds

The space inside the caged molecules is generally called cavity of a cage. This space is an ideal space for any molecule to get encapsulated with appropriate size. By using appropriate cages, the reactive species can be protected from the outer environment and stabilized for a longer time.

4.2 Recognition of guest ions or molecules

The host-guest chemistry is known from the early days. The presence of appropriate size and well defined cavity of caged molecule make them an ideal host for recognition of varied guest ions or molecules. The small cations, like Li^+, Na^+ and K^+, are usually bound at the outside of the cage, whereas the larger cations, like Rb^+ and Cs^+, are bound inside the cage (Figure 3). Zhang and co-workers reported the synthesis of a rigid porphyrin-based cage compound, which showed high selectivity (>1000) in binding C70 compound over C60.



Scheme 6. Synthesis of caged molecule by imine and olefin metathesis

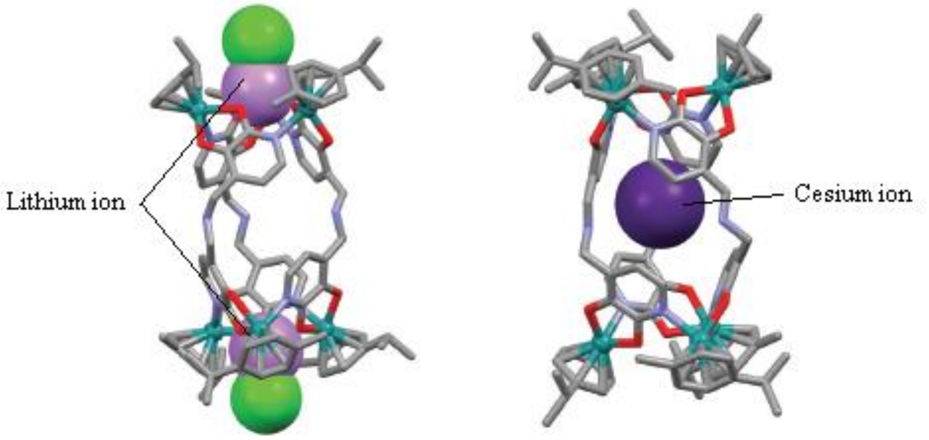


Figure 3. Recognition of ions by caged molecules

4.3 Caged molecules as permanent porous materials:

The caged molecules also showed a zeolitic behavior and played the role of permanent porous materials. The porosity behavior can be switched on and off by changing the polymorphism of crystalline cages influenced by the solvent employed.

4.4 Ionic transport

The metal–organic polyhedral (MOP) cages are actively involved in the ionic transport and single molecule detection behavior. They are employed for both cationic and anionic transport. For example, Furukawa et al. synthesized a charge-neutral MOP-18, [$(Cu_2)_{12}$-(5-dodecyloxy-1,3-benzenedicarboxylate$)_{24}$]. This caged compound had overall size of 5 nm having a hydrophilic cuboctahedral core cavity with the diameter of 13.8 Å. This was used in the preparation of synthetic ion channel that has successfully been used to transport protons and alkali-metal ions across the lipid membranes.

4.5 Pharmaceutical applications

The caged compounds have been successfully applied in drug delivery to specific locations within the human body. The metal–organic self-assemblies with proper functionalities and appealing drug hosting and release potential are a new input to the field. The caged molecules offer storage, carriers and controlled release. Literature is filled with publications where the use of caged molecules in drug release studied.

5. Symmary

The caged molecules exist as cage for other molecules. They exist in a closed pattern having space in the middle where something can be located or trapped or encapsulated.

- The caged molecules are either organic or inorganic including coordination in nature.
- In general, a caged molecule is a shape-persistent macrocycles that have a defined interior space, large enough to host other molecules, and do not crumple to a more dense or twisted structure.
- The caged molecule possesses features like permanent porosity, highly selective guest binding/encapsulation, solubility, chemical and thermal stability etc.
- The caged molecule can be synthesized by two popular methods like irreversible bond formation method which includes cross-coupling reactions or amidation such as amide-bond formation nucleophilic aromatic substitutions, the formation of carbon–carbon bonds etc. The other method is reversible bond formation method like imine bond formation, imine and olefin metathesis etc.

- The caged molecules have been utilized in variety of fields. They are utilized to stabilize the reactive compounds, recognize the guest ions or molecules. They provide permanent porous materials and helps in ionic transport. Their applications are found in all sectors of industry such as food, pharmaceutical, chemistry, chromatography, biotechnology, agriculture, cosmetics, hygiene, medicine, textiles, and the environment.

Subject	Chemistry
Paper No and Title	14: Organic Chemistry- IV (Advanced Organic Synthesis, supramolecular chemistry and carbocyclic rings)
Module No and Title	24: Dendrimers
Module Tag	CHE_P14_M24

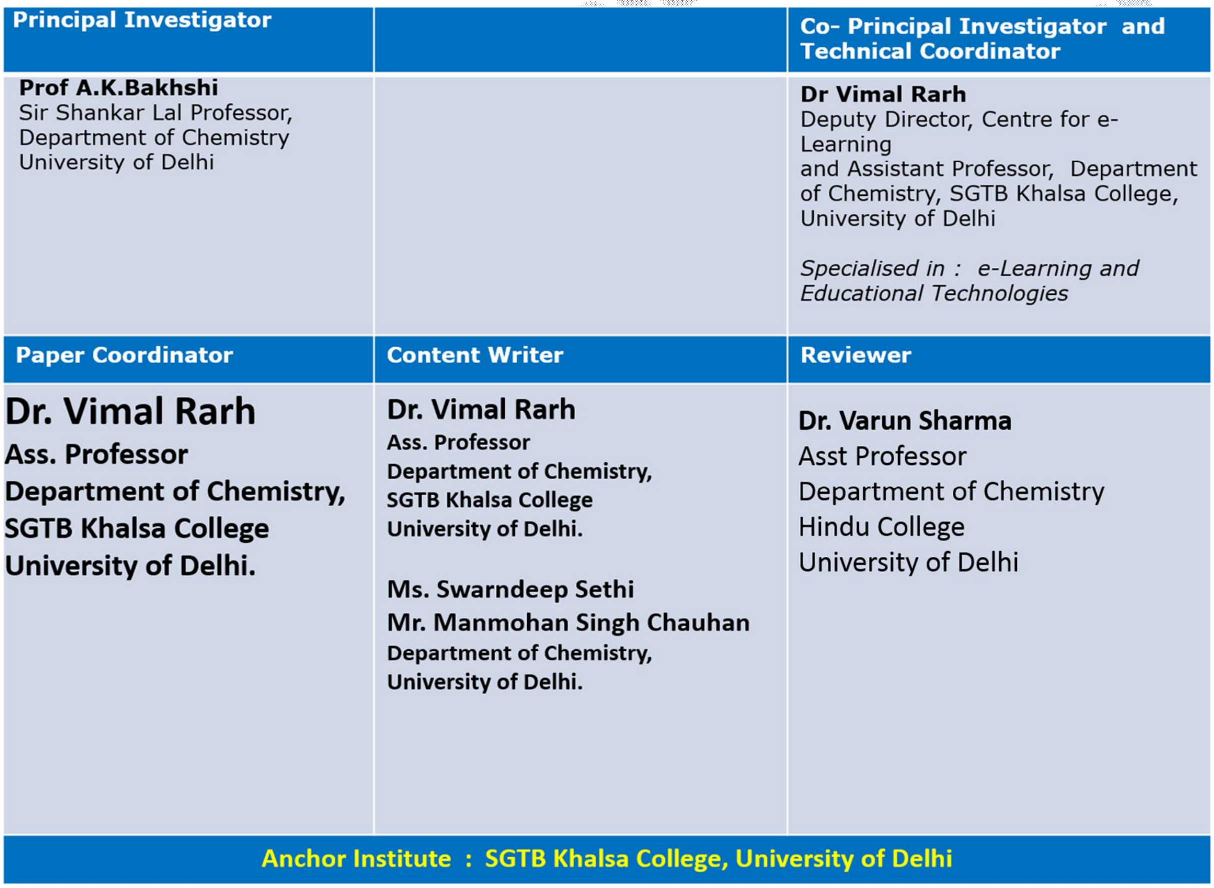


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TABLE OF CONTENTS

1. Learning Outcomes

After studying this module, you shall be able to

- Basic knowledge of dendrimer
- Preparation of dendrimer
- Physical property and characterisation of dendrimer
- Host-Guest chemistry of dendrimer
- Supramolecular dendrimer assemblies
- Application of dendrimer in medical field

2. Introduction

Dendrimer taken from Greek word *Dendron* which means tree and *meros* denoting part, since the monomer exhibit a repetitive branching, which is responsible for their unique character. Dendrimers are highly branched three-dimension architecture, which synthesized by the monodicpersed macromolecules. A dendrimer have tree like fashion, which is grown from a central core.

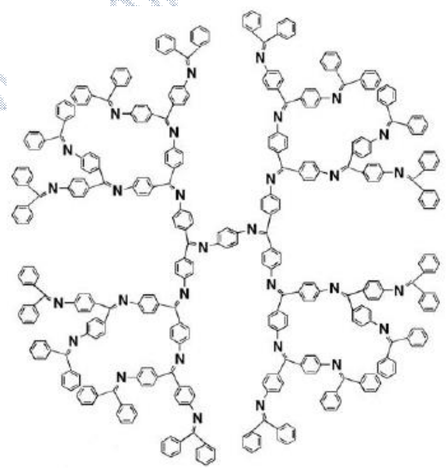

Fig. 1: Structure of Dendrimer

3. Size and Structure of Dendrimers

Dendrimers are usually nanometers to tens of nanometers in size. Comparatively, the general size of a dendrimer is larger than a typical closed fullerene (diameter, ╓0.7 nm) and smaller than aminocrosphere (diameter, 0.1-10µm). Actually the size of dendrimer depends upon the number of steps which are used for building them (as dendrimers are constructed by stepwise connection of several parts.)

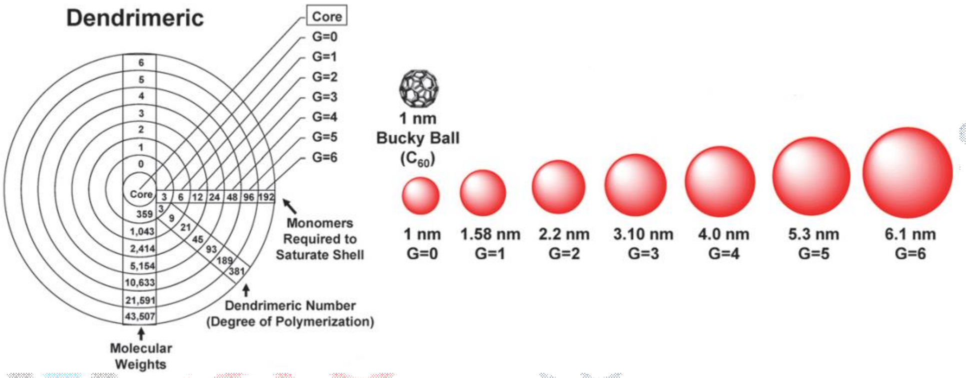

Fig. 2: Size of Dendrimers

Structurally, a dendrimer begins with a multifunctional core. Numerous molecules like ammonia, pentaerythritol, benzene, adamantane, porphyrin, or even fullerene can be used as dendrimer cores. From this core, an oligomer is generated by the attachment of multifunctional repeating unit with core functional group. This oligomer contained a central core and a number of functionalized pendant arms. This is the *first generation dendrimer.* If second monomer unit are attached with functional group of the first generation material, a much larger and highly branched dendrimer form. This is the *second generation dendrimer.* A well defined, three-dimensional polymeric dendrimer build by this iterative process.

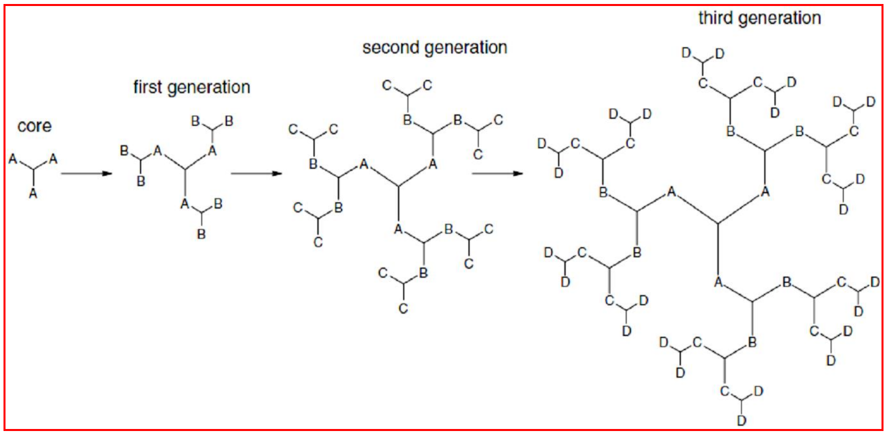

Fig. 3: Generation of a dendrimer

4. Synthesis of Dendrimers

Two strategies have been proposed for preparation of dendrimers:

1. *Divergent method* describes the successful attachment of one set of branching units, (characterized by their multiplicity) to central core. Numerous reactions are performed on the same molecule. At least a coupling and a deprotection step is required in successive addition of each generation so that growth occurs at the rate of one generation at a time rather than by uncontrolled polymerization. Thus many synthetic pitfalls are avoided during dendrimer synthesis by using divergent method.

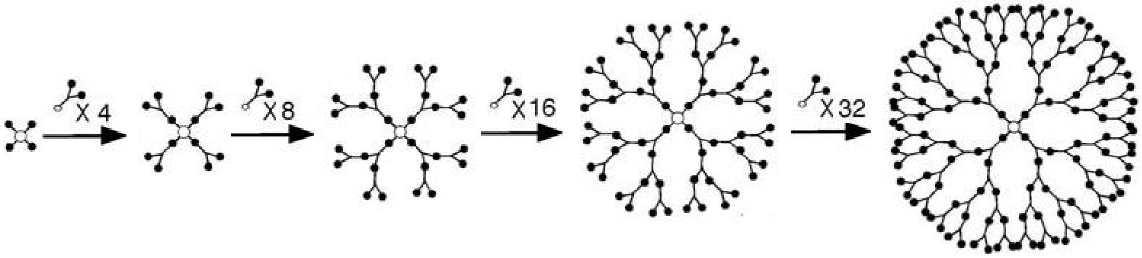

Fig. 4: Synthesis of dendrimer by using *Divergent Method*

2. *Convergent method* includes the building of dendrimer by starting from outside. In this type of a method, separate fragments are build for the dendrimer synthesis and in the final step, all fragments are linked to a common core. Thus, number of individual reaction

steps are reduced for a single molecule reaction. We can understand by an example shown in figure 5. In the first step, three monomeric units are connected. Next, other monomeric units are connected with two of these three monomers. A large part of dendrimer increases due to this step wise coupling and finally it is fused together to built up a spherical dendrimer.

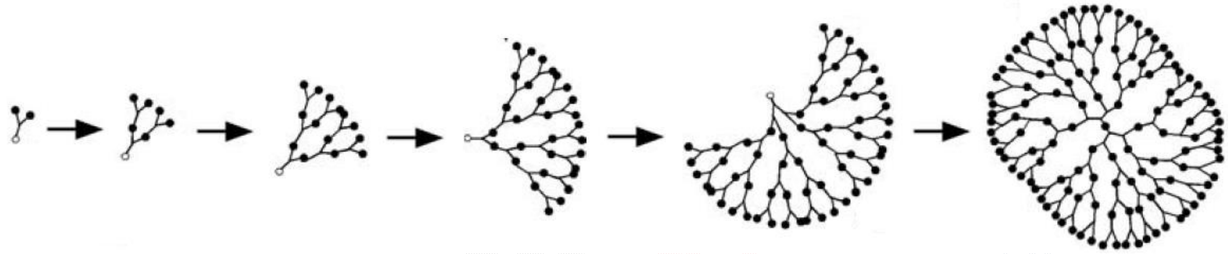

Fig. 5: Synthesis of Dendrimer by using *Convergent Method*

Various structures of dendrimers can be prepared in stepwise processes. The synthesis of blocktype dendrimer is shown in figure 6. For the synthesis of blocktype dendrimer, one side of the central molecule is activated, then hemispherical dendrimer in selectively formed. These type of processes provide ñhalf & halfò type dendrimers. For the synthesis of amphiphilic block type dendrimers, the hydrophilic groups and hydrophobic groups are introduced separately. This type of dendrimer forms a monolayer on the surface of water.

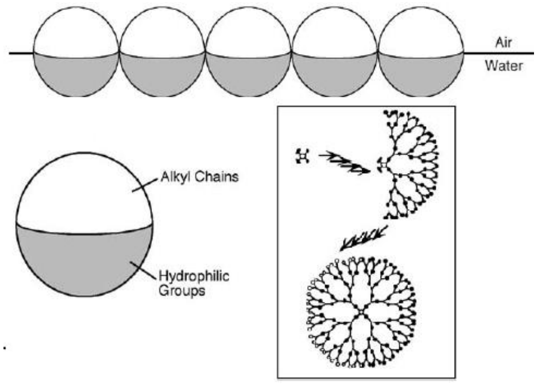

Fig. 6: Structure and synthesis of a block dendrimer, and schematic showing a block dendrimer monolayer on the surface of water

Star-shaped dendrimers (Figure 7) can be synthesized by using stepwise dendrimer growth and subsequent linear polymerization protocol. By following this strategy, a dendrimer with oligosaccharide chains on its outer surface was produced. This type of dendrimer is densely covered with sugar residues thus, providing it ball-like shape and therefore it is known as ósugar ballô. The sugar ball is a useful model for investigation of sugar based biological recognition processes such as virus binding.

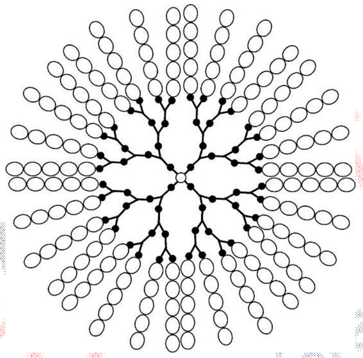

Fig. 7: Star Shaped dendrimer

5. Characterisation of Dendrimers

It is tough to determine the purity of dendrimer (percentage of defect free dendrimer) due to their large size and high symmetry. Various characterisation techniques such elemental analysis, chromatography (*e.g.* HPLC), NMR spectroscopy are used, but small amount of impurities are generally not exposed in higher-generation dendrimers. Some other methods such as mass spectroscopy, modern ionisation techniques like electrospray ionisation (ESI), and matrix-assisted laser desorption ionisation (MALDI) are widely used for the determination of purity of a dendrimer. We can understand the characterisation of a dendrimer through the ESI-MS spectrum of the fifth generation poly(propylene imine) dendrimer (Figure 8). The dendritic purity at each stage may be calculated by an iterative procedure by using the knowledge of the mass spectra of all of the previous generations of the dendrimer. The simulated spectrum, which agrees well with experiment, gives a polydispersity of 1.002 (= *Mw*/*Mn*; the ratio of observed versus theoretical molecular weight) and a dendritic purity of 23 %.

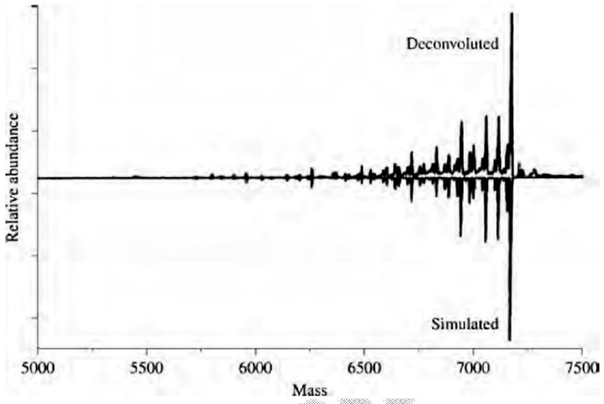

Fig.8: Experimental and calculated ESI–MS spectra for poly(propylene imine) dendrimers

6. Physical Properties of Dendrimers

Physical property wise, dendrimers depend on the nature of the component groups and the interactions between them to a large extent. The surface density and the number of available functional groups of dendrimer can be reduce due to **back-folding** of dendrimer. Indeed, there is an entropic penalty in adopting an open, extended and porous structure. In high molecular weight compounds, solution properties of linear macromolecules are differ as compared to dendrimers. The molecular weight of a dendrimer increases exponentially and the volume occupied by a dendrimer increases cubically with every generation, this means the viscocity of dendrimer does not increase with molecular mass, but reaches a maximum at a certain limiting generation. The size of dendrimer also depends on the solvent. Dendrimers adopts a more open structure in solvents for which they have a high affinity.

7. Application of Dendrimers

Dendrimers are applied in various useful synthesises and properties like supramolecular assemblies, nanodevices, Magnetic Resonance Imaging (MRI), electron transformation, drug delivery etc.

Supramolecular Dendrimer Assemblies : Dendrimers can also be assembled non-covalently. Fréchet type dendrimers have been used for this strategy. Fréchet type dendrimer is appended to a double isophthalic acid functionalised molecular cleft. Isophthalic acid is self-complementary and forms a hexagonal assembly of six units (Figure 9).

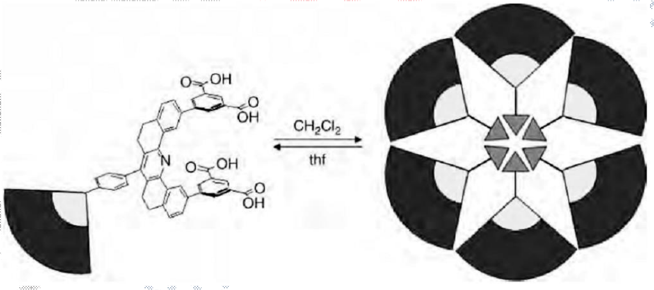

Fig. 9: Hexameric assembly of dendrons by isophthalic acid hydrogen bonding interactions

The highly stable assembly is obtained due to the presence of two hexagonal units and their insulation from the surrounding medium by a dendrimer portion. Fréchet-type dendrimers have also been used as ligands for lanthanide(III) ions in a novel variation of the convergent strategy using focal point functionalised dendrons (Figure 10).

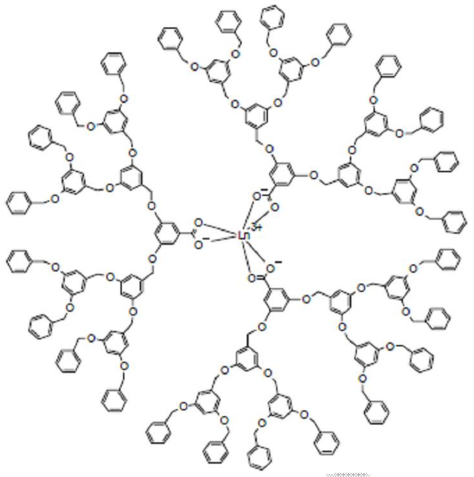

Fig. 10: Lanthanide(III) ion containing dendrimer

In this type dendrimer assembled supramolecule, the focal point is a carboxylate moiety. It is an excellent ligand for the oxophilic lanthanides. Lanthanide fluorescence is improved by the isolation final of the lanthanide ion and the antenna effects of the dendrons. These kinds of species are reminiscent of the light harvesting and conversion devices. The ócomplex-as-metals, complexes-as-ligandsô strategy is an excellent way to prepare metallodendrimers.

Dendritic Nanodevices: Organic dendrimers such as the ónanostarô dendrimer (Figure 11) exhibit energy transfer and light-harvesting properties, because of their fully delocalised nature, which allows orbital overlap and hence Dexter-type excitation transfer. Dendritic cascade type coordination complexes also showed light energy transfer property, in which light energy is transferred from the outside of an inorganic dendrimer to a core chromophore. This type of process mimics the energy transfer cascade in natural photosynthesis. The emission intensity of ónanostarô dendrimer, which is based on a perylene chromophore, is 400 times greater than that of the control molecule 1-ethynylperylene.

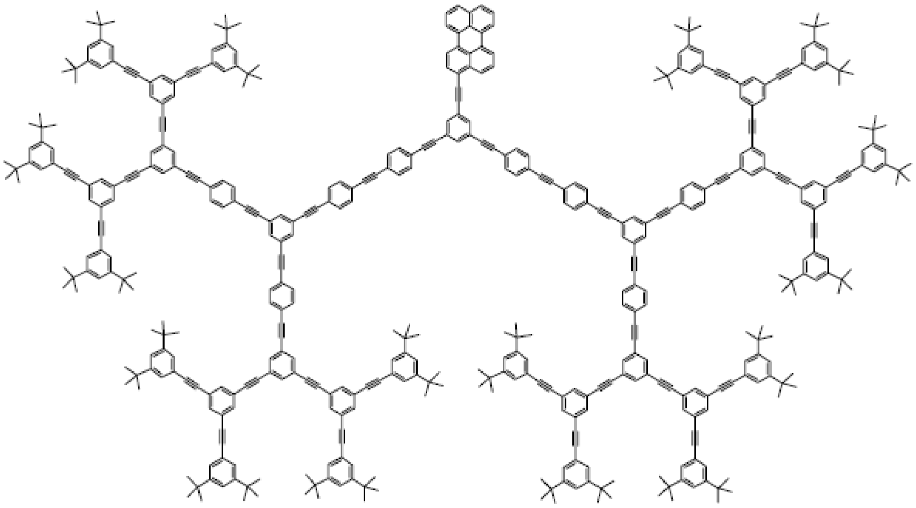

Fig. 11: 'Nanostar' dendrimer

Dendrimer in Electron Transformation: A dendrimer can be made to induce adsorption of counterionized functional molecules after attachment with ionized groups onto the outer surface of a dendrimer. Anionic groups containing porphyrin dendrimer have been shown to adsorb the electron acceptor methylviologen (MV^{2+}) (Figure 12).

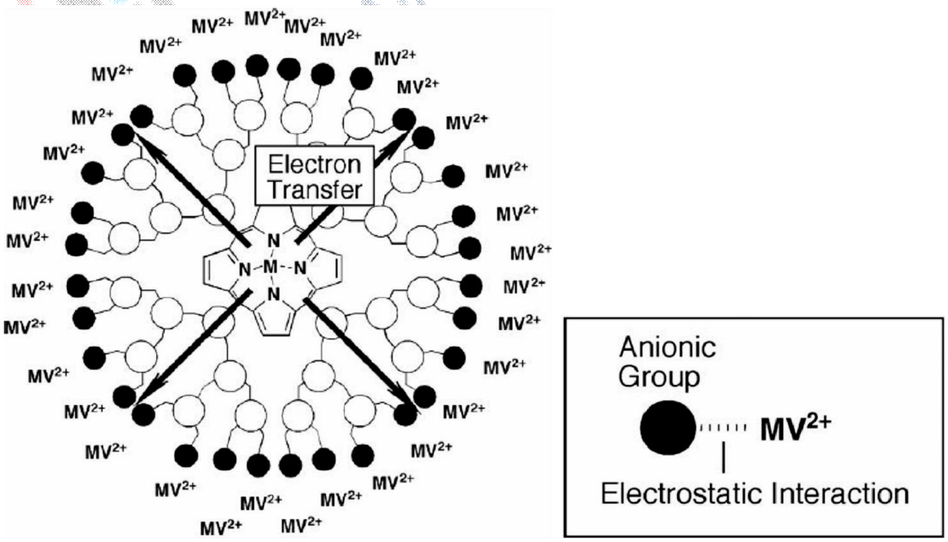

Fig. 12: Electron transfer via a dendrimer core

Electron transfer is induced by the photoexcitation of the central porphyrin to the adsorbed methylviologens. The size of dendrimer also affects the transfer of an electron. As the size of the dendrimer increases, electron back-transfer gets effectively suppressed and a long-lived electron separation state is achieved. The number of units increases toward the outside of the molecule, the dendrimeric structure become useful for functions such as accumulating energy on the outside and passing it to the center. This dendrimer function mimcs the light-harvesting process associated with photosynthesis. We can understand this concept by considering isomerization of azobenzene by energy collection (Figure 13). As shown in figure 13, infrared light excites the benzene groups in each unit. The transformation of the central azobenzene from a *cis* configuration to a *trans* form is induced by the collected energy. Without a dendrimer shell, this transformation cannot be achieved by irradiating azobenzene. This is because sufficient energy is not passed to azobenzene which can be accumulated by it and cause the transformation. This takes place due to energy loss through molecular collisions.

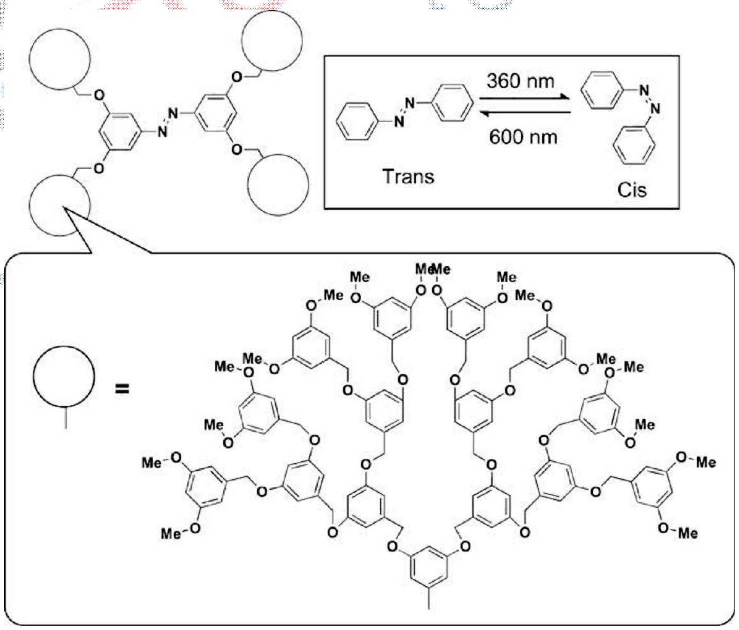

Fig. 13: Azobenzene isomerization through energy collection

Dendrimer in Magnetic Resonance Imaging (MRI) application: Dendrimer devices are also useful in magnetic resonance imaging (MRI) applications. The dendrimers act as carriers for paramagnetic Gd(III) ions. A large number of Gd(III) ions can be bound per dendrimer. The residence time of the dendrimer-lanthanide conjugate in the bloodstream is thus increased due to the large size of dendrimer and this allows the radiologist to perform more detailed imaging studies. Moreover the relaxation properties of the Gd(III) ions are dramatically improved compared to small molecule analogues.

Attachment of the exterior surface of the dendrimer also allows a significant degree of biological recognition between the contrast agent and a target site. Another biological application of dendritic nanodevices is their correlation antibody assays. The regular spacing between antibody and solid support introduced by replacing a secondary antibody spacer with a dendrimer reduces non-specific interactions between an immobilised antibody and an analyte and this improves manufacturing properties. Dendrimers have also been used as vectors. It carries genetic material into cells and as anti-cancer agents after combining with platinum based anti-cancer drugs such as *cis*-platin. The cancer cells are more permeable to the large dendrimers than normal cells. The high density of surface functionality of dendrimer allows it to build multivalent interactions between functionalized dendrimer and biomolecules. This feature of dendrimer has been used in the bonding of dendrimer-saccharide conjugates to proteins such as lectins. The viral inhibition activity improved after the multiple interactions.

Dendrimers also play an important role as a drug delivery agent for therapeutic drugs. This specific property of a dendrimer makes it possible to bind those guests and then let them dissociate at a known rate. This ócontrolled releaseô property makes dendrimers potential candidates as drug delivery agents as shown in figure 14.

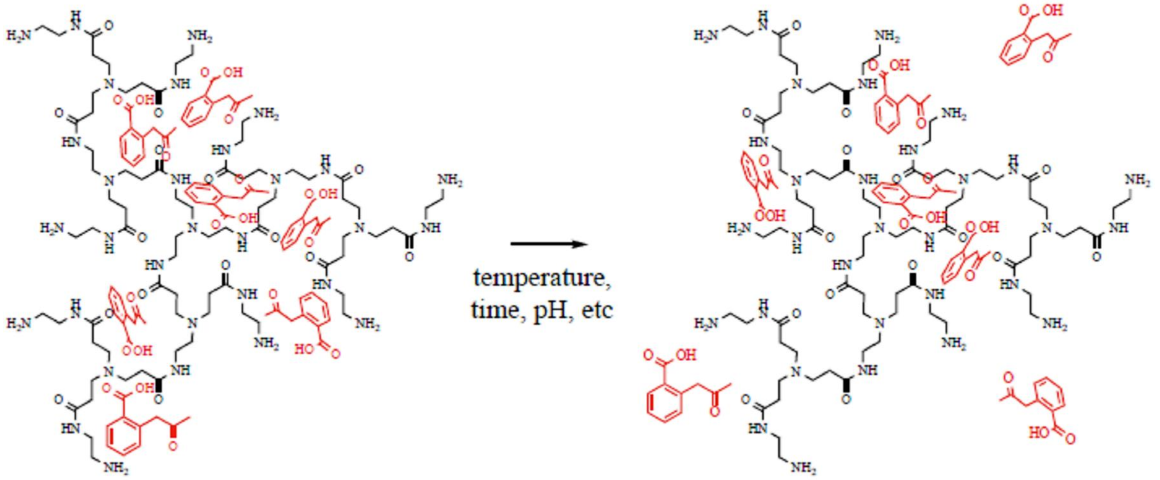

Fig. 14: Controlled release of therapeutic drugs by a dendrimer

8. Summary

- Dendrimer is ótreeô shaped compound which has branch type functional group which makes it appropriately analogous to a molecular tree.
- Dendrimers are synthesized by divergent and convergent methods.
- Dendrimers are characterized by NMR, mass spectroscopy, electrospray ionisation (ESI), and matrix-assisted laser desorption ionisation (MALDI).
- Dendrimers are widely applicable as a carrier agent in various type of biological active compounds.

Subject	Chemistry
Paper No and Title	**14: Organic Chemistry- IV (Advanced Organic Synthesis, supramolecular chemistry and carbocyclic rings)**
Module No and Title	**23: Gelators, Fibres and Adhesives**
Module Tag	**CHE_P14_M23**

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1. Learning Outcomes

After studying this module, you shall be able to understand:

- Basics of gelators
- Compounds responsible for gelator formation
- Applications of gelators
- Basics of fibre
- Classification of fibres
- Applications of fibres
- Basics of adhesives
- Classification of adhesives
- Applications of adhesives

2. Gelators

2.1 Introduction

Any substance capable of forming a gel is termed as gelators. A gel is a soft, solid or solid-like material that contains both solid and liquid components. The solid components are called the gelators. This is present as a mesh/network of aggregates, which immobilizes the liquid component. Dorothy Jordon Lloyd proposed in 1926: "only one rule seems to hold for all the gels and that is that they must be built up from two components, one which is a liquid at the temperature under consideration and the other which, the gelling substance proper, often spoken of as the gelator, is a solid. The gel itself has the mechanical properties of a solid i.e. it can maintain its form under stress of its own weight and under any mechanical stress it shows the phenomenon of strain."

Gels can be classified in different ways based upon the chemical nature of components or physical state of bulk phase. In general, gels are classified as chemical gels and physical gels. In chemical gels, the formation of crossed-linked network occurs through covalent bonding where as in case of physical gels, the formation of crossed-linked network occurs through non-covalent interactions. During the formation of gels, organic molecules are involved as solid components. These are sometimes also called as organogelators. On the basis of components, organogelators are classified as:

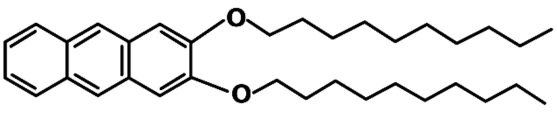
(i) One-component organogelators and
(ii) Two-component organogelators

2.2 One-component organogelators

In one-component organogelators, a compound is present in solution and forms gel with the solvents. The gelators molecules are stacked one after one to form gel networks by non-covalent interactions such as π- π stacking, hydrogen bonding, Van der Waals interaction etc. and hence comes under physical gels. Different types of compound given below have been used as one-component organogelators.

2.2.1 Anthracene derivatives

The compound, 2,3-bis(*n*-decyloxy)anthracene, (**1**) is a good organogelator and works at low concentration for wide range of solvents ranging from alkanes to alcohols, ethers, ketones or halogenated molecules. The molecules of **1** are self-associated by Van der Waals interactions and dipolar force. This gelator also has ability to grow organically modified hybrid silica fibres. Another anthracene derivative, 2,3-bis(*n*-decyloxy)anthraquinone (**2**) is also an efficient gelator of organic solvents.



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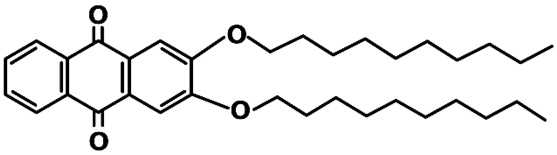

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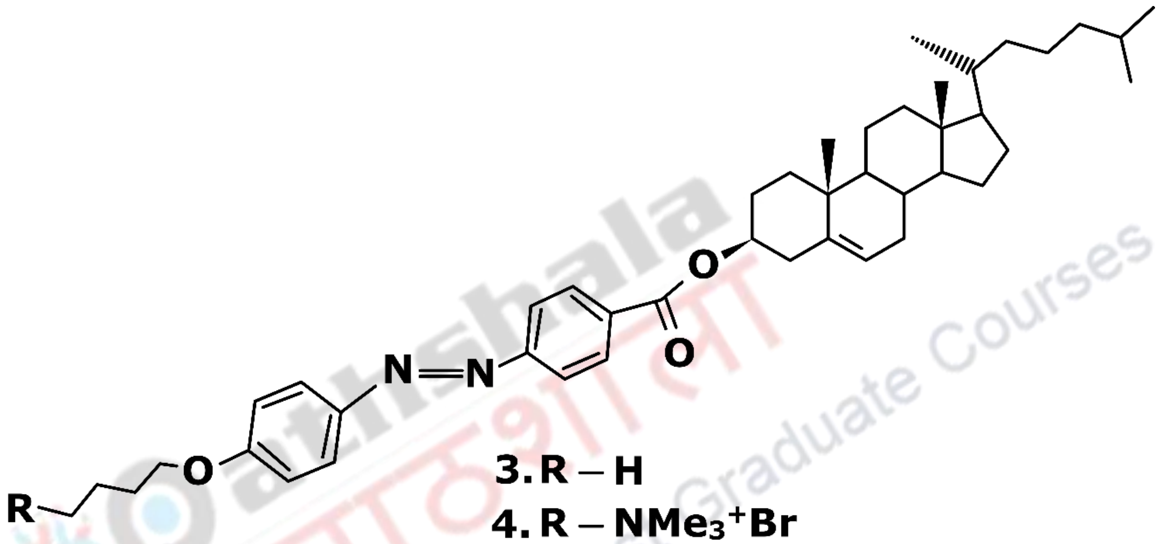
2.2.2 *Steroidal-benzene conjugates*

The steroidal-aromatic conjugate organogelators consist of an aromatic group linked to steroidal moiety through a suitable linking group. The compounds **3** and **4** possess the gelation properties in various organic solvents.

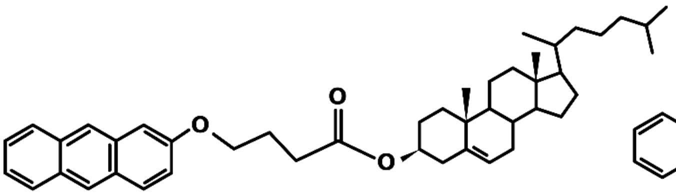


3. $R - H$

4. $R - NMe_3{}^{+}Br$

2.2.3 *Steroidal-anthracene derivative conjugates*

The cholesteryl 4-(2-anthryloxy) butyrate (CAB, **5**) is a steroidal-anthracene conjugates and gelate a wide range of solvents like alkanes, alkenes, alcohols, aldehyde, carboxylic acid esters, amines and aromatic solvents. Another conjugate compound **6** also gives gelation properties with organic solvents. The replacement of 2-anthryl part of compound **6** by other groups like phenanthryl, pyrenyl, or 9-anthryl did not give the gelation properties with organic solvents. The driving force for the formation of aggregates leading to the gelator molecules was due to π- π stacking, Van der Waals interaction and other non-covalent interactions.



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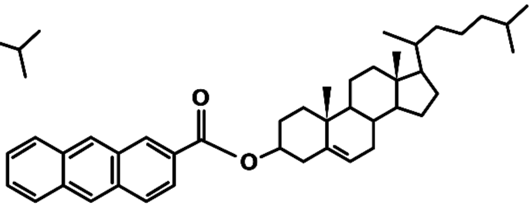

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2.2.4 Terpenoid-benzene conjugates

A terpenoid-benzene conjugate **7** is able to form gel with different alcoholic and mixed solvents. This compound gives stable and efficient gels with aliphatic alcohols at <1 wt% of the gelators.

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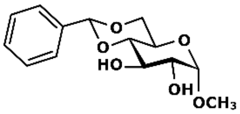
2.2.5 Sugar-based organogelators

The sugar based compounds also acts as strong organogelators for various organic solvents. The compounds **8-14** like methyl benzylidene monosaccharides are very effective organogelators. They form aggregate with the solvent molecules through the formation of a hydrogen bond. The formation of the hydrogen bond can be authenticated by FT-IR and temperature dependent NMR spectroscopy. The polar sugar parts can form a chain of intermolecular hydrogen bonds in organic solvents and exposes the aromatic parts to the solvent.



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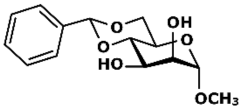

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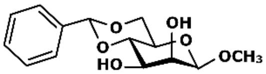

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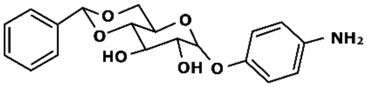

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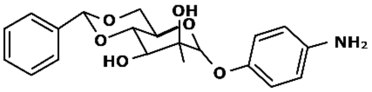

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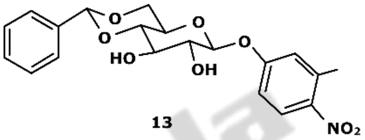

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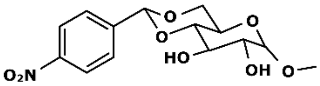

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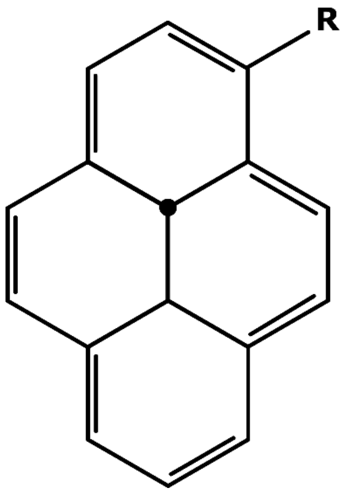
2.3 *Two-component organogelators*

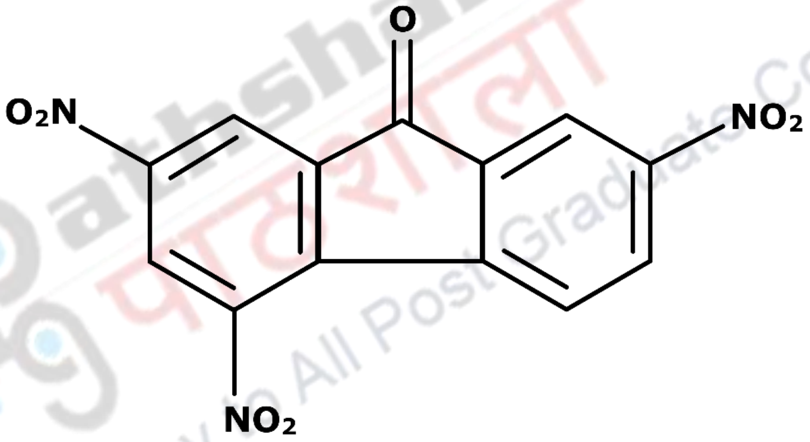
In a two-component gelator system, one component can be present in isotropic solution, and only on additions of the second component, a gel is actually formed. In this system, one compound forms a complex with another compound using donor-acceptor interaction, hydrogen bonding etc. Different types of compound given below have been used as two-component organogelators.

2.3.1 *Pyrene-based gelators*

The pyrene derivative compounds (**15-18**) formed gel with different organic solvents in presence of trinitrofluorenone (TNF, **19**) due to charge-transfer interaction between pyrene unit and TNF. The gels so formed have been found to be stable at room temperature for several days.



15 R = $COO(CH_2)_{15}CH_3$
16 R = $COO(CH_2)_7CH_3$
17 R = $(CH_2)_{11}CH_3$
18 R = $O(CH_2)_{13}CH_3$



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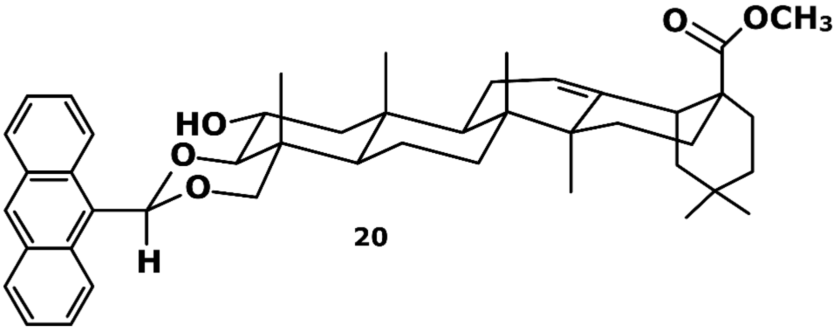
2.3.2 Terpenoid-based two-component gelator

The derivative of natural product arjunolic acid (**20**) forms thermo reversible gel with organic solvents in the presence of electron deficient guest like picric acid (**21**). The change in color from yellow to deep red was observed during gelation. The charge transfer interaction between the aromatic part of the triterpene derivative and picric acid has been observed and checked with temperature dependent UV-VIS spectroscopy.



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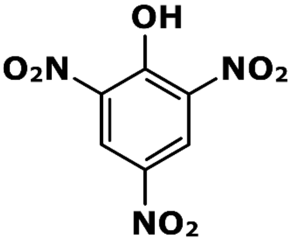

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2.4 *Applications of Gelators*

The primary applications of gelators are to form useful gels. The low-molecular weight-gelators are more important and received more attention in comparison to their polymeric counterpart for a number of applications. This is due to their thermo-reversible nature and prompt response to external stimuli. A good gelator must show critical balance between hydrophilic and hydrophobic interactions in the gelation process. The presence of an aromatic ring in small molecule gelator is very helpful in inducing self-aggregation towards gelation. The aromatic moiety having planar nature favors π–π stacking interactions between the molecules involved and leads to the formation of 3-D networks of gels. The gels formed have wide applications in different aspects of life including electronic and photonic applications like organic electronics imaging, sensing applications etc.

3. Fibres

3.1 *Introduction*

The word ‘Fiber’ is derived from the Latin word ‘Fibra’ which means a slender, elongated, threadlike object or structure. In English and French it is called fiber. It is defined as one of the delicate, hair portions of the tissues of a plant or animal or other substances that have length hundred times its diameter. In general, it is a morphological term for substances characterized by their flexibility, fineness and high ratio of length to cross sectional area.

The history of fibres is as old as human civilization. The fibres had been utilized dates back to the early Egyptians and Chinese who used papyrus mats in the pyramids and the Buddhist temples to reinforce and consolidate the foundations. The utilization of silk in semi-technical applications also goes back in history where the Mongolian armies wore silk next to their skin to reduce penetration of incoming arrows. The use of silk in wound dressing and open cuts in web and fabric form also dates back to the early Chinese and Egyptians eras. The fibres have enormous applications to mankind since history to present day and this will continue in future also.

3.2 Classification

Fibers are classified as given in figure 1.

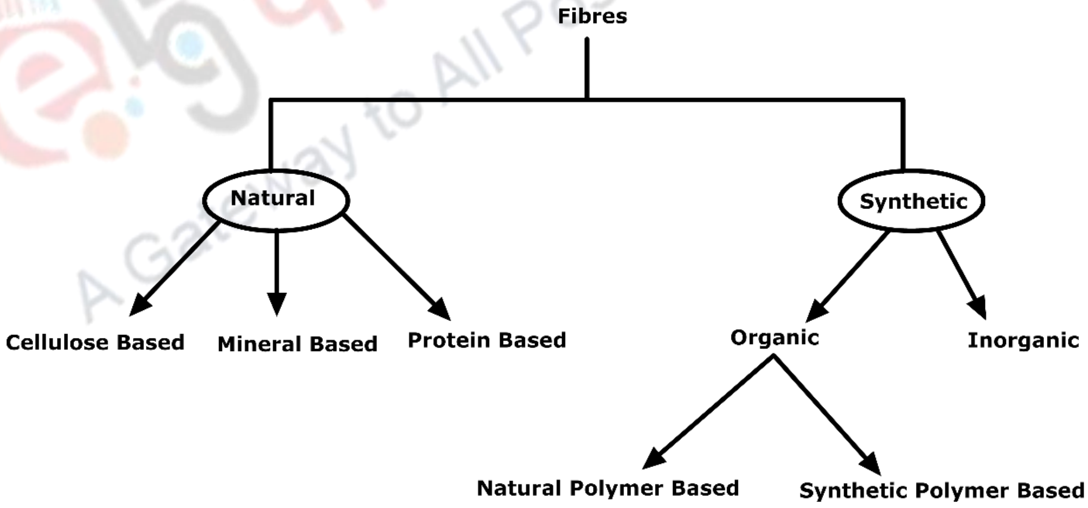


Figure 1. Classification of fibres

3.2.1 Natural fibres: Any fine hair like substance that are obtained from any natural sources are natural fibres. They are further grouped into three broad categories:

Cellulose based fibres
Mineral based fibres
Protein based fibres

Cellulose based fibres: They are also sometimes called plant fibres. They are extracted from plants and are also classified on the basis of part of the plant used. For example, cotton is cellulose based fibre (Figure 2) and obtained from seeds of cotton plants. The cellulose based fibres are also obtained from the stalk of plants like rice, maize, oat, wheat. Jute is another example of this class of fibres. This is extracted from the bark of the white jute plant, *Corchorus capsularis* and to a lesser extent from tossa jute (*C. olitorius*).

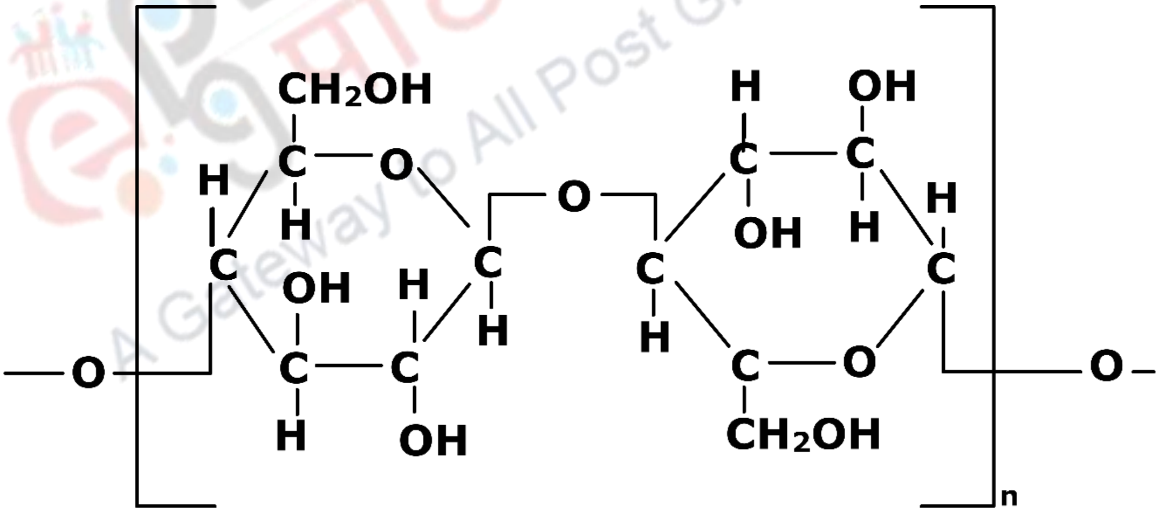


Figure 2. Chemical structure of cotton

Mineral based fibres: The inclusion of mineral based fibres under natural fibres is conditional. They are not renewable and include clay based, silicates, absestosiform etc. Usually they are obtained by spinning or drawing molten minerals.

Protein based fibres**:** They are also called animal fibers like silk and wool. The silk is obtained from the glands of insects (Figure 3), wool from hairy mammals and avian fiber from birds.

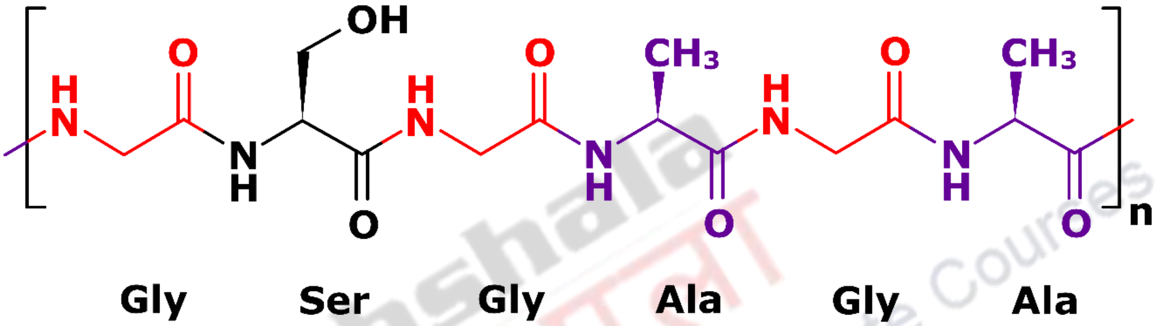


Figure 3. Chemical structure of silk fibroin

3.2.2 Synthetic fibres: The synthetic fibres are also called man-made or chemical fibres. They are synthesized in laboratories using chemicals. They are broadly classified into two types:

Organic fibers: Organic fibers are synthesized from petrochemicals based raw materials which are polymerized into long, linear fibers. They are further subdivided into two groups:

Natural polymers based
Synthetic polymers based

Natural polymers based: These are also called regenerated fibres or semi-synthetic fibres. These are derived from naturally occurring polymers. For instance, rayon (Figure 4) is made of the same cellulose polymers that make up cotton, hemp, flax, and the structural fibres of wood. The rayon is obtained from cellulose by reaction with sodium hydroxide (NaOH) and carbon disulfide (CS_2) and regeneration with sulfuric acid.

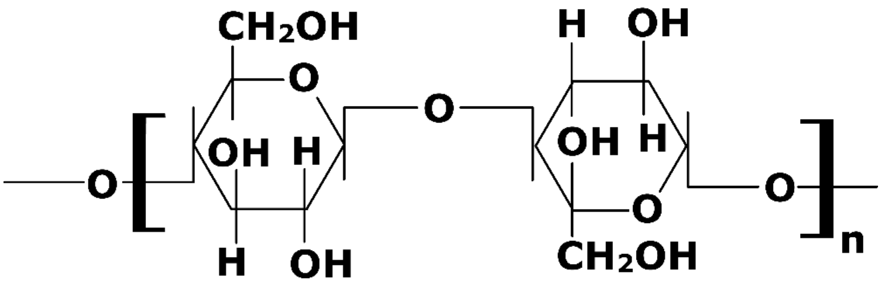


Figure 4. The chemical structure of rayon

Synthetic polymers based: The synthetic polymer based fibre is a class of synthetic fibre. They are made of polymers that do not occur naturally but instead are produced entirely in the chemical plant or laboratory. They are always obtained from by-products of petroleum or natural gas. These polymers include nylon and polyethylene terephthalate, acrylics, polyurethanes and polypropylene etc.

The first synthetic polymer based fibre that appeared on the world market was nylon 6,6 (Figure 5) in 1939. It was produced by DuPont and gained fast public popularity. The nylons are also referred to as polyamides in which the amide linkage is the common factor.

Another popular fibre known as polyester was also first introduced as Dacron by DuPont in 1951. This is today the second most used fibre after cotton and other synthetic fibres in terms of both production and consumption. The most popular polyester, polyethylene terephthalate (PET) is made by the condensation polymerisation of ethylene glycol and terephthalic acid (Figure 6). The product is further processed by melt extrusion and drawing.

Polyacrylic fibre is a polyacrylonitrile and is wool-like fibre produced by the polymerization of acrylonitrile. This is an addition polymer (Figure 7). They can spin into fibres by dry or wet spinning methods. Other addition polymers like polyolefin fibres such as polyethylene and polypropylene made from ethylene and propylene are also find their applications. Polyethylene has moderate physical properties with a low melting temperature of about 110°C for its low density form and about 140°C for its high density form which severely restricts its application in low temperature applications. Polypropylene has better mechanical properties and can withstand temperatures of up to 140 °C before melting at about 170°C

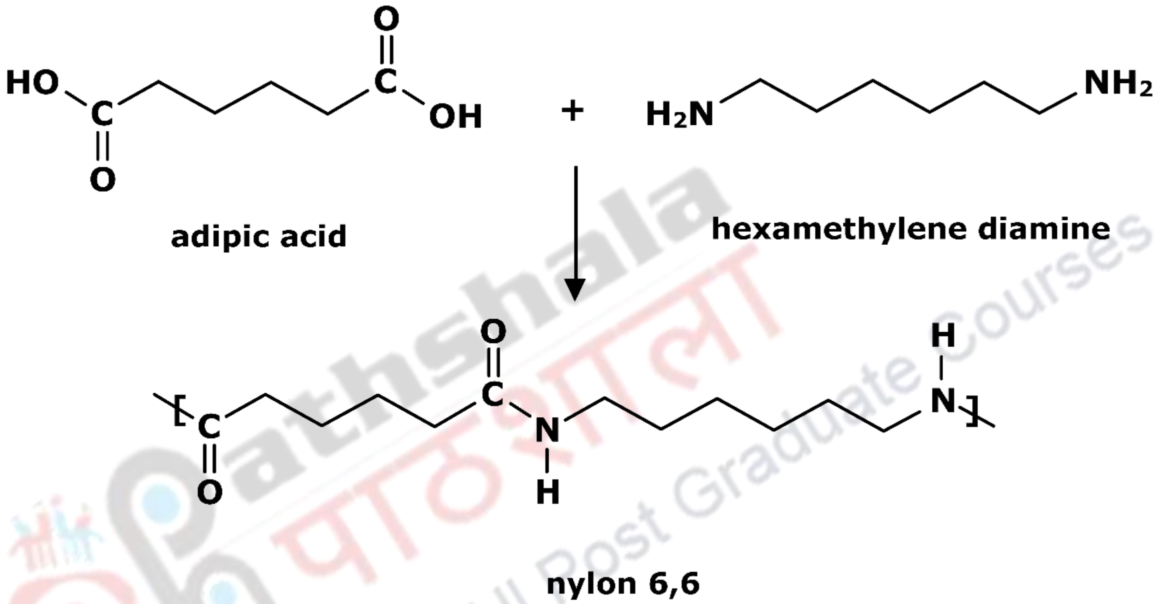


Figure 5. Synthesis of nylon 6,6

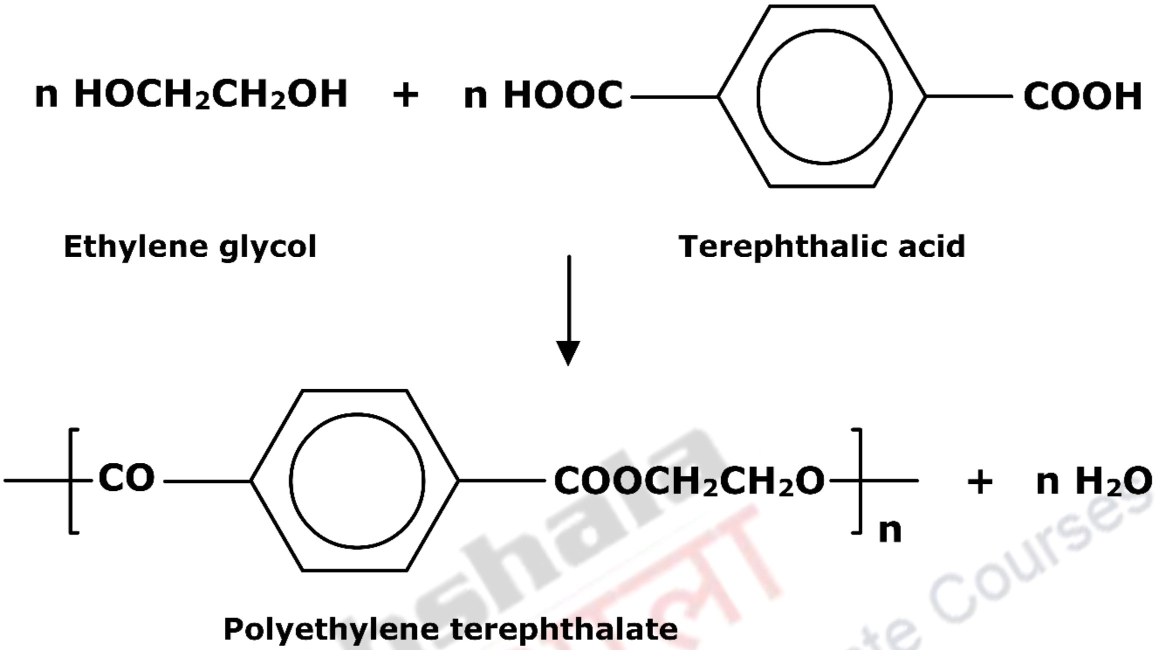


Figure 6. Synthesis of polyethylene terephthalate (PET)

Figure 7. Synthesis of polyacrylonitrile

Inorganic or metallic fibres: The fibres which are produced from materials those are present in the earth's crust and that are inorganic rather than polymeric in nature. Examples that are currently being used or considered as sources of fiber are glass, metals, carbon, asbestos and ceramics.

A comparison of natural and synthetic fibres is summarized in table 1.

Table 1. A comparison of properties between natural and synthetic fibres

Property	**Natural fibre**	**Synthetic fibre**
Origin	Natural	Completely man made
Length	Decided by nature	Controlled by man
Type	Staple or filament form	Mostly filament form but sometimes cut into Staple form
Spinneret	No need	Essential for filament production
Spinning process	Not required	Required (melt, wet or dry) for filament production
Chemical solution	Not required for yarn production	Essential for yarn production
Comfort	Very comfortable to wear	Not so comfortable
Dust and impurities	Present	Not present
Fiber structure	Not possible to change	Possible to change
Color	Grows with natural color	Artificial colors are added
Crimp	Natural crimp is present	Crimp is applied on filament
	Mostly hydrophilic	Mostly hydrophobic
Dye	Easy to dye	Not so easy to dye
After burning	It becomes ash	It melts
Smell after burning	Hair burn or paper burn	Chemical smell
Cost	High	Comparatively low
Environmental concerns	Environmental friendly	Not so environmental friendly
Durability	Less durable	More durable
Use	Limited	Multi tasking

3.3 Applications of fibres

Fibres have their utilities in all walks of life. Few important and notable applications are listed below:

1. Transport applications are an important end-use area for fibres. The products have their applications in tyre, belt, safety belts and air bags.
2. The fibres are utilized as technical textiles in industrial products such as filters, conveyor belts and abrasive belts, as well as reinforcements for printed circuit boards, seals and gaskets and other industrial equipment. The use of nonwovens outweighs that of woven and other fabric types. The consumption in 2000 is estimated at 700000 tonnes and a little over 400000 tonnes, respectively.
3. The fibres are also an important component for hygiene applications such as wipes, babies' diapers (nappies) and adult sanitary and incontinence products. Although, attempts have been made to develop and introduce more efficient biodegradable fibres for such end-uses at low cost to avoid land-fills and other environmental hazards.
4. The fibres have its utility in household also. Hollow fibres with excellent insulating properties are widely used in bedding and sleeping bags. The fibre has also replaced foams in furniture due to fire and other health hazards posed by such materials.
5. The woven fabrics are used in carpet and furniture backings and in some smaller, more specialized areas such as curtain header tapes.
6. Nylon 6,6 is a popular household carpet fibre
7. Polyethylene and polypropylene polymeric fibre have a density less than that of water which allows them to float as ropes, nets and other similar applications. The availability, low cost and good resistance to acid and alkaline environments of polypropylene has greatly influenced its growth and substantial use in geotextile applications.
8. The cloths and clothing components are the biggest consumer of fibres. This category include sewing threads, interlinings, waddings, insulation and the main outer and lining fabrics of garments.

9. The fibres find its applications in agriculture, horticulture and fishing also. These industries used fibre in the form of nets, ropes and lines and materials for covering, protection and containment applications.

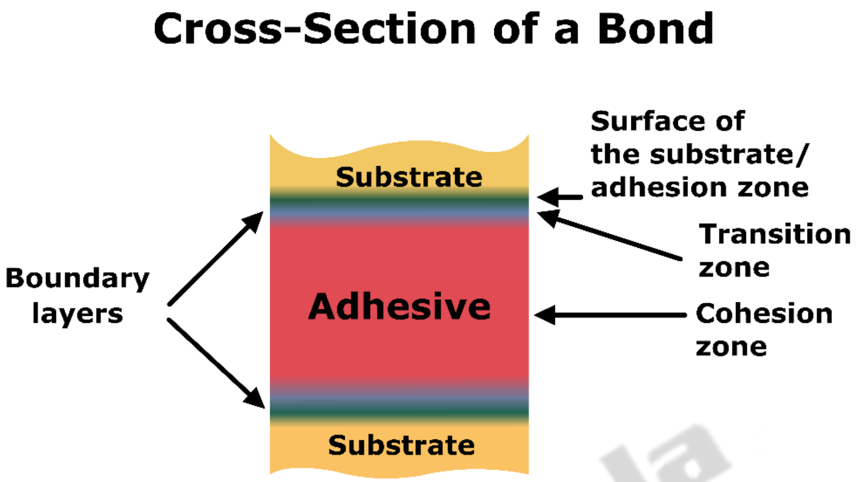
10. The fibres are also used for making temporary structures such as tents, marquees and awnings at the tie of natural calamities.

4. Adhesives

4.1 Introduction

An adhesive is a material used for holding two surfaces together either by applying on one surface only or on both the surfaces. The basic definition of an adhesive as used by the Adhesive Sealant Council in America is ‘a material used for bonding that exhibits flow at the time of application’. According to Wu, ‘adhesion refers to the state in which two dissimilar bodies are held together by intimate interfacial contact such that mechanical force or work can be transferred across the interface. The interfacial contact is usually arising from van der Waals forces, chemical bonding, or electrostatic attraction.

In today’s life, adhesives are used everywhere, starting from postage *stamp to* highly technological manufacturing. The adhesives have taken the place of other joining processes like age old, bolts and welding and hence reduced the cost of manufacturing and labour. The major customers of adhesive companies are the construction sector, automotive manufacturers, aircraft manufacturers, and packaging industries. The adhesives industry is one of the largest in the world and comprising of the multi-billion dollar industry. They can be used to join metals, ceramics, rubber, plastics, cork and other combinations of materials (Figure).



Some important requirements for a substance to act as an adhesive are:

a. It must wet the surface on which it is applied
b. It must stick to the surface, once applied.
c. It must develop strength after it has been applied.
d. It should remain stable.

The joining of two materials using adhesives has some advantages and disadvantages.

Advantages of using adhesives

a. Joins thin or thick materials, similar or dissimilar materials of any shape
b. Leads to uniform distribution of stress and larger stress-bearing area
c. Reduce or prevent electrochemical corrosion
d. Make joints with smooth contours and protect against a variety of environmental factors
e. Insulate against heat transfer and electrical conductance
f. Reduce vibration and absorb shock
g. Have excellent strength/weight ratio with quicker action

Disadvantages of using adhesives

a. Proper choice of adhesive is required for specific purposes.
b. Surface preparation played significant role to obtain durable bonds.
c. Long cure times needed, particularly where high cure temperatures are not used
d. Cleanliness is required for most adhesives
e. For initial fixing, holders are necessities.
f. The process is temperature sensitive.
g. Natural origin adhesives are susceptible to attack by bacteria, mold, rodents etc.

4.2 Classification of adhesives

Adhesives can be classified on the basis of many aspects as given below:

4.2.1 On the basis of sources

Natural adhesives: The natural adhesives are based on vegetable and animal-based sources. The organic materials like casein, blood, albumin, hide, bone, fish, starch, etc and inorganic materials like sodium silicate acts as natural adhesives. Most of their applications are limited to paper, paperboard, foil, and light wood. Theses adhesives have a long shelf life but low strength properties.

***Synthetic adhesives*:** The adhesives that are not natural are synthetic. The adhesives like elastomeric, thermoplastic, thermosetting, alloys, structural adhesives are synthetic.

4.2.2 On the basis of chemical composition

***Thermosetting adhesives*:** The adhesives that cannot be heated and melted after the initial cure are known as thermosetting adhesives. The curing takes place by chemical reactions at appropriate temperature depending on the type of adhesive. This type of adhesives requires considerable pressure. Examples of thermosetting adhesives are polyester, polyimide, urea-formaldehyde, polybenzimidazole etc.

Thermoplastic adhesives**:** Thermoplastic adhesives can be melted without significant change in their properties and do not cross-link during cure. They are single-component system. Wood glues are thermoplastic emulsions. These are common household items. They harden by evaporation of water from an emulsion. Examples of these types of adhesives are cellulose acetate, polyvinyl acetals, cellulose acetate butyrate, polyvinyl alcohol etc.

Elastomeric adhesives**:** These materials are polymeric in nature. They have better toughness and elongation. Most of these adhesives are solvent dispersions of water emulsions. They have relatively low bond strength but flexibility is excellent. Some examples of elastomeric adhesives are natural rubber, styrene-butadiene rubber, poly-isobutylene silicone etc.

Adhesive alloys**:** Adhesive alloys forms by the ccombination of resins of two different chemical groups chosen from the thermosetting, thermoplastic, or elastomeric adhesives. In most of these adhesives, heat and pressure are required for curing. They are solvent-based dispersions. They are stronger over wider temperature ranges. Examples of adhesive alloys are epoxy-phenolic, neoprene-phenolic, epoxy-polysulfide etc.

4.2.3 On the basis of function

Structural adhesives**:** Structural adhesives are of high strength and performance. They hold structures together and capable of resisting high loads. Polyaromatics, polyester and polyurethane are some example of this type.

Non-structural adhesives**:** Non-structural adhesives do not withstand substantial loads. They only hold materials in place. Examples include adhesives that fill gaps and rubber cements that used to stick paper to paper in office applications.

4.2.4 On the basis of physical form

Liquid adhesives**:** These exist in liquid state and applied by means of mechanical spreaders.

Paste adhesives**:** These adhesives have high viscosities and applied on vertical surfaces with very less tendency to sag or drip. An example is modified epoxy adhesive that has superior strength in metallic and composite structure like BR® 95 paste adhesive.

Tape and Film adhesives**:** These adhesives lead to a uniform thickness and offer the advantages of easy dispensing. These are available as pure sheets of adhesive, or with film or paper reinforcement.

Powder or Granule adhesives**:** These adhesives exist in either powder of small granules. They are heated or dissolved in a solvent to get converted to a liquid form and then further applied to the required surfaces.

4.3 Applications of adhesives

The applications of adhesives depend upon the selection of materials, quality, performance of the product and economy involved. They have unlimited applications from household to big industries.

Some of the most frequent applications of adhesives are given below:

1. In small scale industries like food products related industry, toys or stationary items, adhesives play an important role in packaging and processing.
2. In large scale industries, adhesives are used in assembling spare parts of machines, car paints or branding them with labels.

3. In construction industries, adhesives are applied for uniform distribution of stress. In addition to this, for painting and furnishing and home décor adhesives play an important role.
4. They are used in households for various day to day applications from glue sticks, cellotapes or gums.
5. In the paper industry where they are used in multiwall bags, in paper backs, as book-binding and case making, corrugated paper etc.
6. They are also used in gummed tape, textiles.
7. They are used in n rubber gasket to steel bonding, paper to steel etc.
8. They are used in some applications of wood to wood bonds, metal to plywood bonds, metal to metal, metal to plastic bonding.
9. They are used as dental cements.
10. They are used in electrical tapes, sealing tapes, ceramic tile adhesives, flooring adhesives, pipe adhesives and pressure sensitive tapes etc.
11. They are used in formation of micaboard and used in abrasives, making laminated safety glasses, brake linings, foundry industry, fibre bonding, plywood.
12. They are used in making hot melt adhesives and for flooring, paper lamination, flocking adhesives etc.
13. They are used for bonding stone chips as concrete, grains to form mortar for bricks etc.
14. They play an important role in the medical device industry.

5. Summary

- This module deals with gelatos, fibres and adhesives.
- A gelator is a gel forming substance.
- On the basis of components, organogelators are classified as one-component organogelators and two-component organogelators.
- In one-component organogelators, a compound is present in solution and forms gel with the solvents.
- The gelators molecules are stacked one after one to form gel networks by non-covalent interactions such as π- π stacking, hydrogen bonding, van der waals interaction etc.
- Different types of compound have been used as one-component organogelators. For example, Anthracene derivatives, Steroidal-benzene conjugates, Steroidal-anthracene derivative conjugates, Terpenoid-benzene conjugates, Sugar-based organogelators etc.
- In a two-component gelator system, one component can be present in isotropic solution, and only on additions of the second component, a gel is actually formed. Examples are Pyrene-based gelators, Terpenoid-based gelators.
- Fibre is defined as one of the delicate, hair portions of the tissues of a plant or animal or other substances that have length hundred times its diameter.
- Fibers are classified as natural fibres and synthetic fibres.
- Natural fibres are obtained from any natural sources.
- Synthetic fibres are also called man-made or chemical fibres. They are synthesized in laboratories using chemicals.
- Fibres have their utilities in all walks of life. Few important and notable applications are listed in the module.
- An adhesive is a material used for holding two surfaces together either by applying on one surface only or on both the surfaces.
- Adhesives can be classified on the basis of many aspects such as on the basis of sources, on the basis of chemical composition, on the basis of function and on the basis of physical forms.

- The applications of adhesives depend upon the selection of materials, quality, performance of the product and economy involved. They have unlimited applications from household to big industries.

Subject	Chemistry
Paper No and Title	14: Organic Chemistry- IV (Advanced Organic Synthesis, supramolecular chemistry and carbocyclic rings)
Module No and Title	22: Novel liquid crystals
Module Tag	CHE_P14_M22_e-Text

Principal Investigator		Co- Principal Investigator and Technical Coordinator
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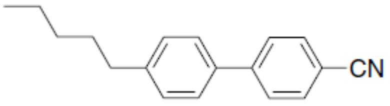
1. Learning Outcomes

After studying this module, you shall be able to:

- Know about liquid crystals and their nomenclature and shape.
- Understand the behavior of liquid crystals with different temperature range.
- Learn about supramolecular liquid crystals.
- Know how liquid crystals are used in daily life.

2. Introduction

*Mesomorphic*or *liquid crystalline* defined as true long-range order in liquids. The term 'liquid crystal' is highly evocative of the true state of the substance that contain the facile deformability and some of the bulk order of the crystalline state and dynamics of the liquid phase. Actually, liquid crystals is an intermediate phase between solid and liquid or in some cases, a series of liquid phases also. The origin of this anisotropic behavior is mainly a function of molecular shape. Mesogens are molecules which are formed by liquid crystals. Mesogens generally have either long and cylindrical (rodlike), such as 42-*n*-pentyl-4-cyanobiphenyl(**13.3**) and cholesteryl nanonoate(**13.4**) or flat and circular (disclike) shape, like *hexakis*((4-octylphenyl)ethynyl)benzene(**13.5**) and *bis*(3,4-nonyloxybenzoyl)methanato copper(II) (**13.6**).



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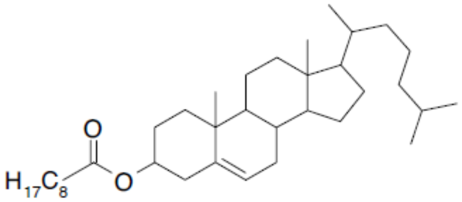

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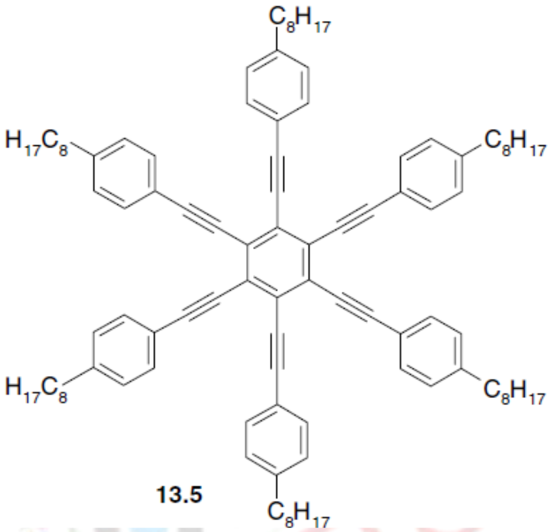

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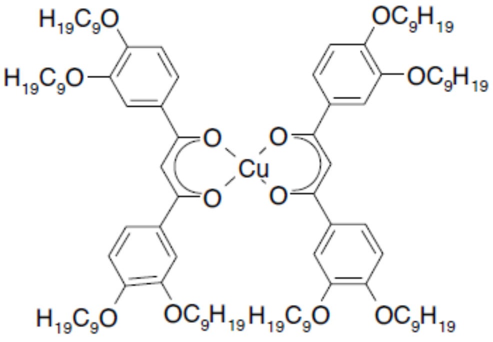

13.6

Fig. 1: Shape of mesogens

Polymer or aggregates such as elongated micelles behavior also been found in mesogens. Mesogenic behavior is also found in alkyl-chain-substituted hydrogen-bonded 2,6-diaminopyridine-uracil (PU) system. Due to highly anisotropic shape of mesogens, a line up with one another in various ordered ways was found, partly as a result of intermolecular interactions, and partly because the molecules are bulky and the liquid phase is relatively viscous. Mesogens are highly fluid and domains may be deformed very easily, this behavior show that liquid crystals should be highly temperature dependent.

3. Effect of Temperature on Liquid Crystal

Liquid crystalline behavior occurs above the melting point of the pure solid. At low temperature, the molecular motion is slow and the energies of intermolecular interactions are strong but as the temperature is increased, molecular motion increases and the phase of liquid crystal may be change.

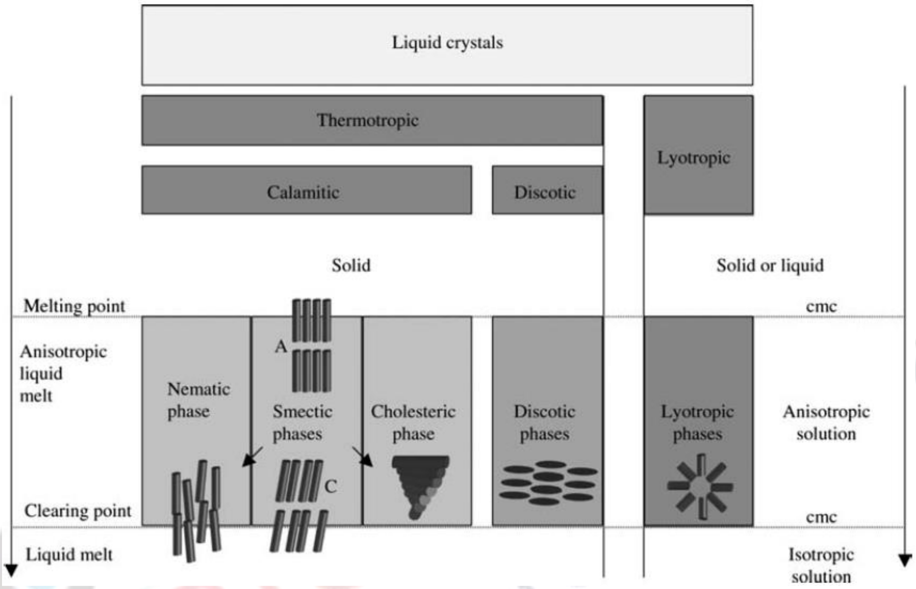

Fig. 2: Fundamental classes of liquid crystalline behavior (temperature increases downwards)

The thermal behavior is the basis for the first fundamental distinction in liquid crystals. As a function of temperature, substances that form mesophases, called *thermotropic*, whereas the influence of a solvent or medium (micelles) called *lyotropic*. The gradual melting of a crystalline solid causes the thermotropic phases. As the temperature increases, molecular vibrations increase and at the melting point, the liquid form generated due to the intermolecular (supramolecular) interactions are broken one by one. The other way to break down a solid lattice is to dissolve it in a solvent. In lyotropic phase, as the melting, not all of the crystal is broken up, it depends on the concentration, and degrees of solute order may exist within the solution.

Thermotropic liquid crystals are two types: *Calamitic* and *discotic*. **Calamitic** phases (derived from the Greek for ‘tube’) are caused by rod like mesogens. **Disctotic** phases are caused by disc like species. Calamitic phases may be either *nematic* (from the Greek for ‘thread’), *smectic*(from the Greek for ‘soap’) or *cholesteric* (named after the cholesterol derivatives such as **13.4**, which exhibit this behavior). A high degree of long range orientational order of molecules is a characteristic property of the nematic phase. The least order of all calamtic phases represent the nematic phase and in systems that possess more than one mesophase. The nematic phase occurs before the melting point.

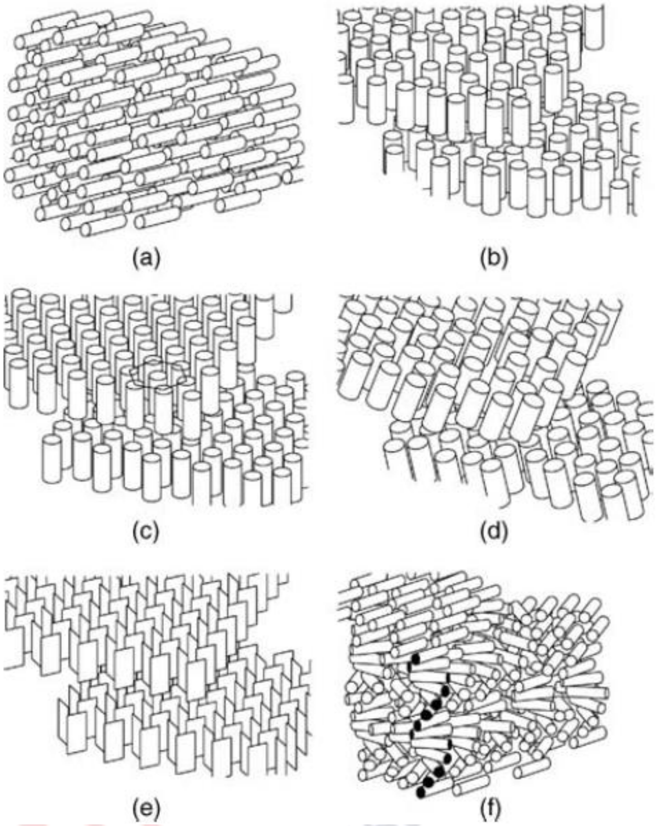

Fig. 3: Schematic representation of calamitic liquid crystalline phases: (a) nematic, (b) smectic A, (c) smectic B, (d) smectic C, (e) smectic E and (f) cholesteric

Smectic phases represent a higher degree of order then nematic. Two-dimensional ordered layer arrangements occur in smectic phases and the thickness of layer is equal to the length of the molecular rods. Between layers, the interactions are limited, allowing one layer to slip easily with respect to the other. Smectic phases such as A and C (Figure 3b and Figure 3d) have less ordered smectic phases and within layer theys exhibit as liquid. Between rods, increasing order is observed with hexagonal arrangements (smectic B) and herringbone arrangement of flatter rods such allowing no rotation about the rod axis (smectic E). With the most ordered phases, exhibiting a high degree of viscosity, 12 different smectic phases have been characterized. On warming, ordered phases shift to less ordered such as $S_E/S_G \rightarrow S_B \rightarrow S_F \rightarrow S_C \rightarrow S_D \rightarrow S_A$. For example, *n*-octyl derivative of compound (Figure 4) undergoes a total of three phase transitions. At 24 ˚C, smectic A phase occurred, at 34 ˚C, smectic A phase transferred into nematic phase and at 42.6 ˚C, finally it decompose to an isotropic melt.

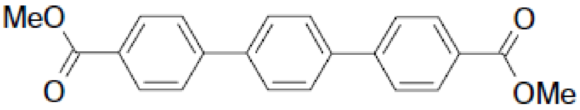

Fig. 4: n-octyl derivative of this compound undergoes a total of three phase transitions

4. Design of Liquid Crystalline Material

The systematic studies designed to elucidate the molecular properties that give rise to liquid crystalline behavior. The design of a large range of liquid crystalline materials has been enabled by these principles. The conventional wisdom may be summarized as follows:

- Within rigid molecular frameworks, the molecular shape should be thin or flat.
- The molecular length should be at least 1.3 nm (13 Å), consistent with the presence of long alkyl groups on many room-temperature liquid crystals.
- The structure should not be branched or angular.
- A highly anisotropic polarisability is required in order to enhance intermolecular dispersive interactions. This is favoured by the presence of easily polarisable groups and permanent dipoles.
- A low melting point is preferable in order to avoid metastable, monotropic liquid crystalline phases. Low-temperature mesoporphic behaviour in general is technologically more useful, and alkyl terminal groups promote this.

The main criterion for Liquid crystalline behaviour is structurally rigid and high anisotropic shape and as a result many liquid crystalline materials based on substituted benzene rings (particularly *p*-disubstituted). A long and extended shape found in *para* arrangement. For example, stilbene and Schiff’s base derivatives (figure 5).

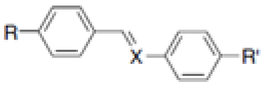

Fig. 5: Stilbene and Schiff's base derivatives (having para arrangement) show long and extended shape

Liquid crystalline behaviour of these compounds is promoted more efficiently by *trans* conformation of central bond compared to *cis* isomers because of the resultant elongated molecular shape.

5. Supramolecular Liquid Crystals

Hydrogen bonding is one of the important interactions in nature. Hydrogen bonding is versatile approach for the design of liquid crystalline materials to the control of simple molecularly assembled structures and the induction of dynamic function. By the hydrogen bonding, a variety of liquid crystals has been prepared by self-assembly processes. Many type of structures such as rod-like and disk like low molecular weight complexes and polymeric complexes with side-chain, main-chain, network and guest-host have been built from complimentary and identical hydrogen-bonded molecules.

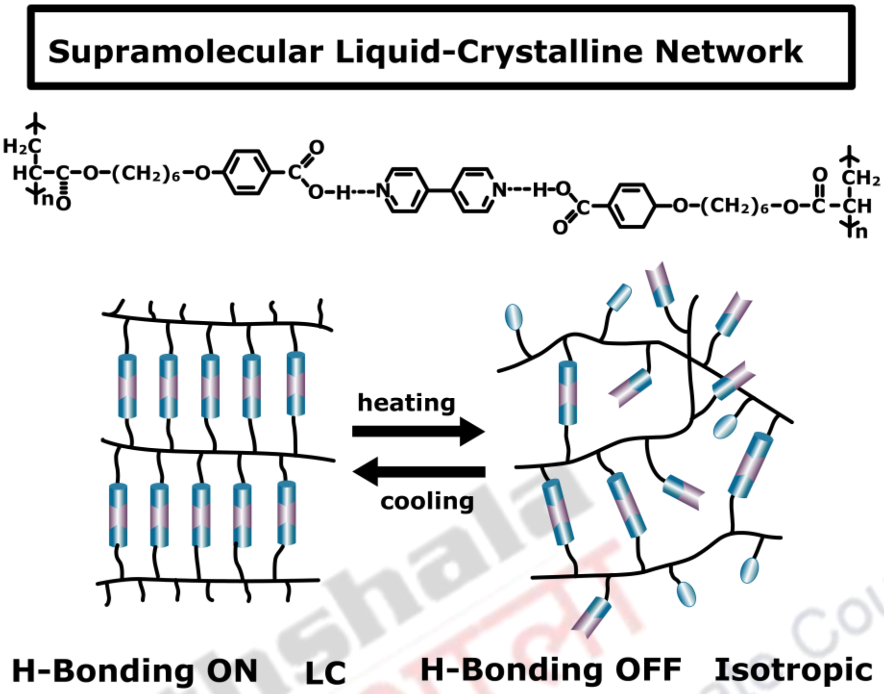

Fig. 6: Supramolecular Liquid crystalline network

We can understand these behaviour with the example of carboxylic acid dimer along with Lehn’s 2,6-diaminopyridine-uracil system. It is the example of the use of supramolecular interactions to assemble mesogens. Same as, the hydrogen bonding interactions which occur between 4-butoxybenzoic acid and *trans*-[4-ethoxy(benzyol)oxy]-4’-stibazole, which gives mesogenic rod like structures (Figure 7).

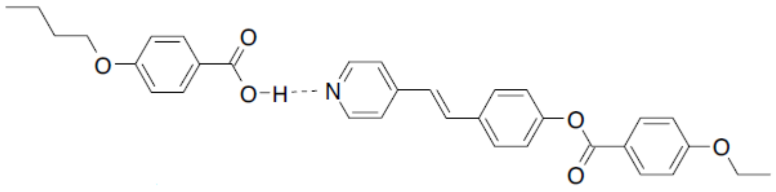

Fig. 7: Hydrogen bonding interactions occurring between 4-butoxybenzoic acid and *trans*-[4-ethoxy(benzyol)oxy]-4’-stibazole giving rise to mesogenic rod like structures

A heteromolecular hydrogen bond occurs between carboxylic acid and the pyridine groups and it results in a thermally stable rigid rod-like assembly. This assembly displays nematic phases up to 214 ˚C.

New liquid crystals based on dendrimers, bent or bowl-shaped cores, non-cavalent bonding, metal coordination or the ones which rely on microphase separation to force mesophase formation have been formed. For example, the phase change occurs in the common guanosine quartet assembly that changes from a smectic (rod shaped) to hexagonal columnar (disc-shaped) phase on the addition of sodium ions, which template the quartet formation (Figure 8). The metal ions chelated by the oxygen atoms and the liquid crystals re-organises into a circular geometry.

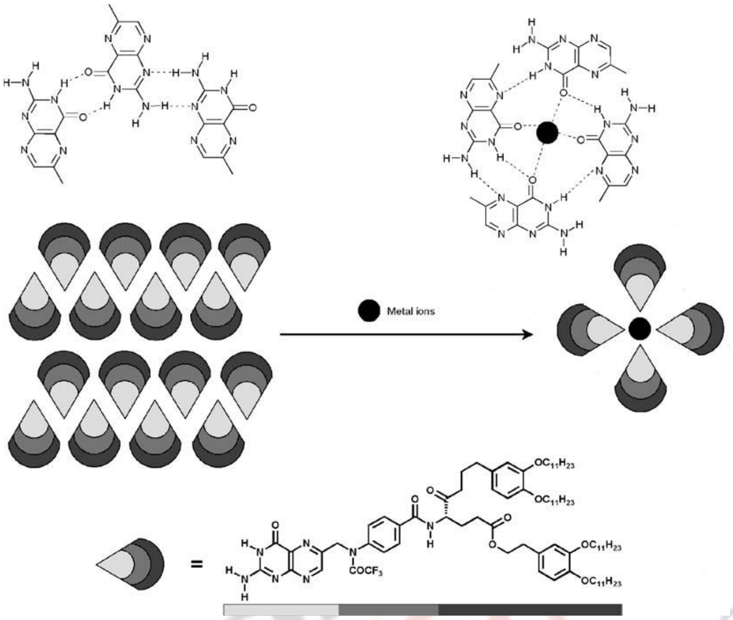

Fig. 8: A ribbon structure of a folic acid derivative self-assembles into a disc-like tetramer based on a G-quartet motif showing liquid crystalline behaviour on the addition of a metal ion such as Na^+

Unusual supramolecular interactions such as halogen bonding has also been reported in supramolecular liquid crystals. As shown in figure 9, the highly activated iodine atom in pentafluoroiodobenzene results in a strong N---I interaction. These type of interactions are comparative strong to hydrogen bonds and upon cooling the melt at 84 ˚C temperature, resulting in the formation of a smectic A liquid crystalline phase.

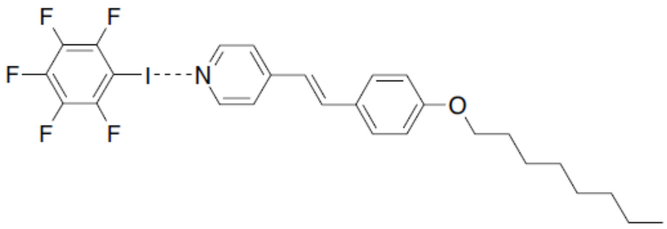

Fig. 9: Figure depicting the highly activated iodine atom in pentafluoroiodobenzene results in a strong N---I interaction

Two component hydrogen bonded mixtures of dendrimers and T-shaped branched amphiphiles are also a rich source of mesophases. This type of interaction was found in between the dendrimer and T-shaped amphiphile (Figure 10).

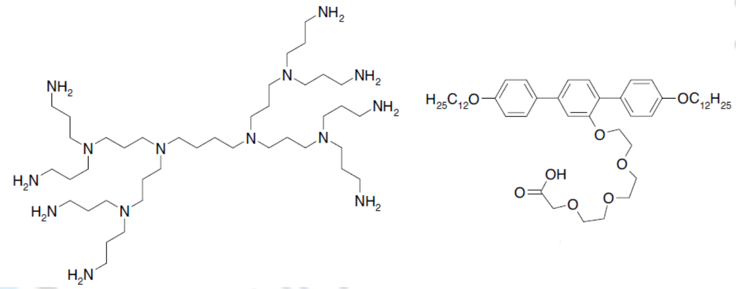

Fig. 10: Two component hydrogen bonded interaction between the dendrimer and T-shaped amphiphile

Recently the surfactant templating of low melting *inorganic* salts like $ZnCl_2$ based new class of liquid crystals has been reported. The inorganic component useful for the formation of glasses with strands comprising linked tetrahedra. A new hybrid liquid crystalline phases are develop by the addition of amphiphiles and it depends on the inorganic-organic composition ration and the temperature. This type of materials has been named *metallotropic*.

6. Application of Liquid Crystals

Various type of technological applications are shown by the liquid crystals. They are used in accurate temperature measurement, where the liquid crystalline phase changes can give temperature resolution of up to 0.007 K in a 1 K range. Temperatures between -20 ˚C and +250 ˚C can be measured on liquid crystalline thermometers on a less precise level. Liquid crystals are cheap and toxicologically harmless and widely used in the areas as diverse as medicine and even as wall thermometers in ‘give away’ advertising gimmicks. In various areas of analytical chemistry, liquid crystals are also used. Dissolution of the sample in a liquid crystalline nematic phase results in the orientation of the sample molecules in a precise and regular manner, facilitating measurement of anisotropic properties, such as circular dichroism phenomena, by IR and UV–visible spectroscopy. In chromatographic separation of closely related isomers (*e.g.*, Haloarenes), the liquid crystals are also used. Various NMR applications are also show by liquid crystals. The most important application of liquid crystals is in crystals displays (LCD). LCDs work on the principle that an applied electric field will alter the molecular orientations and result in changes in the optical behaviour. Twisted nematic cells (TNC) based LCDs are used in full-colour computer monitor displays. A thin layer of nematic liquid crystal is sandwiched between two transparent glass plates. The glass plates are treated with a director before use and it has an orientation effect on the liquid crystalline phase, much like the mesogen orients itself by interactions with its neighbours. A helical twist in the nematic phase is produced by the 90 degree rotation of two plates to each other, with twist angle of 90 degree from one side to the other (Figure 11). This 90 degree twist followed by the polarization of plane-polarised light passing through the layer. The orientated liquid crystalline layer is placed between crossed polarisers, resulting in a display that is transparent to light at rest in the absence of an electric field.

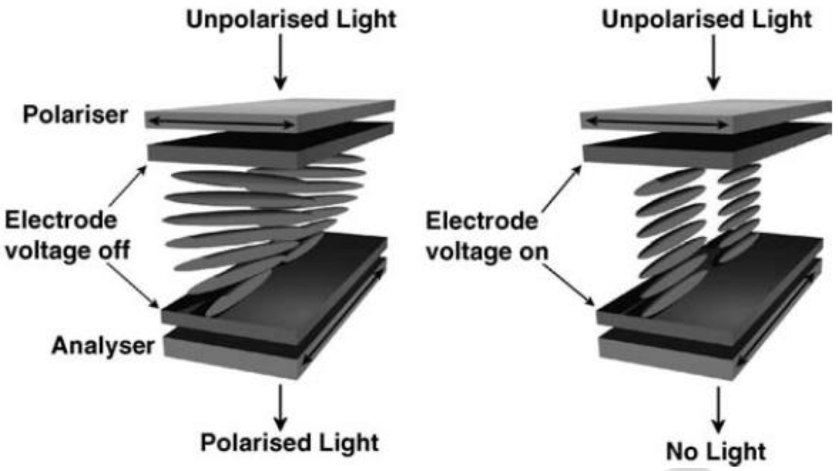

Fig. 11: Operation of a twisted nematic cell

7. Summary

- Liquid crystal is a phase between solid and liquid
- The shape of liquid crystal highly effected by the temperature, the shape of liquid crystal is change with the variation in temperature
- Hydrogen bonding play an important role in the synthesis of supramolecular liquid crystals
- Liquid crystals are widely used in daily life.

Subject	Chemistry
Paper No and Title	14: Organic Synthesis: Disconnection Approach
Module No and Title	17: Principles of molecular associations and organizations: Non-covalent synthesis
Module Tag	CHE_P14_M17

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1. Learning Outcomes

After studying this module, you shall be able to:

- Learn about the basics of supramolecular chemistry.
- Know about non-covalent interactions.
- Understand the concepts of self-assembly and self-organization.
- Learn and analyse host-guest chemistry.

2. Introduction

Supramolecular chemistry is a highly interdisciplinary field of science covering the chemical, physical, and biological features of the organized chemical species of greater complexity than molecules themselves, which are held together and organized by means of intermolecular (non-covalent) binding interactions. In other words, this can also be defined as ‘chemistry of molecular assemblies and of the intermolecular bond’. Professor Jean-Marie Lehn, won the Nobel Prize in 1987 for his work in the area of supramolecular chemistry. Basically, supramolecular chemistry was defined in terms of the non-covalent interactions between a ‘host’ and a ‘guest’ molecule.

The non-covalent interactions such as electrostatic interactions, hydrogen bonding and van der Waals forces define the inter component bond between the molecular individuals and populations. These non-covalent interactions are as important in supramolecular chemistry as covalent interactions in classical organic chemistry. The energy of these non-covalent interactions is much smaller than 200-400 kJmol^{-1} which is typical for covalent chemical bonds. In addition to relatively strong ion-ion electrostatic interactions of ca. 100-350 kJmol^{-1} and hydrogen bonding of ca. 10-120 kJmol^{-1}, they include much smaller London dispersion forces, ion-induced dipole and dipole-dipole interactions that are in the range of 5-50 $kJmol^{-1}$ strong. Supramolecular chemistry covers the crystals, solutions and also the polymers in which non-covalent interactions play such an important role.

In general, supramolecular chemistry involves the self-assembly and host-guest systems using a variety of interactions, some of which are clearly non-covalent (*e.g.* hydrogen bonds) and some of which possess a significant covalent component (*e.g.* metal–ligand interactions) It also has diversified enormously and includes charge-transfer complexes, inclusion complexes (incorporating e.g. Cram's hemicarcerands and cyclodextrins), mono- and polylayers, micelles, vesicles, liquid crystals and cocrystals consisting of at least two different kinds of molecules which form highly specific domains differing in the objects studied and research techniques. The specificity and separateness of the charge-transfer complexes and those of liquid crystals seem generally recognized. On the other hand, as concerns inclusion complexes or other molecular aggregates consisting of only few molecules, higher molecular aggregates, and cocrystals formed by at least two types of molecules the situation is not that clear.

3. Non-Covalent Interactions

The supramolecular chemistry generally concerns non-covalent bonding interactions such as ion-ion interactions, ion-dipole interactions, dipole-dipole interactions, hydrogen bonding, cation-π interactions, anion-π interactions, π-π interactions, closed shell interactions, van der Waals forces and crystal close packing. The term ‘non-covalent’ encompasses an enormous range of attractive and repulsive effects.

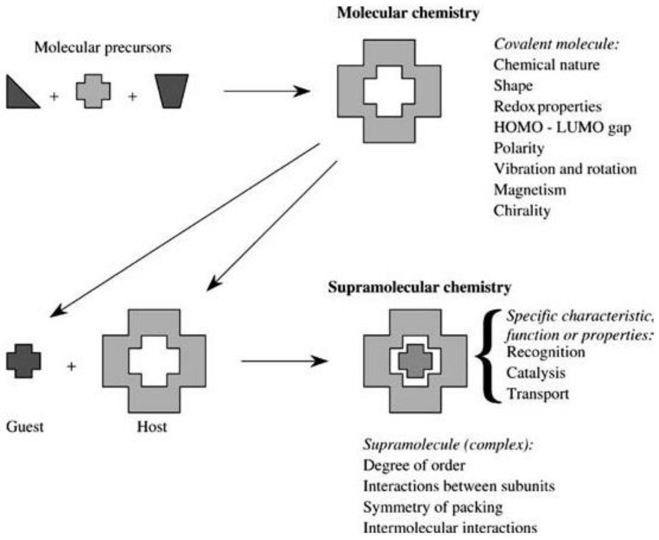


Fig. 1: Comparison between the scope of molecular and supramolecular chemistry according to Lehn

The ion-ion interaction as in ionic cubic lattice of solid sodium chloride in which each Na^+ cation is surrounded by six Cl^- anions. The Na^+ cation is able to organise six complementary donor atoms about itself in order to maximize non-covalent ion–ion interactions. The ionic cubic lattice of solid sodium chloride breaks down in solution because of solvation effects to give species such as the labile, octahedral $Na(H_2O)_6^+$. The bond strength of ionic bonding is comparable in strength to covalent bonding and bond energy in the range of 100–350 kJ mol^{-1}.

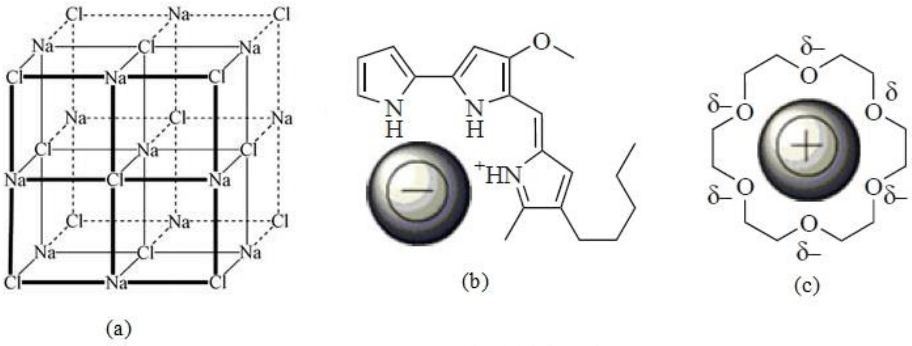


Fig. 2: (a) The ionic cubic lattice of solid sodium chloride (b) showing supramolecular ion-ion interactions by anion and an organic cation and (c) showing the supramolecular ion-dipole interactions by metal cation and crown ether

The bonding of an ion, such as Na^+, with a polar molecule, such as water, is an example of an ion–dipole interaction, which range in strength from *ca.* 50 – 200 kJ mol^{-1}. This kind of bonding is seen both in the solid state and in solution. The ion-dipole interactions in supramolecular structures of the complexes of alkali metal cations with macrocyclic (large ring) ethers termed crown ethers in which the ether oxygen atoms play the same role as the polar water molecules, although the complex is stabilized by the chelate effect and the effects of macrocyclic pre-organization.

A hydrogen bond (H-bond) may be regarded as a particular kind of dipole–dipole interaction in which a hydrogen atom attached to an electronegative atom (or electron withdrawing group) is attracted to a neighbouring dipole on an adjacent molecule or functional group. H-bonds are commonly written D–H··A and usually involve a hydrogen atom attached to an electronegative atom such as O or N as the donor (D) and a similarly electronegative atom, often bearing a lone pair, as the acceptor (A). The typical range for H-bond strength is from *ca.* 10–120 kJ mol^{-1} and the typically H-bonded O···O distances are 2.50–2.80 Å in length, though interactions in excess of 3.0 Å may also be significant. An excellent example of H-bonding in supramolecular chemistry is the formation of carboxylic acid dimers. Figure 3(a), which results in the shift of the *v*(OH) infrared stretching frequency from about 3400 cm^{-1} to about 2500 cm^{-1}, accompanied by a significant broadening and intensifying of the absorption. H-bonds are ubiquitous in supramolecular chemistry. In particular, H-bonds are responsible for the overall shape of many proteins, recognition of substrates by numerous enzymes, and (along with π-π stacking interactions) for the double helix structure of DNA.

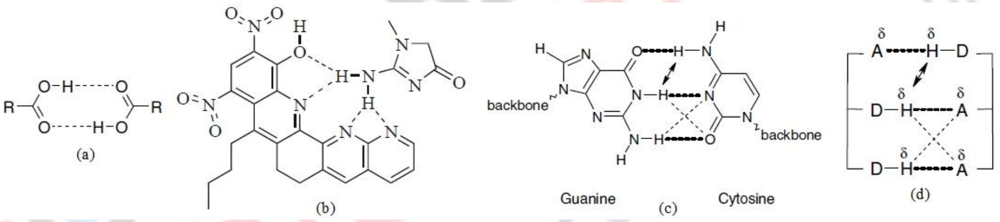


Fig. 3: Supramolecular Hydrogen bonding (H-bonding) interactions in (a) carboxylic acid dimers (b) organic molecule and (c) & (d) guanine and cytosine base pairs of DNA

The π-π interactions occur between aromatic rings so sometimes it is also called aromatic π-π stacking interactions, often in situations where one is relatively electron rich and one is electron poor. The typical range for π-π interactions strength is from *ca.* 50–500 kJ mol^{-1}. There are two types of π-interactions: face-to-face and edge-to-face (Figure 4). Face-to-face π-stacking interactions are responsible for the slippery feel of graphite and its useful lubricant properties. Similar π-stacking interactions between the aryl rings of nucleobase pairs also help to stabilize the DNA double helix. Edge-to-face interactions may be regarded as weak forms of hydrogen bonds between the slightly electron deficient hydrogen atoms of one aromatic ring and the electron rich π-cloud of another. Strictly they should not be referred to as π-stacking since there is no stacking of the π-electron surfaces. Edge-to-face interactions are responsible for the characteristic herringbone packing in the crystal structures of a range of small aromatic hydrocarbons including benzene.

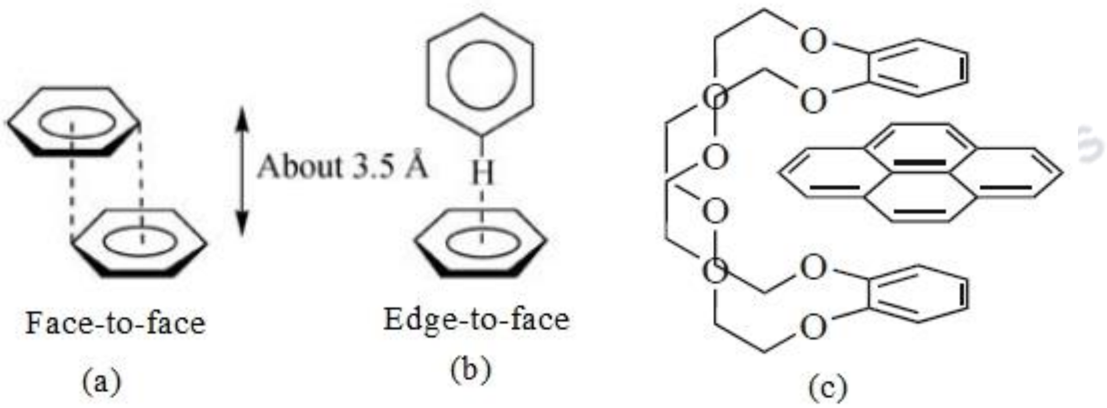
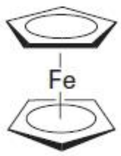


Fig. 4: Supramolecular π-π interactions in the molecular structures

Cation-π interactions: Transition metal cations such as Fe^{2+}, Pt^{2+} *etc.* are well known to form complexes with olefinic and aromatic hydrocarbons such as Zeise's salt $[PtCl_3(C_2H_4)]^-$ and ferrocene $[Fe(C_5H_5)_2]$. The bonding in such complexes is strong and could by no means be considered non-covalent, since it is intimately linked with the partially occupied *d*-orbitals of the metals. Even species such as $Ag^+\cdots C_6H_6$ have a significant covalent component. The interaction of alkaline and alkaline earth metal cations with C=C double bonds is, however, a much more non-covalent 'weak' interaction, and is suggested to play an important role in biological systems. For example, the interaction energy of K^+ (Figure 5) and benzene in the gas phase is ~80 kJ mol^{-1}. By comparison, the association of K^+ with a single water molecule is similar at 75 kJ mol^{-1}.

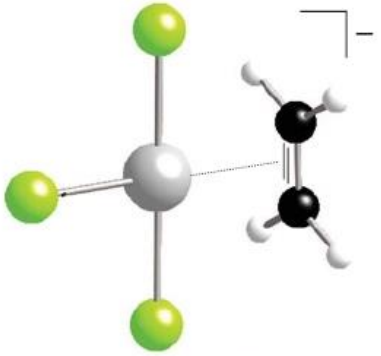
The reason for this is that the K^+ ion is more soluble in water than in benzene is related to the fact that many water molecules can interact with the potassium ion, whereas only a few bulkier benzene molecules can fit around it. The interaction of non-metallic cations such as RNH_3^+ with double bonds may be thought of as a form of X—H ···π hydrogen bond.

Anion-π interactions: Cation-π interactions are favorable however the interaction of an anion with π-electron density seems like it should be repulsive and indeed the affinity of the aromatic ring containing cryptand figure 6(a) for halides rapidly falls off in the order $F^- >> Cl^- > Br^- \sim I^-$ because of anion-π repulsions in the case of the larger halides, with all except F^- showing a constant anion-ring centroid distance of *ca*. 3.7 Å. However, there is a charge difference between an overall neutral aromatic ring and an anion and therefore in principle the possibility exists for an electrostatic attraction. Such short anion-π interactions have been noted for organometallic calixarene derivatives shown in figure 6(b) where the aromatic ring bears a significant positive charge. Anion-π interactions have also been implicated as controlling elements in self-assembly reactions of Ag(I) complexes with π-acidic aromatic rings.



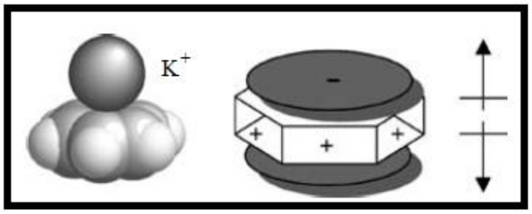
ferrocene

(a)



Zeise's salt

(b)



(c)

Fig. 5: Cation-π interactions in molecular structures (a) ferrocene (b) Zeise's salt and (c) schematic representation of cation-π interactions in between K^+ ion and benzene and quadrupole moment of benzene

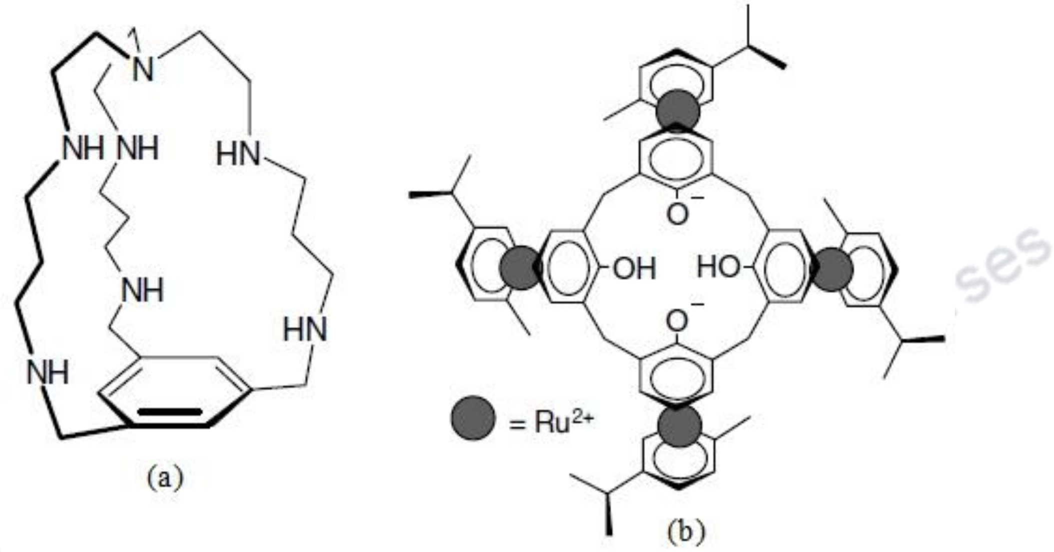


Fig. 6: Molecular structures which are involve in anion-π interactions (a) aromatic ring containing cryptand and (b) organometallic calixarene derivative

Van der Waals interactions arise from the polarization of an electron cloud by the proximity of an adjacent nucleus, resulting in a weak electrostatic attraction. The typical range for Van der Waals interactions strength is from *ca.* 0.50–40 kJ mol^{-1}. These Van der Waals interactions are non-directional and hence possess only limited scope in the design of specific hosts for selective complexation of particular guests. In general, van der Waals interactions provide a general attractive interaction for most 'soft' (polarisable) species with the interaction energy proportional to the surface area of contact. In supramolecular chemistry, they are most important in formation of 'inclusion' compounds in which small, typically organic molecules are loosely incorporated within crystalline lattices or molecular cavities, *e.g.* the inclusion of toluene within the molecular cavity of the *p*-*tert*-butylphenol-based macrocycle, *p*-*tert*-butylcalix[4]arene (Figure 7(a)).

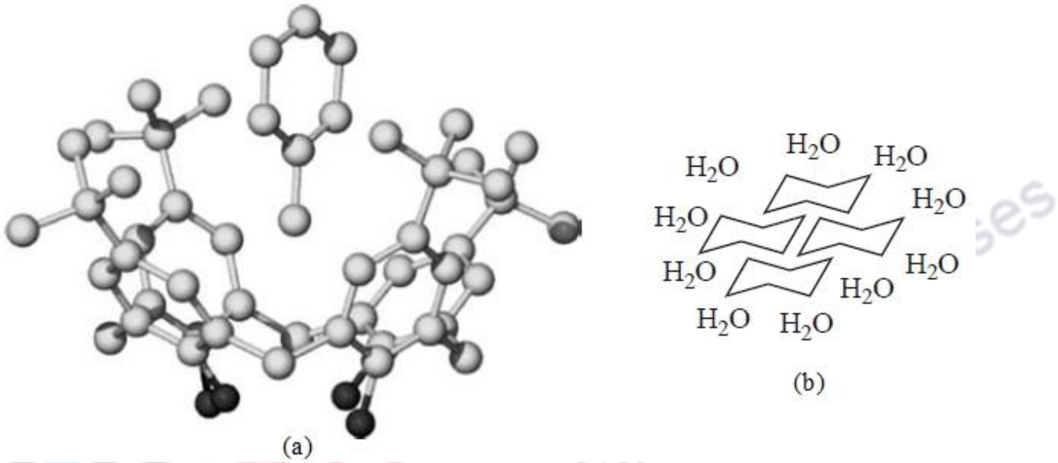


Fig. 7: (a) X-ray crystal structure of a typical van der Waals inclusion complex *p*-*tert*-butylcalix[4]arene·toluene and (b) hydrophobic van der Waals interactions

Dipole-dipole interactions: Alignment of one dipole with another can result in significant attractive interactions from matching of either a single pair of poles on adjacent molecules (type I) or opposing alignment of one dipole with the other (type II) (Figure 8) with energies in the range 5–50 kJ mol^{-1}. Organic carbonyl compounds show this behaviour well in the solid state and calculations have suggested that type II interactions have an energy ~20 kJ mol^{-1} which is comparable to a moderately strong hydrogen bond. The boiling point of ketones such as acetone (56 ºC), however, demonstrates that dipole–dipole interactions of this type are relatively weak in solution.

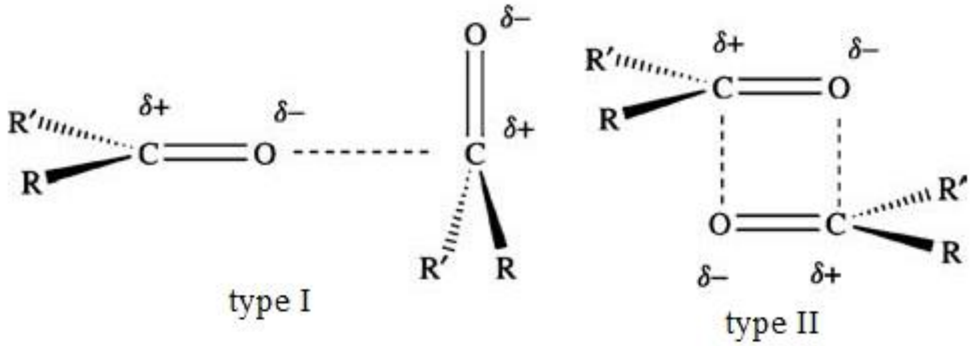
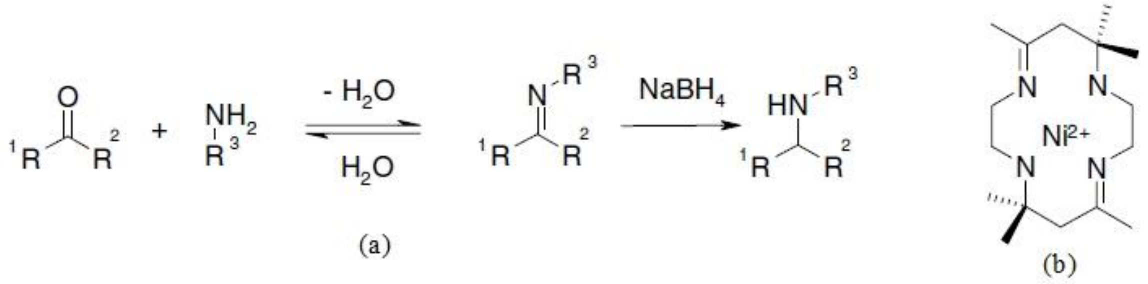


Fig. 8: Dipole-dipole interactions in carbonyls

4. Self-Assembly and Self-Organization

Self-assembly is the spontaneous and reversible association of molecules or ions to form discrete/extended entities at either the molecular, covalent or the supramolecular, non-covalent level. Within self-assembly processes, we must distinguish molecular self-assembly and supramolecular self-assembly. Molecular self-assembly concerns the formation of covalent bonds as part of a special synthetic procedure. The assembly is subject to control by the reaction stereochemistry and the conformational features of the intermediates, *e.g.* the formation of amine–aldehyde condensation macrocycles (Figure 9). The formation of supramolecular self-assemblies results from the recognition-directed spontaneous association of a well-defined and limited number of molecular components under the intermolecular control of the non-covalent interactions such as coordination interactions, hydrogen bonds and dipolar interactions that hold them together. The reversibility of supramolecular self-assembly is the key to resulting systems' ability to shift through the available components to form the thermodynamically most favourable structure. In other words supramolecular self-assembly concerns the spontaneous association of either a few or many components resulting in the generation of either discrete oligomolecular supramolecules or of extended polymolecular assemblies such as molecular layers, films, membranes, etc. The name *tecton* (from τέκτων: builder) has been proposed for designating the components that undergo self-assembly.



(a) (b)

Fig. 9: (a) The Schiff base condensation and the reduction of the product to give an amine (b) macrocycle synthesized by aldol condensation of acetone and $[Ni(en)_3]^{2+}$

Self-organization could be considered as a set intersecting self-assembly, ordered self-assembly, that would (1) contain the systems presenting a spontaneous emergence of order in either space or time or both; (2) cover spatial (structural) and temporal (dynamic) order of both equilibrium structures and of non-equilibrium, dissipative structures, incorporating non-linear chemical processes, energy flow and the arrow of time; (3) concern only the non-covalent, supramolecular level; (4) be multicomponent and result in the formation of polymolecular assemblies presenting supramolecular organization and long-range order (with or without regularity and periodicity) by virtue of specific interactions operating either through recognition events between the molecular components or in a dynamic process. The higher the degree of confinement or order (1D, 2D, 3D, 4D) of self-assembled entities, the more they may be considered as organized (molecular layers, membranes, micelles, colloids, liquid crystals, molecular crystals) entities. Self-organization thus involves interaction (between parts) and integration (of the interactions) leading to collective behaviour, such as is found in a phase change or in the generation of spatial or temporal waves. The phenomenological description of the macroscopic features of self-organizing systems must eventually find an etiological explanation at the microscopic, molecular, and supramolecular levels.

Self-assembly and self-organization of a supramolecular architecture are both multistep processes implying information and instructed components of one or several types. And these may distinguished from mere templating. Templating is a synthetically most efficient procedure involving the use of temporary or permanent "helper" species, of organic or inorganic nature, for the stepwise assembly of molecular or supramolecular structures of high complexity. Self-assembly and self-organization require molecular components containing two or more interaction sites and thus capable of establishing multiple connections. Self-complementary components associate with themselves undergoing homoassembly, whereas complementary components (pleromers) associate with one another giving heteroassembly.

5. Host-Guest Compounds

In host-guest compounds generally we consider a molecule (a ‘host’) binding another molecule (a ‘guest’) to produce a ‘host–guest’ complex or supramolecule. Commonly the host is a large molecule or aggregate such as an enzyme or synthetic cyclic compound possessing a sizeable, central hole or cavity. The guest may be a monatomic cation, a simple inorganic anion, an ion pair or a more sophisticated molecule such as a hormone, pheromone or neurotransmitter. More formally, the host is defined as the molecular entity possessing *convergent* binding sites (*e.g.* Lewis basic donor atoms, hydrogen bond donors *etc*.). The guest possesses *divergent* binding sites (*e.g.* a spherical, Lewis acidic metal cation or hydrogen bond acceptor halide anion). In turn a binding site is defined as a region of the host or guest capable of taking part in a non-covalent interaction. The host–guest relationship has been defined by Donald Cram and he also received the Nobel Prize with Professor Jean-Marie Lehn and J. Pedersen for their work in area of supramolecular chemistry.

The supramolecular host–guest chemistry generally shows the stability of a host–guest complex in solution. The chemistry of clathrates (figure 10), or more generally, inclusion, relates to hosts that are often stable only in the solid (crystalline) state and dissociate on dissolution in a solvent. Gas hydrates, urea clathrates and a wide variety of crystalline solvates fall into this category. On the other hand, molecular hosts for ions (figure 11) such as the crown ethers, cryptands and spherands, or hosts for neutral molecules (figure 12) such as the carcerands and cryptophanes, display significant binding both in the solid state and in solution.

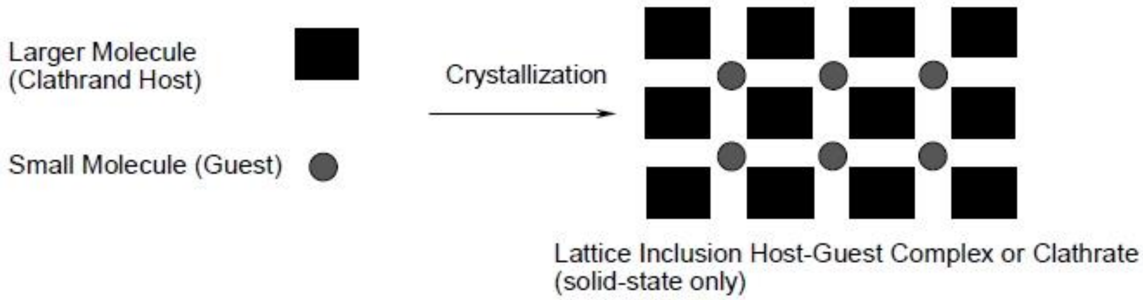
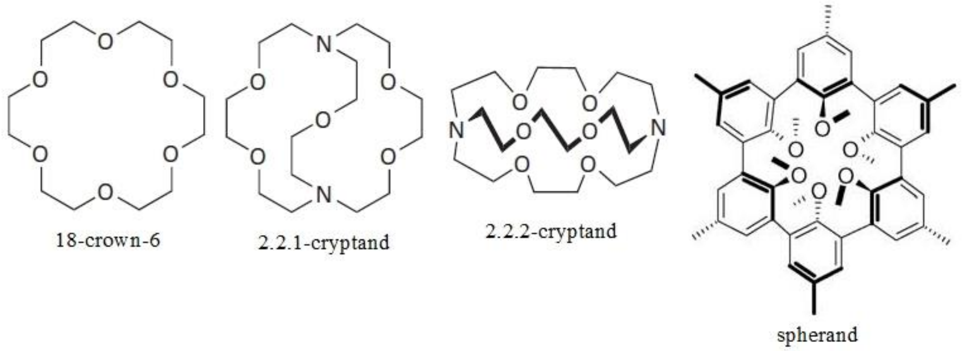
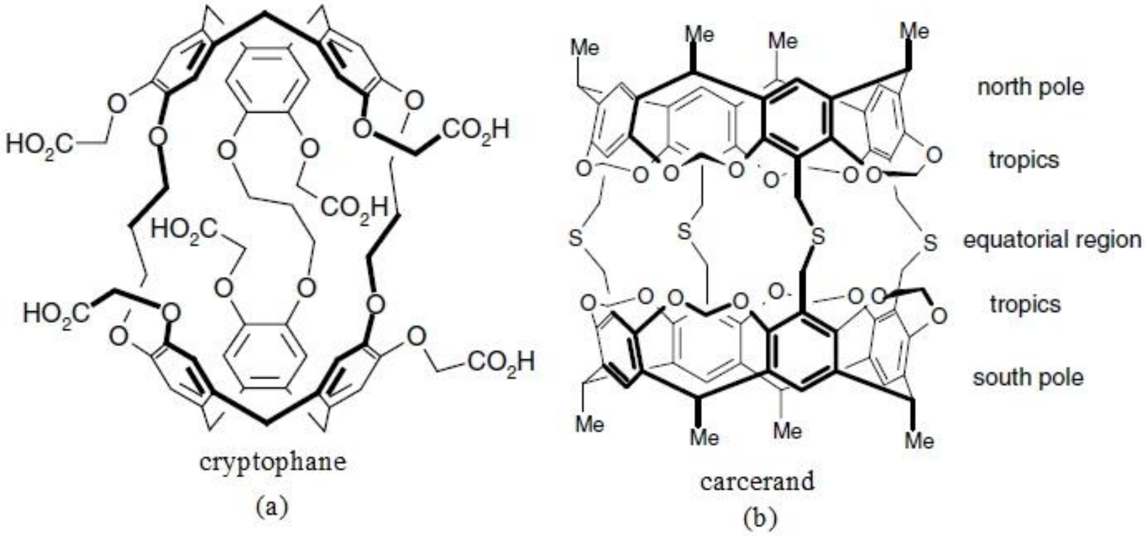


Fig. 10: Inclusion of guest molecules in cavities formed between the host molecules in the lattice resulting in conversion of a clathrand into a clathrate



18-crown-6 2.2.1-cryptand 2.2.2-cryptand spherand

Fig. 11: Supramolecular host molecules for ions



cryptophane (a) carcerand (b)

Fig. 12: Supramolecular hosts for neutral molecules

6. Summary

In this module you have learnt that:

- Supramolecular chemistry deals with the organized chemical species of greater complexity than molecules themselves, which are held together and organized by means of intermolecular (non-covalent) binding interactions.
- The supramolecular chemistry generally concerns non-covalent bonding interactions such as ion-ion interactions, ion-dipole interactions, dipole-dipole interactions, hydrogen bonding, cation-π interactions, anion-π interactions, π-π interactions, closed shell interactions, Van der Waals forces and crystal close packing.
- In general, supramolecular chemistry involve the self-assemble and host-guest systems using a variety of interactions, some of which are clearly non-covalent (*e.g.* hydrogen bonds) and some of which possess a significant covalent component (*e.g.* metal–ligand interactions).
- Self-assembling systems do not involve hosts and guests but rather self-complementary molecules or complementary partners (tectons).
- In host-guest compounds a host component with convergent binding sites and a guest component with divergent binding sites are involved.
- Host molecules which are generally involved in supramolecular chemistry such as the crown ethers, cryptands and spherands for ions, and hosts for neutral molecules such as the carcerands and cryptophanes, display significant binding both in the solid state and in solution.

Subject	Chemistry
Paper No and Title	14: Organic Chemistry- IV (Advanced Organic Synthesis, supramolecular chemistry and carbocyclic rings)
Module No and Title	Module 18: Self-assembly and self-organisation
Module Tag	CHE_P14_M18

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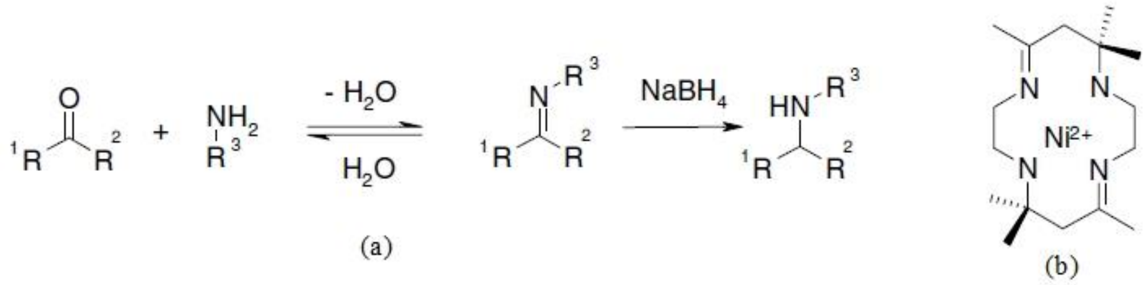
1. Learning Outcomes

After studying this module, you shall be able to:

- Basics about the self-assembly and self-organisation processes.
- Distinguish between molecular self-assembly and supramolecular self-assembly.
- Self-assembly of inorganic architectures.
- Self-assembly of organic architectures.

2. Introduction: Self-assembly and self-organisation

Self-assembly is the spontaneous and reversible association of molecules or ions to form discrete/extended entities at either the molecular, covalent or the supramolecular, non-covalent level. Within self-assembly processes, we must distinguish **molecular self-assembly** and **supramolecular self-assembly**. Molecular self-assembly concerns the formation of covalent bonds as part of a special synthetic procedure. The assembly is subject to control by the reaction stereochemistry and the conformational features of the intermediates, *e.g.* the formation of amine–aldehyde condensation macrocycles (Figure 1). The formation of supermolecular self-assemblies results from the recognition-directed spontaneous association of a well-defined and limited number of molecular components under the intermolecular control of the non-covalent interactions such as coordination interactions, hydrogen bonds and dipolar interactions that hold them together. The reversibility of supramolecular self-assembly is the key to resulting systems' ability to sift through the available components to form the thermodynamically most favourable structure. In other words supramolecular self-assembly concerns the spontaneous association of either a few or many components resulting in the generation of either discrete oligomolecular supermolecules or of extended polymolecular assemblies such as molecular layers, films, membranes, etc. The name ***tecton*** (from τέκτων: builder) has been proposed for designating the components that undergo self-assembly.



(a)

(b)

Figure 1: (a) The Schiff base condensation and the reduction of the product to give an amine (b) macrocycle synthesized by aldol condensation of acetone and $[Ni(en)_3]^{2+}$.

Self-organization could be considered as a set intersecting self-assembly, ordered self-assembly, that would (1) contain the systems presenting a spontaneous emergence of order in either space or time or both; (2) cover spatial (structural) and temporal (dynamic) order of both equilibrium structures and of non-equilibrium, dissipative structures, incorporating non-linear chemical processes, energy flow and the arrow of time; (3) concern only the non-covalent, supramolecular level; (4) be multicomponent and result in the formation of polymolecular assemblies presenting supramolecular organization and long-range order (with or without regularity and periodicity) by virtue of specific interactions operating either through recognition events between the molecular components or in a dynamic process. The higher the degree of confinement or order (1D, 2D, 3D, 4D) of self-assembled entities, the more they may be considered as organized (molecular layers, membranes, micelles, colloids, liquid crystals, molecular crystals) entities. Self-organization thus involves interaction (between parts) and integration (of the interactions) leading to collective behaviour, such as is found in a phase change or in the generation of spatial or temporal waves. The phenomenological description of the macroscopic features of selforganizing systems must eventually find an etiological explanation at the microscopic, molecular, and supramolecular levels.

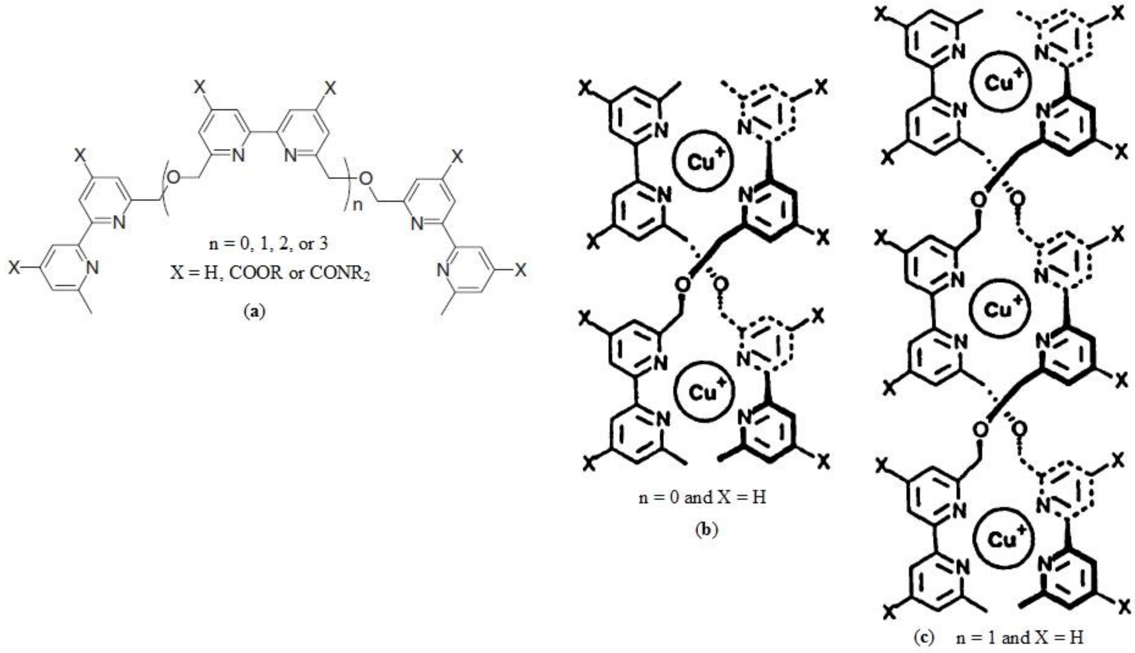
Self-assembly and self-organization of a supramolecular architecture are both multistep processes implying information and instructed components of one or several types. And these may distinguished from mere templating. Templating is a synthetically most efficient procedure involving the use of temporary or permanent "helper" species, of organic or inorganic nature, for the stepwise assembly of molecular or supramolecular structures of high complexity. Self-assembly and self-organization require molecular components containing two or more interaction sites and thus capable of establishing multiple connections. Self-complementary components associate with themselves undergoing **homoassembly**, whereas complementary components (pleromers) associate with one another giving **heteroassembly**.

3. Self-assembly of inorganic architectures

Inorganic self-assembly and self-organization involve the spontaneous generation of well-defined metallo-supramolecular architectures from organic ligands and metal ions. The latter serve both as cement holding the ligands together and as centre orienting them in a given direction. In the process, full use is being made of the structural and coordination features of both types of components, which in addition convey redox, photochemical or chemical functionality, depending on their nature.

The formation of any complex species from an organic ligand and a metal ion is in principle an assembly process, which occurs spontaneously. The emphasis here lies in the design of the ligands and the choice of the metal ions in order to produce defined architectures in a controlled fashion from multiple subunits. Metal ions have properties of special interest as components of supramolecular systems and linkers for self-assembly. They provide (1) a set of coordination geometries, (2) a range of binding strengths, from weak to very strong, and of formation and dissociation kinetics, from labile to inert, and (3) a variety of photochemical, electrochemical and reactional properties. In addition, and most significantly, they allow the reversible assembly-disassembly of supramolecular architectures and represent switchable interaction sites, for instance, by electrochemical interconversion between oxidation states of different coordination geometries.

For example, a self-assembly of double helicates is shown in figure 2. In the presence of Cu(I) ions and a organic ligand (Figure 2(**a**)) containing 2,2'-bipyridine (bipy) groups, a spontaneous assembly takes place giving double-stranded helicates, in which two ligand strands are wrapped around each other in a double-helical fashion with Cu(I) ions holding them together. It results from the tetrahedral-like coordination imposed by each $Cu(bipy)^{2+}$ site and from the design of the ligands, which disfavours binding to only a single strand. In such instances, double-helix formation requires self-recognition by the two helicands and that leads to preferential formation of the double-helical structures. In other words, helicate formation amounts to a tetrahedral reading of the molecular information stored in the bipy strands.



n = 0, 1, 2, or 3
X = H, COOR or $CONR_2$
(a)
n = 0 and X = H
(b)
(c) n = 1 and X = H

Figure 2: (a) A organic ligand containing 2,2’-bipyridine (bipy) group, (b) and (c) are the double helical self-assembly of Cu(I) ion.

Only metal ions presenting the appropriate coordination features with bipy will form double helicates. This is also shown to be the case for Ag(I), which yields the tri-, tetra-, and pentahelicates, as confirmed by determination of the crystal structure of the silver trihelicate in figure 3.

Using oligo-bipy ligands, the formation of triple helicates becomes possible through a modification of the steric instruction by shifting the 6,6'-disubstitution, as in figure 2(a), to a 5,5'-disubstitution (figure 4(a)), which should remove the hindrance towards binding of three bipy units to an octahedral metal centre.

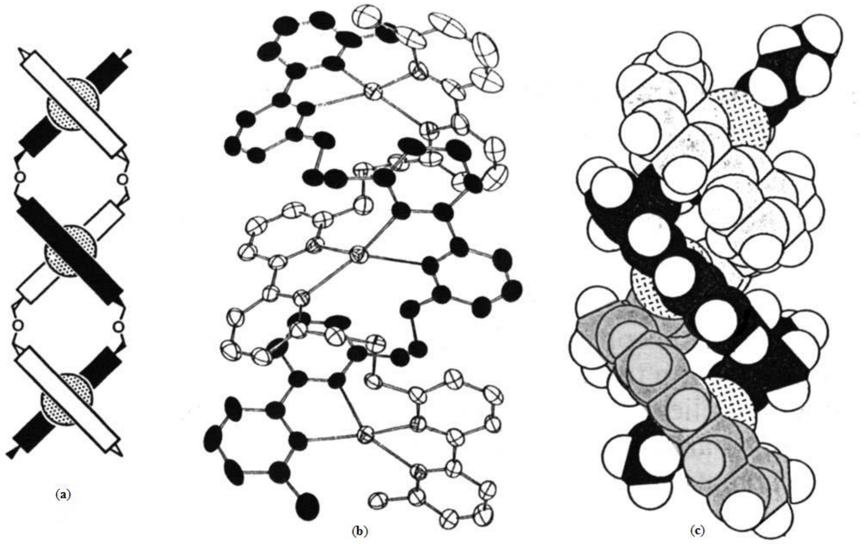


Figure 3: (a) Schematic representation of a trinuclear double helicate silver self-assembly $[Ag_3(BP_3)_2](CF_3SO_3)_3$: and (b) the structural view by ORTEP plot, the spheres represent 20% probability and (c) MOLDRAW plot with radii criteria, giving a space filling model.

A trinuclear triple-helical complex figure 4 is indeed formed spontaneously by self-assembly from three 5,5'-disubstituted tris(bpy) strands and three Ni^{II} ions.

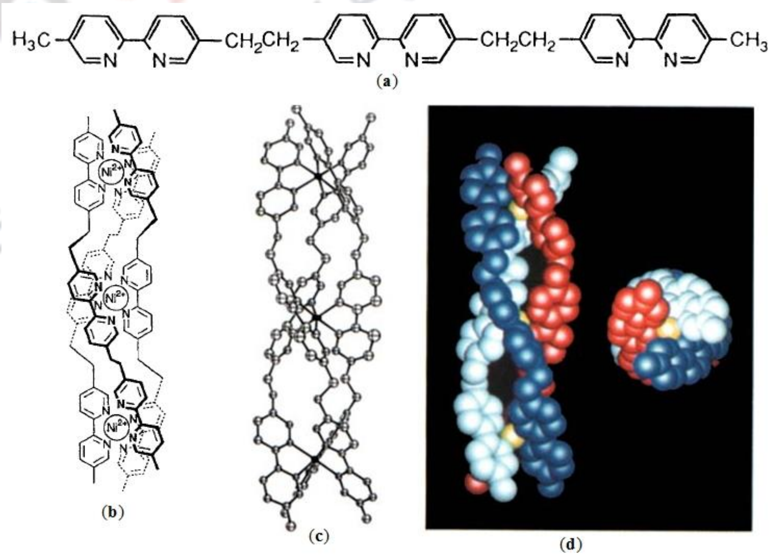


Figure 4: (a) 5,5'-disubstituted tris(bpy) organic ligand; (b) trinuclear self-assembly of triple helical Ni^{II} complex; (c) and (d) crystal structural representation of the self-assembled trinuclear triple helical Ni^{II} complex.

The nature and the coordination geometry of the metal ions involved in the self-assembly of helicates, in addition to, three main features that bear structural information determining the nature and shape of the helical species formed may be distinguished: (1) the precise structure of the binding site; it specifies in particular the ability to coordinate metal ions with a given geometry as well as the number of strands bound; (2) the spacer separating the binding sites; it must favour inter- over intrastrand binding, and it influences the tightness of the helix (the pitch) through the rotation of one metal centre with respect to the next; (3) most importantly the configuration of the coordination centres determines whether the structure is indeed of helical nature; helicity implies that all metal centres have the same screw sense.

The self-assembly of the helicates and related structures involves just one type of ligand and metal ion. Further progress in the understanding and the control of the self-assembly and self-organization of inorganic superstructures requires the conception of systems capable of spontaneously generating well-defined architectures from a larger set of components, comprising at least two types of ligands and/or metal ions. The design and choice of these components must fulfill criteria at all three levels of molecular programming and information input that determine the output of the desired final species: recognition, orientation and termination.

Multiligand multimetal self-assembly has been achieved by means of a flat ligand containing three chelating subunits, hexaphenylhexaaza-triphenylene figure 5(a) and bipy derived ligands. The ditopic bis-bipy component figure 5(**b**) is employed, two units of figure 5(**a**) and three of 5(**b**) bind six Cu(I) ions to form the cylindrical complex 5(**c**) (Figure 5). This amounts to the self-assembly of five ligands of two different types and six metal ions, altogether eleven particles, to give the closed, cage-like entity in one stroke.

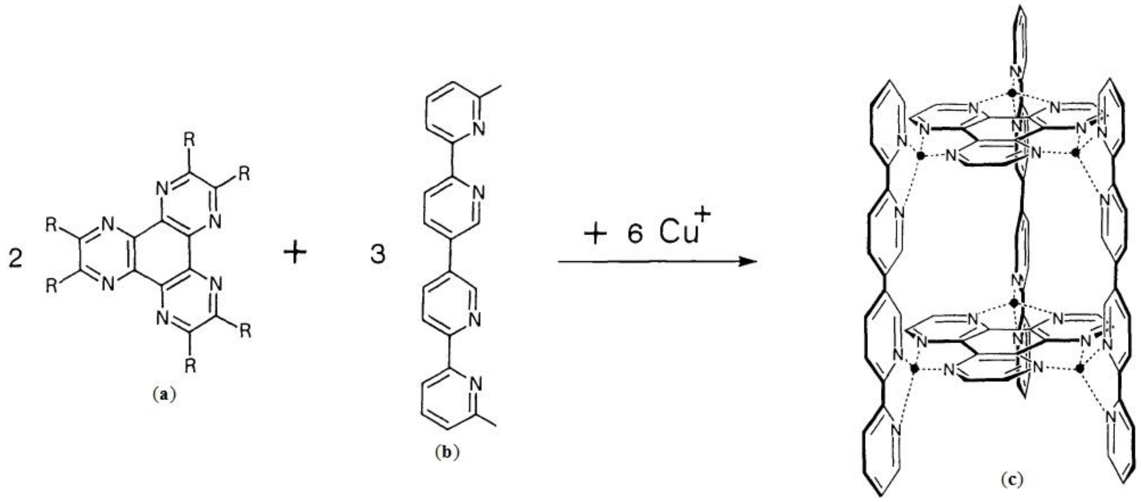


Figure 5: Scheme of formation of a self-assembly of a multicomponent cylindrical complex.

Various other inorganic superstructures are also shown as self-assembly such as a rack-like arrangement schematically represented in figure 6, would be formed by the complexation of several metal ions to rigid, linear sequences of binding sites. A ladder superstructure figure 6(**c**) may result from the complexation of linear ligands of the type of 4(**a**) and bispyrimidine derivatives 6(**a**) or extended units 6(**b**) with tetrahedral metal centres.

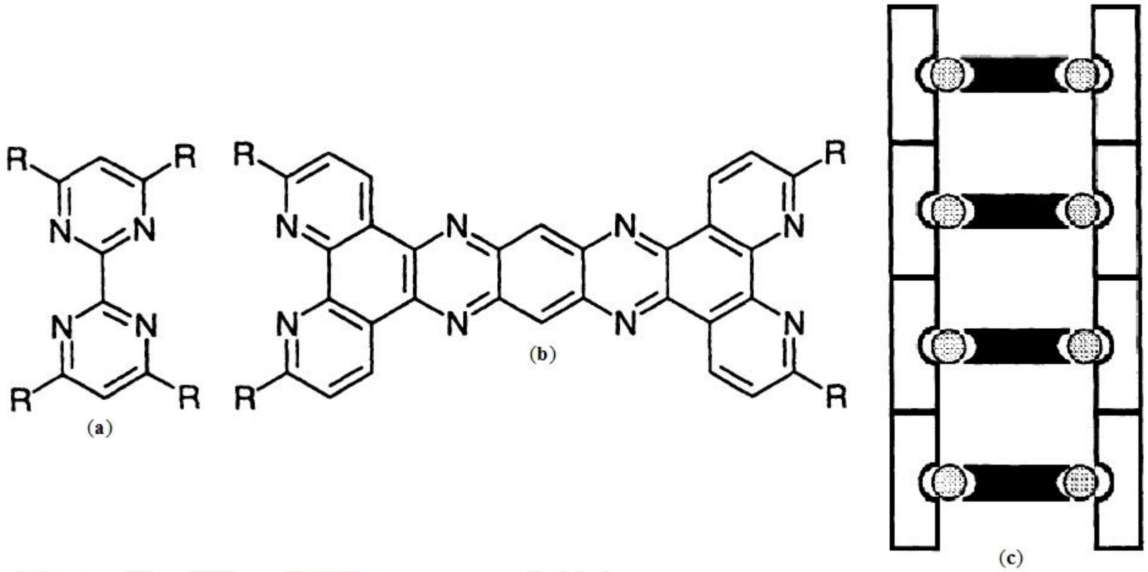


Figure 6: (a) and (b) are organic bispyrimidine ligands and (c) is the resulting ladder like self-assembly constructed from these organic ligands.

4. Self-assembly of organic supramolecular structures

The self-assembly of organic supramolecular species makes use of interactions other than metal ion coordination, such as electrostatic, hydrogen bonding, van der Waals, stacking or donor-acceptor effects as found in proteins, nucleic acids, liquid crystals and molecular complexes. The spontaneous generation of organized structures depends on the design of molecular components capable of self-assembling into supramolecular entities presenting the desired architectural and functional features. The nature of the species obtained will be determined by the information stored in the components. Thus, the self-assembly process may be directed by molecular recognition between two or more complementary subunits so as to form a given supramolecular architecture. If these molecular units incorporate specific optical, electrical, magnetic, binding, etc., properties their ordering may induce a range of novel features. Depending on the subunits involved the association may lead either to supermolecules or to organized assemblies, such as membranes, molecular layers and films, mesophases, polymeric species or solid state lattices.

The self-assembly of supramolecular structures via molecular recognition between complementary hydrogen bonding components has developed into well-defined arrangements of molecules in solution, in liquid crystals and in the solid state. The build-up of two-dimensional and three-dimensional architectures requires the presence in the molecular components of two or more hydrogen bonding subunits whose disposition determines the final supramolecular architecture. When two subunits are incorporated into a single group, it will then possess two recognition faces and may be termed a **Janus molecule**, a double faced H-bonding recognition unit. If the faces are the same or different the unit is homotopic or heterotopic, if the unit is self-complementary and may be termed plerotopic. Considering tridentate sites, 2,6-diaminopyridine and uracil are complementary single site groups figure 7(**a**), while 7(**b**) is plerotopic by virtue of its two complementary sites. On the other hand barbituric acid (BA) and 2,4,6-triaminopyrimidine (TAP) or -triazine (TAT) are Janus molecules containing two identical recognition sites and these may associate either as a linear or as a cyclic structure (figure 8). Each recognition site may be monodentate, bidentate or tridentate depending on whether it contains one, two or three hydrogen bond donor (D) or acceptor (A) centres. Of course, the stability and selectivity of the associations depend on the nature and position of the centres.

The bases of nucleic acids are well known heterocyclic groups that interact through hydrogen bonding, usually forming base pairs through Watson-Crick type association. In which flavin adenine dinucleotide contains complementary adenine group and uracil site of the flavin.

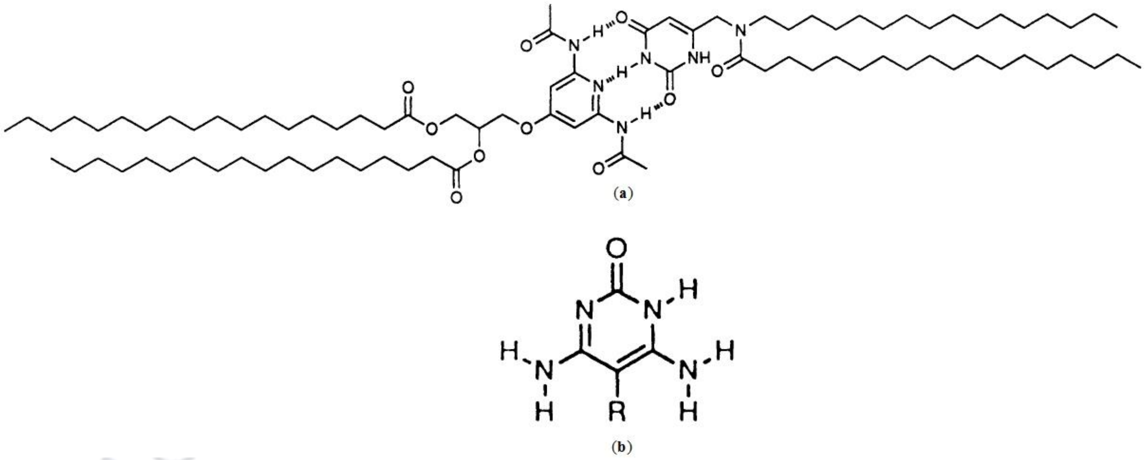


Figure 7: (**a**) complementary single site groups of 2,6-diaminopyridine and uracil and (**b**) is plerotopic group.

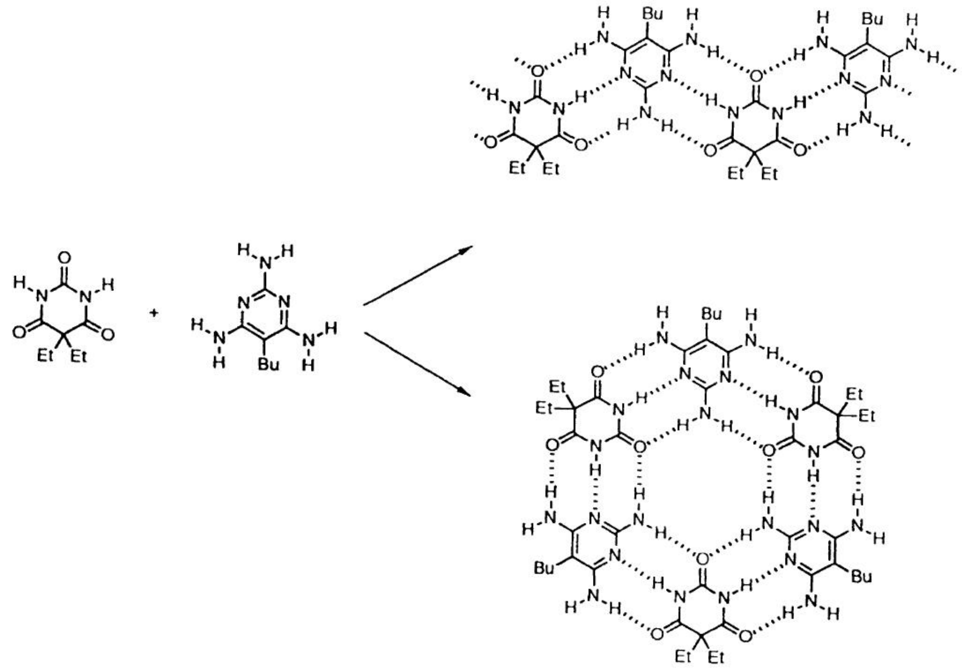
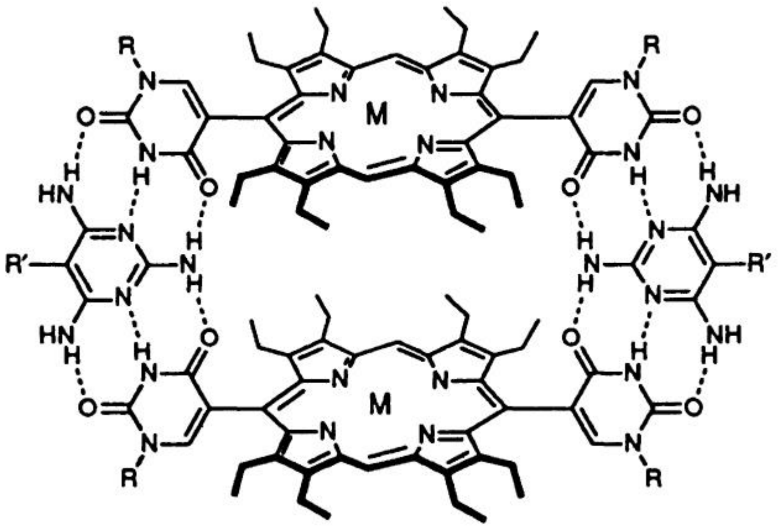


Figure 8: Self-assembly of either a supramolecular ribbon (right top) or a supramolecular macrocycle (right bottom) from barbituric acid and 2,4,6-triaminopyrimidine units.

The self-assembly of a porphyrin (or its Zn(II) complex) bearing two uracil groups by means of two TAP units yields a supramolecular bis-porphyrin cage figure 9 into which a bipy guest molecule may bind by coordination to the Zn(II) sites in a synergic fashion.



M = 2 H or Zn(II)

Figure 9: self-assembly of a supramolecular bis-porphyrin cage.

5. Summary

In this module you have learnt that:

- Self-assembly is the spontaneous and reversible association of molecules or ions (tectons) to form larger, more complex supramolecular entities according to the intrinsic information contained in the molecules themselves.
- Fundamentally self-assembly is a convergent process in which a number of components assemble into, ideally, a single final, stable structure. Self-assembly is thus very distinct from chemical emergence which is a divergent process in which complexity evolves over time.
- Self-assembly broadly divided into two classes 1. Self-assembly of inorganic structures and 2. Self-assembly of organic structures.
- Inorganic self-assembly and self-organization involve the spontaneous generation of well-defined metallo-supramolecular architectures from organic ligands and metal ions.
- The self-assembly of organic supramolecular species makes use of interactions other than metal ion coordination, such as electrostatic, hydrogen bonding, van der Waals, stacking or donor-acceptor effects as found in proteins, nucleic acids, liquid crystals and molecular complexes.

Subject	Chemistry
Paper No and Title	14: Organic Chemistry- IV (Advanced Organic Synthesis, supramolecular chemistry and carbocyclic rings)
Module No and Title	Module 20: Molecular and supramolecular devices
Module Tag	CHE_P14_M20

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Anchor Institute : SGTB Khalsa College, University of Delhi

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1. Learning Outcomes

After studying this module, you shall be able to:

- Basics about the use of supramolecular entities as molecular devices.
- Energy and electron transfer processes.
- Semiochemistry.
- Molecular and supramolecular devices as photonic, electronic and ionic.

2. Introduction

Molecular devices have been defined as structurally organized and functionally integrated chemical systems; they are based on specific components arranged in a suitable manner, and may be built into supramolecular architectures. Thus a supramolecular device is a complex system made up of molecular components with definite individual properties. These properties are intrinsic to a particular molecular component whether it is part of the device or not. Another way of saying this is that the interaction energy between the components of the supramolecular device must be small compared with other energy parameters relevant to the system. Such a definition of a supramolecular device does not exclude the 'traditional' concept of host and guest or receptor and substrate. Molecular recognition events between host and guest may be an intrinsic part of the operation of a supramolecular device, which might, for example, be designed to bind and then signal the presence of a guest.

The function performed by a device results from the integration of the elementary operations executed by the components. In other words we can say that photonic, electronic or ionic devices depending on whether the components are respectively photoactive electroactive or ionoactive, i.e., whether they operate with (accept or donate) photons, electrons, or ions. This defines fields of molecular and supramolecular photonics, electronics and ionics. Two basic types of components may be distinguished: 1) **Active components:** that perform a given operation (accept, donate, transfer) on photons, electrons, ions, etc.; 2) **Structural components:** that participate in the build-up of the supramolecular architecture and in the positioning of the active components, in particular through recognition processes; in addition, **ancillary components** may be introduced to modify or perturb the properties of the other two types of components. A major requirement would be that these components, and the devices that they bring about, perform their function(s) at the molecular and supramolecular levels as distinct from the bulk material.

3. Molecular Recognition, Information and Signals Semiochemistry

Molecular recognition events represent the basis of information processing at the supramolecular level. They may give rise to changes in electronic, ionic, optical, and conformational properties and thus translate themselves into the generation of a signal. By making the use of three dimensional information storage/readout operating in molecular recognition, in combination with substrate transformation and translocation, one may be able to design components for devices that would be capable of processing information and signals at the molecular and supramolecular levels.

The molecular recognition events can occur only if the correct selective binding of the complementary active components takes place (see Figure 1) and this processes may play a role in several key steps: (1) the building up of the device from its components; (2) its incorporation into supramolecular arrays; (3) the selective operation on given species (e.g., ions); (4) the response to external physical or chemical stimuli (light, electrons, ions, molecules, etc.) that may regulate the operation of the device and switch it on or off; (5) the nature of the signals generated and of the signal conversion effected (photon-photon, photon-electron, electron-electron, electron-ion, ion-ion, etc.).

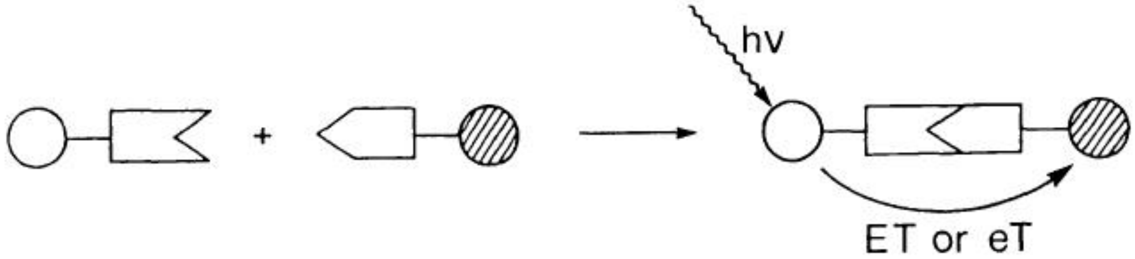


Figure 1: Molecular recognition-dependent photochemical molecular devices.

Recognition-dependent informed devices represent the molecular and supramolecular entities by which molecular recognition events may be transduced into processes and signals, through the design of suitable components responding to external stimuli and suitable for incorporation into the final superstructure. Recognition expressed via a chemical transformation, in the nature or in the rate of formation of the products, amounts to the generation of a specific molecular signal and the resulting area of investigation has been termed semiochemistry (from the Greek σημεῖον: sign, signal)

Semiochemistry is the name given to the area of supramolecular chemistry which is broadly concerned with signalling devices. The term comes from ‘semiotics,’ meaning the study of signs or symbols and their use or interpretation. The basic concept of a molecular sensor is that the substrate (guest, analyte) must be attracted to a receptor portion of the sensor (Figure 2). This is a straightforward molecular recognition event, and the receptor can be any of the systems, such as crown ethers, cryptands, cavitands. The binding must be selective for the target substrate in the presence of a range of other potential guest species, depending on the system and its environment. In endo receptors the binding (information) sites are oriented into a molecular concavity; exo receptors, with outward-directed sites, present "informed" surfaces on which recognition may occur. The receptor must also be in communication with a signalling unit that is responsive to the guest binding, which generates a signal in the form of an emission of electromagnetic radiation (photochemical sensing), a current (electrochemical sensing) or an otherwise externally measurable change (*e.g.* in colour or pH).

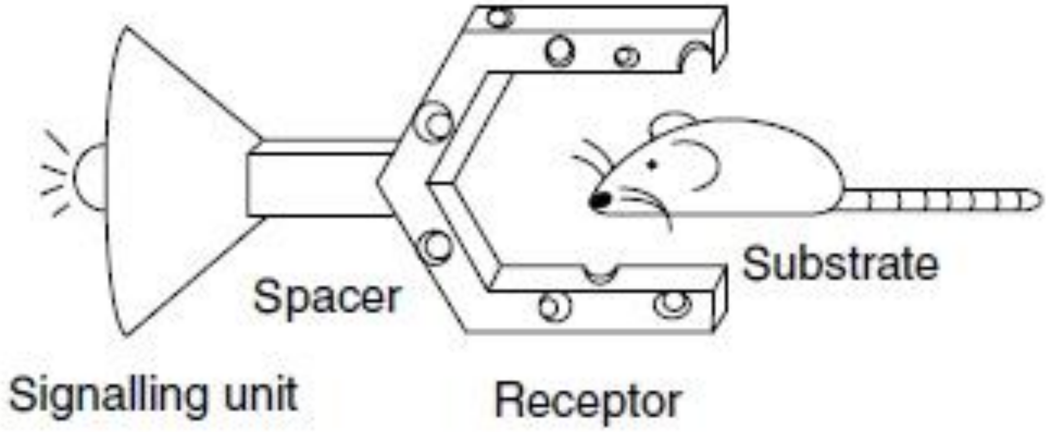


Figure 2: Model representation of chemical sensor.

4. **Supramolecular Photochemistry. Molecular and Supramolecular Photonic Devices**

Supramolecular photochemistry in which the use of photochemically active components as a supramolecular device and the formation of supramolecular entities from photoactive components may be expected to pertub the ground-state and excited-state properties of the individual species (*i.e.* chromophores), giving rise to novel properties such as energy migration, photoinduced charge separation, perturbations of optical transitions and polarisabilities, modification of ground- and excited-state redox potentials, photoregulation of binding properties, selective photochemical reactivity *etc.*

When a molecular chromophore is irradiated with electromagnetic radiation of a wavelength corresponding to the energy required to promote an electron to an accessible electronic excited state, energy is absorbed resulting in the promotion of an electron from a ground-state molecular orbital to one of higher energy. This is known as primary charge separation and results in a high-energy electron and a positively charged ‘hole’. The energy of the excited-state electron can either be dissipated as heat by relaxation by the solvent (nonradiative decay), emitted radiatively (luminescence) or used to carry out a chemical reduction (Figure 3). Luminescence involving direct radiative decay, in which the electron returns immediately to the ground state from a singlet excited state, is termed *fluorescence*. Fluorescent emissions are usually of lower energy than the absorbed energy because the electron is promoted into a vibrationally excited state from which it relaxes non-radiatively before fluorescing back to the electronic ground state (Figure 3).

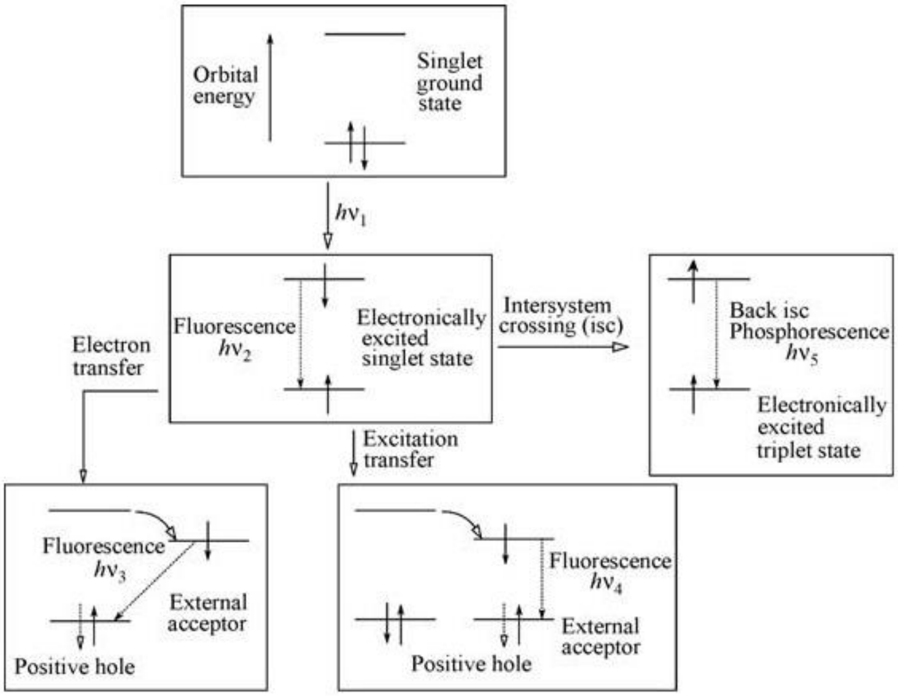


Figure 3: Possible radiative events following photoexcitation. ISC: Intersystem crossing

Phosphorescence is the process in which the electron undergoes a change of spin state (intersystem crossing) to triplet state then the triplet excited state (long-lived) may undergo vibrational relaxation to a lower energy level emitting a kind of luminescence. Fluorescent and phosphorescent processes may be distinguished by time-resolved spectroscopic measurements because phosphorescence takes much longer to decay than fluorescence.

The results of photoexcitation may be divided into three broad categories:

1. Re-emission of the absorbed energy as light (fluorescence or phosphorescence).

2. Chemical reaction of the excited state (secondary charge separation, isomerisation, disassociation *etc*.).

3. Non-radiative vibrational quenching of the excitation by solvent.

The process re-emission of the radiation by luminescence is of interest in sensing and signalling applications, while chemical reactions are of interest in applications such as molecular switches and photocatalysis. Strictly speaking absorption and re-emission type processes are termed molecular ‘photophysics’ while light-induced chemical reactions or chemical processes are termed ‘photochemistry’.

Supramolecular photochemistry, may involve three steps: binding of substrate and receptor, mediating a photochemical process (such as energy, electron or proton transfer), followed by either restoration of the initial state for a new cycle or by a chemical reaction (Figure 4).

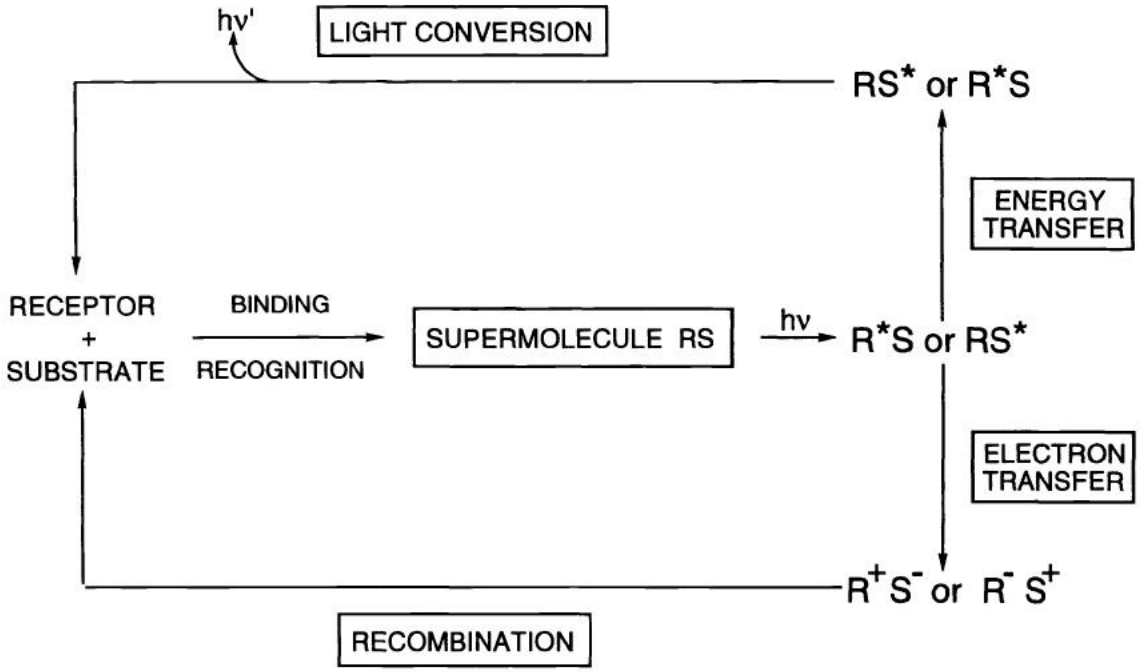
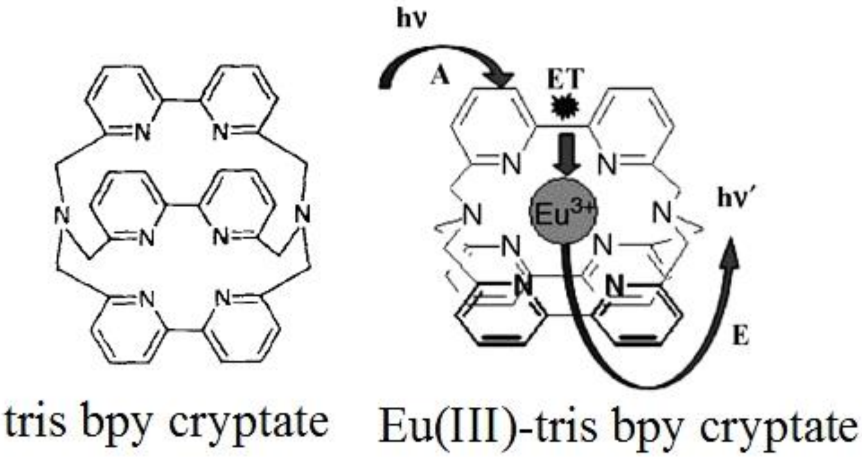


Figure 4: Representation of photoinduced energy transfer and electron transfer processes involved in supramolecular photochemistry. Generation of R*S, RS*, R^+S^-, or R^-S^+ may be followed by a chemical reaction.

In principle, supramolecular photonic devices require a complex organization and adaptation of the components in space, energy, and time, leading to the generation of photo-signals by energy transfer (ET) or electron transfer (eT), substrate binding, chemical reactions, etc.

4.1 Light Conversion and Energy Transfer Devices

A light conversion molecular device may be realized by an Absorption-Energy-Transfer-Emission (A-ET-E) process in which light absorption by a receptor molecule is followed by intra-molecular energy transfer to a bound substrate which then emits. An optimum device may be designed if the light absorber or antenna, light emitter and the degree of coupling between them may be tuned separately. The combination of coupled absorber and emitter thus produces a light-conversion device with optimal properties such as maximum light collection and emission at the desired wavelength. This occurs in the europium(III) and terbium(III) cryptates of the macrobicyclic ligand [bipy.bipy.bipy]. UV light absorbed by the bipy groups is transferred to the lanthanoid cation bound in the molecular cavity, and released in the form of visible lanthanoid emission via an A-ET-E process, as shown in Figure 5. These Eu^{III} and Tb^{III} complexes display a bright luminescence in aqueous solution, whereas the free ions do not emit under the same conditions.



tris bpy cryptate Eu(III)-tris bpy cryptate

Figure 5: The A-ET-E process is shown for the Eu(III)-tris bpy cryptate.

4.2 Photoinduced Electron Transfer in Photoactive Devices

The photogeneration of charge separated states by photoinduced electron transfer (PeT) is of interest for initiating photocatalytic reactions (e.g., natural and artificial photosynthesis) and for the transfer of photosignals (e.g., through a membrane). A schematic diagram of a simple example of such a process is shown in Figure 6 in which a three component entity containing a photosensitizer PS linked to an electron donor D and an electron acceptor A, possessing suitable redox properties in their ground and excited (for PS) states so that irradiation of PS leads to electron transfer from D to A yielding the charge separated triad D^{+}-PS-A^{-}.

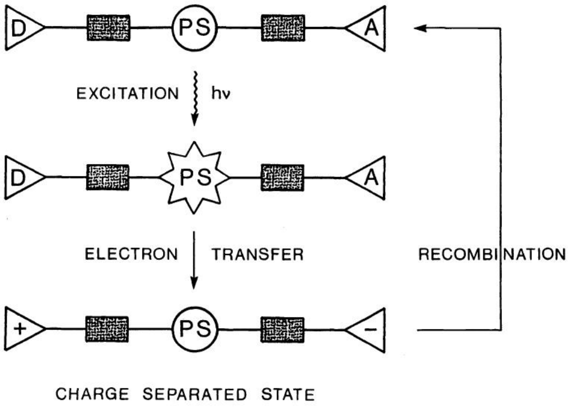


Figure 6: Schematic representation of a center for photoinduced charge separation consisting of a photosensitizer PS, a donor D and an acceptor A as well as insulating spacer group.

An example of a photoinduced charge separation is shown Figure 7 in which a macropolycyclic coreceptors containing both a photosensitive porphyrin group and binding sites for silver(l) ions as acceptor centres. This results in quenching of the singlet excited state of the Zn-porphyrin center by an efficient intracomplex electron transfer, leading to charge separation and generating a porphyrinium cation of long lifetime.

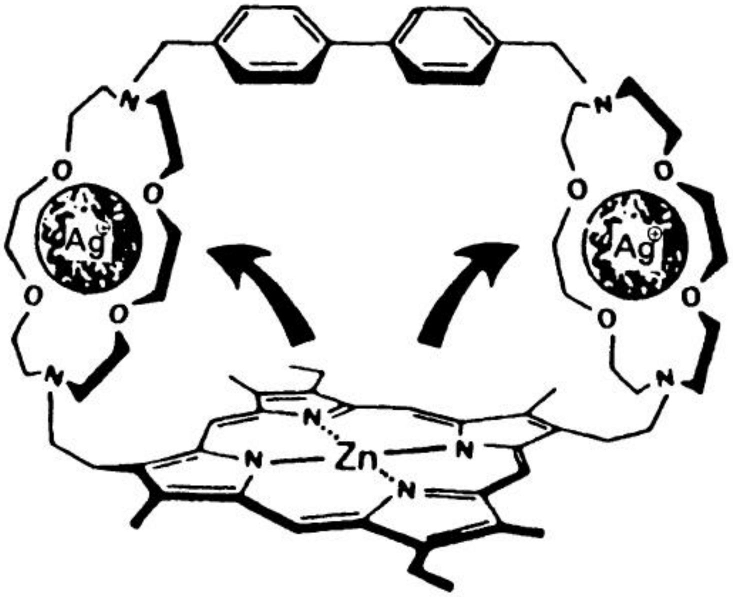


Figure 7: A macropolycyclic Zn-porphyrin coreceptors containing both a photosensitive porphyrin group and binding sites for silver(I) ions as acceptor centres.

5. Molecular and Supramolecular Electronic Devices

Molecular electronic devices are conceptually most resemble electronic and computer components. If individual electronic components that may be coupled together, such as wires, switches, rectifiers *etc.*, can be produced, then the conceptual basis exists to manufacturing molecule-sized (*i.e.* nanoscale) electronic devices with concomitant gains in speed, efficiency, capacity and reduced use of resources.

Much attention has been given to design electronic devices that would operate at the level of the molecular and the supermolecular. Very extensive work has been performed on electroactive materials such as organic metals (e.g., conducting polymers and charge transfer salts) or molecular semiconductors that may lead to devices based on organic materials. This defines a field of molecular and supramolecular electronics concerning the properties of single molecules, of oligomolecular associations and of polymolecular architectures such as Langmuir-Blodgett films within and between which electron transfer processes may occur.

To realize such devices involves several steps. It is first necessary to imagine a component molecule that may possess the desired features, synthesize it, and study its properties. The second step is to incorporate it into supramolecular architectures, such as membranes or other organized structures, and to investigate whether the resulting entity possesses the required properties. The third step requires the connection of the basic unit to other components, in order to address it via relay molecules or with an external physical signal. Pursuing the design of molecular electronic circuitry may have many spin-offs along the way, in addition to raising novel questions about the handling of molecules.

5.1 Supramolecular Electrochemistry

Supramolecular electrochemistry is the resulting electrochemical effects from redox responsive receptor-substrate binding and the molecular devices operating on electrons are basic elements for converting molecular recognition events into electronic signals. The redox responsive receptor molecules are based on two types of component: substrate binding sites and electroactive groups. A number of substances have been studied in which the redox properties of groups such as metallocenes, quinones or paraquat are modified on substrate binding. Conversely, redox interconversion of these groups allows the reversible switching between states of high and low affinity. The mutual effects of redox changes and binding strength in a receptor-substrate pair thus may make it possible to achieve electrocontrol of complexation and, conversely, to modify redox properties by binding. As a consequence of these electrochemical effects, molecular receptors may be used to convert the chemical information present in binding and recognition processes into electronic signals.

Multinuclear metal complexes possess a rich electrochemistry and may serve as electron reservoirs. Thus, dinuclear Cu(I) and Ni(II) complexes exchange two electrons in one step and four electrons in two steps, respectively. Attachment of several redox groups such as ferrocene, viologen or Ni(ll) cyclam to a core provides electron reservoirs that may be capable of powering multielectron catalytic reactions. Polyoxymetallates also take up a number of electrons (up to 32). Biological multiredox centres are found, for instance, in the electron transfer protein cytochrome c_3 that contains four heme groups, whose redox properties are affected by local solvation as in synthetic porphyrins.

5.2 Electron Conducting Devices. Molecular Wires

The basic properties of a molecular wire are that it should connect to two components (generally an electron acceptor and an electron donor) and conduct an electrical signal or impulse between them. The three main classes of electron transfer processes may be considered: (1) electron transport by redox active molecules acting as mobile carriers through membranes; this may or may not also involve electron transfer from one carrier to another during an encounter; (2) electron hopping between suitable redox active groups attached to a backbone or assembled via non-covalent interactions; (3) electron conduction along a continuous conjugation path formed by π-bonds (see Figure 8), which may also involve other electron transmitting groups such as strained σ-bonds, etc.; it represents an electron channel, and embodies specifically the idea of a molecular wire.

Thus the molecular wire concept is analogous to the channel-mediated mechanism, since it is expected to involve a rapid current flow, but the ideal electronic device would result solely in electron flow rather than the flow of alkali metal cations.

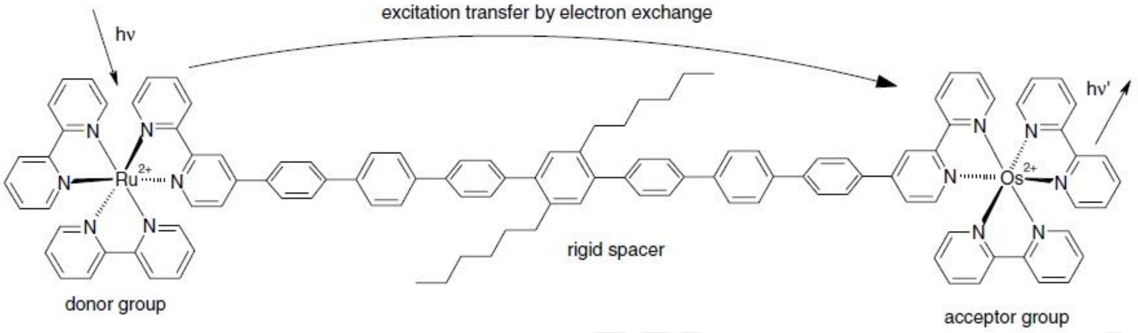


Figure 8: The triplet excitation transfer[3] between the ruthenium(II) donor and the osmium(II) acceptor in $[Ru(bpy)_3]^{2+}(ph)_7\text{-}[Os(bpy)_3]^{2+}$.

The design of a molecular wire should satisfy three criteria: (1) contain an electron- conducting chain; (2) possess terminal electroactive and polar groups for reversible electron exchange; (3) be long enough to span a typical molecular supporting element such as a monolayer or a bilayer membrane (see Figure 9).

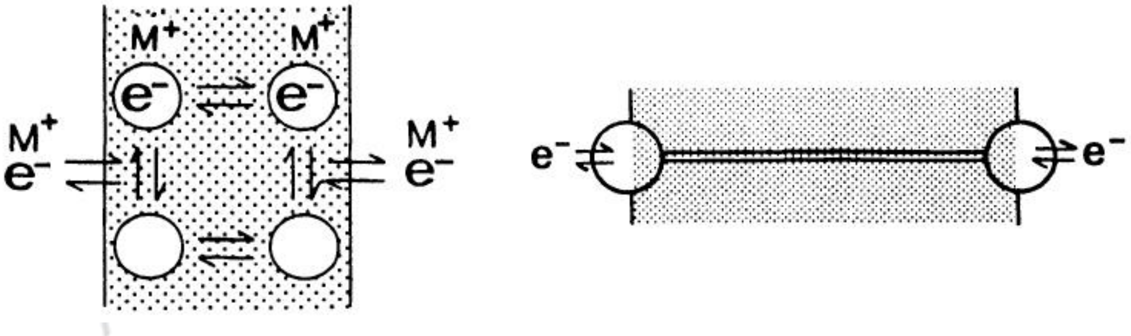


Figure 9: Transmembrane electron transfer processes: carrier mediated via a redox carrier (left) or channel mediated via a molecular wire (right). Both processes may be coupled to light by introduction of photoactive groups in the carrier or in the wire.

Electron transfer occurred between an external reducing phase and an internal oxidizing phase on incorporation of zwitterionic caroviologens $CV^{2\pm}$ compound into phospholipid vesicles. Using only a small amount of incorporated $CV^{2\pm}$ (about 150 active molecules per vesicle) an acceleration factor of 4-8 over background was obtained. This clearly indicated that $CV^{2\pm}$ did induce electron conduction.

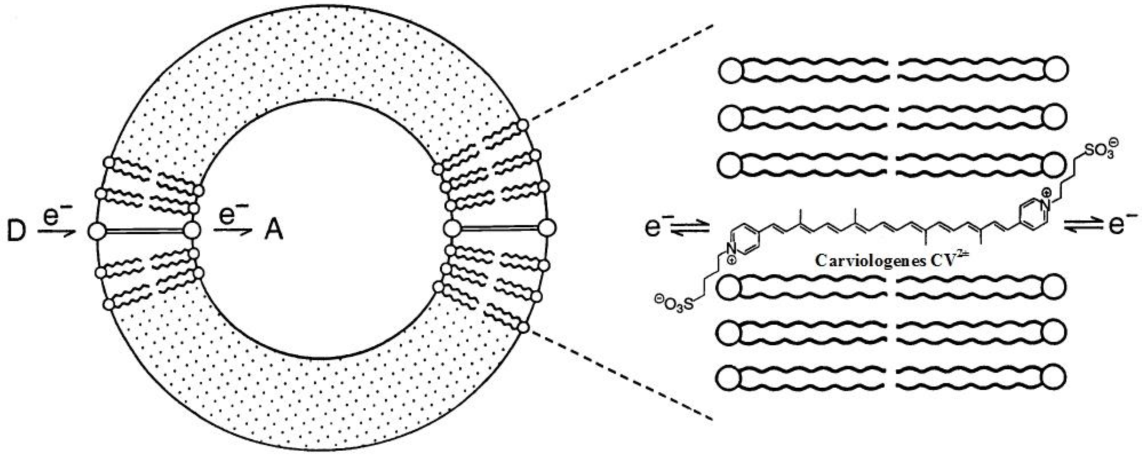


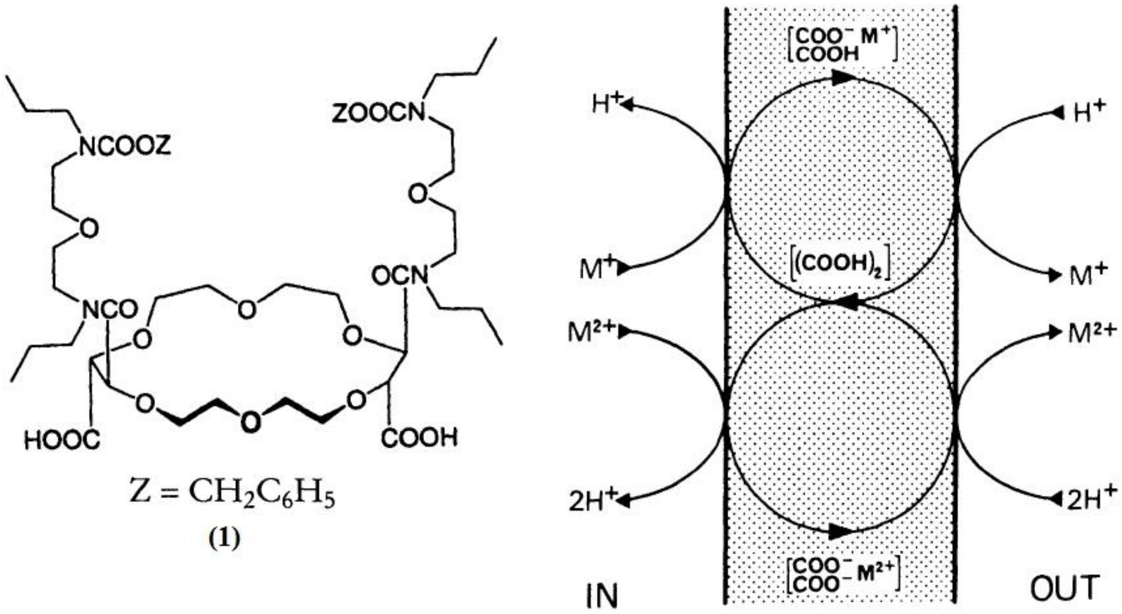
Figure 10: Schematic representation of transmembrane electron transfer from a reducing agent (such as sodium dithionite) to an oxidizing agent (such as potassium ferricyanide) by a zwitterionic caroviologen (CV$^{2\pm}$) incorporated in the bilayer membrane of a phospholipid vesicle.

6. Molecular and Supramolecular Ionic Devices

The numerous receptor, reagent, and carrier molecules are potential components of molecular and supramolecular ionic devices that are capable of handling inorganic and organic ions via highly selective recognition, reaction, and transport processes with coupling to external factors and regulation. Such components and the devices that they may build up form the basis of a field of molecular ionics, the field of systems operating with positively or negatively charged ionic species as support for signal and information storage, processing, and transfer. In view of the size and mass of ions, ionic devices may be expected to perform more slowly than electronic devices. However, ions have a very high information content by virtue of their multiple molecular (charge, size, shape, structure) and supramolecular (binding geometry, strength and selectivity) features.

The molecular recognition events involved may be directly related to information and signal processing by ions, as is the case in biology. Indeed, biological signals and communication events are based on ionic and molecular species (sodium, potassium, calcium, chloride, acetylcholine ions, etc.). Selective ion receptors represent basic units for ionic transmitters or detectors; selective ion carriers correspond to ionic transducers. These units may be fitted with triggers and switches sensitive to external physical (light, electricity, heat, pressure) or chemical (other binding species, regulating sites) stimuli for connection and activation.

Binding, transport and triggering may be performed by separate species, each having a specific function, as in multiple carrier transport systems. This allows a variety of combinations between photo- or electroactive components and different receptors or carriers. Light- and redox-sensitive groups incorporated into receptors and carriers affect binding and transport properties. Co-receptors and co-carriers provide means for regulation via cofactors, co-bound species that modulate the interaction with the substrate. Thus, a simple ionizable group, such as a carboxylic acid function, represents a proton switch and leads to proton-gated receptors and carriers responding to pH changes, as seen for instance in the regulation of transport selectivity by a lipophilic carrier (Figure 11, (**1**)), containing a single cation receptor site and two ionizable carboxylic acid groups, was found to transport selectively Ca^{2+} in the dicarboxylate form and K^+ when monoionized, thus allowing pH control of the process. This striking change in transport features as a function of pH involves pH regulation of Ca^{2+}-K^+ selectivity in a competitive (Ca^{2+}, K^+) symport coupled to (Ca^{2+}, $2H^+$) and (K^+, H^+) antiport in a pH gradient, which provides a proton pump (Figure 11, (**2**)).



$Z = CH_2C_6H_5$

(1)

(2)

Figure 11: (**1**) A lipophilic carrier and (**2**) A competitive divalent/monovalent cation symport coupled to $M^{2+}/2H^+$ and M^+/H^+ antiport in a pH gradient by a macrocyclic lipophilic carrier such as (**1**); the state of the carrier is indicated as diprotonated, $[(CO_2H)_2]$, or complexed, $[(CO_2^-)_2, M^{2+}]$ and $[(CO_2H)(CO_2^-), M^+]$.

Ion transfer takes place through mobile carriers or ion channels (see Figure 12); a rotating shuttle process may also be considered. Artificial transmembrane channels have been much less explored than carriers, probably because of the inherently larger molecular structures involved, despite the fact that biological transport is thought to occur mainly via channel-type species. Various routes to the design of ion channels and ion-responsive membrane systems have been investigated. One may imagine a variety of ion channel types depending on the nature of the ion binding sites, on the way in which they are arranged, on the molecular type and on the overall structural features. Some are represented schematically in Figure 13.

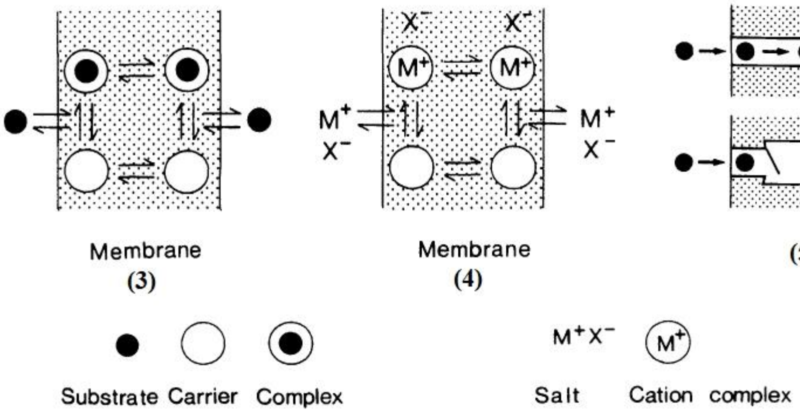


Figure 12: Transport processes. Carrier mediated, via a neutral species (**3**), of an ion pair (**4**). Channel mediated (**5**, top), gated channel (**5**, bottom).

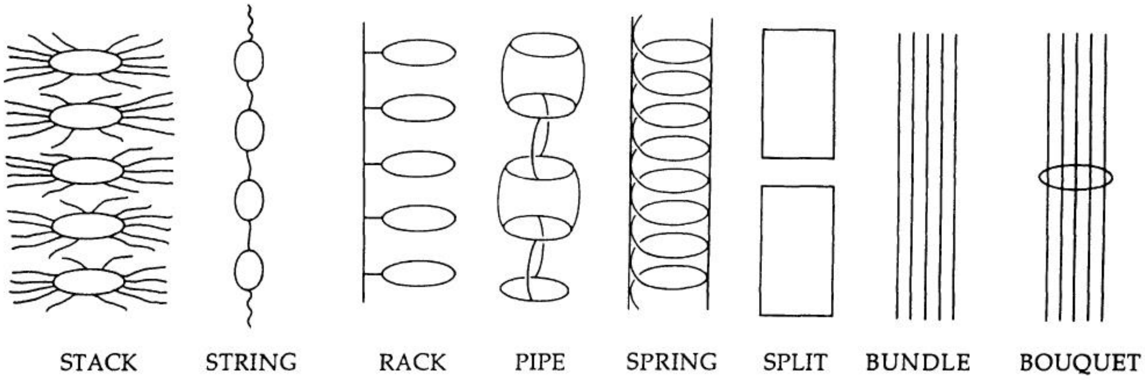


Figure 13: Schematic representation of different possible types of ion channel structures (from left to right): stack, string, rack, pipe of macrocycles, helical strand, two half-channel units, self-aggregated and macrocycle core bearing bundles of chains.

7. Summary

In this module you have learnt that:

- The understanding of the design and properties of molecular and supramolecular devices as basis for the development of chemical information processing and signalling as well as for the exploration of their relationships with related biological phenomena.

- The development of circuitry and functional materials at the nanometric scale by the formation of photonic, electronic, ionic switching devices from molecular components and their incorporation into well-defined organized assemblies.
- A supramolecular device comprises two or more components linked either covalently or noncovalently with distinct functions that are properties of the individual components.
- Supramolecular sensors comprise binding, transduction and actuator components either in a single molecule or as part of an indicator displacement assay.
- Molecules can display characteristics of electronic components such as the conduction of energy or electrons.

Subject	Chemistry
Paper No and Title	14: Organic Chemistry- IV (Advanced Organic Synthesis, supramolecular chemistry and carbocyclic rings)
Module No and Title	Module 19: Supramolecular reactivity and catalysis
Module Tag	CHE_P14_M19

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Anchor Institute : SGTB Khalsa College, University of Delhi

TABLE OF CONTENTS

1. Learning Outcomes

After studying this module, you shall be able to:

- Supramolcular catalysis process.
- Host-guest interactions and types of receptor molecules.
- Biological mimics
- Cocatalysis

2. Introduction

In this module basically we focus on supramolecular chemical reactivity predominantly in accelerating or understanding chemical reactions. There are close parallels between artificial, abiotic supramolecular reactivity and biochemistry, for example in the study of enzymes and Nature's catalysts. Synthetic catalysts can both model natural ones and allow the design of new different kinds of reactions. Supramolecular catalysis lies somewhere between chemical catalysis (transition metal and organocatalysis) and biology.

Supramolecular catalytic reactions involve binding of a well defined substrate (reactant) to the receptor (catalyst) and the catalytic process complete in three steps (see **Figure 1**) 1) Selective binding of reactant(s) based on their recognition by the receptor that may bear reactive group(s). 2) Transformation of the bound species. 3) Release of the products and regeneration of the catalyst. First two steps binding and transformation in this catalytic process, are the important steps because both steps take part in the molecular ***recognition*** of the ***productive*** substrate and require the correct molecular information in the reactive receptor. Compared to molecular catalysis, a binding step is involved that selects the substrate and precedes the reaction itself.

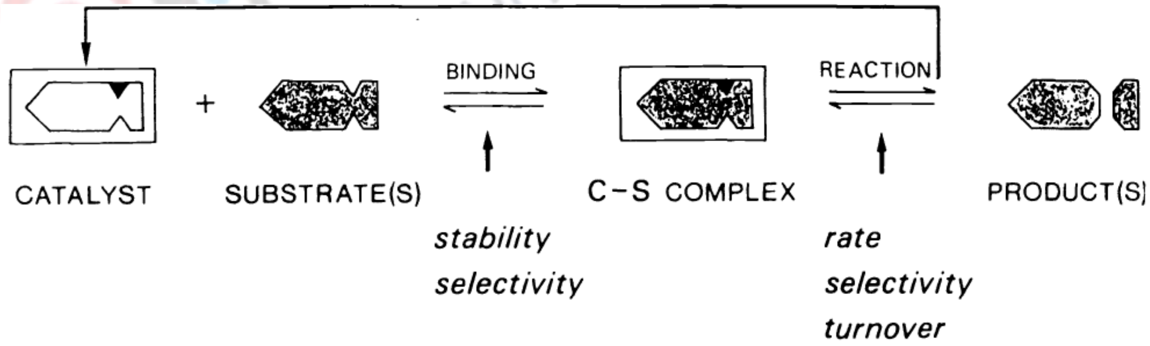


Figure 1 Schematic representation of the supramolecular catalysis process.

Supramolecular catalysis obeys the general rule stating that catalytic action consists in stabilization of a transition state of the reaction and in the rapid release of the product (see **Figure 2**). In a reaction catalyzed by the formation of a supramolecular transition state complex, substrates are inserted into either an active site of an enzyme, a host cavity, a layer, a micelle, a vesicle or micropores bringing their functional groups into a close contact for relatively long time. In addition, the incorporation can stabilize favorable conformations of the substrates.

Functional groups in the active site or cavity such as hydrogen bonding donor or acceptor groups can additionally exert ‘true’ catalytic action.

Supramolecular catalysis may be divided according to the type of the aggregate involved since it can be based on a catalytic action of a macrocyclic host, that of microemulsions, micelles or vesicles or on the catalytic activity of mesoporous materials.

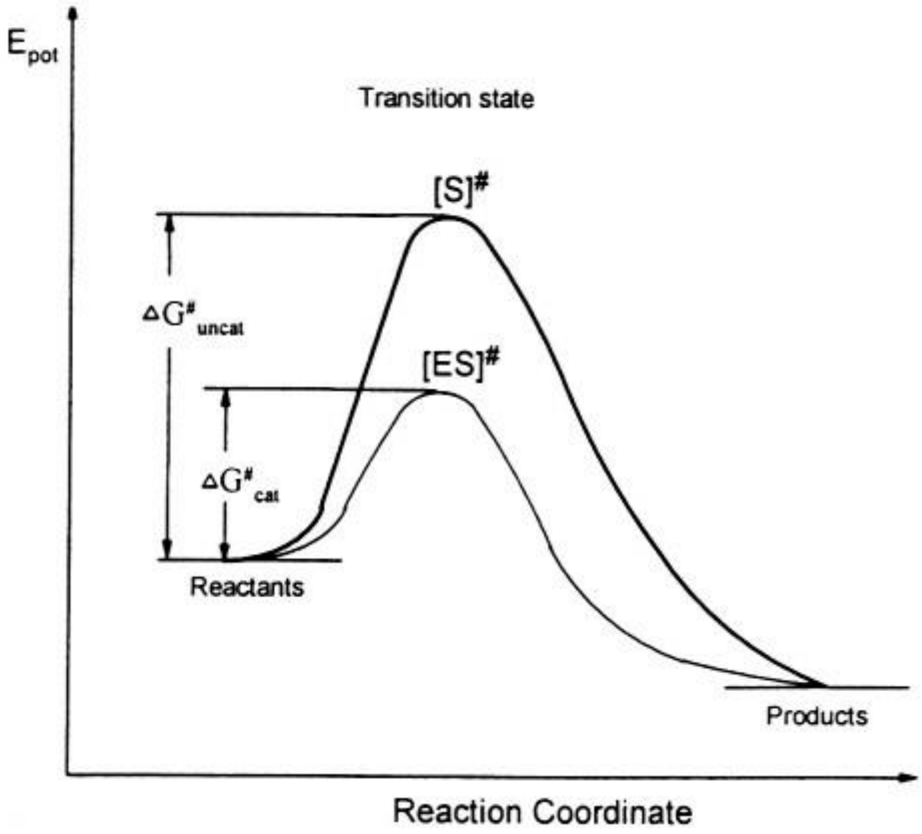


Figure 2 Transition state plots for the supramolecular catalysis process.

3. Catalysis by Reactive Macrocyclic Cation Receptor Molecules

The most important example for catalysis by reactive macrocyclic cation receptors is the deacylation of O-acetylhydroxylamine CH_3COONH_2 in presence of the macrocyclic polyether bearing four carbonyl groups derived from tartaric acid. The ability of [18]-O_6 macrocyclic polyethers to bind primary ammonium ions opens the possibility to induce chemical transformations on such substrates (see **Figure 3**). Activation and orientation by binding was observed for the hydrolysis of O-acetylhydroxylamine, which forms such a stable complex with the macrocyclic tetracarboxylate receptor that it remains protonated and bound even at neutral pH, despite the low pK_a (ca. 2.15) of the free species. As a consequence, its hydrolysis is accelerated and exclusively gives acetate and hydroxylamine, whereas in the presence of K^+ ions, which displace the substrate, it yields also acetylhydroxamic acid, $CH_3CONH\text{-}OH$ (ca. 50%). Thus, strong binding may be sufficient for markedly accelerating a reaction and affecting its course, a result that also bears on enzyme-catalysed reactions. Chemical transformations may be induced by reaction between a bound substrate and functional groups borne by the macrocyclic receptor unit.

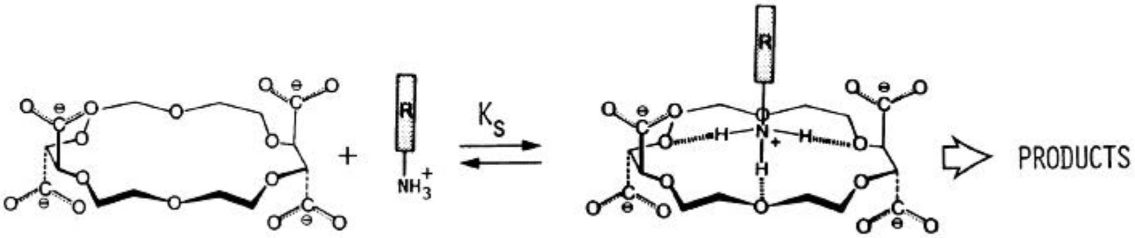


Figure 3: Scheme of binding of a primary ammonium group by the NH^{3+} to the cavity of [18]-O_6 macrocyclic polyether.

Ester cleavage processes have been most frequently investigated in enzyme model studies. Macrocyclic polyethers fitted with side chains bearing thiol groups cleave activated esters with marked rate enhancements and chiral discrimination between optically active substrate. The tetra-L-cysteinyl derivative of macrocycle [18]-O_6 polyether binds p-nitrophenyl (PNP) esters of amino acids and peptides, and reacts with the bound species, releasing p-nitrophenol as shown in **Figure 4**. The reaction displays (1) substrate selectivity with (2) marked rate enhancements in favor of dipeptide ester substrates, (3) inhibition by complexable metal cations that displace the bound substrate, (4) high chiral recognition between enantiomeric dipeptide esters, and (5) slow but definite catalytic turnover.

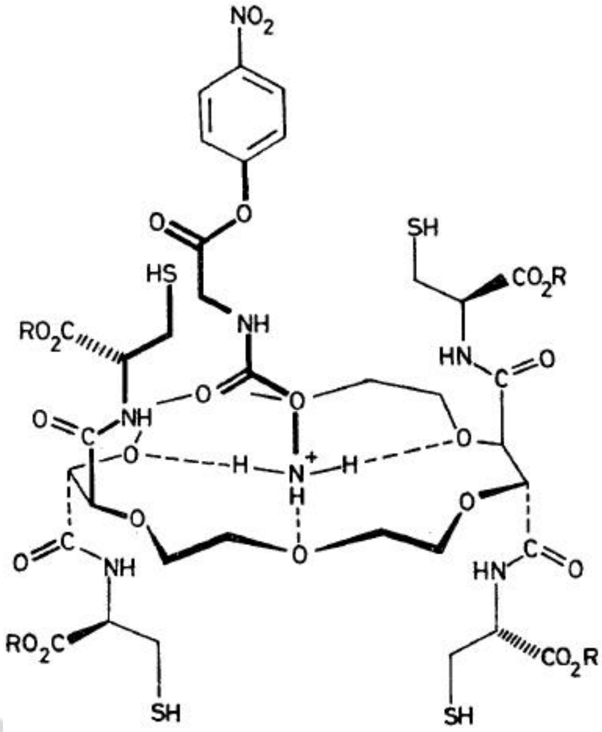


Figure 4: Schematic representation of the complex of receptor [18]-O_6 with the dipeptide substrate, glycyl-glycine p-nitrophenyl ester salt.

A well-understood example as mimics for transacylases has also been addressed by Cram, who used chiral corands as shown in **Figure 5**, bearing thiolate nucleophiles situated above and below the plane of the macrocycle. Corands of this type can bind primary ammonium cations via charge-assisted N-H···O hydrogen bonds. The host is complementary to the organic cation because of the matching of the three-fold symmetry of the -NH^{3+} group with the pseudo-six-fold arrangement of the corand binding sites. In the case of chiral guests, chiral recognition is observed as a consequence of steric interactions between the substituents on the naphthenyl groups (-CH_2SH in corand) and the substituents on the guest. Guest binding was accompanied by transacylation, in which an acyl group is transferred from guest to the host thiol group as a result of nucleophilic attack by the thiol (see **Figure 6**). In each case, the resolved S-host was used, and it was found that in the intermediate the stabilisation of the S-host/Lamino ester pair was significantly greater than the S–D diastereoisomer. The system thus displays kinetic selectivity in the sense that the substrates of L-handedness react more quickly than those of D-chirality because the reaction transition state is more stable for the S–L pair. This kinetic selectivity depends strongly on the nature of the amino acid derivative, which determines the identity of the R group on the substrate. For small amino esters such as alanine derivatives (R = Me), the ratio $k_{S,L}/k_{R,L}$ is 1, *i.e.* no selectivity. The selectivity increases rapidly with the bulk of R, however, with rate selectivity factors of 6.4 for R = Me_2CHCH_2, 8.2 for R = $C_6H_5CH_2$ and 9.4 for R = Me_3CH.

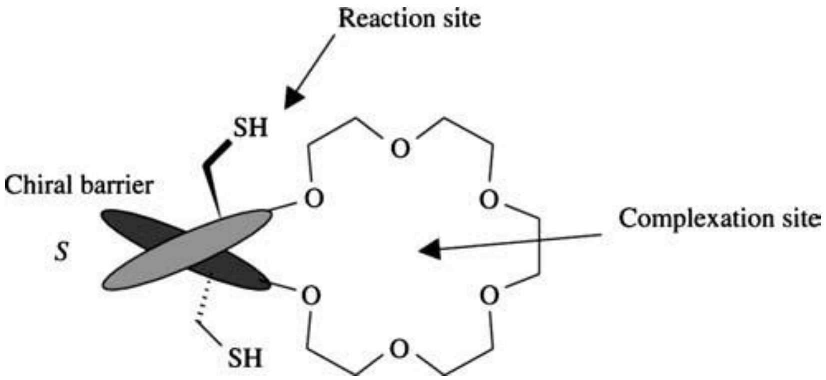


Figure 5: Key features of chiral corand transacylase mimics.

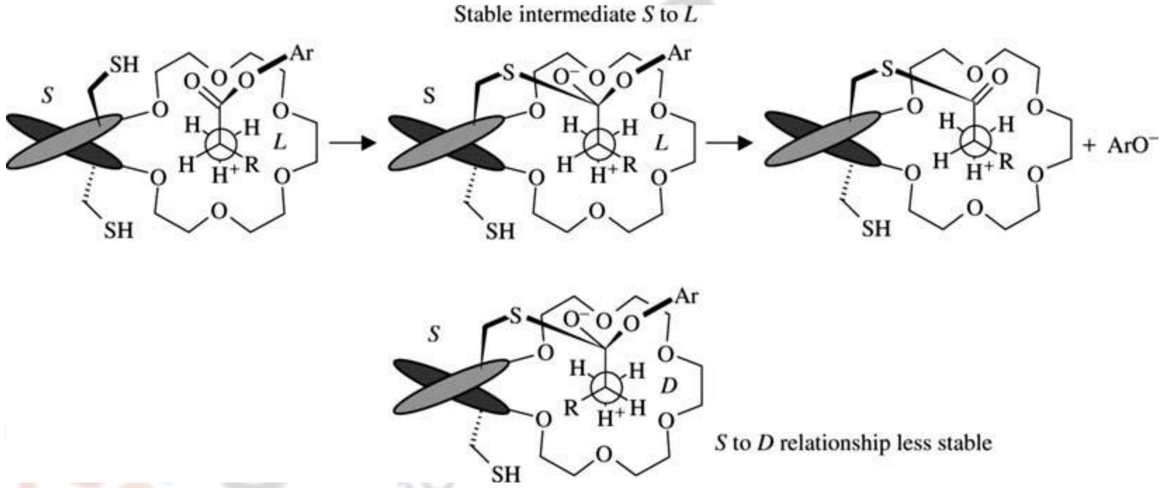
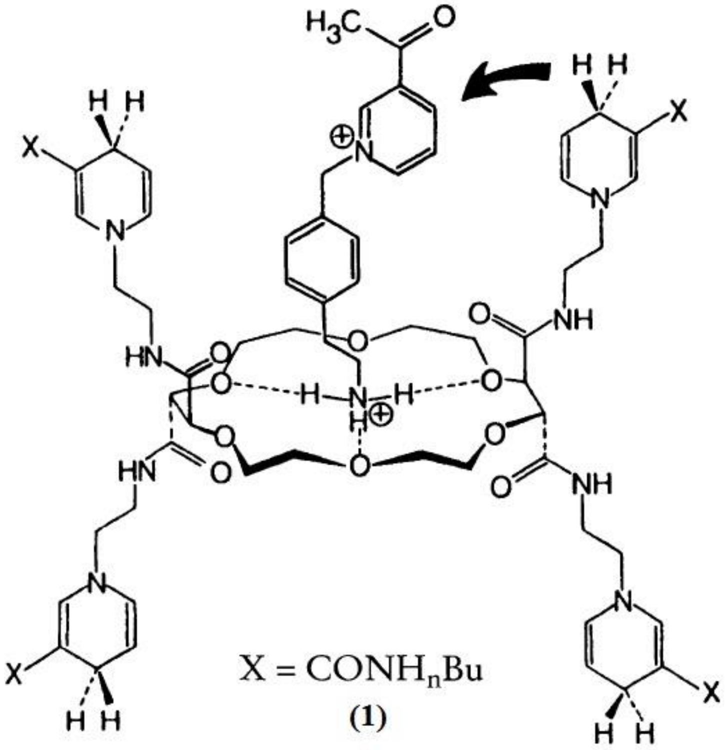


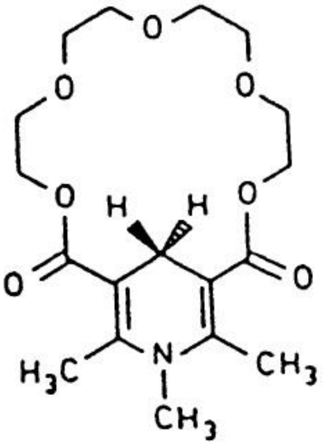
Figure 6: Scheme of transacylation step carried out by above described corand (Ar = *p* -$C_6H_4NO_2$).

Hydrogen transfer has been induced with macrocyclic receptors bearing 1,4-dihydropyridyl (DHP) groups. Bound pyridinium substrates are reduced by hydrogen transfer from DHP side chains within the supramolecular species (**1**); the first order intra complex reaction is inhibited and becomes bimolecular on displacement of the bound substrate by complexable cations. Reactions with carbonyl or sulphonium substrates have been performed with other DHP containing macrocycles, such as (**2**).



X = CONH$_n$Bu

(1)



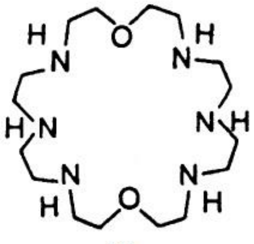
(2)

4. Catalysis by Reactive Anion Receptor Molecules

Generally, the anion hosts are also obey the same rules that govern the magnitude of binding constants and host selectivity in cation hosts (primarily based on preorganisation, complementarity, salvation and size and shape effects), their application is made much more difficult because of some of the intrinsic properties of anions, listed below.

- Anions are relatively large and therefore require receptors of considerably greater size than cations. For example, one of the smallest anions, F^-, is comparable in ionic radius to K^+ (1.33Å versus 1.38Å).
- Even simple inorganic anions occur in a range of shapes and geometries, *e.g.* spherical (halides), linear (SCN^-, N_3^-), planar (NO_3^-, $PtCl_4^{2-}$), tetrahedral (PO_4^{3-}, SO_4^{2-}), octahedral (PF_6^-, $Fe(CN)_6^{3-}$) as well as more complicated examples as in the case of biologically important oligophosphate anions.
- In comparison to cations of similar size, anions have high free energies of solvation and hence anion hosts must compete more effectively with the surrounding medium, *e.g.* $\Delta G_{hydration}(F^-) = -465$ kJ mol^{-1}, $\Delta G_{hydration}(K^+) = -295$ kJ mol^{-1}.
- Many anions exist only in a relatively narrow pH window, which can cause problems especially in the case of receptors based upon polyammonium salts where the host may not be fully protonated in the pH region in which the anion is present in the desired form.
- Anions are usually coordinatively saturated and therefore bind only *via* weak forces such as hydrogen bonding and van der Waals interactions, although they can form dative bonds.

The development of anion coordination chemistry and anion receptor molecules has made it possible to perform molecular catalysis on anionic substrates of chemical and biochemical interest, such as adenosine triphosphate (ATP). ATP hydrolysis was found' to be catalyzed by a number of protonated macrocyclic polyamines. In particular, [24]-N_6O_2 (**3**) strongly binds ATP and markedly accelerates its hydrolysis to ADP and inorganic phosphate over a wide pH range. The reaction presents first-order kinetics and is catalytic with turnover. It proceeds via initial formation of a complex between ATP and protonated (**3**), followed by an intracomplex reaction which may involve a combination of acid, electrostatic, and nucleophilic catalysis. Structure (**4**) represents one possible binding mode of the ATP-(**3**) complex and indicates how cleavage of the terminal phosphoryl groups might take place. A transient intermediate, identified as phosphoramidate (**5**), is formed by phosphorylation of the macrocycle by ATP and is subsequently hydrolyzed. Studies with analogues of ATP indicated that the mechanism was dissociative in character within a preassociative scheme resulting from receptorsubstrate binding. In this process, catalyst (**3**) presents prototypical ATPase activity; i.e., it behaves as a proto-ATPase.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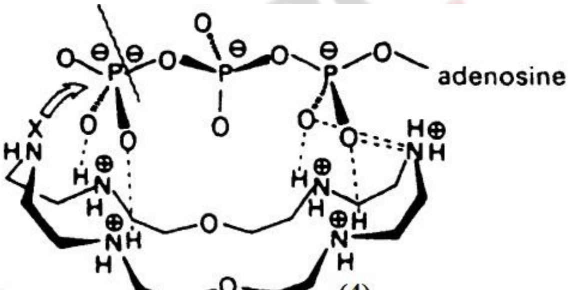

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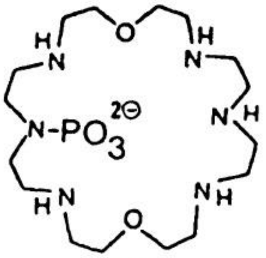
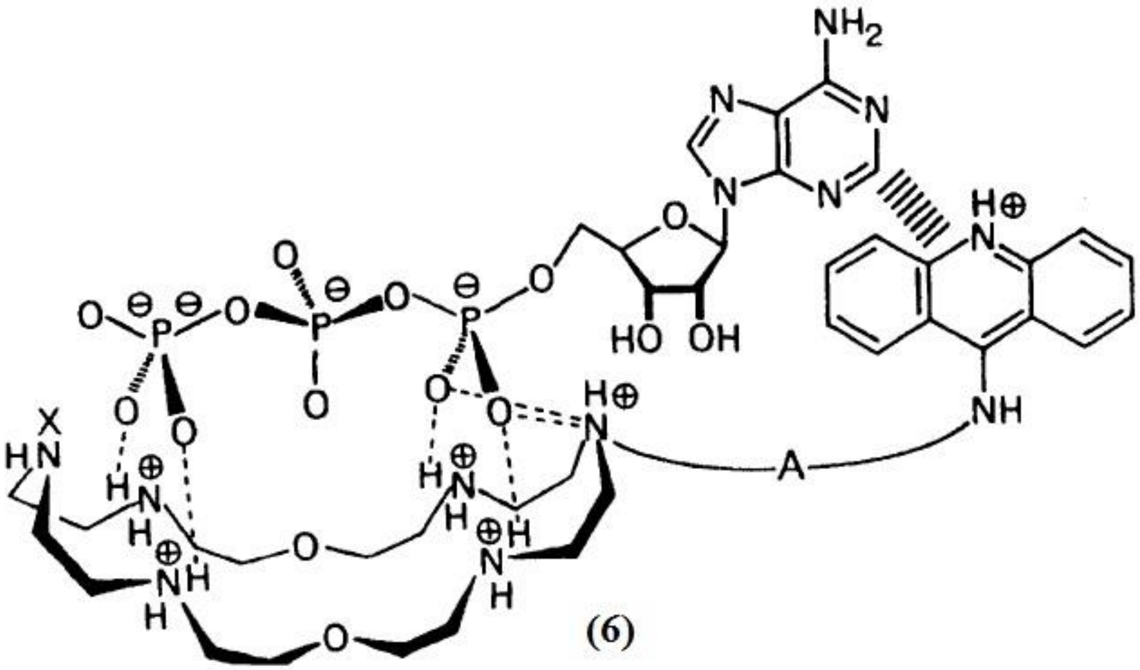


(5)

Multiple recognition and catalysis in ATP hydrolysis with increased ATP/ADP selectivity has been achieved with a multifunctional anion receptor containing a macrocyclic polyamine as anion binding site, an acridine group as stacking site and a catalytic site for hydrolysis (structure (**6**)). Phosphoryl transfer is accelerated by other types of hydrogen-bonding receptors.



(6)

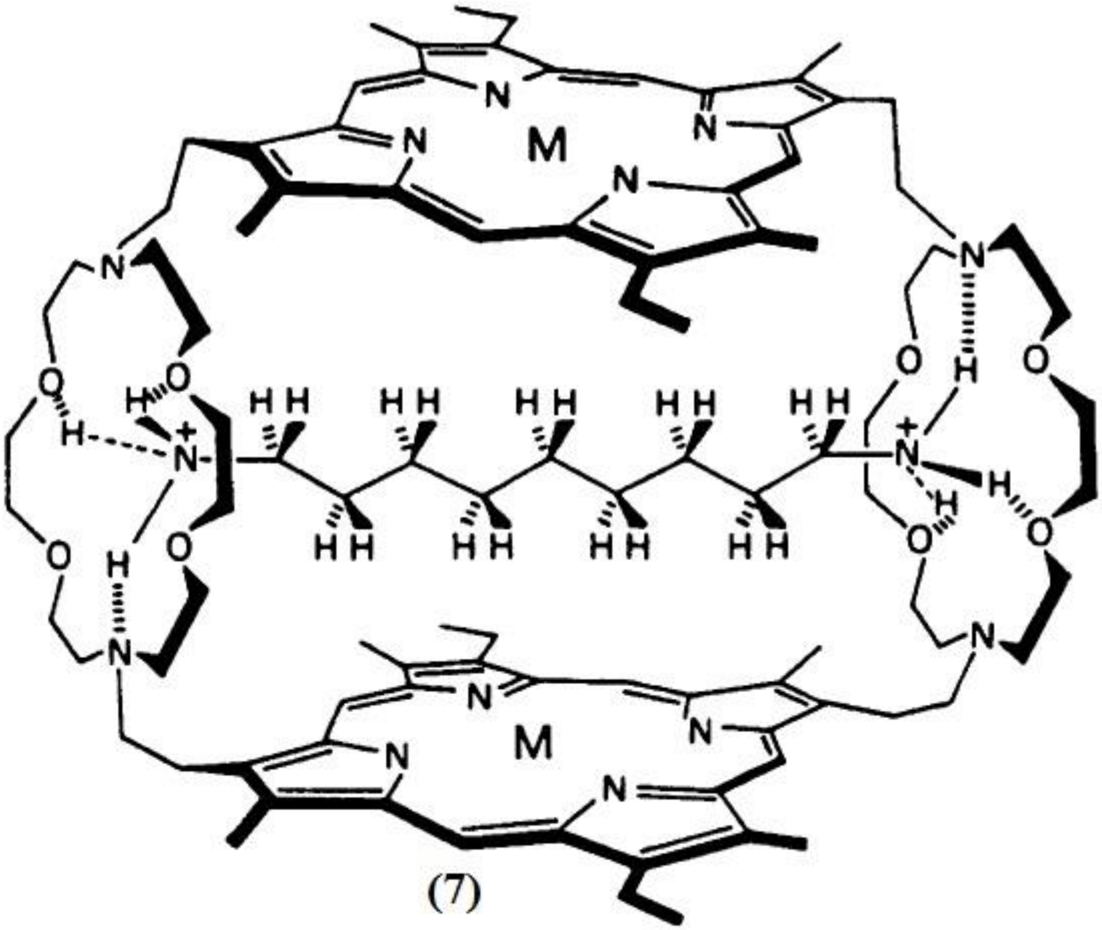
5. Catalysis with Cyclophane Type Receptors

The term ‘cyclophane’ literally means any organic molecule containing a bridged aromatic ring. By definition, cyclophane hosts (e. g. calixarenes and resorcarenes) must contain at least one macrocyclic ring and thus must achieve closure by some means of curvature. Cyclophane hosts commonly bind both neutral molecules and organic cations, and there is sometimes even some ambiguity as to whether a guest is protonated by, for example, a hydrogen bond acid host or vice versa, resulting in charge-assisted binding. Cyclophanes may or may not contain a molecular cavity large enough to host guest species, but in some cases cavities are unnecessary to achieve high binding affinity as long as binding sites exhibiting stereoelectronic (steric and electronic) complementary to the guest and are properly positioned (preorganised) on the surface of the host. Thus cyclophanes can exhibit capsular or nesting types of binding, or even apolar surface interactions, often leading to aggregation. Cavities are frequently encountered however, because of the entropic and enthalpic gains associated with spherical or three-dimensional encapsulation of the guest by a host with convergent binding sites.

A number of studies have made use of functionalized cyclophanes for developing supramolecular catalysts and enzyme models. Their catalytic behaviour is based on the implementation of electrostatic, hydrophobic and metal coordination features for effecting various reactions in aqueous media. Hydrophobic species bearing hydrocarbon chains present vitamin B_{12} or vitamin B_6 type activity. Such systems lend themselves to inclusion in membrane or micellar media. They thus provide a link with catalysis in more or less organized media such as membranes, vesicles, micelles, polymers. Water soluble cyclophanes showing, for example, transaminase, acetyl transfer, pyruvate oxidase or nucleophilic substitution activity have been described. Cyclophane catalysts offer a rich playground for developing novel reactions and enzyme models in view of the variety of their structural types, the large cavities they contain and the possibility to attach several functional groups.

6. Supramolecular Metallocatalysis

Supramolecular metallocatalysts consist in principle of the combination of a recognition subunit (such as a macrocycle, a cyclodextrin, a cyclophane, etc.) that selects the substrate(s) and of a metal ion, bound to another subunit that is the reactive site. Complexed metal ions presenting free coordination positions may present a variety of substrate activation and functionalization properties. Heterotopic coreceptors such as (**7**) bind simultaneously a substrate and a metal ion bringing them into proximity, thus potentially allowing reaction between them. Approaches towards the development of artificial metalloenzymes have been made, based on cyclodextrins or macrocycles and involving various metal ions, such as Zn(ll), Cu(ll), Co(lll), for facilitating hydrolysis, epoxidation, hydrogen transfer, etc. Metalloporphyrins have been used for epoxidation and hydroxylation and a phosphine-rhodium complex for isomerization and hydrogenation. Cytochrome P-450 model systems are represented by a porphyrin-bridged cyclophane, macrobicyclic transition metal cyclidenes or β-cyclodextrin-linked porphyrin complexes that may bind substrates and perform oxygenation reactions on them. A cyclodextrin connected to a coenzyme B_{12} unit forms a potential enzyme-coenzyme mimic. Recognition directed, specific DNA cleavage reagents also make use of the reactivity features of various complexed metallic sites. The remarkable facilitation of amide hydrolysis by dinuclear copper complexes and related processes may open routes towards metallocleavage of proteins. Selective metalloprocesses, in particular asymmetric reactions utilizing external chiral ligands, such as hydrogenation, epoxidation, hydroxylation, etc. are of great value for organic synthesis and are being actively investigated. Supermolecular metallocatalysts, by combining a substrate recognition unit with a catalytic metallic site, offer powerful entries to catalysts presenting shape, regioand stereoselectivity.



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7. Cocatalysis: Catalysis of Synthetic Reactions

A further step lies in the design of systems capable of inducing bond formation rather than bond cleavage, thus effecting synthetic reactions as compared to degradative ones. To this end, the presence of several binding and reactive groups is essential. Such is the case for coreceptor molecules (**7**) in which subunits may cooperate for substrate binding and transformation. They should be able to perform cocatalysis by bringing together substrate(s) and cofactor(s) and mediating reactions between them within the supramolecular structure (**Figure 5**).

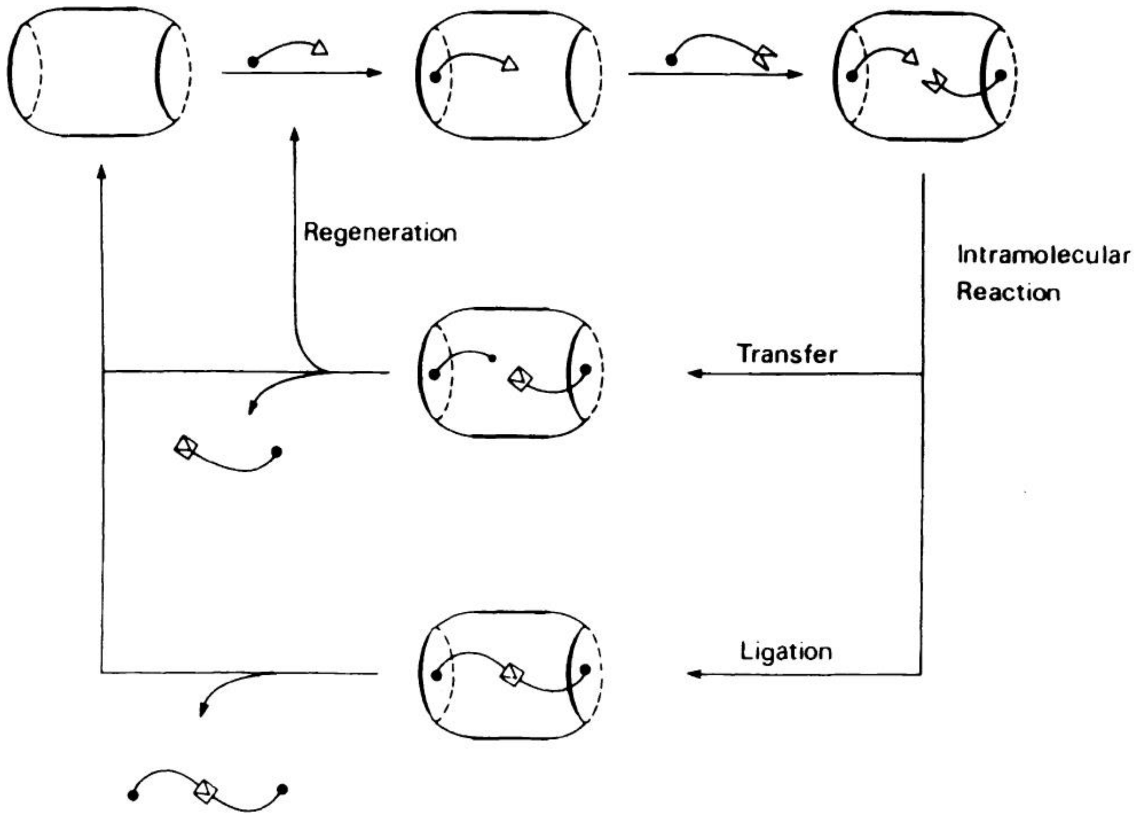


Figure 5: Schematic illustration of cocatalysis processes: group transfer and ligation reactions occuring within the supramolecular complex formed by the binding of substrates to the two macrocyclic subunits of a macrotricyclic coreceptor molecule.

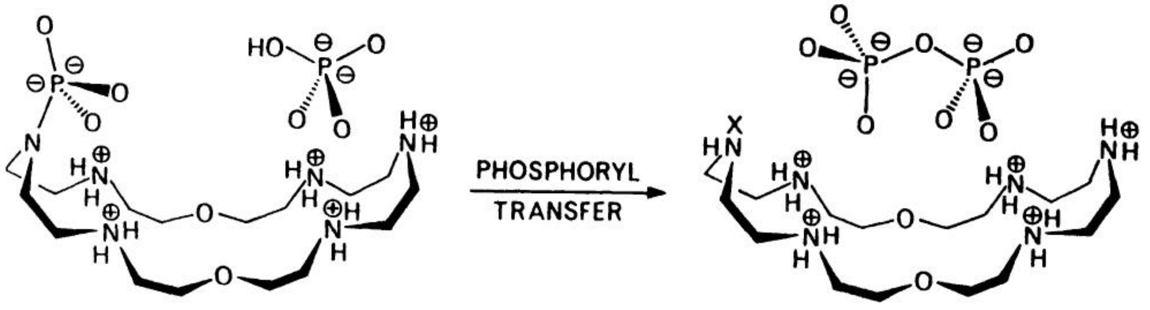


Figure 6: Cocatalysis: pyrophosphate synthesis by phosphoryl transfer mediated by macrocycle (**3**) Via the phosphorylated intermediate (**5**).

Processes of this type have been realized in supramolecular phosphorylation reactions. Indeed, the same [24]-N_6O_2 macrocycle (**3**) as that already used in the studies of ATP hydrolysis was also found to mediate the synthesis of pyrophosphate from acetylphosphate (AcP). Substrate consumption was accelerated and catalytic with turnover following the steps: (1) substrate AcP binding by the protonated molecular catalyst (**3**); (2) phosphorylation of (**3**) within the supramolecular complex, giving the phosphorylated intermediate PN (**5**); (3) binding of the substrate HPO$_4^{2-}$ (P); (4) phosphoryl transfer from PN to P with formation of pyrophosphate PP (**Figure 6**); (5) release of the product and of the free catalyst for a new cycle. PP is also formed in the hydrolysis of ATP in the presence of divalent metal ions. The fact that (**3**) is a ditopic coreceptor containing two diethylenetriamine subunits is of special significance for both PN and PP formation. These subunits may cooperate in binding AcP and activating it for phosphoryl transfer via the ammonium sites, in providing an unprotonated nitrogen site for PN formation and in mediating phosphoryl transfer from PN 81 to P. Thus (**3**) would combine electrostatic and nucleophilic catalysis in a defined structural arrangement suitable for PP synthesis via two successive phosphoryl transfers, displaying kinase type activity (**Figure 6**). This process was extended to the phosphorylation of various substrates, in particular to the synthesis of ATP from ADP in mixed solvent and in aqueous solution in the presence of Mg^{2+}, probably via formation of a ternary catalytic species (**8**). The latter abiotic ATP generating system has been coupled to sets of ATP consuming enzymes resulting in the production of NADH by a combined artificial/natural enzymatic process (**Figure 7**).

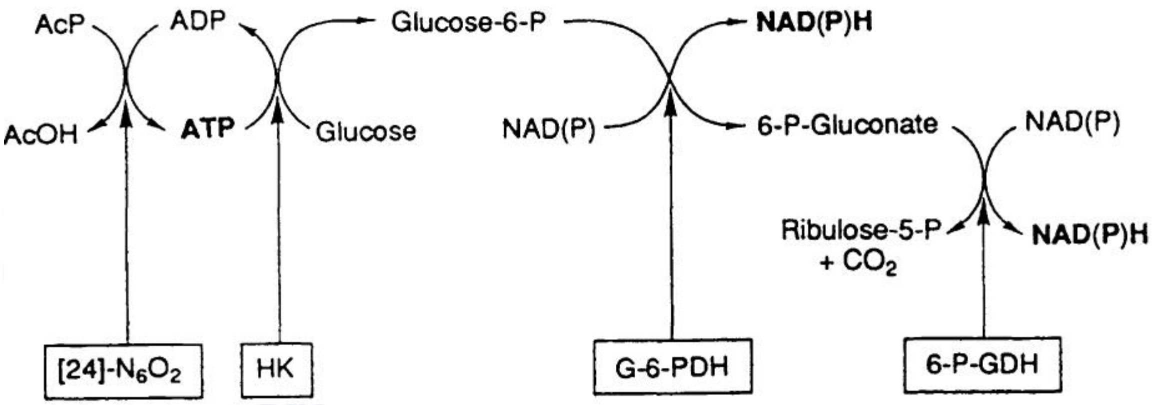
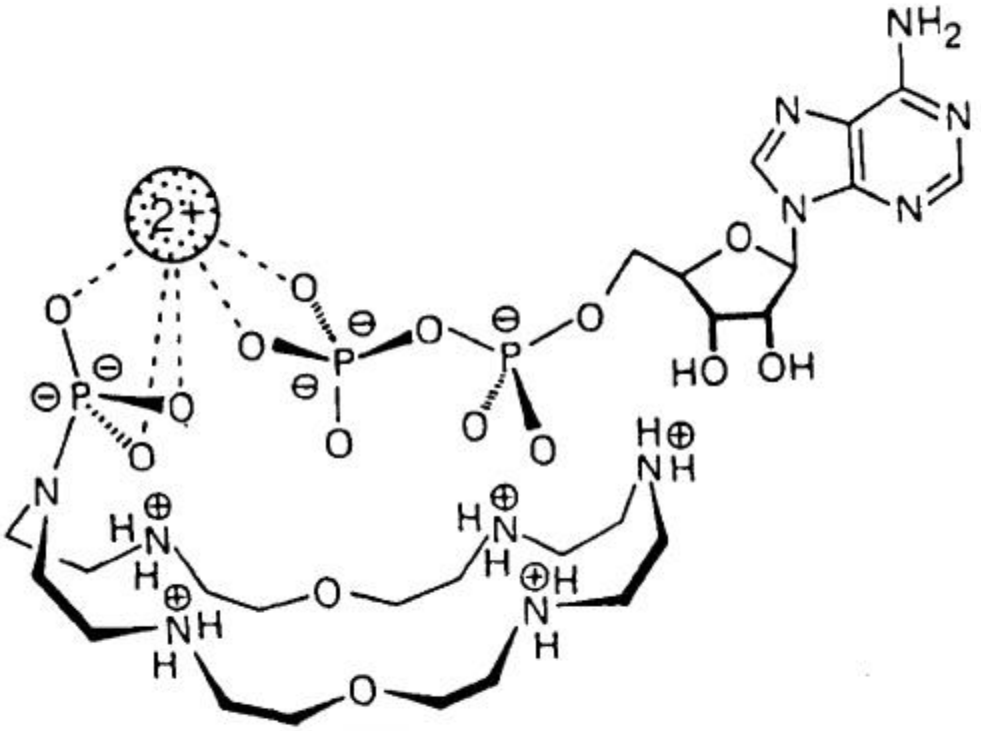


Figure 7: Sequence of transformations catalysed by the supramolecular ATP-generating system [(**3**), AcP, Mg^{2+}, ADP] ((**3**) = [24]-N$_6$O$_2$) and the enzymes hexokinase (HK), glucose-6-phosphate dehydrogenase (G-6-PDH) and 6-phospho-gluconate dehydrogenase (6-P-GDH).



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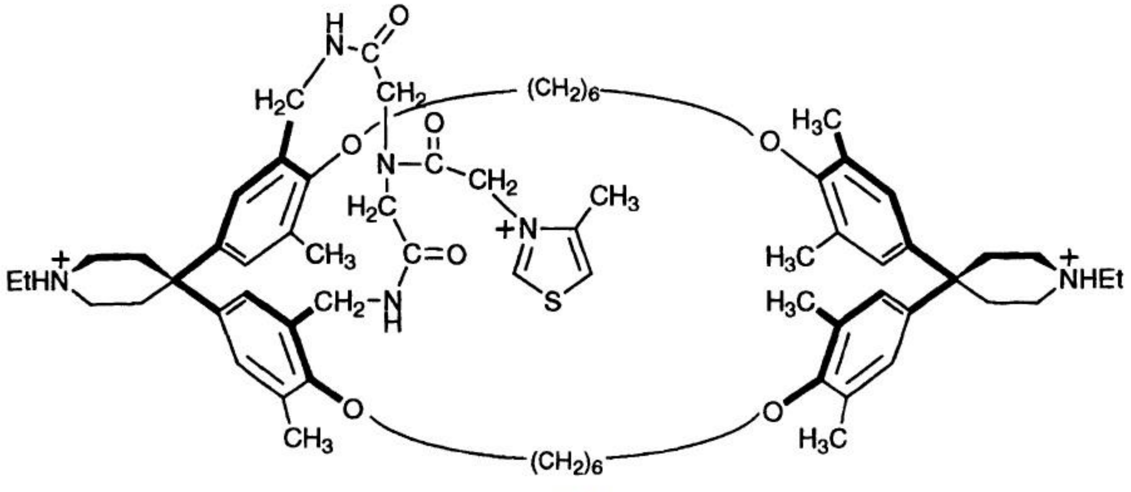

(9)

Templates possessing two hydrogen bonding subunits bind two substrates forming a ternary complex in which the substrates are positioned so as to facilitate bond formation between them. In a related way, the rate and stereoselectivity of a bimolecular Diels-Alder reaction are substantially increased by binding both the diene and the dienophile within the cavity of a tris-porphyrin macrocycle. A macrobicyclic thiazolium cyclophane (**9**) functions as a model of thiamine pyrophosphate-dependent ligases and effects benzoin condensations. Acyl transfer is catalysed by formation of a ternary complex between a cyclophane receptor and two substrates. Difunctional binding and catalysis has been observed in functionalized cyclodextrins and in a hydrogen bonding cleft. Functionalized crown ethers have been used as reagent for peptide synthesis.

8. Biomolecular and Abiotic Catalysis

The design of supramolecular catalysts may make use of biological materials and processes for tailoring appropriate recognition sites and achieving high rates and selectivities of reactions. Modified enzymes obtained by chemical mutation or by protein engineering represent biochemical approaches to artificial catalysts. This is also the case for the generation of catalytic proteins by induction of antibodies. Antibodies to reactive haptens are able to facilitate the transformation of the bound species. Generating antibodies against analogues of transition states should lead to transition state stabilization and facilitate the process. Such *catalytic antibodies* or *abzymes* have been produced for a variety of reaction and an active field of research has developed along such lines. It represents an approach to substrate specific, efficient and selective catalysis of supramolecular type which is of much basic and applied interest. The strong affinity for the transition state (TS) of the reaction of a given substrate leads it along the way and thus facilitates the process. In line with the remarks made at the beginning of this chapter, the antibodies should be generated not against a transition state analogues (TSA) itself but against a (TSA-X) isoster lacking the group(s) X, which belong(s) to the reactive function(s) of the protein that is (are) expected to perform the reaction. This requires designing a (TSA-X) species in which the face presenting the (-X) gap be ideally chosen so as to lead to the induction in the antibody of the desired reactive functional group at the correct position.

9. Summary

In this module you have learnt that:

- Supramolecular reactivity and catalysis possess several properties such as: substrate recognition, reaction within the supermolecule, rate acceleration, inhibition by competitively bound species, structural and chiral selectivity, and catalytic turnover.
- In particular, the transacylation reactions mentioned above operate on activated esters as substrates, but the hydrolysis of unactivated esters and especially of amides under "biological" conditions, presents a challenge that chemistry has met in enzymes but not yet in abiotic supramolecular catalysts.
- Development of supramolecular catalysts performing synthetic reactions that create new bonds rather than cleave them. By virtue of their multiple binding features, coreceptors open the way to the design of cocatalysts for ligation, metallocatalysis, and cofactor reactions, which act on two or more co-bound and spatially oriented substrates.
- Supramolecular catalysts are by nature *abiotic* chemical reagents that may perform the same *overall* processes as enzymes, without following the detailed pathway by which the enzymes actually effect them or under conditions in which enzymes do not operate.

- Furthermore and most significantly, this chemistry may develop systems realizing processes that enzymes do not perform while displaying comparable high efficiencies and selectivities.