

CHM 421 ORGANIC SYNTHESSES

ORGANIC SYNTHESIS: Most organic compounds can be prepared by different routes and criteria are needed to select the best method. Generally the best synthesis of a substance involves the conversion of the most available and cheapest starting materials into the desired product and it should be with the least number steps and in the highest possible overall yield.

In commercial synthesis, cost of starting materials and economy of operation play a dominant role.

Organic chemists have traditionally undertaken synthesis as the final proof of molecular structure for natural products from plants and animal sources. Identity between the natural substance and the compound produced by synthesis confirms the molecular structure deduced by chemical and physical methods. In more practical terms, synthesis can provide the supply of useful compounds like quinine, penicillin, prostaglandins, vitamins and insect attractants not available in adequate quantities from nature.

Synthesis can also be used to prepare substances previously unknown but predicted to have useful properties either to test theories or to create new chemical products. Synthetic chemistry is a major Endeavour in the research laboratory of the chemical industry.

DESIGN OF A SYNTHETIC: There are great numbers of synthetic routes leading to any given target molecule. It is preferable to select routes with fewest steps and the cheapest or most available starting materials. However, the yields of organic reactions are in practice, rarely 100%. In a multi – step sequence, the overall yield is the mathematical product of the yields of all the individual steps. The serious decrease in efficiency is caused by poor yield leads to an important guiding principle to be applied when choosing between alternative routes.

1. The central test of a good route is to have a minimum number of steps
2. The reaction selected should have at least a good precedent of high yield
3. The reaction selected must be closely examined to be as certain as possible that no competing rxn will seriously lower the yield and lead to difficult problems of separation.

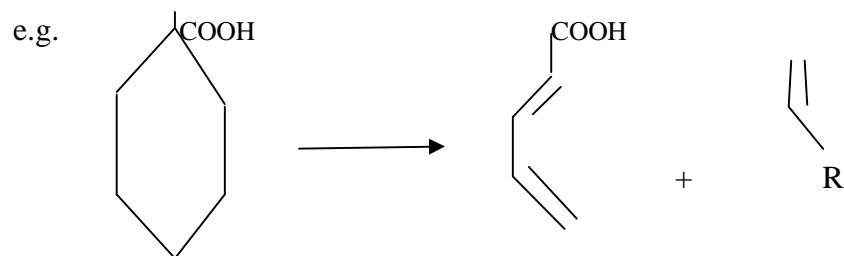
SYNTHESIS DESIGN: It is usually to work backwards from the target to the structures available as starting materials



Product Synthon

The structure of the target molecule can be formally divided into 2 parts:-

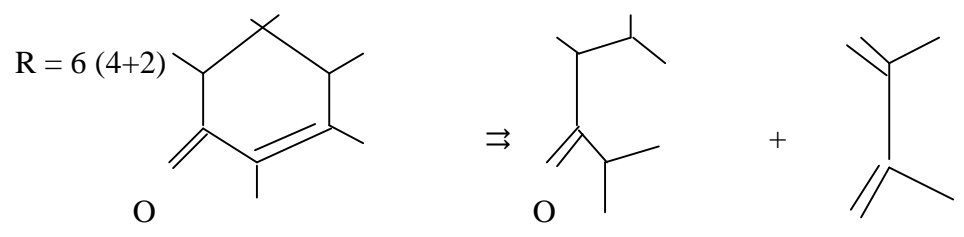
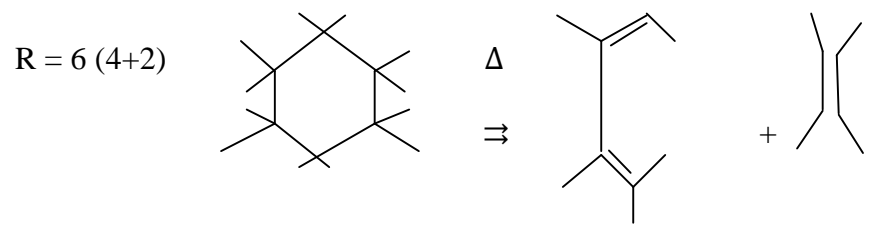
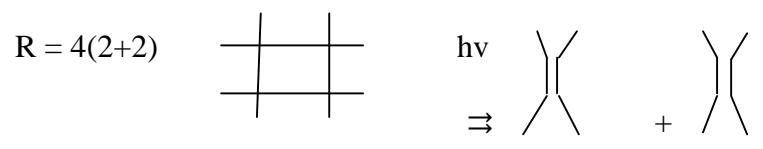
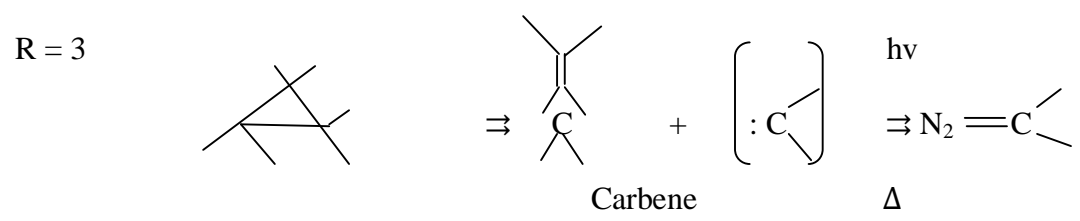
- (i) Its carbon skeleton
- (ii) Functional group located on that skeleton.



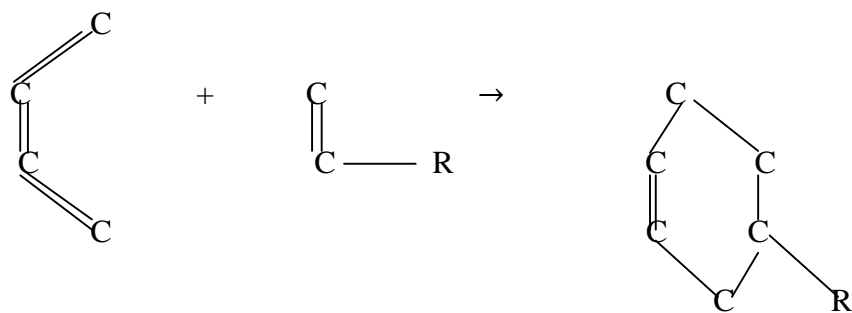
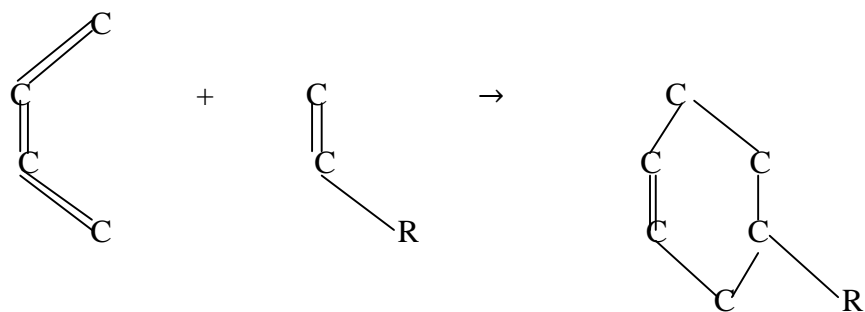
The structure of the target must be constructed from smaller units (synthons)

ANNELATION REACTION: - Ring forming reactions are of special importance since many of the usual synthetic targets contain cyclic skeleton. In order to synthesis a ring from 2 separate synthons, we must construct 2 bonds of that ring, the 1st to pull the synthons together and the second to cyclise them.

An annelation reaction is one which creates both bonds in one step, or at least in one laboratory operation cycle addition such as Dial Alder's rxn is an example. If the ring size is Rr and the two synthons contribute m & n atoms to the ring, then, $r = m+n$ and the operation is an (m+n) annelation. E.g.



DIEL – ALDER’S REACTION: - This is a rxn undergone by conjugated diene. It is the most important type of (the) rxn. These are addition rxn in which the ring system are formed continue the elimination of any compound in general term the Diel – Alder’s rxn may be written as follows:



A- diene

B (dienophile)

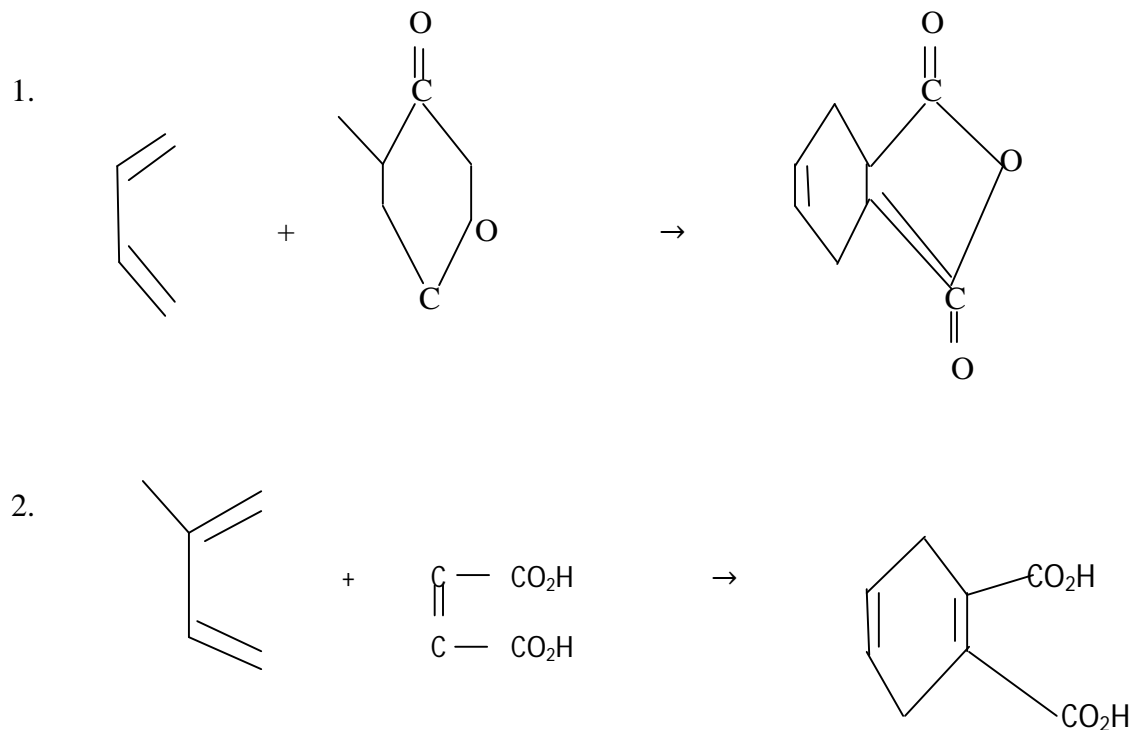
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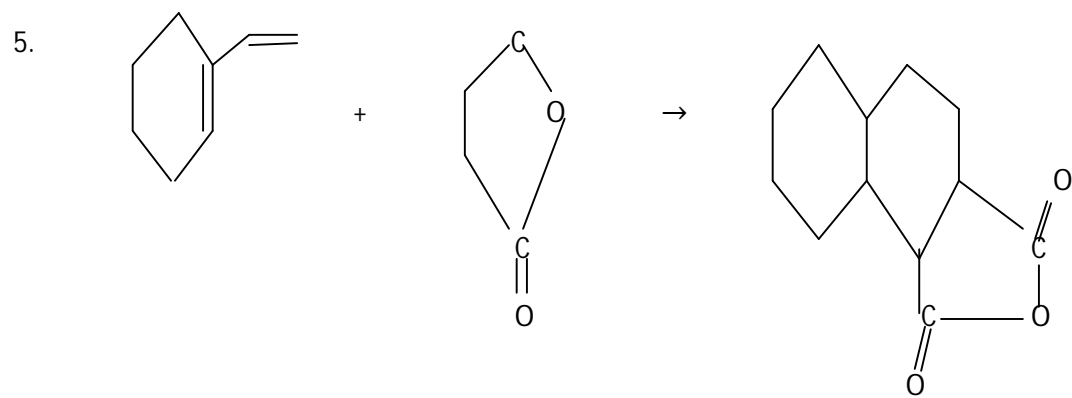
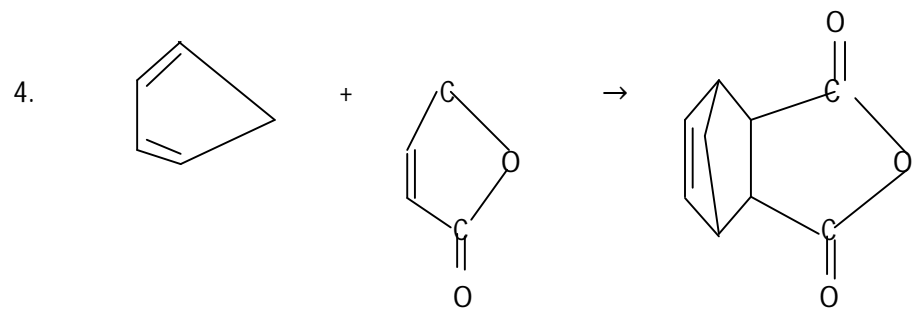
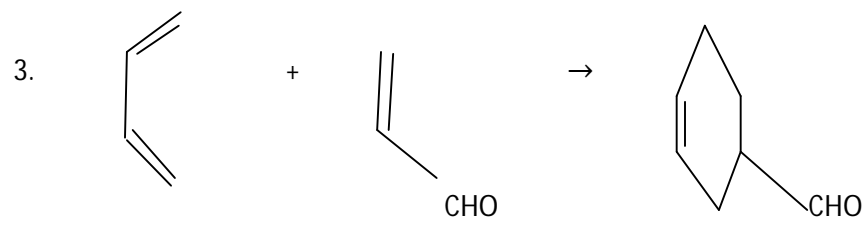
Compound A is usually referred to as the diene (whether it be a conjugated diene, polyene, enyne or diene). Compound B is usually referred to as a dienophile. R is usually a group which contains a carbonyl group attached to one of the ethylenic or acetylenic carbon atoms. E.g. The dienophile is usually an α, β unsaturated carbonyl. E.g. α, β unsaturated acids and anhydrides, esters, aldehydes or ketones.

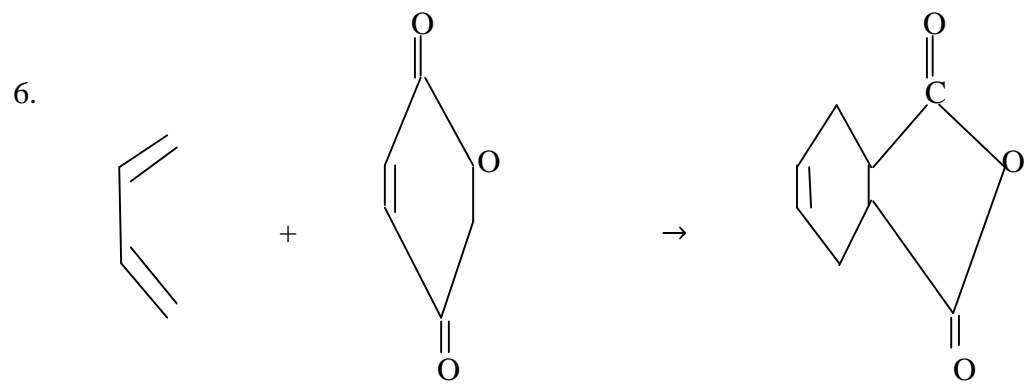
The dienophile may also be quinone. The presence of a carbonyl group (I effect) in the dienophile is essential, compounds which contain – I group such as nitro or cyano can also behave as dienophile.

The dienes may be of various types as cycle, acyclic allylic, semicyclic compounds containing 2 double bonds in conjugation, bicyclic compounds, aromatic h/c containing at least 3 linear benzene rings e.g Anthracene also, heterocyclic compounds (furan)

It is important to note that only cisoid and not transoid dienes enter into Diels-Alder's rxn.



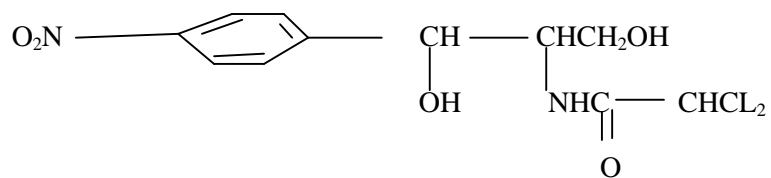




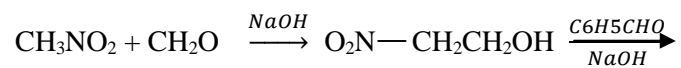
SPECIAL TECHNIQUES

A variety of indigenous techniques have been invented by research xmistis to overcome special obstacles to successful synthesis. These methods are best described by illustrating their use in actual synthesis

- 1) **SYNTHESIS OF CHLORAMPHENICOL** :- It is an aromatic compound of commercial importance and was isolated from cultures of certain enlarge and was found to possess the structure stated below:-

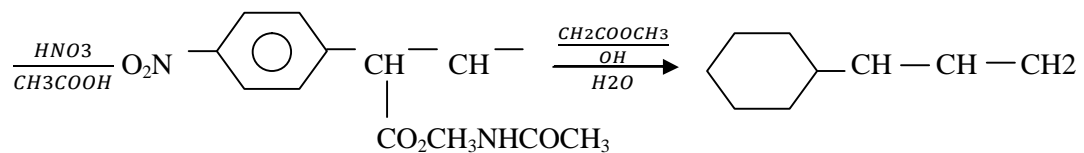
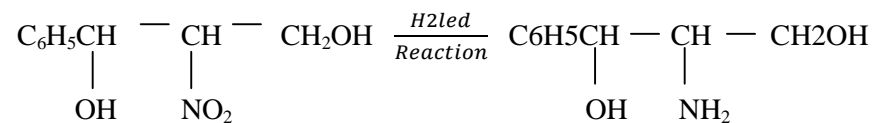


PREPARATION



Nitro HCHO

Methane methanol



2) SYNTHESIS OF VITAMIN A

This is important in nutrition.

The starting material is readily available terpene, citral see is converted to β ionone to (a) provide the cyclic end of the target.

Preparation

diagramn

INDUSTRIAL SYNTHESIS OF VINYL CHLORIDE

Vinyl chloride is used to make PVC of it is the second largest tonnage polymer.

PREPARATION

(1).Acetylene or Ethyne base the

Diagram

The reaction proceeds through an intermediate vinyl Hg (oc) compound as shown:

Diagram

% yield is 80-95%

DESIRABILITY OF THE METHOD (MERITS)

1. It is a one-stage process process.
2. Relatively mild reaction condition.
3. Endothermic reaction, no heat is required. Hence, money is saved. Pyrolysis:-heating (2) high temperation.
4. Favourable stoichiometry i.e almost 100% yield, all draw materials appear in the product. The only disadvantages of this method as the supply of raw materials (acetylene) see are expensive.

It is a highly corrosive gas of transportation is costly. The high cost of acetylene provides a considerable economic incentive to base vinyl chloride manufacture on a cheaper to carbon raw material such as ethylene.

(2). Ethylene dichloride process

This involves the use of ethylene.

Diagram

The reaction can be carried out in gas phase at a temperature of 360-400k.

The reaction flows free radical mechanical.

Diagram

It can also take place in liquid phase in the presence of FeCl_3 at 340k.

The reaction follows ionic mechanical

Diagram

This method has an advantage of being based on a cheaper h/c i.e. diagram than the acetylene process. This route has the major drawback of converting half the chlorine set to it to HCl of this severely limited use of ethane or ethylene in vinyl chloride manufacture.

(3). THE BALANCE ROUTE PROCESS

One elegant way to go around those disadvantages of the ethylene dichloride process is to use the so called balance route. In this, acetylene based of ethylene based process is reacted in parallel, the HCl produced by ethylene do chloride pyrolysis is being fed to the acetylene based process.

Diagram

The balanced route has been operated in bp inUK. However, this solution to the problem of HCl by-product is not as attractive as it appears at first sight for two reasons.

Firstly, the process requires three reaction stages, so that capitals of operating cost are increased.

Secondly, half the h/c fed is still the expensive acetylene in this form described, it is not a favoured way of making vinyl chloride.

(4). KNETE PROCESS

Modified form of the above process was developed. In this a mixture of acetylene produced by h/c cracking is reacted first with HCl under such conditions that only acetylene reacts.

The resultant vinyl chloride is removed from the gas stream. The remaining ethylene is then reacted with chloride to give ethylene dichloride which is then pyrolysed to give vinyl chloride of HCl.

Diagram

The essential difference between this process of the balanced-route describe is that substantial savings in the separation cost of ethylene of acetylene are made. However, high capitals of energy cost are still incurred of the conversation of acetylene or ethylene mixture still requires three stages. The route is not commercially attractive.

(5). OXY-CHLORINATION-DEACON'S PROCESS (MOST ACCEPTED)

This involves the conversion of HCl to chlorine (deacon process) by oxidation with air or a copper chloride at 720K. One way of avoiding wastage of chlorine will be to use Deacon's process to convert HCl by-product from ethylene dichloride pyrolysis back to chlorine.

Diagram

However, this method involves an extra stage to the process, with the resultant increase in capital and operating cost.

A more elegant approach is to carry out the oxidation of the HCl in the presence of ethylene.

A more recently developed process has been able to carry out the reaction and has been found to be the most successful way of producing vinyl chloride.

Diagram

CHLOROPRENE: - (2-CHLOROBUTAN-1, 3-DIENE)

Diagram

It is a monomer for neoprene one of the highest synthetic rubbers. The original method of manufacture is by addition of HCl to vinyl chloride made by dimerisation of acetylene.

Diagram

This process is now subject to competition for processes based on raw materials other than acetylene e.g. from butadiene as raw material.

Diagram

Butadiene is chlorinated in gas phase at 570K to give a mixture of trans 1, 4-dichlorobut-2-ene and 3, 4-dichlorobut-1-ene.

Diagram

The reaction is a free-radical mechanism and conditions must be carefully designed to avoid the occurrence of the variety of side reactions. The 3, 4-dichlorobut-1-ene (b.p. 396K) which is the product required for the final stage of the process is separated from the mixture of 1, 4-dichlorobut-2-ene (b.p. 428K).

The 1, 4-dichlorobut-2-ene is subject to isomerisation on the presence of Cu or other salts to produce further 3, 4-dichlorobut-1-ene.

Diagram

In the final stage of the process, the intermediate carbonium ion can be re-arranged to give 3, 4-dichlorobut-1-ene is dehydrochlorinated (btHCl) by heating with alcoholic KOH.

Diagram

PREPARATION OF INSECTICIDE OF DDT

Insecticides are important group of organic chemical in the industry of they make the major contribution to the quality of life by increasing agricultural efficiency of output.

They also control insect-born diseases. DDT was found to be a highly effective insecticide. It is highly potent of kills a wide range of insect by both contact of ingestion.

It is of low acute iconicity to warm blooded animals. The major disadvantage is that it is chemically stable of therefore persistent.

Diagram

SPECIAL TOPICS

ASCENT OF HOMOLOGOUS SERIES (INCREASING THE NO OF ATOMS IN AN ORGANIC COMPOUND)

Diagram

(2). ARNDT – EISTERT REACTION

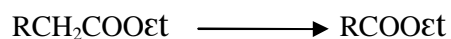
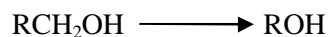
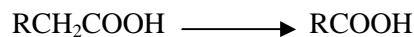
It increases the homologous of carbon atoms (length of carbon atom chain) by using diazomethane (step up process of carboxylic acid).

Diagram

7. Reduction of aldehyde can also be affected by reduction with aluminium isopropoxide Al(isopropyl). It is known as meerwen pondoff reduction.

Diagram

DESCENT OF HOMOLOGOUS SERIES



1. **BARBIER – LORQUIN – WISLAND DEGRADATION REACTION**

(i) Diagram

(ii) Diagram

(iii) If we make use of Ba salt of the carboxylic acid with barium acetate, there will be reduction in the no of carbon atoms.

Diagram

2. **GALLAHER – HOLLANDER REDUCTION: -**

This knocks off two carbon atoms

Diagram

3. **HOFFMAN'S DEGRADATION**

Diagram

4. **SCHMIDT DEGRADATION REACTION**

Diagram

RING CONTRACTION

1. **ZELINSKY'S REACTION**

Diagram

2. Action of nitrous acid on cyclic amines

Diagram

3. Action of silver nitrate on cyclic halides

Diagram

4. Action of caustic alkali on cyclic of chloro ketones

Diagram

5. Diagram

6. Action of GRIGNARD'S REAGENT

Diagram

RING EXPANSION

1. OXIDATION OF CYCLIC KETONE

The oxidants are usually KMnO_4 , O_3 , or nitric acid HNO_3

Diagram

2. BY HYDROGENATION

Diagram

3. RING FUSION BY ISOMERISATION (Al_2O_3)

Diagram

USE OF ANHYDRIDE

Diagram

Phthalic anhydride is used for protecting certain compounds when introducing another group e.g. the protection of the amino group

(1). Diagram

(2). PREPARATION OF PERACETIC ACID (ADD ONE ATOM OF OXYGEN)

Diagram

(3). FRIEDEL CRAFTS REACTION: -

Diagram

(4). PREPARATION OF ALCOHOL

Diagram

(5). PERKIN'S REACTION

Diagram

(6). PREPARATION OF COUMARIN

Diagram

1. Preparation of 1-tetralone and tetralin

Diagram

2. Preparation of naphthalene derivative

Diagram

3. Preparation of phenanthrene

Diagram

PHTHALIC ANHYDRIDE

1. Diagram
2. Diagram
3. It is used in the preparation of indicators e.g phenolphthalein

Diagram

4. Preparation of Eosin

Diagram

5. Preparation of Quinizarin

Diagram

6. Preparation of triphenyl methane

Diagram

INSECTICIDE (Δ) DDT

(2). BENZENE HEXACHLORIDE: -

It has insecticidal properties

Diagram

Benzene hexachloride has a fishy smell of causes tainting of food which it comes in contact with

CHLORIDINE

Preparation: -

It flows Dier – Alder's reaction of hexa chloro cyclopenta diene with certain alkene

Diagram

(b). diagram

PREPARATION OF PIERIC ACID

Diagram

(c). diagram.

