

# Organic Reactions and Mechanisms

- **Organic reactions** are chemical reactions involving organic compounds. The basic organic chemistry reaction types are addition reactions, elimination reactions, substitution reactions, pericyclic reactions, rearrangement reactions and redox reactions.
- **A reaction mechanism** is the step by step sequence of elementary reactions by which overall chemical change occurs.

# Nucleophilie

- A reagent which can donate an electron pair in a reaction is called a nucleophile.
- The name nucleophile means nucleous loving and indicates that it attacks regions of low electron density (positive centres) in the substrate molecule.
- Nucleophiles are electron rich.
- They may be negative ions including carbanions or neutral molecules with free electron pair.
- A nucleophile can be represented by a by general symbol  $\text{Nu}^-$
- Examples
- $\text{Cl}^-$ ,  $\text{Br}^-$ ,  $\text{I}^-$ ,  $\text{CN}^-$ ,  $\text{OH}^-$ ,  $\text{RCH}_2^-$ ,  $\text{NH}_3$ ,  $\text{RNH}_2$ ,  $\text{H}_2\text{O}$ ,  $\text{ROH}$

# Electrophiles

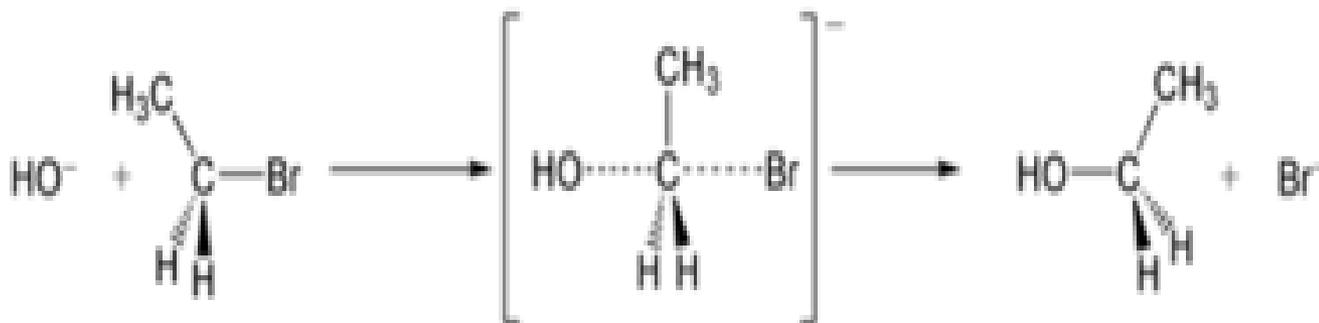
- A reagent which can accept an electron pair in a reaction called an electrophile.
- The name electrophile means electron-loving and indicates that it attacks regions of high electron density (negative centres) in the substrates molecule.
- Electrophiles are electron deficient.
- They may be positive ions including carbonium ions or neutral molecules with electron deficient centres
- An electrophile can be represented by  $E^+$
- Examples
- $H^+$ ,  $Cl^+$ ,  $Br^+$ ,  $I^+$ ,  $NO_2^+$ ,  $R_3C^+$ ,  $^+SO_3H$ ,  $AlCl_3$ ,  $BF_3$

# Organic Reaction Mechanism

- A **reaction mechanism** is the step by step sequence of elementary reactions by which overall chemical change occurs.
- Although only the net chemical change is directly **observable** for most chemical reactions, experiments can often be designed that suggest the possible sequence of steps in a reaction mechanism.

# Mechanism

- There is no limit to the number of possible organic reactions and mechanisms. However, certain general patterns are observed that can be used to describe many common or useful reactions. Each reaction has a stepwise **reaction mechanism** that explains how it happens, although this detailed description of steps is not always clear from a list of reactants alone.



# Types of Organic Reactions

- Organic reactions can be organized into several basic types. Some reactions fit into more than one category. For example, some substitution reactions follow an addition-elimination pathway. This overview isn't intended to include every single organic reaction. Rather, it is intended to cover the basic reactions.

# Types of reactions

- Addition reactions
- Substitution reactions
- Elimination Reactions
- Rearrangement reactions
- Organic Redox reactions

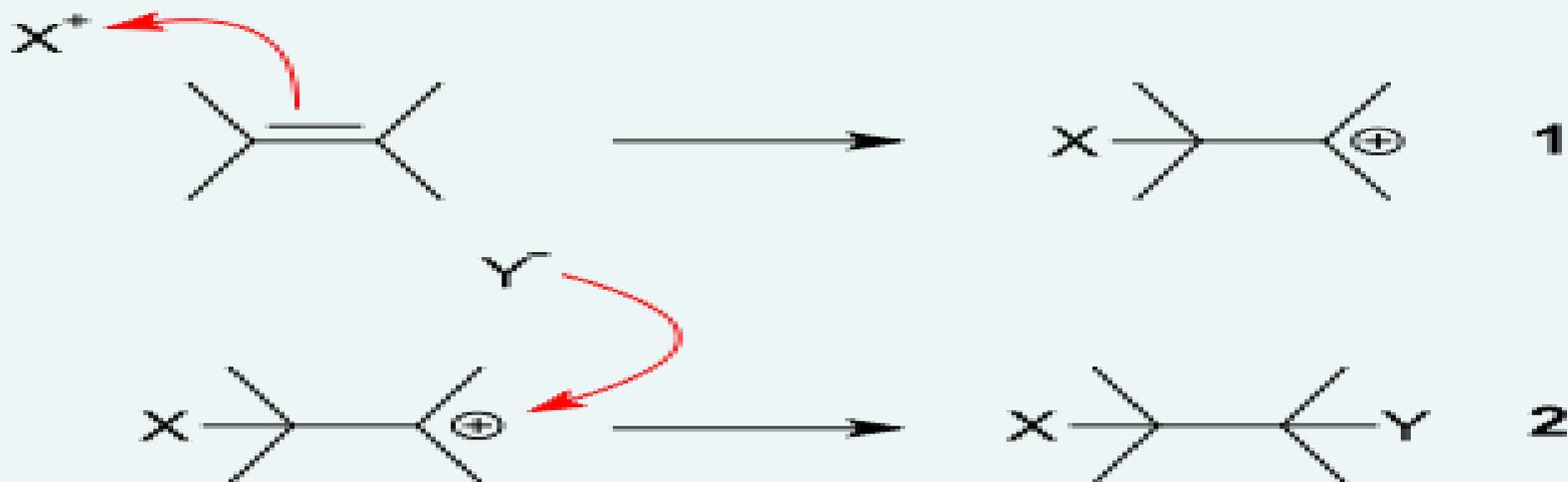
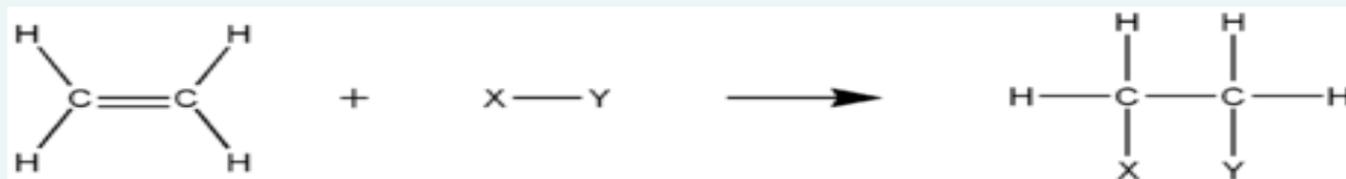
# Types of Reactions

Reaction Type	Sub-type	comments
Addition reactions	Electrophilic Nucleophilic radical	halogenation, hydrohalogenation and hydration
Elimination reaction		Dehydration
Substitution reactions	nucleophilic aliphatic Substitution nucleophilic aromatic substitution nucleophilic acyl substitution electrophilic substitution electrophilic aromatic substitution radical substitution	with $SN^1$ , $SN^2$ and $SNi$ reaction mechanisms
Organic Redox reactions		redox reactions specific to organic compounds
Rearrangements reactions	1,2-rearrangements pericyclic reactions metathesis	

# Addition Reactions - Electrophilic addition

- An **electrophilic addition** reaction is an addition reaction where, in a chemical compound, a  **$\pi$  bond** is broken and two new  **$\sigma$  bonds** are formed. The substrate of an electrophilic addition reaction must have a **double bond** or **triple bond**.
- The driving force for this reaction is the formation of an **electrophile  $X^+$**  that forms a **covalent bond** with an electron-rich **unsaturated C=C bond**. The positive charge on X is transferred to the carbon-carbon bond, forming a **carbocation**.

# Addition Reactions - Electrophilic addition



# Addition Reactions - Electrophilic addition

- In step 1, the positively charged intermediate combines with (Y) that is electron-rich and usually an anion to form the second covalent bond.
- Step 2 is the same nucleophilic attack process found in an SN1 reaction. The exact nature of the electrophile and the nature of the positively charged intermediate are not always clear and depend on reactants and reaction conditions.

# Addition Reactions - Electrophilic addition

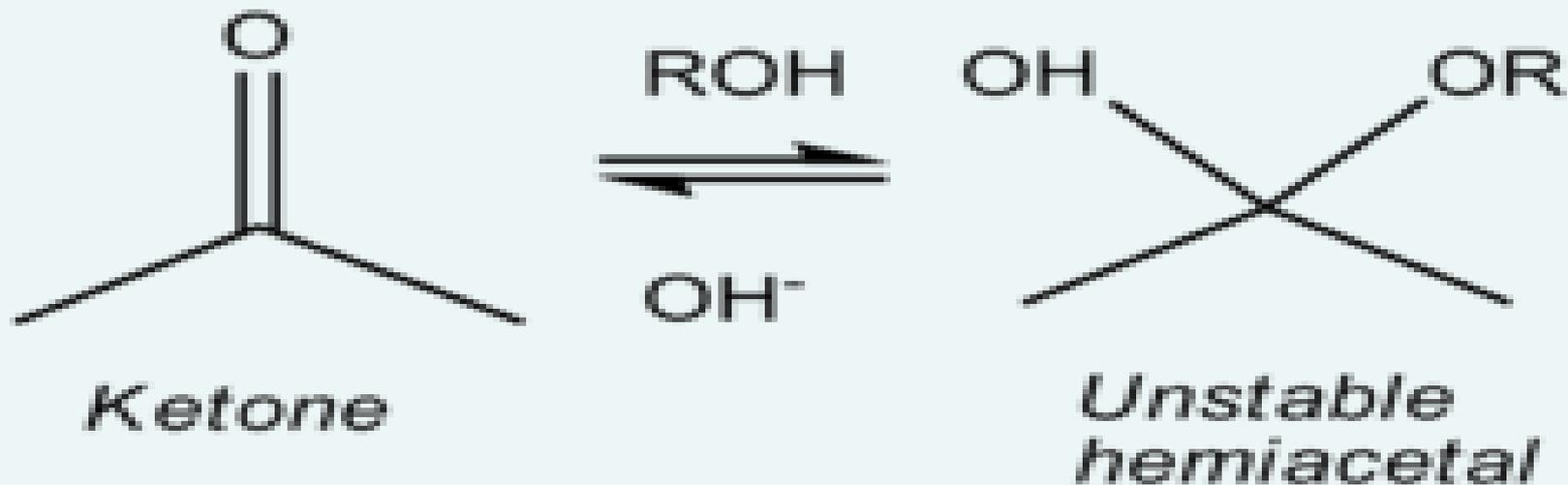
- In all asymmetric addition reactions to carbon, regioselectivity is important and often determined by Markovnikov's rule. Organoborane compounds give anti-Markovnikov additions. Electrophilic attack to an aromatic system results in electrophilic aromatic substitution rather than an addition reaction.
- Typical electrophilic additions to alkenes with reagents are:
  - dihalo addition reactions:  $X_2$
  - Hydrohalogenations:  $HX$
  - Hydration reactions:  $H_2O$
  - Hydrogenations  $H_2$
  - Oxymercuration reactions: mercuric acetate, water
  - Hydroboration-oxidation reactions : diborane
  - the Prins reaction : formaldehyde, water

# Nucleophilic addition

- A **nucleophilic addition** reaction is an addition reaction where in a **chemical compound** a  $\pi$  **bond** is removed by the creation of two new **covalent bonds** by the addition of a **nucleophile**.
- Addition reactions are limited to chemical compounds that have multiple-bonded atoms
- molecules with carbon - hetero multiple bonds like **carbonyls**, **imines** or **nitriles**
- molecules with carbon - carbon double bonds or triple bonds

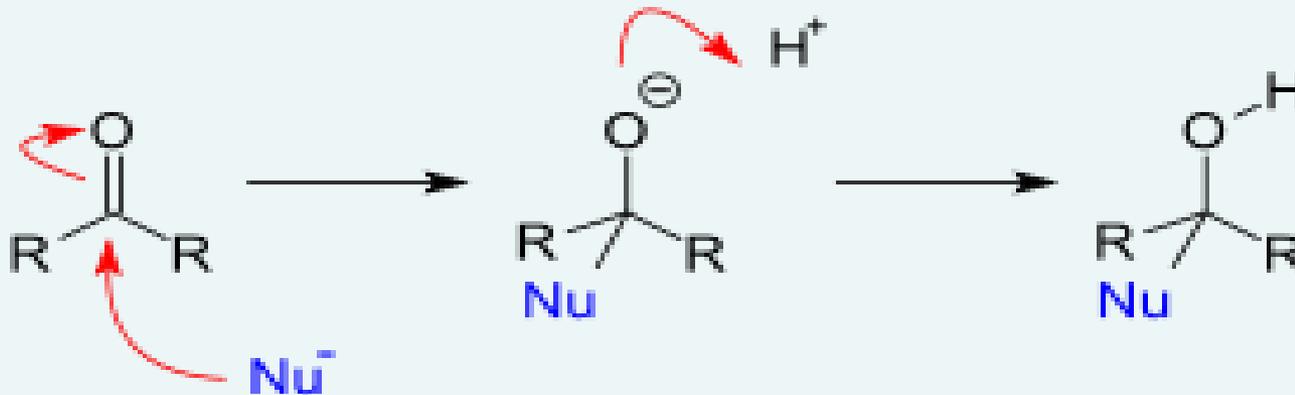
# Nucleophilic addition

- An example of a nucleophilic addition reaction that occurs at the carbonyl group of a ketone by substitution with hydroxide-based compounds, denoted shorthand. In this example, an unstable hemiketal is formed.

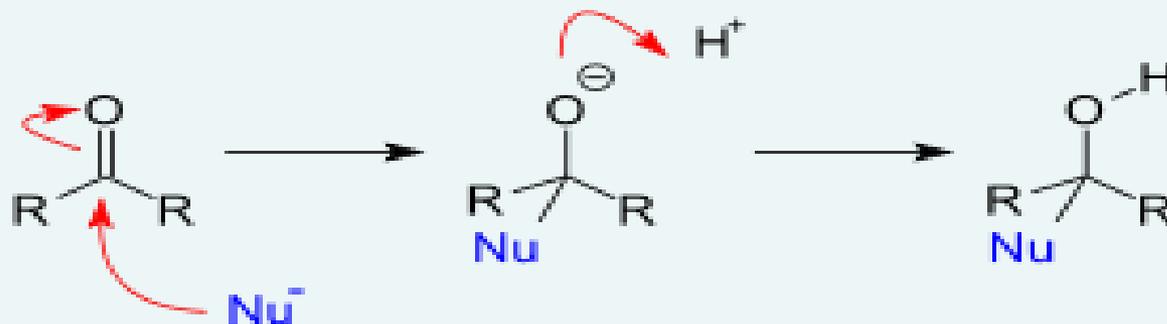


# Nucleophilic Addition to carbon - hetero double bonds

- Addition reactions of a nucleophile to carbon - hetero double bonds such as C=O or CN triple bond show a wide variety. These bonds are **polar** (have a large difference in **electronegativity** between the two atoms) consequently carbon carries a partial positive charge. This makes this atom the primary target for the nucleophile.



# Nucleophilic Addition to carbon - hetero double bonds



- This type of reaction is also called a **1,2 nucleophilic addition**. The **stereochemistry** of this type of nucleophilic attack is not an issue, when both alkyl substituents are dissimilar and there are not any other controlling issues such as **chelation** with a **Lewis acid**, the reaction product is a **racemate**. Addition reactions of this type are numerous. When the addition reaction is accompanied by an elimination, the reaction type is **nucleophilic acyl substitution** or an **addition-elimination reaction**.

- **Carbonyls**

- With a carbonyl compound as an electrophile, the nucleophile can be:
- water in hydration to a geminal diol (hydrate)
- an alcohol in acetalisation to an acetal
- an hydride in reduction to an alcohol
- an amine with formaldehyde and a carbonyl compound in the Mannich reaction
- an enolate ion in an aldol reaction or Baylis-Hillman reaction
- an organometallic nucleophile in the Grignard reaction or the related Barbier reaction or a Reformatskii reaction
- ylides such as a Wittig reagent or the Corey-Chaykovsky reagent or  $\alpha$ -silyl carbanions in the Peterson olefination
- a phosphonate carbanion in the Horner-Wadsworth-Emmons reaction
- a pyridine zwitterion in the Hammick reaction
- an acetylide in the Favorskii reaction

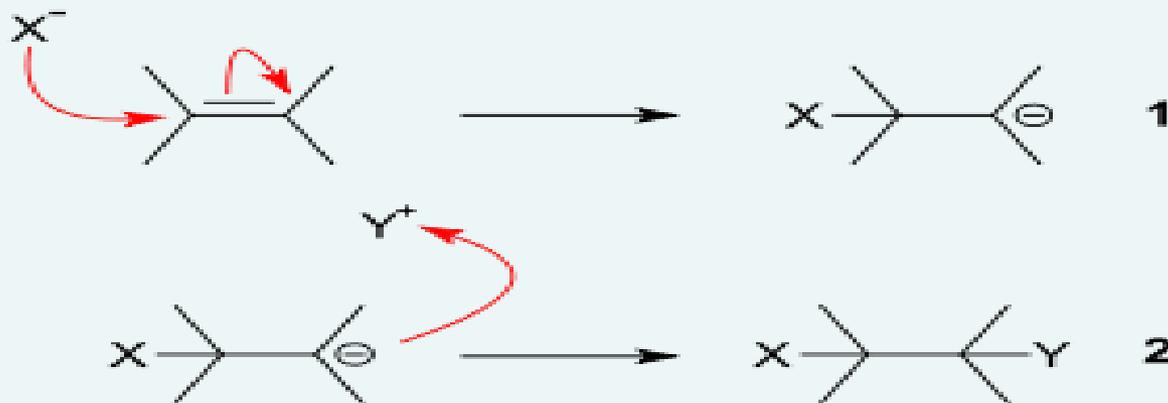
- **Nitriles**

- With nitrile electrophiles nucleophilic addition take place by:
- hydrolysis of a nitrile to an amide or a carboxylic acid
- organozinc nucleophiles in the Blaise reaction
- alcohols in the Pinner reaction.
- the (same) nitrile  $\alpha$ -carbon in the Thorpe reaction. The intramolecular version is called the Thorpe-Ziegler reaction.

- **Imines and other**
- With imine electrophiles nucleophilic addition take place by:
- hydrides to amines in the Eschweiler-Clarke reaction
- water to carbonyls in the Nef reaction.
- With miscellaneous electrophiles:
- addition of an alcohol to an isocyanate to form a carbamate.
- Nucleophiles attack carbonyl centers from a specific angle called the Bürgi-Dunitz angle.

# Nucleophilic Addition to carbon - carbon double bonds

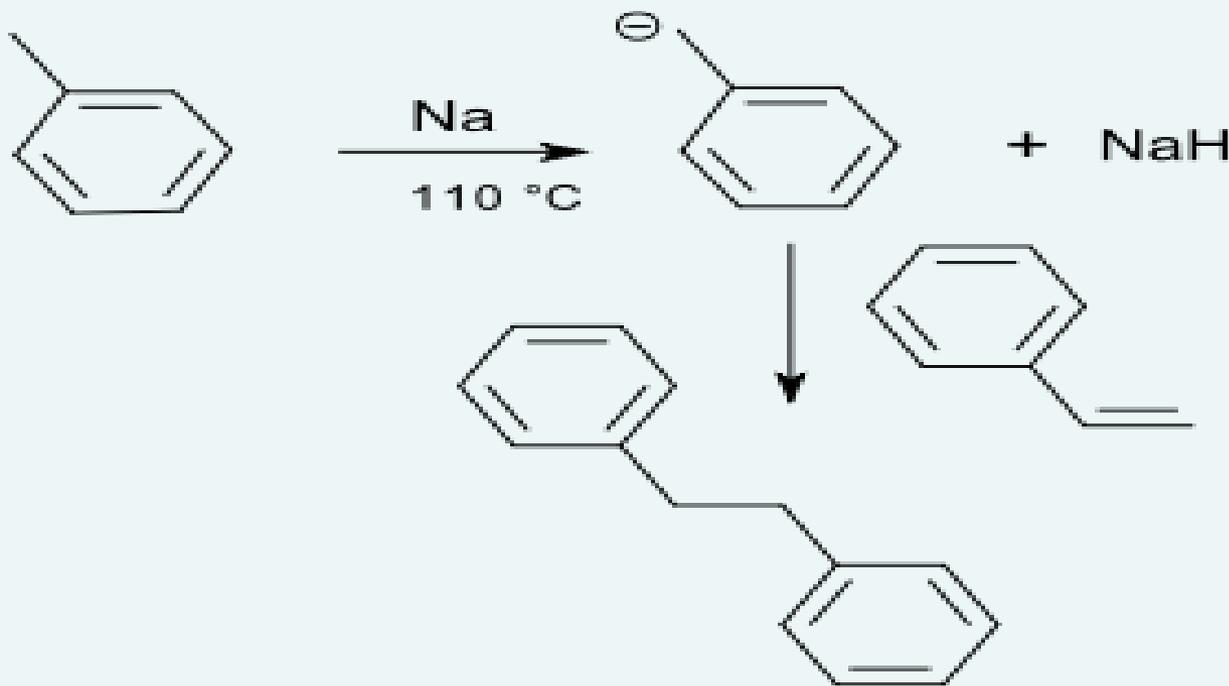
- The driving force for the addition to **alkenes** is the formation of a **nucleophile** X<sup>-</sup> that forms a **covalent bond** with an electron-poor **unsaturated** system -C=C- (step 1). The negative charge on X is transferred to the carbon - carbon bond.



- In step 2 the negatively charged **carbanion** combines with (Y) that is electron-poor to form the second covalent bond.

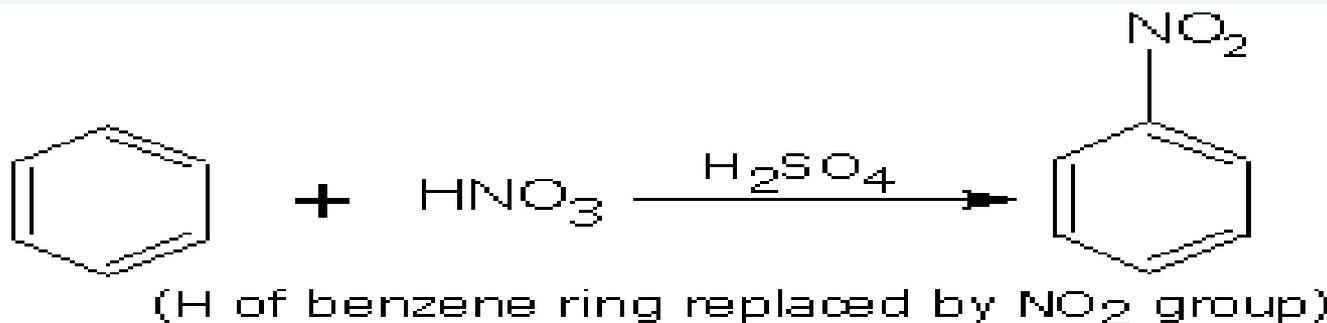
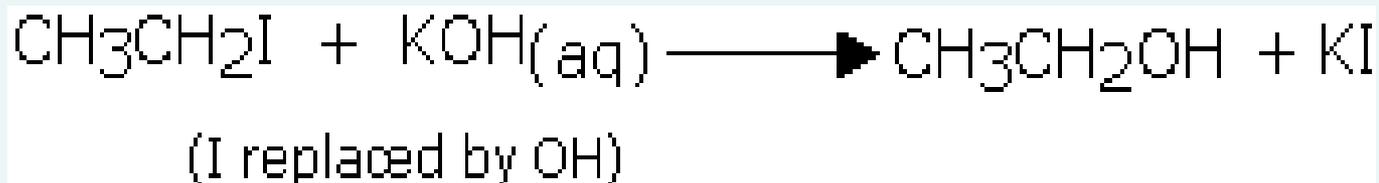
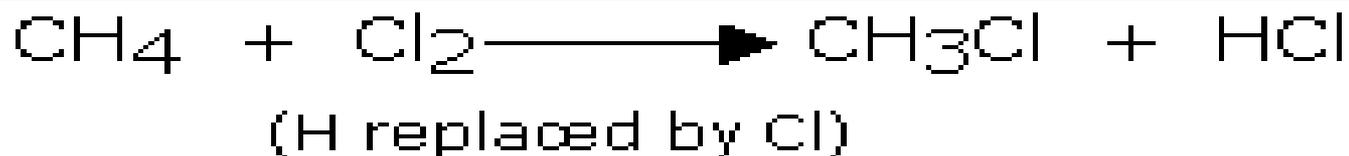
# Nucleophilic Addition to carbon - carbon double bonds

- Ordinary alkenes are not susceptible to a nucleophilic attack (apolar bond). **Styrene** reacts in **toluene** with **sodium** to 1,3-diphenylpropane through the intermediate carbanion:



# Substitution Reactions

The reactions in which an atom or group of atoms in a molecule is replaced or substituted by different atoms or group of atoms are called substitution reaction. For example,



# Nucleophilic Substitution

- **Nucleophilic substitution** is a fundamental class of substitution reaction in which an "electron rich" nucleophile selectively bonds with or attacks the positive or partially positive charge of an atom *attached to a group* or atom called the leaving group; the positive or partially positive atom is referred to as an electrophile.
- Nucleophilic substitution reactions can be broadly classified as
  - Nucleophilic substitution at saturated carbon centres
  - Nucleophilic substitution at unsaturated carbon centres

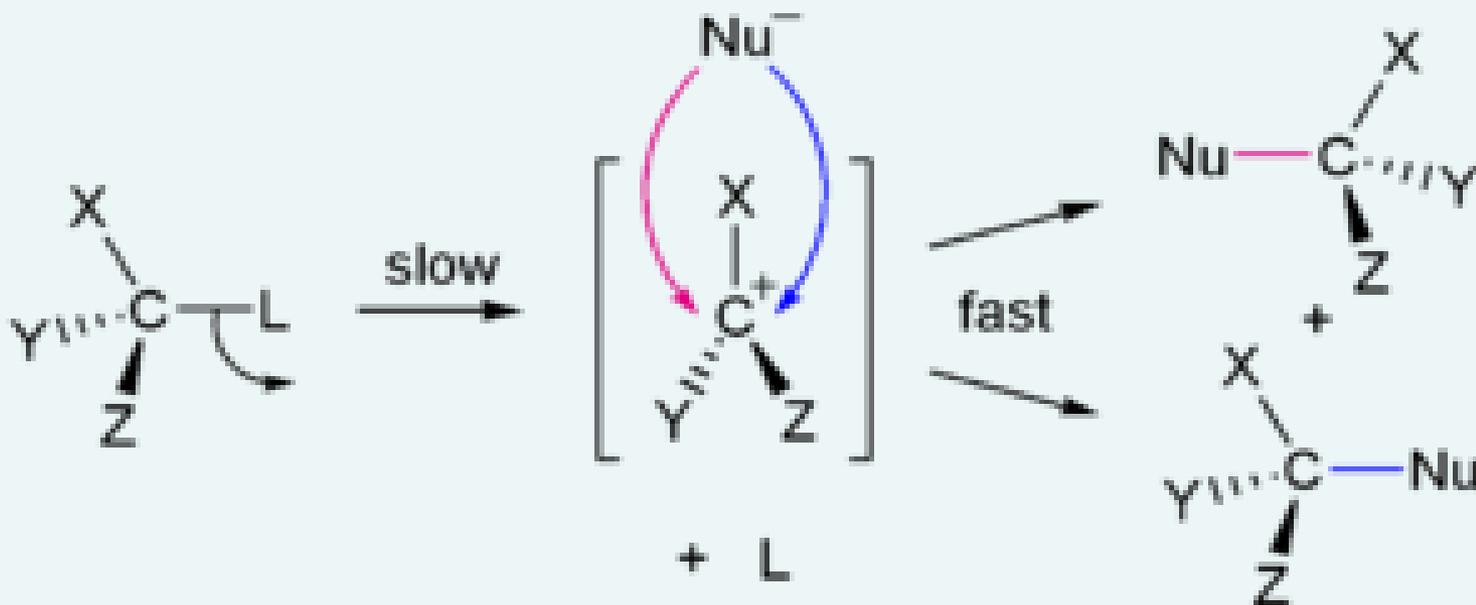
# Nucleophilic substitution at saturated carbon centres

- In 1935, **Edward D. Hughes** and **Sir Christopher Ingold** studied nucleophilic substitution reactions of **alkyl halides** and related compounds. They proposed that there were two main mechanisms at work, both of them competing with each other. The two main mechanisms are the **SN1 reaction** and the **SN2 reaction**. S stands for chemical substitution, N stands for nucleophilic, and the number represents the **kinetic order** of the reaction.

- In the SN2 reaction, the addition of the nucleophile and the elimination of leaving group take place simultaneously. SN2 occurs where the central carbon atom is easily accessible to the nucleophile. By contrast the SN1 reaction involves two steps. SN1 reactions tend to be important when the central carbon atom of the substrate is surrounded by bulky groups, both because such groups interfere sterically with the SN2 reaction (discussed above) and because a highly substituted carbon forms a stable **carbocation**.

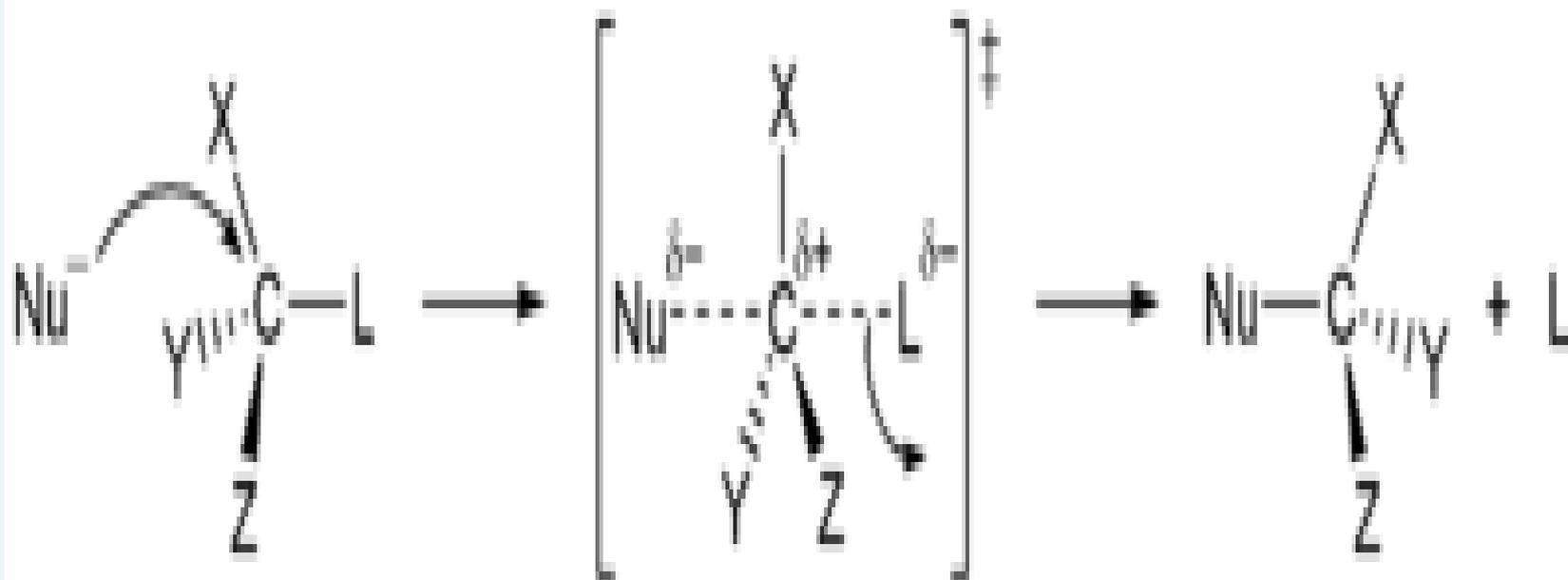
Nucleophilic substitution at carbon atom

# SN<sup>1</sup> Mechanism



Nucleophilic substitution at carbon atom

# SN<sup>2</sup> Mechanism

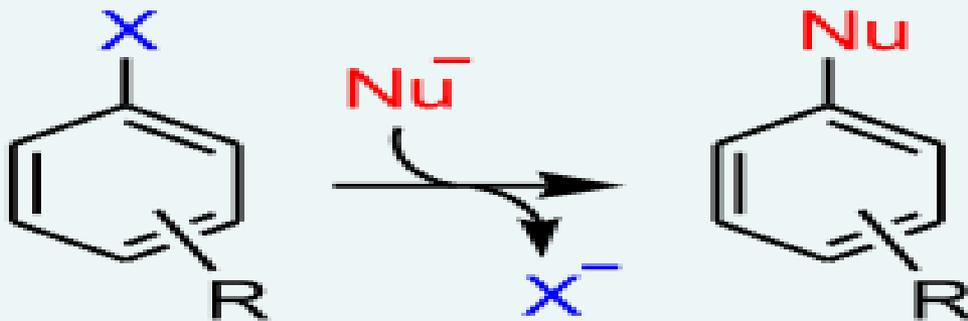


# Nucleophilic substitution at unsaturated carbon centres

- Nucleophilic substitution via the SN1 or SN2 mechanism does not generally occur with vinyl or aryl halides or related compounds.
- When the substitution occurs at the carbonyl group, the acyl group may undergo nucleophilic acyl substitution. This is the normal mode of substitution with carboxylic acid derivatives such as acyl chlorides, esters and amides.

# Nucleophilic Aromatic substitution

- A **nucleophilic aromatic substitution** is a substitution reaction in organic chemistry in which the nucleophile displaces a good leaving group, such as a halide, on an aromatic ring.



$\text{X}$  = halogen etc.  $\text{Nu}$  = nucleophile

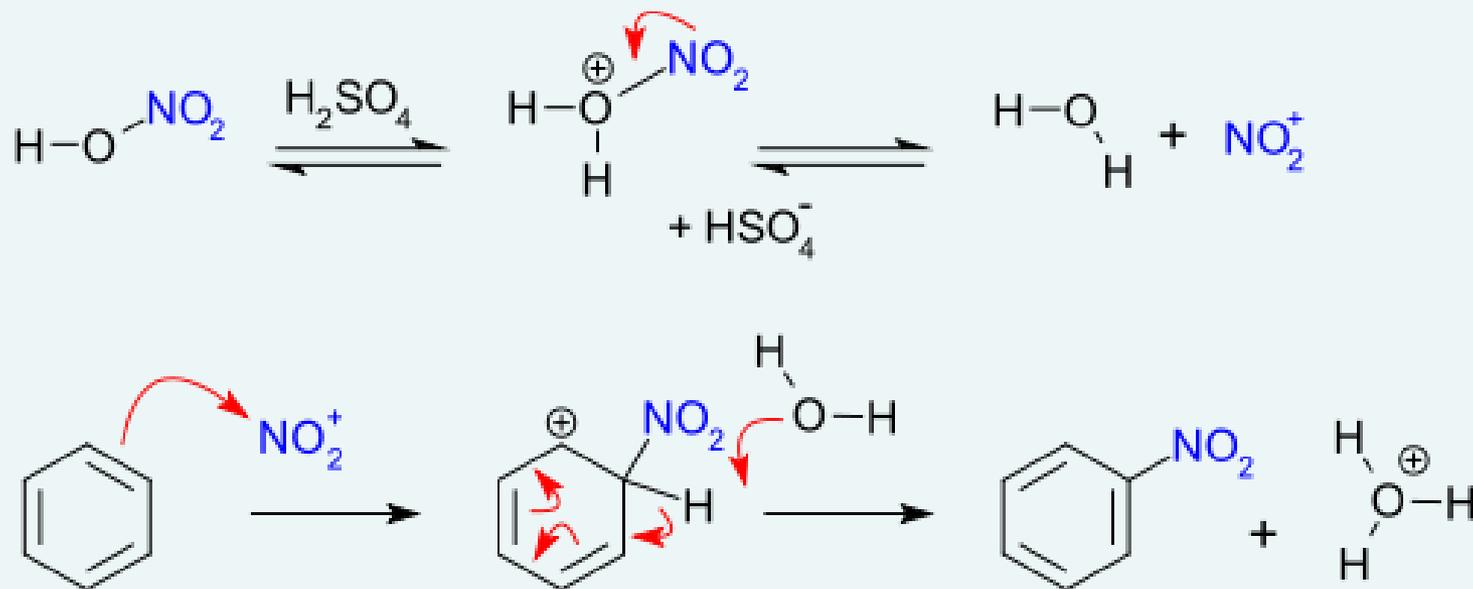
# Nitration



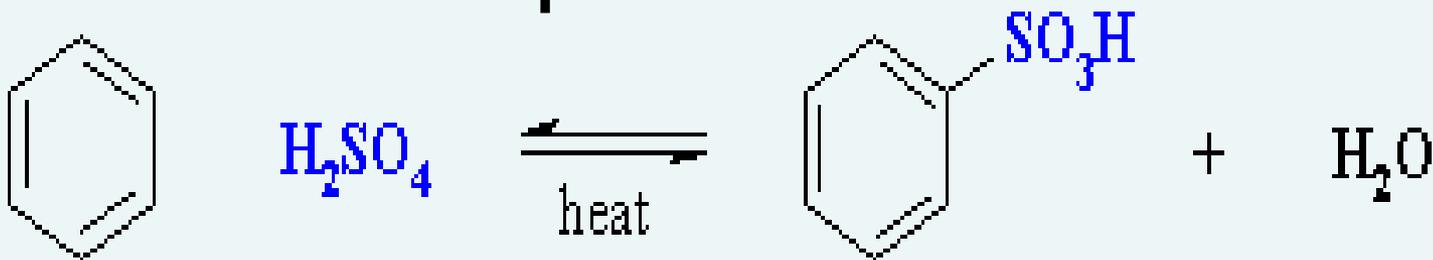
- **Nitration** is a general chemical process for the introduction of a nitro group into a chemical compound. Examples of nitrations are the conversion of glycerin to nitroglycerin and the conversion of toluene to trinitrotoluene. Both of these conversions use nitric acid and sulfuric acid.
- In **aromatic nitration**, aromatic organic compounds are nitrated via an electrophilic aromatic substitution mechanism involving the attack of the electron-rich benzene ring by the nitronium ion.

Aromatic nitro compounds are important intermediates to anilines by action of a reducing agent. Benzene is nitrated by refluxing with concentrated sulfuric acid and concentrated nitric acid at 50 °C. The sulfuric acid is regenerated and hence acts as a catalyst. It also absorbs water.

- The formation of a nitronium ion (the electrophile) from nitric acid and sulfuric acid and subsequent reaction of the ion with benzene is shown below:



# Sulphonation



- **Electrophilic Aromatic Substitution**
- Overall transformation : **Ar-H** to **Ar-SO<sub>3</sub>H**, a sulfonic acid.
- Reagent : for benzene,  $\text{H}_2\text{SO}_4$  / heat or  $\text{SO}_3$  /  $\text{H}_2\text{SO}_4$  / heat (= fuming sulfuric acid)
- Electrophilic species :  $\text{SO}_3$  which can be formed by the loss of water from the sulfuric acid
- Unlike the other electrophilic aromatic substitution reactions, sulphonation is reversible.
- Removal of water from the system favours the formation of the sulphonation product.
- Heating a sulfonic acid with aqueous sulfuric acid can result be the reverse reaction, desulfonation.
- Sulphonation with fuming sulfuric acid strongly favours formation of the product the sulfonic acid.

# MECHANISM FOR SULFONATION OF BENZENE

- **Step 1:**

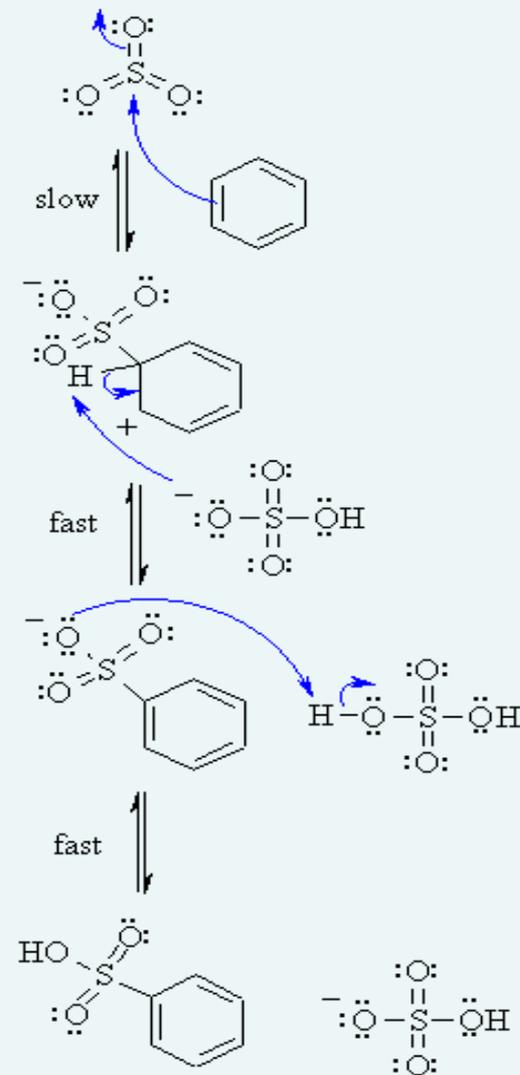
The p electrons of the aromatic **C=C** act as a nucleophile, attacking the electrophilic S, pushing charge out onto an electronegative O atom. This destroys the aromaticity giving the cyclohexadienyl cation intermediate.

- **Step 2:**

Loss of the proton from the sp<sup>3</sup> C bearing the sulfonyl- group reforms the **C=C** and the aromatic system.

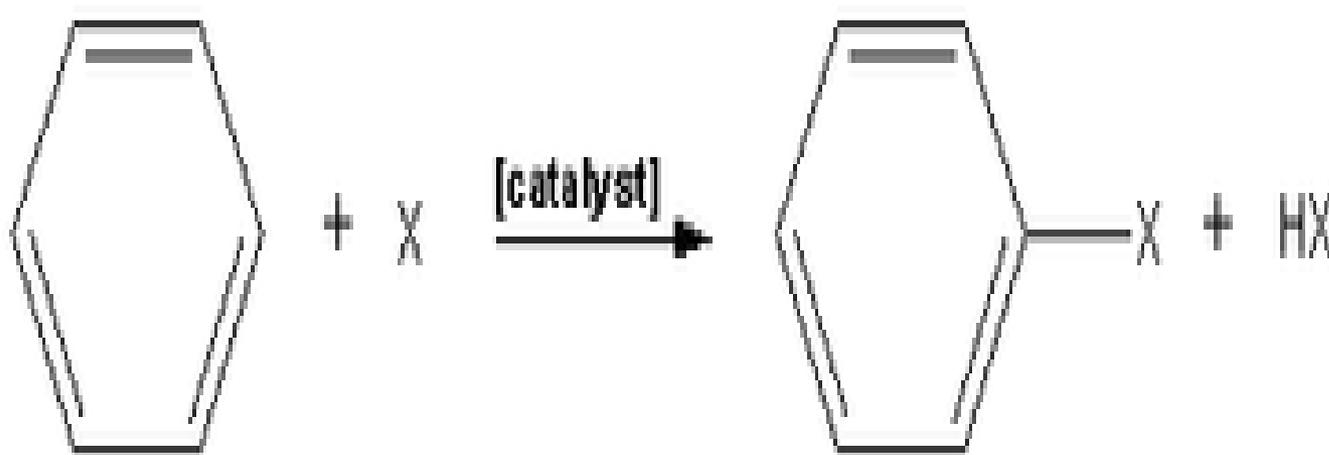
- **Step 3:**

Protonation of the conjugate base of the sulfonic acid by sulfuric acid produces the sulfonic acid

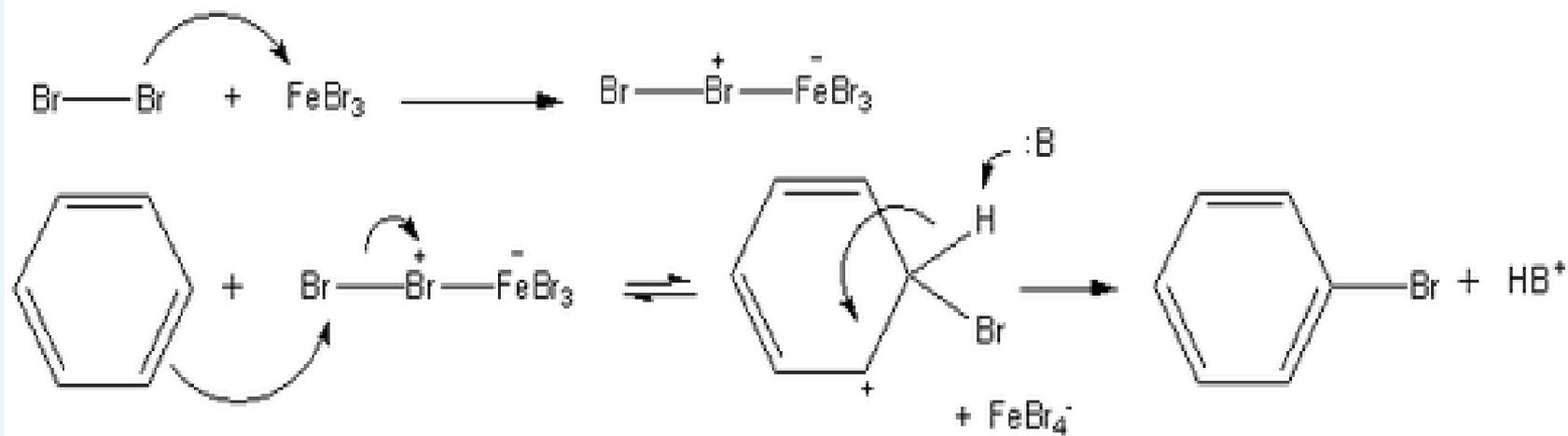


# Halogenation

- An **electrophilic aromatic halogenation** is a type of electrophilic aromatic substitution. This organic reaction is typical of aromatic compounds and a very useful method for adding substituents to an aromatic system.



- A few types of aromatic compounds, such as **phenol**, will react without a catalyst, but for typical benzene derivatives with less reactive substrates, a **Lewis acid** catalyst is required. Typical Lewis acid catalysts include  $\text{AlCl}_3$ ,  $\text{FeCl}_3$ ,  $\text{FeBr}_3$ , and  $\text{ZnCl}_2$ . These work by forming a highly **electrophilic complex** which attacks the benzene ring.

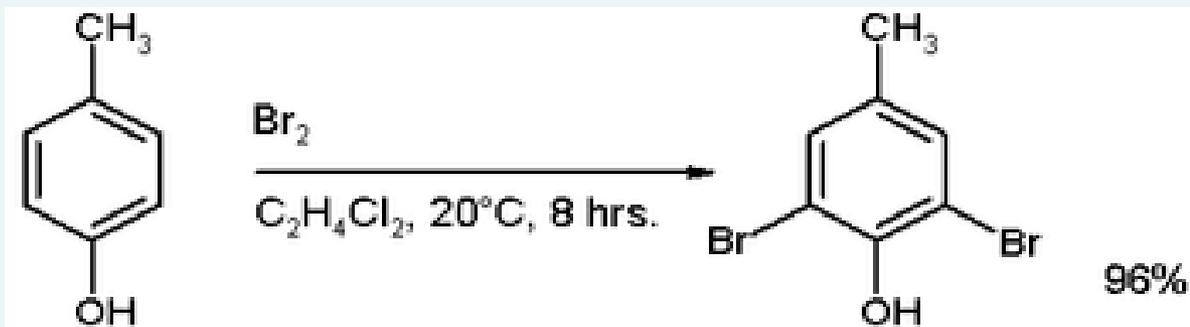


# Reaction mechanism

- The reaction mechanism for chlorination of benzene is the same as bromination of benzene.
- The mechanism for iodination is slightly different: iodine ( $I_2$ ) is treated with an oxidizing agent such as nitric acid to obtain the electrophilic iodine ( $2 I^+$ ). Unlike the other halogens, iodine does not serve as a base since it is positive.
- Halogenation of aromatic compounds differs from the halogenation of alkenes, which do not require a Lewis Acid catalyst.

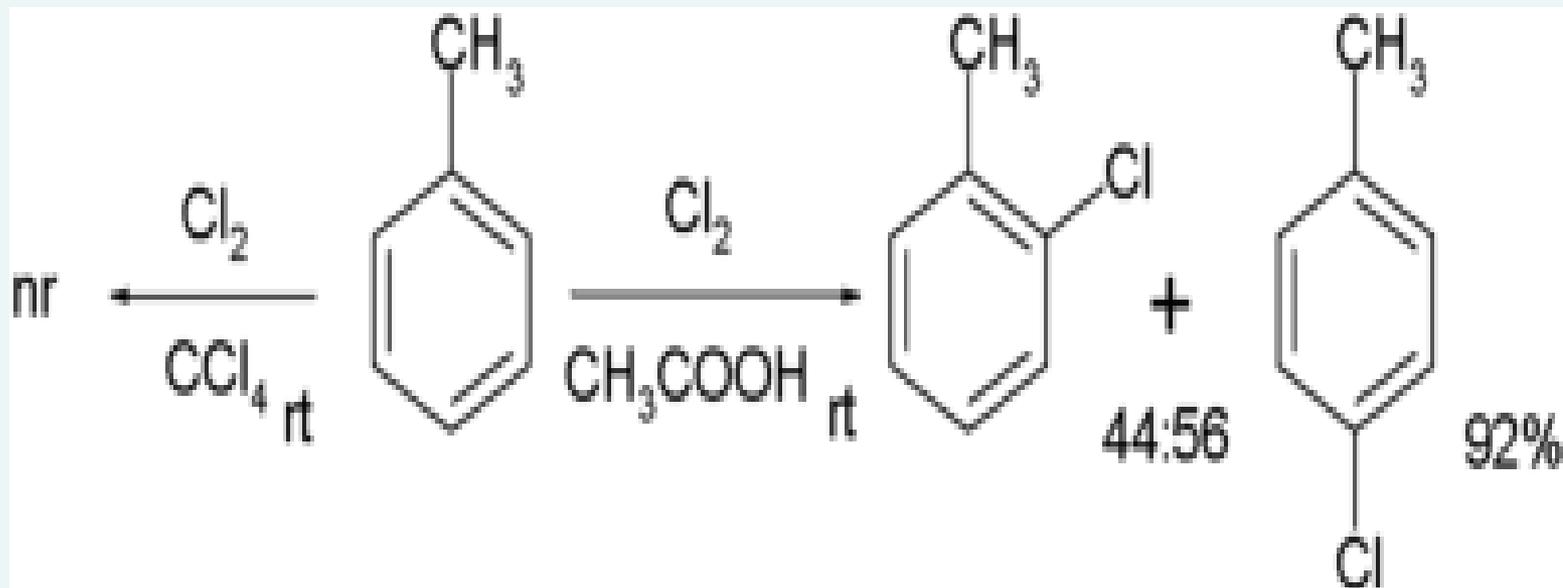
# scope

- If the ring contains a strongly activating substituent such as -OH, -OR or amines, a catalyst is not necessary, for example in the bromination of p-cresol

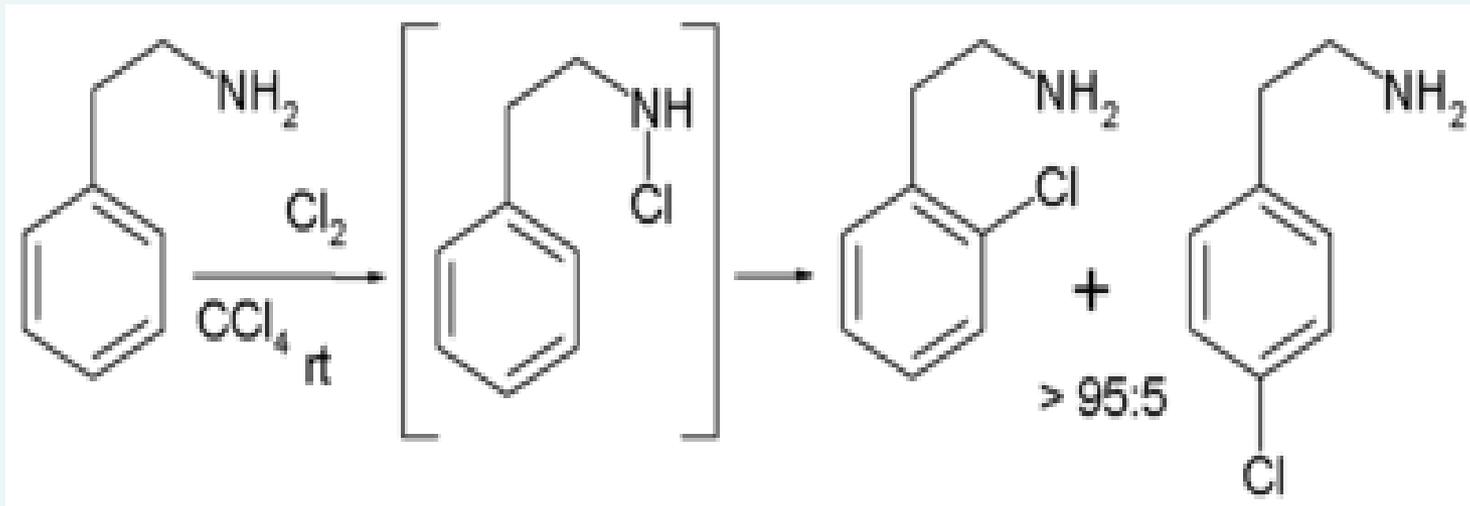


- However, if a catalyst is used with excess bromine, then a tribromide will be formed.

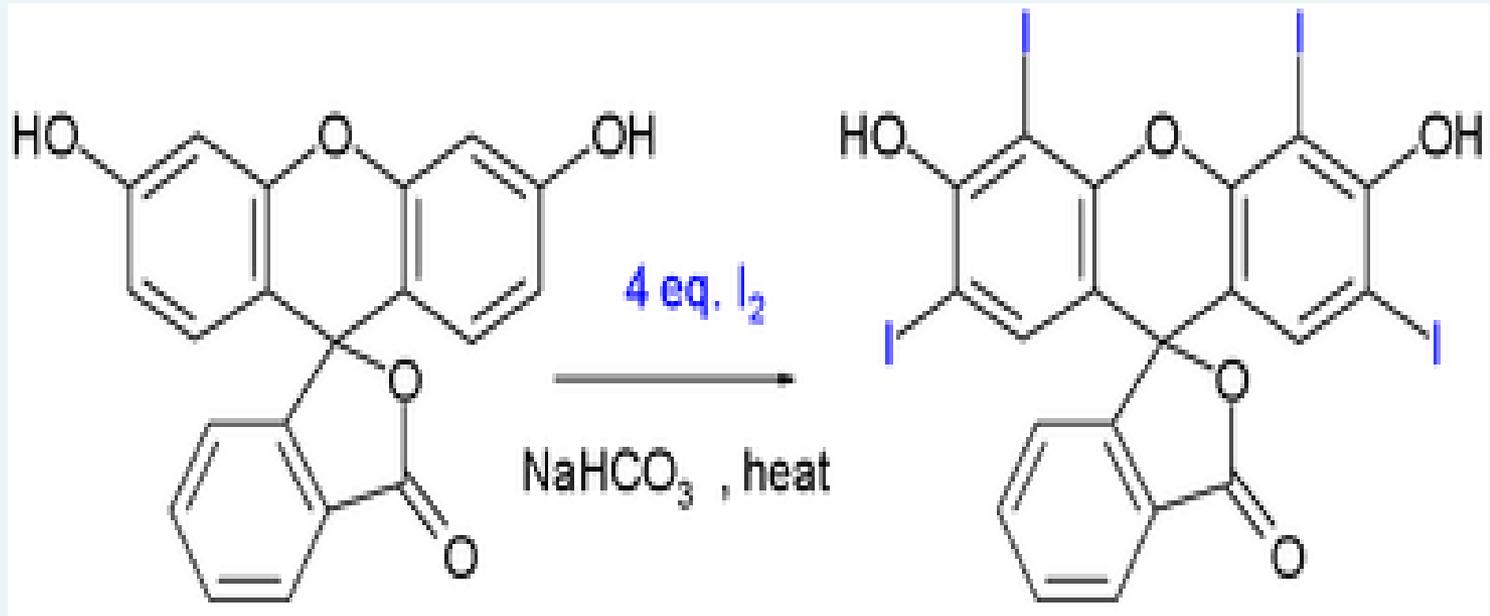
- Halogenation of phenols is faster in polar solvents due to the dissociation of phenol, with phenoxide ions being more susceptible to electrophilic attack as they are more electron-rich.
- Chlorination of toluene with chlorine without catalyst requires a polar solvent as well such as acetic acid. The ortho to para selectivity is low:



- No reaction takes place when the solvent is replaced by tetrachloromethane. In contrast, when the reactant is *2-phenylethylamine*, it is possible to employ relatively apolar solvents with exclusive ortho- regioselectivity due to the intermediate formation of a chloramine making the subsequent reaction step intramolecular.



- The food dye erythrosine can be synthesized by iodination of another dye called fluorescein:



- This reaction is driven by sodium bicarbonate.