6.5 An Example of a Polar Reaction: Addition of $\text{H}_2\text{O}$ to Ethylene

Addition of water to ethylene
- Typical polar process
- Acid catalyzed addition reaction (Electrophilic addition reaction)

\[
\begin{array}{c}
\text{Ethylene} \\
\text{H}_2\text{SO}_4 \text{ catalyst} \\
\text{250 °C} \\
\text{Ethanol}
\end{array}
\]

Polar Reaction
- All polar reactions take place between an electron-poor site and an electron-rich site, and they involve the donation of an electron pair from nucleophiles to electrophiles

An Example of a Polar Reaction: Addition of $\text{H}_2\text{O}$ to Ethylene

Reactants of reaction
- Ethylene
  - An alkene, contains a C=C double bond (overlapping orbitals from two sp$^2$-hybridized carbon atoms)
- C=C double bond
  - Has greater electron density than single bonds
  - Electrons in σ bond are more accessible to approaching reactants
  - Nucleophilic and reacts with electrophile

Water
- In presence of a strong acid, it is protonated to give the hydronium ion $\text{H}_3\text{O}^+$ (proton, H+, donor and electrophile).

Polar reaction
- Electrophile-nucleophile combination
Carbocation
- Formed in step two of the acid-catalyzed electrophilic addition reaction of ethylene and water
- Positively charged carbon species with only six valence electrons
- Electrophile that can accept an electron pair from a nucleophile

An Example of a Polar Reaction: Addition of H\textsubscript{2}O to Ethylene

6.6 Using Curved Arrows in Polar Reaction Mechanisms

Rule 1 – Electrons move from a nucleophilic source (Nu: or Nu\textsuperscript{-}) to an electrophilic sink (E or E\textsuperscript{+})

- Nucleophilic source must have an electron pair available
- Electrophilic site must be able to accept electron pair

Using Curved Arrows in Polar Reaction Mechanisms

Rule 2 – The nucleophile can be either negatively charged or neutral
- Negatively charged (the atom gives away an electron pair and becomes neutral):
- Neutral (the atom gives away an electron pair to acquire a positive charge):
 Rule 3 – The electrophile can be either positively charged or neutral
  • Positively charged (the atom bearing the charge becomes neutral after accepting electron pair):

  ![Positively charged reaction](image)

  • Neutral (the atom acquires a negative charge after accepting electron pair):

  ![Neutral reaction](image)

 Rule 4 – The octet rule must be followed

 ![Octet rule example](image)

 Worked Example 6.2

 Using Curved Arrows in Reaction Mechanisms

 Add curved arrows to the following polar reactions to show the flow of electrons

 ![Worked example reaction](image)
6.7 Describing a Reaction: Equilibria, Rates, and Energy Changes

Every chemical reaction can proceed in either the forward or reverse direction

\[ aA + bB \rightleftharpoons cC + dD \]

- The position of the resulting chemical equilibrium is expressed by the equilibrium constant equation \( K_{eq} \)

\[ K_{eq} = \frac{[C]^c[D]^d}{[A]^a[B]^b} \]

- \([C]\) = equilibrium concentration of C raised to the power of its coefficient in the balanced equation
- \([D]\) = equilibrium concentration of D raised to the power of its coefficient in the balanced equation
- \([A]\) = equilibrium concentration of A raised to the power of its coefficient in the balanced equation
- \([B]\) = equilibrium concentration of B raised to the power of its coefficient in the balanced equation

Describing a Reaction: Equilibria, Rates, and Energy Changes

The value of \( K_{eq} \) tells which side of the reaction arrow is energetically favored

- \( K_{eq} > 1 \)
  - Product concentration term \([C]^c[D]^d\) is much larger than reactant concentration term \([A]^a[B]^b\)
  - Reaction proceeds from left to right
- \( K_{eq} = 1 \)
  - Comparable amounts of both products and reactants are present at equilibrium
- \( K_{eq} < 1 \)
  - Product Concentration \([C]^c[D]^d\) is much smaller than reactant concentration \([A]^a[B]^b\)
  - Reaction proceeds from left to right

Describing a Reaction: Equilibria, Rates, and Energy Changes

Equilibrium Expression (\( K_{eq} \))

- Reaction of ethylene with \( H_2O \)

\[ H_2C=CH_2 + H_2O \rightleftharpoons CH_3CH_2OH \]

\[ K_{eq} = \frac{CH_3CH_2OH \cdot H_2O}{H_2C=CH_2} = 25 \]

Because \( K_{eq} > 1 \)

- the reaction proceeds as written (left to right)
- some unreacted ethylene remains at equilibrium
Describing a Reaction: Equilibria, Rates, and Energy Changes

For a reaction to have a favorable equilibrium constant and proceed from left to right
• the energy of products must be lower than the energy of the reactants (energy must be released)

Gibbs free-energy change ($\Delta G$)
• the energy change that occurs during a chemical reaction (energy difference between reactants and products)
  \[ \Delta G = G_{\text{products}} - G_{\text{reactant}} \]

Describing a Reaction: Equilibria, Rates, and Energy Changes

Gibbs Free-Energy Change, $\Delta G^\circ$
• $\Delta G^\circ$ is negative
  - Reaction is exergonic (energy lost by system and released to surroundings)
  - Has favorable equilibrium constant
  - Can occur spontaneously
• $\Delta G^\circ$ is positive
  - Reaction is endergonic (energy absorbed into system from surroundings)
  - Unfavorable equilibrium constant
  - Cannot occur spontaneously

$\Delta G^\circ$ denotes standard free-energy change for a reaction
• (º) means that the reaction is carried out under standard conditions
$K_{eq}$ and $\Delta G^\circ$ are mathematically related because they both measure whether a reaction is favored

\[ \Delta G^\circ = -RT \ln K_{eq} \quad \text{or} \quad K_{eq} = e^{\Delta G^\circ / RT} \]

where
- $R = 8.314 \text{ J/(K \cdot mol)} = 1.987 \text{ cal/(K \cdot mol)}$
- $T = \text{Kelvin temperature}$
- $e = 2.718$
- $\ln K_{eq} = \text{natural logarithm of } K_{eq}$
- $K_{eq} = 25$ for the reaction of ethylene with $H_2O$
  \[ \ln K_{eq} = \ln 25 = 3.2 \]

$\Delta G^\circ = -RT \ln K_{eq} = -[8.314 \text{ J/(K \cdot mol)}] \times (298 \text{ K}) \times (3.2)$
  \[ = -7800 \text{ J/mol} = 7.9 \text{ kJ/mol} \]
Describing a Reaction: Equilibria, Rates, and Energy Changes

The free-energy change $\Delta G$ made up of two terms:

1. Enthalpy $\Delta H$
2. Entropy $T\Delta S$ (temperature dependent)

$$\Delta G^\circ = \Delta H^\circ - T\Delta S^\circ$$ (standard conditions)

Reaction of ethylene with $H_2O$ at 298 K

$$\text{H}_2\text{C} = \text{CH}_2 + \text{H}_2\text{O} \rightleftharpoons \text{CH}_3\text{CH}_2\text{OH}$$

$\Delta G^\circ = -7.9 \text{ kJ/mol}$
$\Delta H^\circ = -44 \text{ kJ/mol}$
$\Delta S^\circ = -0.12 \text{ kJ/(K \cdot mol)}$

Describing a Reaction: Equilibria, Rates, and Energy Changes

Change in Enthalpy, $\Delta H$

- The heat of reaction
- Calculated as the difference in strength between the bonds broken and the bonds formed under standard conditions
  $$\Delta H^\circ = H^\circ_{\text{products}} - H^\circ_{\text{reactants}}$$ (standard conditions)

- Negative $\Delta H^\circ$
  - The reaction releases heat, exothermic
  - Products are more stable than reactants
  - Have less energy than reactants
  - Have stronger bonds than the reactants

- Positive $\Delta H^\circ$
  - The reaction absorbs heat, endothermic
  - Products are less stable than reactants
  - Have more energy than reactants
  - Have weaker bonds than reactants

Describing a Reaction: Equilibria, Rates, and Energy Changes

Entropy change, $\Delta S^\circ$

$$\Delta S^\circ = S^\circ_{\text{products}} - S^\circ_{\text{reactants}}$$

- The change in molecular disorder during a reaction at standard conditions

- Negative $\Delta S^\circ$
  - Disorder decreases during reaction
  - Addition reaction
    - reaction allows more freedom of movement in products than reactants by splitting one molecule into two
    $$A + B \rightarrow C$$

- Positive $\Delta S^\circ$
  - Disorder increases during reaction
  - Elimination reaction
    - reaction restricts freedom of movement of two molecules by joining them together
    $$A \rightarrow B + C$$
Describing a Reaction: Equilibria, Rates, and Energy Changes

\( K_{eq} \)

- Tells position of equilibrium
- Tells how much product is theoretically possible
- Does not tell the rate of reaction
- Does not tell how fast equilibrium is established

**Rate** → Is the reaction fast or slow?

**Equilibrium** → In what direction does the reaction proceed?

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**TABLE 6.2**

<table>
<thead>
<tr>
<th>Term</th>
<th>Name</th>
<th>Explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \Delta G^\circ )</td>
<td>Gibbs free-energy change</td>
<td>The energy difference between reactants and products. When ( \Delta G^\circ ) is negative, the reaction is <em>exergonic</em>, has a favorable equilibrium constant, and can occur spontaneously. When ( \Delta G^\circ ) is positive, the reaction is <em>endergonic</em>, has an unfavorable equilibrium constant, and cannot occur spontaneously.</td>
</tr>
<tr>
<td>( \Delta H^\circ )</td>
<td>Enthalpy change</td>
<td>The heat of reaction, or difference in strength between the bonds broken in a reaction and the bonds formed. When ( \Delta H^\circ ) is negative, the reaction releases heat and is <em>exothermic</em>. When ( \Delta H^\circ ) is positive, the reaction absorbs heat and is <em>endothermic</em>.</td>
</tr>
<tr>
<td>( \Delta S^\circ )</td>
<td>Entropy change</td>
<td>The change in molecular randomness during a reaction. When ( \Delta S^\circ ) is negative, randomness decreases; when ( \Delta S^\circ ) is positive, randomness increases.</td>
</tr>
</tbody>
</table>

---

6.8 Describing a Reaction: Bond Dissociation Energies

Bond strength is a measure of the heat change that occurs on breaking a bond, formally defined as bond dissociation energy

- Each bond has its own characteristic strength

**Bond Dissociation Energy (D)**

- The amount of energy required to break a given bond to produce two radical fragments when the molecule is in the gas phase at 25\(^\circ\)C

\[ \text{A : B} \xrightarrow{\text{Bond dissociation energy}} \text{A}^\cdot + \text{B}^\cdot \]
Connections between bond strengths and chemical reactivity

- Exothermic reactions are favored by products with stronger bonds and reactants with weaker bonds
  - Bond formation in products releases heat
  - Bond breaking in reactants requires heat

Reactive substances that undergo highly exothermic reactions such as ATP (adenosine triphosphate) are referred to as “energy-rich” or high energy compounds

- ATP has relatively weak bonds (bonds require only a small amount of heat to break)
Glycerol vs. ATP reaction with water
- Bond broken in ATP is substantially weaker than the bond broken in glycerol-3-phosphate

Describing a Reaction: Bond Dissociation Energies

For a reaction to take place
- Reactant molecules must collide
- Reorganization of atoms and bonds must occur

Describing a Reaction: Energy Diagrams and Transition States

Chemists use energy diagrams to graphically depict the energy changes that occur during a chemical reaction
- Vertical axis
  - the total energy of all reactants
- Horizontal axis
  - “reaction coordinate” the progress of the reaction from beginning to end
Activation Energy ($\Delta G^\ddagger$)
- The energy difference between reactants and transition state
- Determines how rapidly the reaction occurs at a given temperature
  - Large activation energy results in a slow reaction
  - Small activation energy results in a rapid reaction
- Many organic reactions have activation energies in the range of 40 – 150 kJ/mol (10 – 35 kcal/mol)
  - If $\Delta G^\ddagger$ less than 80 kJ/mol the reaction takes place at or below room temperature
  - If $\Delta G^\ddagger$ more than 80 kJ/mol the reaction requires heating above room temperature

Describing a Reaction: Energy Diagrams and Transition States

Activation energy leads to transition state

The Transition State
- Represents the highest-energy structure involved in the reaction
- Unstable and cannot be isolated

A hypothetical transition–state structure for the first step of the reaction of ethylene with $\text{H}_2\text{O}^+$
- the $\text{C}=$-$\text{C}$ bond about to break
- the $\text{C}=$-$\text{H}$ bond is beginning to form

Once transition-state is reached the reaction either:
- Continues on to give carbocation product
  - New $\text{C}=$-$\text{H}$ bond forms fully
  - Amount of energy corresponding to difference between transition-state ($\Delta G^\ddagger$) and carbocation product is released
  - Since carbocation is higher in energy than the starting alkene, the step is endergonic ($\Delta G^\circ$, absorbs energy)
- Reverts back to reactants
  - Transition-state structure comes apart
  - Amount of free-energy ($-\Delta G^\ddagger$) is released
Describing a Reaction: Energy Diagrams and Transition States

Each reaction has its own profile

(a) a fast exergonic reaction (small $G^\ddagger$, negative $G^\circ$);

(b) a slow exergonic reaction (large $G^\ddagger$, negative $G^\circ$);

(c) a fast endergonic reaction (small $G^\ddagger$, small positive $G^\circ$);

(d) a slow endergonic reaction (large $G^\ddagger$, positive $G^\circ$).

---

6.10 Describing a Reaction: Intermediates

Reaction Intermediate

- A species that is formed during the course of a multi-step reaction but is not final product
- More stable than transition states
- May or may not be stable enough to isolate
- The hydration of ethylene proceeds through two reaction intermediates, a carbocation intermediate and a protonated alcohol intermediate

---

Describing a Reaction: Intermediates

Each step in a multi-step process can be considered separately (each step has $\Delta G^\ddagger$ and $\Delta G^\circ$)

Overall $\Delta G^\circ$ of reaction is the energy difference between initial reactants and final products

Overall energy diagram for the reaction of ethylene with water
Describing a Reaction: Intermediates

Biological reactions occur at physiological conditions
- Must have low activation energy
- Must release energy in relatively small amounts

Enzyme catalyst changes the mechanism of reaction to an alternative pathway which proceeds through a series of smaller steps rather than one or two large steps

Worked Example 6.3

Drawing Energy Diagram for Reactions
Sketch an energy diagram for a one-step reaction that is fast and highly exergonic

6.11 A Comparison between Biological Reactions and Laboratory Reactions

Solvent
- Laboratory reaction
  - Organic liquid, such as ether or dichloromethane
  - Used to dissolve reactants
  - Used to bring reactants into contact with each other
- Biological reaction
  - Aqueous medium inside cell

Temperature
- Laboratory reaction
  - Takes place over wide range of temperatures (typically 80-150°C)
- Biological reaction
  - Takes place at the temperature of the organism
A Comparison between Biological Reactions and Laboratory Reactions

Catalyst
- Laboratory reactions
  - Either none or very simple
- Biological reactions
  - Catalyzed by enzymes

Enzyme
- A large, globular protein molecule that contains a protected pocket called an active site

Active site
- The pocket in an enzyme where a substrate is bound and undergoes reaction
  - Lined by acidic or basic groups
  - Has precisely the right shape to bind and hold substrate molecule

Reagent size
- Laboratory reactions
  - Usually small and simple (such as Br₂, HCl, NaBH₄, CrO₃)
- Biological reactions
  - Relatively complex reagents called coenzymes
    - ATP is the coenzyme in the hexokinase-catalyzed phosphorylation of glucose
    - Reduced NADH is the coenzyme that effects hydrogenation in many biological pathways
Specificity

- Laboratory reactions
  - Little specificity for substrate (a catalyst such as sulfuric acid might be used to catalyze the addition of water to thousands of different alkenes)
- Biological reactions
  - Very high specificity for substrate (an enzyme will catalyze only a very specific reaction)

### TABLE 6.1
A Comparison of Typical Laboratory and Biological Reactions

<table>
<thead>
<tr>
<th></th>
<th>Laboratory reaction</th>
<th>Biological reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solvent</td>
<td>Organic liquid, such as ether</td>
<td>Aqueous environment in cells</td>
</tr>
<tr>
<td>Temperature</td>
<td>Wide range: ~60 to 150 °C</td>
<td>Temperature of organism</td>
</tr>
<tr>
<td>Catalyst</td>
<td>Either none or very simple</td>
<td>Large, complex enzymes needed</td>
</tr>
<tr>
<td>Reactant size</td>
<td>Usually small and simple</td>
<td>Relatively complex coenzymes</td>
</tr>
<tr>
<td>Specificity</td>
<td>Little specificity for substrate</td>
<td>Very high specificity for substrate</td>
</tr>
</tbody>
</table>