Aryl Halides

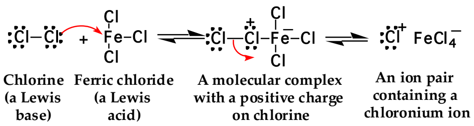
- Aryl halides are halides in which the halogen is attached directly to an aromatic ring.
- Carbon-halogen bonds in aryl halides are shorter and stronger than carbon-halogen bonds in alkyl halides.
- Because the carbon-halogen bond is stronger, aryl halides react more slowly than alkyl halides when carbon-halogen bond breaking is rate determining.

Physical Properties of Aryl Halides

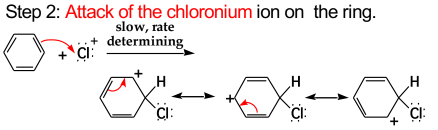
- Resemble alkyl halides
- All are essentially insoluble in water
- Less polar than alkyl halides

Preparation

Step 1: Generation of the electrophile: a chloronium ion.



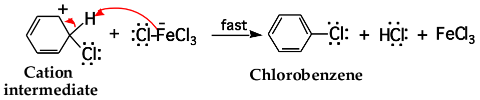
Step 2: Attack of the chloronium ion on the ring.

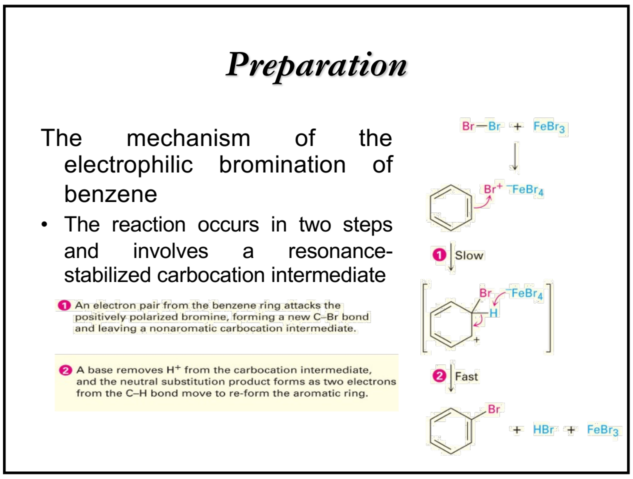


Resonance-stabilized cation intermediate; the positive charge is delocalized onto three atoms of the ring

Preparation

Step 3: Proton ejection regenerates the aromatic character of the ring.





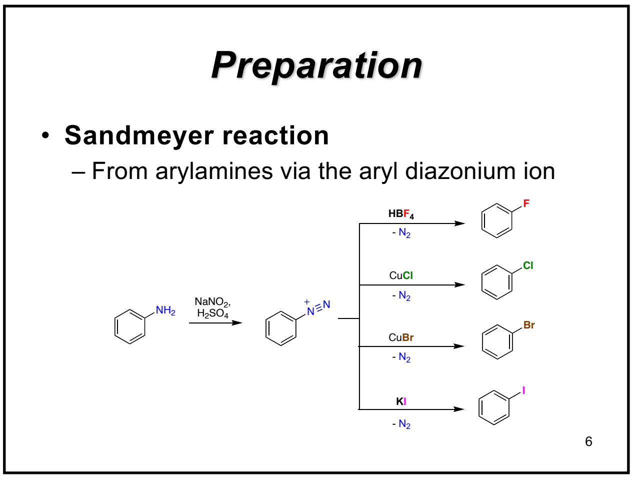
Preparation

The mechanism of the electrophilic bromination of benzene

- The reaction occurs in two steps and involves a resonance-stabilized carbocation intermediate

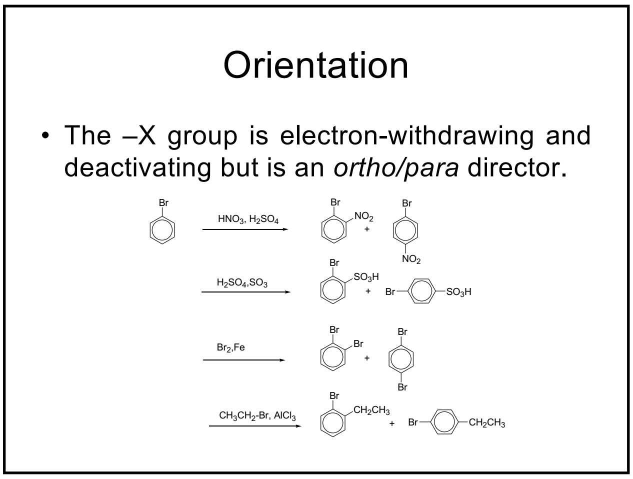
① An electron pair from the benzene ring attacks the positively polarized bromine, forming a new C–Br bond and leaving a nonaromatic carbocation intermediate.

② A base removes H^+ from the carbocation intermediate, and the neutral substitution product forms as two electrons from the C–H bond move to re-form the aromatic ring.



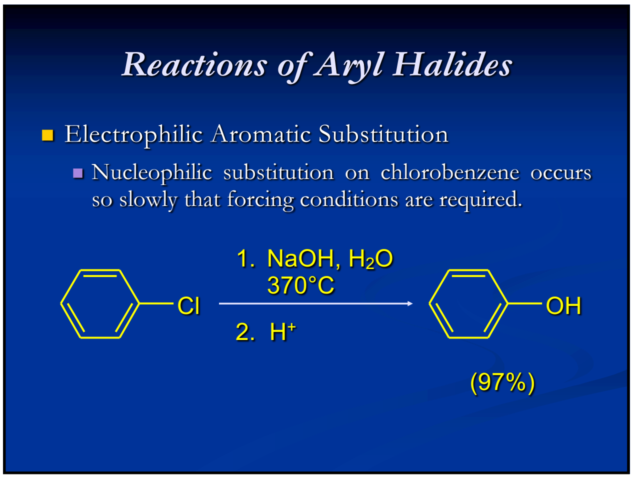
Preparation

- **Sandmeyer reaction**
  - – From arylamines via the aryl diazonium ion



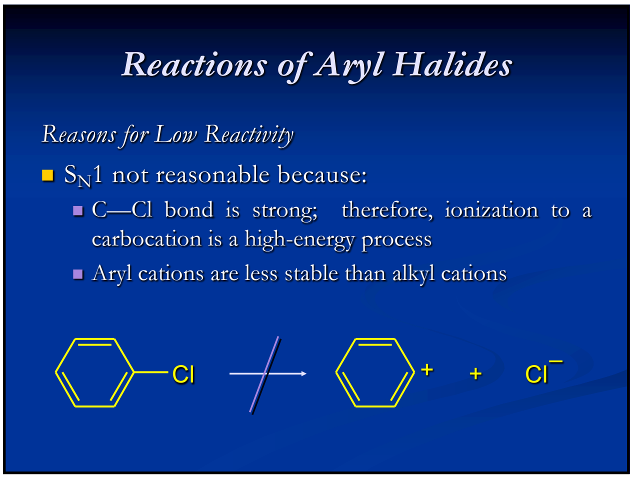
Orientation

- The –X group is electron-withdrawing and deactivating but is an *ortho/para* director.



Reactions of Aryl Halides

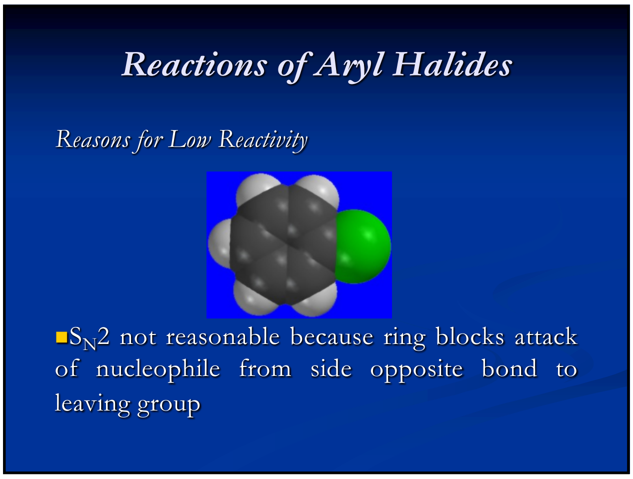
- Electrophilic Aromatic Substitution
  - Nucleophilic substitution on chlorobenzene occurs so slowly that forcing conditions are required.



Reactions of Aryl Halides

Reasons for Low Reactivity

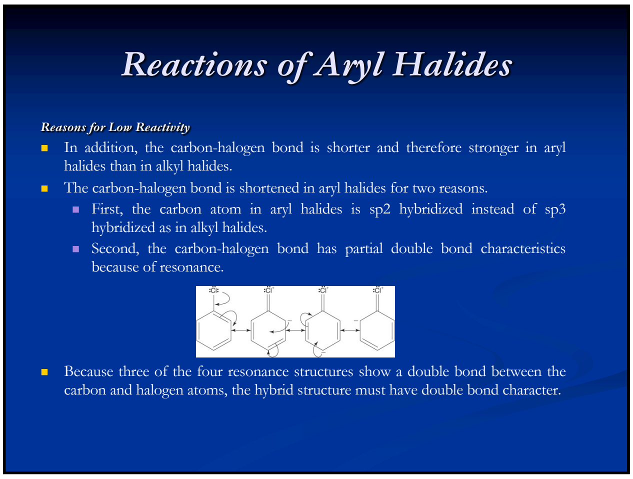
- S_N1 not reasonable because:
  - C—Cl bond is strong; therefore, ionization to a carbocation is a high-energy process
  - Aryl cations are less stable than alkyl cations



Reactions of Aryl Halides

Reasons for Low Reactivity

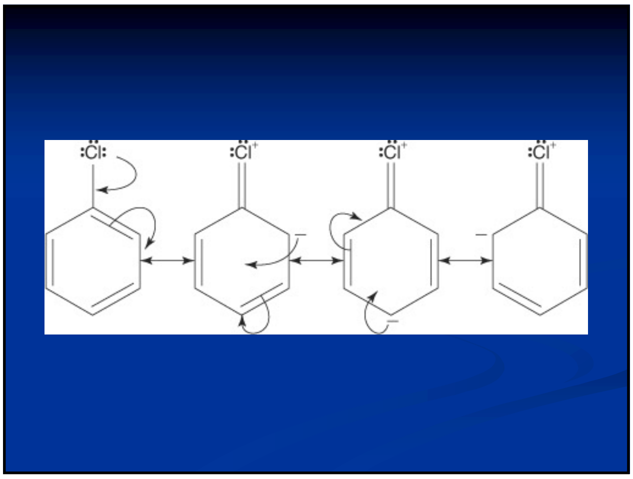
- S_N2 not reasonable because ring blocks attack of nucleophile from side opposite bond to leaving group

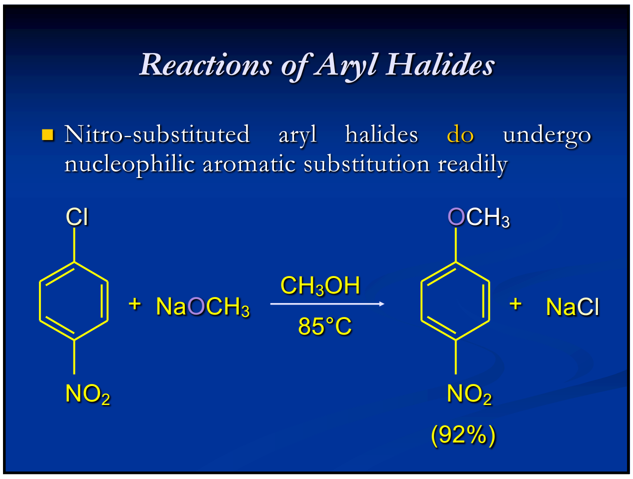


Reactions of Aryl Halides

Reasons for Low Reactivity

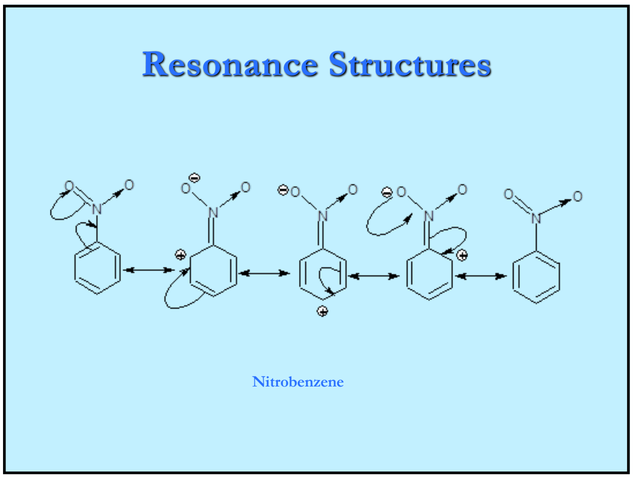
- In addition, the carbon-halogen bond is shorter and therefore stronger in aryl halides than in alkyl halides.
- The carbon-halogen bond is shortened in aryl halides for two reasons.
  - First, the carbon atom in aryl halides is sp2 hybridized instead of sp3 hybridized as in alkyl halides.
  - Second, the carbon-halogen bond has partial double bond characteristics because of resonance.
- Because three of the four resonance structures show a double bond between the carbon and halogen atoms, the hybrid structure must have double bond character.





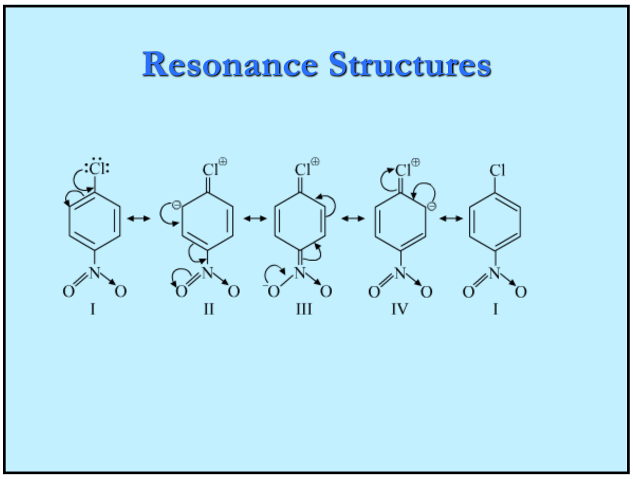
Reactions of Aryl Halides

- Nitro-substituted aryl halides do undergo nucleophilic aromatic substitution readily

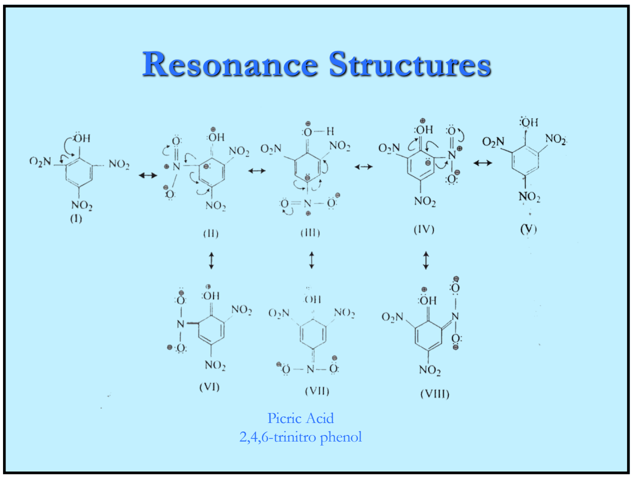


Resonance Structures

Nitrobenzene

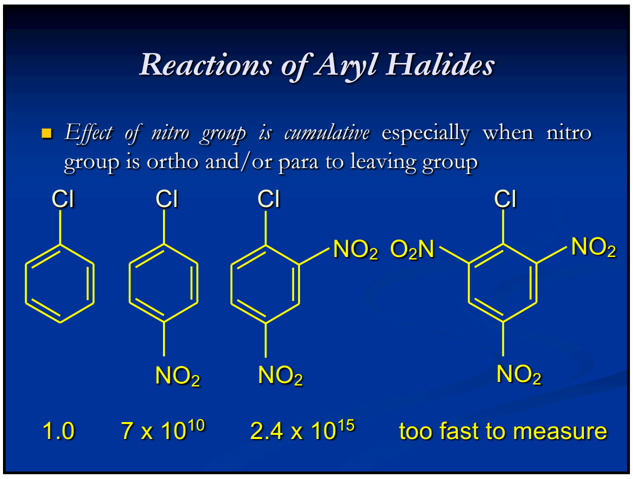


Resonance Structures



Resonance Structures

Picric Acid
2,4,6-trinitro phenol



Reactions of Aryl Halides

- *Effect of nitro group is cumulative* especially when nitro group is ortho and/or para to leaving group

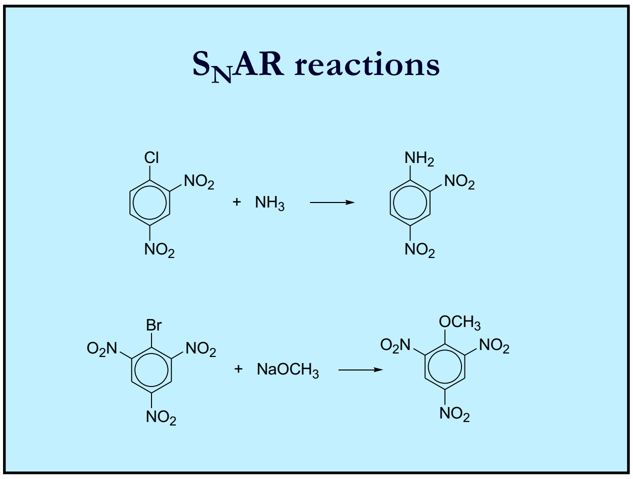
Reactions of Aryl Halides

General Conclusions About Mechanism

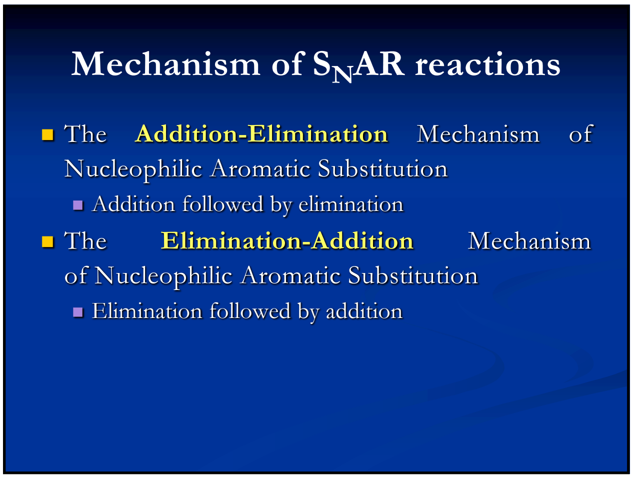
- Bimolecular rate-determining step in which nucleophile attacks aryl halide
- Rate-determining step precedes carbon-halogen bond cleavage
- Rate-determining transition state is stabilized by electron-withdrawing groups (such as NO_2)

S_NAR reactions

- Nucleophilic substitution reactions can occur with aryl halides under specific conditions
  - **A strong electron-withdrawing groups (deactivators) are located ortho and/or para to the carbon atom that's attached to the halogen.**
  - This arrangement makes the carbon susceptible to nucleophilic attack.)

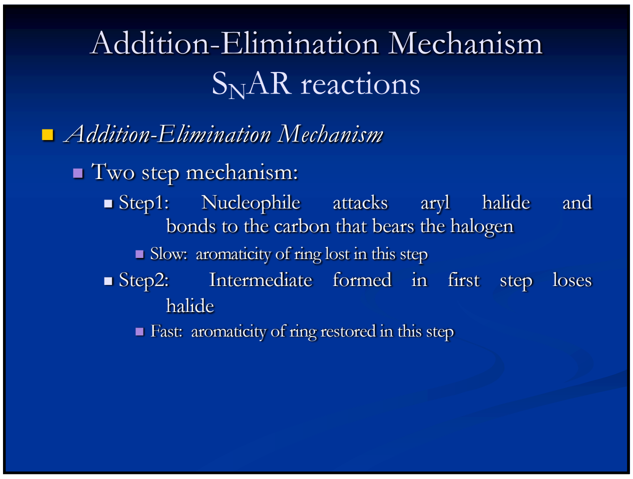


S_NAR reactions



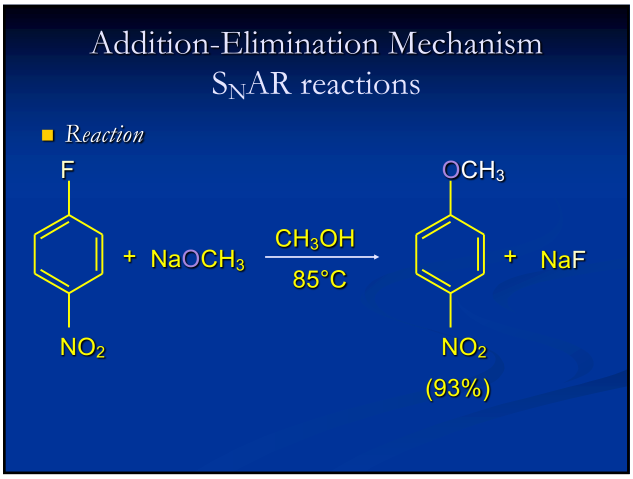
Mechanism of S_NAR reactions

- The **Addition-Elimination** Mechanism of Nucleophilic Aromatic Substitution
  - Addition followed by elimination
- The **Elimination-Addition** Mechanism of Nucleophilic Aromatic Substitution
  - Elimination followed by addition



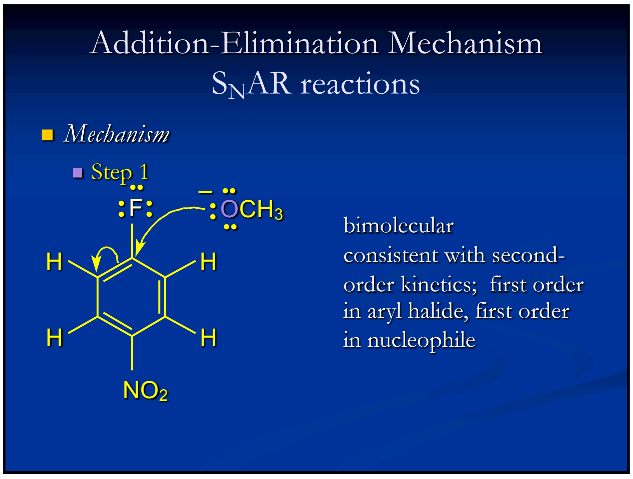
Addition-Elimination Mechanism S_NAR reactions

- *Addition-Elimination Mechanism*
  - Two step mechanism:
    - Step1: Nucleophile attacks aryl halide and bonds to the carbon that bears the halogen
      - Slow: aromaticity of ring lost in this step
    - Step2: Intermediate formed in first step loses halide
      - Fast: aromaticity of ring restored in this step



Addition-Elimination Mechanism S_NAR reactions

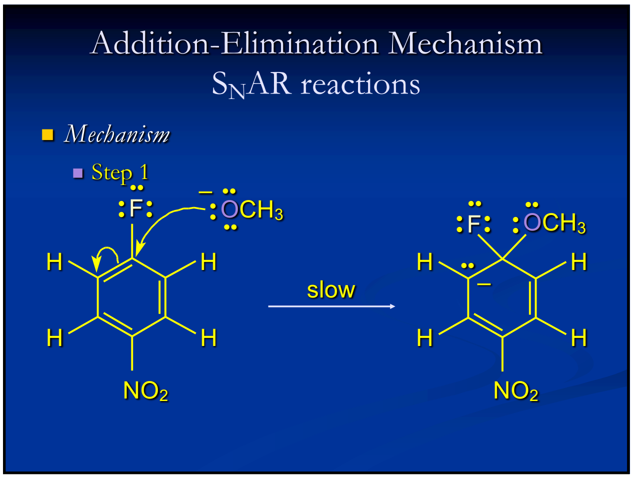
- *Reaction*



Addition-Elimination Mechanism S_NAR reactions

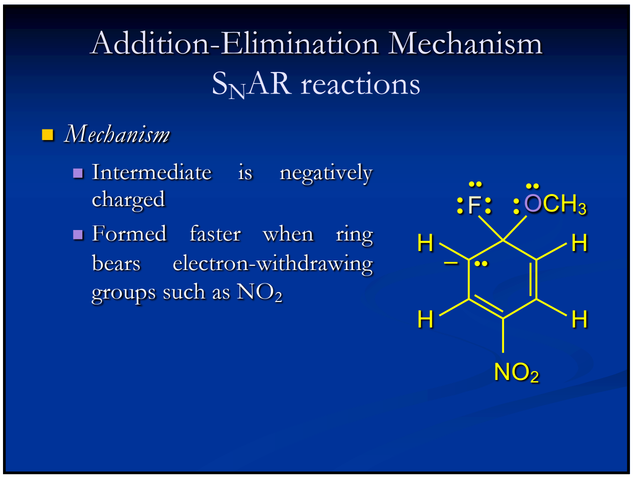
- *Mechanism*
  - Step 1

bimolecular consistent with second-order kinetics; first order in aryl halide, first order in nucleophile



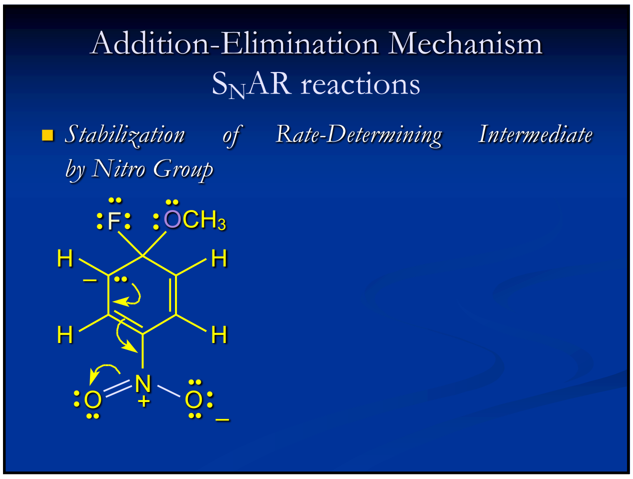
Addition-Elimination Mechanism
S_NAR reactions

- *Mechanism*
  - Step 1



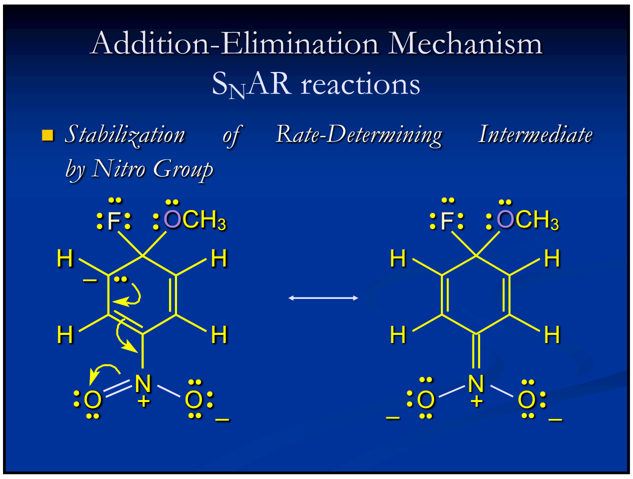
Addition-Elimination Mechanism
S_NAR reactions

- *Mechanism*
  - Intermediate is negatively charged
  - Formed faster when ring bears electron-withdrawing groups such as NO_2



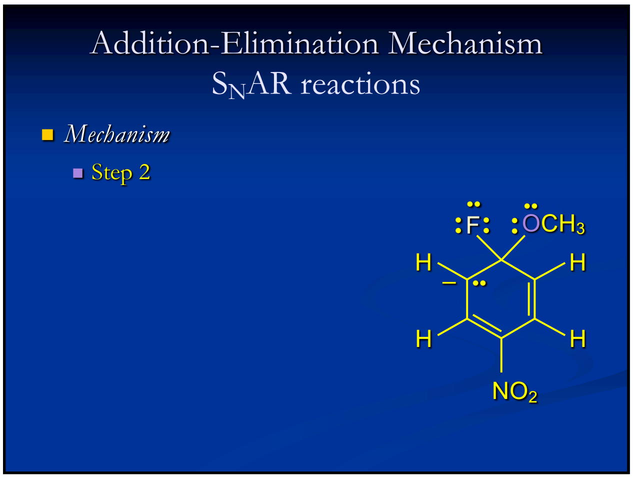
Addition-Elimination Mechanism
S_NAR reactions

- *Stabilization of Rate-Determining Intermediate by Nitro Group*



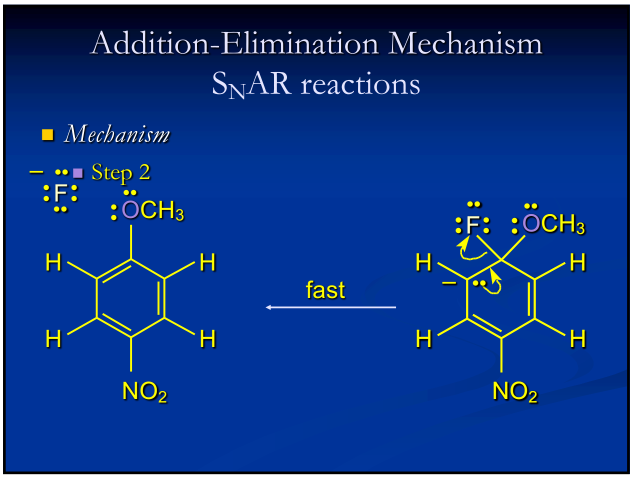
Addition-Elimination Mechanism
S_NAR reactions

- *Stabilization of Rate-Determining Intermediate by Nitro Group*



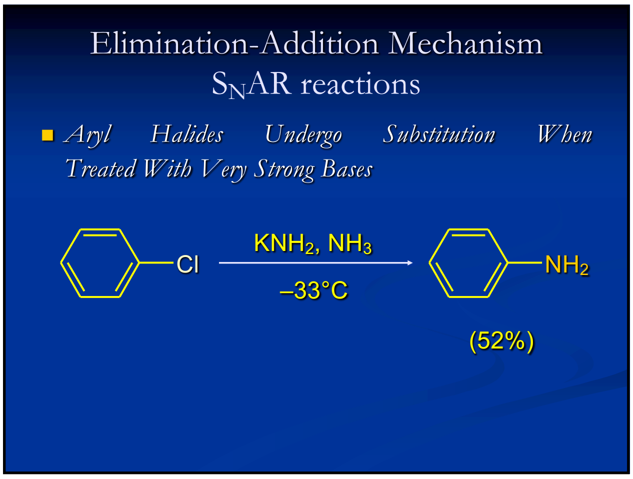
Addition-Elimination Mechanism
S_NAR reactions

- *Mechanism*
  - Step 2



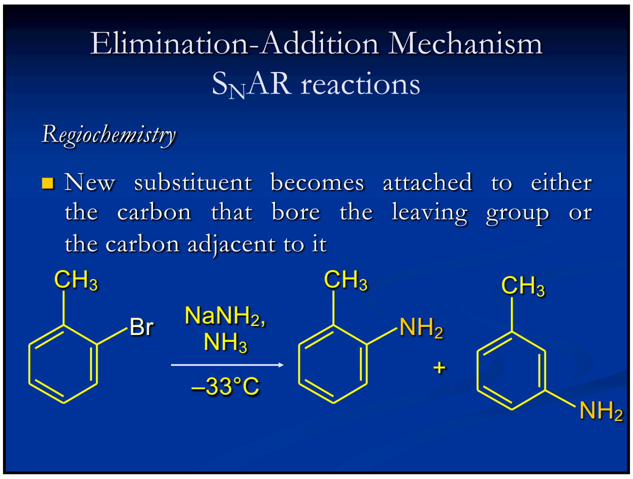
Addition-Elimination Mechanism
S_NAR reactions

- *Mechanism*
  - Step 2



Elimination-Addition Mechanism
S_NAR reactions

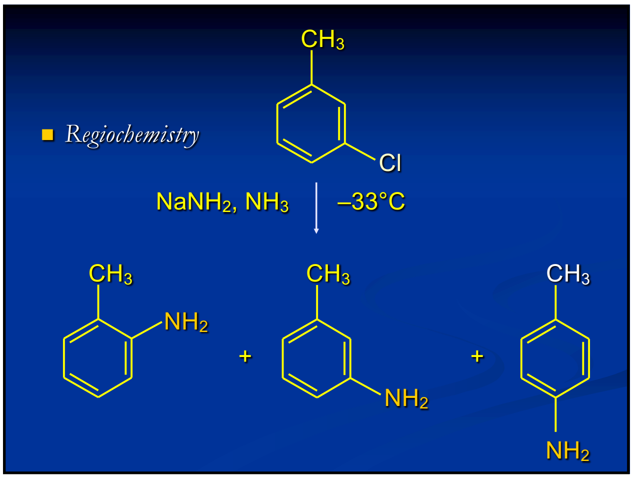
- *Aryl Halides Undergo Substitution When Treated With Very Strong Bases*



Elimination-Addition Mechanism
S_NAR reactions

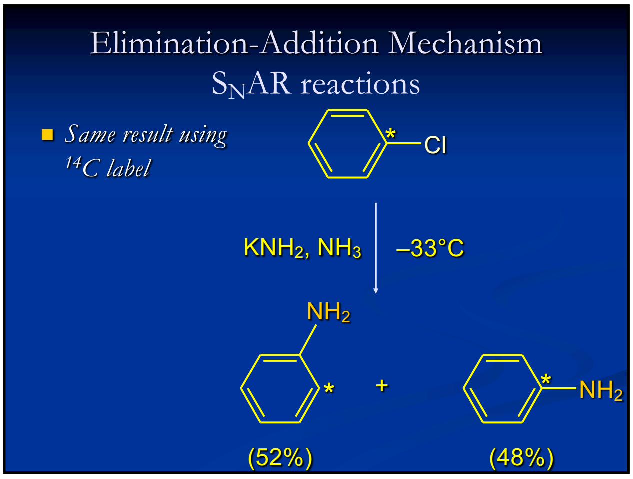
Regiochemistry

- New substituent becomes attached to either the carbon that bore the leaving group or the carbon adjacent to it



- *Regiochemistry*

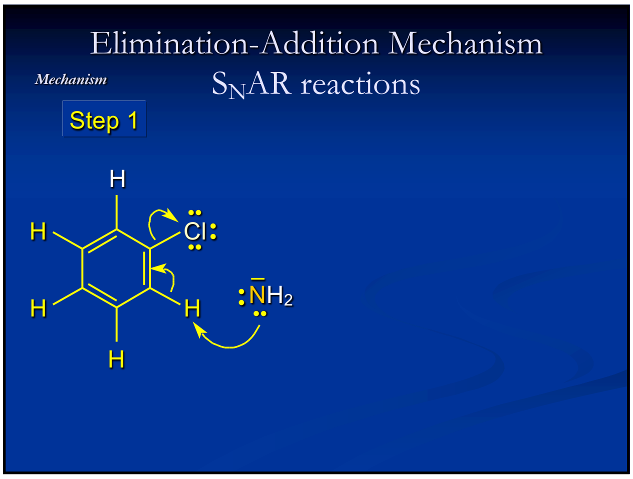
33



Elimination-Addition Mechanism
S$_N$AR reactions

- *Same result using ^{14}C label*

34

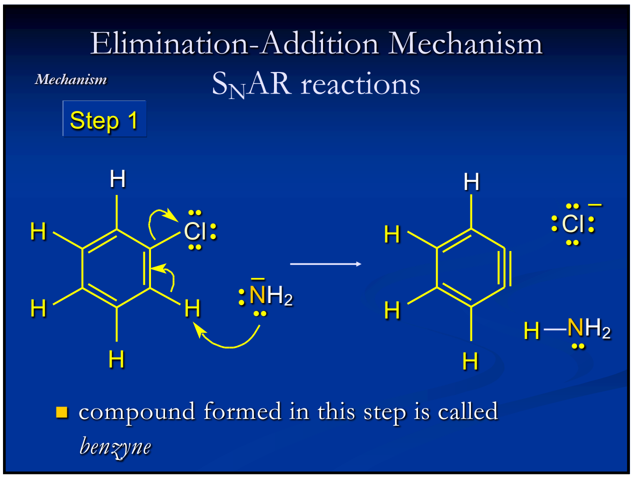


Elimination-Addition Mechanism
S$_N$AR reactions

Mechanism

Step 1

35



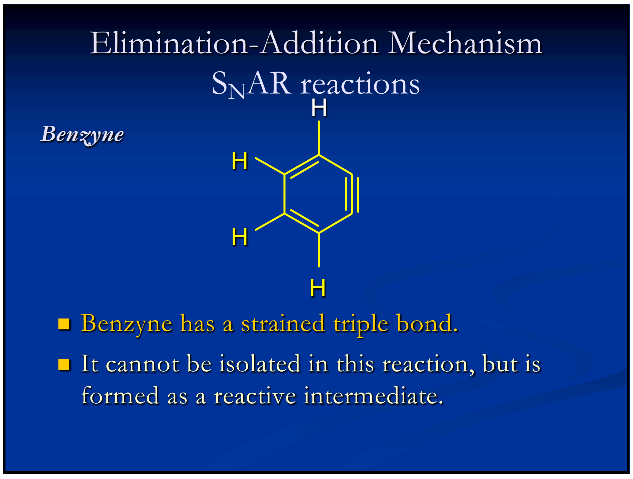
Elimination-Addition Mechanism
S$_N$AR reactions

Mechanism

Step 1

- compound formed in this step is called *benzyne*

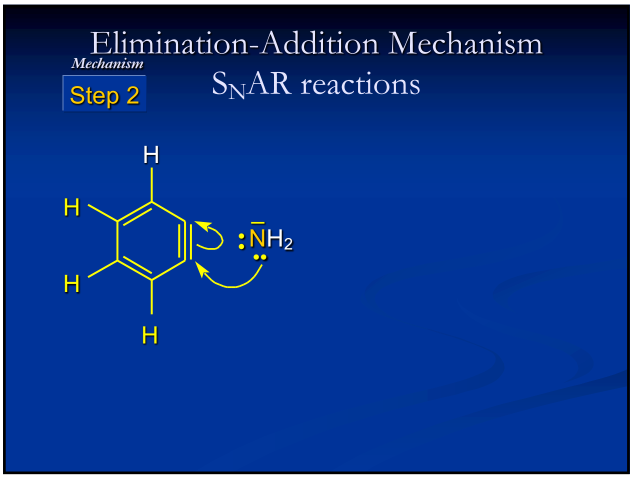
36



Elimination-Addition Mechanism
S_NAR reactions

Benzyne

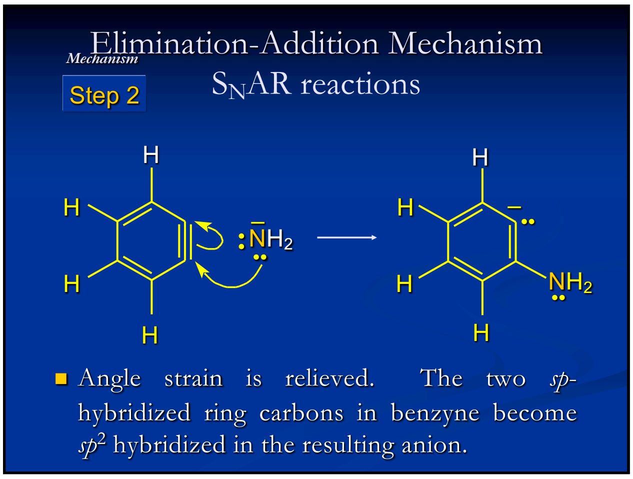
- Benzyne has a strained triple bond.
- It cannot be isolated in this reaction, but is formed as a reactive intermediate.



Elimination-Addition Mechanism
S_NAR reactions

Mechanism

Step 2

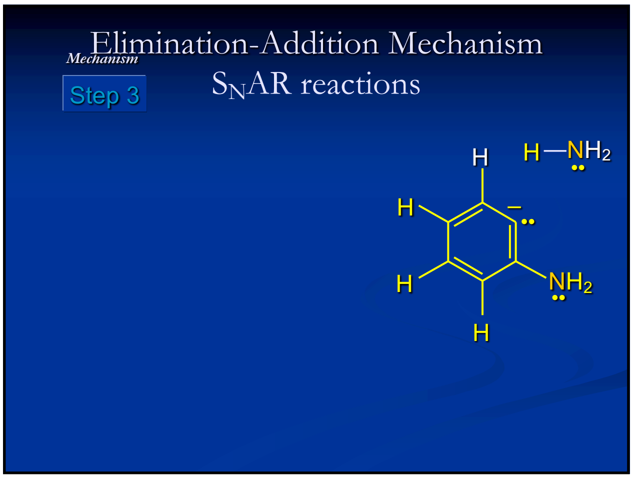


Elimination-Addition Mechanism
S_NAR reactions

Mechanism

Step 2

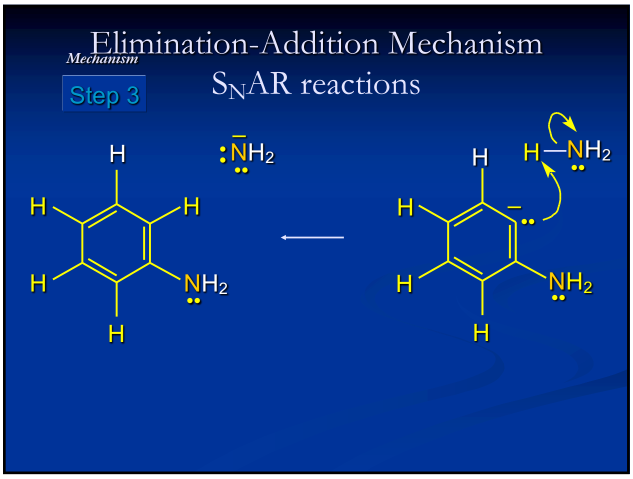
- Angle strain is relieved. The two *sp*-hybridized ring carbons in benzyne become *sp*^{2} hybridized in the resulting anion.



Elimination-Addition Mechanism
S_NAR reactions

Mechanism

Step 3

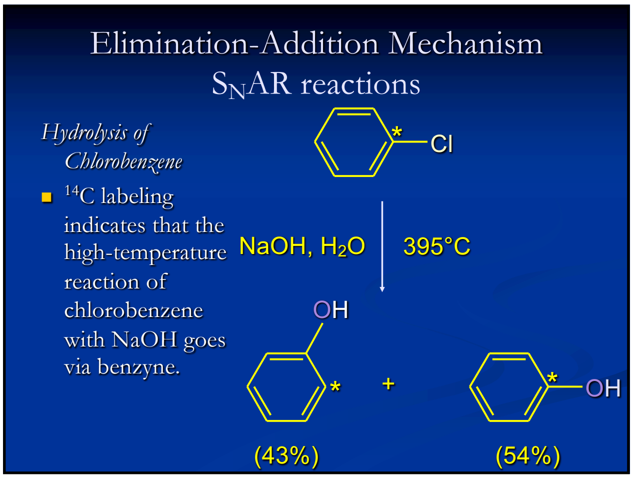


Elimination-Addition Mechanism

S_NAR reactions

Mechanism

Step 3

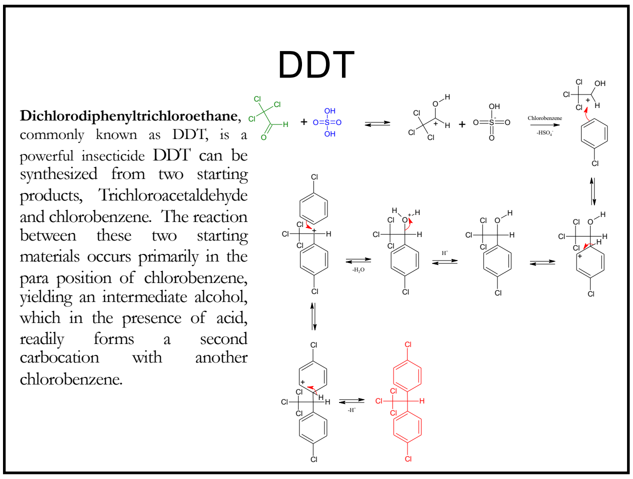


Elimination-Addition Mechanism

S_NAR reactions

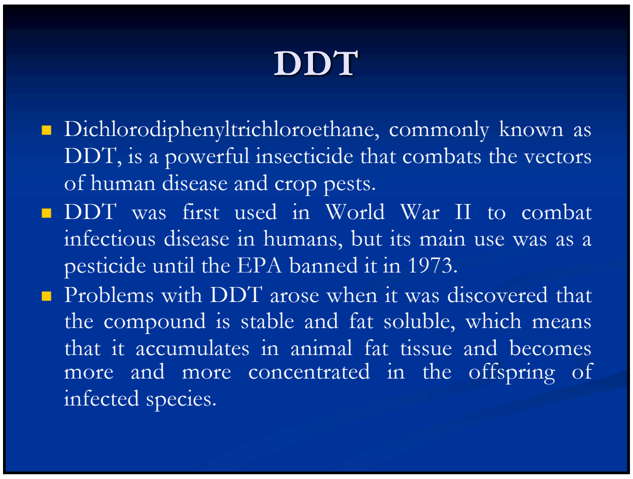
Hydrolysis of Chlorobenzene

- ^{14}C labeling indicates that the high-temperature reaction of chlorobenzene with NaOH goes via benzyne.



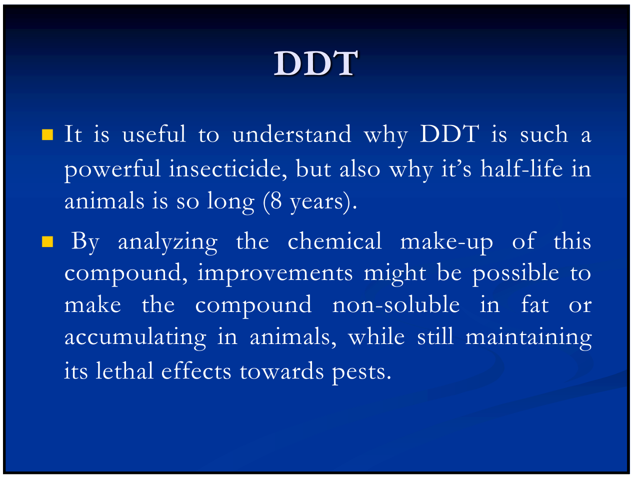
DDT

Dichlorodiphenyltrichloroethane, commonly known as DDT, is a powerful insecticide DDT can be synthesized from two starting products, Trichloroacetaldehyde and chlorobenzene. The reaction between these two starting materials occurs primarily in the para position of chlorobenzene, yielding an intermediate alcohol, which in the presence of acid, readily forms a second carbocation with another chlorobenzene.



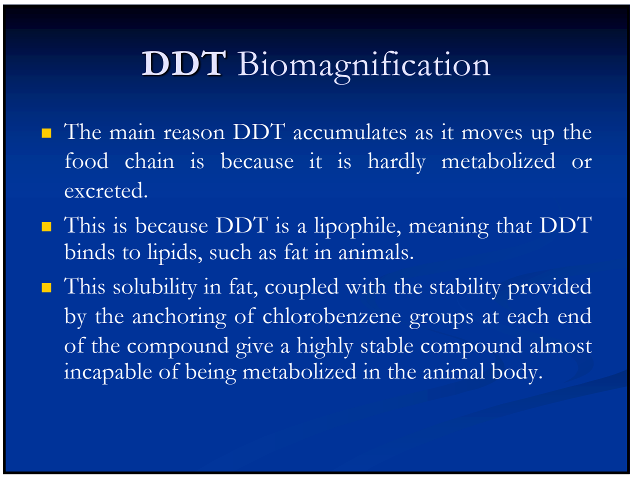
DDT

- Dichlorodiphenyltrichloroethane, commonly known as DDT, is a powerful insecticide that combats the vectors of human disease and crop pests.
- DDT was first used in World War II to combat infectious disease in humans, but its main use was as a pesticide until the EPA banned it in 1973.
- Problems with DDT arose when it was discovered that the compound is stable and fat soluble, which means that it accumulates in animal fat tissue and becomes more and more concentrated in the offspring of infected species.



DDT

- It is useful to understand why DDT is such a powerful insecticide, but also why it's half-life in animals is so long (8 years).
- By analyzing the chemical make-up of this compound, improvements might be possible to make the compound non-soluble in fat or accumulating in animals, while still maintaining its lethal effects towards pests.



DDT Biomagnification

- The main reason DDT accumulates as it moves up the food chain is because it is hardly metabolized or excreted.
- This is because DDT is a lipophile, meaning that DDT binds to lipids, such as fat in animals.
- This solubility in fat, coupled with the stability provided by the anchoring of chlorobenzene groups at each end of the compound give a highly stable compound almost incapable of being metabolized in the animal body.