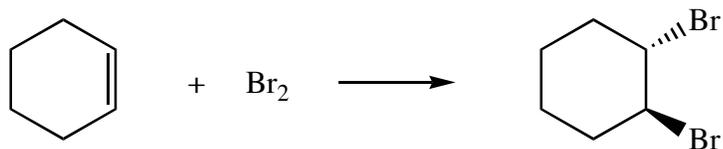


Lecture Notes  
Chem 51A  
S. King

Chapter 6 Understanding Organic Reactions

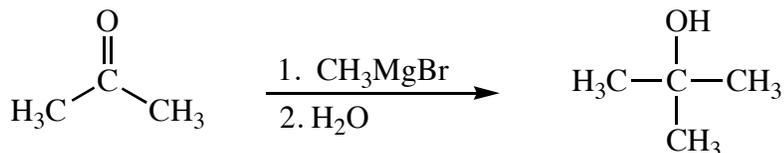
**I. Writing Equations for Organic Reactions**

Certain conventions make organic equations look different than the equations encountered in general chemistry. Reagents can be drawn either to the left of the reaction arrow, or above the reaction arrow, to focus on the organic transformation taking place. Solvent and temperature may be added above or below the arrow. The symbols  $h\nu$  or  $\Delta$  are used for reactions that require heat or light. By-products are often omitted.



Other reaction parameters can also be indicated:

When two or more sequential reactions are carried out without drawing an intermediate compound, the steps are numbered above and below the arrow.

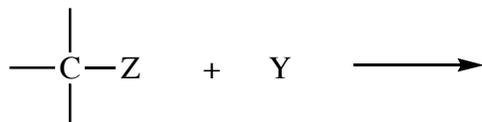


## II. Kinds of Organic Reactions

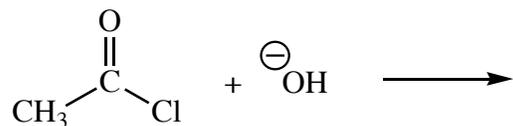
Organic molecules undergo acid-base and oxidation-reduction reactions. They also undergo substitution, elimination, and addition reactions.

### A. Substitution Reactions

Substitution is a reaction in which an atom or a group of atoms is replaced by another atom or group of atoms.

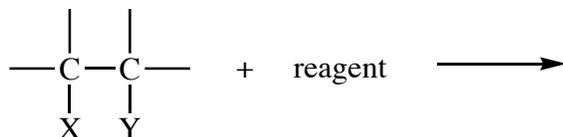


Examples:

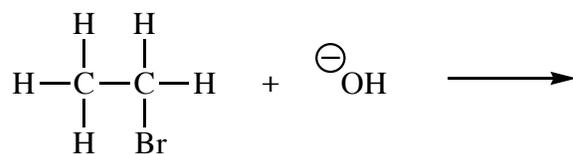


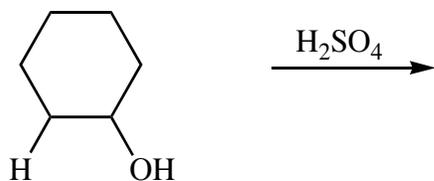
### B. Elimination Reactions

In an elimination reaction, elements of the starting material are “lost” and a  $\pi$ -bond is formed.



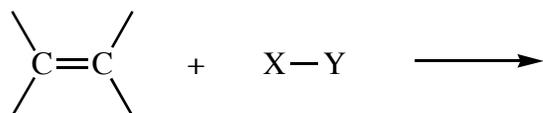
Examples:



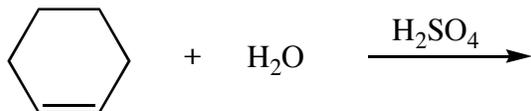
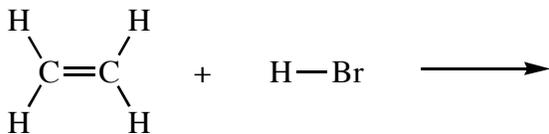


### C. Addition Reactions

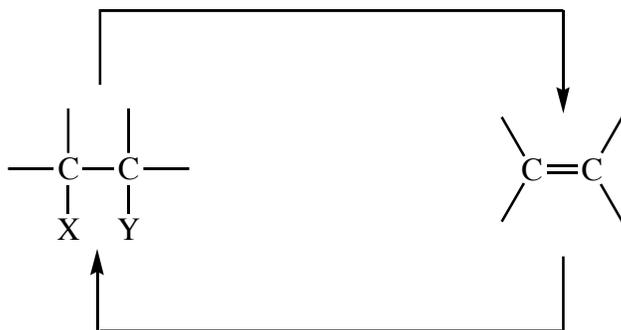
In an addition reaction, elements are added to a starting material:



Examples:



Notice:



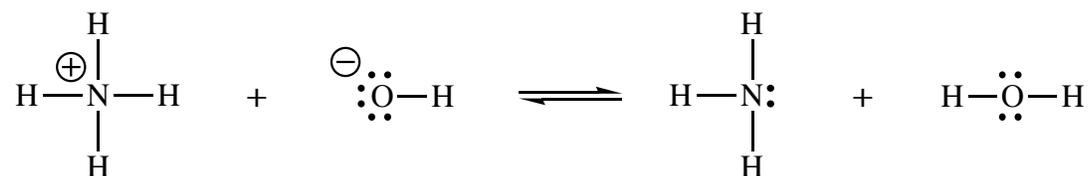
### III. Reaction Mechanism

A reaction mechanism is a detailed description of how bonds are broken and formed as starting material is converted to product. Curved arrows are used to show the mechanism of a reaction.

A reaction can occur in one step or in a series of steps:

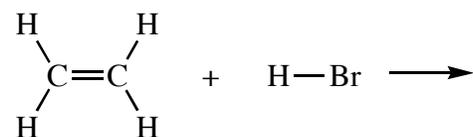
- A one-step reaction is called a **concerted reaction**. Bonds are made and broken in the same step.

Example:



- A **stepwise reaction** involves more than one step. A starting material is first converted to an unstable **reactive intermediate**, which then goes onto to form product.

Example:



#### A. Bond Cleavage

Bonds are broken and formed in all chemical reactions. There are only two ways to break (*cleave*) a bond:

- **Homolysis** (*homolytic bond cleavage*):



☛ *Homolysis generates uncharged reactive intermediates with unpaired electrons (AKA: free radicals)*

• **Heterolysis (*heterolytic bond cleavage*):**



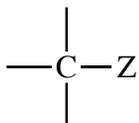
*or*



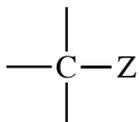
☛ *Heterolysis generates charged intermediates.*

Homolysis and heterolysis of a C-Z bond generates the three most important reactive intermediates in organic chemistry:

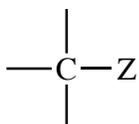
*Heterolysis when Z is more electronegative:*



*Heterolysis when C more electronegative:*



*Homolysis:*



## B. Bond Formation

Radicals react by donating single electrons, whereas compounds without unpaired electrons react by donating or accepting a pair of electrons:



## IV. Bond Dissociation Energy

The bond dissociation energy is the energy needed to homolytically cleave a covalent bond.



The energy absorbed or released in any reaction, symbolized by  $\Delta H^\circ$ , is called the **enthalpy change** or **heat of reaction**.

- When  $\Delta H^\circ$  is positive (+), energy is absorbed and the reaction is endothermic.
- When  $\Delta H^\circ$  is negative (-), energy is released and the reaction is exothermic.

Look at  $\text{H}_2$ :



☛ The stronger the bond, the higher its bond dissociation energy.

Table 6.2 gives the bond dissociation for some common bonds seen in organic chemistry.

Notice some trends:

H—C	H—N	H—O	H—F
104	107	119	136
			H—Cl
			103
			H—Br
			88
			H—I
			71

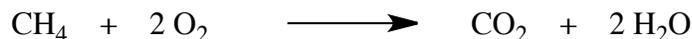
Bond dissociation energies can be used to calculate the enthalpy change in a reaction in which several bonds are broken and formed.  $\Delta H^\circ$  indicates the relative strengths of bonds broken and formed in a reaction.

- When  $\Delta H^\circ$  is positive, more energy is needed to break bonds than is released in forming bonds. The bonds broken in the starting material are stronger than the bonds formed in the product.
- When  $\Delta H^\circ$  is negative, more energy is released in forming bonds than is needed to break bonds. The bonds formed in the product are stronger than the bonds broken in the starting materials.

**To determine** the overall  $\Delta H^\circ$  for a reaction:

1. Begin with a balanced equation. Add up all bond dissociation energies for bonds broken in starting materials. This (+) value is the **energy needed to break bonds**.
2. Add the bond dissociation energies for all bonds formed in the products. This (–) value represents the **energy released in forming bonds**.
3. Add values from step 1 and step 2.

Example: Calculate the standard enthalpy change for the following oxidation reaction.



#### IV. Thermodynamics and Kinetics

For a reaction to be practical, the equilibrium must favor the products, and the reaction rate must be fast enough to form in a reasonable period of time. These two conditions depend on the thermodynamics and kinetics of the reaction.

- **Thermodynamics** ( $\Delta G^\circ$ ,  $\Delta H^\circ$ ,  $\Delta S^\circ$ ,  $K_{eq}$ ) describes energy and equilibrium. How do the energies of the reactants and products compare? What are the relative amounts of reactants and products at equilibrium?
- **Kinetics** ( $E_a$ ,  $\Delta G^\ddagger$ ,  $k$ ) describes reaction rates. How fast are reactants converted to products?

##### A. Thermodynamics

The equilibrium constant,  $K_{eq}$ , is a mathematical expression that relates the amount of starting material and product at equilibrium.

*Consider the following reaction:*



$$K_{eq} = \frac{[\text{products}]}{[\text{reactants}]}$$

The size of  $K_{eq}$  tells us about the position of equilibrium; that is, it expresses whether the starting materials or products predominate once equilibrium is established.

- When  $K_{eq} > 1$

- When  $K_{eq} < 1$

Q. What determines whether equilibrium favors the products in a given reaction?

A. The relative concentration of reactants and products (*position of equilibrium*) is determined by the relative energies of reactants and products.

☛ *The more stable the compound, the greater its concentration at equilibrium!*

*If products are more stable than reactants:*

*If products are less stable than reactants:*

It is the change in free energy (**Gibbs free energy,  $\Delta G^\circ$** ) between the reactants and the products, which determines whether starting materials or products are favored at equilibrium.

$$\Delta G^\circ = G^\circ_{\text{products}}(\text{free energy of products}) - G^\circ_{\text{reactants}}(\text{free energy of reactants})$$

$K_{eq}$  is related to  $\Delta G^\circ$  by the following equation:

$$\Delta G^\circ = -2.303 RT \log K_{eq}$$

Using this expression, we can determine the relationship between the equilibrium constant and the free energy change between reactants and products.

- When  $K_{eq} > 1$ :

- When  $K_{eq} < 1$ :

**Table 6.3** lists representative values for  $\Delta G^\circ$  and  $K_{eq}$  at 25°C for a reaction  $A \rightarrow B$ .

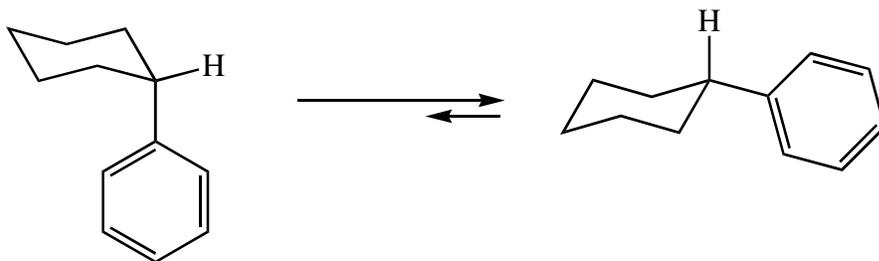
$\Delta G^\circ$ (kcal/mole)	$K_{eq}$	Relative amount of A & B @ equilibrium
+4.2	$10^{-3}$	1000 times as much A as B
+2.8	$10^{-2}$	100 times as much a as B
+1.4	$10^{-1}$	10 times as much A as B
0	1	equal amounts A and B
-1.4	$10^1$	10 times as much B as A
-2.8	$10^2$	100 times as much B as A
-4.2	$10^3$	1000 times as much B as A

Important points:

- Compounds that are lower in energy have increased stability. Thus equilibrium favors the products when they are more stable (lower in energy) than the reactants.
- Because  $\Delta G^\circ$  depends on the logarithm of  $K_{eq}$ , a small energy change corresponds to a large difference in the relative amounts of reactants and products at equilibrium.
- At 25 °C,  $2.303RT = 1.4$  kcal/mole. Thus, the equation simplifies to  $\Delta G^\circ = -1.4 \log K_{eq}$ .

- These equations can be used for any process with two states at equilibrium, like the rapidly converting chair conformations of a cyclohexane ring.

**Example:** The energy difference between the two chair conformations of phenylcyclohexane is  $-2.9$  kcal/mole. Use the values in Table 6.3 to determine the relative amounts of each chair conformation at equilibrium.



The Gibbs standard free energy has an enthalpy component  $\Delta H^\circ$ , and an entropy component,  $\Delta S^\circ$ :

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

$\Delta H^\circ$  gives the relative strengths of bonds broken and formed in a reaction.

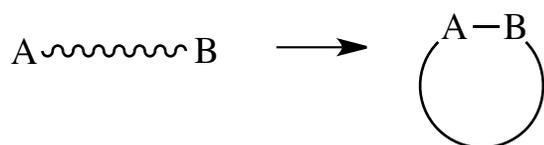
$\Delta S^\circ$  is the change in freedom of motion (*degree of disorder*) in a reaction. reactants.

$$\Delta S^\circ = (\text{freedom of motion of the products}) - (\text{freedom of motion of the reactants})$$

- $\Delta S^\circ$  is positive (+) when the products are more disordered than the reactants.
- $\Delta S^\circ$  is negative (-) when the products are less disordered (*more ordered*) than the reactants.

- **Reactions resulting in an increase in entropy are favored.**

Restricting freedom of motion in a molecule decreases its entropy!



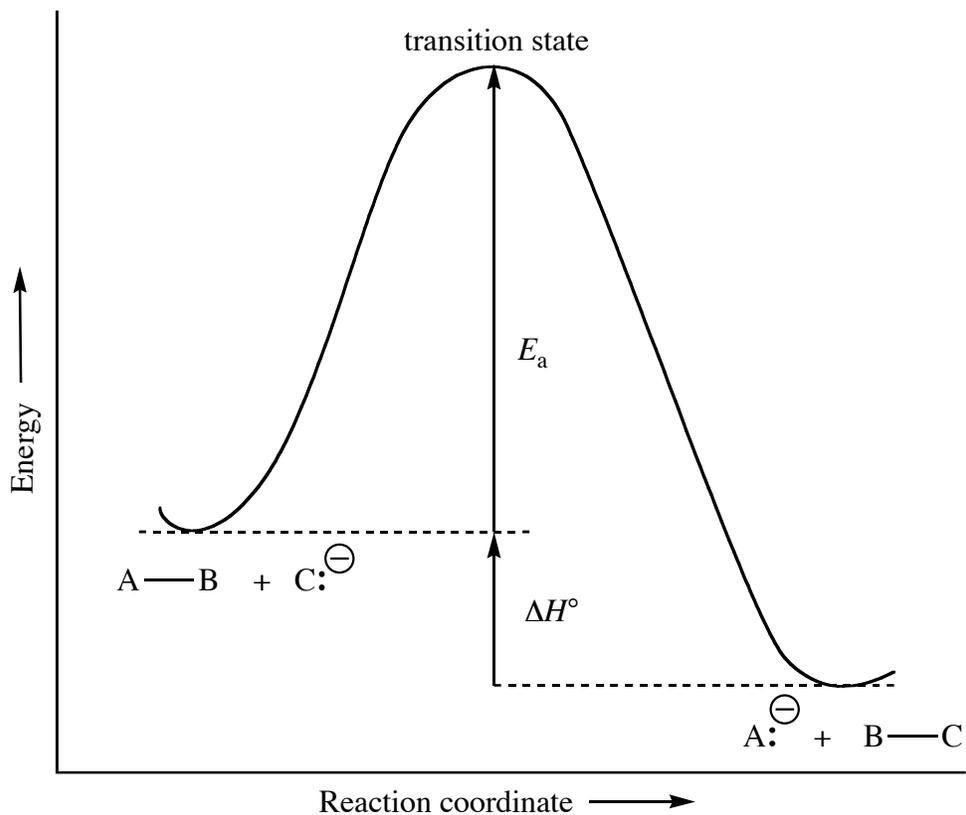
☛ Negative values of  $\Delta H^\circ$  and positive values of  $\Delta S^\circ$  contribute to making  $\Delta G^\circ$  (-)!

If the  $T\Delta S^\circ$  value is small, then  $\Delta G^\circ \approx \Delta H^\circ$ , and you can **approximate**  $\Delta G^\circ$  by calculating  $\Delta H^\circ$ . *This can be a dangerous practice because many organic reactions occur with a significant change in entropy, or occur at high temperatures!* Nonetheless, for most of the reactions in this textbook, this approximation is made.

## B. Energy Diagrams

An energy diagram is a schematic representation of the energy changes that take place as reactants are converted to products. An energy diagram indicates how readily a reaction proceeds, how many steps are involved, and how the energies of reactants, products and intermediates compare.

Look at the following energy diagram for the a concerted reaction between molecule **A–B** with **C:** to form **A:** and **B–C**.



Important points:

- As starting materials **A–B** and **C:** approach one another, their electron clouds feel some repulsion, causing an increase in energy, until a maximum value is reached. This unstable energy maximum is the **transition state**. In the transition state, the bond between **A** and **B** is partially broken, and the bond between **B** and **C** is partially formed.
- At the transition state, the bond between **A** and **B** can reform to regenerate starting material, or the bond between **B** and **C** can form to generate product.
- The energy difference between reactants and products is  $\Delta H^{\circ}$ . Because products are lower in energy than reactants, the reaction is exothermic and energy is released.
- The energy between the transition state and the starting material is called the energy of activation,  $E_a$ .

- The energy of activation is the minimum amount of energy needed to break bonds in the reactants. It represents an energy barrier that must be overcome for the reaction to occur.
- The larger the  $E_a$ , the greater the amount of energy that is needed to break bonds, and the slower the reaction rate.

**C. Kinetics:** What is the rate of the reaction and what factors govern this rate?

*A reaction can have a large  $K_{eq}$  and negative  $\Delta G^\circ$ , but be extremely slow!*

The rate of reaction can be defined as the number of reactant molecules converted to product per unit of time.

$$\text{rate of reaction} = \left( \begin{array}{c} \text{number of collisions} \\ \text{per unit of time} \end{array} \right) \times \left( \begin{array}{c} \text{fraction with} \\ \text{sufficient energy} \end{array} \right) \times \left( \begin{array}{c} \text{fraction with the} \\ \text{proper orientation} \end{array} \right)$$

**Two factors govern the second term, the fraction with sufficient energy:**

**1. The size of the energy barrier, or energy of activation,  $E_a$ .**

If the energy barrier is high, a smaller fraction will have a sufficient energy to overcome the energy barrier.

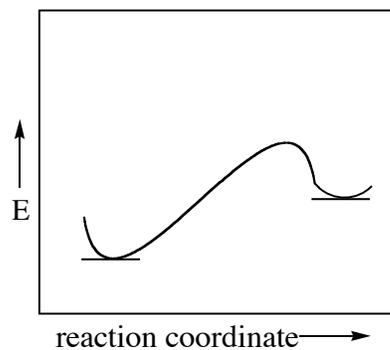
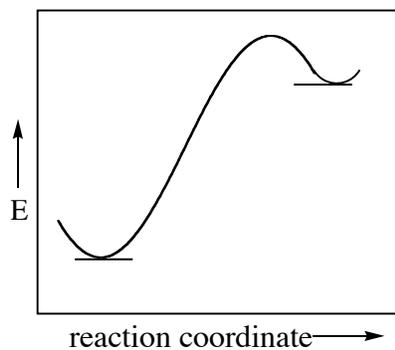
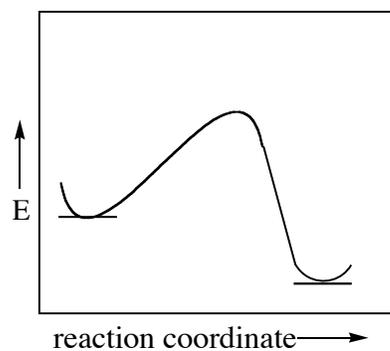
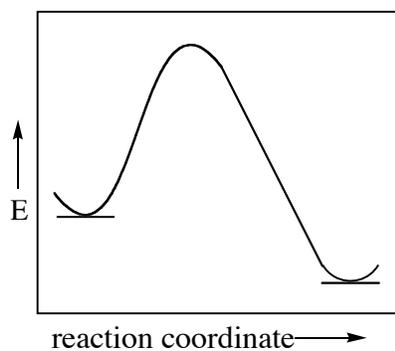
The rate constant is related to the energy of activation,  $E_a$ , by the Arrhenius equation:

$$k = Ae^{-(\Delta E_a/RT)}$$

- As  $E_a$  gets larger,  $e^{-(E_a/RT)}$  must get smaller
- As  $E_a$  gets smaller, the rate of the reaction increases.
- Small differences in  $E_a$  produce very large differences in rates.

Why?

**Compare:**



**2. The temperature:** Molecules obtain the energy needed to overcome  $E_a$  from their thermal motion.

$$k = Ae^{-(\Delta E_a/RT)}$$

Why? Increasing the temperature increases the average kinetic energy of the molecules - There is a large increase in the number of collisions with sufficient energy to overcome the energy barrier for the reaction.

The  $E_a$  values for most organic reactions are 10-35 kcal/mole. When  $E_a < 20$  kcal, the reaction goes readily at room temperature. When  $E_a > 20$  kcal, higher temperatures are needed. As a rule of thumb, increasing the temperature by 10 °C doubles the reaction rate.

☛ **Increasing the concentration also increases the rate of a reaction because it increases the number of collisions in a given period of time.**

#### D. Rate Equations

The rate of a chemical reaction is determined by measuring the decrease in concentrations of reactants over time, or the increase in products over time. A rate law (*or rate equation*) is an equation that shows the relationship between the rate of a reaction and the concentration of the reactants. A rate law is determined experimentally and it depends on the mechanism of the reaction.

In the ~~one-step~~ reaction of molecule **A-B** with **C:-** to form **A:-** and **B-C**, for example, it was found that the concentration of both reactants affected the rate.



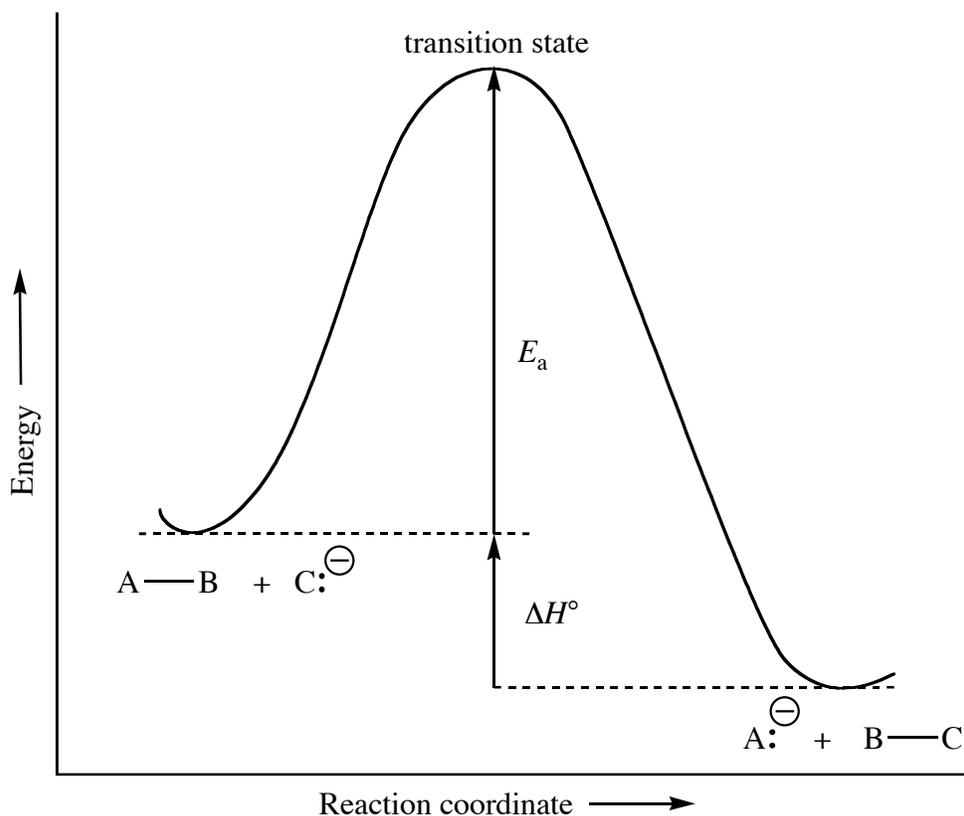
- The rate constant,  $k$ , is a fundamental characteristic of a reaction. It is a complex mathematical term that takes into account the dependence of rate on temperature and the energy of activation.

- The order of the rate equation equals the sum of the exponents of the concentration terms in the rate equation.
- Because the rate of this reaction is proportional to the concentration of only two reactants, it is called a second-order reaction.
- The reaction is bimolecular.

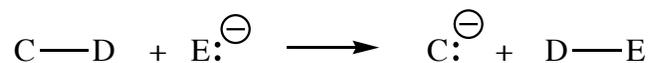
The rate law is consistent with a concerted (*one step*) mechanism:



With the following energy diagram:



The situation is different in the reaction of molecule **C–D** with **E:<sup>⊖</sup>** to form **C:<sup>⊖</sup>** and **D–E**. It was found that the rate of the reaction depended only on the concentration of **C–D**:



- Because the rate of this reaction is proportional to the concentration of only one reactant, it is a first-order reaction.

A mechanism that is consistent with this rate law is a two-step process:



- Species  $\text{D}^{\oplus}$  is a reactive intermediate. It is formed as a product of step 1, and then goes on to react with  $\text{E:}^{\ominus}$  in step 2.

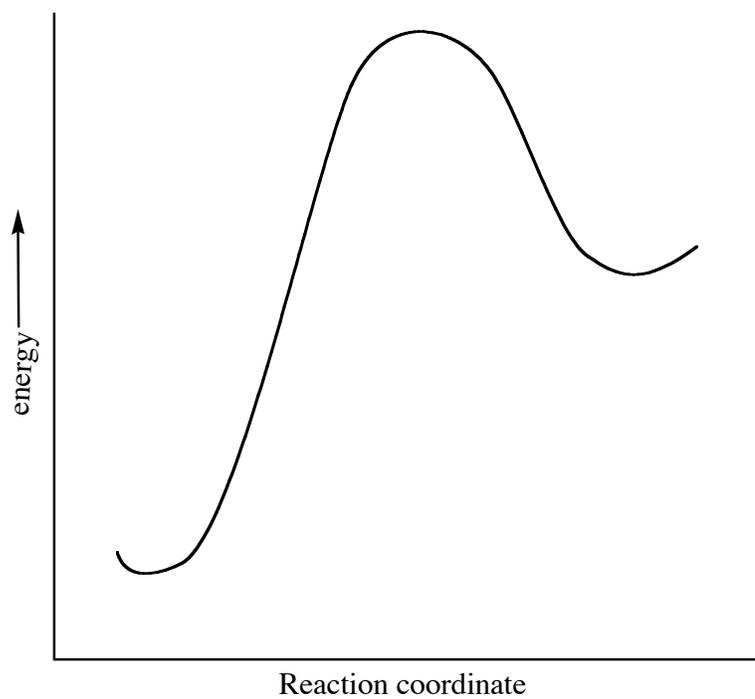
### E. Multistep Reactions and the Rate Limiting Step

Each step of a multistep reaction has its own characteristic rate, and therefore its own transition state. The reaction can occur no faster than its slowest step. In a multistep reaction, the slow step is called the *rate-determining step*. Only the concentrations of reactants affecting the rate-determining step appear in the rate equation. Since the rate depends on the concentration of **C–D**, then only **C–D** appears in the rate determining step.

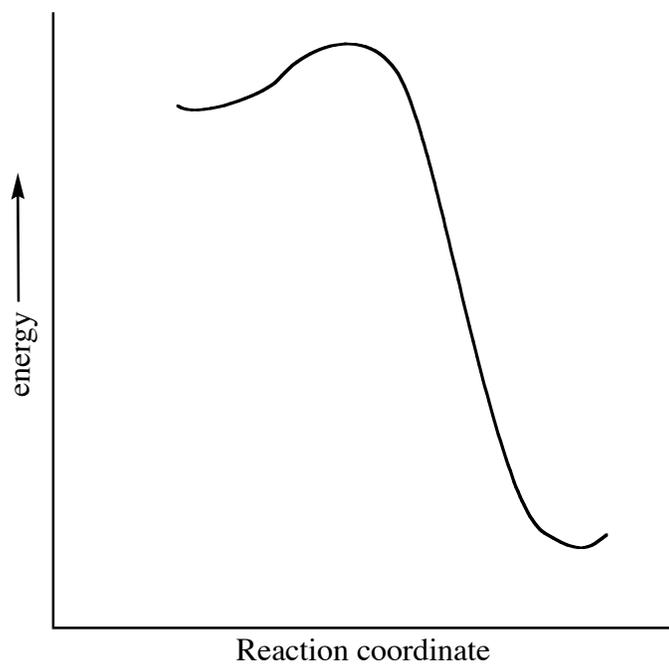
Which step is the rate determining step?

Let's construct the energy diagram for this two-step process:

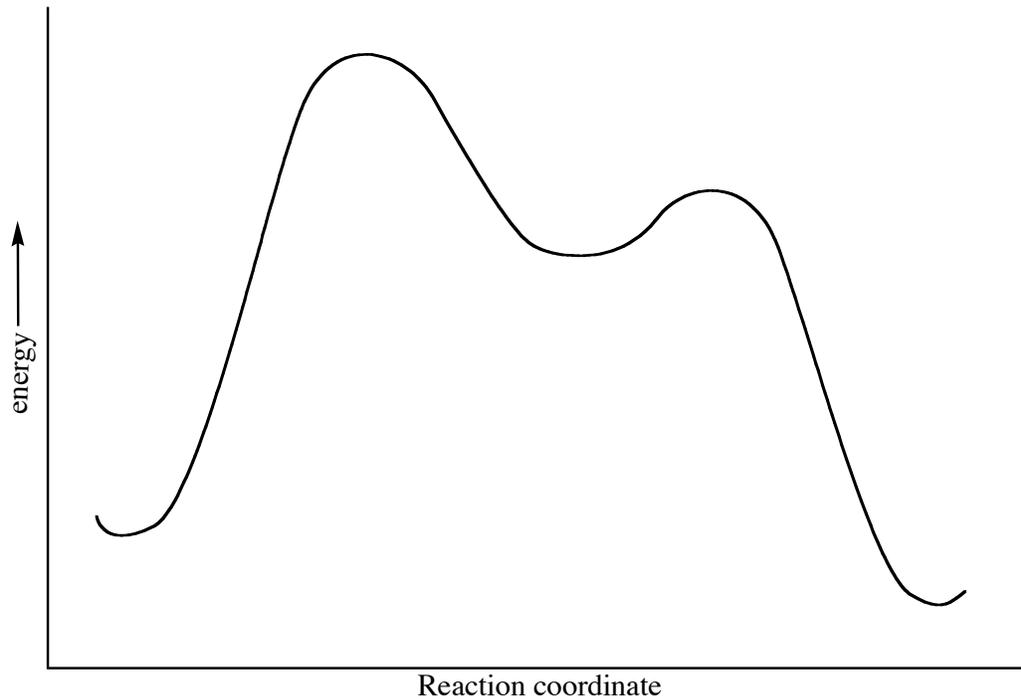
Step 1: C-D bond breaks:



Step 1: E: attacks D<sup>+</sup>:



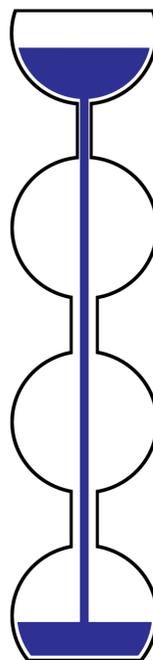
The two steps combined into a single energy diagram:



In a multistep reaction, the *rate-determining step (r.d.s)* is the step with the transition state of highest free energy.

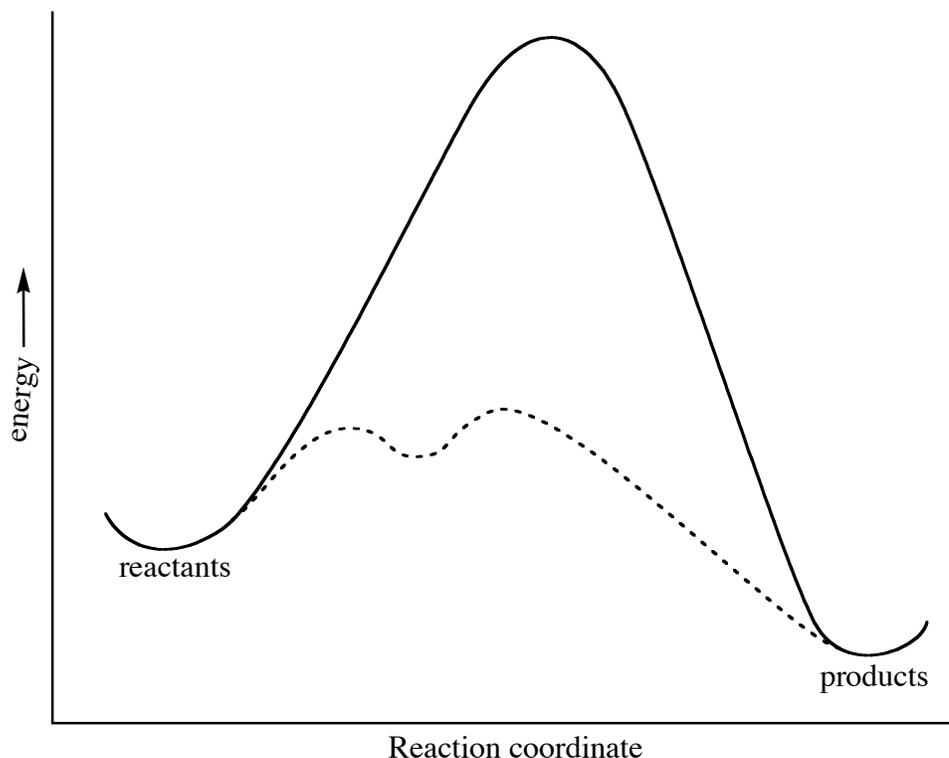
- The rate of the overall reaction *cannot* be higher than the rate of the rate-determining step! **Why?**

Look @ the modified hourglass:



## F. Catalysts

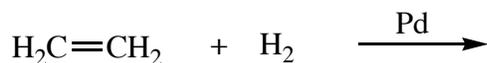
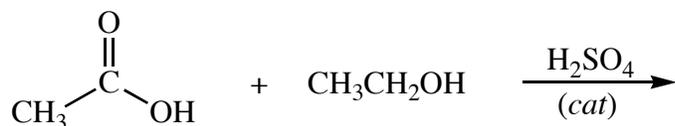
A **catalyst** is a substance that increases the rate of a chemical reaction without itself being consumed or changed in the reaction. A catalyst increases the rate of a chemical reaction by providing a lower energy pathway with a transition state that is more stable. Because only a small amount of catalyst is needed relative to starting material, it is said to be present in a **catalytic amount**.



- The reaction is exothermic, but the  $E_a$  is too high for the reaction to occur at an appreciable rate without the catalyst.
- Addition of a catalyst lowers  $E_a$ ,  $\therefore$  the reaction can occur at an appreciable rate.

The catalyst can lower  $E_a$  by either providing a way to convert the reactant into an unstable species, or lowering the energy of activation by providing a different pathway for the reaction to take place.

Common catalysts in organic reactions are acids, bases or metals. Two examples are shown below:



Enzymes are biological catalysts. They are composed of amino acids held together in a very specific three-dimensional shape. An enzyme contains a region called its active site, which binds an organic reagent, called a substrate. When bound, this unit is called the enzyme-substrate complex. Once bound, the organic substrate undergoes a very specific reaction at an enhanced rate.

An enzyme facilitates a reaction in a number of ways:

- Reacting groups are brought together at the active site in the proper orientation for reaction.
- Some of the amino acid side chains of the enzyme serve as catalytic groups. And many enzymes have metal ions at their active site that act as catalysts.
- Groups on the enzyme can stabilize transition states and intermediates by van der Waals interactions, electrostatic interactions, and hydrogen bonding.