BASIC CONCEPTS IN REACTION MECHANISMS
• We have a tendency of representing any reaction in the form of a balanced chemical equation that summarizes the overall reaction by showing only the beginning of the reaction (starting materials) and the end of the reaction (the products).

\[
\begin{align*}
\text{Reactants} & : \quad \text{CH}_4 + 3\text{Cl}_2 & \xrightarrow{\text{Heat}} & \quad \text{CHCl}_3 + 3\text{HCl} \\
\text{Starting materials} & : \quad \text{Methane} & \quad \text{Chloroform} & \quad \text{Products}
\end{align*}
\]

• However, it is important to recognize that these chemical changes occur in a stepwise fashion by electron reorganization in the bonds undergoing cleavage in the process of forming the new bonds.
Reaction Mechanism

What is a Reaction Mechanism?

• To understand the reactions, one ends to look at the movement of electrons during the bond reorganizations that occur.

• A detailed explanation of the electron reorganizations that take place in the course of these reactions is usually illustrated in the reaction mechanism.

• A reaction mechanism is a reasonable, stepwise illustration of how the electrons in the bonds of the starting materials of a reaction are reorganized into its products under a given set of reaction conditions.
Reaction Mechanisms
Homolytic vs Heterolytic Bond Cleavage

• When a covalent bond breaks such that each of the bonded atoms retains one of the bonding electrons, the process is called homolytic bond cleavage or homolysis.

\[
\text{Cl-Cl} \xrightarrow{\text{Heat}} 2\text{Cl}^- \quad \text{Homolytic bond cleavage}
\]

• Covalent bond cleavage that occurs with both electrons staying with one of the atoms is an heterolytic bond cleavage or heterolysis.

\[
\text{H-Cl} \rightarrow \text{H}^+ + \text{Cl}^- \quad \text{Heterolytic bond cleavage}
\]

• The chemical species that are generated during these homolytic and heterolytic processes are reactive and thus responsible for propagating the chemical reactions.
Reaction Mechanisms
Reactive Species in Chemical Reactions

• A brief look at these chemical species would guide rationalize how reactions proceed once they are generated.

• Whereas homolytic bond cleavage provides radicals (7 electron species), heterolytic bond cleavage provides cations (+ve) and anions (-ve) as the reactive species.

• Radical species are mostly generated in non-polar bonds, while polarized bonds possess positively polarized (electrophilic) centres that can interact with electron rich or negatively charged species (nucleophiles) during a reaction.
Reaction Mechanisms
Reactive Species in Chemical Reactions

• The genesis of naming these chemical species as electrophiles or nucleophiles and how they interact with others to bring out chemical change can be rationalized by looking at the structure of the atom.

  ![Diagram showing nucleus and electron shell](nucleus-electron-shell.png)

  Nucleus (protons and neutron) (positively charged)

  Electron shell (negatively charged)

• Since the nucleus is positively charged, only negatively charged/electron-rich species or ones that have free/lone pairs of electrons would be attracted to it.
Reaction Mechanisms
Reactive Species in Chemical Reactions

- **Nucleophiles** (nucleus-loving species) are electron-rich reactants that form bonds by sharing its electrons with a substrate.
- **Electrophiles** (electron-loving species) are electron-deficient reactants that seek electrons and form bonds by sharing the electrons of a substrate.
- A **radical** (more precisely, a free radical) is an atom or molecule that has unpaired valence electrons. These unpaired electrons make free radicals highly reactive towards other substances or even towards themselves.
Reaction Mechanisms
Writing Reasonable Reaction Mechanisms

• Given an overall reaction, you may be required to propose a logical and stepwise reaction mechanism to account for the products formed.
• Each reaction mechanism you propose would logically comprise of several steps.
• Each step of the reaction mechanism is called an elementary step.
• Each elementary step would be balanced in terms of atoms and charges.
• Curly arrows are used in each elementary step to show the electron flow in the reacting species.
• The curly arrow originates from the source of electrons (electron rich site) to an electron deficient site (where the new bond forms).
Reaction Mechanism

Guidelines for Writing Reasonable Reaction Mechanisms

1. Inspect the starting materials and products to determine what has happened in the reaction. What bonds have been broken and what new bonds have been formed?

2. Identify the nucleophilic centres in all the reagent molecules and determine which is the most nucleophilic. Then identify the electrophiles present and determine which is the most electrophilic.

3. If the combination of the two centres appears to lead to the desired product, position the nucleophilic and electrophilic centres within bonding distance.
4. Draw a curly or curvy arrow from the nucleophile to the electrophile. It must start on the filled orbital or negative charge and finish on the empty orbital or positive charge.

5. Inspect the structure to verify that the atoms changed do not have too many bonds; if so one of them must be broken to avoid a ridiculous structure.

6. Write out the structures of the products specified by the curly arrows. Break the bonds that are the sources of the arrows and make those that are the targets.
Reaction Mechanism
Guidelines for Writing Reasonable Reaction Mechanisms

7. Inspect the charges on individual atoms in each elementary step of the reaction mechanism to verify that the overall charge is not changed.

8. Once you have drawn the curly arrows, the structure of the products is already determined by the new bond linkages formed.

9. Just write the structure that the curly arrows show you.

10. If the structure obtained is wrong, then the curly arrows were wrong; so go back and correct them.
Reaction Mechanisms
Sample Homolysis in Formation of CH₃Cl

Overall Reaction

\[
\text{H–C–H} + \text{Cl–Cl} \xrightarrow{\text{Heat}} \text{Cl–C–H} + \text{H–Cl}
\]

- Since the bonds in the starting materials (methane and chlorine) are not polarized, homolytic cleavage is the likely bond-cleavage.
- Balance the atoms in each elementary step.

Elementary steps of a reaction

(i) \( \text{Cl–Cl} \xrightarrow{\text{Heat}} 2 \text{Cl}^\cdot \) (Initiation step)

(ii) \( \text{Cl}^\cdot + \text{H–C–H} \rightarrow \text{H–Cl} + \text{C–H}^\cdot \) (Propagation step)

(iii) \( \text{Cl}^\cdot + \text{C–H}^\cdot \rightarrow \text{Cl–C–H} \) (Termination step)
Reaction Mechanisms
Sample Heterolysis in Formation of CH$_3$Cl

- Since the starting materials have polarized bonds, heterolytic cleavage is the likely bond-cleavage.
- Balance the atoms and charges in each elementary step.

Overall Reaction

H-C-OH + H-Cl $\xrightarrow{\text{Heat}}$ Cl-C-H + HOH

Elementary steps of the reaction mechanism:

(i) H-Cl $\xrightarrow{\text{Electrophile}}$ H$^+$ + Cl$^-$

(ii) H-C-OH + H$^+$ $\xrightarrow{\text{Nucleophile}}$ H-C-O-H$^+$

(iii) Cl$^-$ + H-C-O-H $\xrightarrow{\text{Nucleophile}}$ Cl-C-H + HOH
Writing Reasonable Reaction Mechanisms
A Summary

• Observe the law of conservation of matter (Matter can neither be created nor destroyed in an isolated system) by balancing the atoms in each elementary step of the reaction mechanism.

• Balance the charges in each elementary step of the reaction mechanism. By balancing the charges, you recognize that energy can not be created from nothing.

• Use curved arrows to show electron movement from an electron rich site to an electron deficient site in the reacting species of each elementary step of a reaction mechanism.
Writing Reasonable Reaction Mechanisms

A Summary

• Ensure the valence of atoms is observed. Carbon should have a maximum of four bonds to be neutral. A three bonded carbon should have an appropriate charge based on how it is generated.

• In a catalysed reaction, the catalyst will always be part of the first elementary step and will always be regenerated in the last step of the reaction mechanism.

• Use the reagents you are given to generate any reactive species you need in the mechanism, but do not use any species before you show where and how it comes by.

• Finally, make sure that the formation of each product in the overall reaction is explained in the reaction mechanism.
Practice Questions
Writing Organic Reaction Mechanisms

• Refer to the reaction mechanism for the acid-catalysed preparation of aspirin and suggest a reasonable alternative.
• Acetanilide (Antifebrin), was once used as an analgesic and antipyretic agent before its use was discontinued due to toxicity concerns. It is prepared based on the reaction shown below.

• Propose a reasonable and stepwise reaction mechanism for the above reaction.
Propose a reasonable and stepwise reaction mechanism for the above reaction.