

## Chapter 5

### The Mechanics of Reactions

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In the preceding chapter finding the acidity constant ( $K_a$ ) for an acid in a table did not always satisfy us. If we wanted to know why one acid or base was stronger than another, we carefully analyzed the structures of the molecules. This allowed us not only to satisfy our curiosity, but also to predict the relative acidities or basicities of molecules with unknown  $K_a$  values. Likewise, simply knowing the reactants and products of chemical reactions is not enough. We want to know why and how a reaction occurs in order to understand the reaction and to predict the effects of changing conditions on a related reaction. Before we learn any more reactions in later chapters, this chapter will give us tools for understanding why and how reactions work.

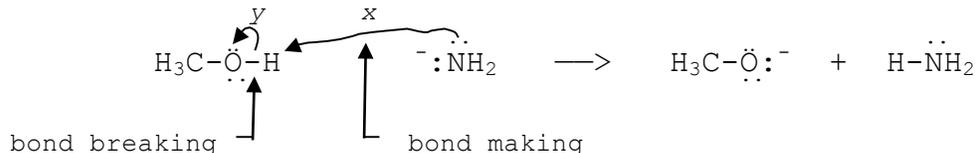
#### 5.1 Mechanisms and Electron Arrows

In the preceding chapter we began to understand organic reactions by discerning the attraction between electrophiles and nucleophiles. The next step is to understand the idea of a **reaction mechanism**. A mechanism is a sequential picture of the making and breaking of bonds during a reaction. Some reactions are **concerted** in that they occur in concert by one-step mechanisms, where all bond making and breaking occur simultaneously. Acid-base reactions typify these. Other reactions occur by multistep mechanisms, where some bonds are made or broken before others.

Although organic reactions are countless, the types of mechanisms are relatively few. Mechanisms provide patterns for reactions. They help us see the similarities of related reactions and organize these reactions into types. Furthermore, they allow us to successfully predict the outcome of a new reaction by analogy to a similar reaction with a similar mechanism. Thus, mechanisms deter rote memorization of reactions as unrelated facts.

Organic chemists like to clarify mechanisms with **electron arrows**. This device is sometimes called a curved arrow because its curved shape distinguishes it from straight reaction arrows, which point from reactants to products in a chemical equation. Electron arrows show the flow of electron pairs making and breaking bonds during reactions. (Another kind of electron arrow that shows the flow of a single electron will be used in Chapter 23.) They also suggest attractions between electron pairs and atoms in the reactants. Consider the mechanism of an acid-

base reaction:



Electron arrow x shows a lone pair on nitrogen forming a  $\sigma$  bond to a hydrogen. Because hydrogen normally accommodates only one bond, electron arrow y shows the hydrogen-oxygen bond breaking and releasing the bonding pair onto the oxygen. Because the bonds are made and broken simultaneously, this reaction is concerted with a one-step mechanism.

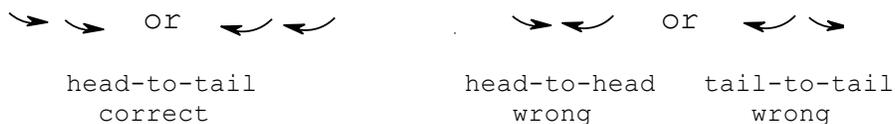
Let us now apply four rules of electron arrows to the above mechanism.

1. *Every electron arrow begins at an electron pair, either bonding or nonbonding.* If the step involves a nucleophile and electrophile, the first arrow begins at the *nucleophilic* electron pair. Our example correctly shows each of the two arrows beginning at an electron pair. Moreover, the first arrow, arrow x, begins at the nucleophilic lone pair on nitrogen. Thus properly drawing electron arrows reinforces identification of the nucleophile.

2. *The electron pair tracked by an electron arrow remains attached to an atom.* In our example, we infer from arrow x that nitrogen accompanies the lone pair in its bond formation. Arrow y suggests that the electron pair of the breaking bond remains with oxygen throughout the reaction.

3. *Every electron arrow ends at an atom, not at a bond.* If the step involves a nucleophile and electrophile, the first arrow ends at the *electrophilic* atom. This rule confirms the tendency of electrons, including nucleophilic pairs, to seek nuclei of atoms. Our example's two arrows both end at atoms. Furthermore, the first arrow, arrow x, ends at the electrophilic hydrogen. (Although electron pairs seek atoms, some chemists unfortunately end some electron arrows at bonds, not atoms.)

4. *In a series of arrows for one mechanistic step, every succeeding arrow begins by the atom where the preceding arrow ends.* In other words, a second arrow picks up where the first arrow leaves off. So successive arrows lie head-to-tail, never head-to-head or tail-to-tail:



Our example's arrows lie properly, head-to-tail.

If followed precisely and thoughtfully, these rules make writing electron arrows and mechanisms easier and more meaningful.

Section 1.5 included three rules for electron arrows generating resonance forms, which resemble the rules 1, 3, and 4 here. For example:

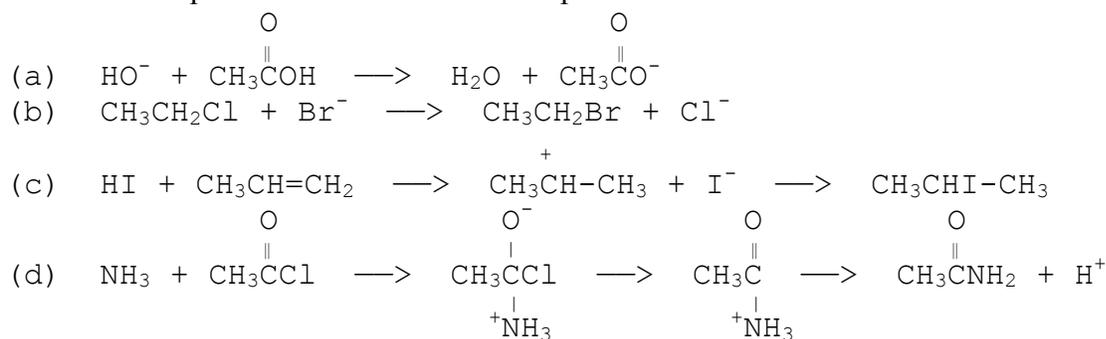


Note how each arrow begins at an electron pair and ends at an atom. Also, the two arrows meet head to tail. Of course, electrons do not actually move between fictitious resonance forms. (Don't

confuse the electron flow of a mechanism with the artificial electron bookkeeping of interconverting resonance forms, despite their similar electron arrows.)

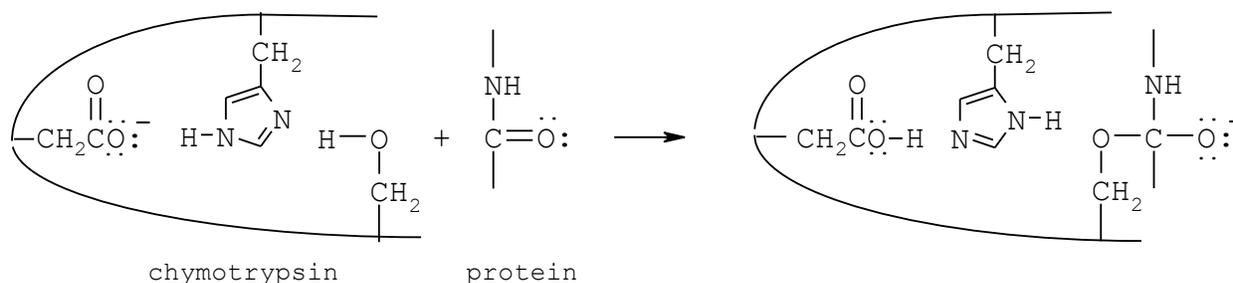
### Puzzle 5.1

Show suitable electron arrows for the following mechanistic steps. Also indicate the electrophilic and the nucleophilic atoms for each first step.



### Puzzle 5.2

Chymotrypsin is a digestive, intestinal enzyme that catalyzes the hydrolysis of other proteins. Show the electron arrows for one mechanistic step of the hydrolysis:



## 5.2 Equilibrium and Free Energy

How far will a reaction go before it yields no more product? Its equilibrium provides the answer. Already in the preceding chapter we have applied the concept of equilibrium to reactions of acids and bases. In establishing an acid-base or other equilibrium, the predominant reaction runs from the more reactive molecules toward the more stable, less energetic molecules. These less energetic molecules predominate at greater concentrations after equilibrium is reached.

Yet various kinds of energy exist. What kind of energy determines the predominant direction of an equilibrium? We often use **enthalpy,  $H$** , a kind of molecular potential energy, to measure the energy of molecules. The net reactive energy of a molecule, however, includes another factor: **entropy,  $S$** . Entropy measures chaos or disorder. The more freedom of movement available to a molecule, the greater is its entropy. For example, pentane with so many possible conformations has more freedom of movement and entropy than does cyclopentane with far fewer conformations. Also, in a reaction where two molecules unite to produce only one molecule, the two reactant molecules have more freedom of movement and more entropy than the one product

molecule.

The molecule's net energy that is free for reaction is called **free energy,  $G$** . This combines enthalpy and entropy according to the equation:

$$G = H - T \cdot S$$

where  $T$  is temperature in kelvins. For a reaction at constant temperature involving reactants and products in standard states (1 atm pressure, 1 M concentration):

$$\Delta G^\circ = \Delta H^\circ - T\Delta S^\circ$$

where:

$$\begin{aligned} \Delta G^\circ &= G^\circ_{\text{products}} - G^\circ_{\text{reactants}} \\ \Delta H^\circ &= H^\circ_{\text{products}} - H^\circ_{\text{reactants}} \\ \Delta S^\circ &= S^\circ_{\text{products}} - S^\circ_{\text{reactants}} \end{aligned}$$

Note that these expressions for change all subtract the earlier attribute from the later one.

An equation links free energy change and the equilibrium constant,  $K$ :

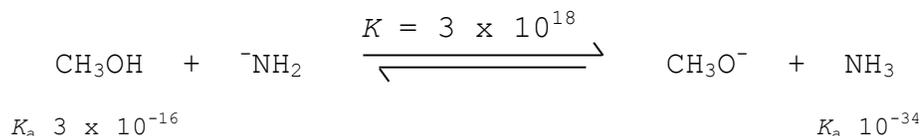
$$\Delta G^\circ = -RT \ln K$$

$R$  is the universal gas constant, 8.31 J/K·mol. Thus if  $\Delta G^\circ$  is positive, then  $\ln K$  is negative,  $K$  is less than one, and the forward reaction is unfavorable. The more positive is  $\Delta G^\circ$ , the more unfavorable is the forward reaction.

**as  $\Delta G^\circ \uparrow$ ,  $K \downarrow$  and extent of forward reaction  $\downarrow$**

In other words, it is unfavorable for products to have more free energy than reactants. This agrees with the intuitive notion that energetically "uphill" reactions are difficult. On the other hand, if  $\Delta G^\circ$  is negative, then  $\ln K$  is positive and  $K$  is more than one. Thus, a favorable forward reaction requires a negative, "downhill"  $\Delta G^\circ$ , with reactants having more free energy than products. In other words, equilibrium yields mostly products only if they are less energetic and more stable, according to the rule of "survival of the weakest" (Section 4.4).

Reconsider the acid-base reaction of Section 5.1:



The  $K_a$  values for the two acids, methanol and ammonia, are  $3 \times 10^{-16}$  and  $10^{-34}$ , respectively. Therefore,  $K = 3 \times 10^{-16}/10^{-34} = 3 \times 10^{18}$ . Evidently the forward reaction goes practically to completion. At 25°C:

$$\begin{aligned} \Delta G^\circ &= -RT \ln K \\ &= (-8.31 \text{ J/K}\cdot\text{mol}) (298 \text{ K}) \ln (3 \times 10^{18}) \\ &= -105,000 \text{ J/mol} = -105 \text{ kJ/mol} \end{aligned}$$

So, in their standard states the reactants have 105 kJ/mol more free energy than do the products, and the products prevail.

We know that a negative  $\Delta G^\circ$  indicates a forward reaction with a favorable equilibrium, but what kinds of enthalpy and entropy changes contribute to a favorable free energy change? According to an earlier equation:

$$\Delta G^\circ = \Delta H^\circ - T\Delta S^\circ$$

a *negative*  $\Delta H^\circ$  helps  $\Delta G^\circ$  become *negative*. In other words, an exothermic, "downhill" enthalpy helps the reaction forward.

**as  $\Delta H^\circ \downarrow$ ,  $\Delta G^\circ \downarrow$  and extent of forward reaction  $\uparrow$**

Mathematically and chemically a negative  $\Delta H^\circ$  is neither necessary nor sufficient for a favorable, negative  $\Delta G^\circ$ . Yet, many successful reactions have negative  $\Delta H^\circ$  values.

Also according to the last equation, a *positive*  $\Delta S^\circ$  supports a *negative*, favorable  $\Delta G^\circ$  ( $T$ , the absolute temperature, is always positive). Entropy increases during many successful reactions, although a positive  $\Delta S^\circ$  is neither sufficient nor necessary for a negative  $\Delta G^\circ$ . The greater  $\Delta S^\circ$ , the smaller and more favorable is  $\Delta G^\circ$ .

**as  $\Delta S^\circ \uparrow$ ,  $\Delta G^\circ \downarrow$  and extent of forward reaction  $\uparrow$**

This reaction has a favorable, positive  $\Delta S^\circ$ :



The three product molecules have more freedom than the two reactant molecules.

Table 5.1 summarizes the desirable and the necessary conditions for a reaction favored by equilibrium.

Table 5.1 Desirable and Necessary Conditions for a Favorable Equilibrium

Desirable conditions		Necessary conditions	
$\Delta H^\circ$	$\Delta S^\circ$	$\Delta G^\circ$	$K$
< 0	> 0	< 0	> 1

Usually  $\Delta H^\circ$  greatly exceeds  $T\Delta S^\circ$  in magnitude. Consider this reaction at 25°C:



$\Delta H^\circ$  is found to be -137 kJ/mol, whereas  $T\Delta S^\circ$  is only -36 kJ/mol. Because the negative, unfavorable  $T\Delta S^\circ$  is relatively small, the negative, favorable  $\Delta H^\circ$  provides a negative, favorable  $\Delta G^\circ$ :

$$\begin{aligned}\Delta G^\circ &= \Delta H^\circ - T\Delta S^\circ \\ &= -137 - (-36) = -101 \text{ kJ/mol}\end{aligned}$$

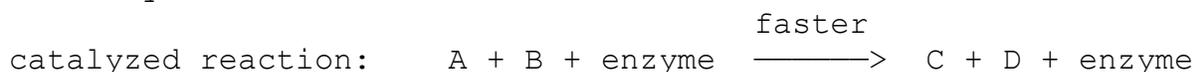
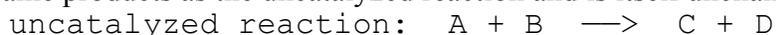
Therefore,  $\Delta G^\circ$  and  $\Delta H^\circ$  often have the same sign. Consequently, instead of dealing with the more complex, less intuitive concept of free energy, we may sometimes in later chapters simplify our estimates of favorable reactions by considering  $\Delta H^\circ$  alone.

### Puzzle 5.3

- (a) At 25°C what  $\Delta G^\circ$  value would give a  $K$  value of 10?  
 (b) At 25°C what  $\Delta G^\circ$  value would give a  $K$  value of 100?  
 (c) At 25°C what  $\Delta G^\circ$  value would give a  $K$  value of 0.10?

### Puzzle 5.4

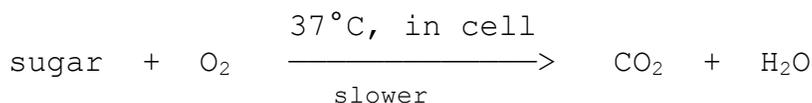
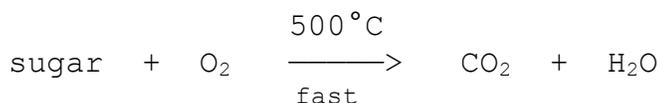
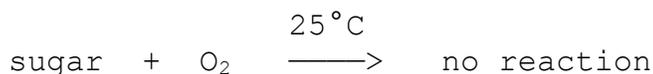
An enzyme is a biological catalyst. Like other catalysts it accelerates the reaction, but gives the same products as the uncatalyzed reaction and is itself unchanged by the end of the reaction.



- (a) Compare  $\Delta H^\circ$  in the uncatalyzed and catalyzed reactions.  
 (b) Compare  $\Delta S^\circ$  in the uncatalyzed and catalyzed reactions.  
 (c) Compare  $\Delta G^\circ$  in the uncatalyzed and catalyzed reactions at the same temperature.  
 (d) Compare  $K$  in the uncatalyzed and catalyzed reactions at the same temperature.

## 5.3 Kinetics

If reactants have more free energy than products, do they necessarily yield lots of product? In other words, does a favorable equilibrium ensure a successful reaction? We have learned how an equilibrium limits the extent of reaction. Now we must consider the rate of reaction, that is, how quickly equilibrium is reached. For example, sugar and oxygen can coexist forever without reaction.

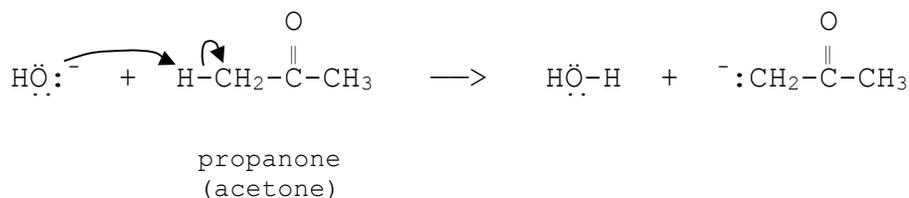


Yet, with a 500°C flame the two chemicals react quickly to produce carbon dioxide and water. In our bodies the two reactants produce the same products but more slowly and at lower temperature.

The equilibria in all three cases are similar and very favorable, but their reaction rates differ greatly. Such reaction rates are explained by the study of **kinetics**.

### 5.3A Collision Theory

Two molecules must collide in order to react with each other. Therefore, as the concentrations of reacting molecules increase, so do the frequency of collision and the reaction rate. Consider the acid-base reaction:



As in any such simple, one-step mechanisms, the reaction rate is proportional to the concentrations of the two reactants, according to the rate equation:

$$\text{rate} = k[\text{HO}^-][\text{propanone}]$$

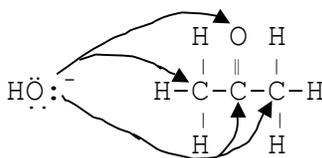
where  $k$  is the proportionality factor, called the **rate constant**. If either reactant concentration is doubled, the rate doubles. If both reactant concentrations are doubled, the rate quadruples.

A balanced reaction equation does not indicate the rate equation. Only kinetics experiments or knowledge of the mechanism (itself derived from kinetics experiments) can lead to the rate equation. For reactions with a more complex, multistep mechanism, the rate equation may or may not include all the reactant concentrations. If the rate equation does not include all reactants, the mechanism must be multistep (e.g., see Sections 6.5A and 7.2B.). If it does include all reactants, one cannot conclude the number of mechanistic steps.

In general:

**reaction rate  $\uparrow$  as  $k \uparrow$  and (often) as [reactant]  $\uparrow$**

The collision of reactant molecules does not necessarily lead to reaction. The molecules must collide with the *proper orientation* so that particular bonds can be made and broken with optimum geometry. In the acid-base reaction above, the oxygen of the hydroxide ion must collide directly with one of the six, equivalent hydrogens of the ketone, not with its carbons or oxygen:



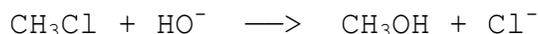
collisions useless for the acid-base reaction

Furthermore, even if the reactant molecules collide with the proper orientation, they may not react. The above reactant molecules must break a bond between hydrogen and carbon. Overcoming any bond or attractive force requires energy. (The energy released from partially forming a bond does not fully compensate for the energy needed to begin breaking a bond.) Thus,

the reactant molecules must bring at least a minimum amount of kinetic energy to their collision to overcome this energy barrier. The reactants are like two cars that must collide at a certain minimum speed to damage their bumpers. Otherwise they harmlessly bump off each other.

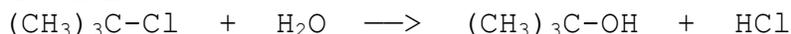
### Puzzle 5.5

(a) Consider the reaction:



The reaction rate is directly proportional to  $[\text{CH}_3\text{Cl}]$  and to  $[\text{HO}^-]$ . Write a rate equation for the reaction. Is it possible to decide if the reaction has a one-step mechanism?

(b) Consider the reaction:



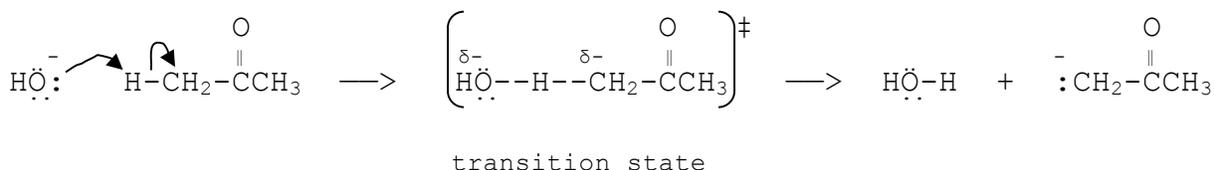
The reaction rate is directly proportional to  $[\text{Me}_3\text{CCl}]$  but is not affected by  $[\text{H}_2\text{O}]$ . Write a rate equation for the reaction. Is it possible to decide if the reaction has a one-step mechanism?

### Puzzle 5.6

Enzymes are huge polymer catalysts. Typically they bind the reactants of their reactions. In terms of collision theory, how could this binding accelerate a reaction?

## 5.3B The Transition State and Energy-Reaction Diagrams

The stage at which the reacting molecules are at their highest free energy before reaching products is called the **transition state** (also known as **activated complex**). This state of minimum stability is depicted below for the acid-base reaction of the preceding section:



The brackets with the double dagger symbol ( $\ddagger$ ) denote the transition state. A depiction of a transition state also features a broken line ( $\cdots$ ), indicating a partial bond being made or broken. The partial charges suggest decreasing charge on the oxygen and increasing charge on the carbon.

An energy-reaction diagram helps us visualize the changes in energy during reaction. Figure 5.1 illustrates the diagram for our present acid-base reaction follows:

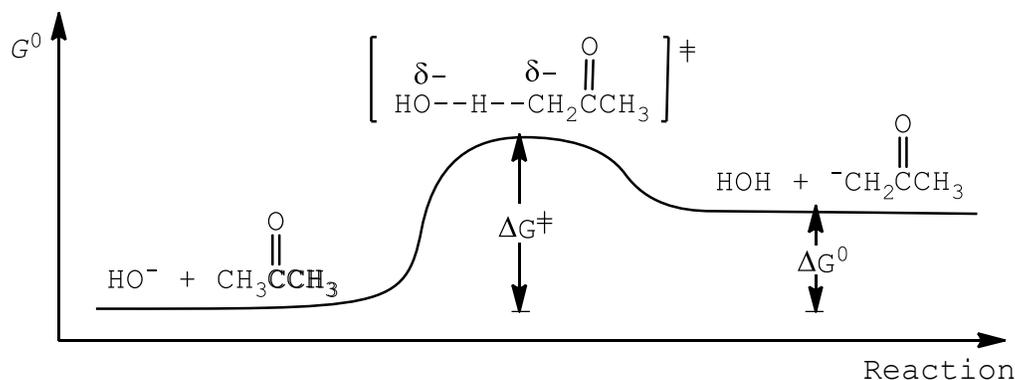
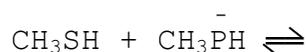


Figure 5.1 Energy-reaction diagram for the reaction of hydroxide ion with propanone.

Here the y-axis represents free energy. The x-axis roughly marks the progress of the reaction. Atop the energy barrier between reactants and products sits the transition state (TS). The height of this barrier, that is, the energy difference between reactants and transition state, is the **free energy of activation** ( $\Delta G^\ddagger$ ) always a positive number. This equals the minimum amount of kinetic energy that the reactants must have to react. The transition state can then quickly proceed "downhill" to products (although it may also return to reactants). A positive value of  $\Delta G^\circ$  reflects the overall "uphill", unfavorable nature of this forward reaction. This is not surprising because Table 4.1 shows that water is a stronger acid than propanone, with  $K_a$  values of  $2 \times 10^{-16}$  and  $10^{-20}$ , respectively.

Puzzle 5.7

Consider the acid-base reaction:



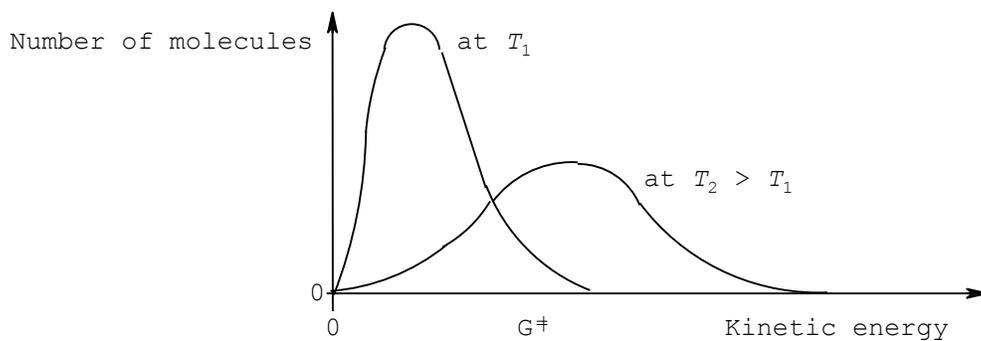
- Draw the products.
- Draw the transition state.
- Are the reactants or the products stronger? Explain in terms of structures.
- Draw an energy-reaction diagram, reflecting the appropriate sign of  $\Delta G^\circ$ .
- Is the free energy of activation positive for both the forward and reverse reactions?

Puzzle 5.8

Draw the transition state for the mechanistic step of Puzzle 5.2, Section 5.1.

### 5.3C Effects of Temperature and Free Energy of Activation

How does a temperature change affect the rate of reaction? Recall the molecular meaning of temperature: the temperature of a substance measures the average kinetic energy ( $KE$ ) of its molecules. The next figure shows how the kinetic energies of molecules in a sample vary at two temperatures.



kinetic energy distribution of molecules at temperatures of  $T_1$  and  $T_2$

Note that increasing temperature increases the average kinetic energy of the reactant molecules. Because the molecules move faster, they collide more frequently. Moreover, as the temperature increases, more molecules have kinetic energy above  $\Delta G^\ddagger$  and can overcome the activation barrier. For both reasons:

**as  $T \uparrow$ , average  $KE \uparrow$ ,  $k \uparrow$ , and reaction rate  $\uparrow$**

The effect can be quite dramatic. A small increase in temperature can greatly accelerate many reactions.

For two reactions under similar conditions, how does a difference in free energy of activation ( $\Delta G^\ddagger$ ) affect the rate of reaction? The more positive  $\Delta G^\ddagger$  is, the fewer the reactant molecules with enough kinetic energy to overcome the activation barrier. As a result:

**as  $\Delta G^\ddagger \uparrow$ ,  $k \downarrow$  and reaction rate  $\downarrow$**

A catalyst accelerates a reaction by lowering  $\Delta G^\ddagger$  (Section 5.4B).

Thus, the collision theory of reactions explains how various factors affect reaction rate. According to the rate equation, reaction rates depend on concentrations of reactants and on the rate constant,  $k$ . In turn,  $k$  depends on orientation requirements for reactant molecules, temperature, and free energy of activation.

#### Puzzle 5.9

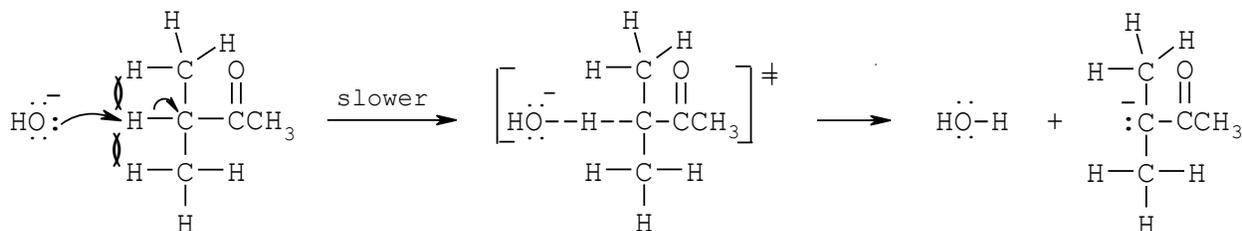
How does each of the following changes affect the rate constant and the rate of a reaction with a one-step mechanism?

- (a) decreasing temperature
- (b) decreasing the concentration of a reactant
- (c) adding a catalyst, which lowers the free energy of activation
- (d) increasing steric hindrance between reactants

#### Puzzle 5.10

Consider a biological reaction catalyzed by an enzyme. Increasing the temperature too much can deform (i.e., denature) the enzyme and cause it to lose catalytic activity. In this case does increasing the temperature necessarily accelerate the reaction? Explain.





sterically hindered

lower  $S_{TS}$ 

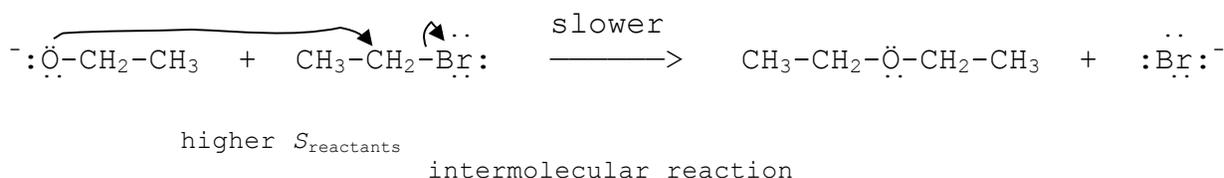
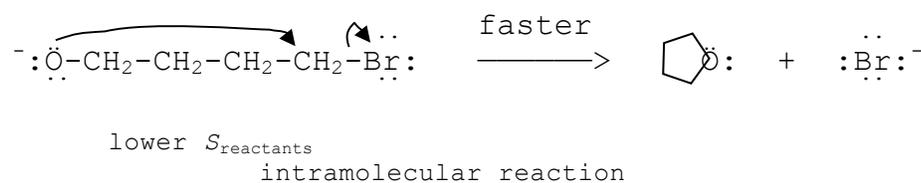
The reaction path for the first reaction is more sterically open and less congested, so the transition state is less ordered with higher entropy. The result is a faster reaction than the second one, where extra methyl groups sterically hinder the approach of the base.

The other way to increase the entropy of activation is to decrease the entropy of the reactants. If the nucleophilic and electrophilic sites are tied together on the same molecule, then they have less freedom and entropy, and are more likely to collide and react. The result is a larger entropy of activation, a smaller free energy of activation, and a faster reaction.

as  $S_{\text{reactants}} \downarrow$ ,  $\Delta S^\ddagger \uparrow$ ,  $\Delta G^\ddagger \downarrow$ , and rate  $\uparrow$

Such a reaction between two reactant sites on the same molecule is an **intramolecular reaction**, in contrast to the usual **intermolecular reaction** between reactant sites on separate molecules.

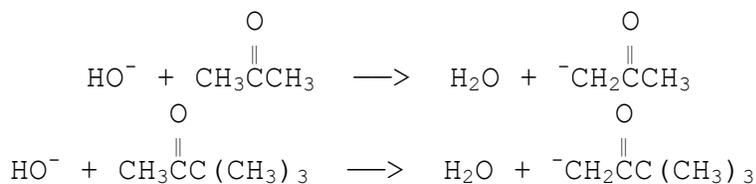
These analogous reactions demonstrate the difference:



In the first, intramolecular reaction the nucleophilic oxide anion and electrophilic alkyl halide reside on the same molecule. Consequently, this reaction has a more favorable, larger entropy of activation than the second, intermolecular reaction, which proceeds more slowly. In general, *its larger entropy of activation accelerates an intramolecular reaction compared to an analogous intermolecular reaction.*

### Puzzle 5.11

In terms of entropy explain why the first reaction below is faster than the second. Hint: it is not a matter of steric hindrance.



## Puzzle 5.12

An enzyme is a biological catalyst that binds reactants into a single complex before they react. In terms of entropy, how does this binding accelerate the reaction?

## 5.4 Equilibrium versus Kinetics

We have seen that equilibrium and kinetics are separate, although related, aspects of a reaction. Equilibrium concerns the final concentrations of reactants and products and depends entirely on their relative free energies, not on the mechanism or transition state. Kinetics concerns the rate at which the reaction reaches equilibrium and depends on the relative free energies of reactants and transition state, not products. Four combinations of favorable or unfavorable equilibrium and kinetics are possible. Two of these combinations we address now.

## 5.4A Unfavorable Equilibrium and Favorable Kinetics

Can a reaction with an unfavorable equilibrium nonetheless reach that equilibrium quickly? Yes, and its energy-reaction diagram would look like Figure 5.1 from Section 5.3B:

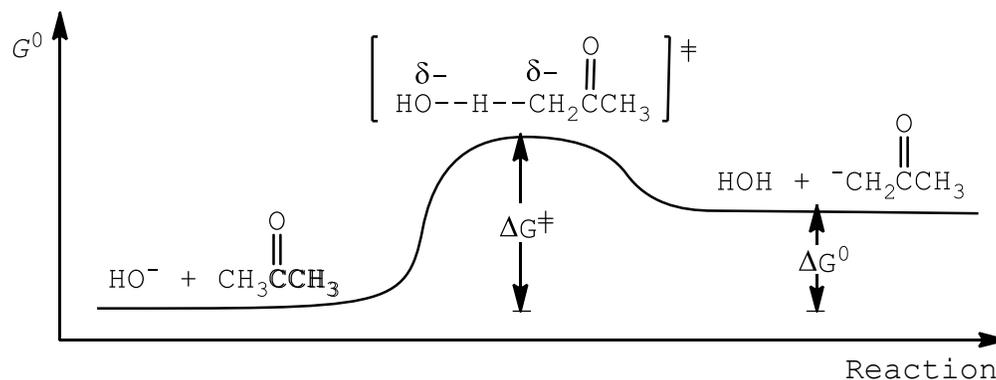


Figure 5.1 Energy-reaction diagram for the reaction of hydroxide ion with propanone.

Note that the products have more energy than the reactants. The resulting positive  $\Delta G^\circ$  hinders the forward reaction.  $K$  is less than 1, and reactant concentrations exceed product concentrations at equilibrium. Nonetheless, as long as reactant concentrations are adequate, this unfavorable equilibrium is reached quickly because of a relatively low activation barrier.

Most acid-base reactions occur very fast, even at room temperature. The typical transition state has little more energy than the more energetic side of the equilibrium. So as long as the equilibrium is not too unfavorable and reactant concentrations are adequate, an acid-base reaction will occur faster than most other reactions. When considering more complex reactions, we must

never overlook the possibility of a very fast acid-base reaction occurring instead.

Puzzle 5.13

Consider the acid-base reaction:



- Draw the structures of the products.
- Are the reactants or the products stronger? Explain in terms of structures.
- Draw an energy-reaction diagram with an appropriate  $\Delta G^\ddagger$  and  $\Delta G^\circ$ .
- How favorable are the equilibrium and the kinetics?

### 5.4B Favorable Equilibrium and Unfavorable Kinetics

Can a reaction with a favorable equilibrium be too slow to occur? Yes, and its energy-reaction diagram would resemble Figure 5.2:

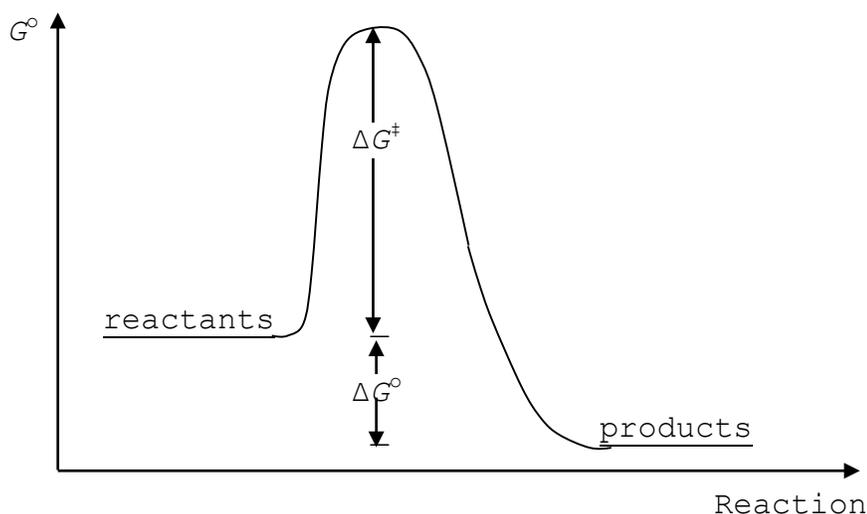


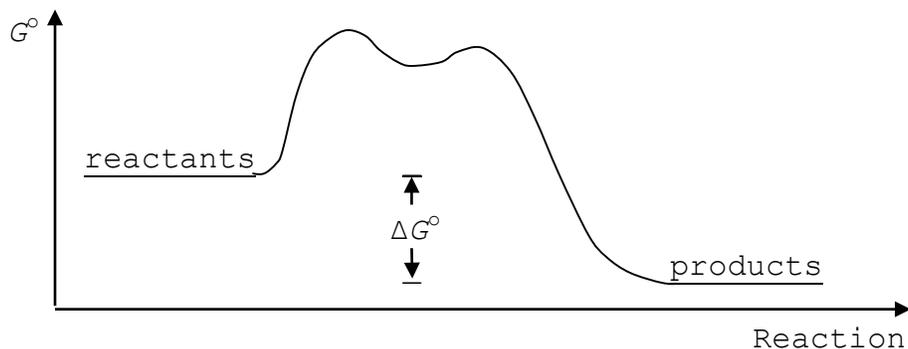
Figure 5.2 The energy-reaction diagram for a very slow reaction with a favorable equilibrium.

The products have less energy than the reactants. So  $\Delta G^\circ$  is negative and favors the forward reaction. This means that  $K$  is greater than 1 and product concentrations exceed reactant concentrations *at equilibrium*. Yet, equilibrium is never reached because of an infinitesimal reaction rate. The large free energy of activation,  $\Delta G^\ddagger$ , prevents reaction at a practical speed at room temperature.

The case of sugar and oxygen, mentioned at the start of Section 5.3, exemplifies such a reaction. At room temperature they do not react. Then how does a flame cause sugar to react? The initial flame raises the temperature high enough so that some molecules can overcome the high activation barrier. By so doing, the reacting molecules produce enough heat in the exothermic reaction ( $\Delta H^\circ < 0$ ) to sustain the high temperatures and the reaction.

How do our bodies sustain this reaction during respiration at a temperature of  $37^\circ\text{C}$ , not much above room temperature? Our cells contain enzymes, which catalyze this and many other reactions. Section 21.6 explains how these enzyme catalysts lower the activation barrier to

facilitate a reaction. The next figure shows a hypothetical case of a catalyzed version of the reaction of Figure 5.2.



energy-reaction diagram for a catalyzed, two-step reaction

In lowering the activation barrier, the typical catalyst increases the number of steps in the mechanism. Here we see a two-step mechanism with two transition states. Note that the catalyst alters the mechanism, but not the energies of reactants and final products. So the position of equilibrium does not change. In effect, the reverse reaction is catalyzed as much as the forward reaction.

#### Puzzle 5.14

Consider the reverse of the reaction illustrated in Figure 5.2.

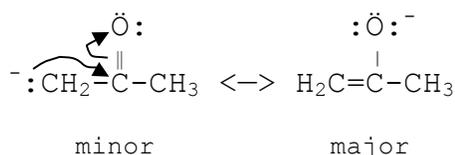
- (a) Draw its energy-reaction diagram. (b) Label its  $\Delta G^\ddagger$  and  $\Delta G^\circ$ .  
 (c) How favorable are the equilibrium and the kinetics?

## 5.5 Reactions with a Two-Step Mechanism

Having briefly considered a hypothetical two-step mechanism involving catalysis, let us carefully examine an actual example of a two-step mechanism.

### 5.5A The Energy-Reaction Diagram for Two-Step Mechanisms

Actually, the acid-base reaction of Figure 5.1 (Section 5.3B) is only the first step of a two-step reaction. The organic anion product of the first step is called an **intermediate**. An intermediate is a temporary, not a final, product. This intermediate is an enolate ion, featured in Chapter 19. Now let us consider its potential for resonance:



The second form is major because its more electronegative oxygen, not its carbon, has the negative

charge (Section 1.5).

This second resonance form suggests a second acid-base reaction with water:

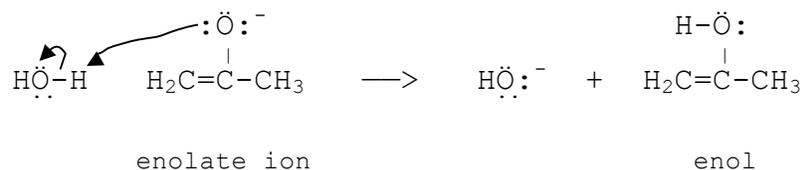


Figure 5.3 combines the consecutive acid-base reactions as a two-step mechanism in a single energy-reaction diagram:

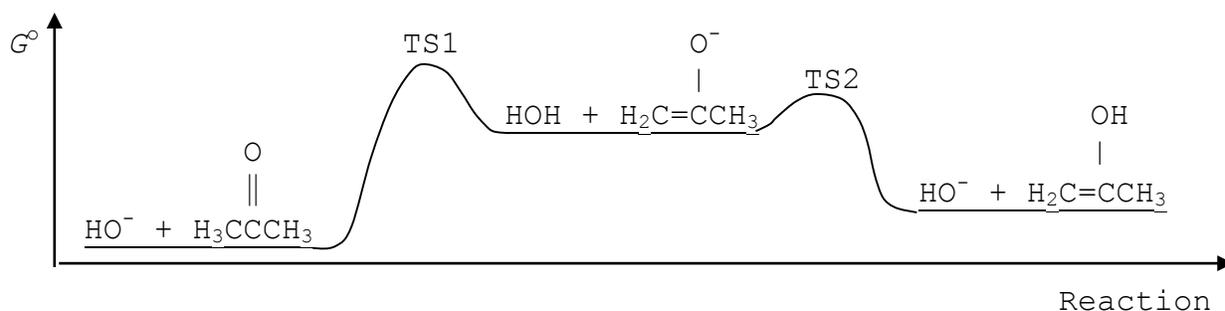
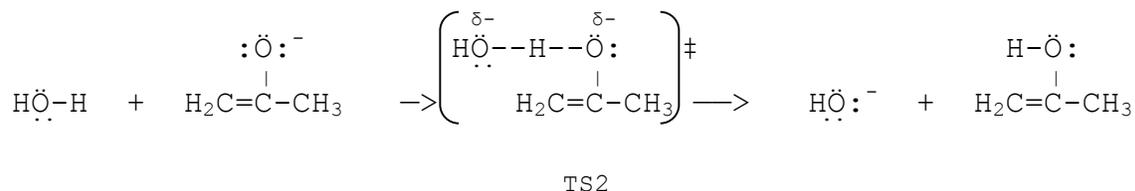


Figure 5.3 Energy-reaction diagram for a two-step mechanism converting propanone to an enol.

Because every step of a mechanism has exactly one activation barrier with one transition state, this two-step mechanism contains two activation barriers and two transition states, TS1 and TS2. To reach the enol (pronounced *ēn' ol*) product, the enolate intermediate and water must cross the second, small activation barrier by way of a TS2:



Note the position of the enolate intermediate in Figure 5.3. An intermediate is not a transition state. A transition state has partial bonds and sits atop an activation hill. An intermediate has no partial bonds and sits in a valley between two activation hills. One intermediate occurs at the end of each mechanistic step except the last.

The overall reaction amounts to an isomerization of propanone to its enol form. Both molecules have the same molecular formula but differ in the position of a hydrogen and a  $\pi$  bond. This isomerization is a succession of two acid-base reactions. Normally such reactions go very fast, as confirmed by the two small activation barriers. Therefore the overall isomerization is very fast. Such fast isomerizations are called **tautomerizations** and two quickly interconverted isomers are called **tautomers**. Most tautomerizations occur by shifting a proton.

Which of the two tautomers has a greater concentration at equilibrium? As always at equilibrium, the more stable, less energetic molecule predominates. Figure 5.3 shows the more stable molecule to be the ketone, propanone. Such tautomers will arise again in Section 9.5B.

## Puzzle 5.15

An oxygen-hydrogen bond is about 50 kJ/mol stronger on average than a carbon-hydrogen bond. Because propanone is more stable than its enol tautomer, is a carbon-carbon  $\pi$  bond or a carbon-oxygen  $\pi$  bond stronger?

## Puzzle 5.16

Glycolysis is the metabolic process that obtains energy by degrading the sugar glucose into smaller molecules. The second step of glycolysis converts glucose-6-phosphate into fructose-6-phosphate:



Show how this conversion can proceed by way of an enol.

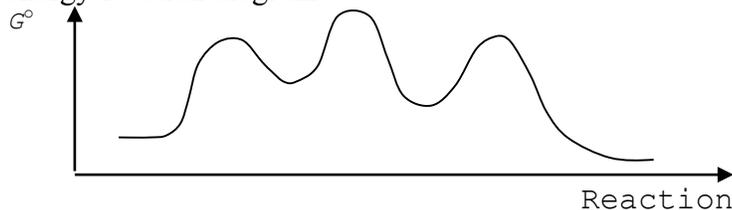
## 5.5B The Rate-Limiting Step

We have already determined that each acid-base reaction step in the above two-step mechanism occurs very fast. But even very fast rates can be fast or slow relative to each other. Which of the above two steps is slower? The first step is slower because its transition state, TS1, has more energy than TS2. The reaction overall can go only as fast as this slower, "bottleneck" step. As fast as the first step creates intermediates, the intermediates become products. Thus, final products are formed just as fast as the rate of the slower step.

The slowest step in a multistep mechanism is called the **rate-limiting** or **rate-determining step** (abbreviated rls or rds, respectively). Wherever the slowest step is in the mechanistic sequence, *the rate of reaction equals the rate of this slowest step, the step with the least stable transition state*. The step with the greatest free energy of activation is not necessarily the slowest. (If two steps are about equally slow, the rate-limiting step can depend on conditions, such as reactant concentrations, solvent, and temperature.)

## Puzzle 5.17

Consider the energy-reaction diagram:



- (a) How many steps does the reaction mechanism have? (b) Which is the rate-limiting step?  
 (c) For the reverse reaction, which is the rate-limiting step?

## Chapter Summary

1. A mechanism, a picture of the making and breaking of bonds during reactions, can be either one-step (i.e., concerted) or multistep.
2. Electron arrows, which show electron pairs making and breaking bonds, are expressed according to four general rules.
3. A reversible reaction seeks an equilibrium position, where less energetic molecules predominate.
4. As the change in free energy ( $\Delta G^\circ$ ) decreases, a reaction proceeds farther and with a larger equilibrium constant ( $K$ ) according to the equation:

$$\Delta G^\circ = -RT \ln K$$

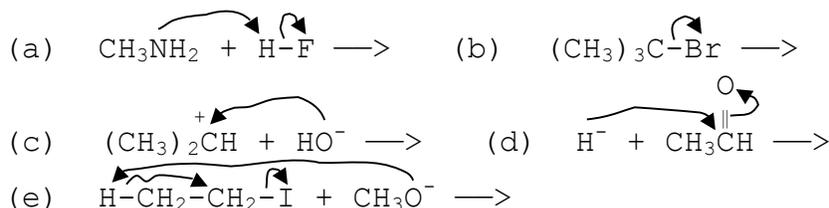
5. A decrease in enthalpy ( $H^\circ$ ) and an increase in entropy ( $S^\circ$ ) lead to a favorable decrease in free energy by the equation:

$$\Delta G^\circ = \Delta H^\circ - T\Delta S^\circ$$

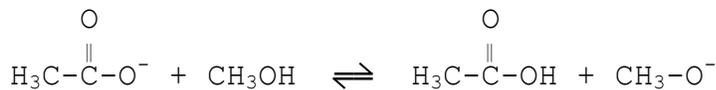
6. By kinetics, the study of reaction rates, we learn how fast a reaction reaches equilibrium.
7. According to the collision theory of reactions, molecules react by colliding with each other with proper orientation and sufficient kinetic energy, equal to the free energy of activation ( $\Delta G^\ddagger$ ).
8. Reacting molecules need kinetic energy to reach the transition state, the structure of highest free energy for molecules reacting during a mechanistic step.
9. An energy-reaction diagram, showing the energies of chemical species as they react, includes one transition state for each step of the mechanism.
10. By giving reacting molecules more kinetic energy, a rise in temperature increases the reaction rate. Also any decrease in free energy of activation, perhaps by addition of a catalyst, increases the reaction rate, by increasing the number of molecules with sufficient kinetic energy.
11. Because of a larger entropy of activation, an intramolecular reaction proceeds faster than an analogous intermolecular reaction. Steric hindrance retards reactions because of a smaller entropy of activation.
12. Equilibrium and kinetics, separate aspects of a reaction, can be favorable or unfavorable in any combination.
13. In multistep mechanisms an intermediate is a temporary product that occurs at the end of every step except the last.
14. The rate-limiting step is the slowest step in a multistep mechanism. Its rate equals the rate of reaction. The rate-limiting step has the transition state with the highest free energy.

## Additional Puzzles

5.18 Indicate the nucleophilic and electrophilic atoms and the products for these mechanisms:

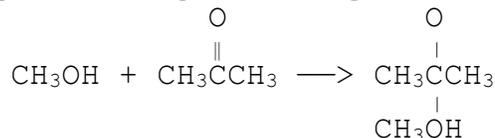


5.19 Consider the equilibrium at 25°C:



- (a) Draw electron arrows for the forward reaction.  
 (b) Aided by Table 4.1, determine  $K$  and  $\Delta G^\circ$  for the forward reaction.  
 (c) Determine  $K$  and  $\Delta G^\circ$  for the reverse reaction.

5.20 Consider a reaction equation missing formal charges:



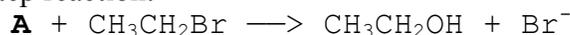
- (a) Supply the formal charges in the product.  
 (b) Indicate the nucleophilic and electrophilic atoms. (c) Draw the electron arrows.  
 (d) Is  $\Delta S^\circ$  positive or negative? Explain. Ignore solvent effects.

5.21 Consider a reaction equation missing formal charges:



- (a) Supply the formal charges in the products.  
 (b) Indicate the nucleophilic and electrophilic atoms.  
 (c) Draw the electron arrows. (d) Draw the transition state.

5.22 Consider the one-step reaction:



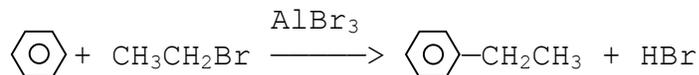
- (a) Identify **A**. (b) Indicate the nucleophilic and electrophilic atoms.  
 (c) Draw the electron arrows.

5.23 Consider the reaction:



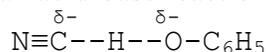
- (a) Which is the nucleophile for the second step? (b) Draw electron arrows for both steps.  
 (c) Draw an energy-reaction diagram for this reaction. Assume that the second step is rate-limiting.

5.24 Consider the reaction:



- (a) If the concentration of benzene or bromoethane doubles, the reaction rate doubles. If the concentration of aluminum bromide doubles, the rate quadruples. Write the rate equation.  
 (b) The aluminum bromide is not consumed in the reaction. What is its function?

5.25 Consider the transition state for an acid-base reaction:



- (a) Write reactants and products appropriate for this transition state. Two correct answers are possible.  
 (b) Aided by Table 4.1, calculate  $K$  for your reaction.  
 (c) Which predominate at equilibrium, reactants or products?  
 (d) Draw the energy reaction diagram for your reaction with a suitable  $\Delta G^\circ$ .

(e) Would the reverse of your reaction have the same transition state?

5.26 How does increasing the temperature affect each of the following:

(a) reaction rate (b) rate constant,  $k$  (c) rate of the reverse reaction (d) equilibrium position

5.27 How does adding a catalyst affect each of the following:

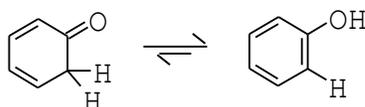
(a) reaction rate (b) rate constant,  $k$  (c) form of the rate equation

(d) rate of the reverse reaction (e) equilibrium position

5.28 (a) Aided by Table 4.1, find a base which reacts with nitric acid,  $\text{HNO}_3$ , with an unfavorable equilibrium and with favorable kinetics.

(b) Draw a suitable energy-reaction diagram.

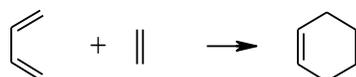
5.29 Consider the tautomerization of the following ketone:



Unlike most enols this enol is more stable than its ketone tautomer. Explain.

5.30 Consider the tautomerization of an enol to propanone by the reverse of the mechanism represented in Figure 5.3 (Section 5.5A). Which is the rate-limiting step?

5.31 Consider the concerted reaction:



(a) Draw the electron arrows.

(b) Is the  $\Delta S^\circ$  positive or negative; favorable or unfavorable? Explain.

(c) A carbon-carbon  $\pi$  bond is weaker than a carbon-carbon  $\sigma$  bond. According to the number of  $\pi$  and  $\sigma$  bonds in the reactants and products, is  $\Delta H^\circ$  positive or negative, favorable or unfavorable? Explain.

(d) From your answers for parts b and c, can you predict if  $K > 1$ ? Explain.

5.32 In each pair of concerted reactions, predict which reaction is faster. Explain.

