

Reaction Mechanisms

Introduction

A reaction mechanism is the detailed, step-by-step description of how a chemical reaction occurs. It provides a theoretical framework that explains how bonds are broken and formed, the role of catalysts, the order in which molecules collide, and the nature of the transient species (intermediates and transition states) involved. Understanding mechanisms is vital because it allows chemists to predict product outcomes, control stereochemistry, and design more efficient synthetic pathways.

Learning Objectives

By the end of this module, you will be able to:

- Write out the detailed, step-by-step reaction mechanisms (SN1, SN2, E1, E2) using curved arrows to show electron flow.
- Identify and differentiate between transition states and reactive intermediates.
- Analyze organic reactions by applying principles of structural stability, kinetics (rate laws), and thermodynamics (energy changes).

Key Concepts and Definitions

Term	Definition
Mechanism	The detailed sequence of elementary steps showing the movement of electrons, intermediates, and transition states.
Curved Arrows	A notation used in mechanisms to show the flow of electron pairs: from a bond or lone pair to an atom or bond.
Transition State (TS)	A short-lived, high-energy arrangement of atoms at the peak of an energy

	barrier. Bonds are partially broken and partially formed.
Intermediate	A chemical species (like a carbocation or carbanion) formed during the reaction that exists for a measurable amount of time. It sits in an energy valley on a reaction coordinate diagram.
Rate-Determining Step (RDS)	The slowest step in a multi-step reaction mechanism, which has the highest activation energy (ΔG^\ddagger) and governs the overall reaction rate.
Kinetic Control	Reaction conditions (low temperature, irreversible) where the product ratio is determined by the rate of formation (lowest ΔG^\ddagger). The kinetic product forms fastest.
Thermodynamic Control	Reaction conditions (high temperature, reversible) where the product ratio is determined by the stability of the products (ΔG). The thermodynamic product is the most stable.

Detailed Discussion

Nucleophilic Substitution Mechanisms (S_N1 and S_N2)

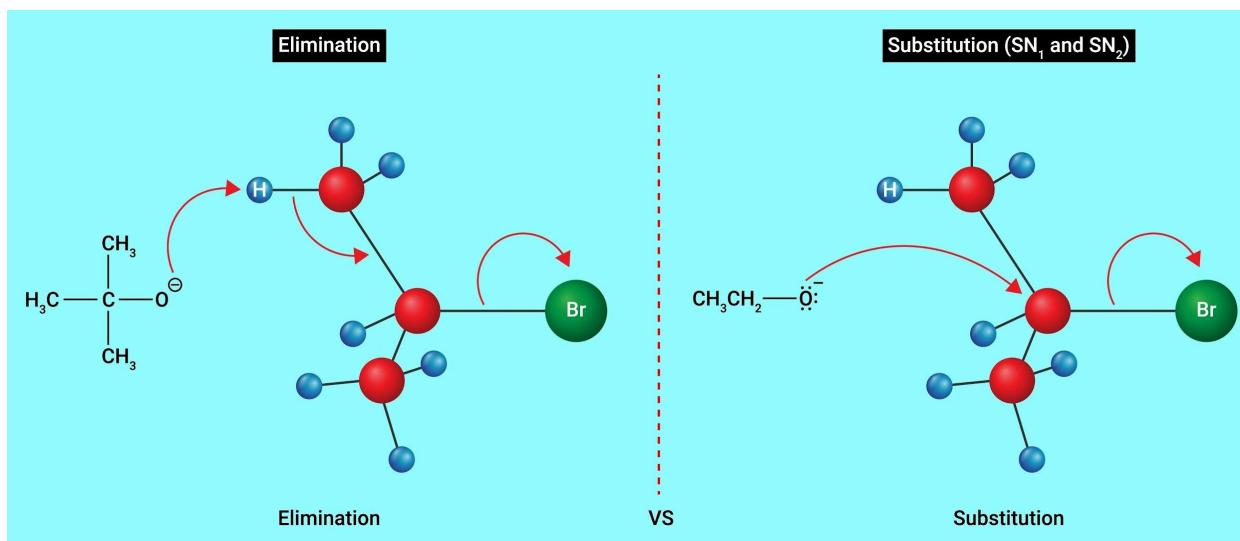
Substitution reactions, a core transformation in organic chemistry, proceed via one of two major mechanisms, which differ fundamentally in their kinetics and stereochemistry.

Feature	S_N2 (Bimolecular)	S_N1 (Unimolecular)
Mechanism	One-step, concerted process.	Two-step process with a carbocation intermediate.
Rate Law	$\text{Rate} = k [\text{Substrate}][\text{Nucleophile}]$ (Second-order)	$\text{Rate} = k [\text{Substrate}]$ (First-order)
Substrate Reactivity	$\text{Methyl} > 1^\circ > 2^\circ >> 3^\circ$	$3^\circ > 2^\circ >> 1^\circ$ (Carbocation)

	(Steric hindrance slows the reaction)	stability)
Stereochemistry	Complete inversion of configuration.	Racemization (formation of a mixture of enantiomers).
Solvent Preference	Polar Aprotic (e.g., DMSO, Acetone)	Polar Protic (e.g., H ₂ O, EtOH)

S_n2 Mechanism:

The nucleophile attacks the carbon atom from the **backside**, opposite to the leaving group. This attack forces the leaving group off in a single step, passing through a high-energy **transition state** where both the nucleophile and leaving group are partially bonded to the central carbon.



S₁ Mechanism:

The leaving group departs first, forming a **planar carbocation intermediate**. This is the **rate-determining step**. The nucleophile then attacks the carbocation from either face, leading to both retention and inversion of configuration (racemization). The presence of the carbocation also makes **rearrangements** possible.

Elimination Mechanisms (E1 and E2)

Elimination reactions often compete with substitution, especially E1 with S_n1, and E2 with S_n2. Elimination forms a π bond.

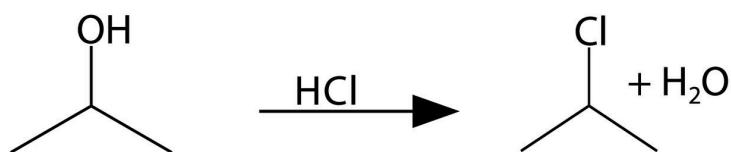
Feature	E2 (Bimolecular)	E1 (Unimolecular)
Mechanism	One-step, concerted process.	Two-step process with a carbocation intermediate.
Rate Law	Rate = k [Substrate] [Base] (Second-order)	Rate = k [Substrate] (First-order)
Stereochemistry	Requires the H and Leaving Group (L) to be anti-periplanar (in the same plane, 180° apart).	Not stereospecific; proceeds via planar carbocation.
Favoring Conditions	Strong, bulky base; high temperature.	Weak base; high temperature.

E2 Mechanism:

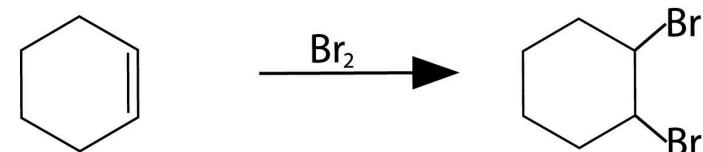
The base abstracts a proton from the carbon adjacent to the leaving group (the β-carbon) simultaneously with the leaving group departing. This concerted movement is favored when the H and the leaving group are in an **anti-periplanar** geometry

Types Of Organic Reactions

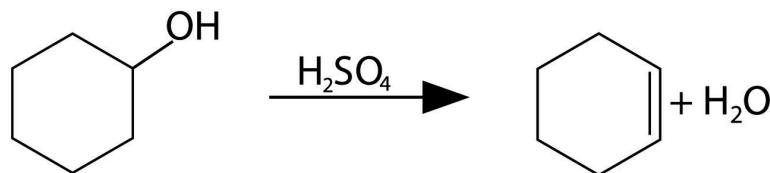
Substitution



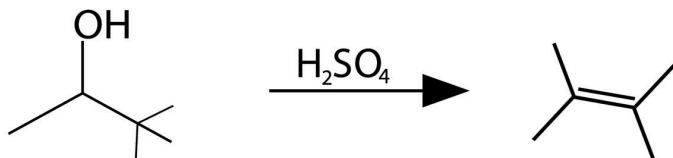
Addition



Elimination



Rearrangement



E1 Mechanism:

Similar to S_n1, the leaving group departs first to form a **carbocation intermediate** (the RDS). In the second, fast step, a weak base or solvent removes a proton from an adjacent carbon, forming the π bond.

Factors Affecting Reaction Pathways (Mechanism Selection)

Choosing the correct reaction mechanism is not random; it is determined by a combination of structural and environmental factors. Understanding these factors allows chemists to predict whether a reaction will proceed via substitution or elimination, and whether it will follow a unimolecular or bimolecular pathway.

Substrate Structure

The structure of the substrate plays a major role in mechanism selection. Primary substrates generally favor SN₂ reactions because they are less sterically hindered, allowing easy backside attack by the nucleophile. Tertiary substrates, on the other hand, favor SN₁ and E₁ mechanisms due to the stability of the carbocation formed after the leaving group departs. Secondary substrates can undergo either substitution or elimination depending on reaction conditions.

Strength of the Nucleophile or Base

Strong nucleophiles favor substitution reactions, particularly SN₂. Strong bases favor elimination reactions, especially E₂. Bulky bases tend to favor E₂ over SN₂ because steric hindrance limits nucleophilic attack but still allows proton abstraction. Weak nucleophiles and weak bases often lead to SN₁ or E₁ mechanisms when carbocation formation is favorable.

Solvent Effects

Solvents significantly influence reaction pathways. Polar protic solvents stabilize ions through hydrogen bonding, which promotes carbocation formation and favors SN₁ and E₁ reactions. Polar aprotic solvents do not strongly solvate nucleophiles, increasing their reactivity and favoring SN₂ mechanisms.

Temperature

Increasing temperature generally favors elimination reactions over substitution. Elimination leads to greater disorder (higher entropy), making it more favorable at higher temperatures. As a result, E₁ and E₂ reactions are commonly observed under heated conditions.

These factors act together rather than independently. A complete mechanistic analysis requires considering all of them simultaneously to predict the dominant reaction pathway.

Thermodynamic and Kinetic Analysis

Reaction mechanisms are best understood through energy diagrams, which illustrate the principles of **thermodynamics** and **kinetics**.

Reaction coordinate diagrams provide a visual representation of the energy changes that occur during a chemical reaction. These diagrams plot free energy on the vertical axis against reaction progress on the horizontal axis, allowing comparison of different mechanisms in terms of kinetics and thermodynamics.

In single-step mechanisms such as SN2 and E2, the reaction coordinate diagram shows a single energy peak corresponding to one transition state. There are no intermediates because bonds are broken and formed simultaneously in a concerted process.

In multi-step mechanisms such as SN1 and E1, the diagram contains multiple peaks and valleys. Each peak represents a transition state, while each valley corresponds to a reaction intermediate, such as a carbocation. The highest energy peak represents the rate-determining step, which controls the overall reaction rate.

Reaction coordinate diagrams also help distinguish between kinetic and thermodynamic control. Under kinetic control, the major product forms through the pathway with the lowest activation energy, even if it is less stable. Under thermodynamic control, the reaction is reversible and the most stable product predominates, regardless of how fast it forms.

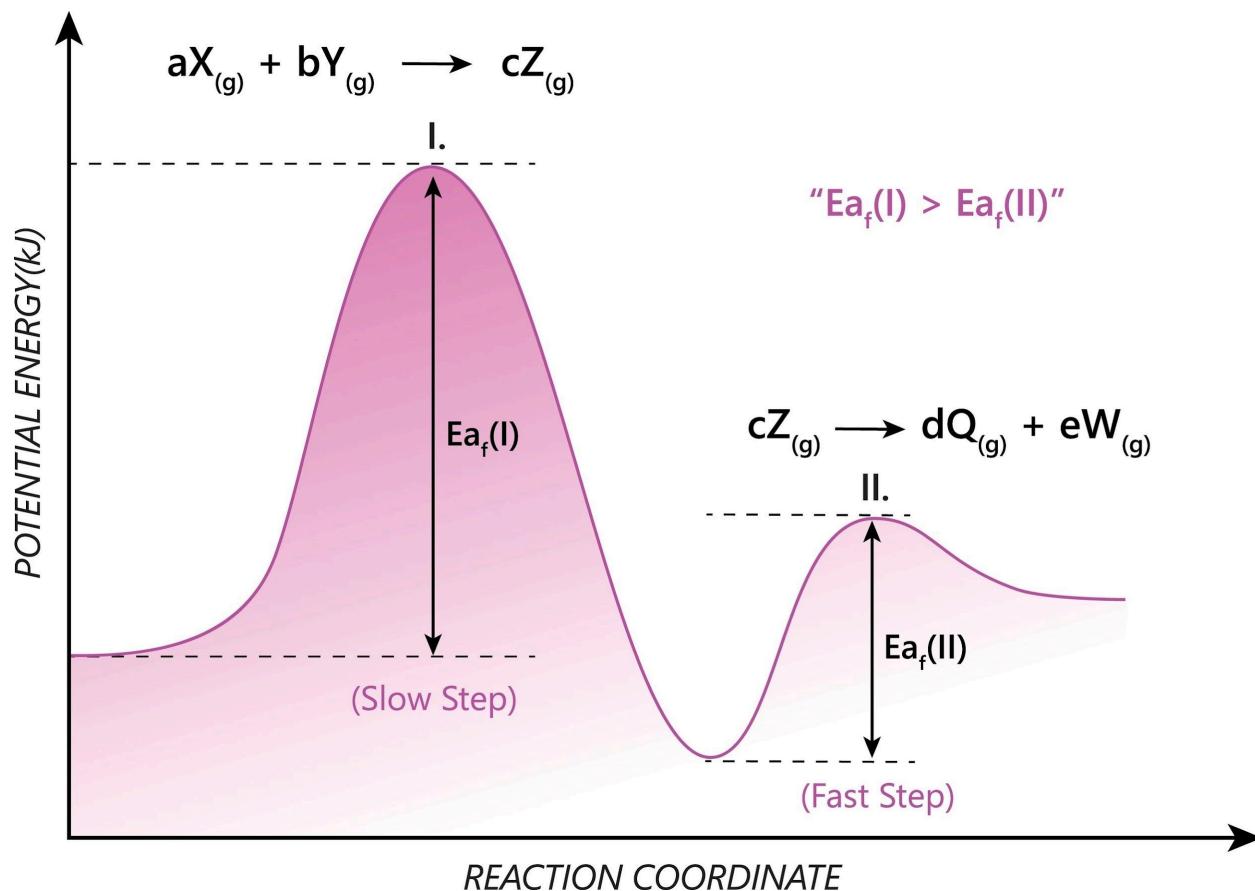
By analyzing reaction coordinate diagrams, chemists can predict reaction rates, identify intermediates, and determine which products are favored under specific reaction conditions.

1. **Thermodynamics (ΔG):** The difference in free energy between the **reactants and the products** determines the **equilibrium** position (K_{eq}) and the **stability** of the products.
 - $\Delta G = \Delta H - T\Delta S$
 - $\Delta G = -RT \ln K_{\text{eq}}$
 - A negative ΔG indicates a thermodynamically favorable reaction.

2. **Kinetics (ΔG^\ddagger):** The difference in free energy between the **reactants and the highest-energy transition state** determines the rate of the reaction. This difference is the **Activation Energy (ΔG^\ddagger)**.
- The lower the ΔG^\ddagger , the faster the reaction rate (k).

Kinetic vs. Thermodynamic Control: When a reaction can produce two different products, the outcome is governed by conditions:

- Low Temperature:** The reaction is often irreversible, and the major product is the one that forms fastest (the **Kinetic Product**), corresponding to the pathway with the lowest ΔG^\ddagger (lowest peak).
- High Temperature:** The reaction is reversible, allowing the products to equilibrate. The major product is the one that is most stable (the **Thermodynamic Product**), corresponding to the product with the **lowest final energy level (ΔG)**.



References:

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