

Chapter 5 – An Overview of Organic Reactions

Chapter Outline

I. Organic Reactions (Sections 5.1 – 5.6).

A. Kinds of organic reactions (Section 5.1).

1. Addition reactions occur when two reactants add to form one product, with no atoms left over.
2. Elimination reactions occur when a single reactant splits into two products.
3. Substitution reactions occur when two reactants exchange parts to yield two new products.
4. Rearrangement reactions occur when a single product undergoes a rearrangement of bonds to yield an isomeric product.

B. Reaction mechanisms - general information (Section 5.2).

1. A reaction mechanism describes the bonds broken and formed in a chemical reaction, and accounts for all reactants and products.
2. Bond breaking and formation in chemical reactions.
 - a. Bond breaking is symmetrical if one electron remains with each fragment.
 - b. Bond breaking is unsymmetrical if both electrons remain with one fragment and the other fragment has a vacant orbital.
 - c. Bond formation is symmetrical if one electron in a covalent bond comes from each reactant.
 - d. Bond formation is unsymmetrical if both electrons in a covalent bond come from one reactant.
3. Types of reactions.
 - a. Radical reactions involve symmetrical bond breaking and bond formation.
 - b. Polar reactions involve unsymmetrical bond breaking and bond formation.
 - c. Pericyclic reactions will be studied later.

C. Radical reactions (Section 5.3).

1. Radicals are highly reactive because they contain an atom with an unpaired electron.
2. A substitution reaction occurs when a radical abstracts an electron from another molecule.
3. An addition reaction occurs when a radical adds to a double bond.
4. Steps in a radical reaction.
 - a. The *initiation step* produces radicals by the symmetrical cleavage of a bond.
 - b. The *propagation steps* occur when a radical abstracts an atom to produce a new radical and a stable molecule.

This sequence of steps is a chain reaction.

- c. A *termination step* occurs when two radicals combine.

5. In radical reactions, all bonds are broken and formed by reactions of species with odd numbers of electrons.

D. Polar reactions (Sections 5.4 – 5.6).

1. Characteristics of polar reactions (Section 5.4).
 - a. Polar reactions occur as a result of positive and negative charges within molecules.
 - b. These charge differences are usually due to electronegativity differences between atoms.
 - i. Differences may also be due to interactions of functional groups with solvents, as well as with Lewis acids or bases.
 - ii. Some bonds in which one atom is polarizable may also behave as polar bonds.

- c. In polar reactions, electron-rich sites in one molecule react with electron-poor sites in another molecule.
- d. The movement of an electron pair in a polar reaction is shown by a curved arrow.
- e. The reacting species:
 - i. A nucleophile is a compound with an electron-rich atom.
 - ii. An electrophile is a compound with an electron-poor atom.
 - iii. Some compounds can behave as both nucleophiles and as electrophiles
- f. Many polar reactions can be explained in terms of acid-base reactions.
- 2. An example of a polar reaction: addition of HBr to ethylene (Section 5.5).
 - a. This reaction is known as an electrophilic addition.
 - b. The π electrons in ethylene behave as a nucleophile.
 - c. The reaction begins by the attack of the π electrons on the electrophile H^+ .
 - d. The resulting intermediate carbocation reacts with Br^- to form bromoethane.
- 3. Rules for using curved arrows in polar reaction mechanisms (Section 5.6).
 - a. Electrons must move from a nucleophilic source to an electrophilic sink.
 - b. The nucleophile can be either negatively charged or neutral.
 - c. The electrophile can be either positively charged or neutral.
 - d. The octet rule must be followed.

II. Describing a reaction (Sections 5.7 – 5.10).

A. Equilibria, rates, and energy changes (Section 5.7).

- 1. All chemical reactions are equilibria that can be expressed by an equilibrium constant K_{eq} that shows the ratio of products to reactants.
 - a. If $K_{eq} > 1$, [products] > [reactants].
 - b. If $K_{eq} < 1$, [reactants] > [products].
 - 2. For a reaction to proceed as written, the energy of the products must be lower than the energy of the reactants.
 - a. The energy change that occurs during a reaction is described by ΔG° , the Gibbs free-energy change.
 - b. Favorable reactions have negative ΔG° and are exergonic.
 - c. Unfavorable reactions have positive ΔG° and are endergonic.
 - d. $\Delta G^\circ = -RT \ln K_{eq}$.
 - 3. ΔG° is composed of two terms – ΔH° , and ΔS° , which is temperature-dependent.
 - a. ΔH° is a measure of the change in total bonding energy during a reaction.
 - i. If ΔH° is negative, a reaction is exothermic.
 - ii. If ΔH° is positive, a reaction is endothermic.
 - b. ΔS° (entropy) is a measure of the freedom of motion of a reaction.
 - i. A reaction that produces two product molecules from one reactant molecule has positive entropy.
 - ii. A reaction that produces one product molecule from two reactant molecules has negative entropy.
 - c. $\Delta G^\circ = \Delta H^\circ - T \Delta S^\circ$.
 - 4. None of these expressions predict the rate of a reaction.
- ### B. Bond dissociation energies (Section 5.8).
- 1. The bond dissociation energy (D) measures the heat needed to break a bond.
 - 2. Each bond has a characteristic strength.
 - 3. In exothermic reactions, the bonds formed are stronger than the bonds broken.

C. Energy diagrams and transition states (Section 5.9).

1. Reaction energy diagrams show the energy changes that occur during a reaction.
The vertical axis represents energy changes, and the horizontal axis represents the progress of a reaction.
2. The transition state is the highest-energy species in this reaction.
It is possible for a reaction to have more than one transition state.
3. The difference in energy between the reactants and the transition state is the energy of activation ΔG^\ddagger .
Values of ΔG^\ddagger range from 40 – 150 kJ/mol.
4. After reaching the transition state, a molecule can go on to form products or can revert to starting material.
5. Every reaction has its own energy profile.

D. Intermediates (Section 5.10).

1. In a reaction of at least two steps, an intermediate is the species that lies at the energy minimum between two transition states.
2. Even though an intermediate lies at an energy minimum between two transition states, it is a high-energy species and usually can't be isolated.
3. Each step of a reaction has its own ΔG^\ddagger and ΔG° , but the total reaction has an overall ΔG° .
4. Biological reactions take place in several small steps, each of which has a small value of ΔG^\ddagger .

III. A Comparison of biological and laboratory reactions (Section 5.11).

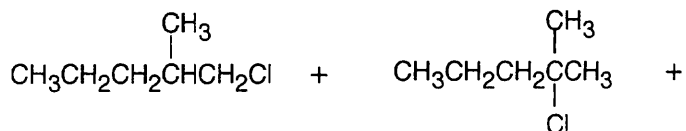
- A. Laboratory reactions are carried out in organic solvents; biological reactions occur in aqueous medium.
- B. Laboratory reactions take place over a wide variety of temperatures; biological reactions take place at the temperature of the organism.
- C. Laboratory reactions are uncatalyzed, or use simple catalysts; biological reactions are enzyme-catalyzed.
- D. Laboratory reagents are usually small and simple; biological reactions involve large, complex coenzymes.
- E. Biological reactions have high specificity for substrate, whereas laboratory reactions are relatively nonspecific.

Solutions to Problems

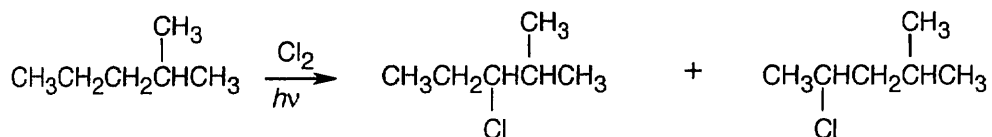
5.1

- (a) $\text{CH}_3\text{Br} + \text{KOH} \longrightarrow \text{CH}_3\text{OH} + \text{KBr}$ substitution
- (b) $\text{CH}_3\text{CH}_2\text{Br} \longrightarrow \text{H}_2\text{C}=\text{CH}_2 + \text{HBr}$ elimination
- (c) $\text{H}_2\text{C}=\text{CH}_2 + \text{H}_2 \longrightarrow \text{CH}_3\text{CH}_3$ addition

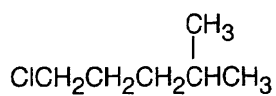
5.2



1-Chloro-2-methylpentane 2-Chloro-2-methylpentane



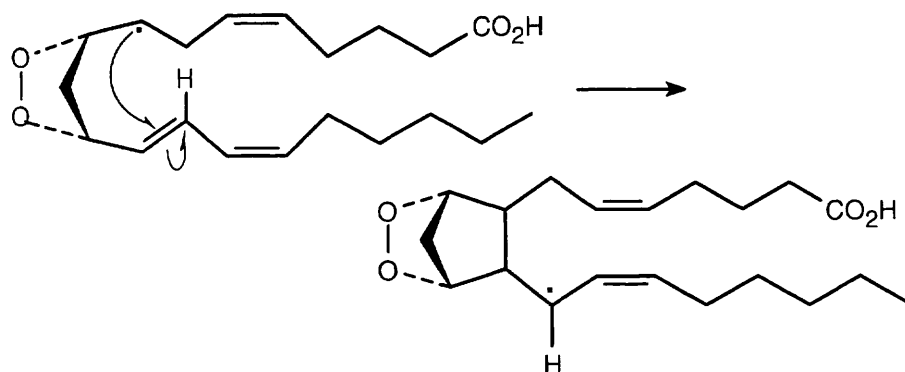
2-Methylpentane 3-Chloro-2-methylpentane 2-Chloro-4-methylpentane



1-Chloro-4-methylpentane

5.3 Strategy: The tails of the arrows show the location of the bond to be broken, and the heads show where the electrons are moving. In radical reactions, the arrow is a fishhook (half-headed).

Solution:



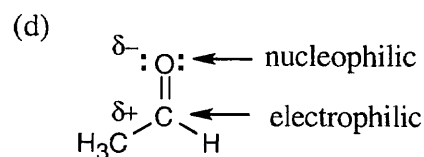
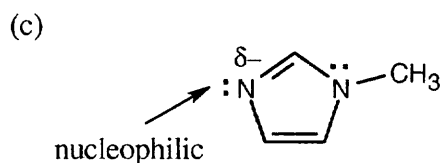
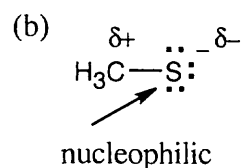
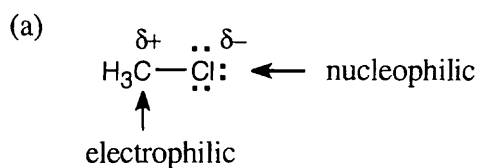
The reaction is a radical addition to a double bond and a rearrangement.

5.4 Strategy: Keep in mind:

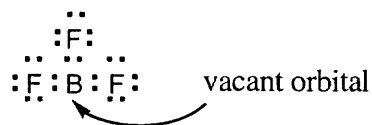
- (1) An electrophile is electron-poor, either because it is positively charged, because it has a functional group that is positively polarized, or because it has a vacant orbital.
- (2) A nucleophile is electron-rich, either because it has a negative charge, because it has a functional group containing a lone electron pair, or because it has a functional group that is negatively polarized.
- (3) Some molecules can act as both nucleophiles and electrophiles, depending on the reaction conditions.

Solution:

- (a) The electron-poor carbon acts as an electrophile.
- (b) CH_3S^- is a nucleophile because of the sulfur lone-pair electrons and because it is negatively charged.
- (c) $\text{C}_4\text{H}_6\text{N}_2$ is a nucleophile because of the lone-pair electrons of nitrogen. (Only one of the nitrogens is nucleophilic, for reasons that will be explained later.)
- (d) CH_3CHO is both a nucleophile and an electrophile because of its polar $\text{C}=\text{O}$ bond.

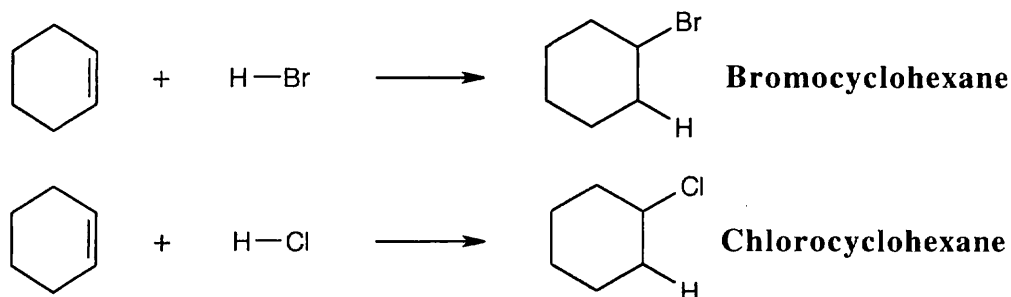


- 5.5 BF_3 is likely to be an electrophile because the electrostatic potential map indicates that it is electron-poor (blue). The Lewis structure shows that BF_3 lacks a complete electron octet and can accept an electron pair from a nucleophile.

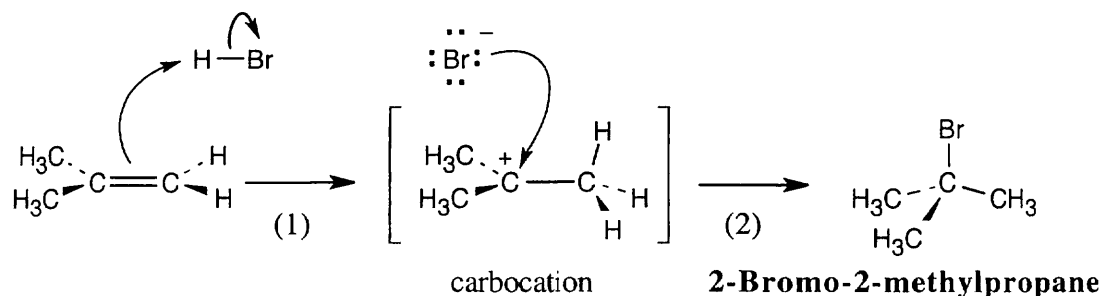


- 5.6 Strategy:** Reaction of cyclohexene with HCl or HBr is an electrophilic addition reaction in which a halogen acid adds to a double bond to produce a haloalkane.

Solution:

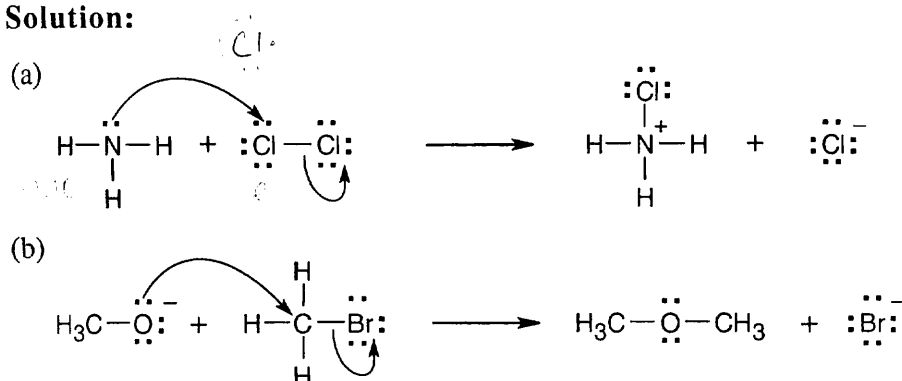


- 5.7** The mechanism is pictured in Figure 5.3. The steps: (1) Attack of the π electrons of the double bond on HBr, forming a carbocation; (2) Formation of a C-Br bond by electron pair donation from Br^- to form the neutral addition product.

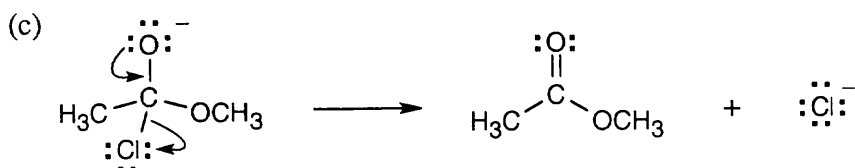


- 5.8 Strategy:** For curved arrow problems, follow these steps:
 (1) Locate the bonding changes. In (a), a bond from nitrogen to chlorine has formed, and a Cl-Cl bond has broken.
 (2) Identify the nucleophile and electrophile (in (a), the nucleophile is ammonia and the electrophile is one Cl in the Cl_2 molecule), and draw a curved arrow whose tail is near the nucleophile and whose head is near the electrophile.
 (3) Check to see that all bonding changes are accounted for. In (a), we must draw a second arrow to show the heterolytic bond-breaking of Cl_2 to form Cl^- .

Solution:

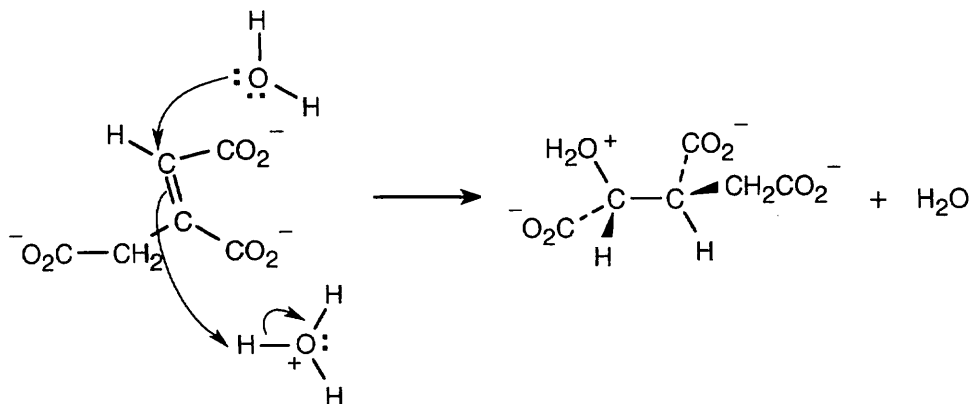


A bond has formed between oxygen and the carbon of bromomethane. The bond between carbon and bromine has broken. CH_3O^- is the nucleophile and bromomethane is the electrophile.



A double bond has formed between oxygen and carbon, and a carbon–chlorine bond has broken. Electrons move from oxygen to form the double bond and from carbon to chlorine.

5.9 This mechanism will be studied in a later chapter.

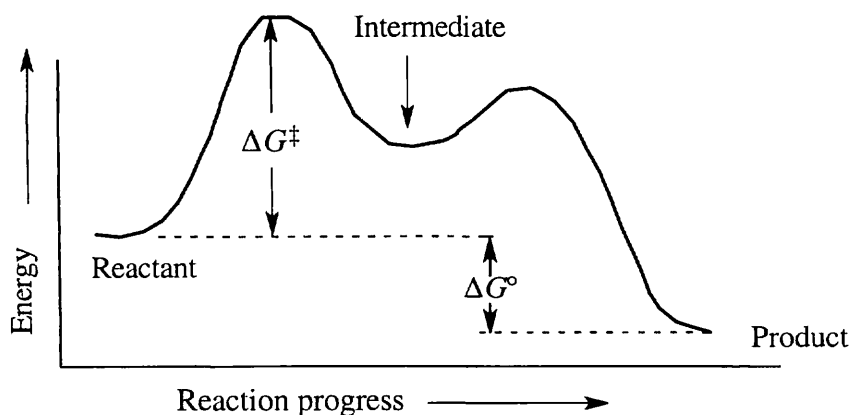


5.10 A negative value of ΔG° indicates that a reaction is favorable. Thus, a reaction with $\Delta G^\circ = -44$ kJ/mol is more favorable than a reaction with $\Delta G^\circ = +44$ kJ/mol.

5.11 From the expression $\Delta G^\circ = -RT \ln K_{\text{eq}}$, we can see that a large K_{eq} is related to a large negative ΔG° . Consequently, a reaction with $K_{\text{eq}} = 1000$ is more exergonic than a reaction with $K_{\text{eq}} = 0.001$.

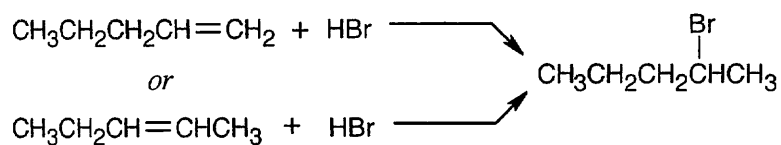
5.12 A reaction with $\Delta G^\ddagger = 45$ kJ/mol is faster than a reaction with $\Delta G^\ddagger = 70$ kJ/mol because a larger value for ΔG^\ddagger indicates a slower reaction.

5.13

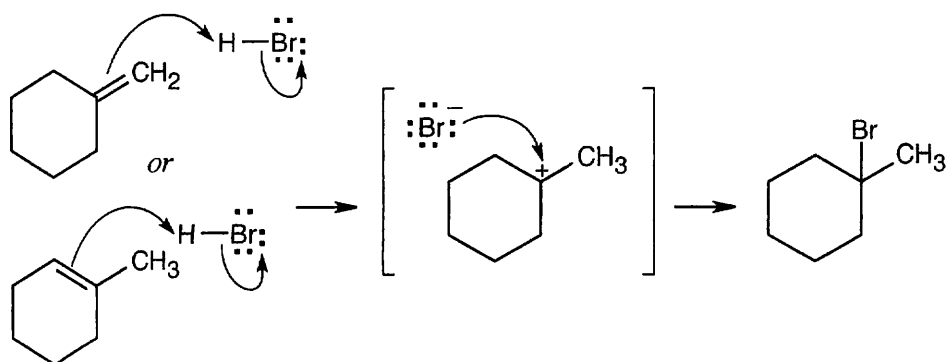


Visualizing Chemistry

5.14

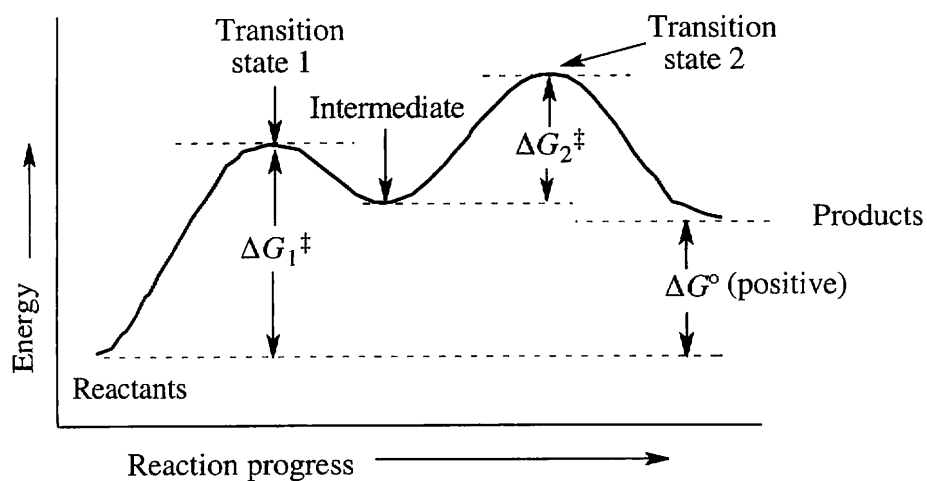


5.15



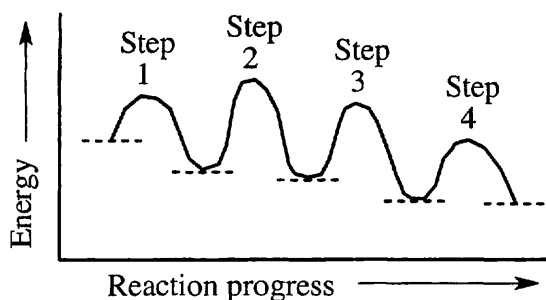
- 5.16 (a) The electrostatic potential map shows that the formaldehyde oxygen is electron-rich, and the carbon–oxygen bond is polarized. The carbon atom is thus relatively electron-poor and is likely to be electrophilic.
 (b) The sulfur atom is more electron-rich than the other atoms of methanethiol and is likely to be nucleophilic.

5.17



- (a) ΔG° is positive.
 (b) There are two steps in the reaction.
 (c) There are two transition states, as indicated on the diagram.

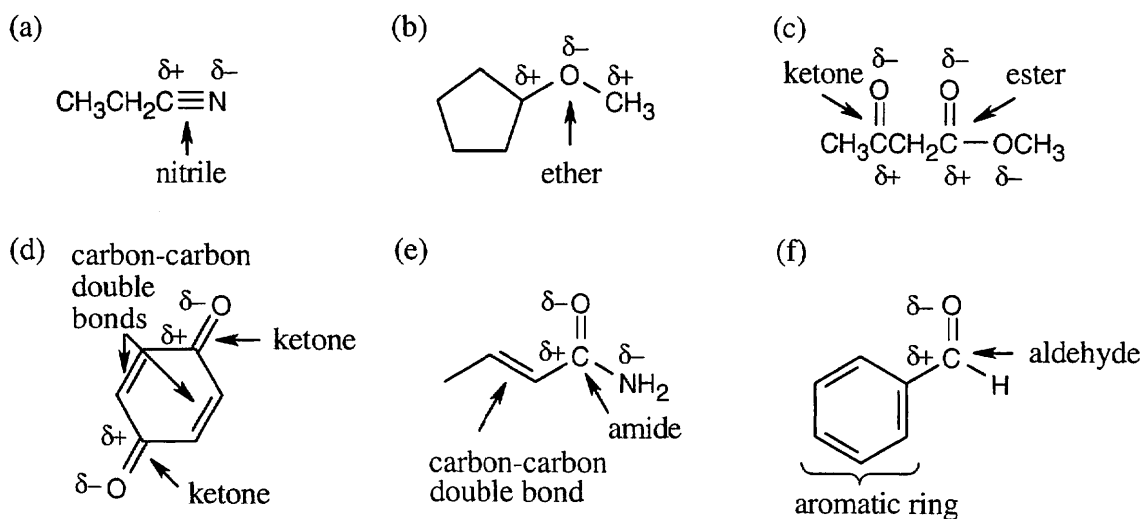
5.18



- (a) The reaction involves four steps, noted above.
 (b) Step 1 is the most exergonic because the energy difference between reactant and product (ΔG°) is greatest.
 (c) Step 2 is slowest because it has the largest value of ΔG^\ddagger .

Additional Problems

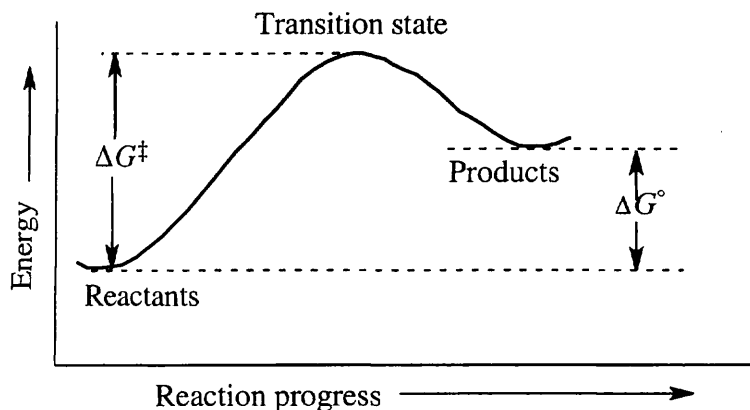
5.19



- 5.20 (a) The reaction between bromoethane and sodium cyanide is a substitution because two reagents exchange parts.
 (b) This reaction is an elimination because two products (cyclohexene and H_2O) are produced from one reactant
 (c) Two reactants form one product in this addition reaction.
 (d) This is a substitution reaction.

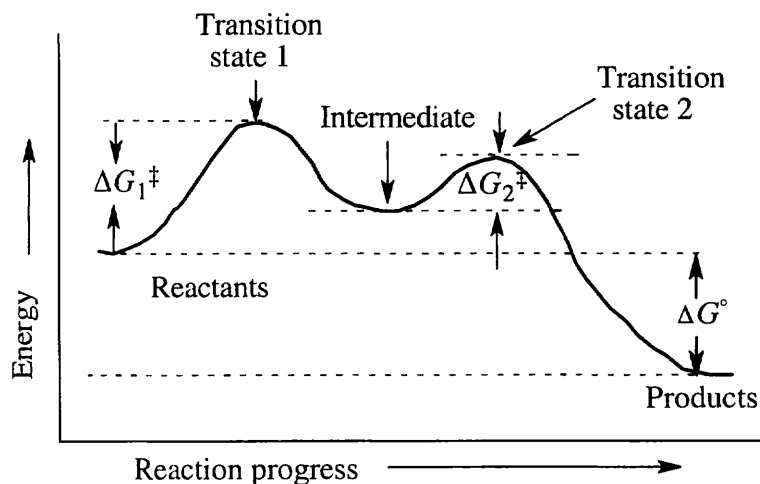
- 5.21 A transition state represents a structure occurring at an energy maximum. An intermediate occurs at an energy minimum between two transition states. Even though an intermediate may be of such high energy that it cannot be isolated, it is still of lower energy than the transition states surrounding it.

5.22



ΔG° is positive because $K_{\text{eq}} < 1$.

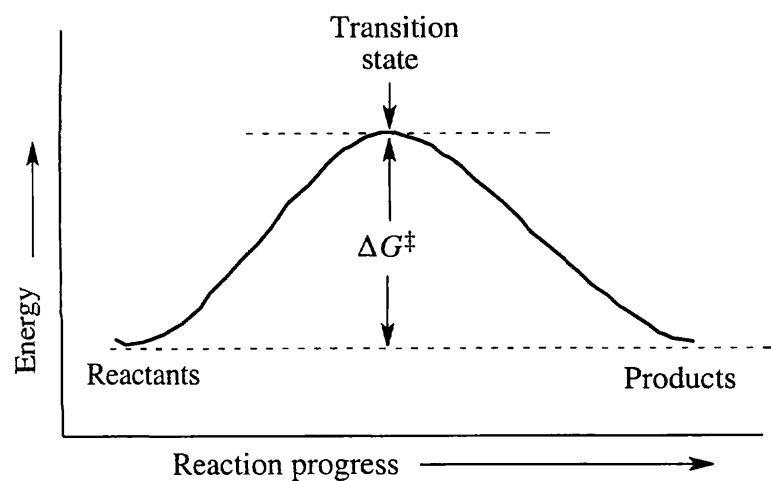
5.23



ΔG° is negative because $K_{\text{eq}} > 1$.

5.24 Problem 5.23 shows a reaction energy diagram of a two-step exergonic reaction. Step 2 is faster than step 1 because $\Delta G_2^\ddagger < \Delta G_1^\ddagger$.

5.25



A reaction with $K_{\text{eq}} = 1$ has $\Delta G^\circ = 0$.

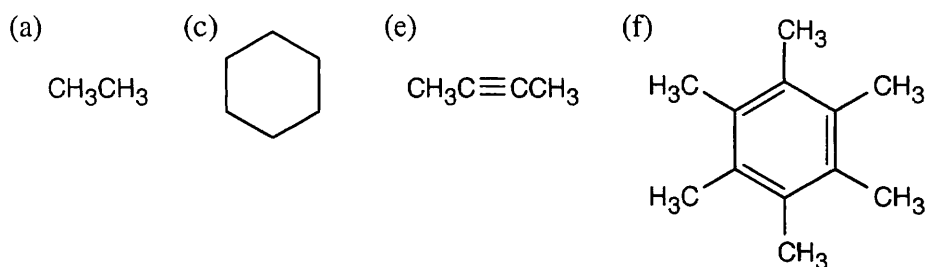
- 5.26 (a) The reaction is exothermic because the sign of ΔH° is negative.
 (b) $\Delta G^\circ = \Delta H^\circ - T\Delta S^\circ$
 $= -44 \text{ kJ/mol} - (298 \text{ K}) [-0.12 \text{ kJ/(K}\cdot\text{mol)}]$
 $= -44 \text{ kJ/mol} + 36 \text{ kJ/mol}$
 $= -8 \text{ kJ/mol}$

The reaction is favorable because the sign of ΔG° is negative.

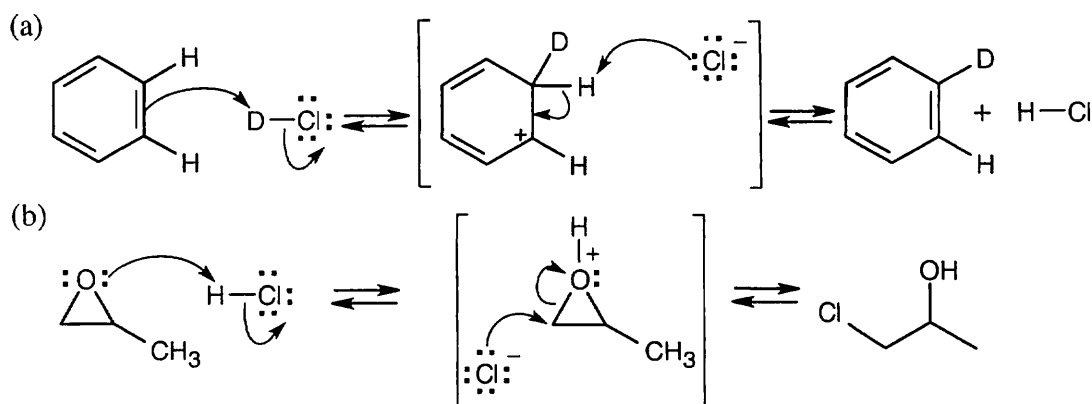
- 5.27 Irradiation initiates the chlorination reaction by producing chlorine radicals. For every chlorine radical consumed in the propagation steps, a new $\text{Cl}\cdot$ radical is formed to carry on the reaction. After irradiation stops, chlorine radicals are still present to carry on the propagation steps, but, as time goes on, radicals combine in termination reactions that remove them from the reaction mixture. Because the number of radicals decreases, fewer propagation cycles occur, and the reaction gradually slows down and stops.

- 5.28 Pentane has three types of hydrogen atoms, $\overset{\text{a}}{\text{CH}_3}\overset{\text{b}}{\text{CH}_2}\overset{\text{c}}{\text{CH}_2}\overset{\text{b}}{\text{CH}_2}\overset{\text{a}}{\text{CH}_3}$. Although monochlorination produces $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{Cl}$, it is not possible to avoid producing $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}(\text{Cl})\text{CH}_3$ and $\text{CH}_3\text{CH}_2\text{CH}(\text{Cl})\text{CH}_2\text{CH}_3$ as well. Since neopentane has only one type of hydrogen, monochlorination yields a single product.

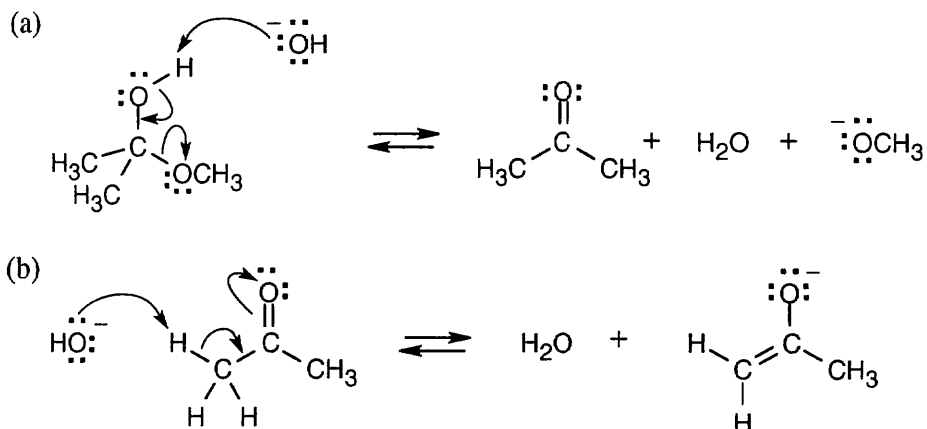
- 5.29 The following compounds yield single monohalogenation products because each has only one kind of hydrogen atom.



5.30



5.31

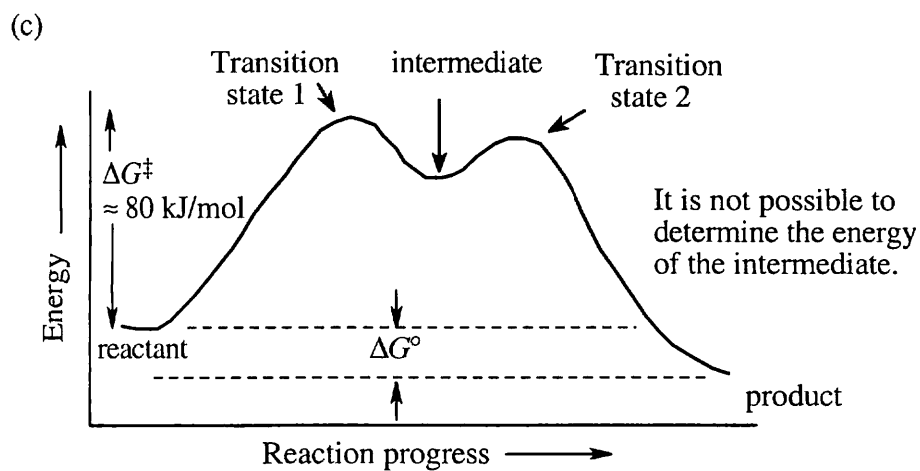


5.32

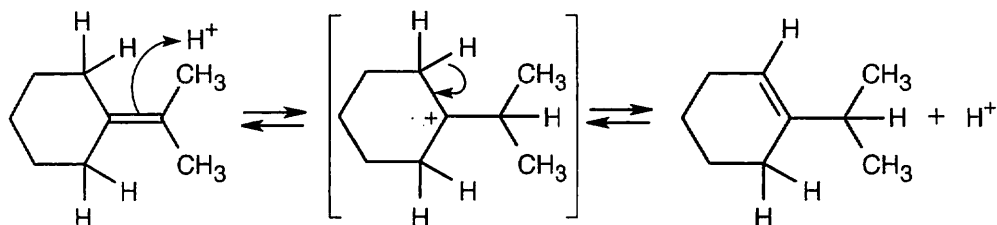
(a)

$$K_{\text{eq}} = \frac{[\text{Products}]}{[\text{Reactants}]} = \frac{0.70}{0.30} = 2.3$$

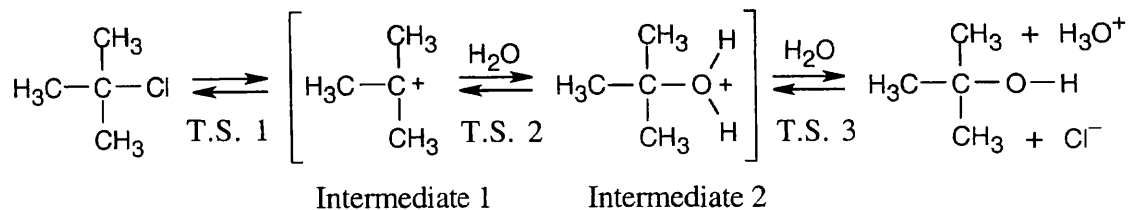
(b) Section 5.9 states that reactions that occur spontaneously have ΔG^\ddagger of less than 80 kJ/mol at room temperature. Since this reaction proceeds slowly at room temperature, ΔG^\ddagger is probably close to 80 kJ/mol.



5.33

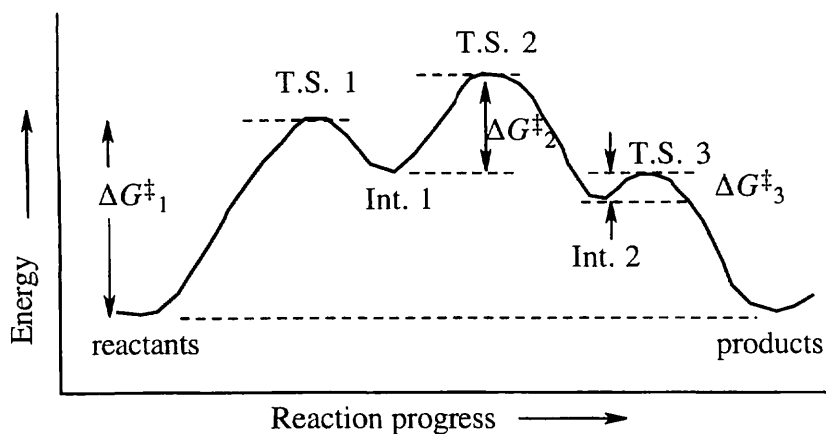


5.34

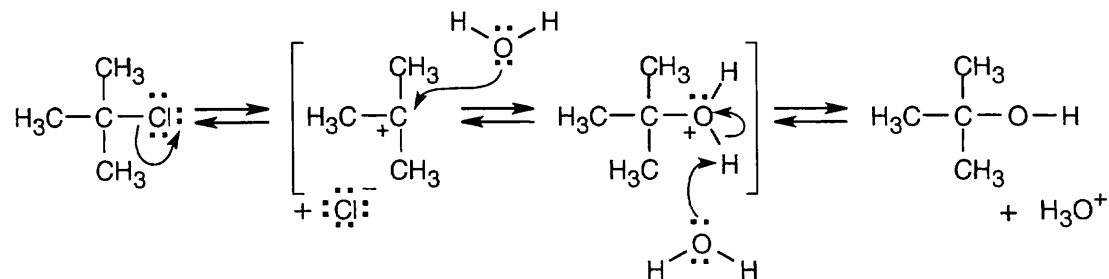


(a) ΔG^\ddagger for the first step is approximately 80 kJ/mol because the reaction takes place slowly at room temperature. ΔG^\ddagger values for the second and third steps are smaller - perhaps 60 kJ/mol for Step 2, and 40 kJ/mol for Step 3. ΔG° is approximately zero.

(b)



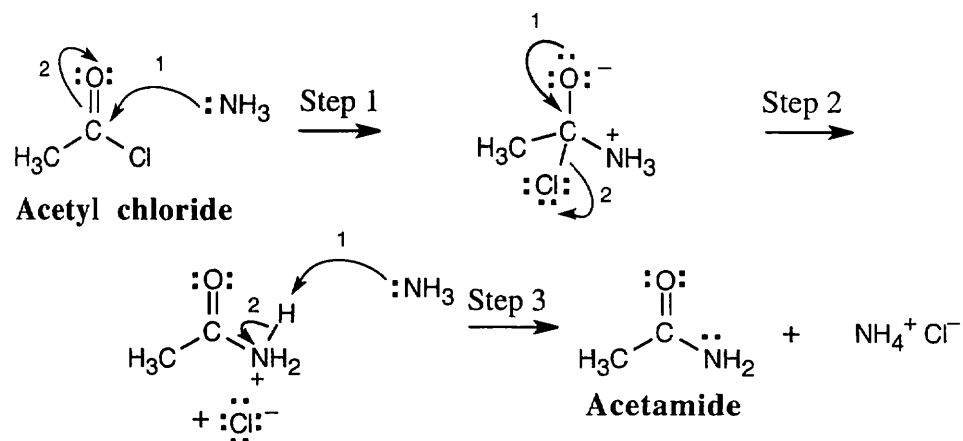
5.35



$$\begin{aligned}
 5.36 \quad \Delta G^\circ &= \Delta H^\circ - T\Delta S^\circ \\
 &= -75 \text{ kJ/mol} - (298 \text{ K})(0.054 \text{ kJ/K}\cdot\text{mol}) \\
 &= -75 \text{ kJ/mol} - 16 \text{ kJ/mol} \\
 &= -91 \text{ kJ/mol}
 \end{aligned}$$

The reaction is exothermic because ΔH° is negative, and it is exergonic because ΔG° is negative..

5.37 Each arrow represents either the formation of a bond or the breaking of a bond. The numbers over the arrows identify the bonds broken and formed.



Bonds formed

Bonds broken

Step 1: C-N (1)

C-O (2)

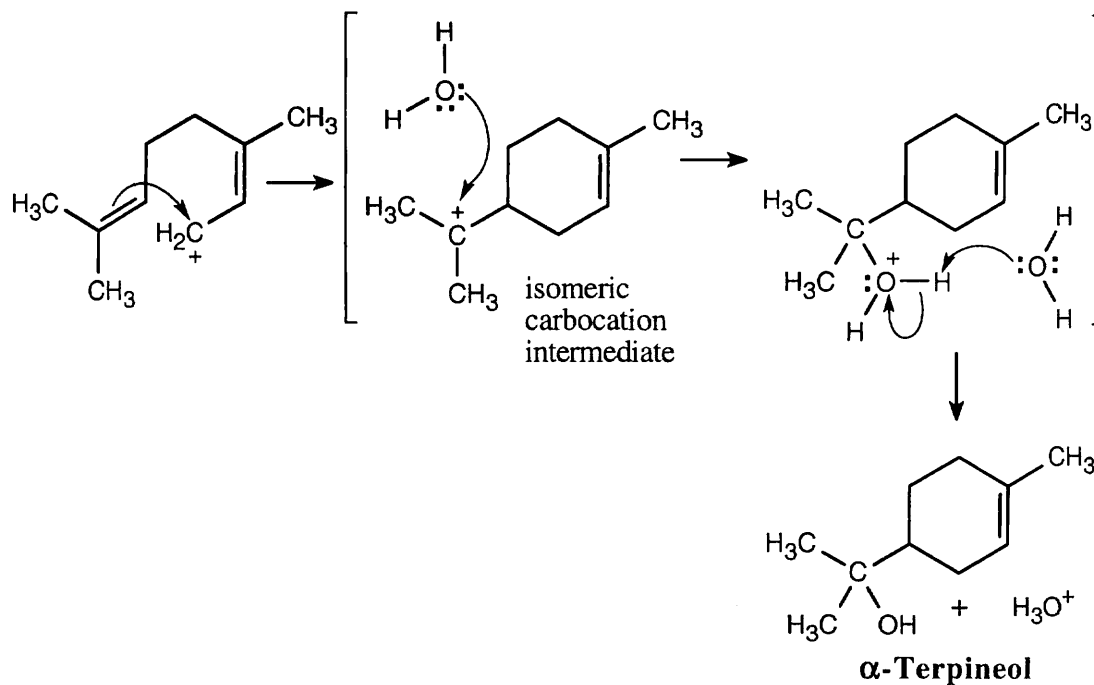
Step 2: C-O (1)

C-Cl (2)

Step 3: N-H (1)

N-H (2)

5.38



Review Unit 2: Alkanes and Their Stereochemistry: Organic Reactions

Major Topics Covered (with Vocabulary):

Functional Groups.

Alkanes:

saturated aliphatic straight-chain alkane branched-chain alkane isomer constitutional isomer
alkyl group primary, secondary, tertiary, quaternary carbon IUPAC system of nomenclature
primary, secondary, tertiary hydrogen paraffin cycloalkane cis-trans isomer stereoisomer

Alkane Stereochemistry:

conformer sawhorse representation Newman projection staggered conformation
eclipsed conformation torsional strain dihedral angle anti conformation gauche conformation
steric strain angle strain heat of combustion chair conformation axial group equatorial group
ring-flip 1,3-diaxial interaction conformational analysis boat conformation twist-boat
conformation polycyclic molecules bicycloalkane

Organic Reactions:

addition reaction elimination reaction substitution reaction rearrangement reaction
reaction mechanism homolytic heterolytic homogenic heterogenic radical reaction
polar reaction initiation propagation termination electronegativity polarizability
curved arrow electrophile nucleophile carbocation

Describing a Reaction:

K_{eq} ΔG° exergonic endergonic enthalpy entropy heat of reaction exothermic endothermic
bond dissociation energy reaction energy diagram transition state activation energy
reaction intermediate

Types of Problems:

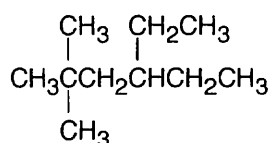
After studying these chapters, you should be able to:

- Identify functional groups, and draw molecules containing a given functional group.
- Draw all isomers of a given molecular formula.
- Name and draw alkanes and alkyl groups.
- Identify carbons and hydrogens as being primary, secondary or tertiary.
- Draw energy vs. angle of rotation graphs for single bond conformations.
- Draw Newman projections of bond conformations and predict their relative stability.
- Understand the geometry of, and predict the stability of, cycloalkanes having fewer than 6 carbons.
- Draw and name substituted cyclohexanes, indicating cis/trans geometry.
- Predict the stability of substituted cyclohexanes by estimating steric interactions.
- Identify reactions as polar, radical, substitution, elimination, addition, or rearrangement reactions.
- Understand the mechanism of radical reactions.

- Identify reagents as electrophiles or nucleophiles.
- Use curved arrows to draw reaction mechanisms.
- Understand the concepts of equilibrium and rate.
- Calculate K_{eq} and ΔG° of reactions, and use bond dissociation energies to calculate ΔH° of reactions.
- Draw reaction energy diagrams and label them properly.

Points to Remember:

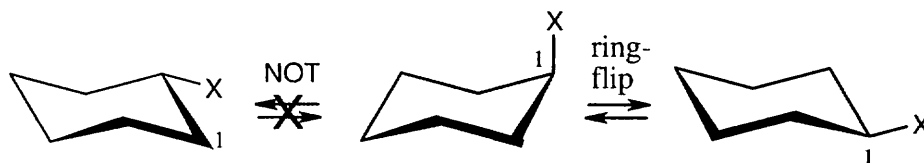
- * In identifying the functional groups in a compound, some groups have different designations that depend on the number and importance of other groups in the molecule. For example, a compound containing an $-OH$ group and few other groups is probably named as an alcohol, but when several other groups are present, the $-OH$ group is referred to as a hydroxyl group. There is a priority list of functional groups in the Appendix of the textbook, and this priority order will become more apparent as you progress through the text.
- * It is surprising how many errors can be made in naming compounds as simple as alkanes. Why is this? Often the problem is a result of just not paying attention. It is very easy to undercount or overcount the $-CH_2-$ groups in a chain and to misnumber substituents. Let's work through a problem, using the rules in Section 3.4.



Find the longest chain. In the above compound, the longest chain is a hexane (Try all possibilities; there are two different six-carbon chains in the compound.) Identify the substituents. The compound has two methyl groups and an ethyl group. It's a good idea to list these groups to keep track of them. Number the chain and the groups. Try both possible sets of numbers, and see which results in the lower combination of numbers. The compound might be named either as a 2,2,4-trisubstituted hexane or a 3,5,5-trisubstituted hexane, but the first name has a lower combination of numbers. Name the compound, remembering the prefix *di-* and remembering to list substituents in alphabetical order. The correct name for the above compound is 4-ethyl-2,2-dimethylhexane.

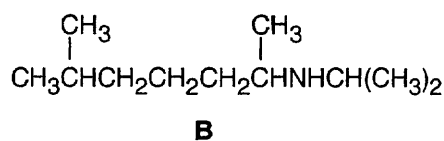
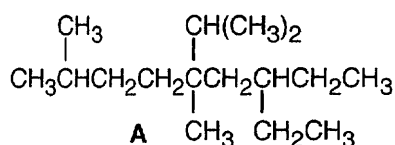
The acronym FINN (from the first letters of each step listed above) may be helpful.

- * When performing a ring-flip on a cyclohexane ring, keep track of the positions on the ring.

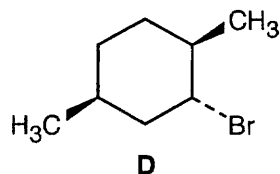
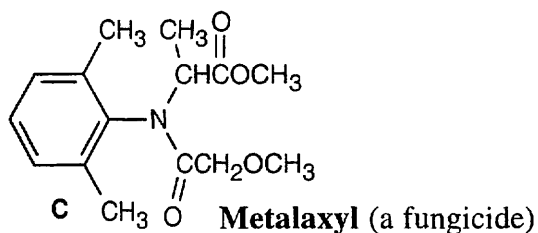


- * In virtually all cases, a compound is of lower energy than the free elements of which it is composed. Thus, energy is released when a compound is formed from its component elements, and energy is required when bonds are broken. Entropy decreases when a compound is formed from its component elements (because disorder decreases). For two compounds of similar structure, less energy is required to break all bonds of the higher energy compound than is required to break all bonds of the lower energy compound.

Self-test

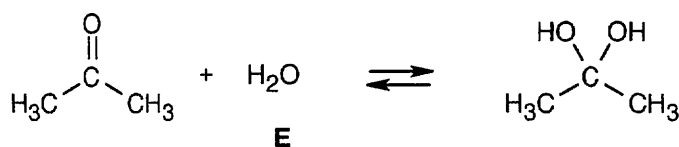
**Metron S** (an antihistamine)

Name **A**, and identify carbons as primary, secondary, tertiary or quaternary. **B** is an amine with two alkyl substituents. Name these groups and identify alkyl hydrogens as primary, secondary or tertiary.



Identify all functional groups of **C** (metalaxyl).

Name **D** and indicate the cis/trans relationship of the substituents. Draw both possible chair conformations, and calculate the energy difference between them.



What type of reaction is occurring in **E**? Would you expect that the reaction occurs by a polar or a radical mechanism? If K_{eq} for the reaction at 298 K is 10^{-3} , what sign do you expect for ΔG° ? Would you expect ΔS° to be negative or positive? What about ΔH° ?

Multiple Choice

- Which of the following functional groups doesn't contain a carbonyl group?
(a) aldehyde (b) ester (c) ether (d) ketone
- Which of the following compounds contains primary, secondary, tertiary and quaternary carbons?
(a) 2,2,4-Trimethylhexane (b) Ethylcyclohexane (c) 2-Methyl-4-ethylcyclohexane
(d) 2,2-Dimethylcyclohexane
- How many isomers of the formula $\text{C}_4\text{H}_8\text{Br}_2$ are there?
(a) 4 (b) 6 (c) 8 (d) 9

4. The lowest energy conformation of 2-methylbutane occurs:
(a) when all methyl groups are anti (b) when all methyl groups are gauche
(c) when two methyl groups are anti (d) when two methyl groups are eclipsed
5. The strain in a cyclopentane ring is due to:
(a) angle strain (b) torsional strain (c) steric strain (d) angle strain and torsional strain
6. In which molecule do the substituents in the more stable conformation have a diequatorial relationship?
(a) cis-1,2 disubstituted (b) cis-1,3 disubstituted (c) trans-1,3-disubstituted
(d) cis-1,4 disubstituted
7. Which of the following molecules is not a nucleophile?
(a) BH_3 (b) NH_3 (c) HO^- (d) $\text{H}_2\text{C}=\text{CH}_2$
8. Which of the following reactions probably has the greatest entropy increase?
(a) addition reaction (b) elimination reaction (c) substitution reaction (d) rearrangement
9. At a specific temperature T , a reaction has negative ΔS° and $K_{\text{eq}} > 1$. What can you say about ΔG° and ΔH° ?
(a) ΔG° is negative and ΔH° is positive (b) ΔG° and ΔH° are both positive (c) ΔG° and ΔH° are both negative (d) ΔG° is negative but you can't predict the sign of ΔH° .
10. In which of the following situations is ΔG^\ddagger likely to be smallest?
(a) a slow exergonic reaction (b) a fast exergonic reaction (c) a fast endergonic reaction
(d) a slow endergonic reaction