

**DEPARTMENT OF CHEMISTRY  
FOURAH BAY COLLEGE  
UNIVERSITY OF SIERRA LEONE**

# **CHEM 123**

**Organic Reaction Mechanisms, Aromatic Chemistry  
and Naturally-Occurring Compounds**

<b>CREDIT HOURS</b>	<b>2.0</b>
<b>MINIMUM REQUIREMENTS</b>	<b>Pass in CHEM 113</b>
<b>REQUIRED FOR</b>	<b>CHEM 222 and CHEM 223</b>

## CHEM 123 – ORGANIC REACTION MECHANISMS

### PART 1 – ORGANIC REACTION MECHANISMS

#### COURSE OUTLINE

What are reaction mechanisms and how are they represented in organic chemistry? What do curly arrows represent and how should we use them? Why do alkenes and arenes react with electrophiles? Why do haloalkanes and carbonyls react with nucleophiles? Why do alkanes react only with free radicals?

What is the mechanism of nucleophilic substitution and which reactions proceed by this mechanism? What is the difference between first order and second order nucleophilic substitution? How can we detect which of the mechanisms is taking place and how can we explain the difference?

What is the mechanism of electrophilic addition and which reactions proceed by this mechanism? Why are isomeric products often formed and how can we predict which product is more likely?

What is the mechanism of free radical substitution and which reactions proceed by this mechanism? Why are so many reaction products possible and to what extent can we control which products are formed?

What are the different elimination mechanisms and which reactions proceed by which mechanism? Why are isomeric products often formed?

What is the mechanism of nucleophilic addition and which reactions proceed by this mechanism?

What is the mechanism of electrophilic substitution and which reactions proceed by this mechanism?

What is the mechanism of nucleophilic addition-elimination and which reactions proceed by this mechanism?

#### CONTENTS

1.	General principles of organic reaction mechanisms; curly arrows and movement of electron pairs, half-arrows and movement of single electrons; electrophiles, nucleophiles and free radicals
2.	Electrophilic addition: alkenes with HBr, Br <sub>2</sub> , H <sub>2</sub> SO <sub>4</sub> ; unsymmetrical alkenes and Markovnikoff products
3.	Nucleophilic substitution: haloalkanes with aqueous NaOH, KCN, ammonia and primary amines; SN1 and SN2
4.	Differences between SN1 and SN2; kinetics, optical activity, type of haloalkane; rate of reaction of different haloalkanes
5.	Elimination: different elimination mechanisms – haloalkanes with ethanolic KOH, acid-catalysed dehydration, different products
6.	Free radical substitution: alkanes with halogens; alternative products
7.	Nucleophilic addition: carbonyls with HCN and NaBH <sub>4</sub>
8.	Electrophilic substitution: alkylation, acylation, halogenation and nitration of benzene
9.	Nucleophilic addition-elimination and condensation reactions
10.	A comparative overview of reaction mechanisms in organic chemistry

## CHEM 123 – ORGANIC REACTION MECHANISMS

### PART 2 – AROMATIC AND NATURALLY OCCURRING COMPOUNDS

#### COURSE OUTLINE

What are the main features of aromatic compounds? What is the structure of benzene? What are the main reactions of benzene? What are the main derivatives of benzene and what are their properties?

What are phenols? What is their structure and what are their typical reactions? How do they compare to other alcohols?

What are heterocyclic aromatic compounds and what are their structures?

What are carbohydrates? What are the different types of carbohydrate and how do they differ? What is starch, how is it made and how is it broken down?

What are proteins? How are they made and how are they broken down? What are amino acids and what are their main chemical properties?

What are lipids and what is their structure? How are lipids made and how are they broken down? What are fatty acids?

What is soap? How does it work and how is it made? What are soapless detergents?

What is cellulose? What is its structure and what are its main properties?

#### CONTENTS

1.	Characteristics of Aromatic Compounds; structure of benzene and its main derivatives
2.	Chemical properties of benzene and its derivatives
3.	Structure and chemical properties of phenols
4.	Heterocyclic aromatic compounds
5.	Carbohydrates (monosaccharides, disaccharides, oligosaccharides and polysaccharides): structures and chemical properties
6.	Starch: structure, formation and chemical properties
7.	Proteins and amino acids: structure, formation and chemical properties
8.	Lipids (fats, oils waxes): structures, formation and chemical properties
9.	Soap and soapless detergents: structure, formation and chemical properties
10.	Cellulose: structure, formation and chemical properties

*items in italics are covered at senior secondary level*

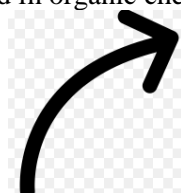
# PART 1 – ORGANIC REACTION MECHANISMS

## Lesson 1 – introduction to Mechanisms

### (a) Introduction to Mechanisms

#### (i) Electrophiles, nucleophiles and electron pairs

- A mechanism is a description of how a chemical reaction takes place; it describes the sequence of steps, which bonds are broken and formed and in what order
- In organic chemistry, mechanisms are most concerned with the movement of electrons onto, within, or away from an organic molecule:
  - In most reactions, electrons move in pairs; electron pairs can be lone pairs (ie on an atom) or bonding pairs (ie in between two atoms); covalent bonds can be both broken and formed by the movement of electron pairs; the movement of electron pairs is represented in organic chemistry with a double-headed curly arrow:



- When a pair of electrons moves out of a covalent bond, the bond breaks and the electron pair will move onto one of the atoms in the bond; the atom which receives the electron pair will become negatively charged and the atom which does not will become positively charged; usually the electrons move towards the more electronegative atom



This type of covalent bond breakage is known as **heterolytic fission**

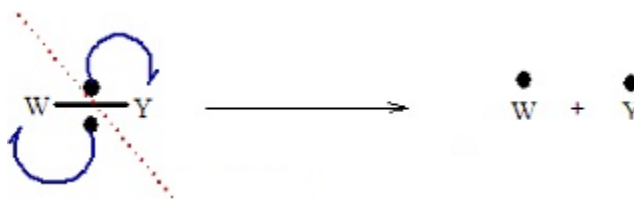
- Some organic molecules react by donating an electron pair to another species; this other species acts as an **electron pair acceptor** in the reaction; a species which can accept a pair of electrons from an organic molecule is called an **electrophile**
- Some organic molecules react by accepting an electron pair from another species; this other species acts as an **electron pair donor** in the reaction; a species which can donate a pair of electrons to an organic molecule is called a **nucleophile**
- Organic mechanisms which largely involve heterolytic fission and start with a species accepting an electron pair from an organic molecule are called electrophilic mechanisms
- Organic mechanisms which largely involve heterolytic fission and start with a species donating an electron pair to an organic molecule are called nucleophilic mechanisms

(ii) Free radicals and unpaired electrons

- In some reactions, electrons move individually; this is common when one of the species involved in the reaction has an unpaired electron; a species with an unpaired electron is known as a **free radical**; it is indicated by a single dot on the species with the unpaired electron; if the unpaired electrons from two different radicals move towards each other, a covalent bond is formed; the movement of single electrons is represented in organic chemistry with a single-headed curly arrow:



- When the individual electrons move out of a covalent bond in opposite directions, the covalent bond breaks and two different radicals are formed:



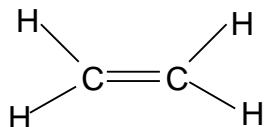
This type of covalent bond breakage is called **homolytic fission**

- Organic mechanisms which largely involve homolytic fission are known as free radical mechanisms

## Lesson 2 – Electrophilic Addition: Reactions of Alkenes

## (a) Electrophilic Addition

- Alkenes are hydrocarbons containing a carbon-carbon double bond; the atoms around the carbon-carbon double bond adopt a planar arrangement and the bond angle is  $120^\circ$



The presence of the C=C bond gives alkenes a number of chemical properties that are not seen in alkanes

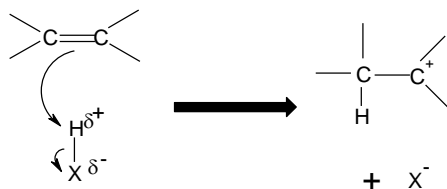
- Since the alkene contains  $\pi$ -bonds, it is possible to break the  $\pi$ -bond and form  $\pi$ -bonds with other species; as a result alkenes (unlike alkanes) are capable of undergoing addition reactions; addition reactions are generally faster than substitution reactions since only weak  $\pi$ -bonds are broken, rather than stronger  $\sigma$ -bonds
- The  $\pi$ -bond in an alkene is an area of **high electron density**; it can thus attract **electrophiles** and undergo heterolytic fission; possible electrophiles are hydrogen halides (H-Cl, H-Br and H-I) and halogens (Br-Br, Cl-Cl and I-I); alkenes also undergo an electrophilic addition reaction with  $\text{H}_2\text{SO}_4$

Alkenes are therefore able to undergo **electrophilic addition** reactions

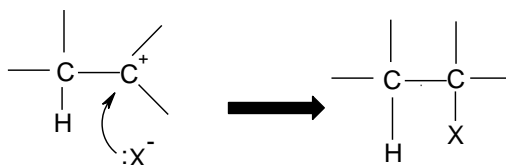
## (b) with hydrogen halides

- Eg  $\text{CH}_2=\text{CH}_2 + \text{H-Br} \rightarrow \text{CH}_3\text{CH}_2\text{Br}$

The H in the H-X bond has a positive dipole and is attacked by the pair of electrons on the C=C bond, which undergoes heterolytic fission:



The halide ion then attacks the carbocation to form a haloalkane:



This reaction takes place readily at room temperature

## CHEM 123 – ORGANIC REACTION MECHANISMS

### (c) with halogens

- Eg  $\text{CH}_2=\text{CH}_2 + \text{Br}_2 \rightarrow \text{CH}_2\text{BrCH}_2\text{Br}$

The Br-Br molecule is non-polar but in the presence of alkenes the electrons move to one side of the molecule and it acquires a temporary dipole (in other words a dipole is induced by the alkene). The  $\delta^+$  Br is then attacked by the alkene:

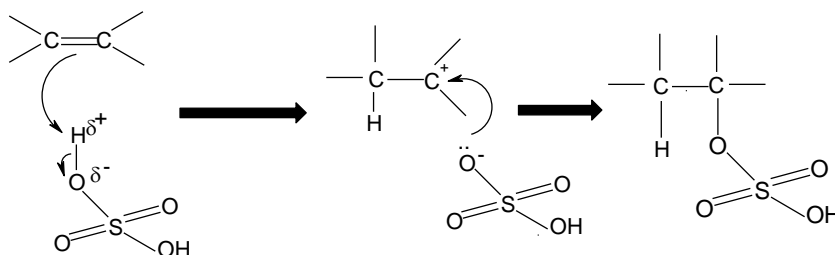


A dibromoalkane is formed; the reaction takes place readily at room temperature

### (d) with $\text{H}_2\text{SO}_4$

- Eg  $\text{CH}_2=\text{CH}_2 + \text{H}_2\text{SO}_4 \rightarrow \text{CH}_3\text{CH}_2\text{HSO}_4$

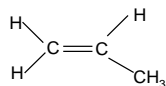
Alkenes will undergo an electrophilic addition reaction with cold concentrated sulphuric acid (the H-O bond is polar)



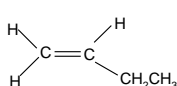
### (e) unsymmetrical alkenes

- Unsymmetrical alkenes are those in which the two carbon atoms in the double bond are not attached to the same groups:

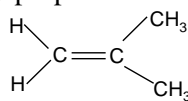
propene



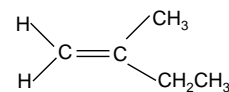
but-1-ene



2-methylpropene



methylbut-1-ene

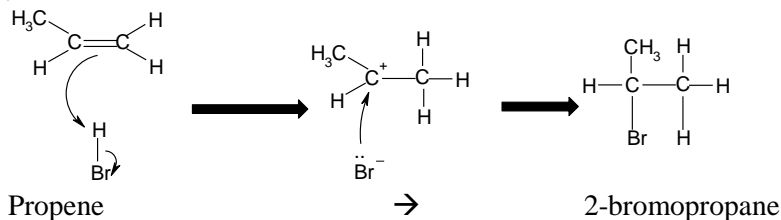


## CHEM 123 – ORGANIC REACTION MECHANISMS

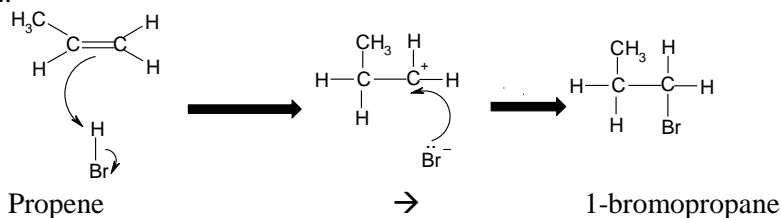
- If unsymmetrical alkenes react with unsymmetrical electrophiles such as H-X or H<sub>2</sub>SO<sub>4</sub>, there are two possible products:

Eg propene with hydrogen bromide

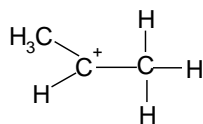
Route 1:



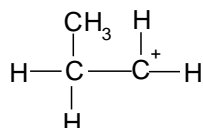
Route 2:



- The two products are not formed in equal quantities; the likelihood of one product being formed over the other depends on the stability of the **carbocation intermediate**
- In route 1, the intermediate is a **secondary carbocation**, as the carbon holding the positive charge is attached to **two** other carbon atoms:



- In route 2, the intermediate is a **primary carbocation**, as the carbon holding the positive charge is attached to **one** other carbon atom:



- Secondary carbocations are more stable than primary carbocations; tertiary carbocations are even more stable than secondary cations; this is because the alkyl groups (CH<sub>3</sub>-, C<sub>2</sub>H<sub>5</sub>-) are “electron pushing” and push electron density onto the C<sup>+</sup>, which stabilises it; the more alkyl groups on the carbocation, the more stable it is
  - Therefore the product of route 1 (2-bromopropane) is a more likely product than the product of route 2 (1-bromopropane); thus 2-bromopropane will be the **major** product and 1-bromopropane will be the **minor** product
  - In general, the more stable carbocation will be the one which is more highly substituted; the more electronegative part of the electrophile is thus more likely to attach itself to the more highly substituted carbon atom; this is known as **Markownikoff's rule**; the major product of the addition reaction is known as the Markownikoff product; the minor product of the addition reaction is known as the anti-Markownikoff product
- Symmetrical alkenes only give one product when electrophiles are added; unsymmetrical alkenes only give one product if the electrophile is symmetrical; thus two products are only obtained when both the alkene and the electrophile are unsymmetrical

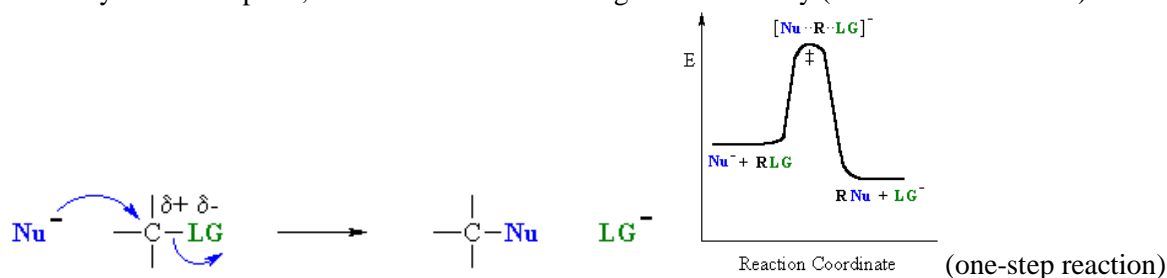


## Lesson 3 – Nucleophilic Substitution: Reactions of Haloalkanes I

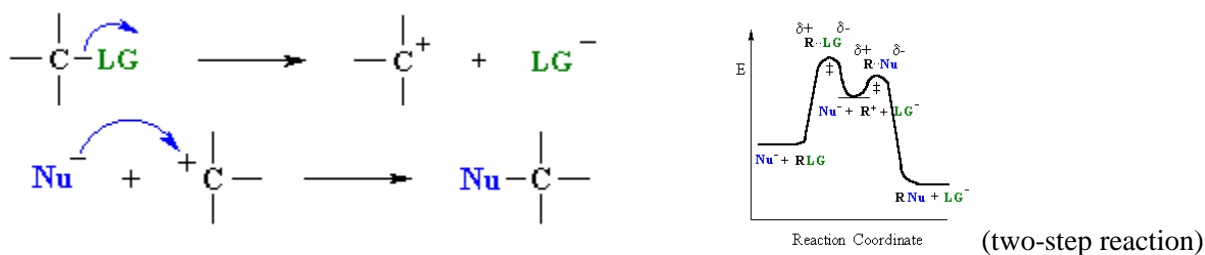
## (a) Nucleophilic Substitution

- The C-X bond is polar, and the carbon is  $\delta^+$ ; therefore haloalkanes can react with **nucleophiles**; the nucleophile generally replaces the halogen atom on the molecule; thus haloalkanes can undergo **nucleophilic substitution** reactions
- Nucleophiles which react with haloalkanes include  $\text{OH}^-$  ions,  $\text{CN}^-$  ions and  $\text{NH}_3$
- Nucleophilic substitution mechanisms can proceed via two different routes:

(i) Attack by the nucleophile, with the halide ion leaving simultaneously (this is known as  $\text{S}_{\text{N}}2$ )



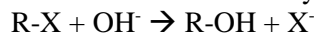
(ii) Spontaneous heterolytic fission of the C-X bond to form a carbocation, followed by attack of the carbocation by the nucleophile (this is known as  $\text{S}_{\text{N}}1$ )



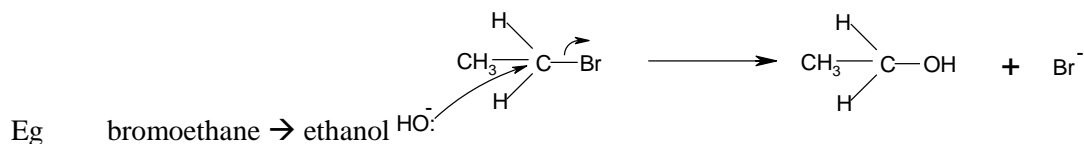
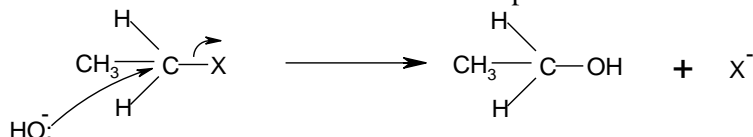
- The relative tendency of a haloalkane to undergo nucleophilic substitution by the  $\text{S}_{\text{N}}1$  or  $\text{S}_{\text{N}}2$  mechanism depends on:
  - the relative stability of the carbocation intermediate; the more stable the carbocation, the greater the tendency to favour  $\text{S}_{\text{N}}1$ ; haloalkanes which form tertiary carbocations are the most likely to proceed via  $\text{S}_{\text{N}}1$ , followed by haloalkanes which form secondary carbocations and haloalkanes which form primary carbocations
  - the ease with which the C atom can be attacked by the nucleophile; if the C atom is surrounded by lots of H atoms or other small atoms, there is more space for attack and  $\text{S}_{\text{N}}2$  is more likely; the less space there is for nucleophilic attack, the less likely  $\text{S}_{\text{N}}2$  becomes
- Haloalkanes which form primary carbocations are called primary haloalkanes; they are most likely to react via the  $\text{S}_{\text{N}}2$  mechanism (eg bromoethane, 1-bromopropane); haloalkanes which form secondary carbocations are called secondary haloalkanes (eg 2-bromopropane) and haloalkanes which form tertiary carbocations are called tertiary haloalkanes (eg 2-methyl, 2-bromopropane); tertiary haloalkanes are most likely to proceed via the  $\text{S}_{\text{N}}1$  mechanism

**(b) Reaction with hydroxide ions**

- Haloalkanes react with hydroxide ions when boiled under reflux with aqueous NaOH or aqueous KOH:



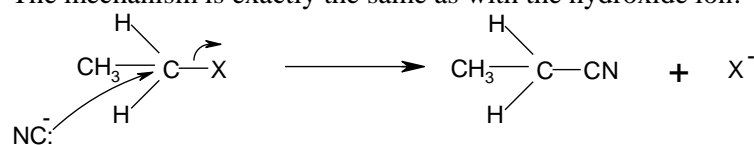
In the SN2 mechanism, the nucleophile (ie the hydroxide ion) attacks the  $\delta^+$  carbon atom from behind, forcing the X atom to leave as the halide ion. It is a one-step mechanism:



**(c) Reaction with cyanide ions**

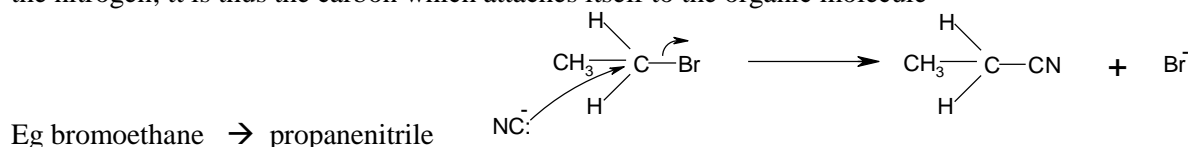
- Cyanide ions are nucleophiles and react with haloalkanes by nucleophilic substitution to give nitriles; the haloalkane should be boiled under reflux with KCN in aqueous ethanol:  $R-X + CN^- \rightarrow R-CN + X^-$

The mechanism is exactly the same as with the hydroxide ion:



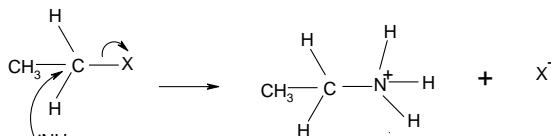
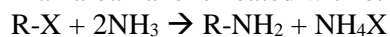
(SN2 mechanism)

- Note that the  $CN^-$  ion has the following structure:  $:\overset{-}{C} \equiv N$ ; thus the lone pair of electrons is on the carbon, not the nitrogen; it is thus the carbon which attaches itself to the organic molecule



**(d) Reaction with ammonia**

- If a haloalkane is heated with ethanolic ammonia in a sealed tube, a primary amine is formed:

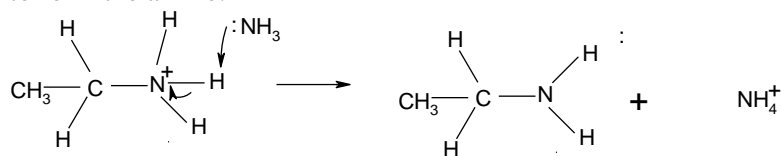


The mechanism is again nucleophilic substitution:

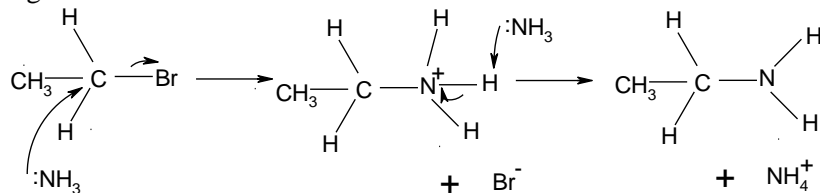
(SN2)

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- The initial substitution step forms the intermediate  $\text{R-NH}_3^+$  ion. The H is removed by another ammonia molecule to form the amine:



Eg bromoethane  $\rightarrow$  aminoethane



It is possible for the amine product to attack the haloalkane in the same way as ammonia does. This would make a series of alternative products called secondary amines. To avoid this, it is necessary to use **excess** ammonia

### (e) Distinguishing experimentally between $\text{S}_\text{N}1$ and $\text{S}_\text{N}2$

#### (i) Using kinetics

- $\text{S}_\text{N}2$  reactions require a collision between the nucleophile and the organic molecule; the rate of these reactions are therefore proportional to the concentration of the nucleophile and the organic molecule; in other words, the reactions show 2<sup>nd</sup> order kinetics ( $\text{S}_\text{N}2$  = substitution, nucleophilic, 2<sup>nd</sup> order);  $\text{S}_\text{N}1$  reactions require only the decomposition of the organic molecule; the rate of these reactions are therefore proportional to the concentration of the organic molecule only; in other words, the reactions show 1<sup>st</sup> order kinetics ( $\text{S}_\text{N}1$  = substitution, nucleophilic, 1<sup>st</sup> order)

#### (ii) Using optical activity

- If the organic molecule is chiral and a single enantiomer, then the product will also be a single enantiomer if the reaction proceeds via  $\text{S}_\text{N}2$ , because the asymmetry remains throughout the mechanism; if the reaction proceeds via  $\text{S}_\text{N}1$ , however, then the asymmetry is lost when the (planar) carbocation intermediate is formed; the carbocation intermediate can be attacked by the nucleophile from both sides with equal probability, producing a racemic mixture of the two optical isomers

### (f) Rates of reaction of haloalkanes with nucleophiles

- Nucleophilic substitution involves the heterolytic fission of the C-X bond; the rate of reaction depends on how quickly this bond can be broken; the C-Cl bond is stronger than the C-Br bond which is stronger than the C-I bond; and hence iodoalkanes react more rapidly than bromoalkanes, which react more rapidly than chloroalkanes
- This happens despite the fact that C-I bonds are less polar than C-Br and C-Cl bonds, which means that the nucleophile is less attracted to the C atom in iodoalkanes; the bond strength outweighs the difference in polarity

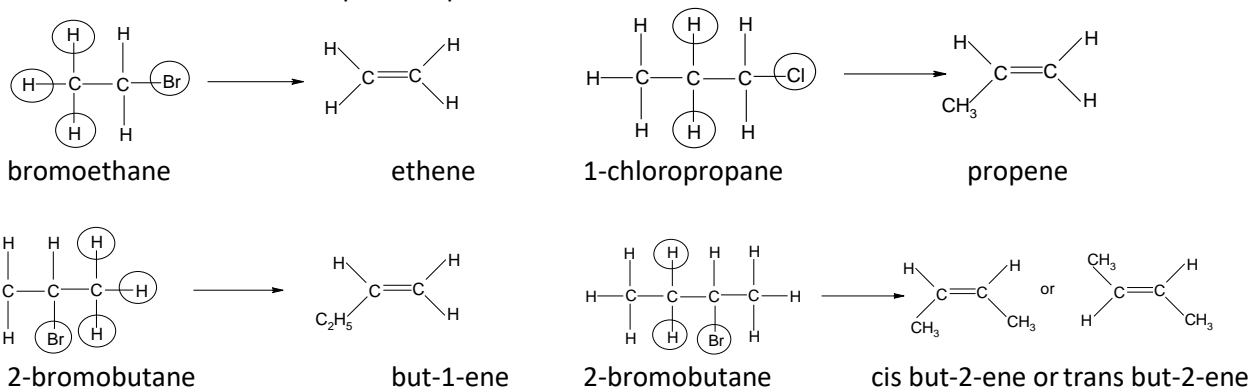
Lesson 4 – Elimination Reactions: Reactions of Haloalkanes II and Reactions of Alcohols

a) Elimination of hydrogen halides from haloalkanes

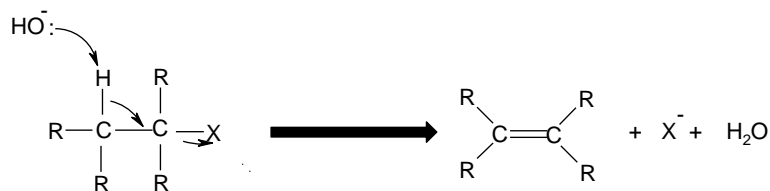
- If haloalkanes are boiled with an ethanolic solution of KOH instead of with an aqueous solution, they will undergo **elimination** of an HX molecule to give an **alkene**:



- NaOH is not used since it is only sparingly soluble in ethanol
- this reaction works best if distillation apparatus is used since the alkene product is volatile
- the hydrogen is always lost from a carbon atom adjacent to the carbon atom attached to the halogen; in the diagram below, all the hydrogen atoms which could be removed have been circled; sometimes this can result in more than one possible product:



- The mechanism of this reaction involves the hydroxide ion attacking a hydrogen atom on the haloalkane:



- Note that the hydroxide ion is behaving as a **base**, not a nucleophile  
Eg 1-chloropropane  $\rightarrow$  propene

- As the hydroxide ion can react with haloalkanes in two ways (nucleophilic substitution or elimination), it is likely that these two reactions are likely to be in competition with each other; it is not possible to ensure that one reaction happens exclusively, the conditions can be adjusted to favour one type of reaction over the other:

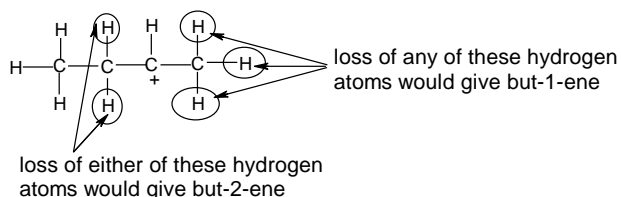
Conditions	Nucleophilic substitution (to make alcohols)	Elimination (to make alkenes)
temperature	Warm	boiling
solvent	water	ethanol
apparatus	Reflux	distillation

- The elimination reaction does NOT proceed via a carbocation intermediate, so it is not possible to predict which of the possible products will be formed in greater quantities
- The reaction does involve the breaking of the C-X bond, so it likely that iodoalkanes will react faster than bromoalkanes, which will in turn react faster than chloroalkanes

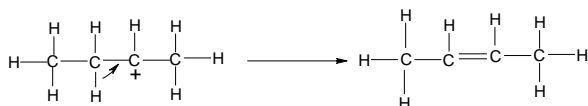
## CHEM 123 – ORGANIC REACTION MECHANISMS

### b) Elimination of water from alcohols

- Alcohols can lose water to form alkenes:  $R_1R_2CHCR_3R_4OH \rightarrow R_1R_2C=CR_3R_4 + H_2O$ ; this reaction is also known as dehydration
- The H which is lost comes from a carbon atom which is adjacent to the carbon atom attached to the OH group which is lost; in some cases, this can lead to more than one product:  
Eg when butan-2-ol undergoes elimination, two different products can be formed depending on which H atom is lost:



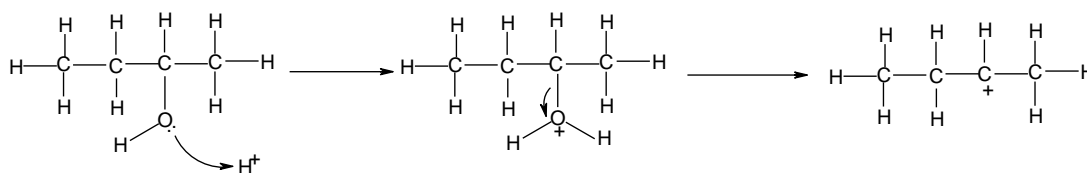
Butan-2-ol  $\rightarrow$  but-2-ene:



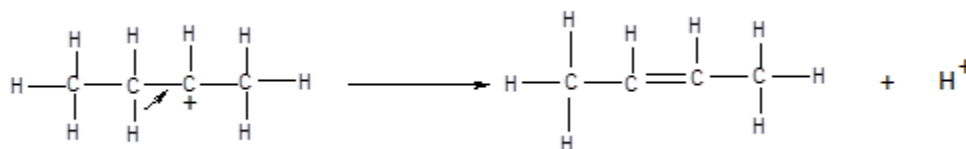
Butan-2-ol  $\rightarrow$  but-1-ene:



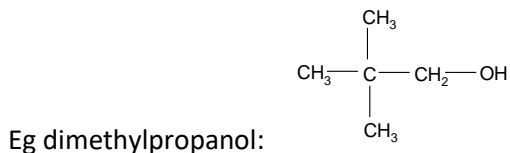
- The OH group on the alcohol accepts a proton, and water is then lost to form a carbocation:



- One of the C atoms next to the C<sup>+</sup> then loses its hydrogen, with the electron pair from the C-H bond being used to form the C=C bond:



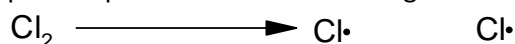
- The H<sup>+</sup> is regenerated and therefore acts as a catalyst; concentrated H<sub>2</sub>SO<sub>4</sub> or concentrated H<sub>3</sub>PO<sub>4</sub> is usually used as the reagent
- NB Alcohols which have no H atoms on the C atom adjacent to the OH group cannot undergo elimination:



## Lesson 5 – Free Radical Substitution: Reactions of Alkanes

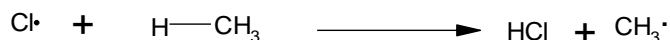
- Alkanes contain C-C and C-H bonds only; these bonds are not significantly polar and the molecule does not have areas of high electron density; as a result alkanes do not react readily with either nucleophiles or electrophiles; alkanes therefore react mainly with free radicals
- Alkanes are also saturated so cannot readily undergo addition reactions; they therefore tend to undergo substitution reactions
- Alkanes can be converted into haloalkanes in a **free radical substitution** reaction:  
Eg  $\text{CH}_4 + \text{Cl}_2 \rightarrow \text{CH}_3\text{Cl} + \text{HCl}$

- In this reaction the free radical which starts the reaction is a chlorine atom, formed when a chlorine molecule breaks up in the presence of ultra-violet light:



The homolytic fission of a covalent bond to produce free radicals is known as **initiation**; the presence of UV light is usually necessary for the homolytic fission of covalent bonds

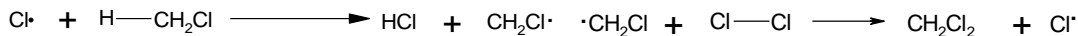
- The radicals will soon collide with an alkane molecule; they will form a covalent bond with one of the H atoms, resulting in an alkyl radical:



The alkyl radical will soon collide with another molecule; most likely a  $\text{Cl}_2$  molecule; this will result in the formation of chloromethane and a Cl radical:



- These steps are known as **propagation** steps; propagation is the reaction of a free radical with a molecule to produce another free radical
- Note that the Cl radicals are recycled during these two propagation steps; the Cl effectively acts as a catalyst and only a small quantity of radicals need to be created during the initiation step to start the reaction; most of the chlorine remains as  $\text{Cl}_2$
- These propagation steps will continue until no more  $\text{CH}_4$  or  $\text{Cl}_2$  remains in the reaction mixture; as the reaction progresses, it is likely that the Cl and  $\text{CH}_3$  radicals will also collide with some of the products of the reaction, such as  $\text{CH}_3\text{Cl}$ ; this in turn will create other radicals such as  $\text{CH}_2\text{Cl}$  which will in turn collide with other molecules to form different products

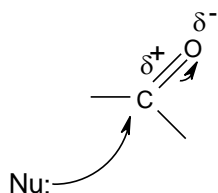


- With larger alkanes, the Cl radicals can collide with any part of the hydrocarbon chain, substituting the Cl into a variety of different positions on the chain
- It is difficult to control the products of free radical substitution reactions, although the extent of further substitution can be reduced by using excess chlorine, or increased by using excess methane
- Eventually some of the radicals will collide with each other to form a single molecule; this is known as termination:
 
$$\text{Cl}\cdot + \text{Cl}\cdot \longrightarrow \text{Cl}_2$$
  - Other termination steps are also possible, such as the combination of alkyl radicals to form a larger alkane
 
$$\cdot\text{CH}_3 + \cdot\text{CH}_3 \longrightarrow \text{CH}_3\text{CH}_3$$
- Free radical substitution reactions therefore tend to produce a large variety of products

Lesson 6 – Nucleophilic Addition (carbonyls) and Nucleophilic Addition-Elimination (acyl chlorides)

(i) Nucleophilic Addition

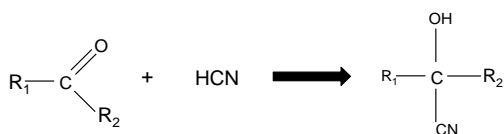
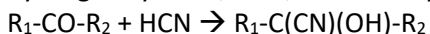
- Carbonyls are unsaturated and can thus undergo addition reactions; the C=O bond is polar so the carbon is a positive centre; carbonyls can react with nucleophiles



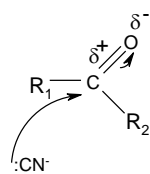
Carbonyls therefore tend to react via **nucleophilic addition** mechanisms

- Example 1: Addition of HCN to make hydroxynitriles:

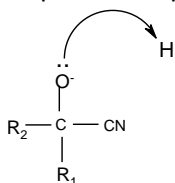
- hydrogen cyanide, HCN, is a nucleophile; it reacts with carbonyls as follows:



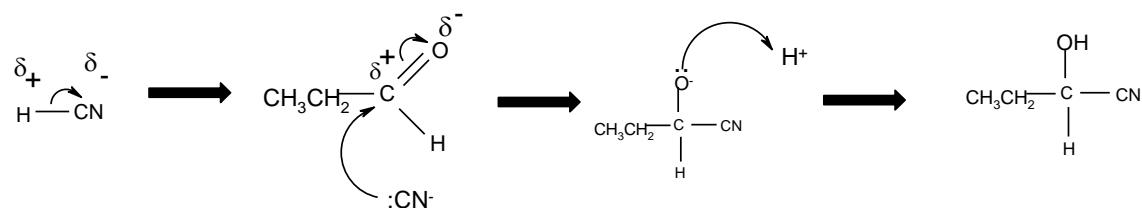
- Step 1: the weak acid HCN dissociates:  $HCN \rightarrow H^+ + CN^-$ , creating the nucleophile  $CN^-$
- Step 2: the nucleophile attacks the C in the C=O and the  $\pi$ -bond breaks heterolytically:



- Step 3: the  $O^-$  picks up the  $H^+$  ion to make the -OH group:



- Eg propanal + HCN  $\rightarrow$  2-hydroxybutanenitrile



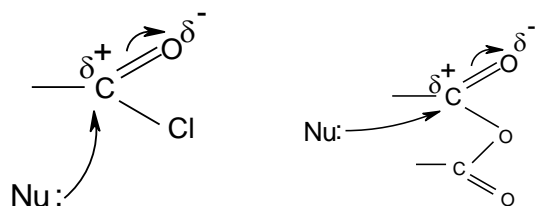
- HCN is a very poisonous gas; it is not safe to carry out this reaction in the laboratory; HCN is made in situ by mixing KCN and HCl:  $KCN(s) + HCl(aq) \rightarrow HCN(g) + KCl(aq)$ ; KCN is also very poisonous but it is safer to store as it is a solid



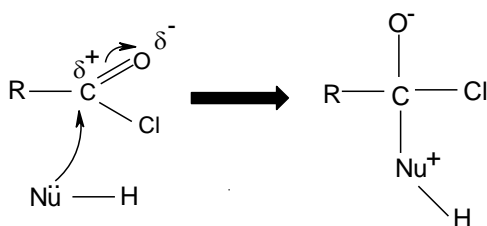


## CHEM 123 – ORGANIC REACTION MECHANISMS

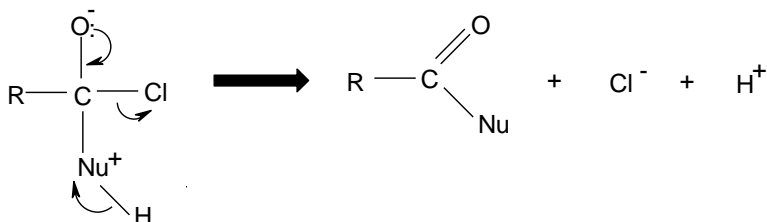
- In both functional groups, the carbon atom is attached to two electronegative atoms and so is very  $\delta^{+ve}$  and attracts nucleophiles readily:



- Acyl chlorides and acid anhydrides react by a mechanism called nucleophilic addition-elimination:
  - Step 1: the nucleophile attacks and the  $\pi$ -bond is broken (addition)

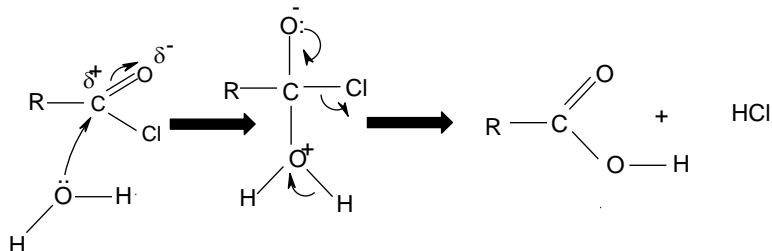


- Step 2: The C-Cl bond then breaks, the H on the nucleophile is lost and the C=O  $\pi$ -bond is reformed:

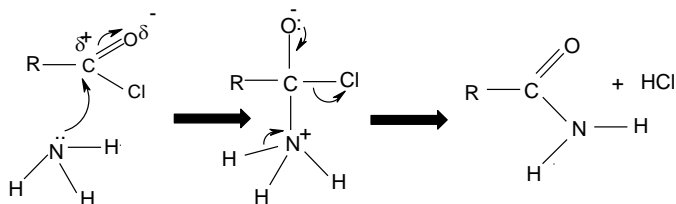


- Step 3: the chloride ion, or another nucleophile may combine with the free proton.

- one possible nucleophile is water:  $R\text{-COCl} + \text{H}_2\text{O} \rightarrow R\text{-COOH} + \text{HCl}$

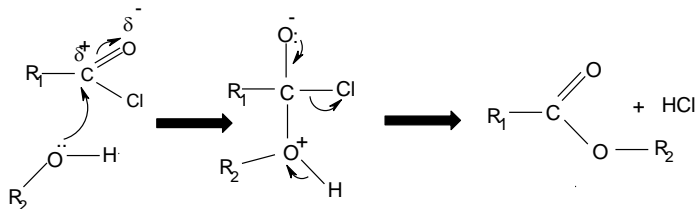


- Another possible nucleophile is  $\text{NH}_3$ :  $R\text{-COCl} + \text{NH}_3 \rightarrow R\text{-CONH}_2 + \text{HCl}$  or  $R\text{-COCl} + 2\text{NH}_3 \rightarrow R\text{-CONH}_2 + \text{NH}_4\text{Cl}$

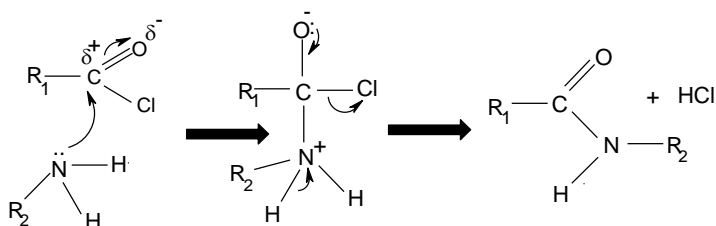


## CHEM 123 – ORGANIC REACTION MECHANISMS

- Alcohols can also act as nucleophiles:  $R_1\text{-COCl} + R_2\text{-OH} \rightarrow R_1\text{-COOR}_2 + \text{HCl}$ ; this is how esters are made



- Amines can also act as nucleophiles:  $R_1\text{-COCl} + R_2\text{-NH}_2 \rightarrow R_1\text{-CONHR}_2 + \text{HCl}$  this is how amides are made



- Acid anhydrides react with all four nucleophiles in the same way; the second product is a carboxylic acid instead of HCl
- Carboxylic acids also form esters and amides via nucleophilic addition-elimination; an acid catalyst is often required to help the  $\text{-OH}$  group leave the molecule
- Acid chlorides react the most quickly, followed by acid anhydrides; carboxylic acids react the most slowly; commercially, acid anhydrides are used rather than acid chlorides as they are cheaper, safer to use and avoid the toxic gas HCl; carboxylic acid reactions are common in Biochemistry

### Questions

**5.3** Write equations and give the mechanism for the following reactions:

- butanone with  $\text{NaBH}_4$
- propanal with HCN
- propanoyl chloride with ammonia
- methanoyl chloride with ethylamine

- 5.4**
- Explain why the product of the reaction in 5.3 (a) does not show optical activity.
  - Write an equation for the reaction of butanoic anhydride with propan-2-ol.
  - Write an equation for the reaction of 2-hydroxybenzoic acid with ethanoic anhydride.
  - Explain why ethanoic anhydride is preferred to ethanoyl chloride for commercial preparations of esters.
  - Explain why the reaction in 5.3 (b) works fastest at a pH between 3 and 5

## CHEM 123 – ORGANIC REACTION MECHANISMS

- 1.1** Explain the meaning of the following terms:
- homolytic fission
  - heterolytic fission
  - Electrophile
  - Nucleophile
  - free radical
- 2.1**
- Why do alkenes react with electrophiles?
  - Explain how bromine can behave as an electrophile
  - Draw the mechanism to show how ethene reacts with bromine
  - Draw the mechanism to show how but-2-ene reacts with HBr
  - Draw the mechanism to show how ethene reacts with concentrated sulphuric acid
  - Draw the structure of the product formed when propene reacts with ICl; give reasons for your choice of product.
- 2.2** The following reactions give two products in unequal amounts; in each case, identify the two products, state which is the major product, explain why it is the major product and give the mechanism for its formation:
- but-1-ene with HBr
  - methylpropene with concentrated sulphuric acid
- 3.1**
- Why do haloalkanes react with nucleophiles?
  - Draw the mechanism to show how bromoethane reacts with hydroxide ions
  - Draw the mechanism to show how 2-methyl, 2-chloropropane reacts with cyanide ions
  - Draw the mechanism to show how 2-iodopropane reacts with ammonia (use the SN2 mechanism)
- 3.2** The rate of the reaction between hydroxide ions and a single enantiomer of 2-iodobutane is found to depend on the concentration of 2-iodobutane but not the concentration of hydroxide ions
- Which mechanism is this reaction taking place by? Explain your answer and outline the mechanism for the reaction
  - Explain how optical activity will change during this reaction.
- 3.3** The rate of the reaction between hydroxide ions and a single enantiomer of 2-chlorobutane is found to depend on the concentration of 2-chlorobutane and the concentration of hydroxide ions
- Which mechanism is this reaction taking place by? Explain your answer and outline the mechanism for the reaction
  - Explain how optical activity will change during this reaction.
  - Suggest a possible reason for why 2-chlorobutane and 2-iodobutane react via different mechanisms
  - Explain which of the reactions will be faster
- 4.1** State two types of reaction that could take place when 1-chlorobutane reacts with potassium hydroxide. Give the mechanism for each reaction and state the role of the hydroxide ion in each case. Suggest conditions which would favour each type of reaction.
- 4.2** State the possible products that could be formed when the following haloalkanes undergo elimination. If more than one product is formed, identify them both and explain how each is formed.
- 1-bromobutane
  - 2-bromobutane
  - 2-bromobutane
  - 2-bromomethylpropane

## CHEM 123 – ORGANIC REACTION MECHANISMS

- 4.3** Identify the organic product or products formed by the dehydration of
- (a) Ethanol
  - (b) butan-1-ol
  - (c) butan-2-ol
  - (d) dimethylpropan-1-ol
- 4.4** Identify three alcohols with the formula  $C_5H_{12}O$  which can give two different alkenes when dehydrated. Identify the alkene products in each case and give the mechanism for the formation of any two of the products.
- 5.1**
- (a) Using full displayed formulae, show the four steps involved in the reaction of **ethane** with chlorine to give chloroethane. State the type of reaction involved in each step.
  - (b) Show by means of additional steps how this mechanism can account for the formation of:
    - (i) 1,1-dichloroethane
    - (ii) butane
- 5.2**
- (a) Explain why alkanes do not react readily with electrophiles or nucleophiles
  - (b) Draw all of the different products with the formula  $C_6H_{13}Cl$  could be formed by the reaction of hexane with chlorine.
  - (c) Draw all of the different products with the formula  $C_6H_{12}Cl_2$  could be formed by the reaction of hexane with chlorine.
  - (d) Draw any three compounds with the formula  $C_{12}H_{26}$  which could be formed by the reaction of hexane with chlorine; in each case, write an equation to show how each product is formed.
  - (e) How many products with the formula  $C_6H_{13}Cl$  could be formed by the reaction of 2-methylpentane with chlorine?

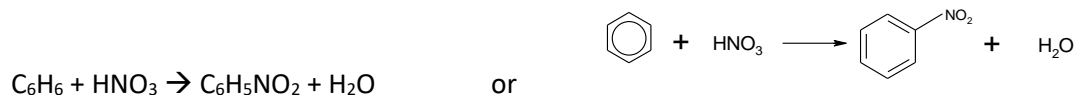
## CHEM 123 – ORGANIC REACTION MECHANISMS

### Lesson 7 – Electrophilic Substitution (Arenes)

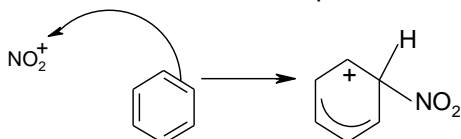
- The delocalization of the electrons in the benzene ring has a significant effect on the stability of the molecule; benzene might be expected to behave like alkenes; i.e. react readily with bromine and hydrogen to undergo addition reactions, but this is not the case; benzene will not decolorise bromine water and does not readily undergo any other addition reactions, as reactions which break up the delocalised system are not favoured; benzene thus tends to undergo substitution, rather than addition reactions
- The delocalized electrons constitute an electron-rich area, and they are thus susceptible to attack by electrophiles; benzene therefore tends to undergo **electrophilic substitution**
- There are three important electrophilic substitution reactions of benzene, all of which follow the same mechanism:

#### a) nitration

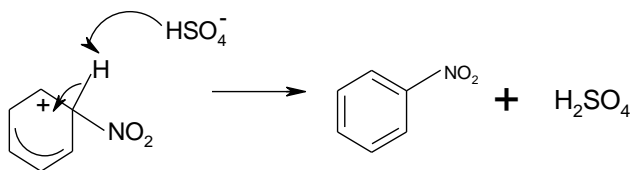
- Benzene reacts with a 50:50 mixture of concentrated nitric and sulphuric acid, under reflux at 50-55°C, to form nitrobenzene:



- **Step 1:** Nitric acid is a weaker acid than sulphuric acid, and acts as a base as the electrophile  $\text{NO}_2^+$  is formed:  
 $\text{H}_2\text{SO}_4 + \text{HNO}_3 \rightarrow \text{H}_2\text{NO}_3^+ + \text{HSO}_4^-$ ;  $\text{H}_2\text{NO}_3^+ \rightarrow \text{H}_2\text{O} + \text{NO}_2^+$
- **Step 2:** The  $\text{NO}_2^+$  is the electrophile and attacks the delocalised ring, breaking it temporarily:



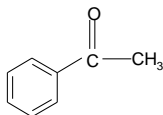
- **Step 3:** The delocalised system then reforms itself by pulling in the electrons from the C-H bond, and the  $\text{H}^+$  recombines with the  $\text{HSO}_4^-$  to form  $\text{H}_2\text{SO}_4$ :



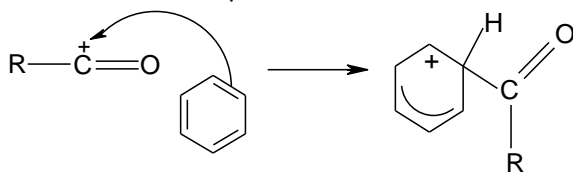
- The sulphuric acid behaves as a catalyst

b) acylation

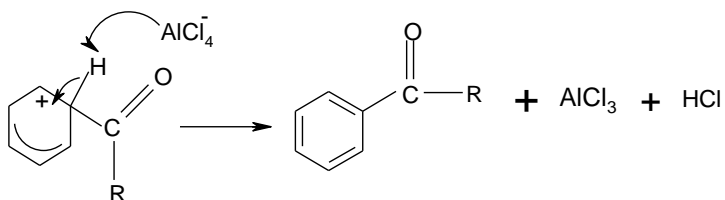
- Benzene reacts with acyl chlorides in the presence of anhydrous  $\text{AlCl}_3$  (or  $\text{FeBr}_3$ ) under reflux at  $50^\circ\text{C}$  to give a phenylketone; this reaction is known as a Friedel-Crafts reaction:  $\text{C}_6\text{H}_6 + \text{R-COCl} \rightarrow \text{C}_6\text{H}_5\text{COR} + \text{HCl}$ ; If ethanoyl chloride is used for example, then the product is phenylethanone:



- **Step 1:** The  $\text{AlCl}_3$  (or  $\text{FeBr}_3$ ) accepts a  $\text{Cl}^-$  from the acyl chloride to form the electrophile  $\text{R-CO}^+$ :  
 $\text{R-CO-Cl} + \text{AlCl}_3 \rightarrow \text{R-CO}^+ + \text{AlCl}_4^-$
- **Step 2:** The electrophile attacks the delocalised ring, breaking it temporarily:



- **Step 3:** The delocalised ring re-forms by taking the electrons from the C-H bond and the  $\text{H}^+$  reacts with  $\text{AlCl}_4^-$  to produce  $\text{HCl}$  gas and regenerate  $\text{AlCl}_3$ :

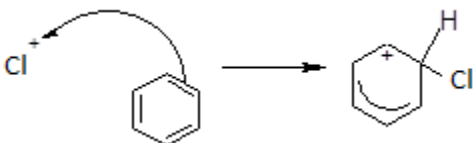


- The  $\text{AlCl}_3$  is a catalyst

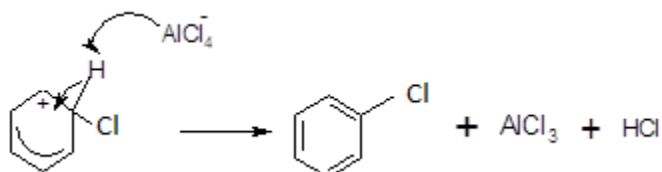
c) halogenation

- Benzene reacts with halogens in the presence of anhydrous  $\text{AlCl}_3$  (or  $\text{FeBr}_3$ ) under reflux at  $50^\circ\text{C}$  to give a halobenzene; this reaction is another example of a Friedel-Crafts reaction:  $\text{C}_6\text{H}_6 + \text{X}_2 \rightarrow \text{C}_6\text{H}_5\text{X} + \text{HX}$ ; the  $\text{AlCl}_3$  again acts as a catalyst

- **Step 1:** The  $\text{AlCl}_3$  accepts a  $\text{X}^-$  from the halogen to form the electrophile  $\text{X}^+$ :  
 $\text{Cl}_2 + \text{AlCl}_3 \rightarrow \text{Cl}^+ + \text{AlCl}_4^-$
- **Step 2:** The electrophile attacks the delocalised ring, breaking it temporarily:

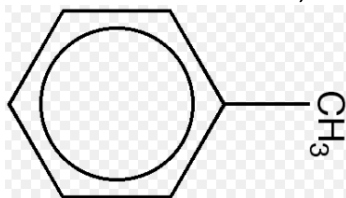


- **Step 3:** The delocalised ring re-forms by taking the electrons from the C-H bond and the  $\text{H}^+$  reacts with  $\text{AlCl}_4^-$  to produce  $\text{HCl}$  gas and regenerate  $\text{AlCl}_3$ :

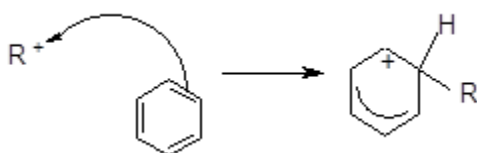


d) alkylation

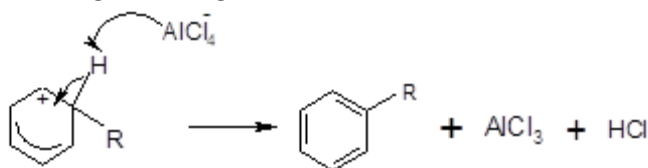
- Benzene reacts with haloalkanes in the presence of anhydrous  $\text{AlCl}_3$  (or  $\text{FeBr}_3$ ) under reflux at  $50^\circ\text{C}$  to give an alkylbenzene; this reaction is another example of a Friedel-Crafts reaction:  $\text{C}_6\text{H}_6 + \text{R-X} \rightarrow \text{C}_6\text{H}_5\text{R} + \text{HX}$ ; the  $\text{AlCl}_3$  again acts as a catalyst; if chloromethane is used as the haloalkane, the product is methylbenzene:



- **Step 1:** The  $\text{AlCl}_3$  (or  $\text{FeBr}_3$ ) accepts a  $\text{Cl}^-$  from the haloalkane to form the electrophile  $\text{R}^+$ :  
 $\text{R-Cl} + \text{AlCl}_3 \rightarrow \text{R}^+ + \text{AlCl}_4^-$
- **Step 2:** The electrophile attacks the delocalised ring, breaking it temporarily:



- **Step 3:** The delocalised ring re-forms by taking the electrons from the C-H bond and the  $\text{H}^+$  reacts with  $\text{AlCl}_4^-$  to produce  $\text{HCl}$  gas and regenerate  $\text{AlCl}_3$ :

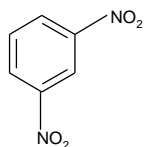


- The same reaction can be achieved by reacting benzene with an alkene together with a hydrogen halide in the presence of  $\text{AlCl}_3$ : eg  $\text{C}_6\text{H}_6 + \text{C}_2\text{H}_4 \rightarrow \text{C}_6\text{H}_5\text{C}_2\text{H}_5$ 
  - step 1: the alkene reacts with the hydrogen halide to form a carbocation, identical to the first step in electrophilic addition: eg  $\text{C}_2\text{H}_4 + \text{HCl} \rightarrow \text{C}_2\text{H}_5^+ + \text{Cl}^-$
  - step 2: the  $\text{AlCl}_3$  accepts the  $\text{Cl}^-$ , preventing the  $\text{Cl}^-$  from joining with the carbocation:  $\text{AlCl}_3 + \text{Cl}^- \rightarrow \text{AlCl}_4^-$
  - step 3: as a result the carbocation can attack the benzene ring: eg  $\text{C}_6\text{H}_6 + \text{C}_2\text{H}_5^+ \rightarrow \text{C}_6\text{H}_6\text{C}_2\text{H}_5^+$
  - step 4: the  $\text{H}^+$  comes off the benzene ring and reacts with the  $\text{AlCl}_4^-$ , restoring the delocalised system and re-forming  $\text{AlCl}_3$  and  $\text{HCl}$   
 $\text{C}_6\text{H}_6\text{C}_2\text{H}_5^+ + \text{AlCl}_4^- \rightarrow \text{C}_6\text{H}_5\text{C}_2\text{H}_5 + \text{AlCl}_3 + \text{HCl}$
  - the  $\text{AlCl}_3$  and the  $\text{HCl}$  are both behaving as catalysts in this reaction

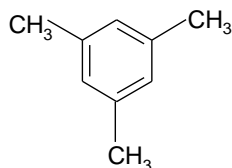
e) further substitution

It is essential that the reaction temperature not be allowed to rise above  $55^\circ\text{C}$  during these reactions. This is because otherwise further substitution will occur:

Eg 1,3 – dinitrobenzene



Eg 1,3,5 - trimethylbenzene



## CHEM 123 – ORGANIC REACTION MECHANISMS

- 6.1** Write equations and give the mechanism for the following reactions:
- butanone with  $\text{NaBH}_4$
  - propanal with  $\text{HCN}$
  - propanoyl chloride with ammonia
  - methanoyl chloride with ethylamine
  - Methanoyl chloride with methanol
- 6.2**
- Explain why the product of the reaction in 6.1 (a) does not show optical activity.
  - Write an equation for the reaction of butanoic anhydride with propan-2-ol.
  - Write an equation for the reaction of 2-hydroxybenzoic acid with ethanoic anhydride.
  - Explain why ethanoic anhydride is preferred to ethanoyl chloride for commercial preparations of esters.
  - Explain why the reaction in 6.1 (b) works fastest at a pH between 3 and 5
- 7.1** For each of the following electrophilic substitution reactions, write an equation for the reaction, identify the electrophile and any catalyst, and outline the mechanism for the reaction:
- Benzene and nitric acid
  - Benzene and propanoyl chloride
  - Benzene and bromine
  - Benzene and 1-chloropropane
  - Benzene and ethene
- 7.2**
- Explain why it is important to keep the temperature below 50 C during electrophilic substitution reactions.
  - The monosubstitution of methylbenzene with chlorine in the presence of aluminium chloride gives three different products. Identify them and outline the mechanism for the formation of any one of the products.
  - The monosubstitution of benzene with propene in the presence of iron (III) bromide and hydrogen bromide gives two different products. Identify them, explain which of the products will be the major product and outline the mechanism for the formation of the major product.