Organic Reactions and Mechanisms

Here are detailed lecture notes on nucleophilic substitution reactions:

Nucleophilic Substitution Reactions

In nucleophilic substitution reactions, a nucleophile replaces a leaving group (typically a halide) in an organic molecule. The nature of the nucleophile, leaving group, and reaction conditions dictate the mechanism. These reactions are categorized into two primary types: SN1 (unimolecular) and SN2 (bimolecular).

1. SN2 Mechanism (Bimolecular Nucleophilic Substitution)

- **Mechanism**: The SN2 reaction involves a single-step mechanism where the nucleophile attacks the carbon atom from the opposite side of the leaving group, leading to a simultaneous formation of a new bond and breaking of the old one. The transition state involves both the nucleophile and the leaving group partially attached to the carbon.

- **Rate Law**: The rate of the SN2 reaction depends on the concentration of both the nucleophile and the substrate:

  $$\text{Rate} = k[\text{alkyl halide}][\text{nucleophile}]$$

  This indicates that the reaction follows second-order kinetics.

- **Stereochemistry**: The SN2 mechanism is characterized by an inversion of configuration at the carbon atom. This is often referred to as "Walden inversion." For instance, the reaction of 2-bromooctane with sodium hydroxide results in 2-octanol, with inversion at the chiral center.

  Example:

  $$\text{CH}_3\text{Br} + \text{OH}^- \rightarrow \text{CH}_3\text{OH} + \text{Br}^-$$

- **Factors Influencing SN2 Reactions**:
  - **Nucleophile**: Strong nucleophiles (like OH^-, CN^-) favor SN2 reactions.
  - **Substrate**: Primary alkyl halides react fastest, while tertiary substrates are highly resistant due to steric hindrance.
  - **Solvent**: Polar aprotic solvents (like acetone) enhance the nucleophilicity and thus the rate of SN2 reactions.

2. SN1 Mechanism (Unimolecular Nucleophilic Substitution)

- **Mechanism**: The SN1 reaction proceeds via a two-step process. First, the leaving group departs, forming a carbocation intermediate. In the second step, the nucleophile attacks the carbocation

to form the final product.

- **Rate Law**: The rate of the SN1 reaction depends only on the concentration of the alkyl halide, as the formation of the carbocation is the rate-determining step:

$$\text{Rate} = k[\text{alkyl halide}]$$

  This indicates that the reaction follows first-order kinetics.

- **Stereochemistry**: Since the carbocation intermediate is planar, the nucleophile can attack from either side, leading to racemization in chiral molecules. For instance, the hydrolysis of 2-bromobutane produces a racemic mixture of 2-butanol.

- **Factors Influencing SN1 Reactions**:
  - **Substrate**: Tertiary alkyl halides react fastest due to the stability of the resulting carbocation. Primary carbocations are too unstable to form.
  - **Nucleophile**: Since the nucleophile does not influence the rate of the reaction, weak nucleophiles can participate in SN1 reactions.
  - **Solvent**: Polar protic solvents (like water or ethanol) stabilize the carbocation intermediate, favoring the SN1 pathway.

3. Ambident Nucleophiles

Ambident nucleophiles, such as cyanide (CN^-), can attack the electrophilic center in two different ways. For example, KCN in an SN2 reaction leads to the formation of an alkyl cyanide, whereas AgCN forms alkyl isocyanide.

Examples:

$$\text{CH}_3\text{CH}_2\text{Br} + \text{KCN} \rightarrow \text{CH}_3\text{CH}_2\text{CN} + \text{KBr}$$

$$\text{CH}_3\text{CH}_2\text{Br} + \text{AgCN} \rightarrow \text{CH}_3\text{CH}_2\text{NC} + \text{AgBr}$$

This concept is crucial for understanding the selectivity and outcome of reactions depending on the choice of reagent.

4. Factors Affecting SN1 and SN2 Reactions

- **Steric Effects**: SN2 reactions are sensitive to steric hindrance, and thus, primary alkyl halides react much faster than secondary or tertiary ones.
- **Carbocation Stability**: The more stable the carbocation (as in tertiary alkyl halides), the more likely the reaction will proceed via the SN1 mechanism.

In summary, nucleophilic substitution reactions are a fundamental part of organic chemistry, with their mechanisms (SN1 or SN2) determined by the nature of the substrate, nucleophile, solvent, and reaction conditions.