



4

Chemical Kinetics

Goal

To understand the physical factors that determine reaction rates.

Objectives

After this chapter, you should be able to

- describe the factors that determine reaction rates.
- identify nucleophiles, electrophiles, and leaving groups.
- use arrow pushing to represent reaction mechanisms.
- draw and interpret reaction energy diagrams.
- draw transition states.
- write a rate expression for a simple chemical reaction and explain how the rate is related to ΔG^\ddagger .

Thermodynamics teaches us about the energetics and favorability of reactions but not whether they are fast or slow. For that we need to understand **kinetics**, the study of rates of reactions and the physical factors that influence those rates. Reactions that are thermodynamically favorable can take millions of years to reach equilibrium. In fact, the velocities of favorable reactions vary over about 15 orders of magnitude. The speed of reactions is critically important for living systems, which must ensure that they occur rapidly enough to be consistent with the rates at which cells grow and divide. Consequently, cells have evolved strategies to accelerate reactions so that they occur on a biological timescale. In this chapter, we will examine the factors that influence reaction rates, and in later chapters, we will explore the strategies that living systems use to increase and control those rates.

Reaction rates are determined by the frequency, orientation, and energy with which molecules collide

Every molecule has a characteristic size, shape, and distribution of electrons. As such, a reaction between two molecules can only occur when they physically contact each other; they must collide to react. The rate at which molecules react with each other to form a product (or deplete a reactant) is determined by the frequency with which they collide, the probability that they collide in an orientation that allows the reaction to occur, and the probability that the molecules that collide do so with enough energy for the reaction to take place.

$$\text{reaction rate} = \text{concentration of reactant molecules} \times \text{velocity of reactant molecules} \times \text{cross-sectional area of reactant molecules} \times \text{probability that molecules collide in the right orientation} \times \text{probability that molecules collide with enough energy to react}$$

Figure 1 Reaction rates depend on multiple factors

Not every collision leads to a reaction, but the rate of a reaction depends on the frequency with which reactant molecules collide, which is influenced by the concentration of the reactants (Figure 1). The larger the number of reactant molecules that are confined within a given volume, the greater the probability of their colliding. The rate of reaction is also influenced by the velocity of the reactant molecules, which again influences the frequency of collisions. The rate of reaction also depends on the cross-sectional areas of the reactant molecules, a property determined by the shapes and sizes of the molecules involved in the reaction.

Reactions can only occur between parts of molecules that are capable of forming new bonds; therefore, the rate of a reaction also depends on the probability that individual molecules collide in the appropriate orientation to react (Figure 1). However, colliding in a productive orientation is not sufficient. Individual molecules also need to collide with enough energy to react. As we have seen, breaking bonds requires energy, and because all reactions involve the breaking of bonds, an input of energy is required to overcome this energetic barrier (or “threshold of free energy”, as we will see below). Even for a favorable reaction in which the products are lower in energy than the reactants, some amount of energy is necessary to overcome this energetic barrier and initiate the bond-breaking reaction.

The rate of a reaction is influenced by temperature, an insight that was formalized by the scientist Svante Arrhenius in the late 1800’s. Temperature increases the frequency with which molecules collide by influencing the velocity of the reactant molecules and the proportion of molecules with sufficient energy to overcome the energetic barrier to react (see Box 1). Therefore, temperature influences two of the five factors in Figure 1, namely the velocity of reactant molecules and the probability that molecules collide with enough energy to react.

To better understand how the five factors influence the rate of reactions, we need to understand how reactions proceed, that is, the sequence of events or pathway by which reactions proceed. The reaction pathway can be represented in two complementary ways: by a molecular mechanism and by a reaction energy diagram. These representations allow us to derive rules that predict reaction outcomes.

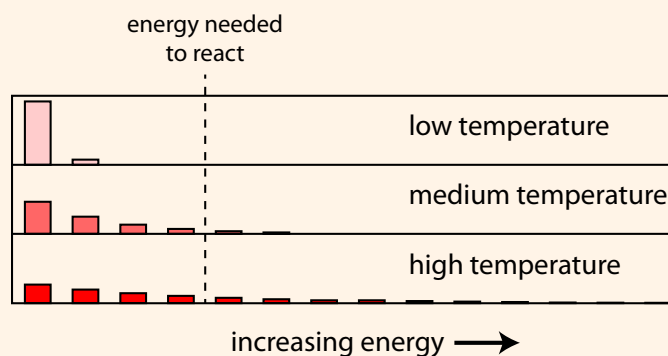
An arrow-pushing formalism describes reaction mechanisms

Put simply, a chemical reaction is a rearrangement of valence electrons that leads to the cleavage and/or formation of bonds. The specific electron movements associated with each reaction are described by the **reaction mechanism**. Reaction mechanisms show where electrons originate in the reactant and where they ultimately reside in the product. This is represented

Box 1 The Boltzmann distribution

Energy is not distributed evenly among molecules in a system, and if you were to examine each individual molecule at any moment, you would find that some molecules have more energy than others. As a consequence, some molecules may have enough energy to react upon colliding, whereas others may not. As temperature increases, however, so does the probability that molecules in the system have enough energy to react.

The Boltzmann distribution describes the probability that a molecule will occupy a specific energy level. Shown below are three simple plots of Boltzmann distributions at different temperatures. Each bar represents the probability of a molecule at that temperature having the indicated energy level (the taller the bar, the higher the probability). Bars farther to the right indicate higher energy levels.



As you can see, at the “low” temperature it is likely that the molecule is at a low energy level, and there is little chance that it has enough energy to react (as indicated by the dotted line). As temperature increases, however, so does the probability that the molecule has enough energy to react. At the “medium” temperature, there is a small chance that a molecule has enough energy to react. At the “high” temperature, the likelihood of a molecule possessing enough energy to react is much higher.

graphically using a formalized system called **arrow pushing** in which the movement of electrons is diagrammed using a series of curved arrows. Arrow pushing diagrams adhere to the following rules:

1. Each arrow represents the movement of one *pair* of valence electrons.
2. Each arrow begins where the electrons originate (either a lone pair of electrons or a bond) and ends where the electrons are going (either an atom or a bond).
3. An arrow that *starts* at an atom represents the movement of a lone pair of electrons.
4. An arrow that *starts* at the center of a bond represents the breaking of that bond.
5. An arrow that *ends* at an atom represents the formation of a new covalent bond or a new lone pair.
6. An arrow that *ends* at a bond represents the addition of a bond to form a double (or triple) bond.

Applying the rules of arrow pushing so that they become second nature requires practice. Box 2 shows examples of mechanisms that are described by individual arrows. Use arrow pushing to draw the reactions shown in the Boxes and then tackle the practice problems.

Box 2 Interpreting the arrow-pushing formalism

Interpretation	Generic Example	Molecular Example
An arrow pointing from a single bond to an atom means that the bond breaks and a lone pair forms on the target atom.	$A-B \longrightarrow A^+ :B^-$	$H-\ddot{Cl}: \longrightarrow H^+ :\ddot{Cl}^-$
An arrow pointing from a lone pair to an atom means that the lone pair electrons form a new bond to the target atom.	$^-B: \longrightarrow A^+ \longrightarrow A-B$	$:\ddot{Cl}^- \longrightarrow H^+ \longrightarrow H-\ddot{Cl}: $
An arrow pointing from a double or triple bond to an atom means that <i>one</i> of the bonds breaks, and those electrons form a new lone pair on the target atom.	$A=B \longrightarrow A^+ -B^-$	$H-\ddot{O}=C-H \longrightarrow H-\ddot{O}^- -C^+ -H$
An arrow pointing from a lone pair to a bond means the lone pair electrons are used to increase the bond order of the target bond (e.g., a single bond becomes a double bond).	$^+A-B^- \longrightarrow A=B$	$H-\ddot{O}^- -C^+ -H \longrightarrow H-\ddot{O}=C-H$

As we saw in Chapter 2, many molecules contain atoms that carry full or partial charges. Reactions between molecules (small molecules or functional groups on macromolecules) often occur when the electrons from an atom carrying a negative charge (full or partial) forms a bond with an atom in another molecule that carries a positive charge (full or partial). For reactions in which a bond is formed between atoms that were not previously bonded, the electron-rich atom from which the electrons originate is known as the **nucleophile**, and the electron-deficient atom is known as the **electrophile** (Figure 2). As their names imply, nucleophiles are attracted to nuclei and electrophiles are attracted to electrons (*philos* being Greek for love).

Another concept that is important in understanding reaction mechanisms is the **leaving group**. This term is used to describe an atom or portion of a molecule that separates from a molecule as a result of a bond breaking during the course of a reaction. Leaving groups always take both electrons from the broken bond with them as they depart.

Figure 2 Nucleophile, electrophile, and leaving group describe specific atoms in reaction mechanisms

(A) Shown is a generic reaction of a nucleophile with an electrophile (*top*) and a specific example involving a reaction between hydroxide and a hydrogen ion (*bottom*). (B) Shown is a generic reaction involving a leaving group (*top*) and a specific example involving a reaction between amide (NH_2^-) and water (*bottom*).

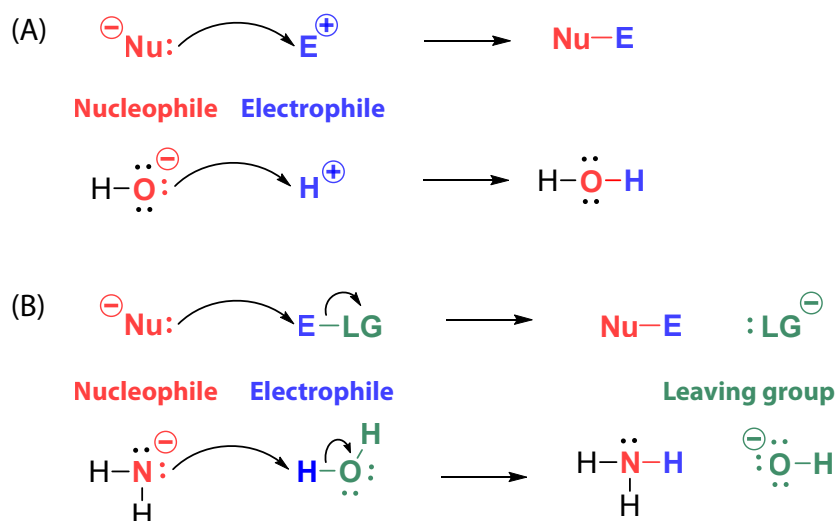
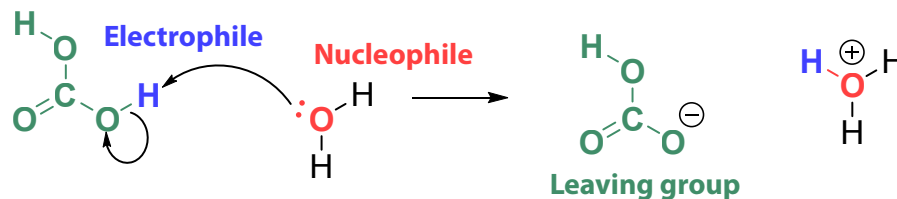


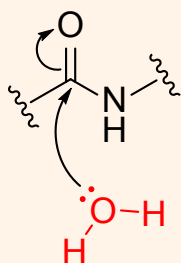
Figure 3 Using arrow pushing to describe the mechanism of carbonic acid dissociation



Let us apply these concepts to the reaction of carbonic acid (H_2CO_3) with water to yield bicarbonate and hydronium ion, as discussed in Chapter 3. The reaction mechanism is described using two arrows (Figure 3). One arrow points from the lone pair of electrons on the water molecule to a hydrogen atom on carbonic acid. This arrow conveys the idea that the oxygen from water is using its lone-pair electrons to form a bond with the hydrogen atom. Since hydrogen can only form one bond at a time, it must break its existing bond to oxygen. Breaking the existing O-H bond is represented by the second arrow, which points from the O-H bond in carbonic acid to the oxygen atom in the same O-H bond. This arrow conveys the idea that the O-H bond is breaking and that the electrons from that bond are being retained by carbonic acid's oxygen as a lone pair. In this reaction, the oxygen in water is a nucleophile and the hydrogen in carbonic acid is an electrophile, as the oxygen in water is using its electrons to form a new bond and hydrogen is the recipient of those electrons. Finally, the remainder of the carbonic acid molecule (HCO_3^-) serves as a leaving group, as it results from the cleavage of the carbonic acid O-H bond; it takes a pair of electrons with it.

Breakout

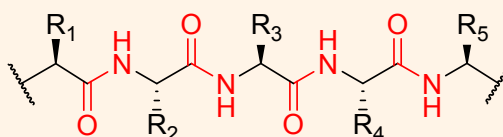
Shown below is the first step of peptide bond hydrolysis, a reaction used by all living systems to break down proteins. Which atom is the electrophile?



- A. The red oxygen.
- B. The black oxygen.
- C. Nitrogen.
- D. Carbon.
- E. The red hydrogen.

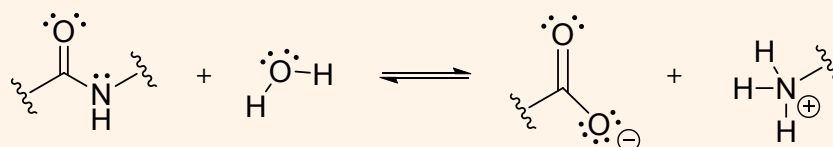
Box 3 Applying arrow pushing to peptide bond hydrolysis

As we will see in Chapter 5 and as shown below, proteins are made from individual amino acid monomers that are connected by peptide bonds (colored in red). The side chains of each amino acid are represented as " R_1 ", " R_2 ", etc.

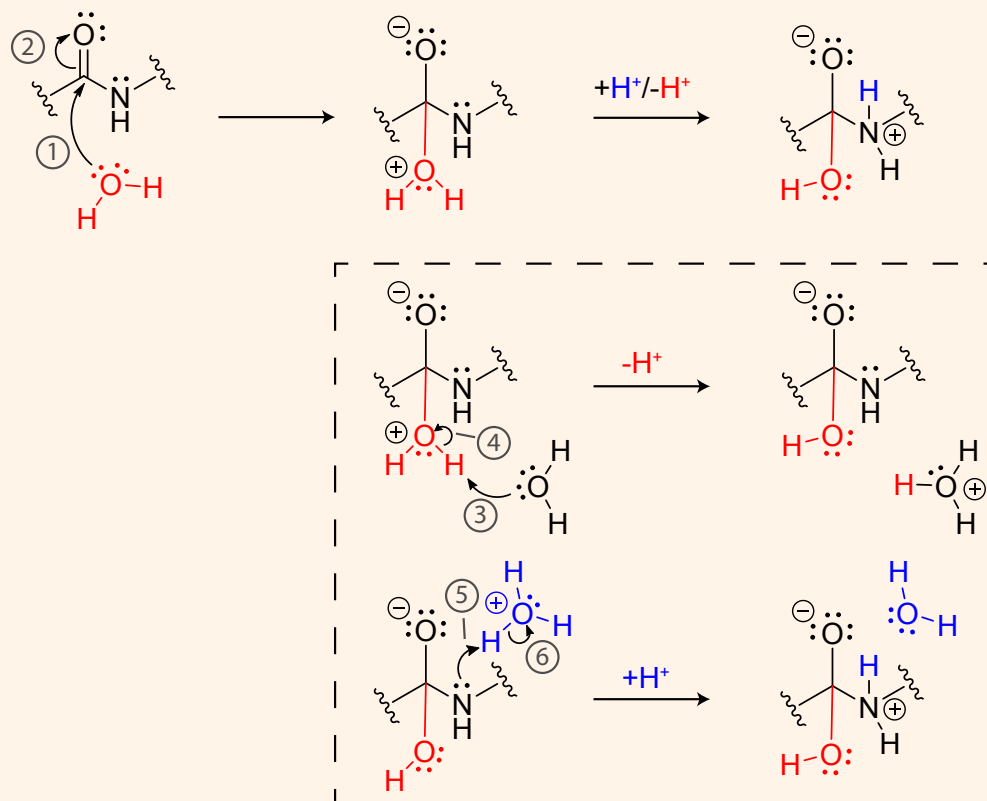


Proteins are broken down to amino acids in cells by hydrolysis. **Hydrolysis** is any reaction in which water reacts with another species to break an existing bond in that species while forming a new bond to the oxygen

of the water molecule. Peptide bond hydrolysis is a reaction that occurs when water reacts with the carbon atom of a peptide bond, resulting in the cleavage of the carbon-nitrogen bond and the formation of a new carbon-oxygen bond:



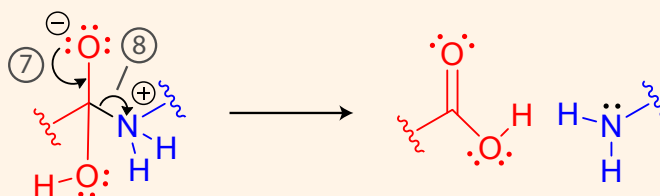
Peptide bond hydrolysis is a multi-step reaction, and as such, we can think of peptide bond hydrolysis as a series of sequential chemical reactions, each with its own arrow-pushing mechanism. In the first step (below), the carbon of the peptide bond (shown in black) and the oxygen of the water molecule (shown in red) react because the carbon is electron-deficient (electrophilic) and the oxygen is electron-rich (nucleophilic). The curly arrows show the movement of electrons as the reaction proceeds. Arrow 1 shows that a lone pair on the oxygen of water is forming a new bond between the oxygen and the carbon. Carbon can only form a maximum of four bonds, so in order to form a new bond with oxygen, one of carbon's other bonds must break. Arrow 2 shows that one of the carbon-oxygen bonds is breaking and forming a lone pair on the oxygen (black). Note that the differences between the starting material and product are only those indicated by the arrows. Note also that the arrow-pushing mechanism involves a chain of curly arrows in which the atom at the beginning of the chain, the oxygen in the water molecule, acquires a positive charge by sharing a lone pair of electrons, and the atom at the end of the chain, the oxygen in the peptide bond, gains a negative charge by acquiring the two electrons it previously shared with the carbon.



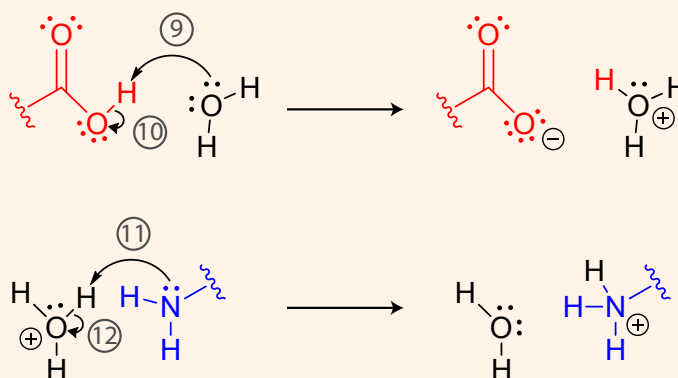
In the next step a proton is transferred from one atom in the molecule to another. You might imagine a direct mechanism for this transfer in which the lone pair on nitrogen reacts with the proton attached to positively charged oxygen shown in red. It is important to remember, however, that these molecules are bathed in water; consequently, this phase of the reaction occurs as a combination of the two reactions shown in the dashed box. In the first reaction, a lone pair from an oxygen atom in a water molecule forms a bond to the hydrogen atom (Arrow 3). Since hydrogen can only form one bond at a time, its other bond must break in order for the new bond to form (Arrow 4). In the second reaction, a lone pair from the nitrogen atom

forms a bond to a hydronium ion (Arrow 5). The bond that previously existed between this hydrogen and the oxygen in hydronium breaks, and the electrons from that bond form a new lone pair on the blue oxygen atom (Arrow 6).

The next step involves the cleavage of the carbon-nitrogen bond. Note that the atoms in this mechanism have been recolored for clarity. Arrow 7 shows that a lone pair on the negatively charged oxygen forms a bond to the carbon atom, creating a double bond. Arrow 8 shows that the carbon-nitrogen bond breaks, with the electrons from that bond forming a new lone pair on nitrogen. At this point hydrolysis of the peptide bond has occurred, but in the cell the reaction is not yet complete.



Completion involves another proton transfer. As before, this transfer occurs via two reactions involving water, as shown below. In one reaction, a lone pair from an oxygen atom in a water molecule forms a new bond to the red hydrogen atom (Arrow 9), and the bond between the red hydrogen and red oxygen breaks, with the electrons from the bond forming a new lone pair on oxygen (Arrow 10). In the other reaction, the lone pair on nitrogen forms a new bond with a hydrogen atom in hydronium (Arrow 11), and the bond between the hydrogen and oxygen in hydronium breaks, with the electrons from the bond forming a new lone pair on oxygen (Arrow 12). These final proton transfers are energetically highly favorable and drive the entire sequence of events that culminate in the hydrolysis of the peptide bond.

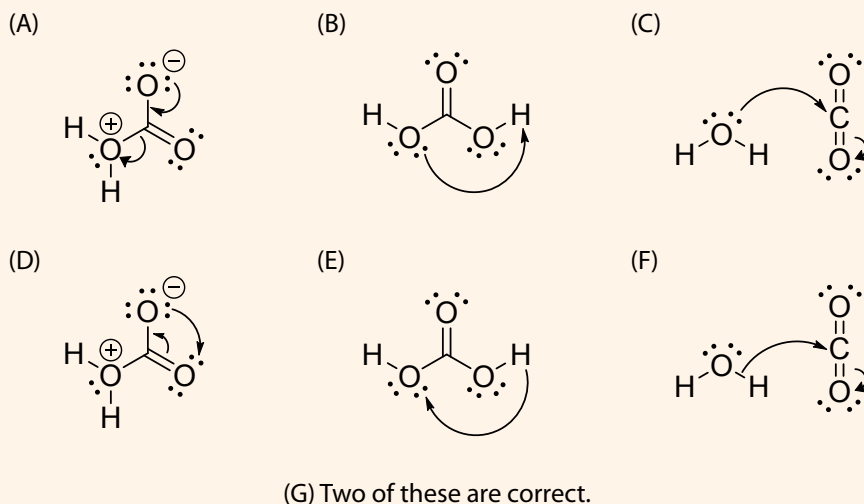
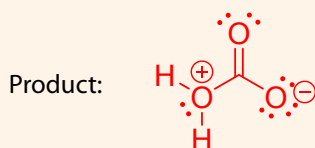


Reaction energy diagrams describe changes in Gibbs free energy as reactants are converted to products

Another way to represent a reaction mechanism is to depict the change in Gibbs free energy as individual reactant molecules react to produce a single set of products. The horizontal axis in the **reaction energy diagram** is the **reaction coordinate**, which is a measure of the extent to which the reactant molecule(s) has proceeded through energetically distinct steps in its conversion into a product molecule(s). The reaction coordinate should not be confused with the time it takes for the reaction to proceed or with progressive changes in the composition of a mixture of many molecules. Molecules are represented in reaction energy diagrams as points whose vertical positions indicate their Gibbs free energy, with more-stable (lower-energy) species closer to the bottom of the diagram. The difference between

Breakout

Which arrow-pushing mechanism would produce the product shown in red?



the left-most and right-most points along the vertical axis equals $\Delta G^\circ_{\text{rxn}}$ (the difference in free energy under standard conditions between reactants and products; Chapter 3). Figure 4 shows a reaction energy diagram representing a thermodynamically favorable reaction (i.e., $\Delta G^\circ_{\text{rxn}}$ is negative, as depicted in red) because the free energy of the products is lower than that of the reactants. Notice that the free energy does not simply decrease along the reaction coordinate as starting material is converted to product. Rather, the free energy (G°) increases to a maximum, representing the **transition state** (to be discussed below), before decreasing to a level below that of the reactants. Bonds are being broken and formed as the reaction proceeds, with different molecules appearing and disappearing during progress along

Figure 4 Using a reaction energy diagram to represent changes in free energy in a reaction pathway

Shown is the reaction diagram for a thermodynamically favorable reaction. The difference in energy between the reactants and products equals $\Delta G^\circ_{\text{rxn}}$, and since the reaction is favorable, the products are at a lower energy than the reactants. The highest energy state over the course of the reaction pathway is the transition state, and the energy difference between the transition state and the reactants is represented by ΔG^\ddagger .

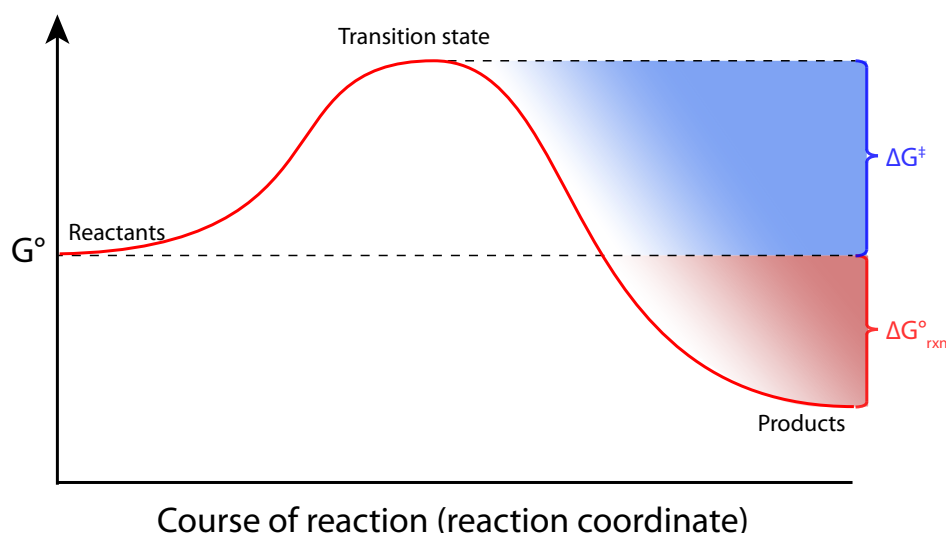
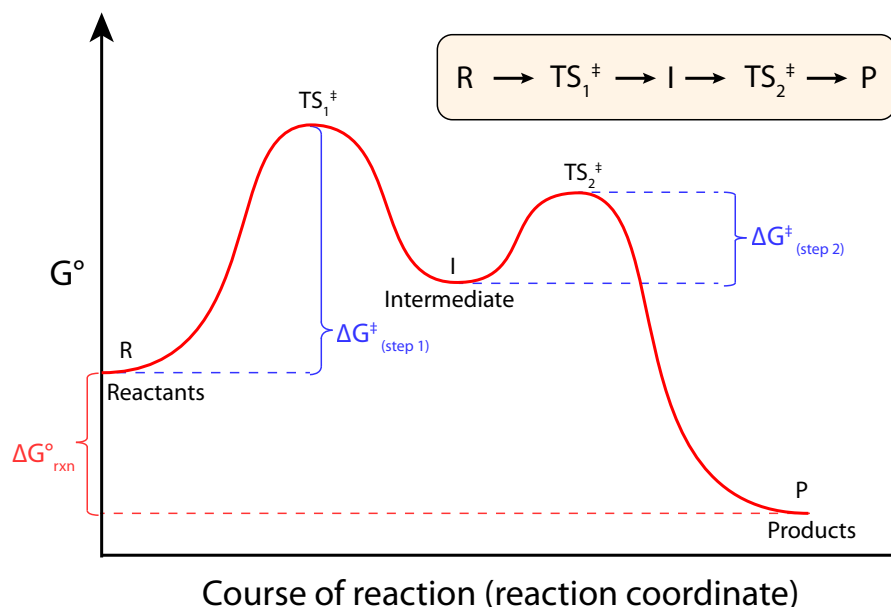


Figure 5 Each step of a multi-step reaction features a transition state

Shown is the reaction energy diagram for a two-step reaction. Each step of the reaction corresponds to a particular transition state and has an accompanying value of ΔG^\ddagger . Multi-step reactions also feature intermediates, which are represented as local minima on the reaction energy diagram.



the horizontal axis. These molecules correspond to species that can be depicted with arrow pushing, as discussed above.

As we have seen, the transition state (TS) represents the maximal energy state along the reaction coordinate. Reactants must attain a threshold of free energy in order to form the transition state and proceed to products. Transition states exist for only an infinitesimal period of time, and as such, they cannot be isolated or observed directly. Despite this, we can make inferences about their structures by analyzing a reaction's mechanism. We think about transition states as the state in which bonds are in the midst of breaking and forming; transition states contain partially formed and partially broken bonds. Valence electrons in the transition state have undergone some form of rearrangement, which required an input of energy. Since its energy is at a maximum, the transition state can spontaneously proceed to products (or revert to reactants) without any additional input of energy. The double dagger (\ddagger) symbol is a descriptor that refers to the transition state and to the change in Gibbs free energy between the reactants and the transition state (ΔG^\ddagger) (blue in Figure 4). ΔG^\ddagger is the “energetic barrier” we mentioned earlier in this chapter.

Some reaction mechanisms proceed through more than one transition state (e.g., TS1[‡] and TS2[‡] in Figure 5). Such multi-step reactions display a local energy maximum for each transition state. In addition, they contain local energy minima that represent intermediates in the reaction. In contrast to transition states, intermediates contain fully formed bonds and can sometimes exist long enough to be observed and characterized.

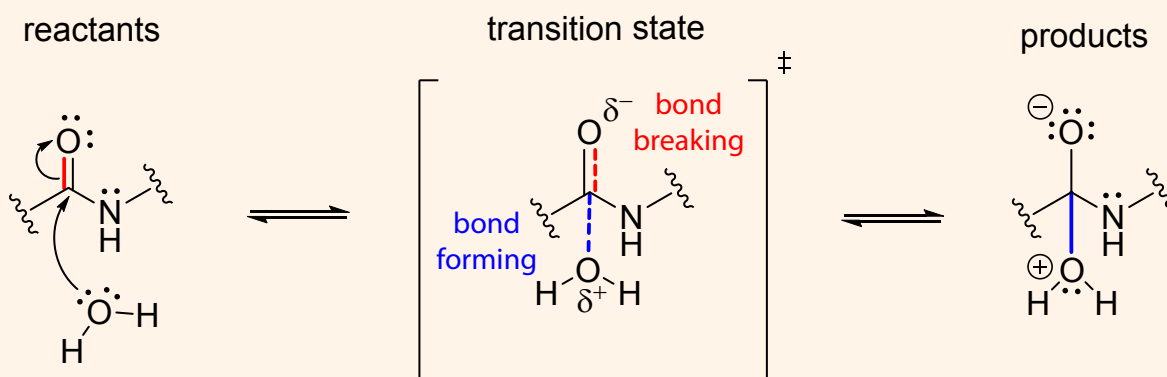
The difference in Gibbs free energy between the reactants and the transition state, ΔG^\ddagger , is *always positive*. If you imagine that at any given moment in a reaction the reactants and the transition state are in a kind of equilibrium, you can apply the concepts from Chapter 3 about free energy differences and equilibrium concentrations of reactants and products to think about how the free energy differences between the reactants and the transition state relate to the concentrations of the two species. Because ΔG^\ddagger is always positive, the concentration of the transition state is always lower than

Box 4 Transition states can be represented as chemical structures

Although transition states cannot be observed directly, their structures can be inferred from the reaction mechanism. To draw a transition state from an arrow-pushing mechanism:

1. Inventory the bonds that are being made and broken in one reaction step.
2. Draw a single structure in which each of these changing bonds is partially formed. Represent partially formed bonds using dashed lines. You should find that the dashed lines in your drawing form a continuous path from one atom to another in the transition state; they are never discontinuous, and they never branch.
3. Assign formal charges in which partially formed bonds represent half a bond, and use δ^- and δ^+ notation to represent “half” charges. You will notice that atoms whose formal charges change during the reaction will have these partial charges. For example, an atom that is negative in the reactant and neutral in the product would be partially negative (δ^-) in the transition state. This is intuitive given that transition states represent species that exist in between the reactant and product. Overall charge is conserved between the reactant, product, and transition state, so the “half” charges in the transition state will always total the overall charge found in both the reactant and product.
4. Lastly, structures of transition states must be denoted as such by drawing them within brackets and marking them with the double dagger symbol (\ddagger).

The transition state for the first step of peptide bond hydrolysis is shown below. The bond that breaks during the reaction is shown in red and the bond that forms is shown in blue.



the concentration of the reactants. The greater the ΔG^\ddagger , the lower the concentration of the transition state.

Since chemical reactions proceed to product by going through the transition state, the rate of a chemical reaction is directly proportional to the concentration of the transition state at any given moment. Thus, the reaction energy diagram is a powerful tool for analyzing chemical reactions because it allows us to assess a reaction's rate as well as its thermodynamic favorability. Reactions with very large ΔG^\ddagger values are said to have high energy barriers or activation energies, exemplifying the idea that the reaction occurs slowly because a lot of energy is needed for the reactants to transform into the transition state. In other words, a reaction with a highly favorable (highly negative) $\Delta G^\circ_{\text{rxn}}$ can be extremely slow if ΔG^\ddagger for the transition state is very high.

$$\begin{array}{l}
 \text{reaction rate} = \text{concentration of reactant molecules} \times \text{velocity of reactant molecules} \times \text{cross-sectional area of reactant molecules} \times \text{probability that molecules collide in the right orientation} \times \text{probability that molecules collide with enough energy to react} \\
 \text{reaction rate} = \text{concentration of reactant molecules} \times \text{rate constant (k)}
 \end{array}$$

Figure 6 The rate constant accounts for all factors affecting rate other than reactant concentration

Reaction rate is determined by reactant concentrations and the rate constant

We are now ready to describe the rate of a reaction in terms of reactant concentrations and a rate constant. We can express the rate of a single-step reaction that proceeds via a single transition state as follows:

$$\text{rate} = k [R_1][R_2]$$

Where $[R_1]$ and $[R_2]$ are the concentrations of reactants R_1 and R_2 and k is the **rate constant**. The rate constant is a term that describes all of the factors other than reactant concentrations that affect the rate of a reaction (Figure 6).

The rate constant is related to ΔG^\ddagger according to the **Arrhenius equation** (shown below as a proportionality) in which e is the base for the natural logarithm (≈ 2.718), R is the gas constant, and T is the temperature in Kelvin:

$$k \propto e^{\frac{-\Delta G^\ddagger}{RT}}$$

We draw two important conclusions from this relationship. First, the rate constant is inversely related to ΔG^\ddagger ; as ΔG^\ddagger becomes larger, the rate constant becomes smaller. We can understand this relationship intuitively, as large values of ΔG^\ddagger are associated with transition states that are difficult to attain (Figure 7). The second conclusion is that the rate constant varies with temperature.

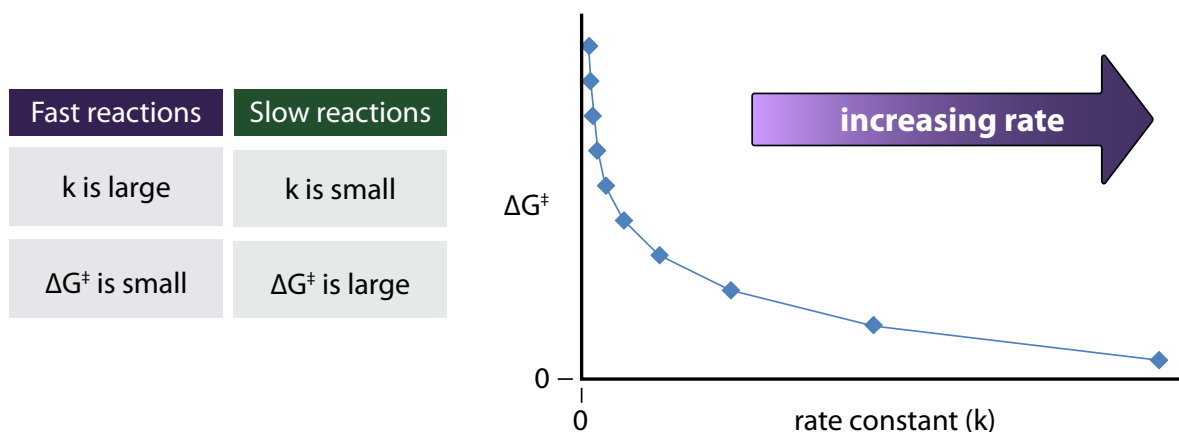


Figure 7 The rate constant k and ΔG^\ddagger correlate with reaction rate

Figure 8 K_{eq} equals the ratio of the forward and reverse rate constants

Shown is the derivation for the relationship between K_{eq} and the forward and reverse rate constants. If we begin with a single-step reaction whose equilibrium constant equals the ratio of product to reactant (*line 1*), we can write expressions for the forward and reverse reaction rates (*line 2*). When the reaction is at equilibrium, we know that the forward and reverse reaction rates are equal, allowing us to set the rate expressions from line 2 equal to one another (*line 3*). Then we can divide both sides of the equation by reactant concentration and the reverse rate constant (*line 4*). Since the reaction is at equilibrium, we can substitute K_{eq} for the ratio of product concentration over reactant concentration in line 4 to produce line 5.

$$\begin{array}{ll}
 (1) & \text{reactant} \xrightleftharpoons[k_{\text{reverse}}]{k_{\text{forward}}} \text{product} \quad K_{eq} = \frac{[\text{product}]}{[\text{reactant}]} \\
 (2) & \begin{array}{l} \text{rate}_{\text{forward}} = k_{\text{forward}} [\text{reactant}] \\ \text{rate}_{\text{reverse}} = k_{\text{reverse}} [\text{product}] \end{array} \\
 (3) & k_{\text{forward}} [\text{reactant}] = k_{\text{reverse}} [\text{product}] \\
 (4) & \frac{k_{\text{forward}}}{k_{\text{reverse}}} = \frac{[\text{product}]}{[\text{reactant}]} \\
 (5) & \frac{k_{\text{forward}}}{k_{\text{reverse}}} = K_{eq}
 \end{array}$$

Finally, the rate constants for the forward and reverse reactions of a one-step process can be related to the equilibrium constant by a simple equation, which is derived in Figure 8:

$$K_{eq} = \frac{k_{\text{forward}}}{k_{\text{reverse}}}$$

Simply put, the equilibrium constant is directly related to the ratio of the forward and reverse rate constants. For example, if the forward rate constant is larger than the reverse rate constant, the equilibrium constant will be greater than one. [Note that the notations used to denote the equilibrium constant (K_{eq}) and the rate constant (k) can be confused with each other. As a rule, the equilibrium constant is written with a capital letter K , and the rate constant is written with a lower-case letter k .]

Favorable reactions with slow kinetics are common in living systems

Thermodynamically favorable reactions that occur very slowly are common in living systems. For example, as we considered in Chapter 3, the cleavage of ATP is highly favorable but extremely slow. Living systems solve this problem by using protein catalysts known as enzymes to accelerate specific reactions. As we shall see in later chapters, these enzymes accelerate reactions by lowering the energy of the transition state, thus reducing ΔG^\ddagger . The use of enzymes to accelerate slow reaction rates has an important advantage for living systems; it enables cells to effectively turn reactions on and off by controlling when and where specific enzymes are present and active. The use of thermodynamically favorable but kinetically slow

reactions enables cells to harness free energy to drive growth, metabolism, movement, propagation, and other features of living systems in a highly controlled and controllable manner.

Summary

The rate of a reaction is determined by the frequency with which reactant molecules collide and the probability that those molecules collide in the correct orientation and with enough energy to react. The rate at which molecules collide is influenced by reactant concentration, molecular velocity, and reactant cross-sectional area. Temperature increases both molecular velocity (and thus collision frequency) and the probability that molecules collide with enough energy to react; consequently, reactions proceed more rapidly at higher temperatures.

Arrow pushing is a formalism that is used to visually represent the movement of valence electrons that occurs during a reaction (i.e., the reaction mechanism). Generally speaking, arrow-pushing diagrams use curved arrows to represent the movement of electron pairs, with arrows beginning at the source of the electrons (i.e., a lone pair or bond) and pointing toward the destination of those electrons (i.e., an atom or a bond). Nucleophile refers to an atom that donates a pair of electrons to form a bond to another atom to which it was not previously bonded. Similarly, electrophile refers to the atom to which a nucleophile forms a new bond. Generally speaking, nucleophiles carry negative charge (full or partial), and electrophiles carry positive charge (full or partial). The formation of a new bond between a nucleophile and electrophile often displaces a group of atoms, called a leaving group, which separates from the electrophile and forms a second molecule.

A reaction mechanism can also be described using reaction energy diagrams in which Gibbs free energy is plotted versus the reaction coordinate. The reaction coordinate is a hypothetical measure of the progress of a reaction involving one set of reactant molecules as they transform into product molecules. The energy difference between the products and reactants on a reaction energy diagram is defined as $\Delta G^\circ_{\text{rxn}}$. Each step of a reaction is indicated by a local maximum on the reaction energy diagram. These maxima represent the energy of the transition state, which is the highest-energy species that forms during each step of a reaction. Bonds are breaking and forming during the transition state, and as such, we show bonds that are changing using dashed lines in graphical representations of transition-state structures. Because bonds break during the transition state, essentially all reactions have an activation energy, ΔG^\ddagger , which describes the amount of energy needed to initiate the reaction. ΔG^\ddagger is the difference in energy between the reactants and the transition state. Since energy is always absorbed during the formation of the transition state, the sign of ΔG^\ddagger is always positive.

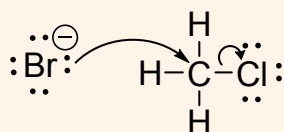
The rate of a reaction can be described quantitatively using a rate expression that expresses reaction rate in terms of reactant concentrations. Rate expressions contain a rate constant k that is inversely related to ΔG^\ddagger ; therefore, reactions with large rate constants have small ΔG^\ddagger values. Reactions with

large rate constants have low activation energy barriers and are likely to proceed quickly. Conversely, reactions with small rate constants have high activation energy barriers and are likely to proceed slowly. Living systems use protein catalysts known as enzymes to accelerate and control the rates of thermodynamically favorable reactions with small rate constants.

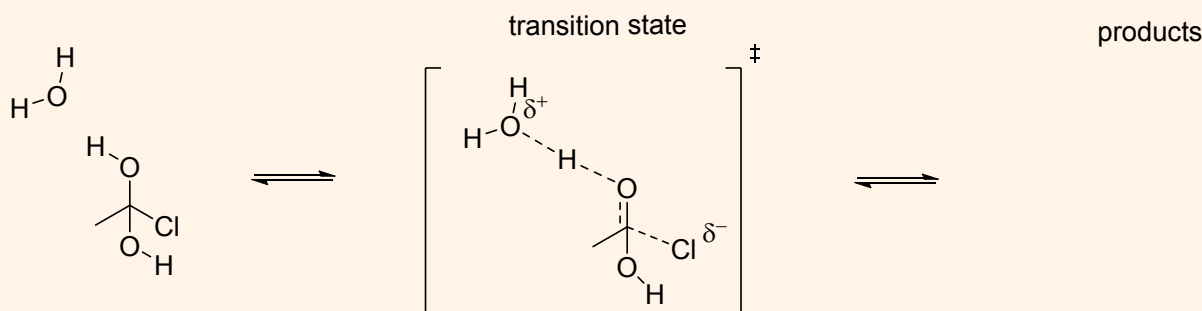
Practice problems

- Which of the following are reasons why the reaction rate increases with temperature? Select all that apply.
 - Collisions between molecules become more frequent.
 - The reaction cross section increases.
 - Molecules are more likely to collide with enough energy to react.

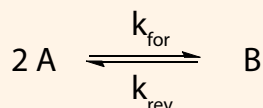
- Consider the arrow-pushing mechanism shown below:



- Which atom is the electrophile? Which atom is the nucleophile?
 - What are the products of this reaction?
- The reactants and transition state for a particular reaction are shown below. Draw (a) the arrow-pushing mechanism that leads from the reactants to the indicated transition state and (b) the structures of the products that result from the reaction.



- Consider the hypothetical one-step reaction shown below.



- Write an equation to express the rate of the forward reaction in terms of reactant concentrations.
- The equilibrium constant for this reaction is measured to be 0.001. Which value is larger, k_{for} or k_{rev} ?

Solutions to practice problems

Question 1:

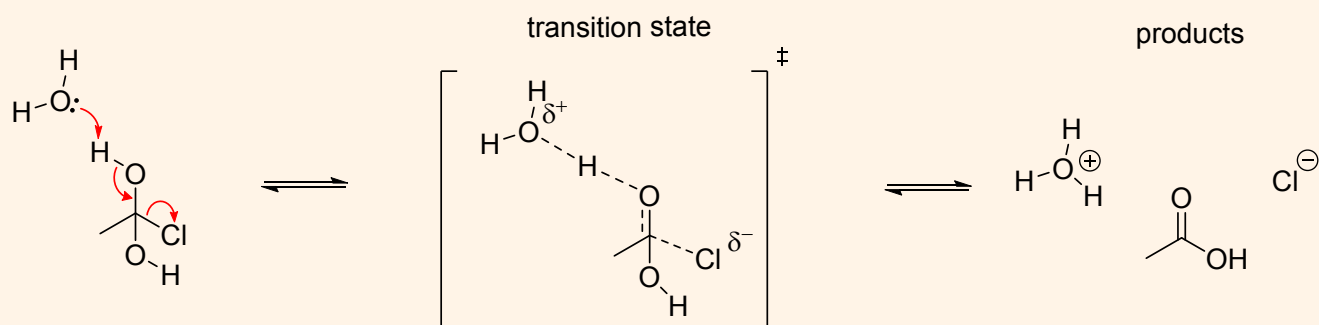
Choices i & iii

Question 2:

a. Carbon; bromine.

b. Methylbromide (CH_3Br) and chloride (Cl^-).

Question 3:



Question 4:

a. Forward rate = $k_{\text{for}} [\text{A}]^2$.

b. The value of k_{rev} is larger.