PHARMACEUTICAL ORGANIC CHEMISTRY-II[nd]

UNIT-4[th]

POLYNUCLEAR HYDROCARBONS

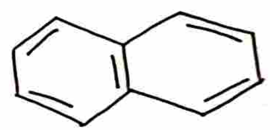
- Synthesis, Reactions, structure and medicinal use of Naphthalene, Phenanthracene, Anthracene, Diphenylmethane, Triphenylmethane and their derivatives.

- Polynuclear hydrocarbons →
  - Polynuclear ↓ Poly + Nuclear (Multiple aromatic rings)
  - hydrocarbons ↓ Hydro + Carbons (Carbon + Hydrogen)

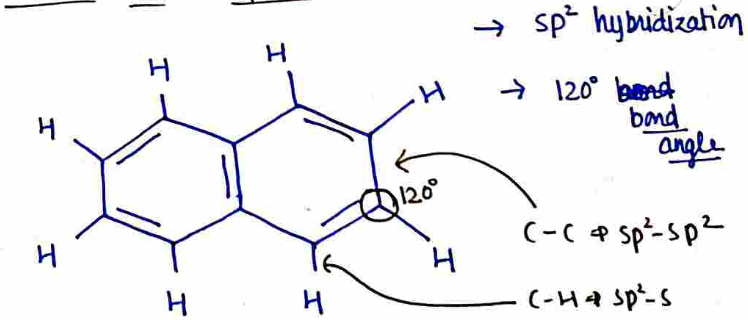
- Polynuclear hydrocarbons (Polynuclear aromatic hydrocarbons) are organic compound which contain only hydrogen and carbon, which further composed in the form of multiple aromatic rings

eg. Naphthalene, Anthracene, Phenanthracene etc—

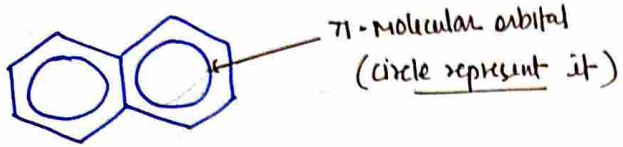
1) **Naphthalene** ⇒



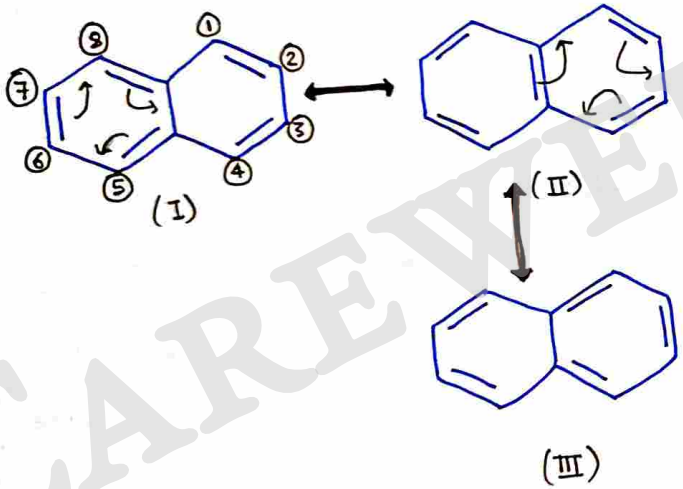
- Structure of naphthalene →



- A common shorthand representation of naphthalene



- According to the resonance theory, naphthalene is considered to be a hybrid of the three form.

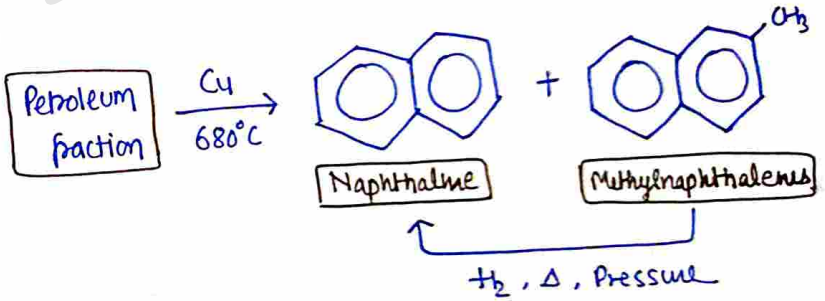


- But In naphthalene, bond length between C-C is different at different position, generally (C_1-C_2) - 1.36 Å & (C_2-C_3) - 1.40 Å

- Naphthalene is less aromatic (more reactive) than benzene

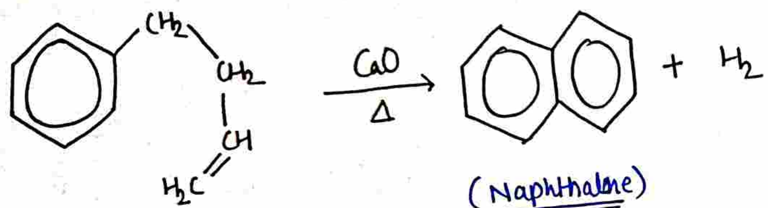
- Synthesis (Method of Preperation)

1) from Petroleum → When petroleum fraction are passed over copper (Cu) Catalyst at 680°C, naphthalene & methylnaphthalene are formed.



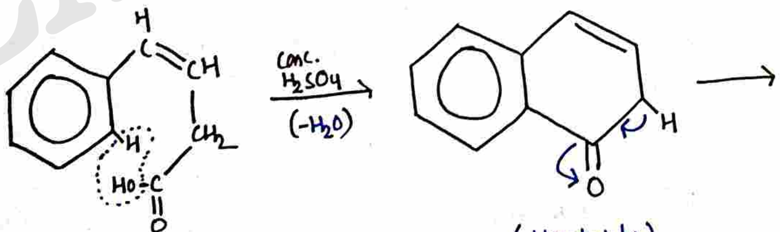
After this, methylnaphthalenes are separated and further converted into naphthalene by heating with hydrogen under pressure. (This rxn called dealkylation).

2) from 4-phenyl-1-butene → When 4-Phenyl-1-butene is passed over red hot calcium oxide, naphthalene is obtained.



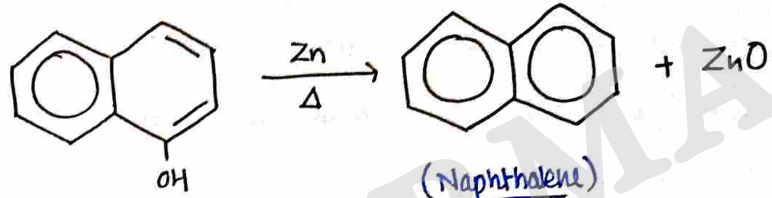
(4-Phenyl-1-butene) (Naphthalene)

3) from 4-Phenyl-3-butenoic Acid → When 4-Phenyl-3-butenoic acid is heated with concentrated Sulfuric acid (H_2SO_4), 1 naphthol is formed, this on distillation with zinc dust give naphthalene



(4-Phenyl-3-butenoic Acid) (Unstable)

on Rearrangement

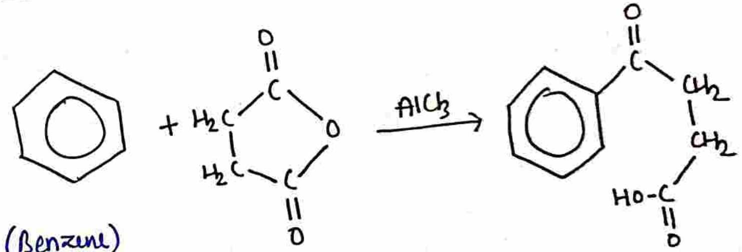


(1-Naphthol) (Naphthalene)

4) By Haworth Synthesis →

This reaction contain five steps →

- **STEP-1st** → (Friedal-craft acylation)

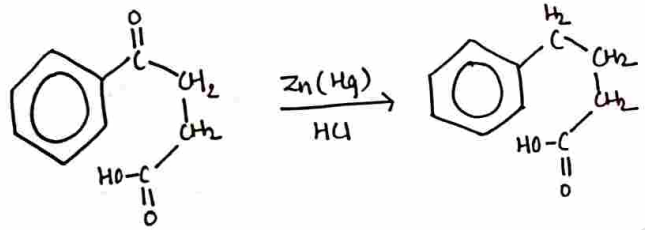


(Benzene) (succinic anhydride) (β-Benzoylpropionic acid)

- Benzene and succinic anhydride are heated in the presence of aluminium chloride to form β-benzoylpropionic acid.

• **STEP-2nd** → (Clemmensen Reduction)

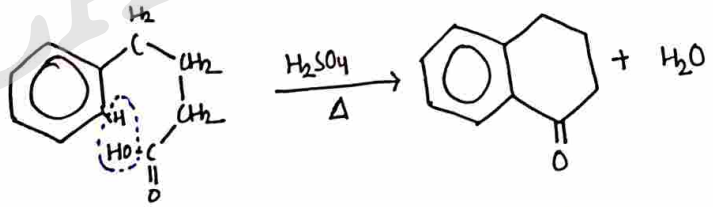
β-Benzoylpropionic acid is treated with amalgamated zinc in the presence of hydrochloric acid (HCl) to give γ-phenylbutyric acid.



(β-Benzoylpropionic acid) (γ-Phenylbutyric acid)

• **STEP-3rd** → (Ring closure reaction)

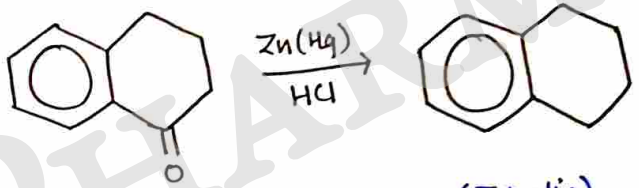
γ-Phenylbutyric acid is heated with conc. H_2SO_4 or polyphosphoric acid to form α-tetralone



(γ-Phenylbutyric acid) (Tetralone)

• **STEP-4th** → (Clemmensen reduction)

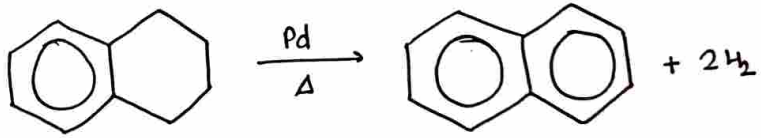
α-Tetralone is heated with amalgamated zinc and hydrochloric acid to give tetraline



(α-tetralone) (Tetralin)

• **STEP-5th** → (Aromatization reaction)

Tetralene is heated with palladium to yield naphthalene



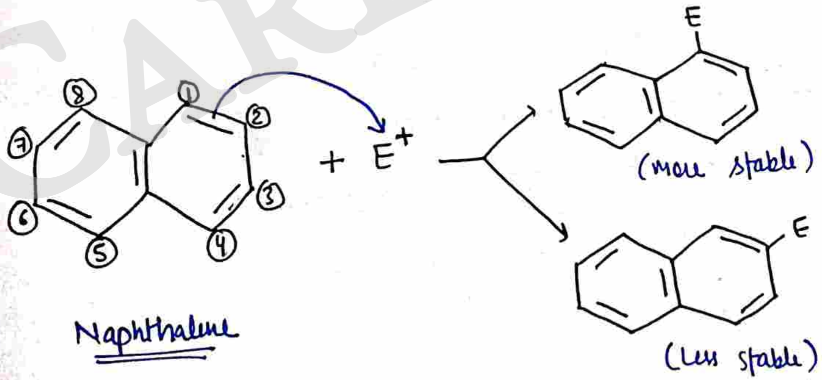
(Tetralin) (Naphthalene)

- **Physical properties of Naphthalene**
  - It is a colorless crystalline Solid.
  - Melting point → 82°C & Boiling point → 218°C
  - Insoluble in water, but soluble in ether, benzene, and hot ethanol.
  - It has a characteristics 'moth ball' odor.

- **Reactions of Naphthalene →**

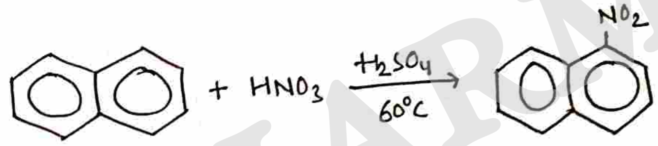
Naphthalene also give electrophilic substitution reaction.

- On reaction E^+ attach on 2 different and make 2 different structure



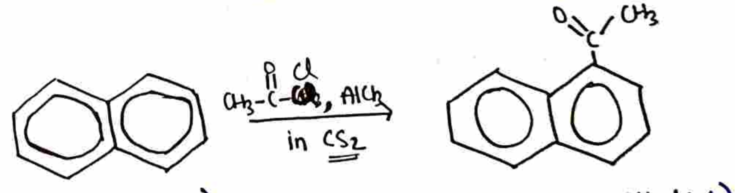
Naphthalene

1) **Nitration** → Naphthalene undergoes nitration with concentrated nitric acid in the presence of sulfuric acid at 60°C to produce 1-nitronaphthalene



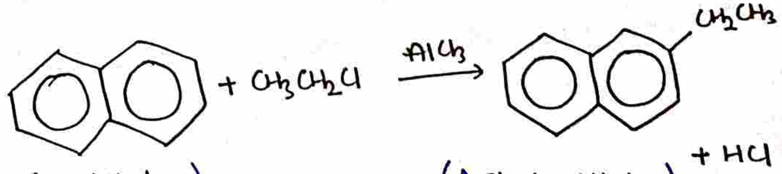
(Naphthalene) (1-Nitronaphthalene)

II) **Friedal-craft acylation** → Naphthalene undergoes acylation with acetyl chloride and aluminium chloride in Carbon disulfide to give 1-acetyl-napthalene



(Naphthalene) (1-Acetylnaphthalene)

III) **Friedal-craft alkylation** →

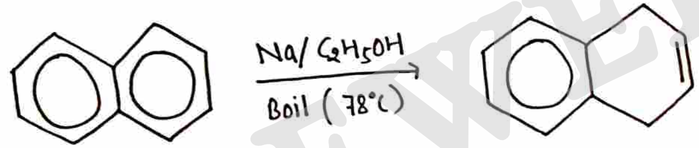


(Naphthalene) (2-Ethylnaphthalene) + HCl

Naphthalene undergoes alkylation with alkyl halides in the presence of aluminium chloride to give 2-alkylnaphthalene [methyl halides do not react].

– Some other reactions ⇒

iv) Reduction → Naphthalene undergoes reduction more readily than benzene, when it react with sodium and ethyl alcohol (bp 78°C) it gives 1,4-dialin (1,4-dihydronaphthalene).



(Naphthalene) (1,4-dihydronaphthalene)

v) Oxidation → Naphthalene is much more easily oxidized than benzene, when it react with chromium trioxide in acetic acid at room temp., it gives 1,4-naphthaquinone

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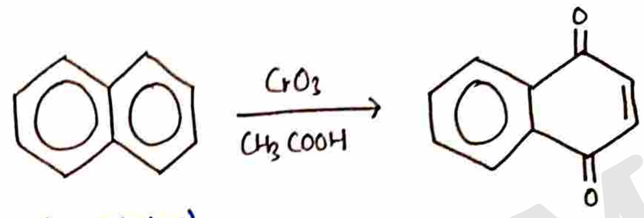
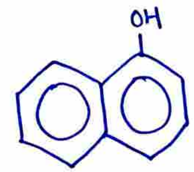


(Naphthalene) (1,4-Naphthaquinone)

• Medicinal use of Naphthalene

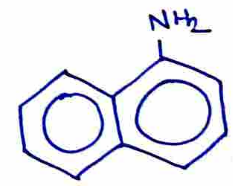
- Naphthalene is used in manufacture of 'moth balls' to protect woden goods, recently p-dichlorobenzene replaced it due to its less obnoxious odor.
- Used in manufacture of phthalic anhydride, carbaryl for insecticides.
- Also used in dyes and several medicinal products.

• Derivatives →



Naphthols

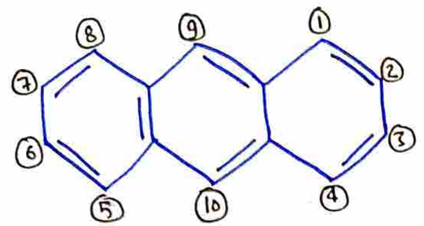
• The hydroxy derivatives of naphthalene.



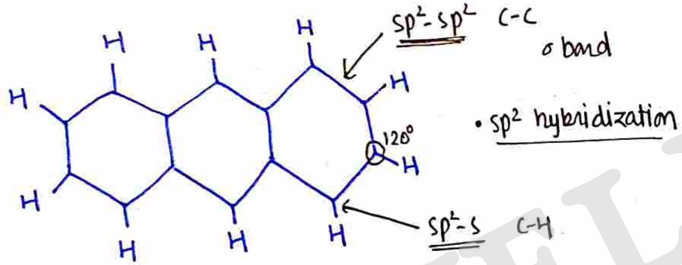
Naphthylamines

• The amino derivatives of naphthalene.

2) Anthracene

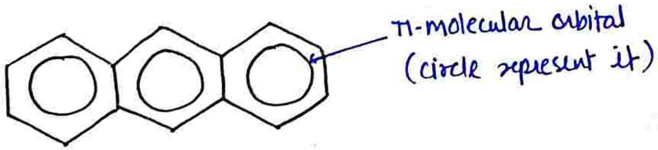


• Structure of anthracene →

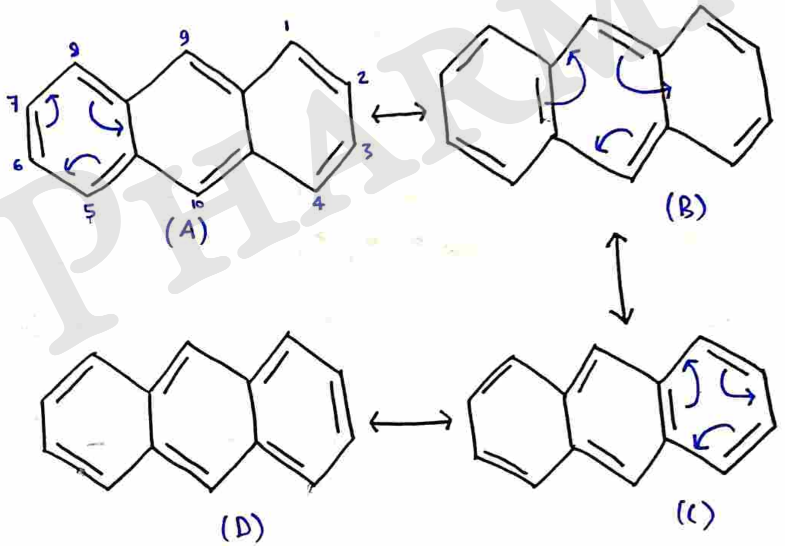


- It has sp^2 hybridization, and the sp^2 hybrid orbitals overlap with each other and with s orbital of the ten hydrogen atom forming C-C and C-H σ bonds.

- A common shorthand representation of anthracene



- According to the resonance theory, anthracene is considered to be a hybrid of the following four canonical form.



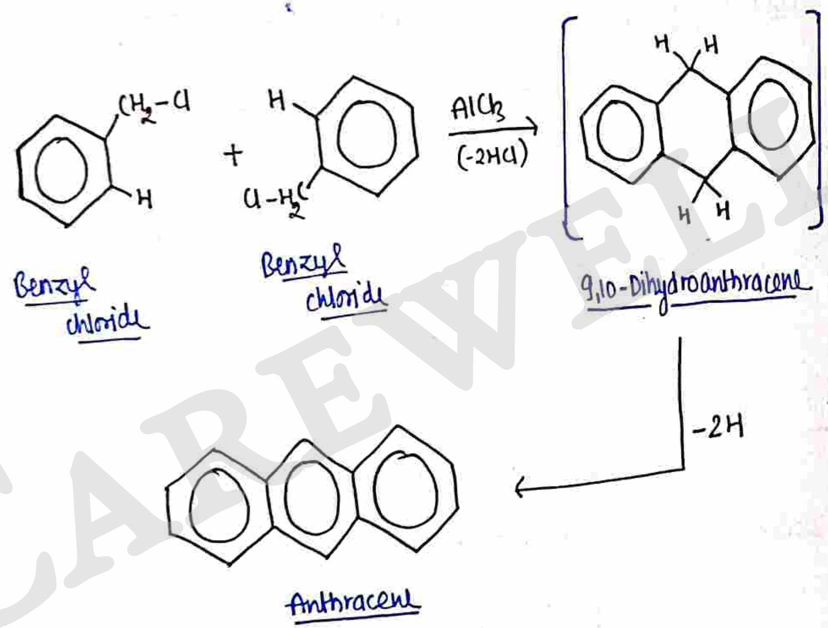
- There are different bond length between carbon-carbon bond.

- Resonance energy of anthracene is 84 kcal/mole. (average 28kcal/mole per ring), which is lower than benzene (36 kcal/mole).

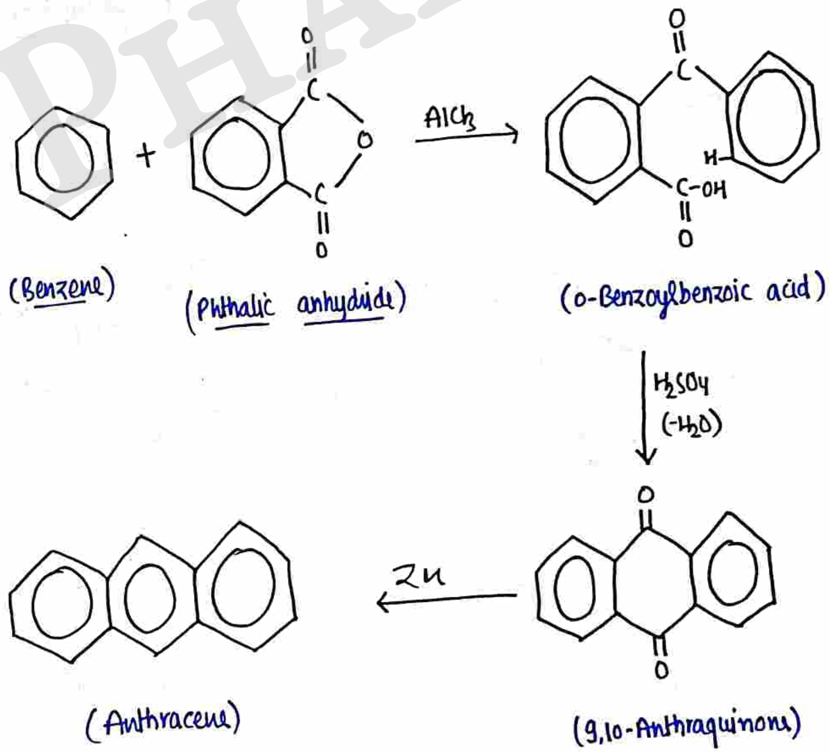
- So, Anthracene is much less aromatic than benzene

- Synthesis (Method of Preparation)

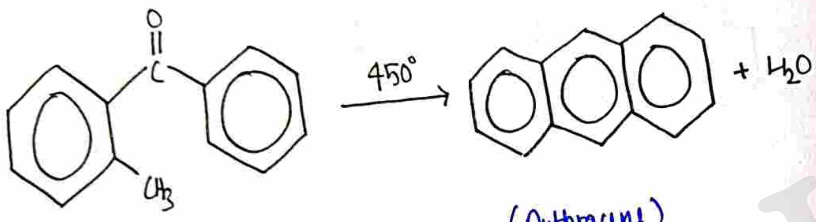
1) By **Friedal-crafts reaction** → Benzene chloride reacts with itself to form 9,10-dihydroanthracene, which readily loses two hydrogen atoms to yield anthracene



II) By **Haworth Synthesis** → This involves the treatement of benzene with pthalic anhydride in the presence of aluminium chloride to form o-benzoylbenzoic acid. Then o-benzoylbenzoic acid heated with concentrated sulfuric acid (H_2SO_4) to give 9,10-anthraquinone. Now, distillation of the anthraquinone with zinc dust yield anthracene



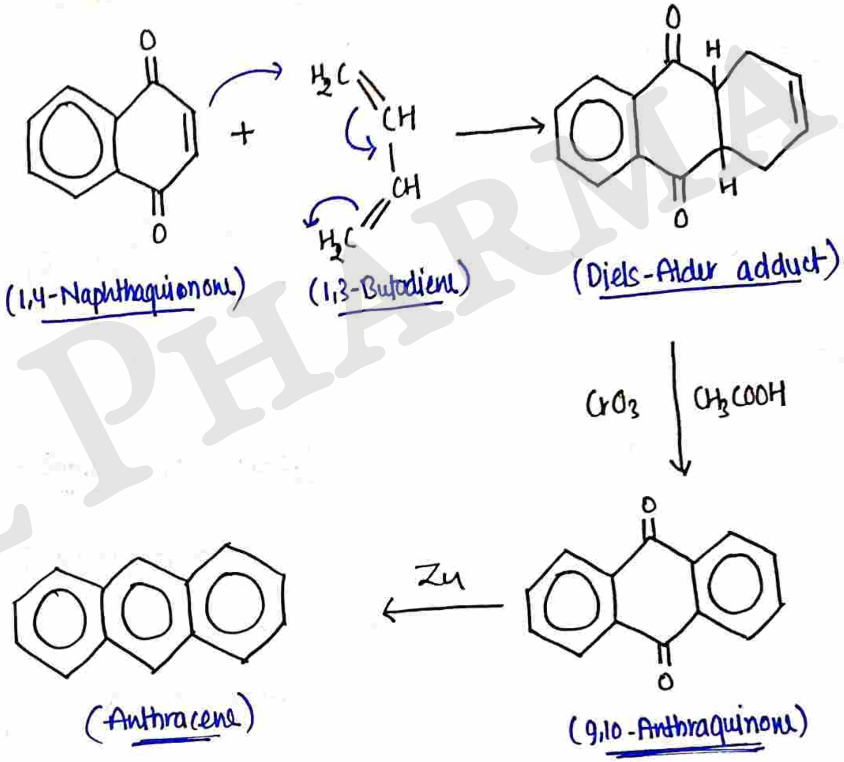
III) By Elbs Reaction → The conversion of a diaryl ketones containing a methyl or methylene group to the carbonyl function is known as the Elbs Reaction.



(o-Methylbenzophenone) (Anthracene)

eg. When o-methylbenzophenone is heated at 450°C, anthracene is formed.

IV) By Diels-Alder Reaction → This involves the reaction of 1,4-napthaquinone with 1,3-butadiene. The product (Diels-Alder adduct) of this reaction is oxidized with chromium trioxide in glacial acetic acid to form 9,10-anthraquinone. Now, Distillation of the anthraquinone with zinc dust yields anthracene.

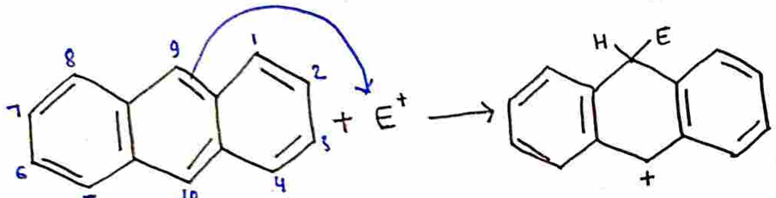


- Physical properties of Anthracene →

- It is colorless solid.
- Melting point → 218°C , Boiling point → 340°C.
- Insoluble in water and dissolve in benzene.

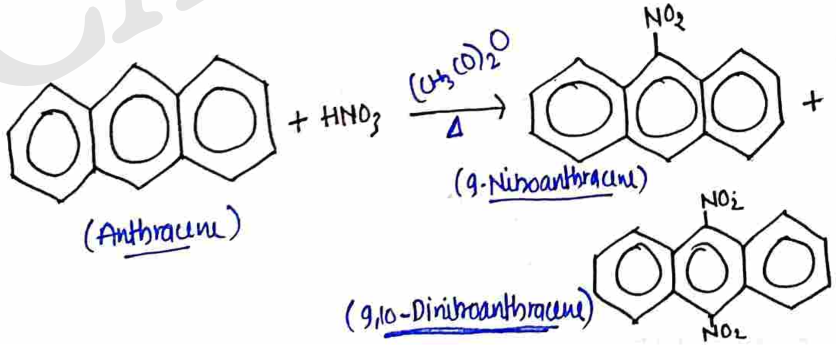
- **Reactions of Anthracene**

It also give electrophilic substitution reaction. These reactions preferentially occurs at the C-9 and C-10 positions.

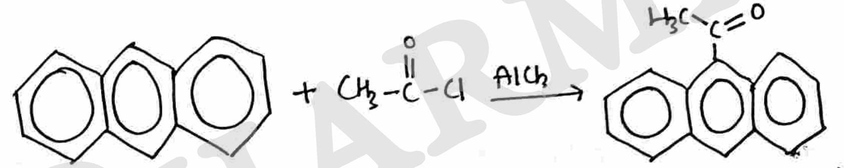


(Anthracene)

1) **Nitration** → Anthracene ⊕ react with concentrated nitric acid in acetic anhydride (H_2SO_4 not used here) at room temperature to yield a mixture of 9-nitroanthracene and 9,10-dinitroanthracene



II) **Friedal-crafts Acylation** → Anthracene undergoes acylation with acetyl chloride and aluminium chloride to form 9-acetylanthracene

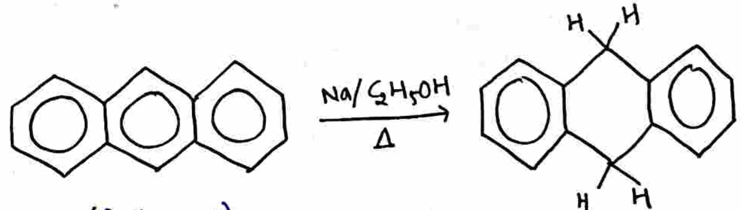


(Anthracene)

(9-Acetylanthracene)

- Some other reactions

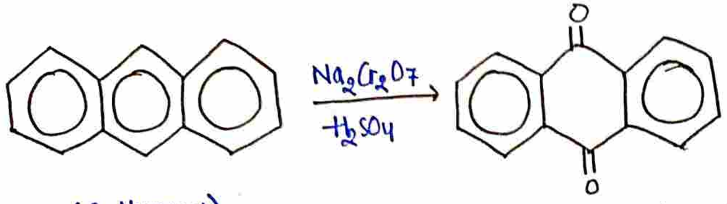
III) **Reduction** → Anthracene undergoes reduction with sodium and ethyl alcohol to form 9,10 dihydroanthracene



(Anthracene)

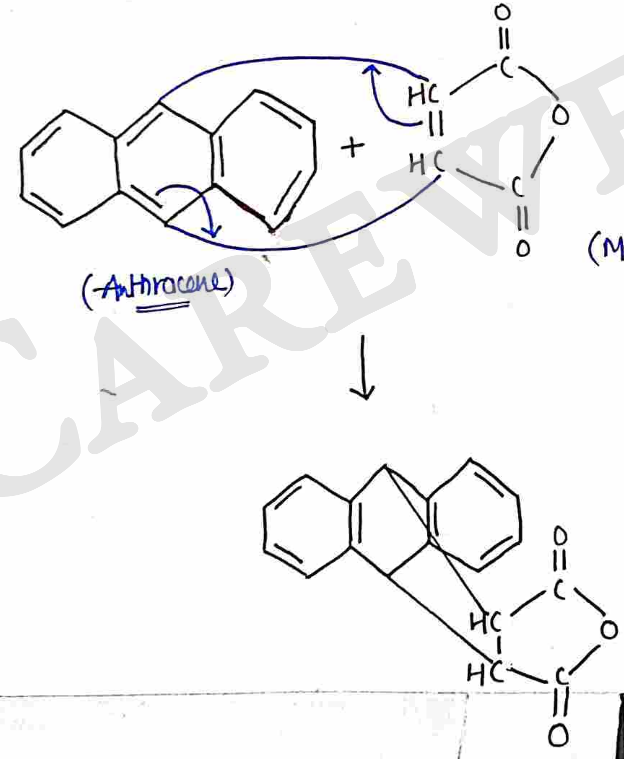
(9,10-Dihydroanthracene)

IV) **Oxidation** → Anthracene undergoes oxidation with sodium dichromate and sulfuric acid to form 9,10-anthraquinone



(Anthracene) (9,10-Anthraquinone) Anthraquinone

v) Diels-Alder Reaction → Anthracene undergoes a Diels-Alder reaction with maleic anhydride to yield the corresponding adduct.

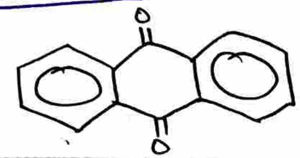


(Anthracene) (Maleic anhydride)

Uses of Anthracene →

- Anthracene is used in the manufacture of anthraquinone.
- Anthraquinone is used in the manufacture of alizarin and several other dyes.
- Used as a preservative in wood and used as an insecticide for crops.
- Used in some drugs,
  Purgative drugs - Senna, Rhubarb, Cascara
  Dithrol - Antifungal.
- Anthraquinone are also used as ~~can~~ anticancer agent.

- Derivatives of Anthracene →
  - Most important derivative of anthracene is anthraquinone (9,10-anthraquinone), which is prepared by oxidation of anthracene

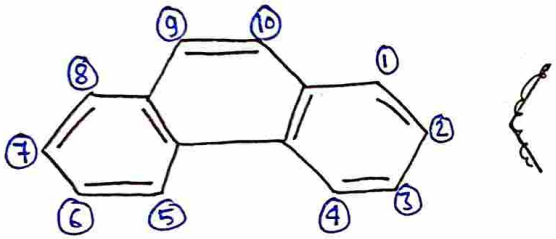


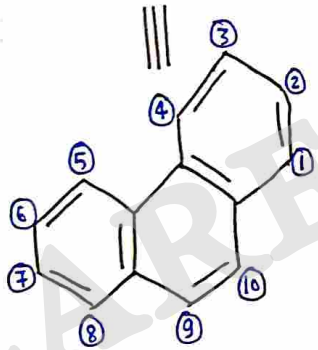
  - Uses are written above ↑

Phenanthrene PHENANTHRENE

Phenanthrene is an isomer of anthracene.

It may be obtained, along with anthracene, from the green oil fraction of coal-tar.

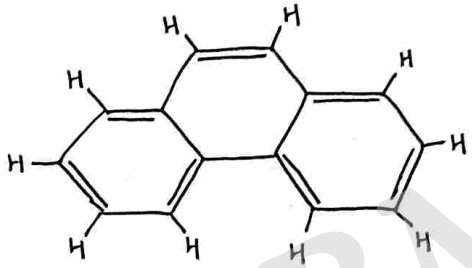




- **STRUCTURE OF PHENANTHRENE**

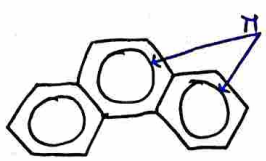
It is also a planar molecules like anthracene and phenanthrene

All fourteen carbon atoms are sp^2 hybridized.



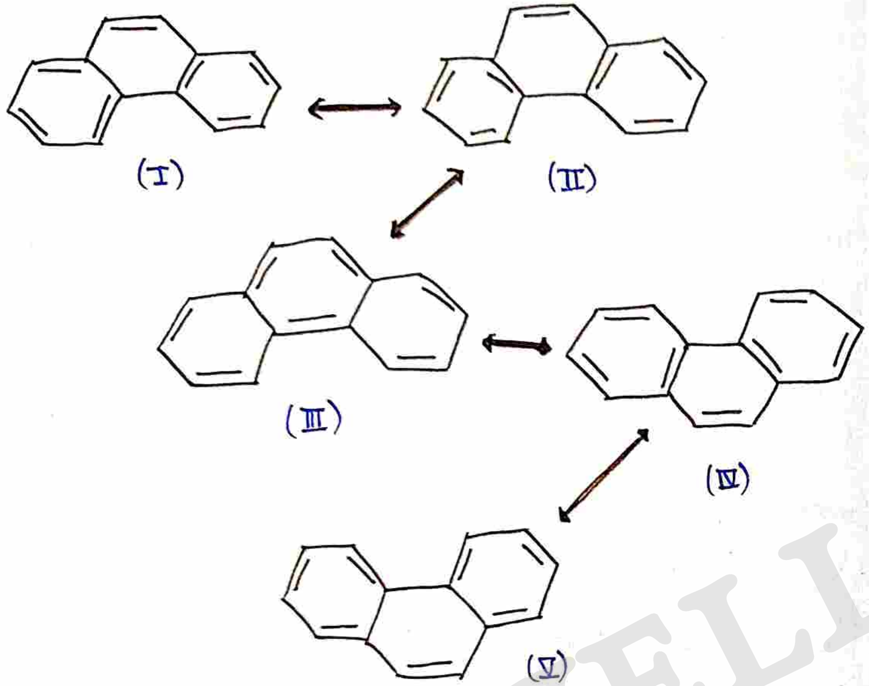
The sp^2 orbitals overlap with each other and with s-orbital of ten hydrogen atom to form C-C and C-H σ bonds.

→ Each carbon atom also possesses a p orbital, and overlap of these p orbital produce a π Molecular orbital.



→ According to resonance theory, phenanthrene is considered to be a hybrid of the following five resonance form:—

(The resonance energy of phenanthrene is 92kcal/mole.)

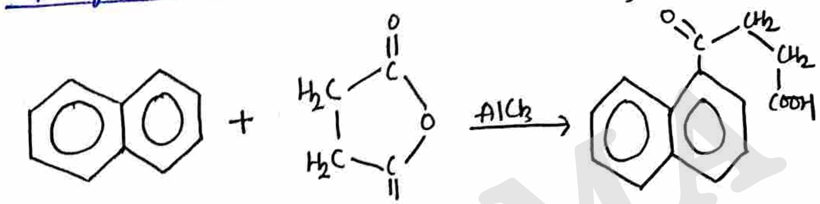


→ All these (Anthracene, naphthalene, phenanthracene) are aromatic and follow huckle rule

- **SYNTHESIS OF PHENANTHRENE**

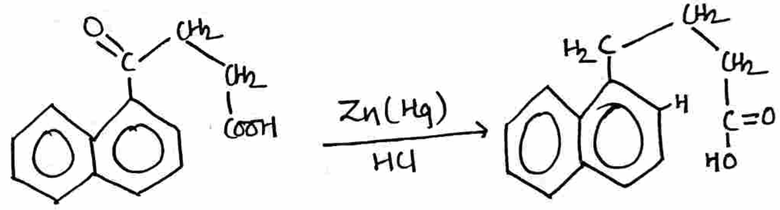
It is obtained by **Haworth Synthesis**:-

1) This involves the treatement of naphthalene with succinic anhydride in the presence of aluminium chloride to form Napthoylpropionic acid. (Friedal craft acylation).



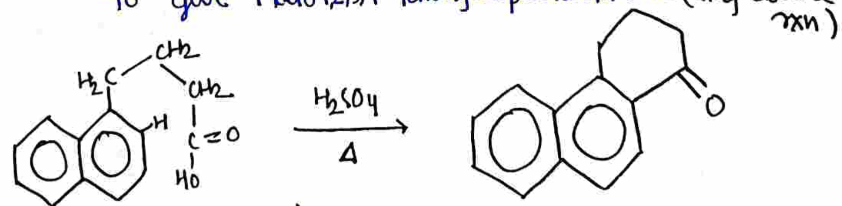
Naphthalene | Succinic anhydride | Naphthoylpropionic acid.

2) Then, Naphthoylpropionic acid treated with amalgated zinc in the presence of hydrochloric acid (HCl) (Clemmensen reduction) to give Naphthylbutyric acid.



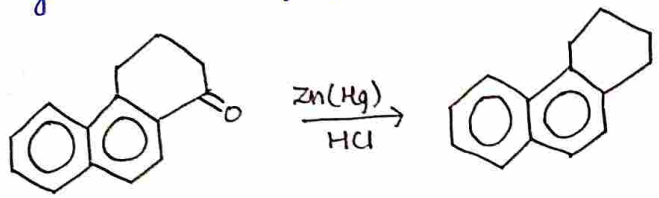
(Naphthoylpropionic acid) | (Naphthylbutyric acid)

3) Now, Naphthylbutyric acid heated with H_2SO_4 to give 1-keto 1,2,3,4-tetrahydrophenanthrene (Ring closure rxn).



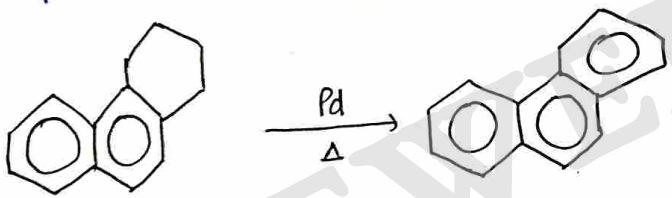
(Naphthylbutyric acid) | (1-keto,1,2,3,4-tetrahydrophenanthrene)

4) 1-keto-1,2,3,4-tetrahydrophenanthrene is treated with amalgated zinc in the presence of HCl to give 1,2,3,4-Tetrahydrophenanthrene. (Clemmensin reduction)



(1-keto.1,2,3,4- tetrahydrophenanthrene) (1,2,3,4-Tetrahydrophenanthrene)

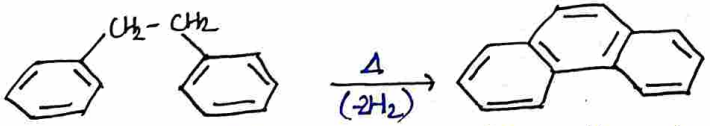
5) Now, 1,2,3,4-Tetrahydrophenanthrene heated with palladium (Pd) to yield phenanthrene



(1,2,3,4-Tetrahydrophenanthrene) (Phenanthrene)

— From Dibenzyl

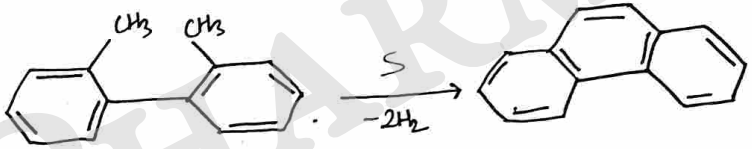
Phenanthrene can be obtained by passing dibenzyl through a red hot tube



(Dibenzyl) (Phenanthrene)

— From 2,2 dimethyl- diphenyl

Phenanthrene can also be obtained by cyclodehydrogenation of 2,2 dimethyl- diphenyl using sulphur



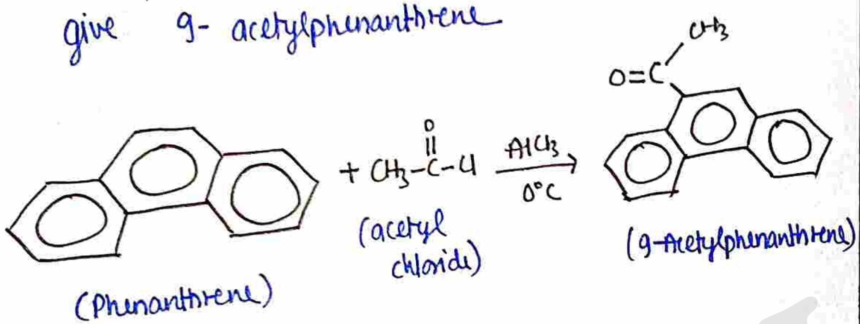
- PHYSICAL PROPERTIES OF PHENANTHRENE
  - It is a colorless solid
  - Melting point 100°C
  - It is insoluble in water, but dissolve readily in ethanol, benzine and ether.

- REACTIONS OF PHENANTHRENE

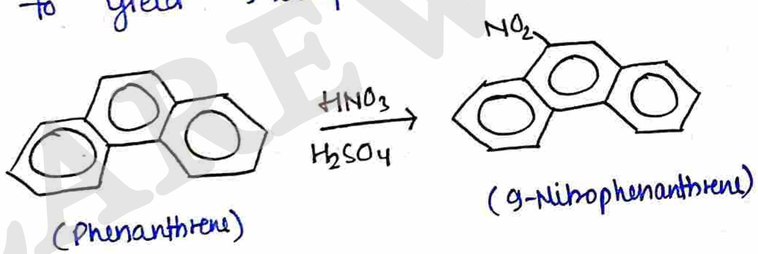
  It undergoes oxidation, reduction, addition and electrophilic substitution reaction.

  As with anthracene, these reactions preferentially occur at the C-9 & C-10 position.

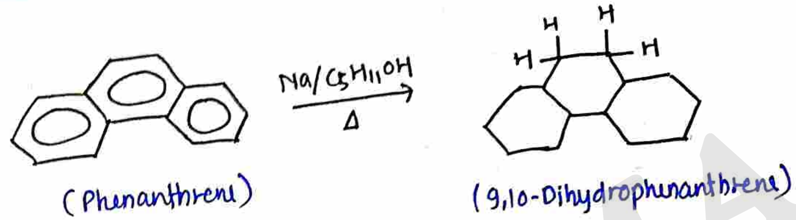
I) **Friedal craft acylation** → Phenanthrene undergoes acylation with acetyl chloride in the presence of aluminium chloride at 0°C to give 9- acetylphenanthrene



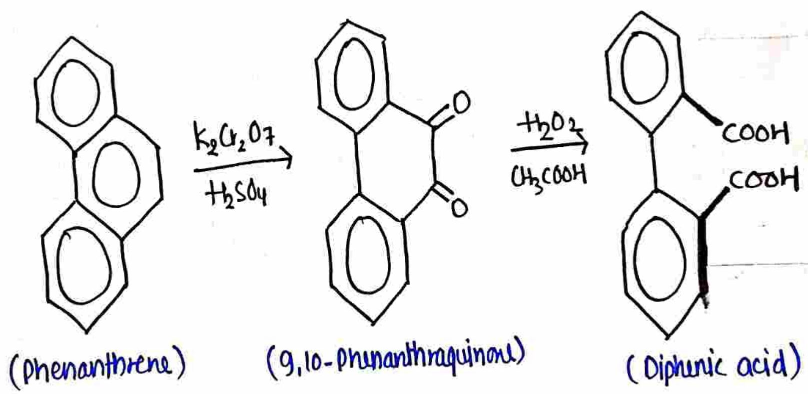
II) **Nitration** → Phenanthrene undergoes nitration with concentrated nitric acid and sulfuric acid to yield 9-nitrophenanthrene



III) **Reduction** → Phenanthrene undergoes reduction with sodium and isopentanol to form 9,10-dihydrophenanthrene



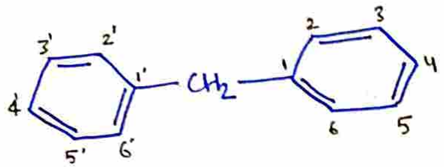
IV) **Oxidation** → Phenanthrene undergoes oxidation with potassium dichromate and sulfuric acid in acetic acid to form 9,10-phenanthraquinone. Further oxidation of this with hydrogen peroxide in acetic acid give diphenic acid.



· **Uses of Phenanthrene**

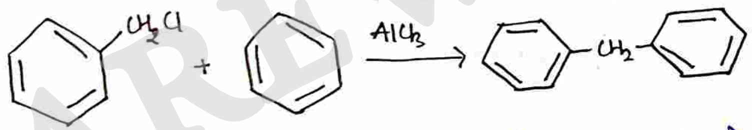
- It is used to make dyes, plastic and pesticides, also used in explosives and drugs.
- Also used to make bile acids, cholestrol & steroids.

DIPHENYL METHANE



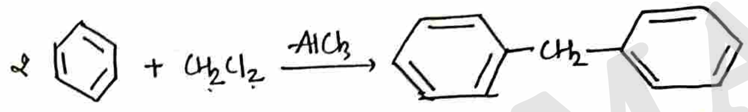
SYNTHESIS (Method of Preparation)

i) Friedal-craft's reaction :- Diphenyl methane is prepared by Friedal-craft's condension between benzyl chloride and benzene



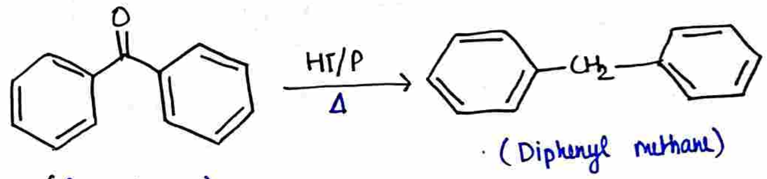
(Benzyl chloride) (Benzene) (Diphenyl methane)

ii) from Benzene → Diphenyl methane is also prepared from two moles of benzene and dichloromethane in the presence of aluminium chloride. (Friedal-craft's condension).



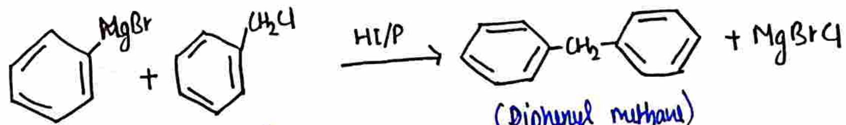
(Benzene) (Dichloro methane) (Diphenyl methane)

iii) from benzophenone → Diphenyl methane is prepared from benzophenone, which is reduced in the presence of red hot phosphorus and hydroiodic acid.



(Benzophenone) (Diphenyl methane)

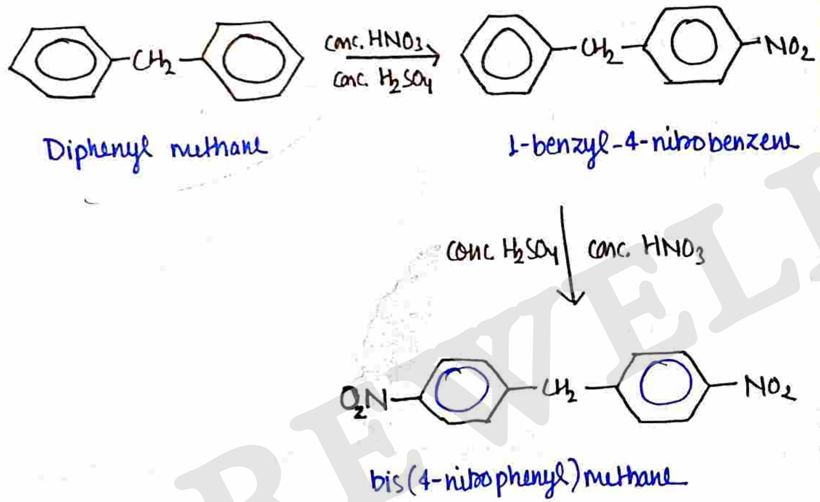
iv) from Grignard reagent → Diphenyl methane is prepared by Grignard reagent.



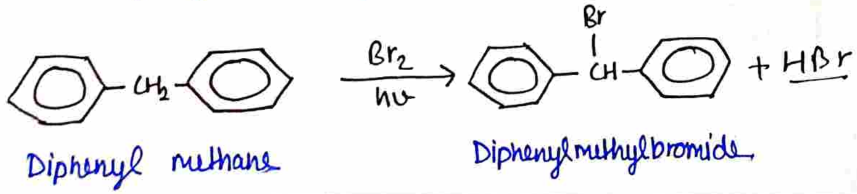
(Grignard reagent) (Benzyl chloride) (Diphenyl methane)

REACTIONS

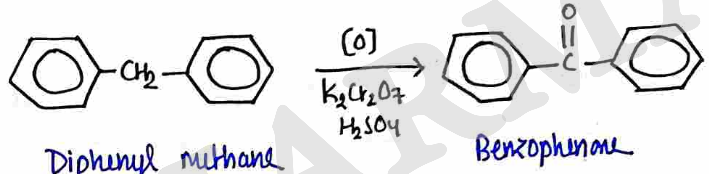
i) **Nitration** :– Diphenyl methane in the presence of concentrated sulphuric acid gives bis (4-nitrophenyl) methane.



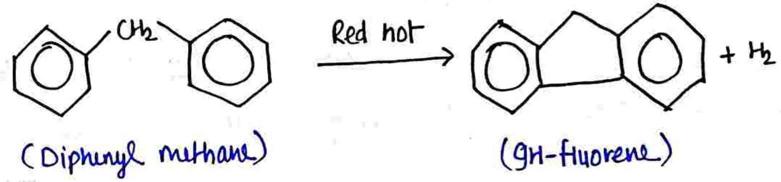
i) **Halogenation** :– Diphenyl methane in the presence of bromine and UV light gives diphenyl methyl bromide.



iii) **Oxidation** :– Diphenyl methane upon oxidation in the presence of potassium dichromate and sulphuric acid gives benzophenone



iv) **Cyclization** :– When diphenyl methane is heated it gives 9H- fluorone



• **Physical properties** :–

⇒ It is a colourless oil

⇒ Melting point → 22 – 24°C

⇒ Boiling point → 264°C

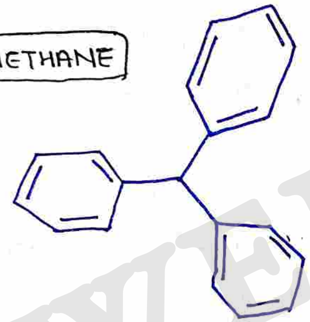
⇒ Molecular formula → $C_{13}H_{12}$

Uses:-

- It is used in the synthesis of methylene diphenyl diisocynate, which is used in the manufacture of polyurethane and as an industrial strength adhesive

TRIPHENYL METHANE

$(C_6H_5)_3CH$

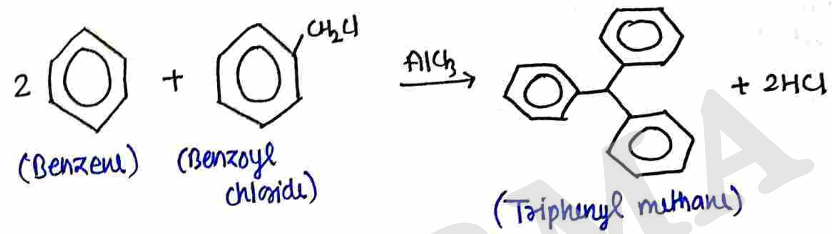


- Synthesis (methods of preparation)

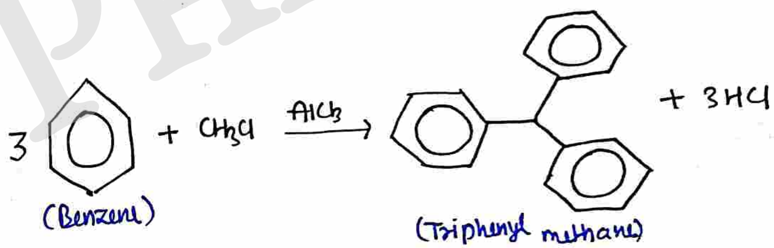
a) Friedal-Craft's reaction → It is prepared by the condensation between benzyl chloride and benzene

$$2C_6H_6 + C_6H_5CH_2Cl \xrightarrow{AlCl_3} (C_6H_5)_3CH + 2HCl$$

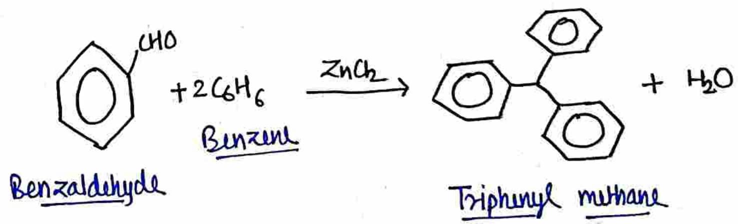
Benzene, Benzyl chloride, Triphenyl methane



b) The condensation between benzene and chloroform gives triphenyl methane



c) The condensation between benzaldehyde and benzene also gives triphenyl methane.



Physical properties of triphenyl methane

⇒ It is a colorless solid.

⇒ Melting point → 92 - 94°C

⇒ Boiling point → 359°C

Uses :-

⇒ Triphenyl methane is a triaryl methane compound used as a backbone of synthetic dyes.

⇒ Triphenyl methane has also been shown to inhibit 3-methylcholanthrene - induced neoplastic transformation of loti cells.