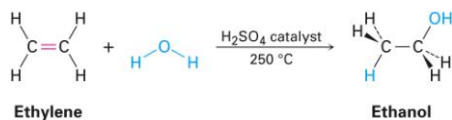


6.5 An Example of a Polar Reaction: Addition of H₂O to Ethylene

Addition of water to ethylene

- Typical polar process
- Acid catalyzed addition reaction (Electrophilic addition reaction)



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

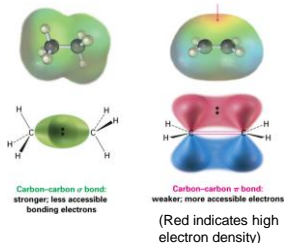
An Example of a Polar Reaction: Addition of H₂O to Ethylene

Reactants of reaction

- Ethylene
 - An alkene, contains a C=C double bond (overlapping orbitals from two sp²-hybridized carbon atoms)

C=C double bond

- Has greater electron density than single bonds
- Electrons in π bond are more accessible to approaching reactants
- Nucleophilic and reacts with electrophile



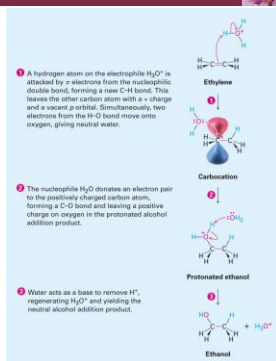
An Example of a Polar Reaction: Addition of H₂O to Ethylene

Water

- In presence of a strong acid, it is protonated to give the hydronium ion H₃O⁺ (proton, H⁺, donor and electrophile).

Polar reaction

- Electrophile-nucleophile combination



An Example of a Polar Reaction: Addition of H₂O to Ethylene

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

6.6 Using Curved Arrows in Polar Reaction Mechanisms

Rule 1 – Electrons move from a nucleophilic source (Nu: or Nu⁻) to an electrophilic sink (E or E⁺)

- Nucleophilic source must have an electron pair available



- Electrophilic site must be able to accept electron pair

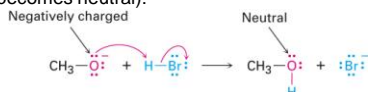
Electrons usually flow to one of these electrophiles.



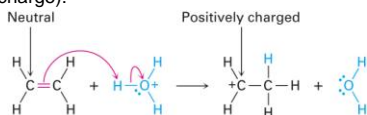
Using Curved Arrows in Polar Reaction Mechanisms

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):



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 (ΔG)

- the energy change that occurs during a chemical reaction (energy difference between reactants and products)

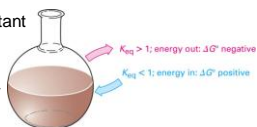
$$\Delta G = G_{\text{products}} - G_{\text{reactant}}$$

Describing a Reaction: Equilibria, Rates, and Energy Changes



Gibbs Free-Energy Change, ΔG°

- ΔG° is negative
 - Reaction is exergonic (energy lost by system and released to surroundings)
 - Has favorable equilibrium constant
 - Can occur spontaneously
- ΔG° is positive
 - Reaction is endergonic (energy absorbed into system from surroundings)
 - Unfavorable equilibrium constant
 - Cannot occur spontaneously



Describing a Reaction: Equilibria, Rates, and Energy Changes



- ΔG° denotes standard free-energy change for a reaction
- $^\circ$ means that the reaction is carried out under standard conditions

K_{eq} and ΔG° are mathematically related because they both measure whether a reaction is favored

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

where

$$R = 8.314 \text{ J/(K} \cdot \text{mol)} = 1.987 \text{ cal/(K} \cdot \text{mol)}$$

T = Kelvin temperature

$$e = 2.718$$

$\ln K_{\text{eq}}$ = natural logarithm of K_{eq}

$K_{\text{eq}} = 25$ for the reaction of ethylene with H_2O

$$\ln K_{\text{eq}} = \ln 25 = 3.2$$

$$\begin{aligned} \Delta G^\circ &= -RT \ln K_{\text{eq}} = -[8.314 \text{ J/(K} \cdot \text{mol)}] (298 \text{ K}) (3.2) \\ &= -7900 \text{ J/mol} = -7.9 \text{ kJ/mol} \end{aligned}$$

Describing a Reaction: Equilibria, Rates, and Energy Changes

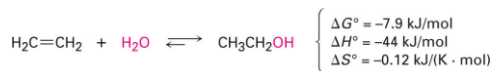


The free-energy change ΔG made up of two terms:

1. Enthalpy ΔH
2. Entropy $T\Delta S$ (temperature depended)

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

Reaction of ethylene with H_2O at 298 K



Describing a Reaction: Equilibria, Rates, and Energy Changes



Change in Enthalpy, ΔH

- 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 ΔH°**
 - The reaction releases heat, **exothermic**
 - Products are more stable than reactants
 - Have less energy than reactants
 - Have stronger bonds than the reactants
- **Positive ΔH°**
 - 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, ΔS°

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

- The change in molecular disorder during a reaction at standard conditions
- **Negative ΔS°**
 - 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 ΔS°**
 - Disorder increases during reaction
 - Elimination reaction
 - reaction restricts freedom of movement of two molecules by joining them together



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?

Describing a Reaction: Equilibria, Rates, and Energy Changes



TABLE 6.2

Explanation of Thermodynamic Quantities: $\Delta G^\circ = \Delta H^\circ - T\Delta S^\circ$

Term	Name	Explanation
ΔG°	Gibbs free-energy change	The energy difference between reactants and products. When ΔG° is negative, the reaction is exergonic , has a favorable equilibrium constant, and can occur spontaneously. When ΔG° is positive, the reaction is endergonic , has an unfavorable equilibrium constant, and cannot occur spontaneously.
ΔH°	Enthalpy change	The heat of reaction, or difference in strength between the bonds broken in a reaction and the bonds formed. When ΔH° is negative, the reaction releases heat and is exothermic . When ΔH° is positive, the reaction absorbs heat and is endothermic .
ΔS°	Entropy change	The change in molecular randomness during a reaction. When ΔS° is negative, randomness decreases; when ΔS° is positive, randomness increases.

6.8 Describing a Reaction: Bond Dissociation Energies

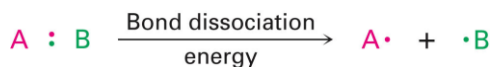


Bond strength is a measure of the heat change that occurs on breaking a bond, formally defined as bond dissociation energy

- 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°C

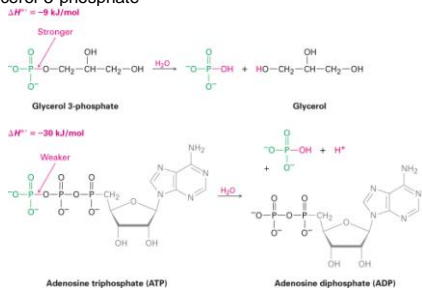


Describing a Reaction: Bond Dissociation Energies



Glycerol vs. ATP reaction with water

- Bond broken in ATP is substantially weaker than the bond broken in glycerol-3-phosphate

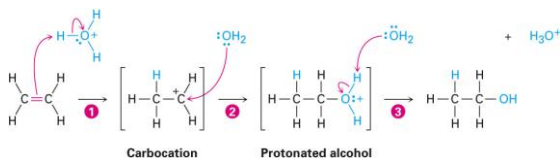


6.9 Describing a Reaction: Energy Diagrams and Transition States



For a reaction to take place

- Reactant molecules must collide
- Reorganization of atoms and bonds must occur

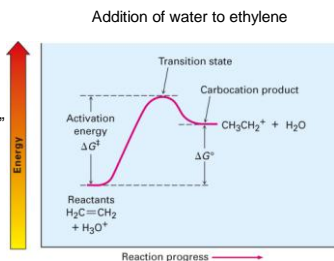


Describing a Reaction: Energy Diagrams and Transition States



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



Describing a Reaction: Energy Diagrams and Transition States

Activation Energy (ΔG^\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 ΔG^\ddagger less than 80 kJ/mol the reaction takes place at or below room temperature
 - If ΔG^\ddagger more than 80 kJ/mol the reaction requires heating above room temperature

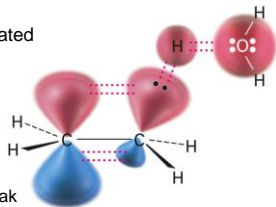
Describing a Reaction: Energy Diagrams and Transition States

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 H_3O^+



- the C=C bond about to break
- the C-H bond is beginning to form

Describing a Reaction: Energy Diagrams and Transition States

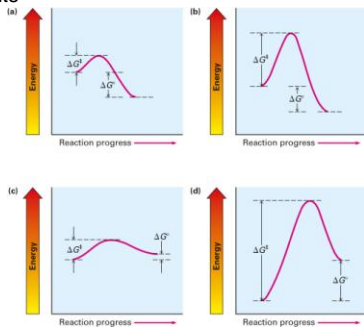
Once transition-state is reached the reaction either:

- Continues on to give carbocation product
 - New C-H bond forms fully
 - Amount of energy corresponding to difference between transition-state (ΔG^\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

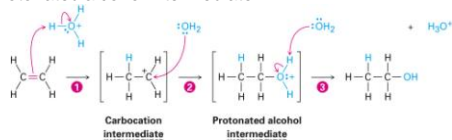
- a fast exergonic reaction (small G^\ddagger , negative G°);
- a slow exergonic reaction (large G^\ddagger , negative G°);
- a fast endergonic reaction (small G^\ddagger , small positive G°);
- a slow endergonic reaction (large G^\ddagger , positive G°).



6.10 Describing a Reaction: Intermediates

Reaction Intermediate

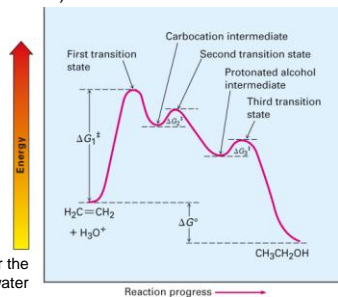
- A species that is formed during the course of a multi-step reaction but is not final product
- More stable than transition states
- May or may not be stable enough to isolate
- The hydration of ethylene proceeds through two reaction intermediates, a carbocation intermediate and a protonated alcohol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



Describing a Reaction: Intermediates

Each step in a multi-step process can be considered separately (each step has ΔG^\ddagger and ΔG°)

Overall ΔG° of reaction is the energy difference between initial reactants and final products



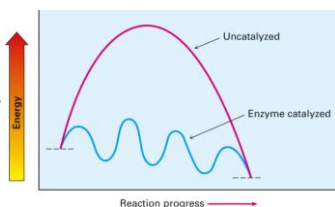
Overall energy diagram for the reaction of ethylene with water

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

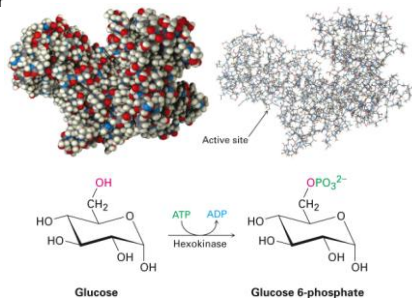
- A large, globular protein molecule that contains a protected pocket called an *active site*

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

A Comparison between Biological Reactions and Laboratory Reactions

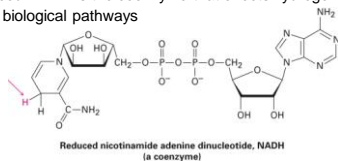
Models of hexokinase in space-filling and wire-frame formats, showing the cleft that contains the active site where substrate binding and catalysis occur



A Comparison between Biological Reactions and Laboratory Reactions

Reagent size

- Laboratory reactions
 - Usually small and simple (such as Br_2 , HCl , NaBH_4 , CrO_3)
- 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



A Comparison between Biological Reactions and Laboratory Reactions



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)

A Comparison between Biological Reactions and Laboratory Reactions



TABLE 6.4

A Comparison of Typical Laboratory and Biological Reactions

	Laboratory reaction	Biological reaction
Solvent	Organic liquid, such as ether	Aqueous environment in cells
Temperature	Wide range; -80 to 150 °C	Temperature of organism
Catalyst	Either none or very simple	Large, complex enzymes needed
Reagent size	Usually small and simple	Relatively complex coenzymes
Specificity	Little specificity for substrate	Very high specificity for substrate
