

# Instructor Supplemental Solutions to Problems

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to accompany

## Organic Chemistry 5th Edition

This manual provides the solutions to the problems that are not provided in the Study Guide and Solutions Manual. These answers are provided as electronic files in Portable Document Format (PDF). Each chapter is provided as a separate file. For the conventions used in these solutions, see the Preface of the *Study Guide and Solutions Manual*.

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# Chapter 1

## Chemical Bonding and Chemical Structure

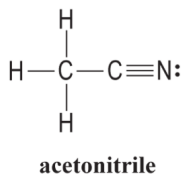
### Solutions to In-Text Problems

- 1.1 (b) The neutral calcium atom has a number of valence electrons equal to its group number, that is, 2.  
(d) Neutral Br, being in Group 7A, has 7 valence electrons; therefore,  $\text{Br}^+$  has 6.

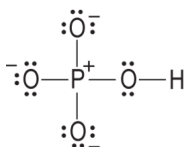
- 1.2 (b) The positive ion isoelectronic with neon must have 10 electrons and 11 protons, and therefore must have an atomic number = 11. This is the sodium ion,  $\text{Na}^+$ .  
(d) Because Ne has atomic number = 10 and F has atomic number = 9, the neon species that has 9 electrons is  $\text{Ne}^+$ .

- 1.3 (b)  $\begin{array}{c} \text{H} - \ddot{\text{N}} - \text{H} \\ | \\ \text{H} \end{array}$       (d)  $\begin{array}{c} \text{H} - \overset{+}{\text{O}} - \text{H} \\ | \\ \text{H} \end{array}$   
ammonia      hydronium ion

- 1.5 The structure of acetonitrile:

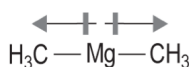


- 1.6 (b) The overall charge is  $-2$ .



- 1.8 (b) Formal charge does not give an accurate picture, because O is more electronegative than H; most of the positive charge is actually on the hydrogens.  
(d) An analysis of relative electronegativities would suggest that, because C is slightly more electronegative than H, a significant amount of the positive charge resides on the hydrogens. However, carbon does not have its full complement of valence electrons—that is, it is short of the octet by 2 electrons. In fact, both C and H share the positive charge about equally.

- 1.9 The bond dipole for dimethylmagnesium should indicate that C is at the negative end of the C—Mg bond, because carbon is more electronegative than magnesium.



- 1.10 (a) Water has bent geometry; that is, the H—O—H bond angle is approximately tetrahedral. Repulsion between the lone pairs and the bonds reduces this bond angle somewhat. (The actual bond angle is  $104.5^\circ$ .)

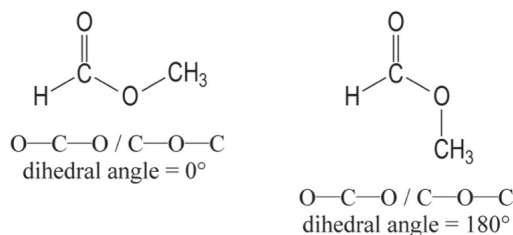
- (c) The formaldehyde molecule has trigonal planar geometry. Thus, both the H—C—H bond angle and the H—C=O bond angle are about 120°.

- 1.11 (a) Bond angles:  $aa$ ,  $ab$ ,  $bc$ ,  $bd$ ,  $cd$ ,  $de$ ,  $df$ , and  $ef$  are all about 120°, because all are centered on atoms with trigonal planar geometry;  $fg$  is predicted to have the tetrahedral value of 109.5. The bond lengths increase in the order

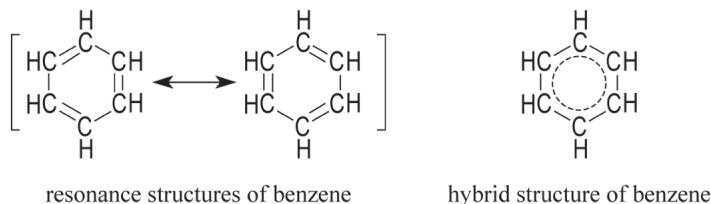
$$a \approx g < e < b < d \approx f < c$$

(In Chapter 4, you'll learn that C—H bonds attached to carbons of double bonds are shorter than C—H bonds attached to carbons of single bonds. For this reason,  $a < g$ .)

- 1.13 (a) Because the carbon has trigonal-planar geometry, the H—C=O bond angle is 120°.  
 (b) The two structures are as follows:

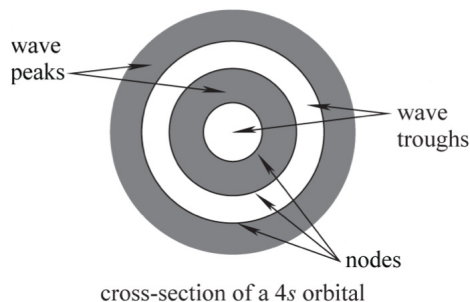


- 1.15 The resonance structures of benzene:



Each bond is a single bond in one structure and a double bond in the other. On average, each bond has a bond order of 1.5.

- 1.17 (b) A 4s orbital is four concentric spheres of electron density, each separated by a node, as shown in “cutaway” diagram (b) in Fig. IS1.1.
- 1.18 (b) The chloride ion,  $\text{Cl}^-$  (atomic number = 17 and one negative charge, therefore 18 electrons): This ion has the same electronic configuration as argon:  $(1s)^2(2s)^2(2p)^6(3s)^2(3p)^6$ . The valence orbitals are the 3s and 3p orbitals, and the valence electrons are the eight electrons that occupy these orbitals.
- (d) The sodium atom (atomic number = 11) has 11 electrons. Therefore its electronic configuration is  $(1s)^2(2s)^2(2p)^6(3s)^1$ . The valence orbital is the 3s orbital, and the valence electron is the one electron that occupies this orbital.



**Figure IS1.1** Cross section of a 4s orbital in the solution to Problem 1.17b.

- 1.19 The pictures and energy levels of the molecular orbitals for parts (a), (b), (d), and (e) are essentially the same as they are for the dihydrogen molecular orbitals in Fig. 1.14 of the text. For part (c), the atomic orbitals involved are  $2s$  orbitals, which have a node. However, the various species differ in their electron occupancies.
- (b) The  $\text{H}_2^-$  ion contains three electrons. This can be conceived as the combination of a hydrogen atom with a hydride ion ( $\text{H}^-$ ). By the aufbau principle, two occupy the bonding molecular orbital, and one occupies the antibonding molecular orbital. This is shown in the electron-occupancy diagram (b) of Fig. IS1.2. Because the bonding molecular orbital contains a greater number of electrons than the antibonding molecular orbital, this species is stable. Notice that in terms of electron occupancy,  $\text{H}_2^-$  and  $\text{He}_2^+$  are identical.
- (d) The  $\text{H}_2^{2-}$  ion can be conceived to result from the combination of two hydride ions ( $\text{H}^-$ ). This species contains four electrons; two occupy the bonding molecular orbital, and two occupy the antibonding molecular orbital. This is shown in the electron-occupancy diagram (d) of Fig. IS1.2. In this species, the energetic advantage of the electrons in the bonding molecular orbital is cancelled by the energetic disadvantage of the same number of electrons in the antibonding molecular orbital. This species consequently has no energetic advantage over two dissociated hydride ( $\text{H}^-$ ) ions, and therefore it readily dissociates.
- 1.22 (a) The oxygen of the hydronium ion has approximately tetrahedral geometry and is therefore  $sp^3$ -hybridized. Two of the  $sp^3$  hybrid orbitals contain an unshared electron pair. One of these becomes the lone pair in  $\text{H}_3\text{O}^+$ ; the other overlaps with a proton ( $\text{H}^+$ ) to give one of the O—H bonds. The other two  $sp^3$  hybrid orbitals contain one electron each; each of these overlaps with the  $1s$  orbital of a hydrogen atom (which contains one electron) to give the three  $sp^3-1s$   $\sigma$  bonds (the O—H bonds) of  $\text{H}_3\text{O}^+$ .
- (b) The H—O—H bond angles in  $\text{H}_3\text{O}^+$  should be somewhat larger than those in water, because there is one less lone pair and a smaller associated repulsion.

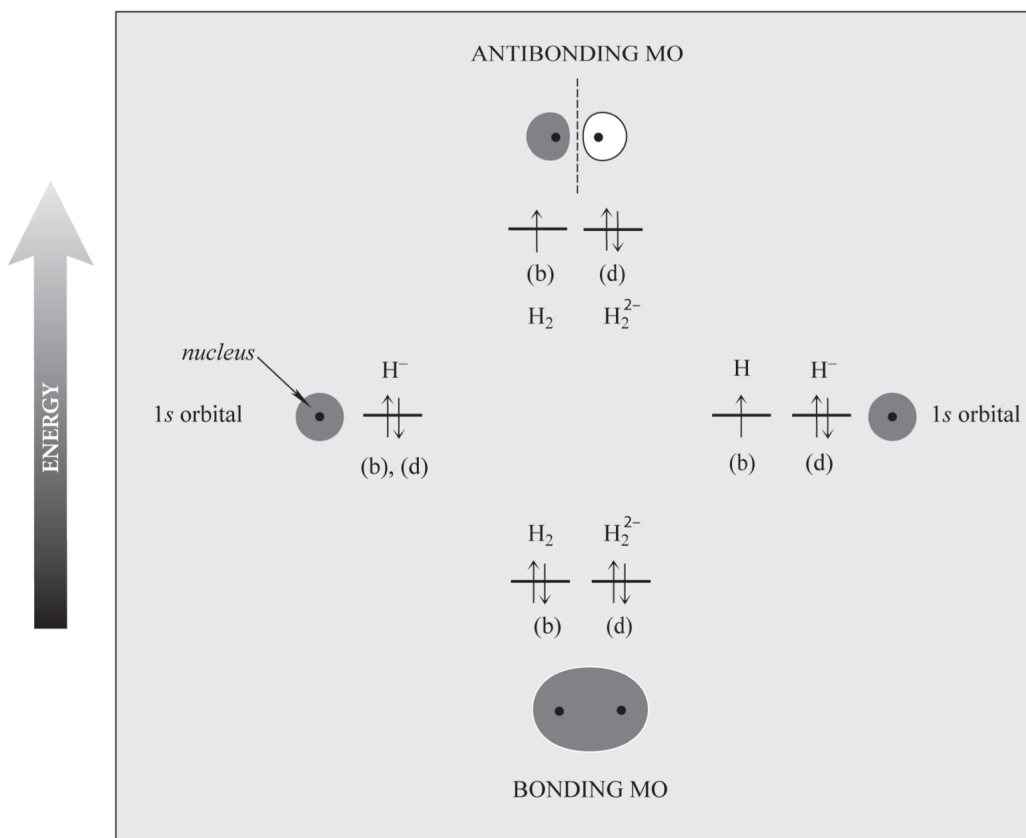
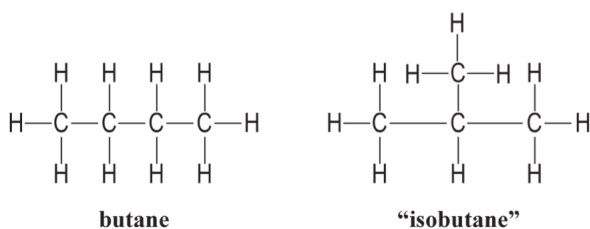
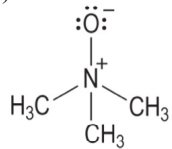
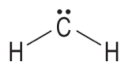
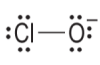


Figure IS1.2 Electron-occupancy diagram for the solution to Problems 1.19b and 1.19d.

## Solutions to Additional Problems

- 1.23 (b) Compound (2), cesium fluoride, would be most likely to exist as an ionic species, because Cs and F come from opposite corners of the periodic table.
- 1.24 The formal charge on all the hydrogens is 0. For the other atoms:
- (b) Nitrogen has a complete octet and a formal charge of 0.  
 (d) Boron has a sextet and a formal charge of 0.  
 (f) Boron has an octet and a formal charge of  $-1$ .
- 1.26 The lengths of the C—C bonds in isobutane have no significance; two are longer merely to accommodate the rest of the structure. Remember that these Lewis structures show only connectivity—not geometry.

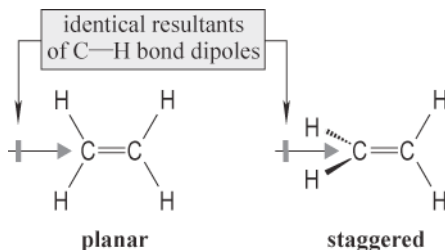


- 1.27 (b)   
**trimethylamine oxide**  
*overall charge = 0*
- (d)   
**methylene**  
*overall charge = 0*
- (f)   
**hypochlorite**  
*overall charge = -1*

- 1.29 Silicon atom (atomic number = 14; therefore 14 electrons):  $(1s)^2(2s)^2(2p)^6(3s)^2(3p_x)^1(3p_y)^1$ . The valence electrons are the two  $3s$  and the two  $3p$  electrons.
- 1.31 (b) The beryllium (Be) bears two groups, and therefore has linear geometry. The H—Be—H bond angle is  $180^\circ$ .  
 (d) The silicon is bound to four chlorines, and is therefore tetrahedral. The Cl—Si—Cl bond angle is  $109.5^\circ$ .  
 (f) The terminal carbons are bound to three groups, and are therefore trigonal planar. The central carbon is bound to two groups, and is therefore linear. Hence, the H—C—H and H—C=C bond angles are  $120^\circ$ ; the C=C=C bond angle is  $180^\circ$ .
- 1.32 (b) Using the method in part (a), the hybrid orbitals in the O—H bonds have about 18.6%  $s$  character; they therefore have 81.4%  $p$  character. Two such orbitals account for 37.2% of an  $s$  orbital. The 62.8% remaining  $s$  character is divided equally between the orbitals containing the unshared pairs—that is, 31.4% for each orbital. Therefore, the hybrid orbitals in the bonds are  $s^{18.6}p^{81.4}$ , or  $sp^{4.4}$  hybrids, and the orbitals containing the unshared pairs are  $s^{31.4}p^{68.6}$ , or  $sp^{2.2}$  hybrids.
- 1.34 We use reasoning analogous to that used in the previous problem. This ion is a hybrid of three identical structures. Hence, each property will be the sum of that property in each structure divided by 3.
- (a) Negative charge on each oxygen:  $(-1 + 0 + -1)/3 = -2/3$ .  
 (b) Bond order of each carbon–oxygen bond:  $(1 + 2 + 1)/3 = 4/3$  or 1.33.
- 1.37 (a) The number of equivalent  $f$  orbitals equals the number of possible values of the quantum number  $m_l$ , which is  $7 (\pm 3, \pm 2, \pm 1, 0)$ . That is, there are  $l + 1 = 7$  equivalent  $f$  orbitals.

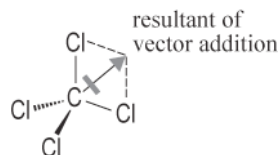
- (b) The orbital designation  $f$  means  $l = 3$ . Orbitals with  $l = 3$  (that is,  $f$  orbitals) first appear in principal quantum level 4.
- (c) There are  $n - 1 = 5 - 1 = 4$  nodes. (Three of them are planar, and one is spherical; see Problem 1.35. Can you sketch a  $4f$  orbital?)

1.40 No matter how any  $\text{CH}_2$  group is turned, the resultant bond dipole is the same:

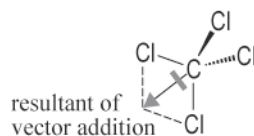


Hence, ethylenes with the two different dihedral angles should both have zero dipole moment because the resultants of the two  $\text{CH}_2$  groups cancel each other in either arrangement. The observation of zero dipole moment does not permit a choice between these two dihedral angles.

- 1.42 To solve this problem, we first have to know the geometry of  $\text{CCl}_4$ . This should be easy: it's tetrahedral, because the carbon is bonded to four identical groups. Now, as suggested in the hint, let's do a vector addition for the bond dipoles of each  $\text{Cl}-\text{C}-\text{Cl}$  pair. (Use a dipole arrow of arbitrary length as long as it is the same for both. We'll use an arrow with the length of the  $\text{C}-\text{Cl}$  bonds.) Here's the result of the vector addition, which we've done graphically, for the first pair. Notice that, because the  $\text{C}-\text{Cl}$  bonds are identical, the resultant must *bisect* the angle between the two bonds.



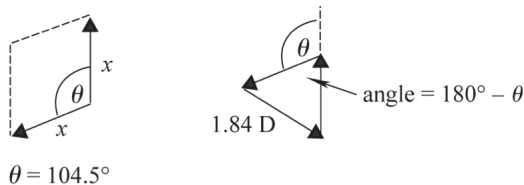
Now let's do the resultant for the second pair. Because the  $\text{C}-\text{Cl}$  bonds are identical to those of the first pair, it follows that the resultant is the same length, and it again bisects the  $\text{Cl}-\text{C}-\text{Cl}$  bond angle. (We've rotated the molecule about an axis along the dipole so we are viewing the other two chlorines from the perspective we used to view the first two—in the plane of the page.)



The two resultants we have just obtained are oriented at an angle of  $180^\circ$ ; that is, they are pointed in opposite directions. Since they are identical in magnitude, they cancel. Hence the dipole moment of  $\text{CCl}_4$  is zero.



- 1.44 This problem requires a construction similar to the one used in Problem 1.43 in which the resultant is known and the individual  $\text{O}-\text{H}$  bond dipoles are unknown.



Applying the law of cosines, with  $x$  as the O—H bond dipoles,

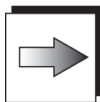
$$1.84^2 = x^2 + x^2 - 2x^2 (\cos (180^\circ - \theta))$$

$$3.39 = 2x^2(1 - \cos 75.5^\circ) = 2x^2(1 - 0.25) = 1.50 x^2$$

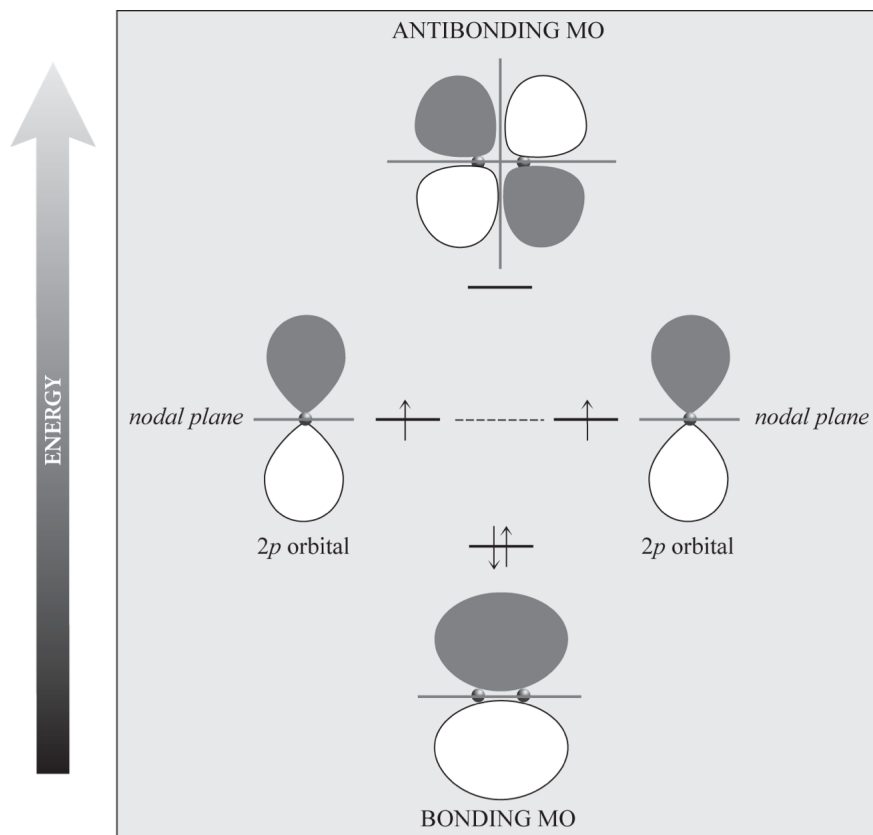
$$x = \sqrt{\frac{3.39}{1.50}} = 1.50 \text{ D}$$

This is the calculated value of the O—H bond dipole, which is very similar to the value assumed in Problem 1.43.

- 1.46 (a) The bonding molecular orbital is derived by the constructive “side-to-side” overlap of peaks with peaks and troughs with troughs. The antibonding molecular orbital is derived by changing the peak to a trough and the trough to a peak in one of the two  $2p$  orbitals. Destructive overlap of troughs with peaks and peaks with troughs gives an additional node in the antibonding orbital. These molecular orbitals are shown in Fig. IS1.3 on the following page.
- (b) The nodes are also shown in Fig. IS1.3. Both of the MOs have the nodes of the original  $2p$  orbitals, which merge into a single node because the nodal plane is common to both orbitals. The antibonding MO has in addition a node between the original orbitals that results from the destructive overlap of a peak and a trough.
- (c) Fig. SG1.8 is the required interaction diagram.
- (d) The resulting bond is *not* a  $\sigma$  bond because it is not cylindrically symmetrical about the internuclear axis.



This type of bond, called a pi ( $\pi$ ) bond, is important in the carbon–carbon double bond. Pi bonds are discussed in Chapter 4.



**Figure IS1.3** An orbital interaction diagram for the side-to-side interaction of two  $2p$  orbitals. The small spheres are nuclei, and the gray lines are nodal planes viewed end-on.





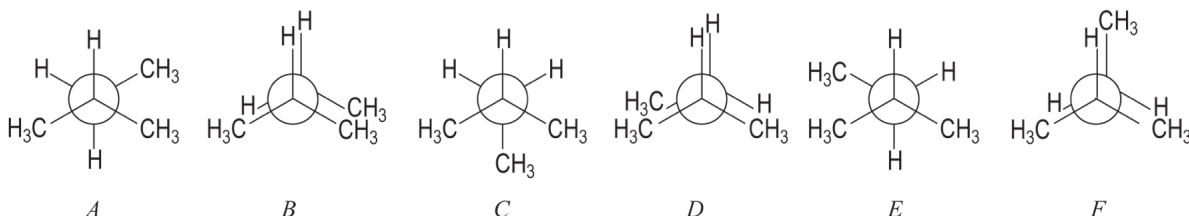
# Chapter 2

## Alkanes

### Solutions to In-Text Problems

2.1 (b) No; all alkanes—indeed, all hydrocarbons—must have an even number of hydrogens. Thus, if  $2n + 2 = 23$ , then  $n$  would have to be 10.5—an impossible number of carbons.

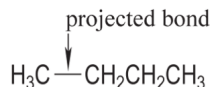
2.3 (a) The staggered conformations of isopentane are *A*, *C*, and *E*; the eclipsed conformations are *B*, *D*, and *F*.



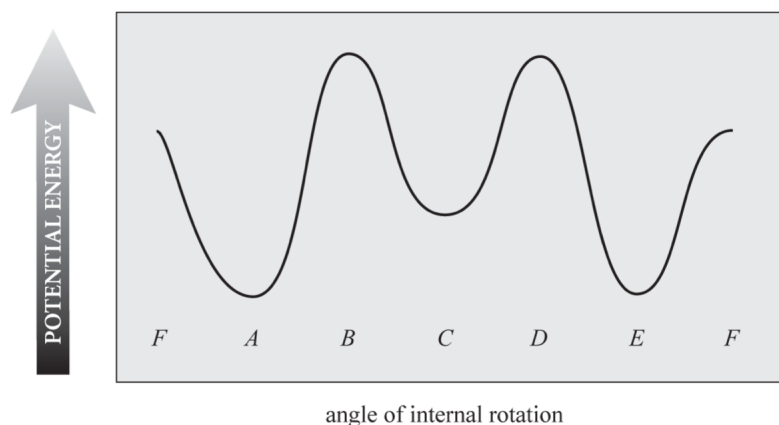
(b) The curve of potential energy versus angle of rotation is shown in Fig. IS2.1. The staggered conformations *B* and *D* have the highest energy because they have eclipsed methyl groups.

(c) Conformations *A* and *E* have the lowest energy because they have one less interaction in which methyl groups are “close together”—that is, the C—CH<sub>3</sub> bonds have a 60° dihedral angle—than conformation *C*; hence, either of these conformations is present in greater concentration than conformation *C*.

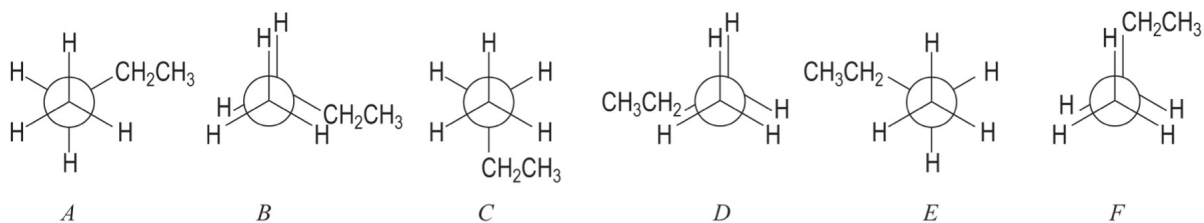
2.4 (a) The projected bond is the carbon–carbon bond at the end of the butane molecule:



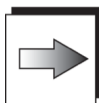
There are three identical staggered conformations and three identical eclipsed conformations.



**Figure IS2.1.** A diagram of potential energy versus angle of internal rotation in isopentane to accompany the solution to Problem 2.3b. The conformations are shown the solution to part (a). Each conformation differs from the adjacent ones by a rotational angle of  $\pm 60^\circ$ .

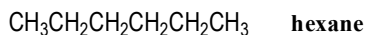


- (b) The curve of potential energy versus angle of internal rotation is essentially identical to the curve for ethane (Fig. 2.3, text p. 52), except that the energy difference between staggered and eclipsed forms is slightly greater. That is, the energies of all staggered forms lie at equal minima, and the energies of all eclipsed forms lie at equal maxima.
- (c) All staggered conformations are present in equal amount because they are identical.

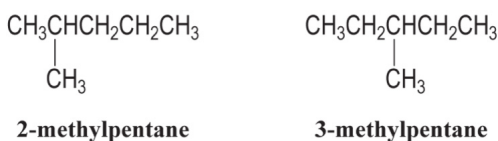


There is a subtlety here. Problem 2.4 has considered the conformation about the C1–C2 bond in isolation. Any staggered conformation about the C1–C2 bond contains a mixture of gauche and anti conformations about the C2–C3 bond.

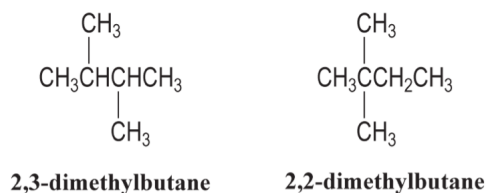
- 2.5 (b) 2,4-Dimethylhexane  
(d) 2,5,5-Trimethylheptane. Rule 8 rules out 3,3,6-trimethylheptane.
- 2.6 (b) Following the systematic approach used in part (a) (see the Study Guide and Solutions Manual), we first draw the structure of hexane itself.



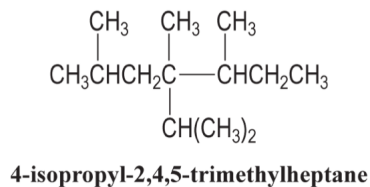
Next, draw the structures with a principal chain of five carbons and one methyl branch:



Finally, we draw the structures with two methyl branches.



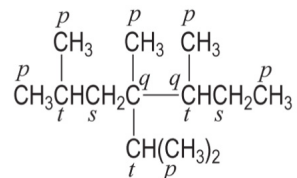
- 2.7 (b) Numbering from either direction gives the branch numbers (4,5,5,6); for that reason, alphabetical citation (rule 10) provides the basis for numbering. The name is 4-ethyl-5,5,6-trimethylnonane.
- 2.9 The structure of 4-isopropyl-2,4,5-trimethylheptane:





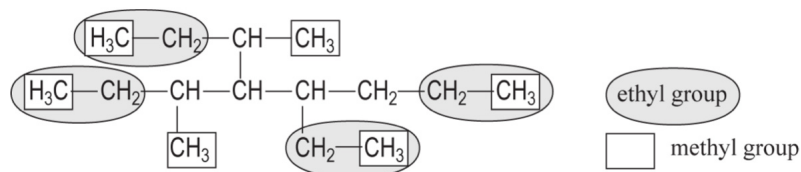
Your structure might look different from this one. Any structure with the same connectivity as this one is correct.

- 2.10 In the following structure, *p* = primary, *s* = secondary, *t* = tertiary, and *q* = quaternary.



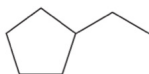
**4-isopropyl-2,4,5-trimethylheptane**

- (b) The primary hydrogens are those in the structure labeled “*p*”; the secondary hydrogens are those at the carbons labeled “*s*”; and the tertiary hydrogens are those at the carbons labeled “*t*.”
- 2.11 Ethyl groups are in the shaded circles; methyl groups are in the boxes. Each ethyl group by definition contains a methyl group.



**4-sec-butyl-5-ethyl-3-methyloctane**

- 2.12 (b)



**ethylcyclopentane**

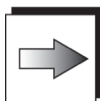
- 2.13 (b) The name is 1-ethyl-2,4-dimethylcyclopentane. Rule 10 (alphabetical citation) and rule 8 dictate the numbers of the substituents.
- 2.14 (b) By the reasoning in part (a), the formula is  $2n - 4$ .
- 2.15 (b) The number of hydrogens differs from the fully saturated number (16) by 4, or two pair. Therefore, the compound has two rings.
- 2.17 (b) Benzene is a very symmetrical compound. The carbon framework is essentially a planar hexagon. Because of its resonance structures, all carbon-carbon bonds have equal length. (See Problem 1.15, text p. 22.) The more symmetrical benzene has an usually high melting point (for a hydrocarbon),  $+5.5^\circ$ . The less symmetrical toluene has a more typical melting point,  $-95^\circ$ .
- 2.19 (b) Because only two layers form, two of the three substances are mutually soluble. From part (a), we know that water and bromoethane are insoluble—they form two layers. From the reading, we know that hexane, a hydrocarbon, is insoluble in water. Therefore, one layer is water and the other is a solution of hexane and bromoethane. If volumes are nearly additive, the hexane-containing layer will be the one with larger volume. But we are not given which layer has the larger volume, so let’s decide the answer in another way.

Because we use equal volumes of hexane and bromoethane, a reasonable conclusion is that the density of the mixture is the average of the two densities, that is,  $(1.46 \text{ g mL}^{-1} + 0.66 \text{ g mL}^{-1})/2 = 1.06 \text{ g mL}^{-1}$ . The mixture is somewhat denser than water and is therefore the lower layer.

- 2.20 (b) Follow the same procedure as in part (a), noting that there is one less mole of water formed per mole of  $\text{CO}_2$  and one less atom of oxygen required.

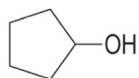


- 2.22 The Oxhide family burns  $(12,000 \text{ miles}/25 \text{ miles gal}^{-1}) = 480$  gallons of gasoline per year. The result from Problem 2.21 is based on 15 gallons; scale the result from that solution to 480 gallons by multiplying it by the factor  $(480/15) = 32$ . This gives a carbon footprint of 8,544 pounds per year of  $\text{CO}_2$  for the Oxhide family car.

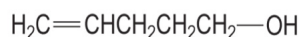


For about 250,000,000 vehicles in the United States, with an average mileage of  $18 \text{ miles gal}^{-1}$ , the carbon footprint is about  $3 \times 10^{12}$  (three *trillion*) pounds of  $\text{CO}_2$ !

- 2.23 (b) Any structure with five carbons, an  $\text{—OH}$  group, and *either* a ring or a double bond is correct. Two of many examples are the following:



**cyclopentanol**

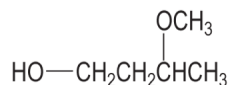


**4-penten-1-ol**

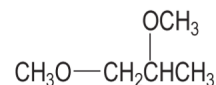
- 2.24 With 12 hydrogens and 5 carbons, this compound cannot have any double bonds or rings. Because amides, carboxylic acids, phenols, and esters each contain one or more double bonds, these groups are ruled out. An amide is ruled out also because it contains nitrogen, which is not present in the compound. The remaining possibilities are a compound with two ether groups, a compound with two alcohol groups, or a compound with both an ether and an alcohol. Examples of each are the following:



a compound with  
two alcohol groups



a compound with  
an alcohol and an ether group

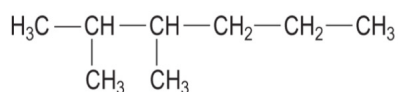


a compound with  
two ether groups

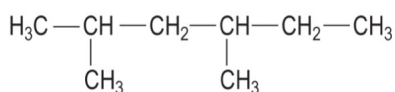
### Solutions to Additional Problems

- 2.25 (b) The second compound has two more carbons than the first, and should have a boiling point that is 40–50° greater—approximately 168–178°.

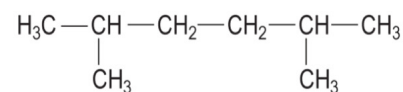
- 2.26 (b) The isomers of octane with six carbons in their principal chains:



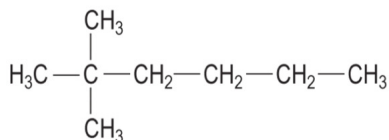
2,3-dimethylhexane



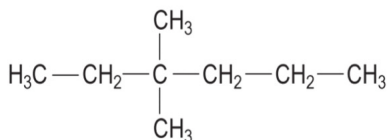
2,4-dimethylhexane



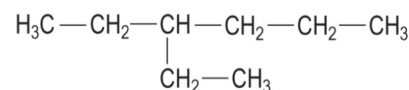
2,5-dimethylhexane



2,2-dimethylhexane

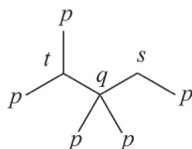


3,3-dimethylhexane



3-ethylhexane

- 2.27 (b)



- 2.28 (b) Cyclopentane has five carbons and only secondary hydrogens:

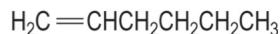


cyclopentane

- (d) The simplest composition has 6 carbons (72.06 atomic mass units) and 12 hydrogens (12.10 atomic mass units) for a molecular mass of 84.16. Cyclohexane or any other six-carbon hydrocarbon containing either one ring or one double bond would fit.



cyclohexane



1-hexene

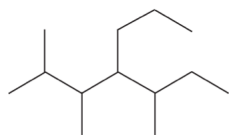
- 2.29 (b) 4-Ethyl-5-methyloctane

- (d) 4-Isopropyloctane

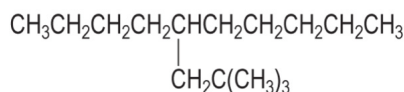
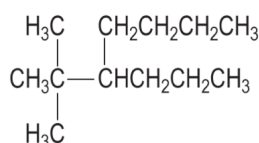


In noncyclic skeletal structures, don't forget to count the carbons on the ends of the chains.

2.30 (b)

**2,3,5-trimethyl-4-propylheptane**

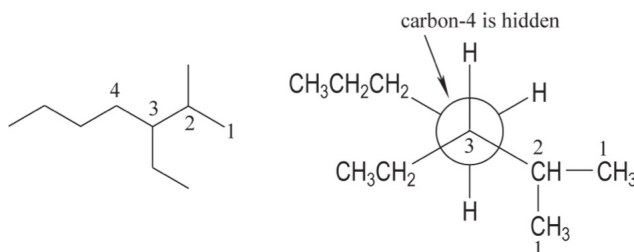
2.31 (b) 5-Neopentyldecane is a correct name.

**5-neopentyldecane**(d) The correct name is 4-*tert*-butyloctane.**4-*tert*-butyloctane**2.32 (b) The systematic name for “pullane” is 1,1-di-*tert*-butyl-2,4-diethylcyclopentane.

Hence, structures *B* and *C* are Newman projections of the same compound, 3-ethyl-2-methylpentane. Compound *A* is 2,3,3-trimethylpentane.

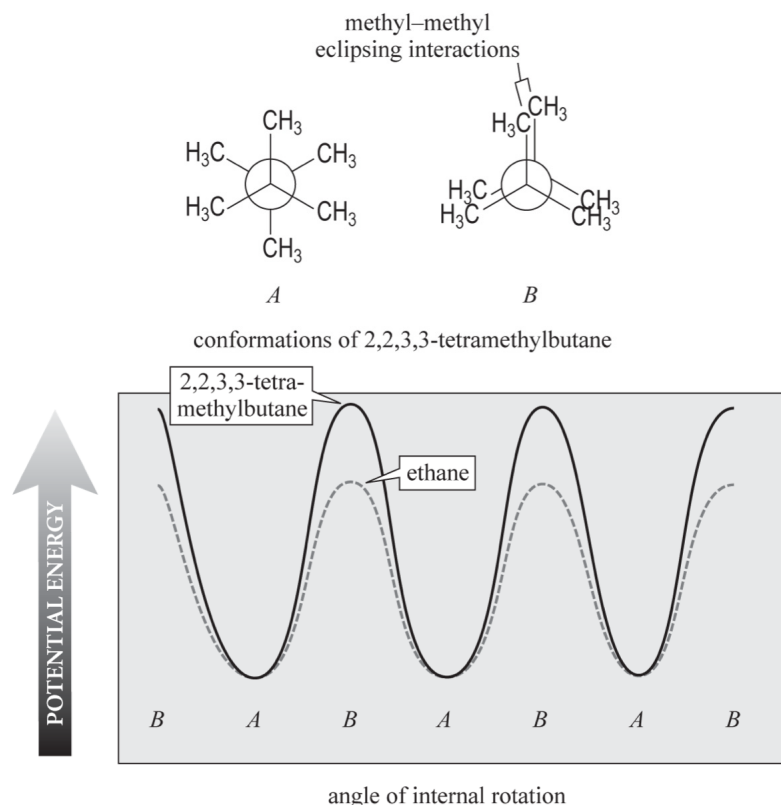
2.33 (b) Structures *A* and *C* both have the connectivity [(CH<sub>3</sub>)<sub>2</sub>CH, CH<sub>2</sub>, CH(CH<sub>3</sub>), CH<sub>2</sub>, CH<sub>2</sub>, CH<sub>3</sub>]. The connectivity of *B* is different. Consequently, structures *A* and *C* represent the same compound, 2,4-dimethylheptane. Compound *B* is 3-ethyl-2-methylheptane.

2.34 (b) The propyl group on carbon-4 has to be gauche to either the ethyl group or the isopropyl group. Because the isopropyl group is larger, the propyl group is gauche to the ethyl group in the most stable conformation.



The ambiguity in drawing the structure is that it has a mirror image, which is not the same, although it has the same energy. (The issue of mirror-image structures is considered in Chapter 6.) If you drew the mirror-image structure, it is equally correct. As noted in the solution to Problem 2.33(b), the name of this compound is 3-ethyl-2-methylheptane.

2.36 Both curves would have the same general appearance, that is, three barriers of equal height. (See Fig. IS2.2.) However, the curve for 2,2,3,3-tetramethylbutane should have greater potential-energy barriers because each eclipsed conformation has three severe methyl–methyl eclipsing interactions, and because eclipsed methyl groups have greater repulsion than gauche methyl groups.

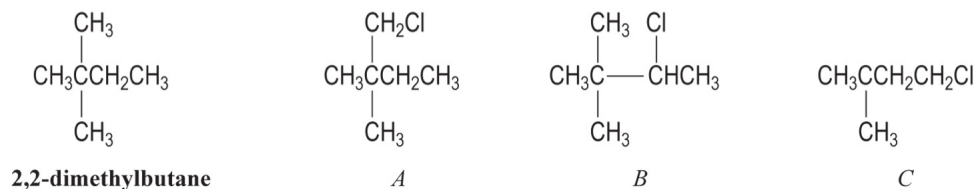


**Figure IS2.2.** Diagrams of potential energy versus angle of internal rotation in 2,2,3,3-tetramethylbutane and ethane to accompany the solution to Problem 2.36. The conformations are shown above the graph. The staggered conformations of ethane and 2,2,3,3-tetramethylbutane are placed at the same energy for comparison purposes. Each conformation differs from the adjacent ones by a rotational angle of  $\pm 60^\circ$ .

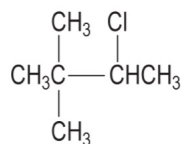
- 2.39 Because severe van der Waals repulsions occur between the *tert*-butyl groups in compound *A* at normal bond lengths and angles, the only way for the molecule to relieve these repulsions is to stretch the appropriate bonds and flatten itself by widening the C—C—C angles. The observed structure is a compromise between the Scylla of van der Waals repulsions and the Charybdis of nonoptimal bond lengths and angles.
- 2.44 (b) Because each ring subtracts two hydrogens from the number present in a noncyclic hydrocarbon ( $2n + 2$ ), the alkane must contain two rings. [See the solution to Problem 2.14(c)]. Two of several possibilities that meet the criteria are the following:



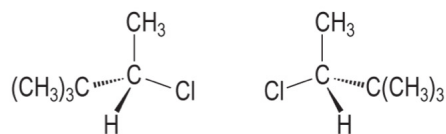
- 2.45 (b) The possibilities are as follows:



Compound *B*, like compound *B* in part (a), can exist as nonsuperimposable mirror-image structures.



B



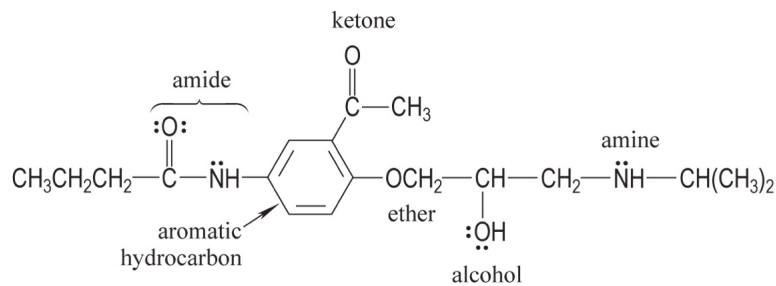
nonsuperimposable mirror-image structures of 2,2-dimethyl-3-chlorobutane

**2,2-dimethyl-3-chlorobutane**

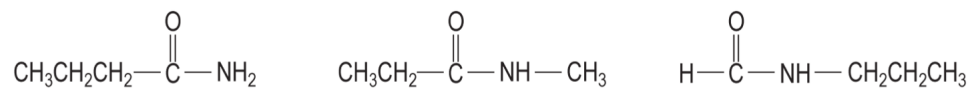
2.46 Consult the inside front cover of the text for a list of common functional groups.

- (b) nitrile  
 (d) ether

2.47 The functional groups in acebutolol are identified and the compound classes are labeled in the following structure.

**acebutolol**

2.48 (b) The following are three of several possibilities:



- (d) A compound with the formula  $\text{C}_4\text{H}_9\text{NO}$  cannot be a nitrile. A nitrile contains a triple bond, which would reduce the number of hydrogens to 7.



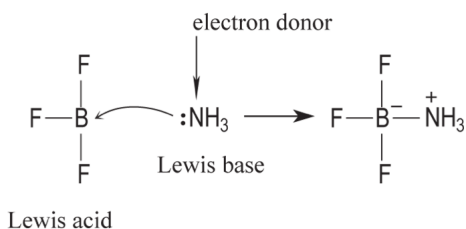
# Chapter 3

## Acids and Bases.

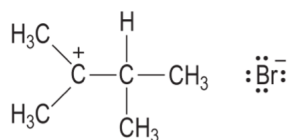
### The Curved-Arrow Notation

#### Solutions to In-Text Problems

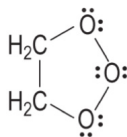
- 3.1 (b) The nitrogen of ammonia donates an electron pair to electron-deficient boron of  $\text{BF}_3$ . (The electron pairs on the fluorine are not shown because they have no direct part in the reaction.)



- 3.2 (b)



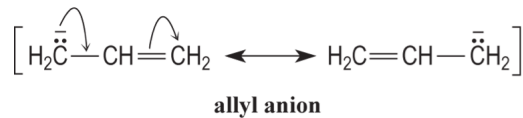
- (d)



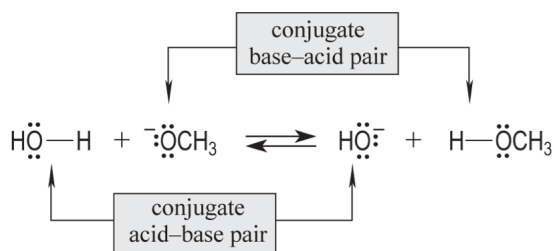
- 3.3 (b)



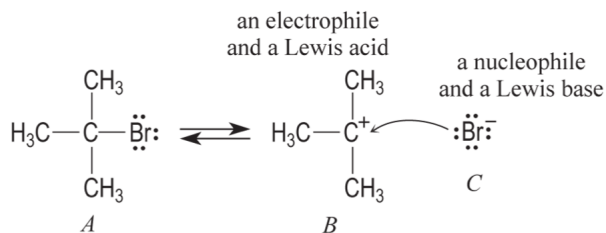
- 3.4 (b)



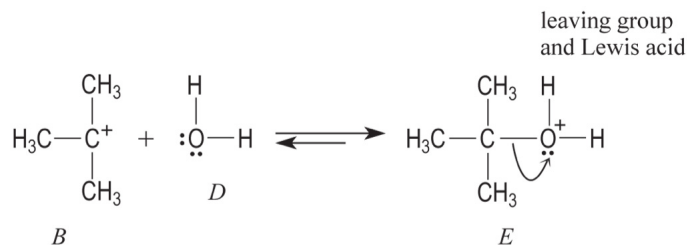
- 3.6 Let  $\text{H}_2\text{O}$  be the acid on the left. Then  $\text{CH}_3\text{OH}$  is the acid on the right. (If you chose  $\text{CH}_3\text{OH}$  as the acid on the left, then switch reactants and products in the reaction below.)



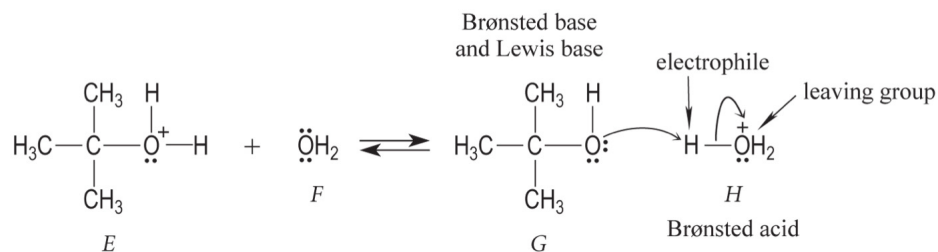
- 3.7 (a) The reverse of reaction 3.18a is a Lewis acid-base association reaction; there is no leaving group.



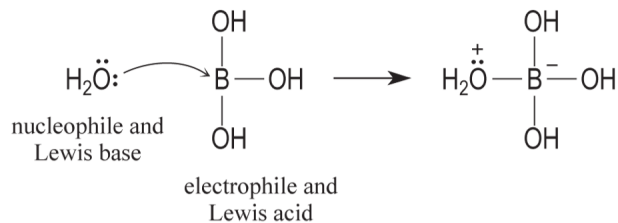
- (b) The reverse of reaction 3.18b is a Lewis acid–base dissociation reaction. There is no nucleophile.



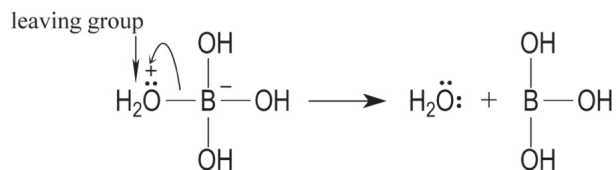
- (c) Like the forward reaction, the reverse of reaction 3.18c is a Brønsted acid–base reaction.



- 3.8 (b) This is a Lewis acid–base association reaction.



The reverse reaction is a Lewis acid–base dissociation reaction:



- 3.9 (b) The curved-arrow notation:



The analogous Brønsted acid–base reaction replaces the ethyl group with H:



3.12 Find the  $K_a$  by changing the sign of the  $pK_a$  and taking the antilog.

(a)  $K_a = 10^{-4}$     (b)  $K_a = 10^{-7.8} = 1.58 \times 10^{-8}$     (c)  $K_a = 10^2 = 100$

3.13 (b) The strongest acid in Problem 3.12 is the one with the largest  $K_a$ —that is, (c).

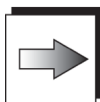
3.14 (b) The acid–base reaction is



The acid on the right side of the equation is H—F ( $pK_a = 3.2$ ), and the acid on the left side is H—CN ( $pK_a = 9.4$ ). Using the procedure in part (a), we find that  $\log K_{\text{eq}} = 3.2 - 9.4 = -6.2$ , and  $K_{\text{eq}} = 10^{-6.2} = 6.3 \times 10^{-7}$ .

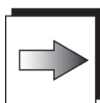
3.16 (b) For this calculation use Eq. 3.30 on text p. 106.

$$\Delta G^\circ = -2.30RT \log K_{\text{eq}} = -5.71 \log(305) \text{ kJ mol}^{-1} = -5.71(2.48) \text{ kJ mol}^{-1} = -14.2 \text{ kJ mol}^{-1}$$



In these solutions and in the Study Guide and Solutions Manual,  $\text{kJ mol}^{-1}$  is used as the unit of energy. If you wish to convert  $\text{kJ mol}^{-1}$  to  $\text{kcal mol}^{-1}$ , simply divide by 4.184  $\text{kJ kcal}^{-1}$ . Also, it is helpful to remember that  $2.30RT$  at 298 K (25 °C) is 5.71  $\text{kJ mol}^{-1}$ .

3.17 (b) If the  $\Delta G^\circ$  is positive, the equilibrium constant is less than unity and the reaction is less favorable; consequently, there should be much less  $C$  and more  $A$  and  $B$  at equilibrium.

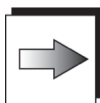


An actual calculation shows that  $[C] = 0.0061$ . Then  $[A] = 0.1 - x = 0.0939 \text{ M}$ , and  $[B] = 0.2 - x = 0.1939$ . The concentration of  $C$  is 10% of that in part (a), a result consistent with the statement in part (b).

3.18 (a) 5.71

3.19 (b) The more acidic species is  $\text{CH}_3\text{—}^+\text{SH}_2$ .

3.20 (b) Compound  $A$  is much more basic than compound  $B$  (charge effect). By the element effect,  $C$  is much more basic than  $A$ ; this follows from the fact that if we rank their conjugate acids, the conjugate acid of  $C$ , ammonia, is less acidic than the conjugate acid of  $A$ ,  $\text{CH}_3\text{OH}$ . Note that a comparison of  $A$  and  $B$  brings into play the amphotericism of methanol: like water, it can act as both an acid and a base in different reactions.



A negatively charged atom is more basic than the same neutral atom. This can be understood on the basis of the charge effect for positively charged atoms by taking into account the relationships of conjugate acids and bases. By the charge effect, an acidic proton on a positively charged atom is more acidic than an acidic proton on the same neutral atom. It follows, then, that the neutral conjugate base of the positively charged acid is less basic than the negatively charged conjugate base of the neutral acid.

3.21 In each set, label the compounds from left to right as  $A$ ,  $B$ , and  $C$ .

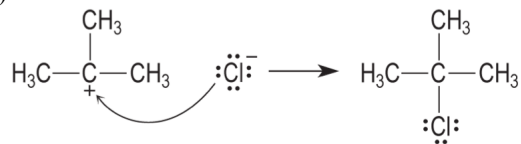
(b) The order of  $pK_a$  values is  $B$  (least acidic)  $> A > C$  (most acidic). The acidity of compound  $A$ , relative to compound  $B$ , is increased by the polar effect of one methoxy ( $\text{—OCH}_3$ ) group. The acidity of compound  $C$  is increased by the polar effect of two methoxy groups.

3.22 (b)  $\Delta G_a^\circ = 2.3RT(pK_a) = (5.71)(4.76) = 27.2 \text{ kJ mol}^{-1}$ . More energy is required to ionize the less acidic compound.

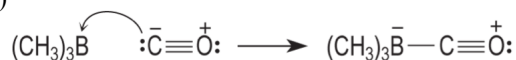
### Solutions to Additional Problems

- 3.24 (b) Every atom has an octet; therefore, this is not an electron-deficient compound.  
 (d) The boron is electron-deficient because it has a sextet of electrons.

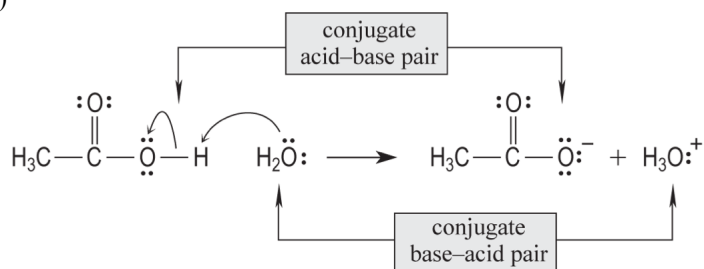
3.25 (b)



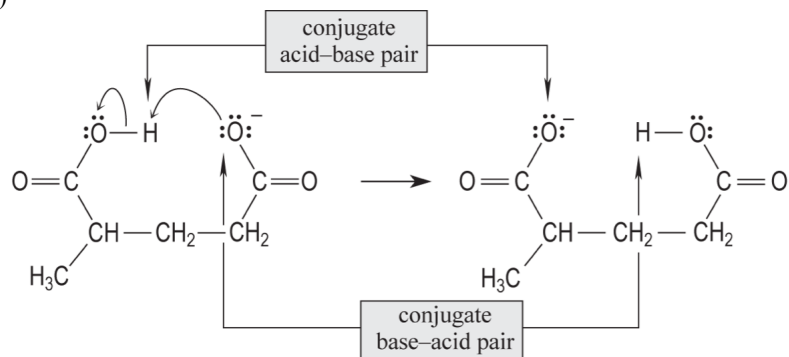
(d)



3.26 (b)



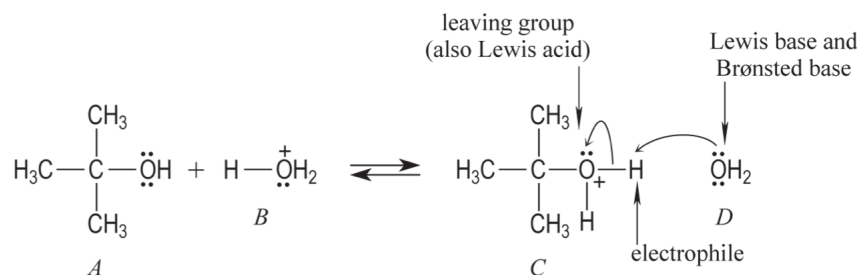
(d)



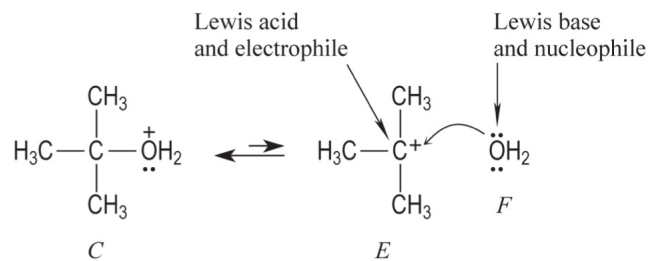
3.28 As in Problem 3.27, every reaction that involves the donation or acceptance of electron pairs, and therefore every reaction in this problem, is (1)—a Lewis acid–base reaction.

- (a) In general, if a reaction in one direction is a Brønsted acid–base reaction, it is also a Brønsted acid–base reaction in the reverse direction. Therefore, *Steps 1* and *3* are (5)—Brønsted acid–base reactions—and (4)—electron-pair displacement reactions.  
 (b) The conjugate acid–base relationship is unchanged by the direction of the reaction. The answer is the same as for Problem 3.27(b).  
 (c) See the equations in part (d).  
 (d) The curved-arrow notation and the labeling of the various species:

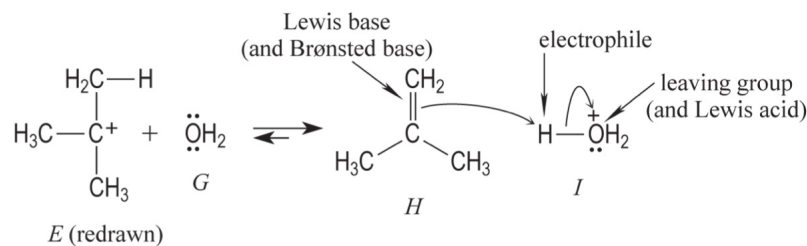
Step 1:



Step 2:



Step 3:

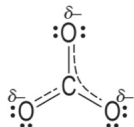


- 3.29 (b) Interconversion of the resonance structures of carbon monoxide with the curved-arrow notation:



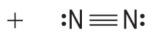
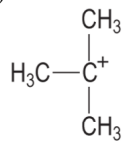
Because the carbon in the structure on the left has a sextet of electrons, it can accept another electron pair.

- 3.31 (b) The resonance structures of the carbonate ion are shown in Problem 1.34, text p. 44. The solution to that problem discusses the significance of these structures. The hybrid structure:

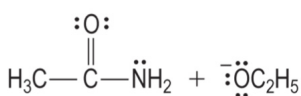


hybrid structure of the carbonate ion

- 3.32 (b)

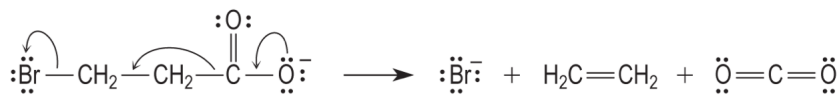


- (d)

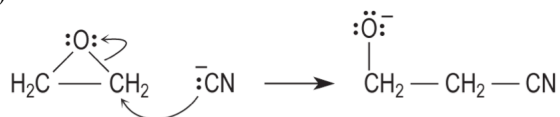


3.33 Remember that an arrow must originate at a *source* of electrons—a bond or an electron pair.

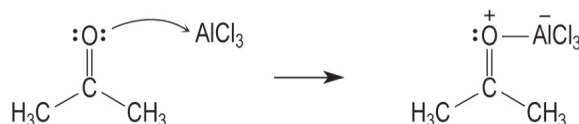
(b)



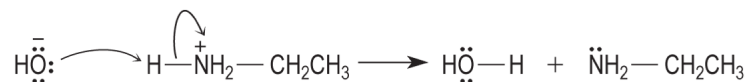
(d)



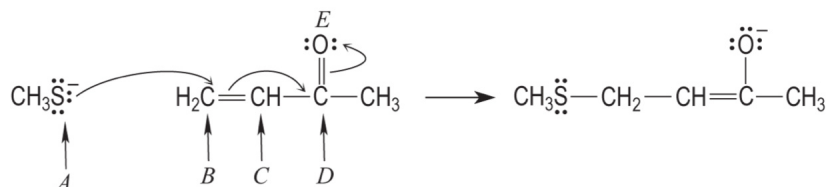
3.34 (b) The reaction is a Lewis acid–base association.



(d) The reaction is a Brønsted acid–base reaction with a proton:



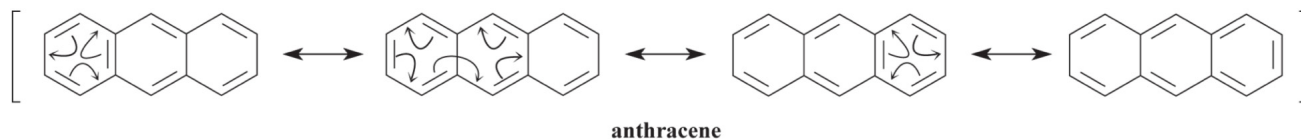
3.35 (b) Species *A* is a Lewis base and a nucleophile. Carbon *B* is an electrophile. Carbon *C* is a leaving group towards carbon *B* but also a nucleophile towards carbon *D*. Carbon *D* is an electrophile. Oxygen *E* serves as a leaving group (and also a Lewis acid). When atoms in double or triple bonds serve as leaving groups, one bond remains intact, so that the leaving group doesn't actually “leave,” but remains tethered within the same molecule. This is the case with atoms *C* and *E*.



3.36 (b) The one curved arrow is shown correctly, but a second one is needed. Otherwise, carbon would have five bonds in the product, and this situation would violate the octet rule.



3.37 (b) The resonance structures of anthracene:



3.38 (b) Let  $K_{\text{eq}}$  be the ratio [anti]/[gauche]; then  $\Delta G^\circ$  for gauche  $\rightleftharpoons$  anti is  $-2.8 \text{ kJ mol}^{-1}$ . (Because gauche has higher energy than anti,  $\Delta G^\circ$  is negative.) Then use Eq. 3.31b in the text.

$$K_{\text{eq}} = 10^{-\Delta G^\circ/2.3RT} = 10^{-(-2.8)/5.71} = 10^{0.49} = 3.1$$

This is the ratio of the anti conformation to any *one* gauche conformation. Taking the total fraction of butane as 1.0, and noting from above that  $[\text{anti}] = 3.1[\text{gauche}]$ ,

$$1.0 = [\text{anti}] + 2[\text{gauche}] = 3.1[\text{gauche}] + 2[\text{gauche}] = 5.1[\text{gauche}]$$

or 
$$[\text{gauche}] = 1.0/5.1 = 0.20$$

Consequently, the total fraction of gauche conformations is  $2 \times 0.20 = 0.40$  (that is, about 40% gauche conformations); and the total fraction of anti conformation is  $1.0 - 0.40 = 0.60$  (that is, about 60% anti conformation) in a sample of butane.

- 3.39 (b) Because of the element effect, both thiols (the compounds with —SH groups) are more acidic than ethanol ( $\text{CH}_3\text{CH}_2\text{OH}$ ). The compound  $\text{ClCH}_2\text{CH}_2\text{SH}$  is the more acidic of the two thiols because of the polar effect of the chlorine substituent.
- (d)  $\text{CH}_3\text{CH}_2\text{OH}$  is less acidic than  $(\text{CH}_3)_2\text{NCH}_2\text{CH}_2\text{OH}$  because of the polar effect of the electronegative nitrogen substituent. In the last compound, not only is the polar effect of the nitrogen present, but also a positive charge, which can stabilize the conjugate-base anion (charge effect). Furthermore, the positively-charged nitrogen is closer to the —OH group. Consequently,  $(\text{CH}_3)_3\text{N}^+\text{—OH}$  is the most acidic of the three compounds and it is thus the strongest acid of all.

3.40 In each part, we apply Eq. 3.25b on text p. 104 and the procedure used in Study Problem 3.6.

- (b) We apply text Eq. 3.25b with  $\text{p}K_a = 15.7$  for  $\text{H}_2\text{O}$ .

$$K_{\text{eq}} = 10^{15.7-10.5} = 10^{5.2} = 1.58 \times 10^5$$



Don't confuse equilibrium constants for the reactions of acids and bases with dissociation constants  $K_a$ . These equilibrium constants use dissociation constants in their calculation, but are not themselves dissociation constants. Similarly,  $\log K_{\text{eq}}$  is related to the  $\text{p}K_a$  values of the two acid–base systems involved, but is not itself a  $\text{p}K_a$ .

- 3.41 (b) Use the same procedure as in part (a) in the Study Guide and Solutions Manual.

$$\Delta G^\circ = -2.3RT \log K_{\text{eq}} = (-5.71)(5.2) = -29.7 \text{ kJ mol}^{-1}$$

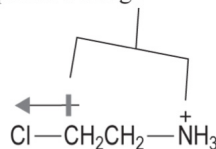
- 3.42 (b) The problem is asking for the standard free energy of dissociation  $\Delta G_a^\circ$ . Use Eq. 3.37 in the text. (Assume 25 °C or 298 K.)

$$\Delta G_a^\circ = 2.3RT(\text{p}K_a) = 5.71(4.31) = 24.6 \text{ kJ mol}^{-1}$$

- 3.45 According to text Fig. 3.2 (text p. 113), selective destabilization of the conjugate acid form of an acid–base pair *raises* the energy of the acidic form relative to its conjugate base and *reduces* its  $\text{p}K_a$ .

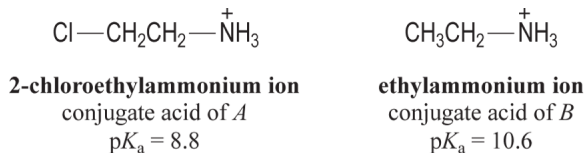
Now let's apply this reasoning to the specific example in the problem. This analysis is similar to the one used in the solution to Problem 3.44. First, assume that the chlorine affects the stability of the *charged species*, which in this case is the conjugate *acid*:

bond dipole of the C—Cl bond  
interacts repulsively with the  
positive charge



The repulsive interaction between the positive charge and the positive end of the C—Cl bond dipole selectively raises the energy of the conjugate acid. This should reduce the  $\text{p}K_a$  of the *conjugate acid* of *A* relative to the  $\text{p}K_a$  of the *conjugate acid* of *B*. This is shown diagrammatically in Fig. IS3.1. This means that *B* is the more basic of the

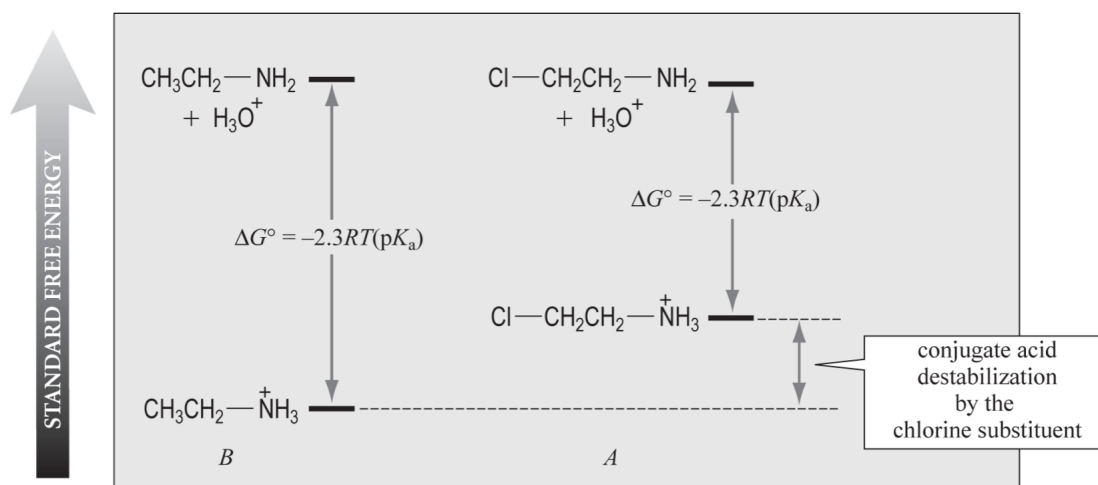
two conjugate bases. The actual data bear out this prediction: chlorine substitution reduces the  $pK_a$  of ethylammonium ion by almost two units:



- 3.47 The  $\Delta G^\circ$  for the reaction is found by taking the logarithm of the equilibrium constant and multiplying it by  $-2.3RT$ .

$$\Delta G_{\text{eq}}^\circ = -2.3RT \log K_{\text{eq}} = -2.3RT(pK_{\text{BH}} - pK_{\text{AH}}) = \Delta G_{\text{a,AH}}^\circ - \Delta G_{\text{a,BH}}^\circ$$

- 3.48 (b) The amide ion is strong enough to react completely with water, and this reaction results in a  $10^{-3} M$  solution of hydroxide ion—that is, a solution  $\text{pH} = 11$ . This is identical to the solution made from  $10^{-3} M$  hydroxide itself, except for the ammonia by-product, which reacts only slightly with water.



**Figure IS3.1.** The effect of chlorine substitution on the energy and  $pK_a$  of the conjugate acid of ethylamine to accompany the solution to Problem 3.46. Note that by raising the energy of the conjugate acid, chlorine substitution reduces the  $pK_a$ . (The two conjugate bases, which are uncharged, are arbitrarily placed at the same energy for comparison purposes.)



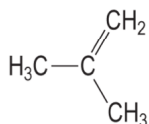
# Chapter 4

## Introduction to Alkenes. Structure and Reactivity

### Solutions to In-Text Problems

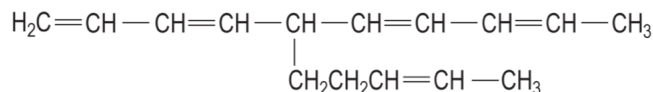
- 4.1 (b) 3-Hexene can exist as both cis and trans isomers; both carbons of the double bond (carbons 3 and 4) are stereocenters.  
(d) 2-Methyl-2-pentene cannot exist as cis, trans isomers because two of the groups at one carbon of the double bond are the same (the methyl groups). This molecule contains no stereocenters.

4.2 (b)

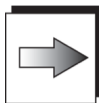


2-methylpropene

(d)

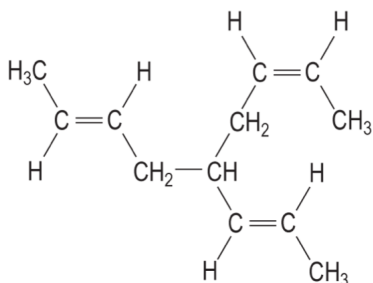


5-(3-pentenyl)-1,3,6,8-decatetraene

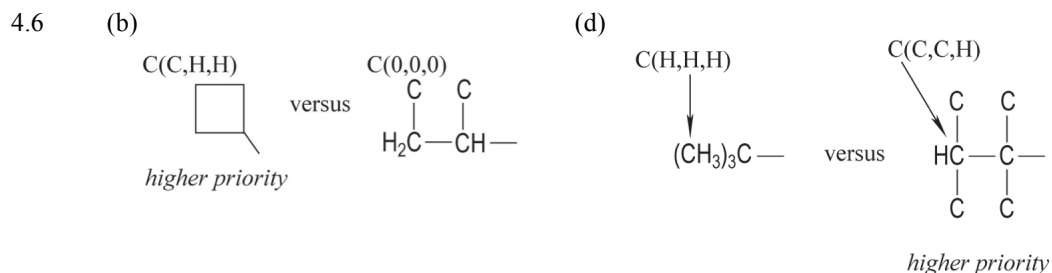


Some chemists were educated in nomenclature to understand that if the position of a substituent is unambiguous it need not be cited by number. Thus, compound (b) could be called methylpropene, because the methyl substituent *must* be on carbon-2. That is, if it is on carbon-1, the compound would not be named as a propene; it would be named as a butene. None of the formal “rule books” on nomenclature support this idea. Hence, we number *all* substituents. The 1993 nomenclature recommendations of the IUPAC went a step further and recommended numbering not only substituents, but also all double bonds, whether ambiguous or not; furthermore, the number is *always* cited before the suffix “ene.” Thus, compound (b) in the 1993 system is called 2-methylprop-1-ene. (The 1993 recommendations are discussed in the sidebar on text p. 134.) A positive aspect of this recommendation is that it creates consistency in the way that all alkene names are constructed. However, this recommendation has not yet been generally accepted, and for that reason it has not been used in this text.

- 4.3 (b) 3-Heptene  
4.4 (b) (Z)-3-Isopropyl-2-hexene  
4.5 (b)



(2E,7Z)-5-[(E)-1-propenyl]-2,7-nonadiene



4.7 (b) Use Eq. 4.7 on text p. 139 to obtain  $U = 3$ .

4.8 (b) The prefix “cyclo” as well as the suffix “ane” indicates that the compound has one ring; consequently,  $U = 1$ .

4.10 (a) This cannot be a correct formula, because a compound containing only C, H, and an odd number of nitrogens must have an odd number of hydrogens.



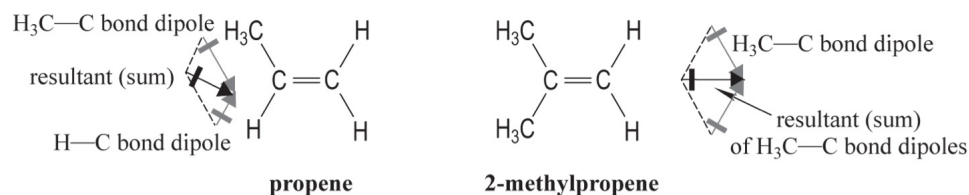
Another way to tell whether a formula is reasonable is to calculate its unsaturation number using Eq. 4.7 on text p. 139. A formula that gives a negative or fractional unsaturation number is not possible.

(b) This could be the formula of an organic compound.

(c) This could not be the formula of an organic compound, because the maximum number of hydrogens possible in a compound containing 10 carbons, 3 nitrogens, and any number of oxygens is 25.

(d) This could be the formula of an organic compound.

4.11 (b) In propene, the  $\text{H}_3\text{C}-\text{C}$  bond dipole adds vectorially to the smaller  $\text{H}-\text{C}$  bond dipole; the resultant is smaller than the  $\text{H}_3\text{C}-\text{C}$  bond dipole itself, as the following diagram shows. In 2-methylpropene, the resultant of the two  $\text{H}_3\text{C}-\text{C}$  bond dipoles is about equal in magnitude to one  $\text{H}_3\text{C}-\text{C}$  bond dipole. (This can be shown analytically if we assume  $120^\circ$  bond angles.) 2-Methylpropene has a somewhat greater dipole moment. (In the following vector analysis, the  $\text{H}-\text{C}$  bond dipoles of the  $\text{CH}_2$  groups are ignored because they cancel in the comparison of the two molecules.)



4.14 (a) The overall  $\Delta H^\circ$  of the process,  $+15.3 \text{ kJ mol}^{-1}$ , must equal the difference in the  $\Delta H_f^\circ$  values of product and reactant. Hence,

$$+15.3 = \Delta H_f^\circ(1\text{-hexene}) - \Delta H_f^\circ(2\text{-ethyl-1-butene})$$

$$+15.3 = -40.5 - \Delta H_f^\circ(2\text{-ethyl-1-butene})$$

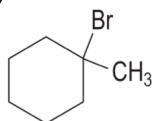
Solving, we have that  $x = \Delta H_f^\circ(2\text{-ethyl-1-butene}) = -55.8 \text{ kJ mol}^{-1}$ .

(b) Because the  $\Delta H_f^\circ$  of 2-ethyl-1-butene is more negative than that of 1-hexene, 2-ethyl-1-butene is the more stable isomer.

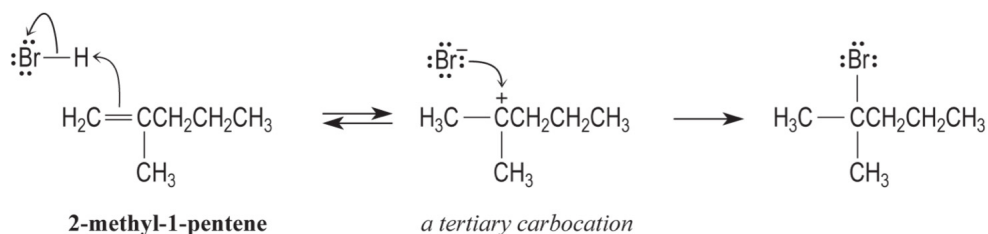
4.16 (b) Compound *B* is more stable than compound *A*, because compound *A*, which is a *cis* alkene, is destabilized by significant van der Waals repulsions between the *tert*-butyl group and the methyl group. Because compound *B* is a *trans* alkene, these destabilizing repulsions are absent.

4.18 (b)  $\text{Br}-\text{CH}_2\text{CH}_2-\text{Br}$

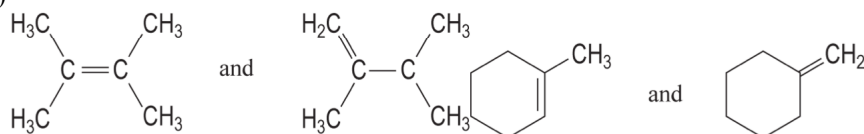
4.19 (b)



4.20 We follow the patterns in text Eqs. 4.18a and 4.18b. First the double bond is protonated on the carbon with *fewer alkyl substituents* by HBr to give a carbocation on the carbon with *more alkyl substituents* and  $\text{Br}^-$ . Note that even through a proton is transferred, we use the curved-arrow notation to show *the flow of electrons*. In the second step, the  $\text{Br}^-$  reacts with the carbocation in a Lewis acid–base association reaction to give the product.

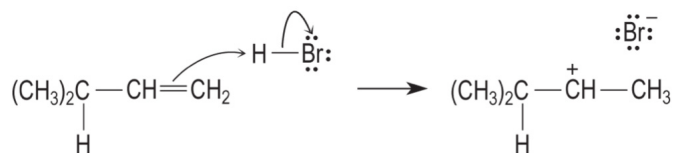


4.21 (b)

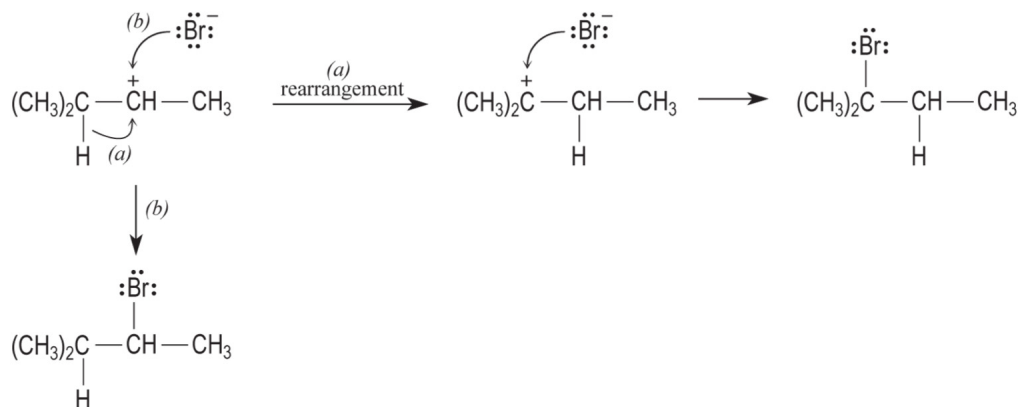


4.22 (b) A rearrangement by the shift of a hydride from the adjacent tertiary carbon gives the same carbocation; hence, this carbocation does not rearrange.

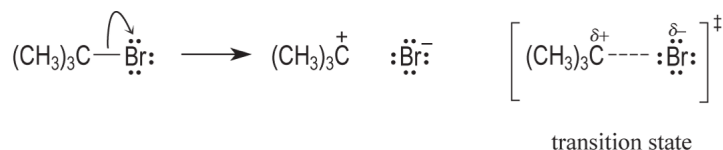
4.23 Protonation of the double bond gives a secondary carbocation:



This secondary carbocation can react by two pathways: (a) rearrangement to a more stable tertiary carbocation followed by reaction of the rearranged carbocation with  $\text{Br}^-$ ; (b) reaction with  $\text{Br}^-$ .



4.25 (b) This is a Lewis acid–base dissociation reaction.



- 4.28 (a) Apply Eq. 4.33b, with :

$$\log \left( \frac{\text{rate}_A}{\text{rate}_B} \right) = \log(10^{-6}) = -6 = \frac{\Delta G_B^{\circ\ddagger} - \Delta G_A^{\circ\ddagger}}{5.71} = \frac{\Delta G_B^{\circ\ddagger} - 90}{5.71}$$

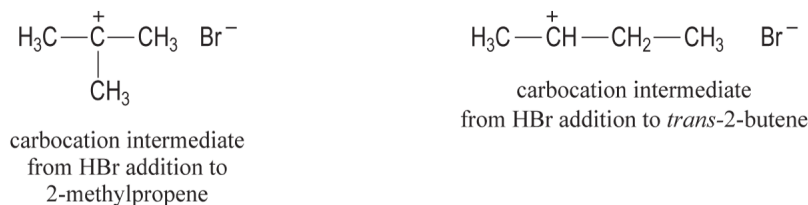
Solving for  $\Delta G_B^{\circ}$ ,

$$\Delta G_B^{\circ\ddagger} = 55.7 \text{ kJ mol}^{-1}$$

- (b) The reaction free-energy diagrams are shown in Fig. IS4.1.  
 (c) The standard free energy of activation of a reverse reaction is the height of the energy barrier measured from the energy of the products. In each case, this is  $10 \text{ kJ mol}^{-1}$  greater than the standard free energy of activation of the forward reaction:  $100 \text{ kJ mol}^{-1}$  for reaction *A*, and  $66 \text{ kJ mol}^{-1}$  for reaction *B*. (See Fig. IS4.1.)

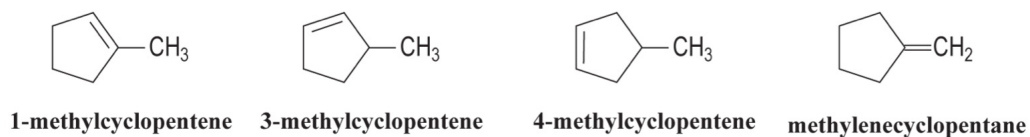
- 4.30 The diagram in Figure IS4.2 meets the criteria in the problem.

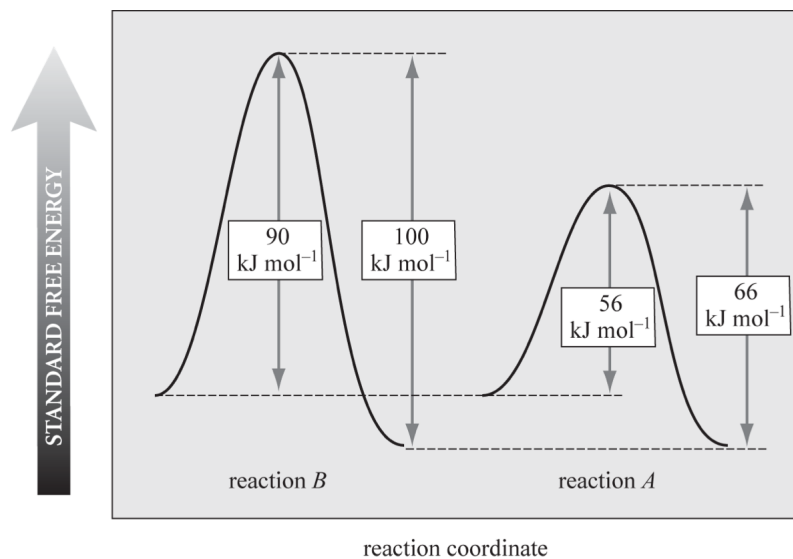
- 4.31 Because the transition states of the two reactions should resemble the respective carbocation intermediates (Hammond's postulate), examine the structures of the two carbocations and determine which should be more stable.



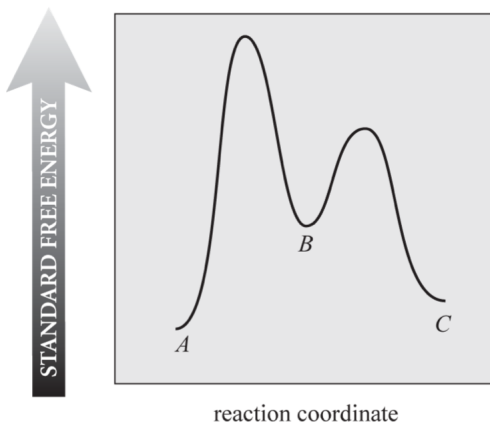
The carbocation intermediate in the addition of HBr to 2-methylpropene is tertiary, and is thus more stable than the carbocation intermediate in the addition of HBr to *trans*-2-butene, which is secondary. If the transition states for the two addition reactions resemble the carbocation intermediates, the transition state for the reaction of 2-methylpropene is also more stable. The relative rates of the two reactions are governed by the *differences* between the standard free energies of the transition states and their respective starting materials. Therefore, we have to consider the free energies of *both* the alkenes and the transition states. *If the two alkenes do not differ appreciably in energy, then the relative rates of the two reactions are governed only by the relative free energies of the two transition states.* (This is a fairly good assumption, because both alkenes have two alkyl branches.) Under this assumption, addition of HBr to 2-methylpropene is faster, because the transition state for this reaction has lower free energy.

- 4.32 (b) The hydrogenation product of (*E*)-1,3-hexadiene is hexane,  $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ .  
 4.33 (b) Any alkene with the carbon skeleton of methylcyclopentane will undergo hydrogenation to give this cycloalkane. There are four such alkenes.



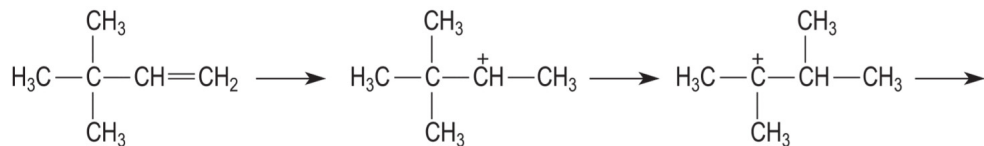


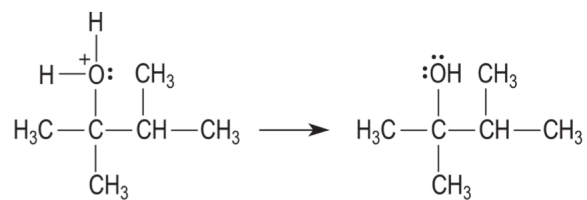
**Figure IS4.1.** A reaction free-energy diagram to accompany the solution to Problem 4.28b. The two curves are drawn to scale. The standard free energies of activation for the forward reactions are shown under their respective curves; the standard free energies of activation for the reverse reactions are shown to the right of their respective curves.



**Figure IS4.2.** The reaction-coordinate diagram to accompany the solution to Problem 4.30.

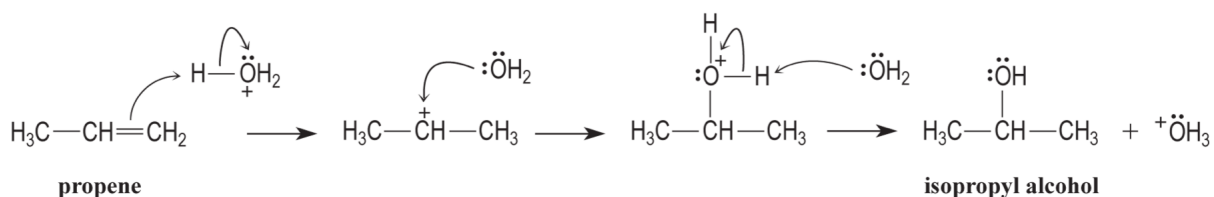
- 4.35 The reaction mechanism is exactly like the one in the solution to Problem 4.34, except that a methyl group migrates in the carbocation intermediate. The various intermediates are shown below; we leave it to you to fill in the other molecules or ions involved as well as the curved-arrow mechanism.





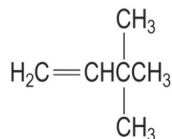
4.36 (b) In the solution to Problem 4.34, the rearrangement of carbocation *A* to carbocation *B* is completely irreversible because of the much greater stability of *B*. Once this carbocation is formed, the only alkenes that can form are those that are derived from it—the ones shown in part (a).

4.38 The hydration of propene involves the usual mechanistic steps of alkene protonation to form a carbocation followed by the nucleophilic reaction of water with the carbocation. The structure of isopropyl alcohol follows from the structure of the carbocation. Notice that a secondary carbocation rather than a primary carbocation is involved. (Why?).

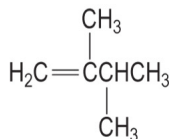


### Solutions to Additional Problems

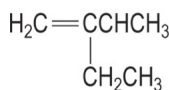
4.40 The structures of the isomeric substituted butenes:



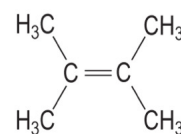
**3,3-dimethyl-1-butene**



**2,3-dimethyl-1-butene**



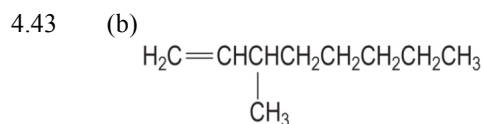
**2-ethyl-1-butene**



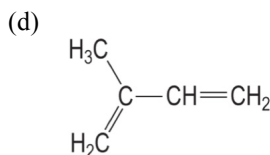
**2,3-dimethyl-2-butene**

4.41 (b) Each of the alkenes from the solution to Problem 4.40 *except* 3,3-dimethyl-1-butene should give one product when it reacts with HBr. 3,3-Dimethyl-1-butene should give one normal addition product and one rearranged product. (The corresponding addition of HCl to the same alkene is shown on text pp. 155–156.)

4.42 (b) 2,3-Dimethyl-2-butene has four alkyl substituents on the double bond. This alkene is more stable than 2,3-dimethyl-1-butene and 2-ethyl-1-butene, each of which has two substituents on the double bond; these are about equally stable. All of these alkenes are more stable than 3,3-dimethyl-1-butene, which has one alkyl substituent on the double bond.



**3-methyl-1-octene**

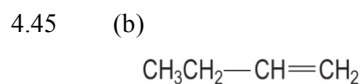


**isoprene**

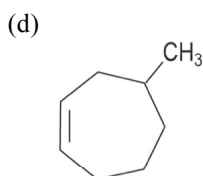
4.44 (b) 6-Methyl-1-heptene

(d) (*E*)-2-Butyl-1,3-pentadiene

(f) (*E*)-5-[(*Z*)-1-propenyl]-1,6-nonadiene



**“3-butene”  
1-butene**



**“6-methylcycloheptene”  
4-methylcycloheptene**

4.46 (b) The stereochemistry is *E*. The Br has higher priority on one carbon stereocenter, but it has lower priority on the other.

(c) The stereochemistry is *E*. The two branches of the ring are treated as separate substituents; the fact that the two branches are tied into a ring has no effect on their relative priorities.

4.47 (b) These are not isomers because they have different molecular formulas (N).

(d) These compounds are constitutional isomers (C) because they have different connectivities.

4.49 (a) An  $sp^3(\text{C})-1s(\text{H})$   $\sigma$  bond

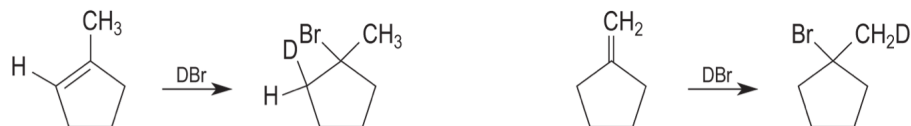
(b) An  $sp^3(\text{C})-sp^2(\text{C})$   $\sigma$  bond

(c) An  $sp^2(\text{C})-sp^2(\text{C})$   $\sigma$  bond and a carbon–carbon  $\pi$  bond

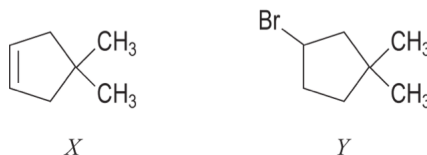
(d) An  $sp^2(\text{C})-sp^2(\text{C})$   $\sigma$  bond

(e) An  $sp^2(\text{C})-1s(\text{H})$   $\sigma$  bond

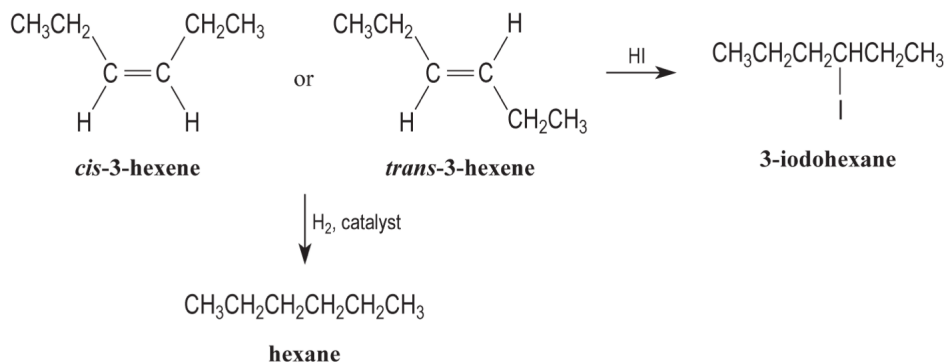
- 4.50 (b) Although the bromine is on the same carbon in the products from the respective alkenes, the hydrogen from HBr (and hence the deuterium from DBr) is not. Consequently, different products are obtained from DBr addition to the two alkenes. In other words, DBr differentiates the proton that is added from the hydrogens that were in the alkene to begin with.



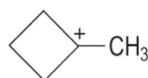
- 4.51 The process to be used in working this problem is thoroughly explained in Study Guide Link 4.3 on p. 43 of the Study Guide and Solutions Manual. The structures of *X* and *Y* are as follows:



- 4.52 Both *cis*- and *trans*-3-hexene should give the same *single* alkyl halide product when they react with HI, and both would undergo catalytic hydrogenation to give hexane:

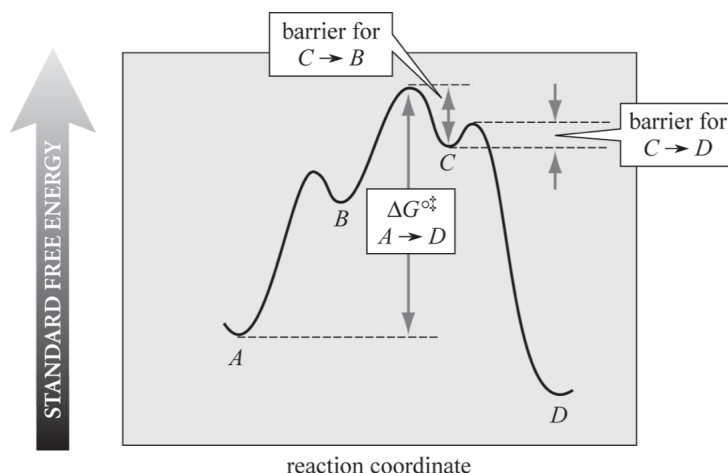


- 4.55 (a) Compound *D* is present in greatest amount when the reaction comes to equilibrium, because it has the lowest standard free energy. Compound *C* is present in least amount because it has the highest standard free energy.  
 (b) The rate-limiting step in this reaction is the  $B \rightleftharpoons C$  step, because it has the transition state of highest standard free energy.  
 (c) The standard free energy of activation is the energy difference between the transition state of highest free energy and the reactant. See Fig. IS4.2 for the  $A \rightarrow D$  case. (What is  $\Delta G^{\ddagger}$  when the reactant is *D*, that is, in the case of the reverse reaction?)  
 (d) The reaction of  $C \rightarrow D$  is faster than the reaction  $C \rightarrow B$  because the energy barrier for the  $C \rightarrow D$  reaction is smaller. The two barriers are labeled in Fig. IS4.3.
- 4.57 (b) The reactive intermediate formed in the rate-limiting step is the carbocation:



- 4.59 Because 3-methyl-1-butene and 2-methyl-1-butene are isomers and produce the same amount of  $\text{CO}_2$  and  $\text{H}_2\text{O}$  when they are burned, the difference in heats of combustion must equal the difference in their heats of formation. The more stable alkene isomer, 2-methyl-1-butene, gives off the smaller amount of heat on combustion. This is diagrammed in Fig. IS4.4. Using this figure, with the  $\Delta H^\circ$  of combustion of 3-methyl-1-butene as  $x$ ,



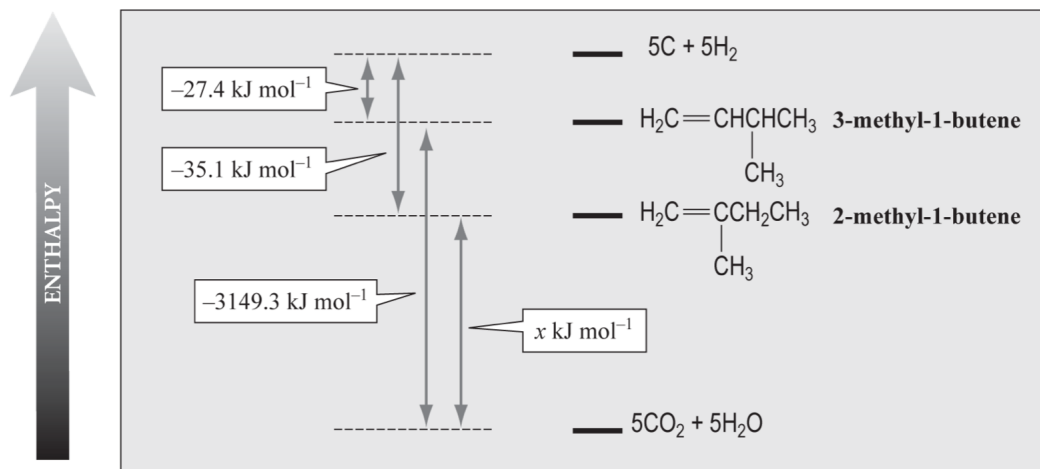


**Figure IS4.3.** Reaction free-energy diagrams to accompany the solutions to Problem 4.55c and 4.55d.

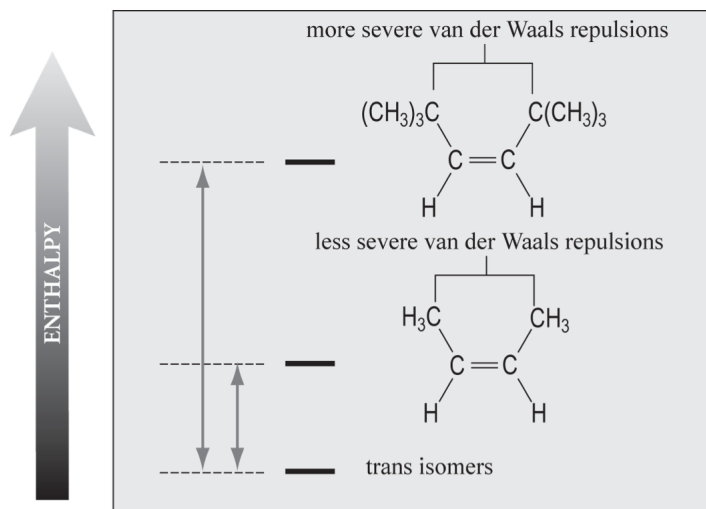
$$x - 35.1 = -3149.3 - 27.4$$

from which we find that  $x = -3141.6 \text{ kJ mol}^{-1}$ . Thus,  $3141.6 \text{ kJ mol}^{-1}$  of heat is liberated when 2-methyl-1-butene is burned. Less energy is liberated than when 3-methyl-1-butene is burned because 2-methyl-1-butene has lower enthalpy than 3-methyl-1-butene. (Why?)

- 4.61 In each *trans*-isomer, the large groups have modest if any van der Waals repulsions with the neighboring hydrogens. However, the *tert*-butyl groups in the *cis*-isomer of (1) suffer more severe van der Waals repulsions than the methyl groups in the *cis*-isomer of (2), because *tert*-butyl groups are much larger than methyl groups. Consequently, relative to the *trans*-isomer, the *cis*-isomer of (1) has much higher energy than the *cis*-isomer of (2). Therefore, more energy is released in the conversion shown in (1) than in the conversion shown in (2). This is summarized in the Fig. IS4.5, in which the two *trans*-isomers have been placed at the same enthalpy for comparison.

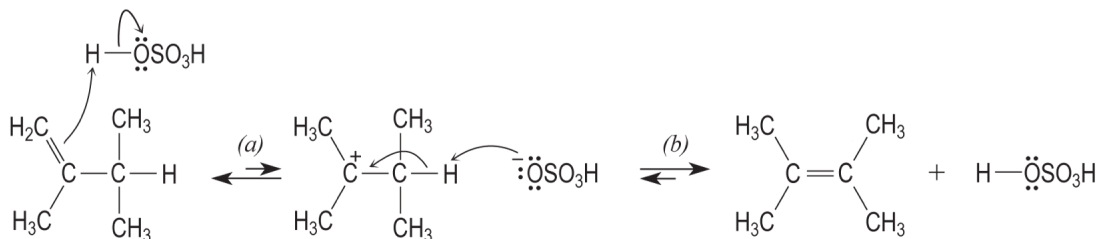


**Figure IS4.4.** A diagram of relative enthalpies (not to scale) to accompany the solution to Problem 4.59.

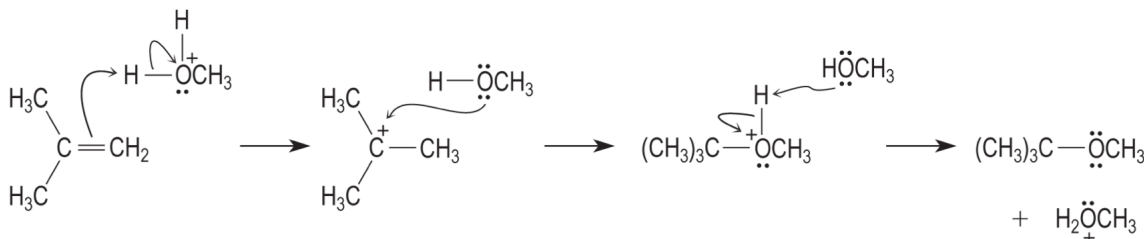


**Figure IS4.5.** Enthalpy relationships for the solution to Problem 4.61. The two *trans*-isomers have been arbitrarily placed at the same enthalpy for comparison.

- 4.64 The mechanism is a sequence of two Brønsted acid–base reactions. In the first (step *a*), the double bond is protonated to give a tertiary carbocation; in the second (step *b*), the carbocation loses a different proton to give the alkene. The equilibrium is driven to the right by the greater stability of the alkene product. (Why is it more stable?)



- 4.65 This is an acid-catalyzed addition to the double bond much like hydration, except that an alcohol rather than water is the nucleophile that reacts with the carbocation intermediate. Notice that the ionized form of  $\text{H}_2\text{SO}_4$  in methanol is protonated methanol ( $\text{CH}_3\text{O}^+\text{H}_2$ ).



- 4.69 This problem can be framed in terms of two reaction coordinate diagrams. To do this for methylenecyclobutane requires a knowledge of the standard free energy of activation for its hydration. Letting the hydration of methylenecyclobutane be reaction *A*, and the hydration of 2-methylpropene be reaction *B*, we use Eq. 4.33b on text p. 160 to obtain

$$\log\left(\frac{\text{rate}_A}{\text{rate}_B}\right) = \log(0.6) = -0.222 = \frac{\Delta G_B^{\ddagger} - \Delta G_A^{\ddagger}}{2.30RT} = -\frac{\Delta G_A^{\ddagger} - \Delta G_B^{\ddagger}}{5.71}$$

or  $\Delta G_A^{\ddagger} - \Delta G_B^{\ddagger} = 1.27 \text{ kJ mol}^{-1}$ . With  $\Delta G_B^{\ddagger} = 91.3 \text{ kJ mol}^{-1}$ , then  $\Delta G_A^{\ddagger} = 92.6 \text{ kJ mol}^{-1}$ .

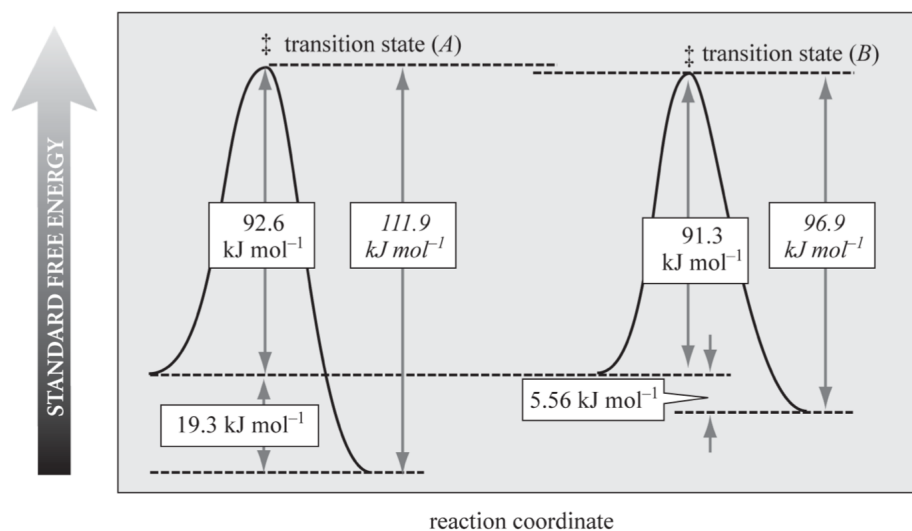
Next, we need to convert the relative hydration equilibrium constants for reactions *A* and *B* into relative standard free energies. A similar equation applies. (This can be derived by combining two equations like Eq. 3.31a on text p. 107.)

$$\log\left(\frac{K_A}{K_B}\right) = \log(250) = 2.40 = \frac{\Delta G_B^{\ddagger} - \Delta G_A^{\ddagger}}{2.30RT} = \frac{-5.56 - \Delta G_A^{\ddagger}}{5.71}$$

or  $\Delta G_A^{\ddagger} = -19.3 \text{ kJ mol}^{-1}$ . We can now construct reaction coordinate-free energy diagrams for the two reactions, which are given in Fig. IS4.6. We have enough information to calculate the standard free energies of activation for the reverse reactions, which are shown in italic type in the figure. Because the standard free energy of activation of the reverse of reaction *A* is larger, it is the slower reaction. The relative rates are calculated from Eq. 4.33b on text p. 160:

$$\log\left(\frac{\text{rate}_B}{\text{rate}_A}\right) = \frac{\Delta G_A^{\ddagger} - \Delta G_B^{\ddagger}}{2.30RT} = \frac{15}{5.71} = 2.63$$

The reverse of reaction *B* is therefore  $10^{2.63}$ , or 427, times faster than the reverse of reaction *A*.



**Figure IS4.6** Reaction coordinate diagrams to accompany the solution to Problem 4.69. The starting alkenes are placed at the same energy for comparison. The numbers in italics are calculated graphically from either the numbers given or calculated in the problem.

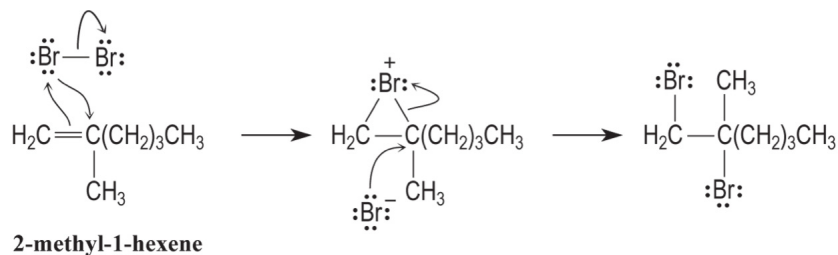


# Chapter 5

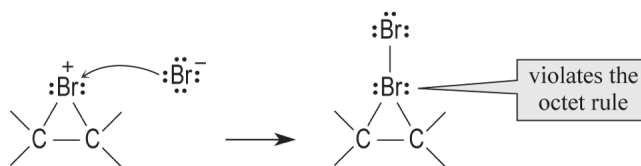
## Addition Reactions of Alkenes

### Solutions to In-Text Problems

- 5.1 (a) The iodine is the electrophile, because it adds to the carbon of the double bond with fewer alkyl substituents. This result does seem to fit the electronegativity pattern for electrophilic addition, as nitrogen is considerably more electronegative than iodine.
- 5.2 (b) The reaction of Br<sub>2</sub> with 2-methyl-1-hexene follows the pattern in Eqs. 5.12 and 5.13 of the text.

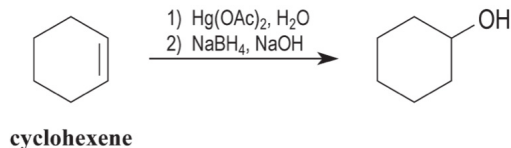


- 5.4 The reaction of bromide ion as a nucleophile at the bromine of the bromonium ion would give a species that violates the octet rule.

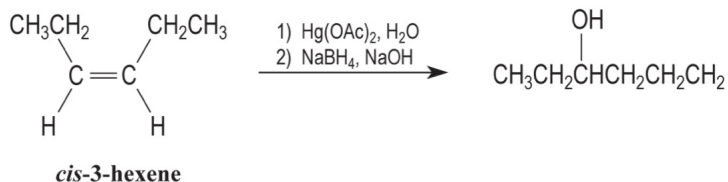


As we'll learn, atoms in periods beyond the third can have more than an octet of electrons, and a structure such as this is not impossible. However, the octet rule can still be used as a guide to reactivity. A reaction of the bromide ion at the carbon of the bromonium ion gives a *much* more stable structure.

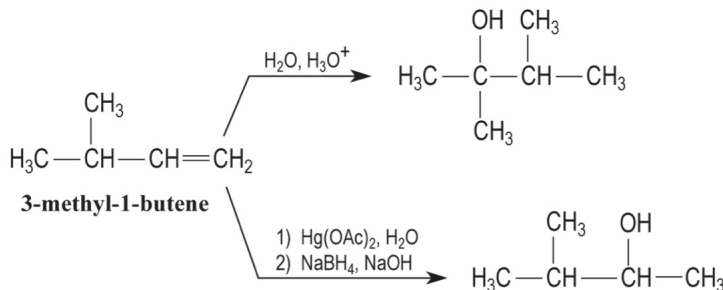
- 5.5 (b) In this part and in part (d), the double bond is symmetrically placed in the molecule; so, regioselectivity is not an issue.



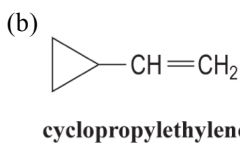
(d)



- 5.6 When 3-methyl-1-butene undergoes acid-catalyzed hydration, rearrangement occurs because carbocation intermediates are involved. (See the solution to Problem 4.35.) Oxymercuration–reduction gives addition without rearrangement because the intermediate is a cyclic mercurinium ion, which does not rearrange.

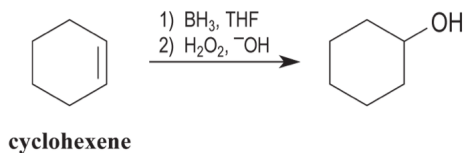


5.7

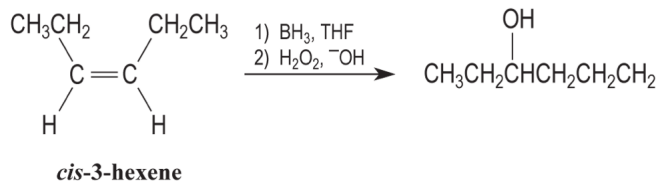


5.8

- (b) In this part and in part (d), the double bond is symmetrically placed in the molecule; so, regioselectivity is not an issue.



(d)

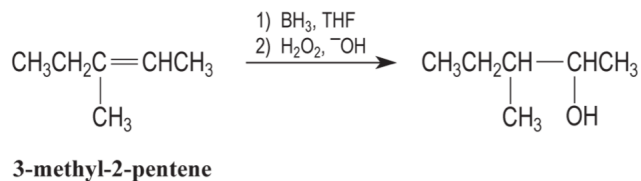


5.9

The products of hydroboration–oxidation are the same as the ones in parts (b) and (d) of Problem 5.5. In both, the alkene is symmetrical; consequently, regioselectivity has no meaning. In part (c), the carbons of the double bond have the same number of alkyl substituents; consequently, there is no reason to expect significant regioselectivity. However, the relative amounts of the products in each case could be different.

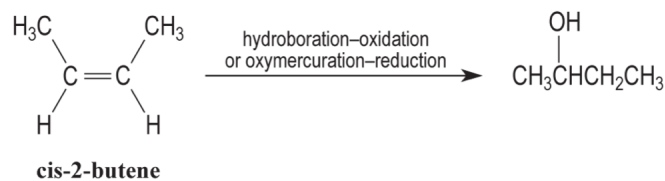
5.10

(b)

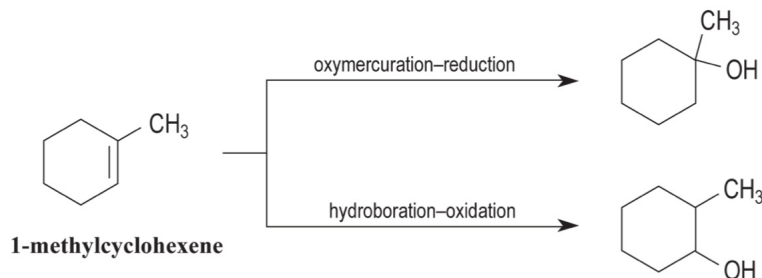


5.12

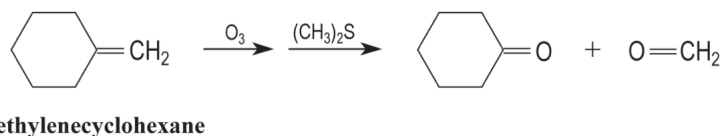
- (a) Because *cis*-2-butene is a symmetrical alkene, it reacts to give the same product in either oxymercuration–reduction or hydroboration–oxidation.



- (b) Because 1-methylcyclohexene has different numbers of alkyl branches at the carbons of its double bond, it gives different products in the two reactions.

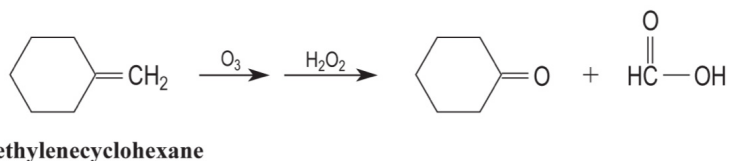


5.13 (b)



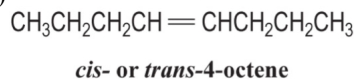
- (d) 2-Methylpentane is an alkane; because it has no double bond, it does not undergo ozonolysis.

5.14 (b)



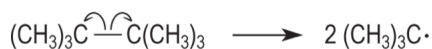
- (d) 2-Methylpentane is an alkane; because it has no double bond, it does not undergo ozonolysis.

5.15 (b)



- 5.16 As the solution to Problem 5.15(b) illustrates, *E* and *Z* isomers of an alkene give the same ozonolysis products. Therefore, ozonolysis cannot be used to determine the stereochemistry at the alkene double bond.

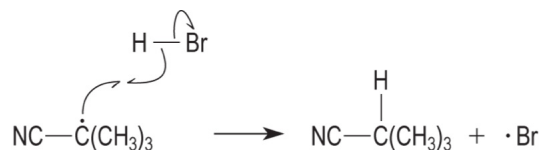
5.17 (a)



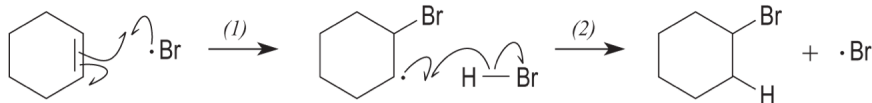
(d)



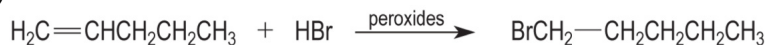
- 5.20 (a) The first initiation step is shown in Eq. 5.49, text p. 203. In the second initiation step, the radical produced in the first initiation step abstracts a hydrogen atom from HBr:



The bromine atom then adds to the  $\pi$  bond of cyclohexene in the first propagation step (1); the resulting radical then reacts with HBr in the second propagation step to give the addition product.



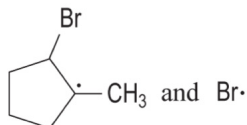
5.21 (a)



1-pentene

1-bromopentane

5.22 (b) The free-radical intermediates in the propagation steps of the peroxide-promoted HBr addition to 1-methylcyclopentene:

5.23 (b) Two  $\text{Cl}-\text{CH}_2$  bonds are formed ( $355 \text{ kJ mol}^{-1}$  each); a  $\text{Cl}-\text{Cl}$  bond ( $239 \text{ kJ mol}^{-1}$ ) and a carbon-carbon  $\pi$  bond ( $\approx 243 \text{ kJ mol}^{-1}$ ) are broken.

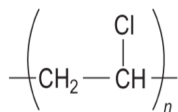
$$\Delta H^\circ = 239 + 243 - 2(355) = -228 \text{ kJ mol}^{-1}$$

5.25 The second propagation step in which Br is abstracted rather than H involves formation of a secondary  $\text{C}-\text{Br}$  bond rather than a secondary  $\text{C}-\text{H}$  bond; the bond broken ( $\text{H}-\text{Br}$ ) is the same. Hence, we use the calculation in the solution of Problem 5.24(a), except that the bond dissociation energy of a  $\text{C}-\text{Br}$  bond is substituted for that of a  $\text{C}-\text{H}$  bond. The closest value in Table 5.3 is the bond dissociation energy of  $(\text{CH}_3)_2\text{CH}-\text{Br}$ ,  $309 \text{ kJ mol}^{-1}$ . The required  $\Delta H^\circ$  is therefore

$$\Delta H^\circ = 368 - 309 = 59 \text{ kJ mol}^{-1}$$

Hence, abstraction of Br is a very *unfavorable* process energetically ( $\Delta H^\circ \gg 0$ ), whereas the abstraction of H is a very favorable process ( $\Delta H^\circ < 0$ ). As is usually the case in free-radical reactions, the relative enthalpies of the processes governs their relative rates. Hence, abstraction of H is *much* more favorable, and therefore is much faster, than abstraction of Br.

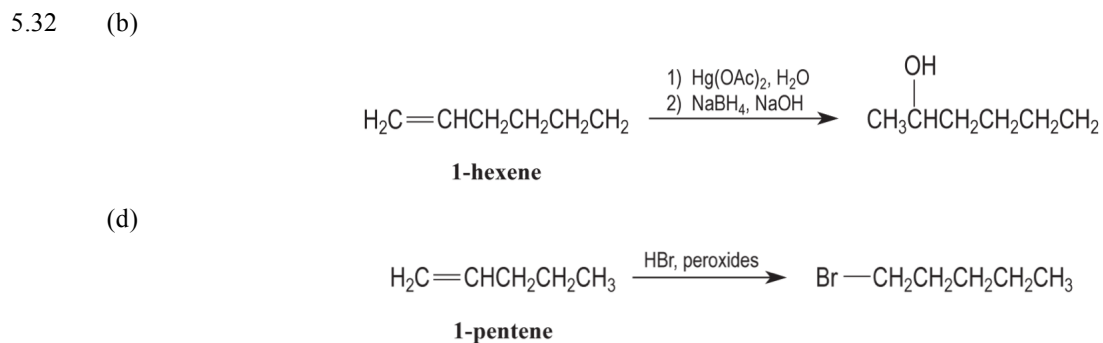
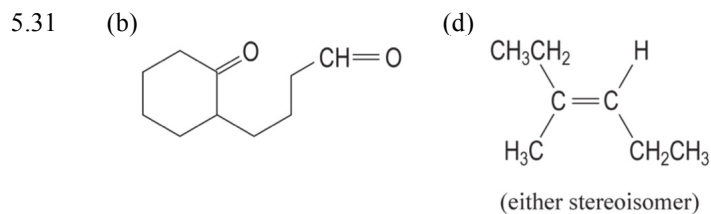
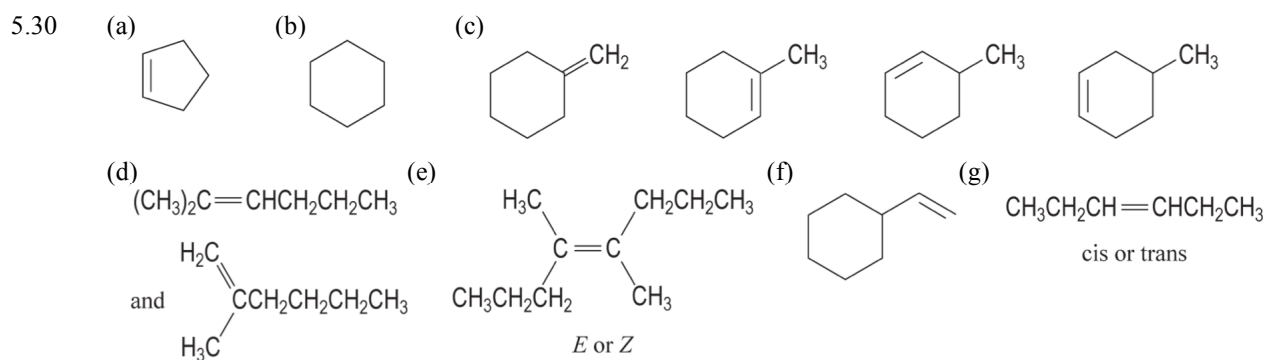
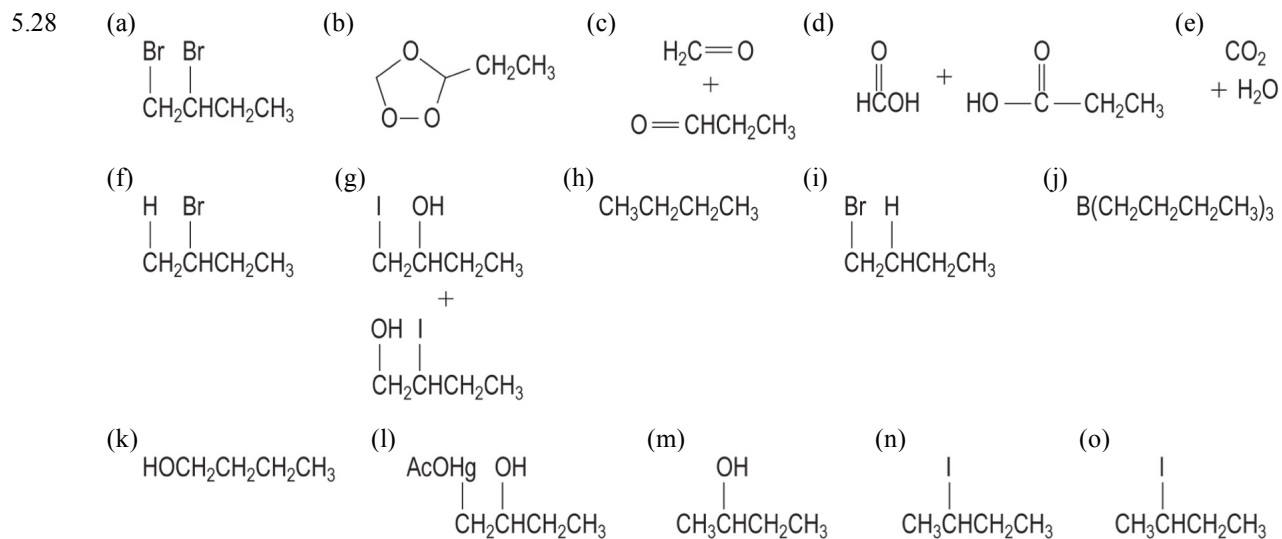
5.26 (b)



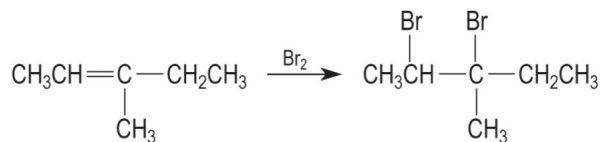
poly(vinyl chloride)



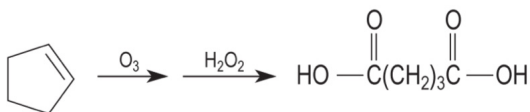
### Solutions to Additional Problems



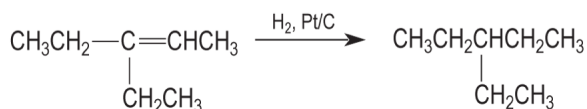
(f)

**3-methyl-2-pentene**

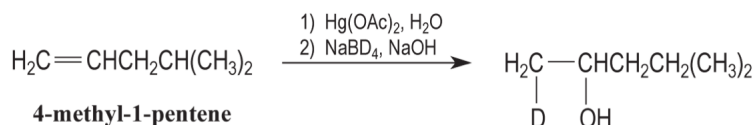
(h)

**cyclopentene**

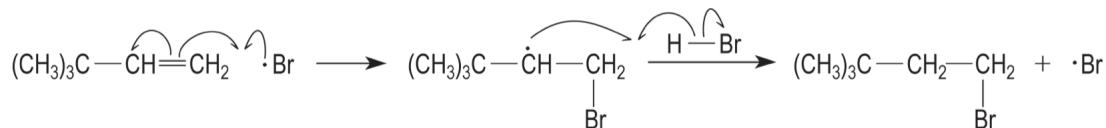
(j)

**3-ethyl-2-pentene**

- 5.33 (b) An oxymercuration–reduction on the alkene used in part (a) gives the desired compound.

**4-methyl-1-pentene**

- 5.36 (a) Only the first two products are formed in the absence of peroxides, and only the third is formed in the presence of peroxides. Different products are formed because different mechanisms and reactive intermediates are involved under the different conditions.
- (b) The mechanism for the formation of the first two products is identical to that shown for reaction of the same alkene with HCl in Eqs. 4.26 and 4.27a–b, text p. 155, except that HBr is used instead of HCl. The first product results from a carbocation rearrangement, and the second from normal regioselective (“Markovnikov”) addition. The third product is the consequence of a free-radical addition mechanism, the propagation steps of which are as follows:

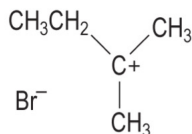


(The initiation steps are shown in Eqs. 5.48 and 5.50 on p. 203 of the text.)

- (c) Peroxide-promoted addition is in competition with normal addition and rearrangement. The normal processes occur at the same rate at which they occur in the absence of peroxides. The fact that *only* the product of peroxide-promoted addition is observed, then, means that this process is much faster than the other, competing, processes.

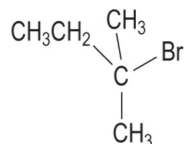
5.37 (b)

reactive intermediate:



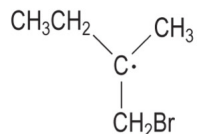
a carbocation

product:



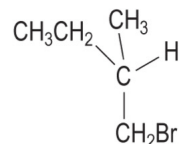
(d)

reactive intermediate:



a free radical

product:

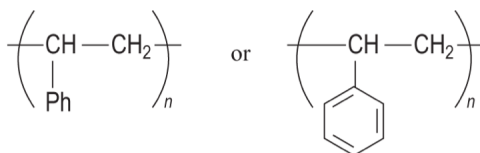


5.42

- (a) The H—CN bond is stronger than the O—H bond, the abstraction of a hydrogen atom from HCN by the *tert*-butoxy radical is endothermic by  $528 - 438 = 90 \text{ kJ mol}^{-1}$ . (These numbers are from Table 5.3 with the bond energy of  $\text{CH}_3\text{O—H}$  as an approximation for that of  $(\text{CH}_3)_3\text{CO—H}$ .) The first initiation step, formation of the *tert*-butoxy radical from a peroxide, is also endothermic. Because *both* initiation steps are highly endothermic, the reaction is not likely to generate a high enough concentration of radicals to initiate a chain reaction.
- (b) This propagation step involves breaking an H—CN bond ( $528 \text{ kJ mol}^{-1}$ ) and formation of a secondary carbon—hydrogen bond ( $-412 \text{ kJ mol}^{-1}$ ). The  $\Delta H^\circ$  of this step is  $528 - 412 = +116 \text{ kJ mol}^{-1}$ . This step is highly endothermic and therefore not reasonable as a propagation step.

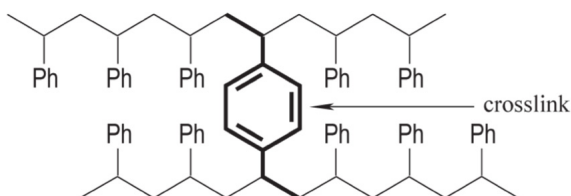
5.45

- (a) The structure of polystyrene:

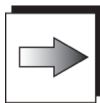


polystyrene

- (b) Because both “ends” of 1,4-divinylbenzene can be involved in polymer formation, addition of 1,4-divinylbenzene serves to connect, or
- crosslink*
- , polymer chains. Such a crosslink is shown with bolded bonds in the following structure:



Notice that because only a small amount of 1,4-divinylbenzene is used, divinylbenzene does not polymerize with itself.



Crosslinks are introduced into polymers to increase their strength and rigidity.

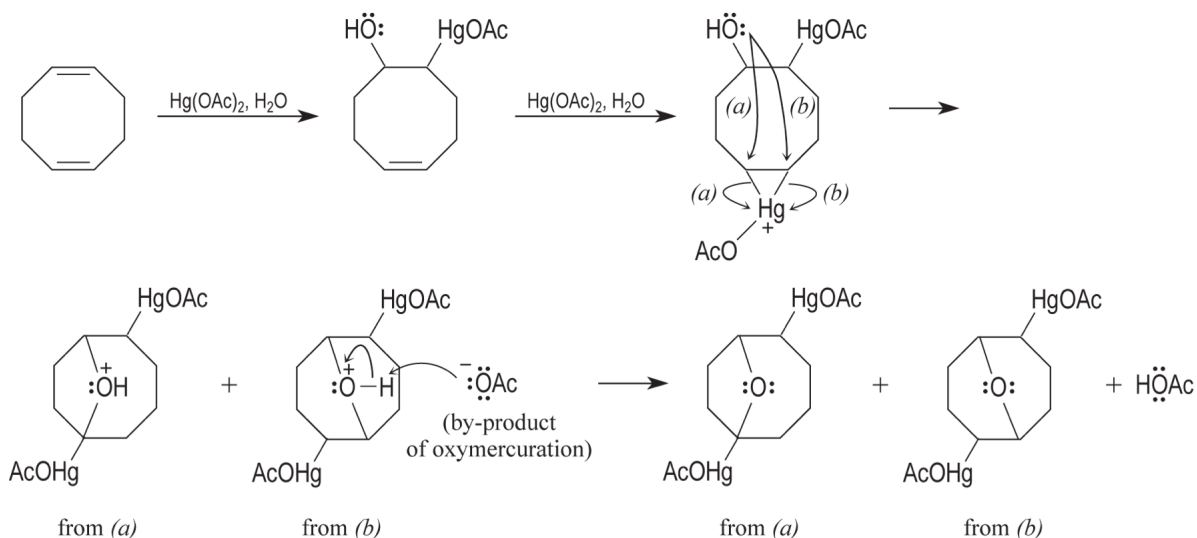
5.47

Compound *A* has the connectivity of octane; because it has an unsaturation number  $U = 1$  and reacts with bromine, it is an alkene. The ozonolysis results show that compound *A* is 4-octene,  $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}=\text{CHCH}_2\text{CH}_2\text{CH}_3$ . Because the double bond is located symmetrically, only one ozonolysis product is formed. Ozonolysis cannot determine whether the compound is *cis* or *trans*.

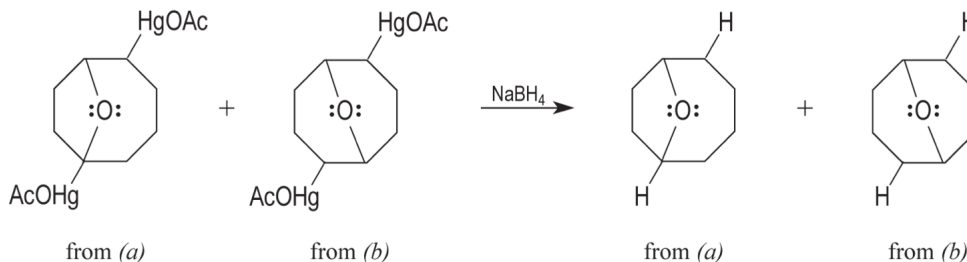
5.48

- (d) The oxygen of a hydroxy group introduced in the oxymercuration reaction of one double bond serves as the nucleophile in the opening of the mercurinium ion formed at the second double bond within the same

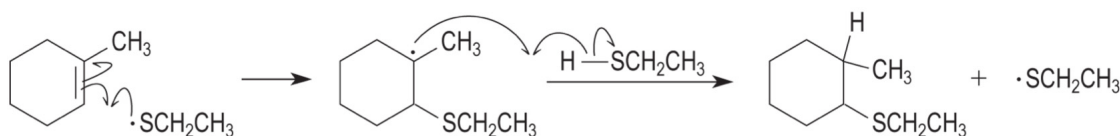
molecule. Two products are formed because the oxygen can react with the mercurinium ion at either of two carbons.



[The acetate ion is a by-product of the first step of oxymercuration; its reaction with the protonated ether is shown only for (b).] Treatment with  $\text{NaBH}_4$  replaces the mercury with a hydrogen.



- (f) The initiation step, reaction of the thiol with an alkoxy radical formed by homolysis of a peroxide, is shown in Eq. 5.55a, text p. 206. The radical produced in that step adds to the  $\pi$  bond of the alkene so as to produce the tertiary free radical, and this radical reacts with the thiol to propagate the chain.



Be sure that you did not form the product by a recombination of two radicals; see the discussion of Eq. 5.56 in Study Problem 5.4, text p. 206.

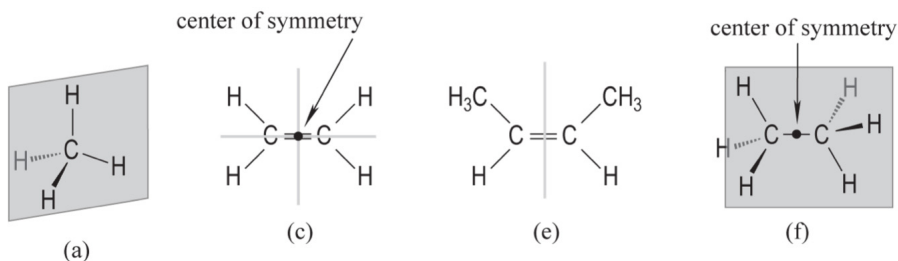
- 5.50 These are both examples of steric effects. Placing three highly branched groups around a central boron results in van der Waals repulsions. These repulsions are severe enough that only two groups can be bound to boron in the case of diisiamylborane, and only one group in the case of thexylborane. (Notice the greater number of alkyl substituents in the “thexyl” group.) Now, alkyl branches stabilize  $sp^2$ -hybridized boron (see the solution to Problem 4.48 on p. 62 of the Study Guide and Solutions Manual) just as they stabilize  $sp^2$ -hybridized carbon; but if the alkyl branches are *themselves* branched, they form a thicket of methyl groups that interact repulsively with each other as more of these branches are accumulated. These repulsive interactions reduce the relative stability of the trialkylboranes—evidently, so much so that they cannot form.

# Chapter 6

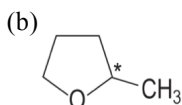
## Principles of Stereochemistry

### Solutions to In-Text Problems

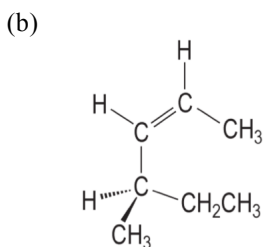
- 6.1 (a) This compound is chiral.  
(b) Methane is achiral.
- 6.3 (a) Planes of symmetry in methane bisect one set of H—C—H bonds and contain the other H—C—H bonds. (There are four such planes.)  
(c) One plane of symmetry in ethylene is the plane of the page; the two others are the planes perpendicular to the page. The center of symmetry is the point in the center of the C=C bond.  
(e) The plane of symmetry in *cis*-2-butene is the plane of the page and the plane perpendicular to the page that bisects the C=C bond.  
(f) The plane of symmetry contains a C—H bond on one carbon as well as the C—C bond, and it bisects an H—C—H bond angle on the other carbon. (There are three such planes.) The center of symmetry is a point at the center of the C—C bond.



- 6.4 The asymmetric carbon is indicated with an asterisk.



- 6.5 Remember that there are many different ways to draw a correct line-and-wedge structure. If your structures don't look like these, and if you're not sure whether yours is correct, make a model of both and check them for congruency. (When possible, we often adopt a "standard" representation in which the bond to the atom of lowest priority—hydrogen in these examples—is the wedged bond, and it is placed to the left of the asymmetric carbon. This makes it very easy to determine configuration. However, this "standard" representation is not necessary.)



(2*Z*,4*R*)-4-methyl-2-hexene

- 6.6 (b) The asymmetric carbon in the given stereoisomer of malic acid has the *S* configuration.

- 6.8 (a) Use Eq. 6.1 on text p. 237:

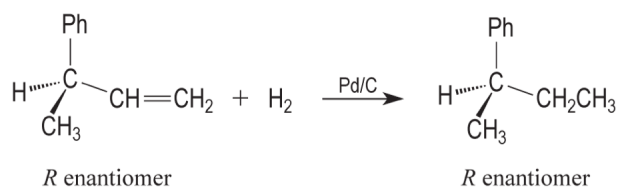
$$\alpha = [\alpha]cl = \frac{(66.5 \text{ deg mL g}^{-1} \text{ dm}^{-1})(1 \text{ dm})(5 \text{ g})}{100 \text{ mL}} = 3.33 \text{ degrees}$$

- (b) The specific rotations of enantiomers must have the same magnitude but the opposite sign. Therefore, the enantiomer of sucrose must have specific rotation =  $-66.5 \text{ deg mL}^{-1} \text{ g}^{-1} \text{ dm}^{-1}$ .

- 6.11 The racemate has no effect on the observed rotation other than to dilute the sample. Hence, after addition of the racemate, the concentration of the excess (*R*)-2-butanol is 0.75 *M*. This corresponds to  $(0.75 \text{ mol L}^{-1})(74.12 \text{ g mol}^{-1})(0.001 \text{ L mL}^{-1}) = 0.0556 \text{ g mL}^{-1}$ . Use this as the value of *c* in Eq. 6.1 with  $[\alpha] = -13.9 \text{ deg mL g}^{-1} \text{ dm}^{-1}$ :

$$\alpha = (-13.9 \text{ deg mL g}^{-1} \text{ dm}^{-1})(0.0556 \text{ g mL}^{-1})(1 \text{ dm}) = -0.773 \text{ deg}$$

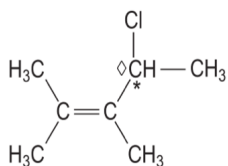
- 6.13 Proceed in the manner suggested by the solution to Problem 6.12. The absolute configuration of the alkene in Eq. 6.2 is known. Carry out the following catalytic hydrogenation:



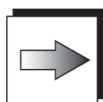
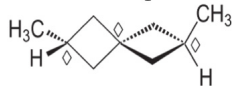
If we assume that hydrogenation proceeds in the normal manner, then the product must have the *R* configuration. Determine the sign of its specific rotation. If positive, then the product shown is the (*R*)-(+)-enantiomer, and it is the dextrorotatory enantiomer; if negative, then the product shown is the (*R*)-(–)-enantiomer, which means that the (*S*)-(+)-enantiomer is the dextrorotatory enantiomer.

- 6.14 (a) For a molecule to have a meso stereoisomer, it must have more than one asymmetric atom, and it must be divisible into constitutionally identical halves (that is, halves that have the same connectivities relative to the dividing line). By these criteria, compound (a) does possess a meso stereoisomer.  
 (b) This compound does not have a meso stereoisomer. A meso compound must have at least two asymmetric carbons.

- 6.17 (b) This compound is chiral.

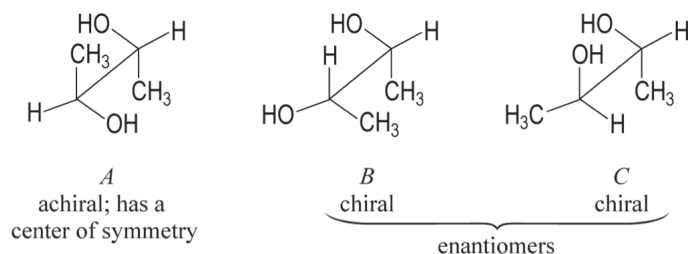


- (d) This compound is chiral and has stereocenters but no asymmetric carbons.

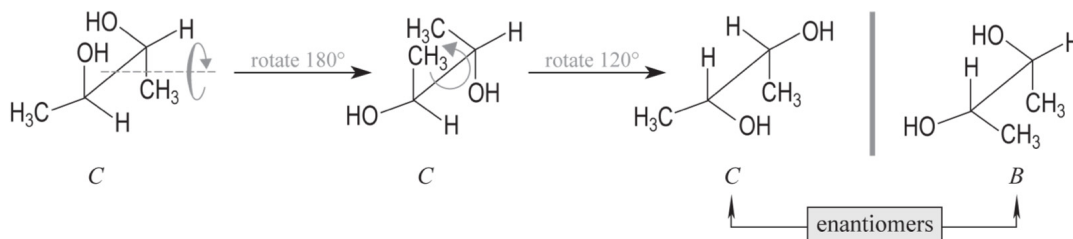


The example in part (d) shows that a tetrahedral stereocenter need *not* be the same thing as an asymmetric carbon.

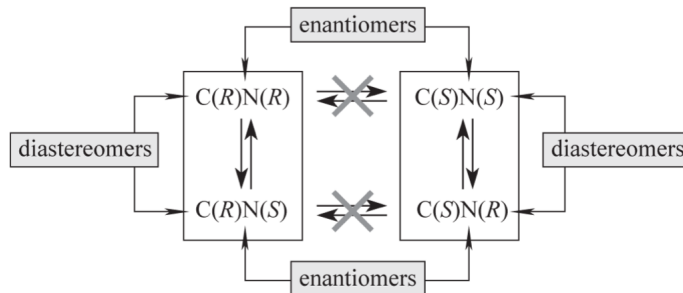
- 6.19 (a) The three conformations of *meso*-2,3-butanediol:



Conformation *A* is achiral; it has a center of symmetry and is congruent to its mirror image. (See Eq. 6.4 on text p. 246.) Conformations *B* and *C* are enantiomers. This relationship can be seen from the following manipulation of conformation *C*:

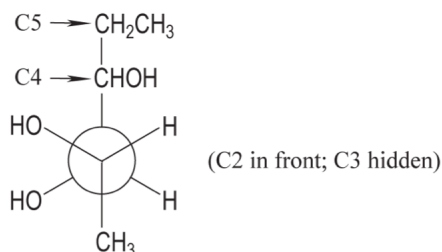


- (b) Because its conformations interconvert rapidly, *meso*-2,3-butanediol cannot be optically active. As the text indicates, molecules that consist of rapidly interconverting enantiomers are said to be achiral. However, at very low temperatures, conformations *B* and *C* could in principle be isolated; each would be optically active, and the two conformations would have rotations of equal magnitudes and opposite signs.
- 6.20 (b) All staggered conformations of propane are achiral (and identical); therefore, even at low temperature, propane could not be resolved into enantiomers.
- (d) Like ethane, 2,2,3,3-tetramethylbutane,  $(\text{CH}_3)_3\text{C}-\text{C}(\text{CH}_3)_3$  consists entirely of achiral (and identical) staggered conformations and therefore cannot be resolved into enantiomers even at very low temperature.
- 6.21 (b) Each of the rapidly interconverting species in part (a) has an enantiomer:  $\text{C}(S),\text{N}(S)$  has an enantiomer  $\text{C}(R),\text{N}(R)$ , and  $\text{C}(S),\text{N}(R)$  has an enantiomer  $\text{C}(R),\text{N}(S)$ . Because inversion of the nitrogen stereocenter does not affect the configuration of the carbon stereocenter, it would be possible to resolve the racemate of this compound into enantiomeric sets of rapidly interconverting *diastereomers*.

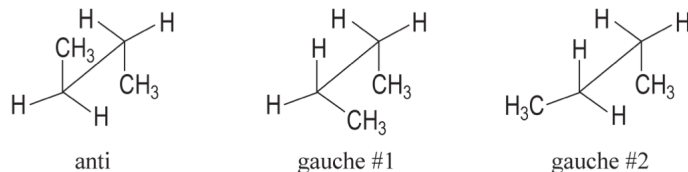


In other words, the set of compounds in one box could be resolved from the set in the other box.

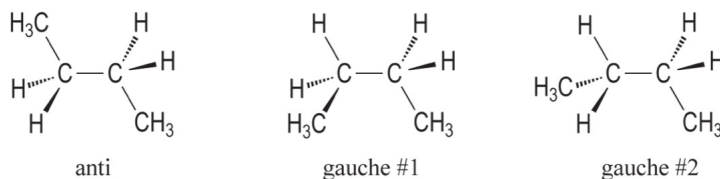
- 6.22 (a) Only the specified bond is shown in Newman projection.



- 6.23 (a) Sawhorse projections of the three conformations of butane:

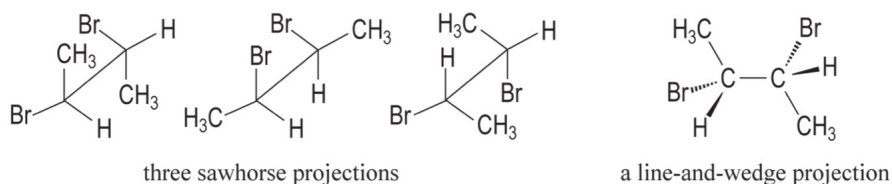


- (b) Line-and-wedge structures for the three conformations of butane:



To convince yourself that this is the meso diastereomer, let either carbon undergo an internal rotation of  $180^\circ$  to see the internal plane of symmetry.

- 6.24 (b) A simple way to provide this answer is to leave the two methyl groups in their same relative positions and reverse the positions of the Br and the H at *one* of the carbons. As in part (a), several other valid projections can be drawn.

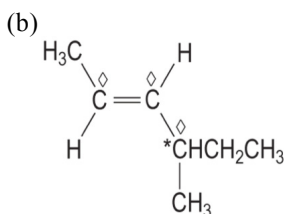


- 6.26 The “resolving agent” was the first crystal that Pasteur separated. The handedness of each subsequent crystal was either “like” that of the first one or “opposite” to it.



### Solutions to Additional Problems

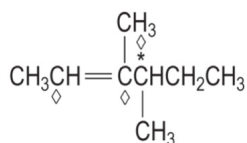
6.27 Asymmetric carbons are indicated with asterisks (\*), and stereocenters with diamonds (◊).



**(E)-4-methyl-2-hexene**

(d) 2,4-Dimethyl-2-pentene,  $(\text{CH}_3)_2\text{C}=\text{CHCH}(\text{CH}_3)_2$ , has no stereocenters or asymmetric carbons.

6.29 The structure:

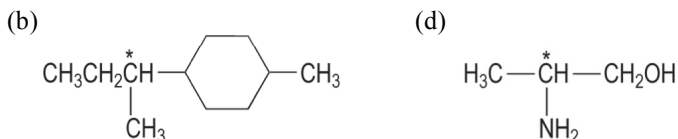


**3,4-methyl-2-hexene**

This compound exists as four stereoisomers: (2*Z*,4*S*), (2*E*,5*S*), (2*Z*,5*R*), and (2*E*,5*R*).

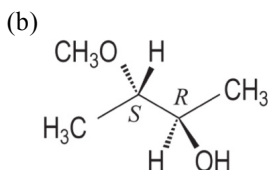
- (a) The carbon stereocenters are carbons 2, 3, and 4, indicated with diamonds (◊) in the structure in part (a).  
 (b) Carbon 4 is an asymmetric carbon, indicated with an asterisk (\*) in the structure in part (a).

6.30 The asymmetric carbons are indicated with asterisks (\*).

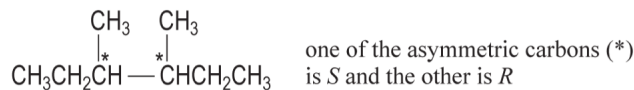


(f) There are no asymmetric carbons in this structure.

6.31

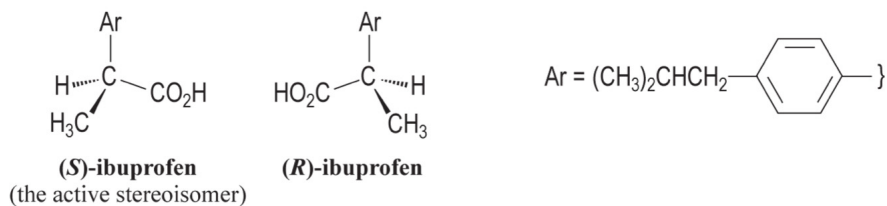


(d) Any meso compound containing two asymmetric carbons must have opposite configurations at the two carbons. Therefore, one of the asymmetric carbons is *S* and the other is *R*.



**3,4-dimethylhexane**

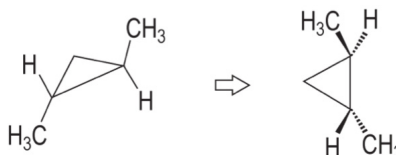
6.33 (a) The line-and-wedge structure of the two enantiomers of ibuprofen:



There are several ways to draw these structures; if you have any doubts as to whether your structures are correct, make models of yours and the ones above and compare them.

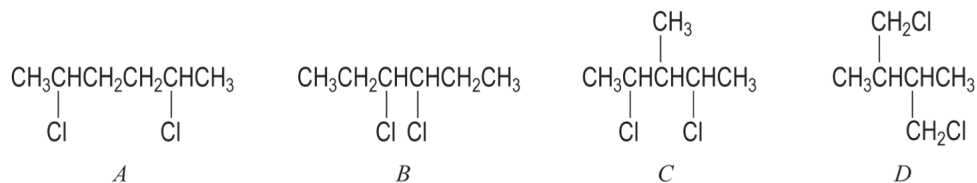
(b) The active stereoisomer is identified in part (a).

6.35 The following stereoisomer of 1,2-dimethylcyclopropane is chiral. If you're not convinced, build a model of it and another model of its mirror image and test them for congruence.



- 6.36
- (b) True by definition.
  - (d) True by definition.
  - (f) False. Some *E,Z* isomers are not chiral (e.g., (*E*)- and (*Z*)-2-butene). Likewise, any meso compound is an achiral diastereomer of a compound containing asymmetric carbons.
  - (h) False, because some stereoisomerism is not associated with chirality—for example, *E,Z* stereoisomerism (double-bond stereoisomerism).
  - (j) False. Molecules with a mirror-image relationship must be either enantiomeric or identical.
  - (l) False. Optical rotation has no general relationship to *R* and *S* configuration.
  - (n) True, because the presence of a plane of symmetry is sufficient (although not necessary) to eliminate chirality.

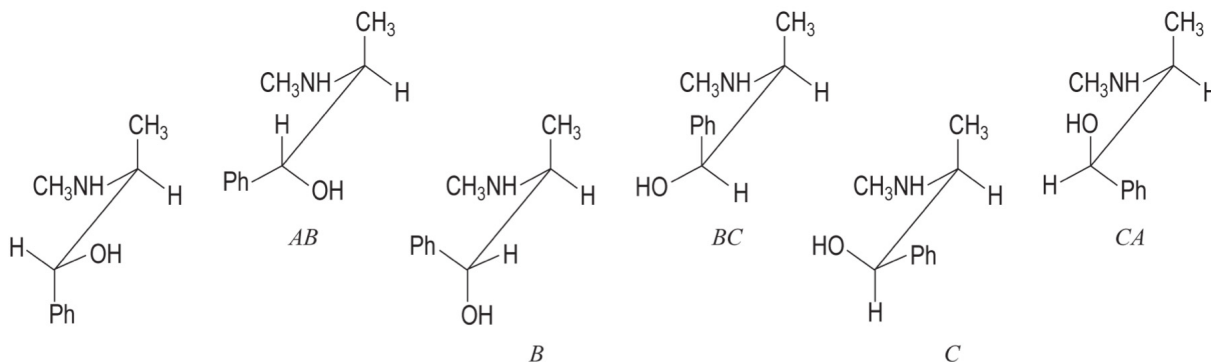
6.38 Meso compounds must be achiral compounds with at least two symmetrically-placed asymmetric carbons and symmetrical branching patterns.



All exist as a single meso compound, except for compound *C*, which can exist as two different meso compounds.



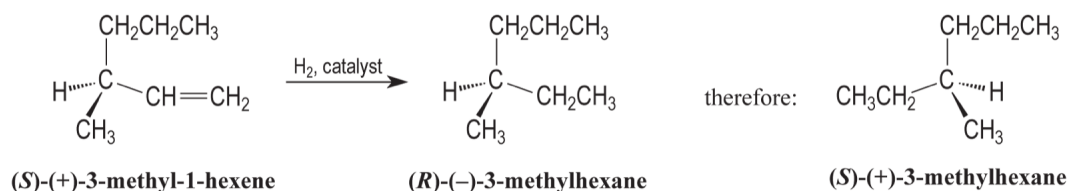
6.40 (a) The sawhorse projections of ephedrine: (The projections labeled with double letters are eclipsed; the projections labeled with single letters are staggered.)



(b) Each of these conformations is chiral. Had any one of them been achiral, ephedrine would not be chiral.

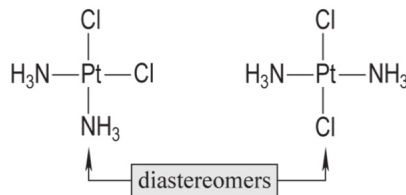
6.43 (b) The rotation of the (–)-enantiomer cancels half of the rotation of the (+)-enantiomer, and the concentration of the (+)-enantiomer is, in addition, halved. Therefore the rotation is 25% of that in part (a)—that is, +0.70 deg.

6.47 (b) Hydrogenation of (*S*)-3-methyl-1-hexene does not break any of the bonds to the asymmetric carbon, and we are given the experimental result that the product, 3-methylhexane, has (–) rotation. Therefore, we can deduce the absolute configuration of (–)-3-methylhexane. Notice that *the relative priorities of the groups at the asymmetric carbon change as a result of the reaction.*



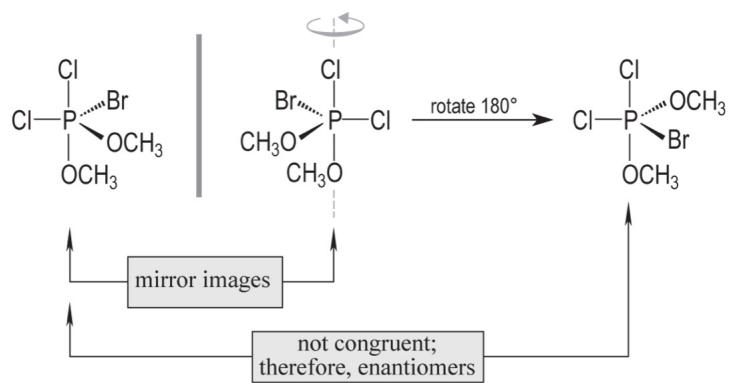
Because (–)-3-methylhexane must have the *R* configuration, it follows that its enantiomer, (+)-3-methylhexane, must have the *S* configuration.

6.50 In a compound of the form  $X_2ZY_2$  with square-planar geometry, there are two ways to arrange groups *X* and *Y* about atom *Z*: with like groups in adjacent corners, or with like groups in opposite corners:



Because these are stereoisomers, and they are not enantiomers, they must be diastereomers. Tetrahedral compounds of the form  $X_2ZY_2$  (for example,  $H_2CCl_2$ ) *cannot* exist as stereoisomers. Hence, the fact that  $Cl_2Pt(NH_3)_2$  exists as stereoisomers with different properties shows that these stereoisomers are diastereomers, and hence that their geometry about platinum is square-planar.

6.52 The ultimate test for chirality is to make the mirror image and test it for congruence:



Because the structure is not congruent to its mirror image, the compound is chiral.

# Chapter 7

## Cyclic Compounds. Stereochemistry of Reactions

### Solutions to In-Text Problems

- 7.3 Following the procedure in the solution to Problem 7.2 (in the Study Guide and Solutions Manual), we first calculate the  $K_{\text{eq}}$  for *tert*-butylcyclohexane:

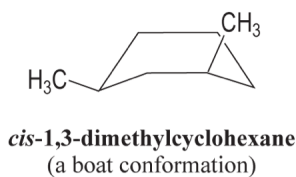
$$K_{\text{eq}} = 10^{-\Delta G^\circ/2.30RT} = 10^{-20/5.71} = 10^{-3.5} = 3.1 \times 10^{-4}$$

From this we calculate, in a total concentration of mol L<sup>-1</sup>,  $[A] = (3.1 \times 10^{-4})[E] \approx 0.00031$ . There is about  $0.051/0.00031 = 168$  times more axial conformation of methylcyclohexane than there is axial conformation of *tert*-butylcyclohexane per mole.

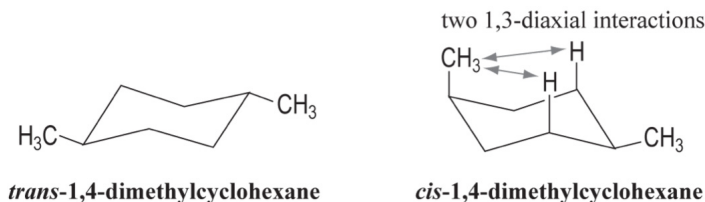
- 7.6 (a) The two chair conformations of *cis*-1,3-dimethylcyclohexane:



- 7.7 (a) A boat conformation of *cis*-1,3-dimethylcyclohexane:

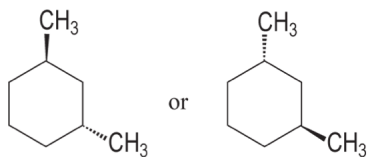


- 7.9 The more stable conformations of the two 1,4-dimethylcyclohexanes:

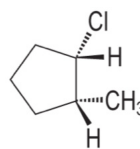


The *cis* isomer has the same number of 1,4 methyl–hydrogen interactions—two—as the axial conformation of methylcyclohexane itself, and thus has a destabilizing contribution of 7.4 kJ mol<sup>-1</sup>. There are no destabilizing interactions in the *trans* isomer.

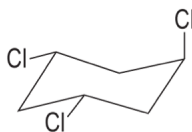
7.10 (b)

*trans*-1,3-dimethylcyclohexane

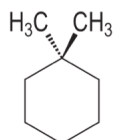
(d)

(1*S*,2*R*)-1-chloro-2-methylcyclopentane

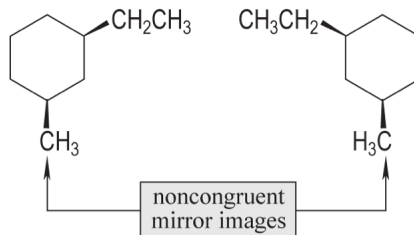
7.11 (b) The most stable conformation is the one that has the greater number of groups in the equatorial position:



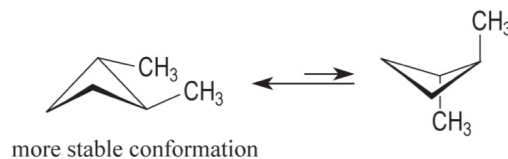
7.12 (b) 1,1-Dimethylcyclohexane is achiral, and therefore cannot be optically active.



1,1-dimethylcyclohexane

(d) *Cis*-1-ethyl-3-methylcyclohexane can be isolated in optically active form.*cis*-1-ethyl-3-methylcyclohexane

7.14 (b) The two structures differ in configuration at both asymmetric carbons. They are enantiomers. (Show that they are noncongruent mirror images.)

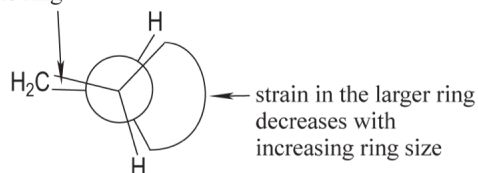
7.15 (b) Cyclobutane undergoes an interconversion of puckered forms analogous to the chair interconversion of cyclohexane. This interchanges axial and equatorial groups. Therefore, one conformation of *trans*-1,2-dimethylcyclobutane—the more stable conformation—has diequatorial substituents, and the other—the less stable conformation—has diaxial substituents.*trans*-1,2-dimethylcyclobutane7.16 (b) *Trans*-1,2-dimethylcyclopropane is chiral.



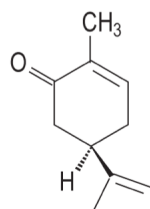
***trans*-1,2-dimethylcyclopropane**  
noncongruent mirror images

- 7.17 (b) Bicyclo[3.2.0]heptane
- 7.20 (b) The model of *trans*-bicyclo[5.3.0]decane is easier to build. The larger is a ring, the easier it is to compress the dihedral angle of the *trans* bonds at the ring junction without introducing significant strain in the ring. This angle must be very close to  $0^\circ$  in order to accommodate a fused cyclopropane, that is, to bridge the ends of *trans* bonds with only one carbon.

a dihedral angle close to  $0^\circ$   
is required for the cyclopropane ring



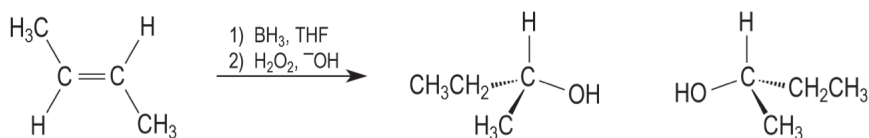
- 7.21 (b) Although both molecules have bridgehead double bonds, the double bond in compound *B* is more twisted, and a model of this molecule is more difficult to build. Consequently, compound *B* is less stable and therefore would have the greater (more positive or less negative) heat of formation.
- 7.22 (b) Premeds could take out their stethoscopes and determine which side of each person the heart is on. Or, you could offer to shake hands. Mr. L would extend what he calls his right hand, but to us it would be his left. Or, you could ask them to smell a spearmint leaf and describe the odor. (*R*)-Carvone, the active principle of spearmint, has a spearmint odor, but its enantiomer (*S*)-carvone smells like caraway (the odor of rye bread). (*R*)-Carvone would smell like caraway to Mr. L.



**(*R*)-(-)-carvone**

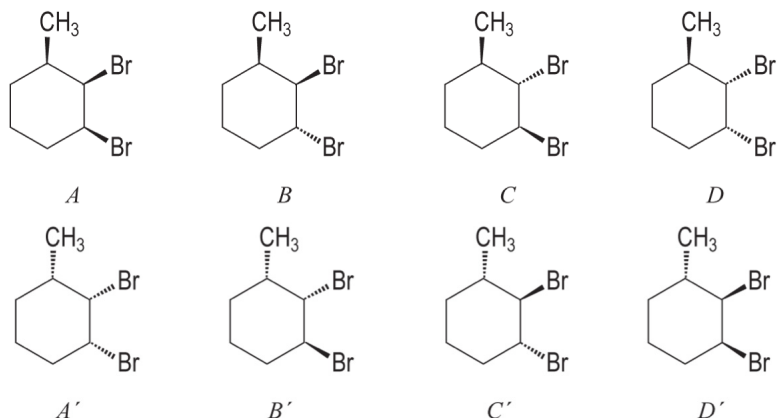
In any case, the point is that the two mirror images are distinguished by comparing a chiral reference element (our bodies, our right hands, or the odors or tastes of enantiomers) with the corresponding elements of the two people.

- 7.24 Hydroboration-oxidation of *trans*-2-butene gives racemic 2-butanol—that is, two enantiomers formed in equal amounts.

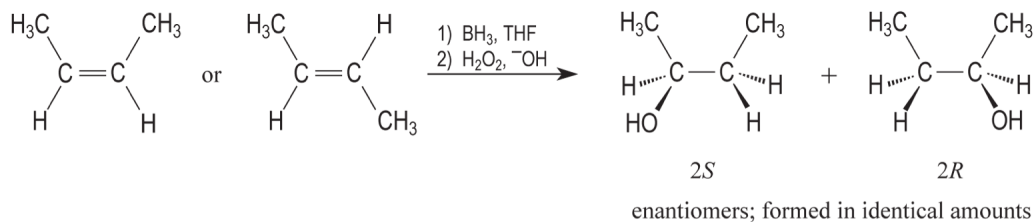


**racemic 2-butanol**

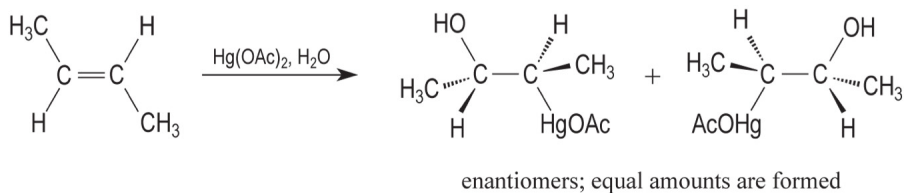
- 7.27 Because the bromines of the product are *trans*, products *B* and *C*, and their respective enantiomers *B'* and *C'*, are the major products. Compounds *B* and *B'* are formed in identical amounts, because they are enantiomers, and compounds *C* and *C'* are formed in identical amounts for the same reason. Compounds *B* and *C*, as well as compounds *B'* and *C'*, are formed in different amounts, because they are diastereomers.



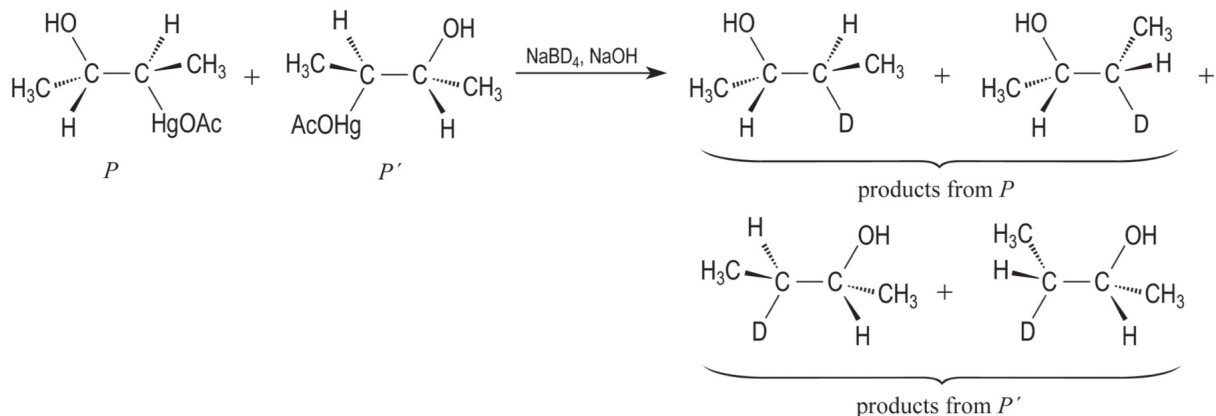
- 7.29 The presence of deuteriums in Problem 7.28 gives rise to diastereomeric products. If the starting material is not isotopically substituted, then the two products are enantiomeric, and the same pair of enantiomers is formed whether the *cis*- or *trans*-alkene is used as the starting material.



- 7.30 (a) Oxymercuration is an *anti*-addition. Two enantiomeric products are formed in equal amounts.



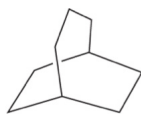
- (b) The enantiomeric products of the reaction in part (a) are shown below as *P* and *P'*. Because the  $\text{NaBD}_4/\text{NaOH}$  reaction occurs with *loss of stereochemistry*, two diastereomers are formed from each of the enantiomers *P* and *P'*. As a result, all four possible stereoisomers are formed.





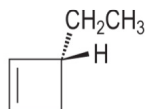
### Solutions to Additional Problems

7.33 (a)



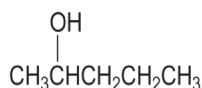
bicyclo[3.2.2]nonane

(b)



(R)-3-ethylcyclobutene

7.35 As the problem indicates, 2-pentanol is a chiral molecule.



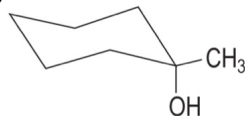
2-pentanol

Distinguishing between enantiomers requires a technique that has a chiral attribute.

- (a) Boiling point does not distinguish between two enantiomers.
- (b) Optical rotation does have a chiral aspect, and therefore can distinguish between two enantiomers. (See Further Exploration 7.3.)
- (c) Because hexane is an achiral solvent, enantiomers have identical solubilities in hexane.
- (d) Density is not a chiral property, and therefore the two enantiomers have identical densities.
- (e) The solubilities of two enantiomers in principle differ in an enantiomerically pure chiral solvent.
- (f) Dipole moment is not a chiral property, and therefore the two enantiomers have identical dipole moments.
- (g) Because taste buds are chiral, they in principle differentiate between two enantiomers.

7.36

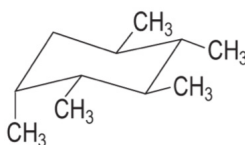
(b)



7.37

(b)

In choosing which conformation to draw, the goal is to put the maximum number of methyl groups possible in equatorial positions.



7.38

(b)

The standard free energy change for the reaction equatorial  $\rightleftharpoons$  axial is  $+9.2 \text{ kJ mol}^{-1}$ ; the axial conformation has the higher standard free energy. The equilibrium constant is calculated by applying Eq. 3.31b, text p. 107.

$$K_{\text{eq}} = 10^{-\Delta G^\circ/2.30RT} = 10^{-9.2/5.71} = 10^{-1.61} = 2.4 \times 10^{-2}$$

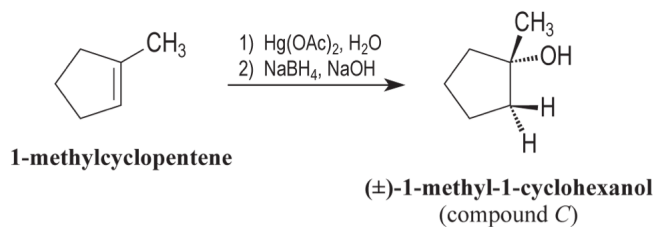
That is, the ratio [axial]/[equatorial] is 0.024. This means that there is  $1/0.024 = 42$  times as much equatorial conformation as there is axial conformation at equilibrium.

7.39

(b)

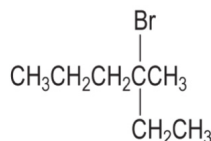
Compound *A* could be formed by oxymercuration–reduction from either *cis*- or *trans*-3-hexene because the alkene is symmetrical and, for that reason, regioselectivity and stereoselectivity are not relevant.

Oxymercuration–reduction of 1-methylcyclopentene gives compound *C*; therefore compounds *B* and *D* are not formed.



7.40 For reaction (2):

(a) The products:

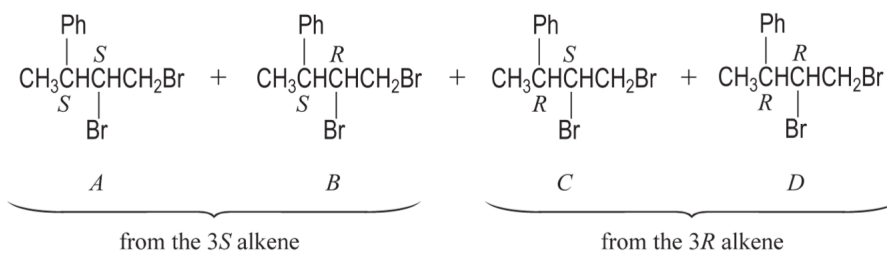


*R* and *S*

- (b) The two products are enantiomers.  
 (c) The two products are formed in identical amounts.  
 (d) The two products have identical boiling points and identical melting points. An enantiomeric resolution would be required to separate the two compounds.

For reaction (4):

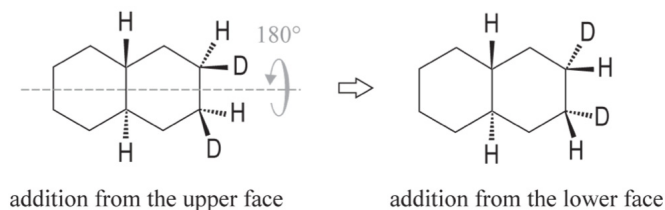
(a) The starting alkene is racemic, and is therefore an equimolar mixture of two enantiomers. To predict the products, make the prediction for each enantiomer separately and then combine the results.



- (b) Compounds *A* and *B*, which come from the *S* enantiomer of the starting material, are diastereomers, as are compounds *C* and *D*, which come from the *R* enantiomer of the starting material. Compounds *A* and *C* and compounds *B* and *D* are also diastereomers. Compounds *A* and *D*, as well as compounds *B* and *C*, are enantiomers.  
 (c) The diastereomers are formed in different amounts; the enantiomers are formed in identical amounts.  
 (d) Any pair of diastereomers have different melting points and boiling points; any pair of enantiomers have identical melting points and boiling points.

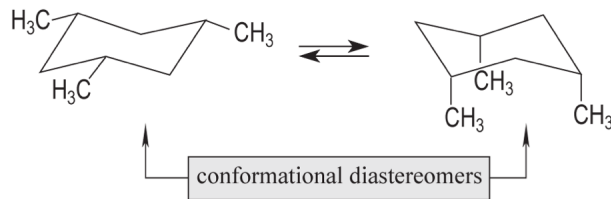
For reaction (6):

(a) The starting alkene is a single enantiomer of a chiral compound. Two *syn*-additions of  $\text{D}_2$  are possible: one from the upper face of the double bond, and one from the lower face.

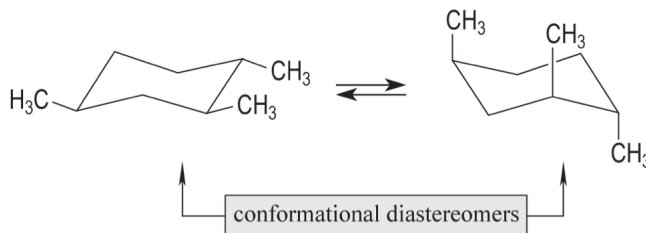


(b)–(d) As the foregoing structures show, the two modes of addition give the same product; so, only one structure is possible.

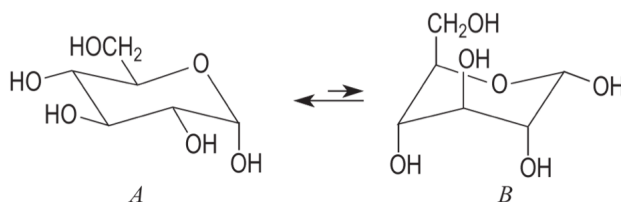
7.41 (b) An achiral trimethylcyclohexane that undergoes the chair interconversion to give conformational diastereomers:



(c) A chiral trimethylcyclohexane that undergoes the chair interconversion to give conformational diastereomers:

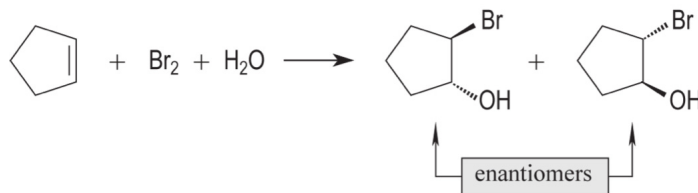


7.43 The chair conformations of glucose:

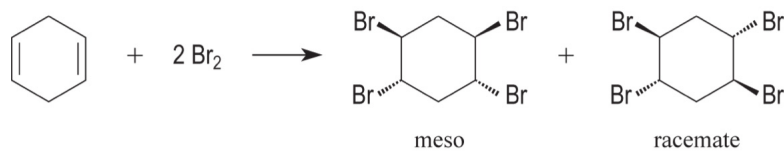


Conformation *A* is more stable because all the substituents (except one) are equatorial.

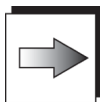
7.44 (b) The bromonium ion derived from the reaction of cyclopentene with bromine undergoes backside substitution by water to give the *trans*-bromohydrin, which is chiral. Because the starting materials are achiral, the chiral product is obtained as a racemate.



7.46 Given that addition of bromine at each double bond is *anti*, two diastereomers of 1,2,4,5-tetrabromocyclohexane can be formed. One is the achiral meso compound, and the other is the racemate.

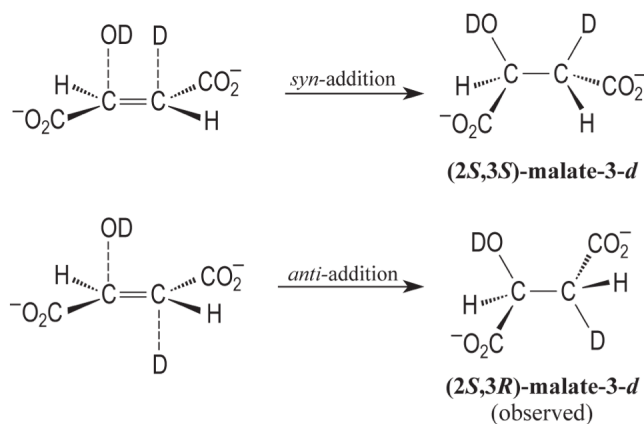


Because these are diastereomers, they have different physical properties; evidently, one melts at 255°, the other at 188°, although the data do not determine which is which.



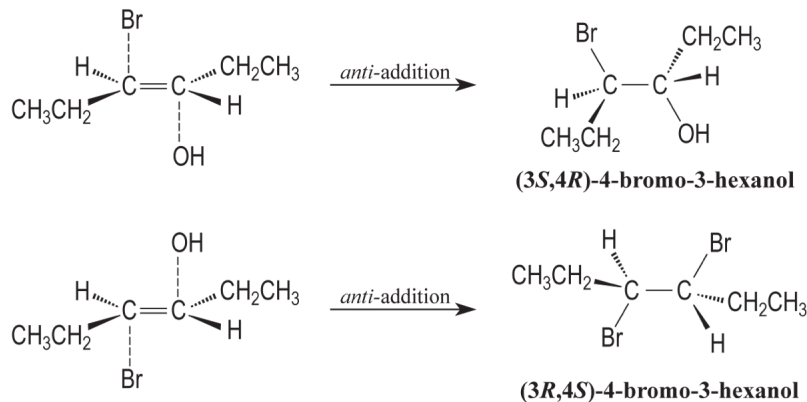
Assuming you had samples of the two compounds but didn't know which was which, what experiment could you do that might identify the two compounds? (*Answer:* Carry out an enantiomeric resolution. The compound that can be separated into optically active components—its two enantiomers—is identified as the racemate.) It turns out that the meso compound is the higher-melting stereoisomer.

- 7.49 (a) The only stereocenter in the molecule is the nitrogen, which rapidly undergoes inversion, a process that rapidly interconverts enantiomers. Consequently, this compound cannot be resolved into enantiomers at room temperature.
- (b) Because nitrogen inversion interconverts enantiomers, the compound cannot be resolved into enantiomers.
- 7.52 (a) Imagine both *syn*- and *anti*-additions to fumarate with the OD entering from the face of the alkene that leads to the product malate-3-*d* in which carbon-2 has the *S* configuration. A *syn*-addition will lead to (2*S*,3*S*)-malate-3-*d*, whereas an *anti*-addition will lead to the observed 2*R*,3*R* product. Therefore, the reaction is an *anti*-addition.

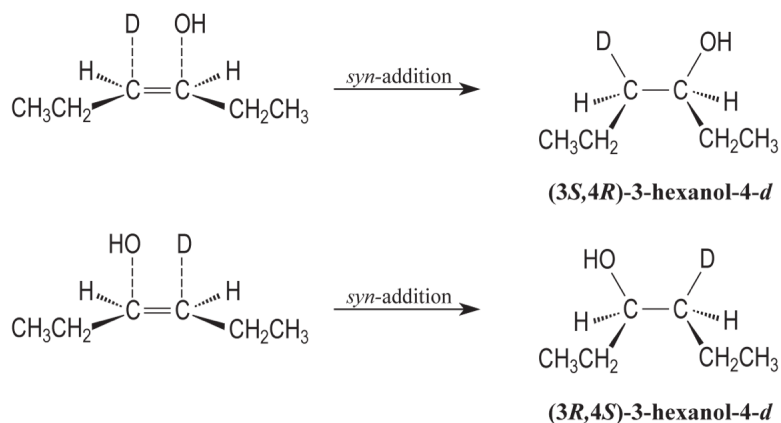


There are experimental techniques—for example, NMR spectroscopy, which is the subject of Chapter 13—that can make the subtle stereochemical distinctions required to solve stereochemical problems like this.

- (b) The use of D<sub>2</sub>O allows us to differentiate the protons of the solvent from those of the starting material. The stereochemistry of the addition cannot be determined without this distinction.
- 7.53 (b) This is essentially like the addition in part (a), except that the nucleophile that reacts with the bromonium ion is water; a bromohydrin is formed rather than a dibromide. (See text pp. 183–184 to review this reaction.) The product is a racemate.

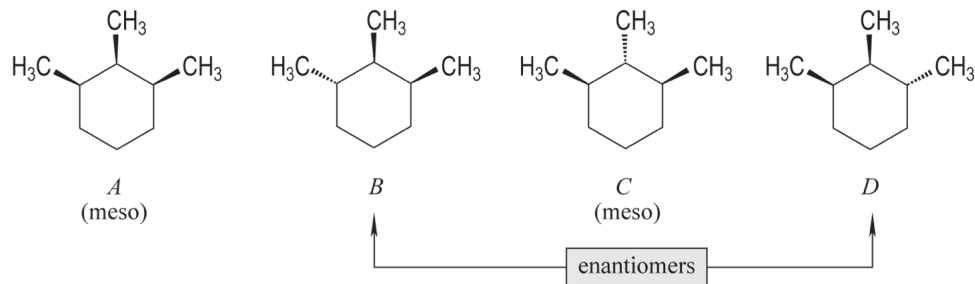


- (d) Analyze the problem as in part (c). The reaction is a net *syn*-addition that gives a racemic product.



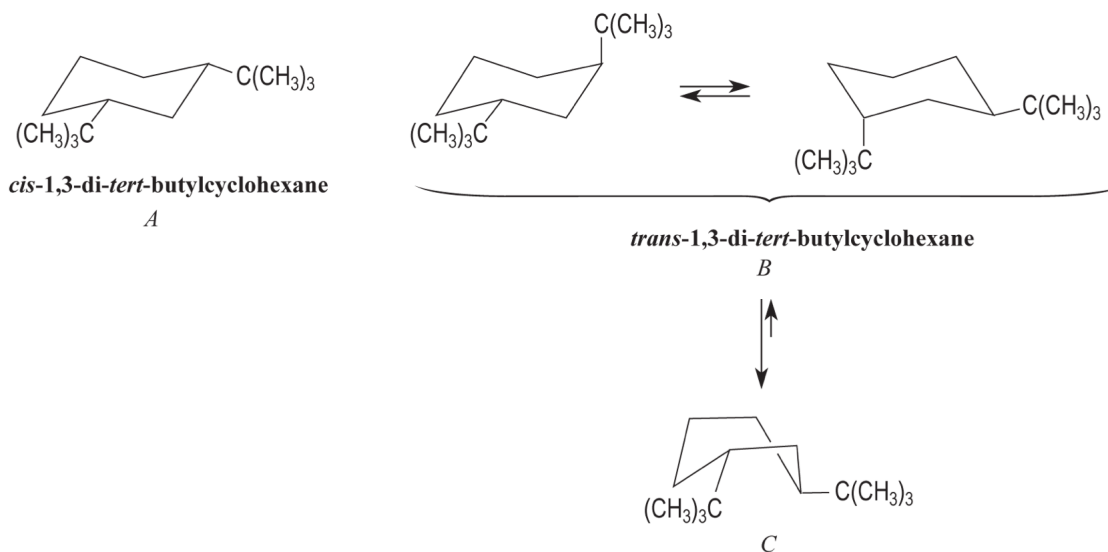
(Convince yourself that the two modes of addition from the bottom face of the alkene give the same products.)

- 7.57 A systematic way to work this problem is to start with all methyl groups in a cis arrangement; then change the stereochemistry one group at a time.



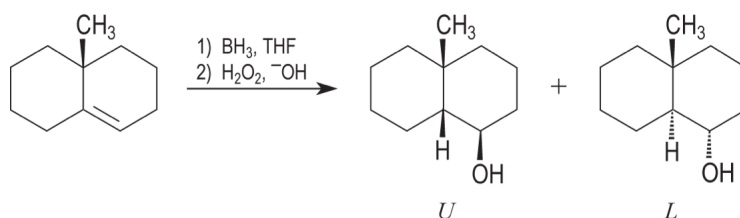
We could go on to start with stereoisomer *A* and change two groups at a time in all possible ways, and then change all three groups. But when we do this, we find that all “new” possibilities are identical to one of the foregoing compounds *A–D*. Therefore, there are four stereoisomers—two meso compounds and two enantiomers.

- 7.60 *Cis*-1,3-di-*tert*-butylcyclohexane can exist in a chair conformation (*A*) in which both *tert*-butyl groups are equatorial. However, in either chair conformation of *trans*-1,3-di-*tert*-butylcyclohexane (*B*), there is an axial *tert*-butyl group. The axial *tert*-butyl group can be avoided if compound *B* exists in a twist-boat conformation *C*, in which both *tert*-butyl groups are equatorial. (This conformation is shown as a boat for simplicity.) Evidently the twist-boat conformation is more stable than either chair conformation containing an axial *tert*-butyl group. The interaction of the methyl groups with the ring hydrogens should be about the same in both conformations *A* and *C*, so that these cancel in the comparison.

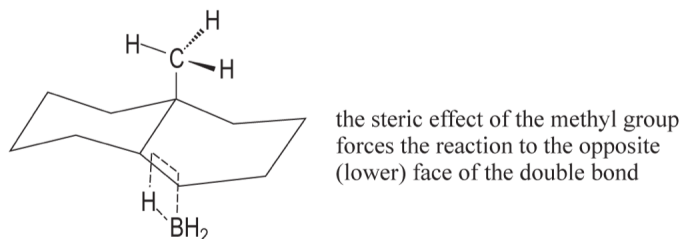


Each interaction shown adds  $3.7 \text{ kJ mol}^{-1}$  to the heat of formation relative to that of *C*. Consequently, *C* has the lowest heat of formation; the heat of formation of *B* is  $(2 \times 3.7) = 7.4 \text{ kJ mol}^{-1}$  greater; and the heat of formation of *A* is  $(3 \times 3.7) = 11.1 \text{ kJ mol}^{-1}$  greater than that of *C*.

- 7.62 (a) *Trans*-decalin, *C*, is more stable than *cis*-decalin, *A* (see Problem 7.19, text p. 269). However, neither compound has angle strain. Compound *B* is least stable because of the strain in its four-membered ring. You can see from Table 7.1, text p. 269, that the strain in a cyclobutane ring ( $4 \times 7.1 = 28.4 \text{ kJ mol}^{-1}$ ) is far more destabilizing than the three 1,3-diaxial interactions ( $3 \times 3.7 = 11.1 \text{ kJ mol}^{-1}$ ) in *cis*-decalin. Therefore, the order of increasing  $\Delta H_f^\circ$  is  $C < A < B$ .
- (b) The ring strain in *B* makes it less stable than *C*; and the twisted double bond in *A* (violation of Bredt's rule) makes it so unstable that it cannot be isolated. Therefore, the order of increasing  $\Delta H_f^\circ$  is  $C < B \ll A$ .
- 7.64 (a) The two diastereomeric products result from addition at the upper (*U*) and (*L*) lower faces of the double bond.



- (b) The methyl group shields the upper face (in steroid terminology, the  $\alpha$  face) of the molecule like an umbrella. Therefore, product *L* is the predominant product.



- 7.67 (a) The approach to this problem is similar to that used in Problem 7.66. The  $\Delta G^\circ$  for this equilibrium,  $\Delta G^\circ(AB)$ , balances two phenyl-hydrogen 1,3-diaxial interactions, on the right, against two methyl-hydrogen 1,3-diaxial interactions, on the left. Since  $\Delta G^\circ > 0$ , the equilibrium is unfavorable; evidently a Ph-H diaxial interaction

has a greater energy cost than a CH<sub>3</sub>-H diaxial interaction. This deduction is consistent with a larger size for the Ph group.

- (b) From the analysis in part (a),

$$\Delta G^\circ(AB) = 4.73 = 2\Delta G^\circ(\text{Ph-H}) - 2\Delta G^\circ(\text{CH}_3\text{-H}) = 2\Delta G^\circ(\text{Ph-H}) - 7.4$$

Solving,

$$\Delta G^\circ(\text{Ph-H}) = (4.73 + 7.4)/2 = 6.1 \text{ kJ mol}^{-1}$$

In Equation (1) of the problem, two Ph-H diaxial interactions and balanced against an equatorial Ph. As we have just calculated, the energy cost, and therefore  $\Delta G^\circ$  for equation (1), is  $2 \times 6.1 \text{ kJ mol}^{-1} = 12.2 \text{ kJ mol}^{-1}$ .

In Equation (2), two Ph-H diaxial interactions ( $13.2 \text{ kJ mol}^{-1}$ ) and a *gauche*-butane interaction ( $2.8 \text{ kJ mol}^{-1}$ ) on the left side are balanced against four methyl-hydrogen diaxial interactions on the right ( $14.8 \text{ kJ mol}^{-1}$ ). The overall  $\Delta G^\circ$  for equation (2) is therefore  $14.8 - 15.0 = -0.2 \text{ kJ mol}^{-1}$ .

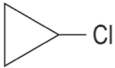
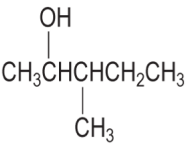
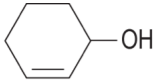
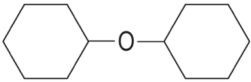
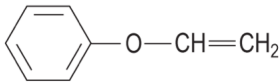
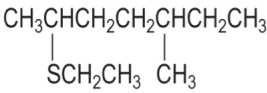




# Chapter 8

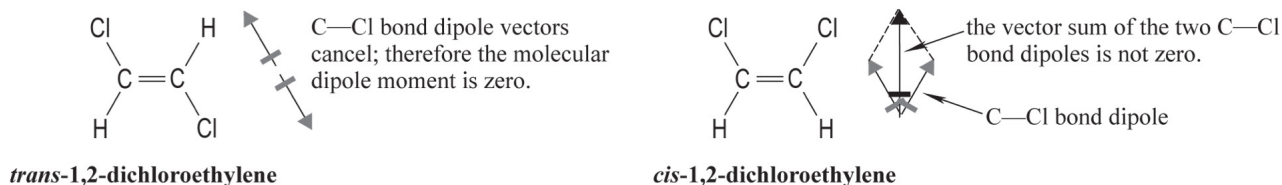
## Introduction to Alkyl Halides, Alcohols, Ethers, Thiols, and Sulfides

### Solutions to In-Text Problems

- 8.1 (b) Hexyl iodide is a primary alkyl halide.  
(c) Cyclopentyl bromide is a secondary alkyl halide.
- 8.2 (b)   
**chlorocyclopropane**
- (d)  $\text{I}-\text{CH}_2-\text{I}$   
**methylene iodide**
- 8.3 (b) (Z)-3-Chloro-2-pentene  
(d) Chloroform ( $\text{HCCl}_3$ ) is the traditional name for trichloromethane.  
(f) 1,3-Dibromocyclobutane
- 8.4 (b)  $(\text{CH}_3)_2\text{CHCH}_2-\text{OH}$   
**isobutyl alcohol**
- (d)   
**3-methyl-2-pentanol**
- (f)   
**2-cyclohexenol**
- 8.5 (b) 1-Butanol  
(d) 2-Chloro-5-methyl-2-cyclopentenol. The 2-refers to the position of the double bond; the position of the  $-\text{OH}$  group is assumed to be the 1-position because it is the principal group. It would not be incorrect to add the 1 to the name: 2-chloro-5-methyl-2-cyclopenten-1-ol.  
(f) 2,5-Cyclohexadienol  
(h) 2-Methyl-2-propanethiol
- 8.6 (b)   
**dicyclohexyl ether**
- (d)  $(\text{CH}_3)_3\text{C}-\text{S}-\text{CH}(\text{CH}_3)_2$   
**tert-butyl isopropyl sulfide**
- (f)   
**phenyl vinyl ether**
- (h)   
**5-(ethylthio)-2-methylheptane**
- 8.7 (b) 2-Ethoxyethanol (or 2-ethoxy-1-ethanol)  
(d) 1-(Isobutylthio)-2-methylpropane

8.8 (b) The structure of 2-butoxyethanol is  $\text{HO—CH}_2\text{CH}_2\text{—OCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ .

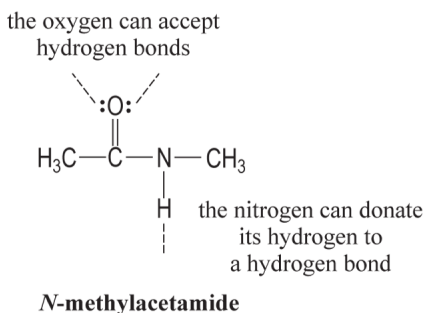
8.12 Because of the molecular geometry of *trans*-1,2-dichloroethylene, the C—Cl bonds are oriented in opposite directions, as are the C—H bonds. Consequently, their bond dipoles cancel, and the molecular dipole moment of *trans*-1,2-dichloroethylene is zero. (The cancellation of the C—Cl bond dipoles is shown in the diagram below; the much weaker C—H bond dipoles also cancel for the same reason.) The corresponding bond dipoles of *cis*-1,2-dichloroethylene do not cancel; consequently it has a significant dipole moment. The interaction of the molecular dipole moments of *cis*-1,2-dichloroethylene molecules provides a cohesive force in the liquid state that is not present in the *trans* stereoisomer. (See text p. 334.) Because such cohesive forces enhance boiling point, *cis*-1,2-dichloroethylene has the higher boiling point of 60.3°.



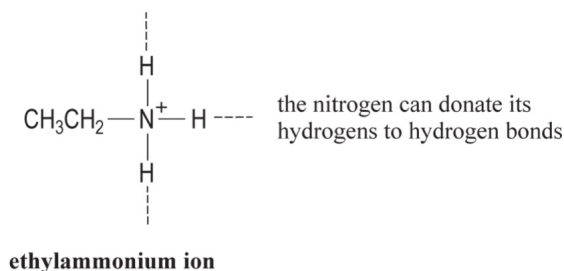
8.13 (b) A chlorine contributes about the same molecular mass (35 units) as an ethyl group (29 units), and alkyl chlorides have about the same boiling points as alkanes of the same molecular mass. Hence, chloromethane has about the same boiling point as propane, which has a lower boiling point than the five-carbon alkene 1-pentene. The alcohol has the highest boiling point because it has about the same molecular mass as 1-pentene, but can donate and accept hydrogen bonds. Consequently, it has the highest boiling point of all. The order of increasing boiling points is, therefore, chloromethane ( $-42^\circ$ ) < 1-pentene ( $30^\circ$ ) < 1-butanol ( $118^\circ$ ).

8.14 (b) Hydrogen fluoride is an excellent hydrogen-bond donor, and the fluorine is an excellent hydrogen-bond acceptor.

(d) *N*-methylacetamide can serve as both a hydrogen-bond donor and a hydrogen-bond acceptor.



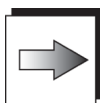
(f) The ethylammonium ion can donate its N—H hydrogens to hydrogen bonds, but it cannot accept hydrogen bonds because it has no unshared electron pairs.



8.15 (b) 2,2,2-Trifluoroethanol is a polar, protic, donor solvent.

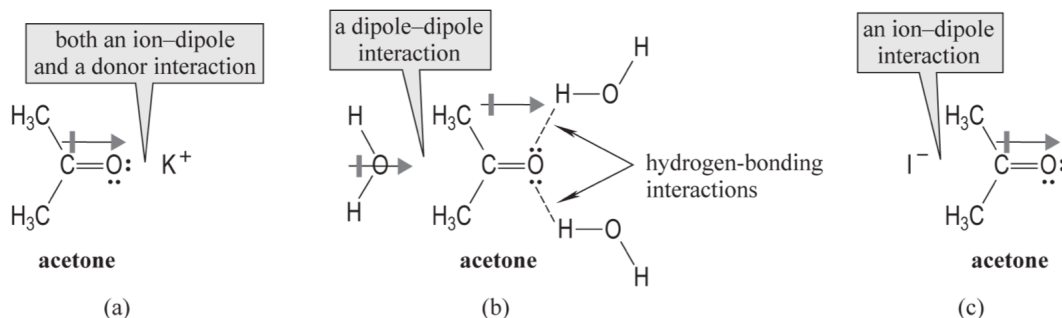
(d) 2,2,4-Trimethylpentane (a major component of gasoline) is an apolar, aprotic, nondonor solvent.

- 8.17 (b) Certainly the 1-nonanol is less soluble in water than methanol is, and its long hydrocarbon chain would both reduce its solubility in water and promote its solubility in methylene chloride. The data on text p. 342 show that even 1-hexanol has a very low solubility in water. The solubility of 1-nonanol would be much lower still. The 1-nonanol would be found primarily in the methylene chloride layer.
- 8.18 Water can accept a hydrogen bond from the hydrogen of the N—H bond, and can donate a hydrogen bond to the oxygen of the C=O bond as well as to the nitrogen. This hydrogen bonding tends to solubilize acetanilide in water. In contrast, the CH<sub>3</sub> group and the phenyl ring cannot form hydrogen bonds with water; consequently, these apolar (“greasy”) groups tend to make acetanilide insoluble.

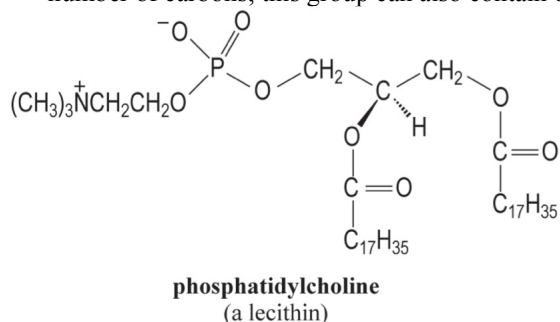


Groups such as alkyl and phenyl groups that reduce water solubility are sometimes termed *hydrophobic groups*.

- 8.20 (a) The interaction with a dissolved potassium ion involves both an ion–dipole interaction and a donor interaction.
- (b) Acetone interacts with water by hydrogen bonding and by dipole–dipole interactions.
- (c) Iodide ion interacts with acetone by an ion–dipole interaction. (In both parts (a) and (c), multiple acetone molecules cluster around the ions; only one is shown here.)



- 8.21 (b) One or both of the C<sub>17</sub>H<sub>35</sub> groups could be substituted by any long, unbranched alkyl group with an odd number of carbons; this group can also contain one or more cis double bonds.



- 8.22 (b) The substitution of an —OH hydrogen by a phosphorus elevates the sequence-rule priority of the phosphorus-containing branch.
- 8.24 (b) The structure of potassium *tert*-butoxide is K<sup>+</sup> <sup>−</sup>O—C(CH<sub>3</sub>)<sub>3</sub>.
- 8.25 (b) Cuprous ethanethiolate [or copper(I) ethanethiolate]
- 8.26 (b) Thiols are more acidic than alcohols, other things being equal (element effect); and a chloro substituent enhances acidity by a polar effect. Thus, ethanol (CH<sub>3</sub>CH<sub>2</sub>OH) is least acidic and has the greatest pK<sub>a</sub>;

2-chloroethanol is more acidic; and 2-chloroethanethiol,  $\text{ClCH}_2\text{CH}_2\text{—SH}$ , is most acidic and has the lowest  $\text{p}K_{\text{a}}$ .

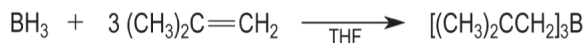


**methyl iodide**

**methylmagnesium iodide**

(a Grignard reagent)

(d) Not all organometallic reagents are prepared from alkyl halides. Here's one from Chapter 5:



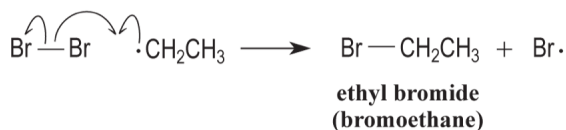
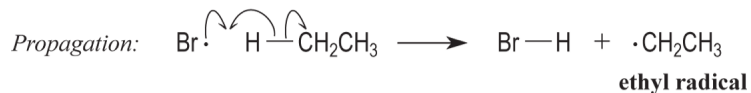
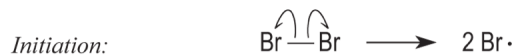
8.28 (b) The product of the reaction is *tert*-butyllithium,  $(\text{CH}_3)_3\text{C—Li}$ , and lithium bromide,  $\text{Li}^+ \text{Br}^-$ .

8.29 (b) The products result from protonolysis of the C—Mg bond: isobutane,  $(\text{CH}_3)_2\text{CHCH}_3$ , and  $\text{HOMgCl}$ , which, under the aqueous reaction conditions, is ionized to  $\text{Mg}^{2+}$ ,  $\text{HO}^-$ , and  $\text{Cl}^-$ . The curved-arrow notation for the protonolysis:



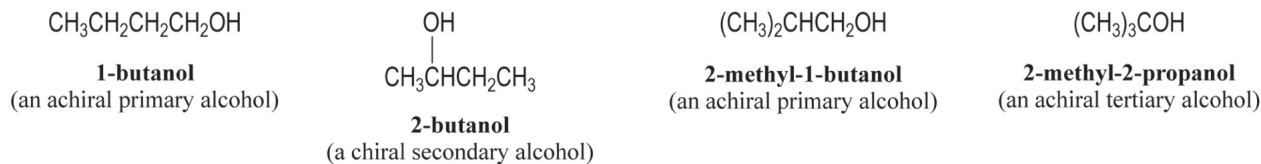
8.30 (b) The compounds formed in the reactions of the Grignard reagents in part (a) with  $\text{D}_2\text{O}$  are  $(\text{CH}_3)_2\text{CH—D}$  and  $\text{CH}_3\text{CH}_2\text{CH}_2\text{—D}$ , respectively.

8.31 The free-radical chain mechanism (initiation and propagation steps) for bromination of ethane:



### Solutions to Additional Problems

8.34 The alcohols with the formula  $C_4H_9OH$ :



8.35 (b) The systematic name of methoxyflurane is 2,2-dichloro-1,1-difluoro-1-methoxyethane.

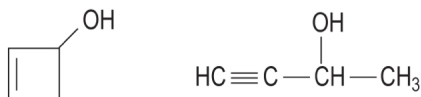
8.36 (b) 3-Methyl-1-butanethiol

8.37 (b) The order of boiling points is *tert*-butyl alcohol < 2-pentanol < 1-hexanol. (The actual boiling points are 82°, 119°, 158°.) This follows the order of molecular masses. The increased branching of 2-pentanol relative to 1-hexanol, and *tert*-butyl alcohol relative to 2-pentanol, makes the differences between these boiling points even greater than they would be for unbranched alcohols of the same molecular masses.

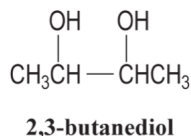
(d) The order of boiling points is propane < diethyl ether < 1,2-propanediol. (The actual boiling points are -42°, 37°, 189°.) Diethyl ether has a higher boiling point than propane because diethyl ether is more polar and because it has a greater molecular mass. 1,2-Propanediol has the highest boiling point because of hydrogen bonding.

8.38 (b) Use the same reasoning as in part (a). The N—H hydrogens of the first compound, acetamide, can be donated in hydrogen bonds between molecules that involve the oxygen or the nitrogen as an acceptor. The second compound, *N,N*-dimethylacetamide, has no hydrogens that can be involved in hydrogen bonding. The hydrogen bonding in the liquid state of acetamide is reflected in its higher boiling point, despite the higher molecular mass of the second compound.

8.39 (b) The unsaturation number is 2, and both rings and/or multiple bonds are allowed in this case. Two of several possibilities are



(d) 2,3-Butanediol exists as a meso stereoisomer and two enantiomers.



8.40 (b) The gas formed is  $D_2$  along with the by-product  $Na^+ ^-OD$ .

(d) The gas formed is ethane,  $CH_3CH_3$ , along with the by-product  $HO^- ^+MgBr$ .

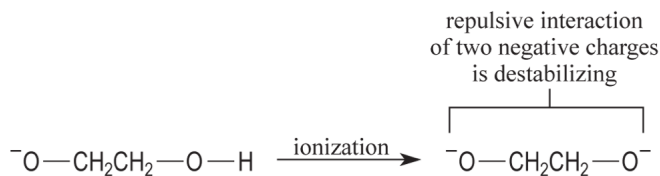
8.41 (b) Allyl methyl ether,  $H_2C=CH-CH_2-OCH_3$ , decolorizes a  $Br_2$  solution, because the  $Br_2$  adds to the double bond. Propyl alcohol,  $CH_3CH_2CH_2OH$ , has no double bond, and does not decolorize a  $Br_2$  solution.

(d) 2-Methylcyclohexanol, an alcohol, reacts with NaH to produce dihydrogen,  $H_2$ . (See Eq. 8.10, text p. 356.) Ethers, lacking an acidic hydrogen, do not react with NaH.

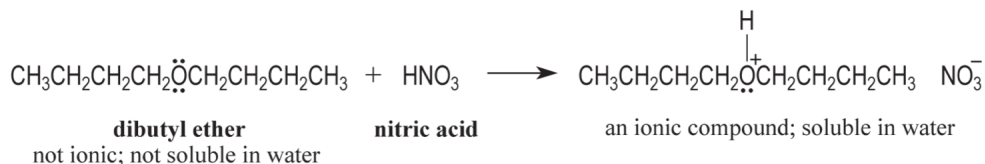
8.42 (b) Although compound *A* is soluble in hydrocarbon solvents, it exists in such solvents as ion pairs and higher aggregates rather than as free ions. The reason is that hydrocarbon solvents have very low dielectric constants ( $\epsilon \approx 2$ ), whereas a high dielectric constant is required to separate ionic aggregates into free ions.

Furthermore, a hydrocarbon offers no solvation by hydrogen bonding to the bromide counter-ion. Hence, this anion remains in proximity to its positive partner.

- 8.43 (b) Isobutane,  $(\text{CH}_3)_3\text{CH}$ , gives two achiral monochlorination products: isobutyl chloride,  $(\text{CH}_3)_2\text{CHCH}_2\text{Cl}$ , and *tert*-butyl chloride,  $(\text{CH}_3)_3\text{C}-\text{Cl}$ .
- 8.44 (b) 2-Chloroethanol < 3-chloro-1-propanethiol < 2-chloro-1-propanethiol. Thiols are more acidic than alcohols (element effect). 2-Chloro-1-propanethiol is the more acidic thiol because the electronegative chlorine is closer to the site of negative charge in the conjugate-base thiolate anion (polar effect).
- (d)  ${}^-\text{O}-\text{CH}_2\text{CH}_2-\text{OH} < \text{CH}_3\text{CH}_2\text{CH}_2-\text{OH} < \text{CH}_3\text{O}-\text{CH}_2\text{CH}_2-\text{OH}$ . 2-Methoxyethanol is most acidic because of the electron-withdrawing polar effect of the oxygen. The anion is least acidic because the negative charge on the oxygen interacts repulsively with a second negative charge formed on ionization of the O—H group:



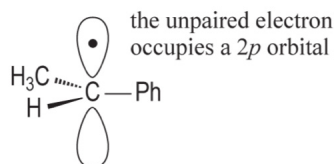
- 8.46 In the presence of concentrated acid, dibutyl ether is protonated. The protonated ether is an ionic compound, and ionic compounds are soluble in water:



- 8.49 The ammonium ion will interact by donating hydrogen bonds to the oxygens of nonactin. (See the solution to Problem 8.23 in the Study Guide and Solutions Manual, which describes the similar interaction of ammonium ion with a crown ether.) It is interesting that both the crown ether and nonactin are selective for binding of the potassium ion, and both also bond the ammonium ion. Evidently, the spatial requirements for both ions is similar. The cavity that fits the potassium ion equally well accommodates a nitrogen and its bound hydrogens.
- 8.50 Hexethyl should be (and is) the more potent sedative, because it is more soluble in membranes, and therefore can readily pass through them. It is more soluble because the longer alkyl chain is more like the interior of a membrane than is the shorter ethyl chain. Furthermore, the long alkyl chain makes hexethyl *less* soluble in water, because large alkyl groups are not effectively solvated by water.
- 8.53 Flick's flailings were fundamentally futile because his ether is also an alcohol. The Grignard reagent was destroyed by the —OH group of the alcohol in a protonolysis reaction:



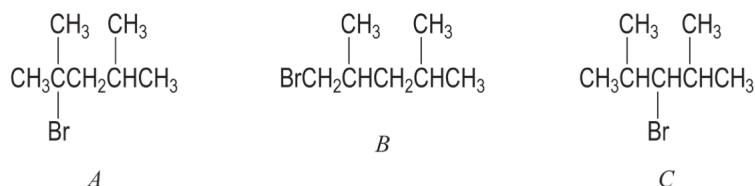
- 8.56 The free radical intermediate in this reaction is  $sp^2$ -hybridized, and is therefore planar and achiral.



a planar and achiral free radical

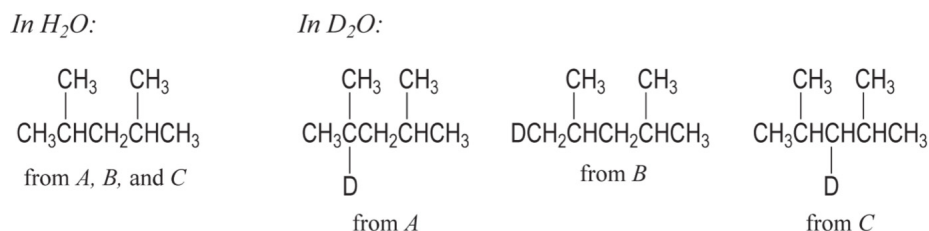
This radical will react with  $\text{Br}_2$  at either the top or bottom lobe of the  $2p$  orbital with equal probability. [See the mechanism in the solution to Problem 8.55(b).] Reaction at the top lobe gives the  $S$  enantiomer; reaction at the bottom lobe gives the  $R$  enantiomer. Because both are formed at the same rates, the product is the racemate, which is not optically active.

- 8.57 The different boiling points indicate that the three alkyl halides are either constitutional isomers or diastereomers. The outcome of the Grignard protonolysis shows that all of the alkyl halides have the same carbon skeleton, that of 2,4-dimethylpentane. The protonolysis in  $\text{D}_2\text{O}$  confirms the fact that the bromines are bound at different places on the carbon skeleton. The only three possibilities for the alkyl halides are

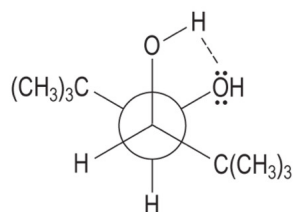


Compound  $B$  is the chiral alkyl halide, and compounds  $A$  and  $C$  are the other two. (The absolute configuration of  $B$  (that is, whether it is  $R$  or  $S$ ) is not determined by the data.)

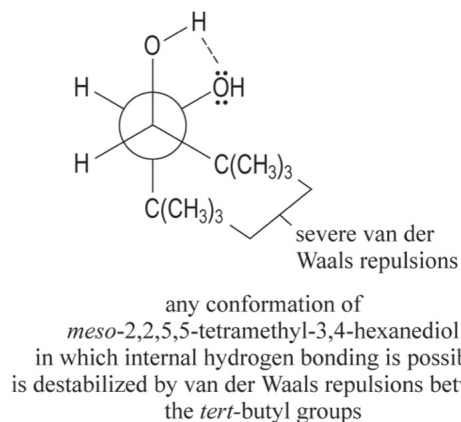
The protonolysis products in  $\text{H}_2\text{O}$  and  $\text{D}_2\text{O}$  are



- 8.59 (b) The solution to part (a) [in the Study Guide and Solutions Manual] shows that intramolecular hydrogen bonding can stabilize conformations that otherwise might be less stable. In this case, intramolecular hydrogen bonding can stabilize the *gauche* conformations of both stereoisomers. Indeed, in either enantiomer of the racemate, such hydrogen bonding can occur in one conformation in which the large *tert*-butyl groups are anti to each other. However, in the meso stereoisomer, the necessity that the hydroxy groups be *gauche* in order for hydrogen bonding to occur also means that the large *tert*-butyl groups must also be *gauche*. The stabilizing effect of intramolecular hydrogen bonding cannot compensate for the magnitude of the resulting van der Waals repulsions between the *tert*-butyl groups.



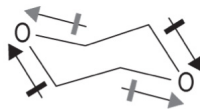
one of the conformations of (3*R*,4*R*)-2,2,5,5-tetramethyl-3,4-hexanediol is stabilized by internal hydrogen bonding, and the *tert*-butyl groups are anti



any conformation of meso-2,2,5,5-tetramethyl-3,4-hexanediol in which internal hydrogen bonding is possible is destabilized by van der Waals repulsions between the *tert*-butyl groups

Convert the Newman projection of the meso stereoisomer to an eclipsed conformation if the meso stereochemistry is not clear.

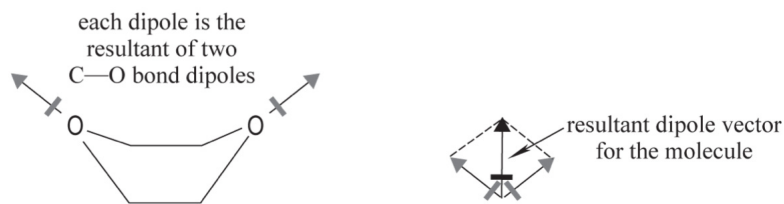
- 8.60 (a) In the chair conformation, for every C—O bond dipole in a given direction, there is another C—O bond dipole of the same magnitude pointing in the opposite direction. Thus, in the following diagram, the gray dipoles cancel each other, and the black dipoles cancel each other.



chair conformation of 1,4-dioxane

Because pairs of dipoles cancel, the overall dipole moment is zero.

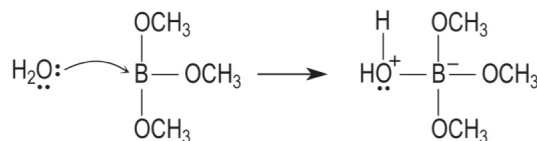
- (b) To the extent that the twist-boat conformation is present, it will contribute a nonzero dipole moment, because the C—O bond dipoles do not cancel in this conformation. (We use the simpler boat conformation to illustrate this idea.)



boat conformation of 1,4-dioxane

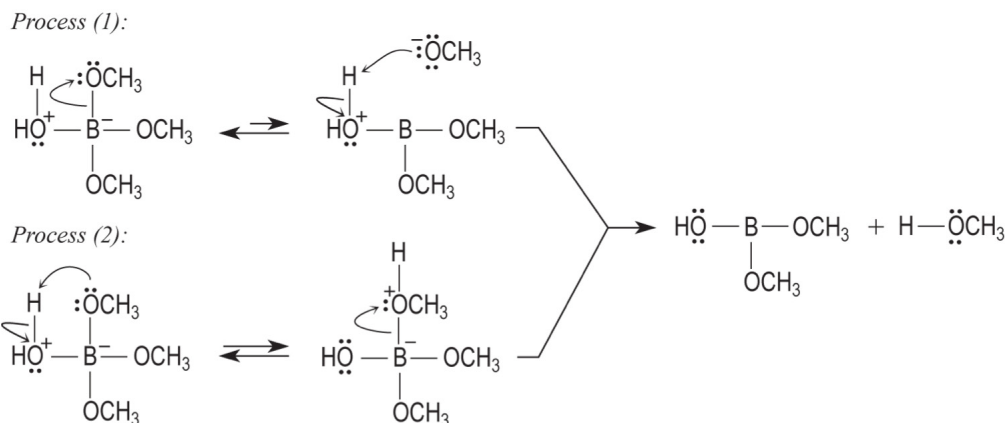
The dipole moment of the twist-boat conformation is actually rather large, but it is present in very small concentration. The dipole moment of any molecule is the weighted average of the dipole moments of individual conformations. In other words, the nonzero dipole moment of 1,4-dioxane results from the presence of a very small amount of a conformation that has a large dipole moment.

- 8.61 (b) The reasoning is much the same as that in part (a). Because the C—O bonds are shorter in the ether *A* than the corresponding C—C bonds in butane *B*, the methyl groups are brought closer together in the gauche conformation of the ether than they are in the gauche conformation of butane. Consequently, van der Waals repulsions in the gauche conformation of the ether are somewhat greater than they are in the gauche conformation of butane. In contrast, the shorter bonds of the ether should have little effect on the energy of the anti conformation, in which the methyl groups are far apart. Hence, the greater energy of the gauche conformation of the ether (relative to the anti conformation) causes less of the gauche conformation to be present at equilibrium. Thus, butane contains more gauche conformation at equilibrium.
- 8.62 (b) This reaction is very much like the one in part (a). The first step is a Lewis acid–base association reaction.



The product then loses a methoxy group. There are two ways that this can happen.





In process (1), the methoxy group dissociates to form a methoxide ion, which then removes a proton from the positively charged oxygen. In process (2), the methoxy oxygen is protonated first. The protonated oxygen then dissociates as methanol. At this stage, either process is a reasonable one. However, protonation makes the leaving oxygen much more electronegative and “willing” to take on an extra electron pair as a leaving group. Moreover, the  $pK_a$  of the protonated oxygen is not very different from that of  $H_3O^+$ . (See Sec. 8.7, text pp. 359ff.) Methoxide,  $^-OCH_3$ , is a strong base, but methanol,  $H-OCH_3$ , is a weak base. As you’ll learn in Chapter 9, *the best leaving groups are relatively weak bases*. Hence, process (2) is the correct one. In the solution to part (a), the analogous protonation does not occur because a neutral F is not basic, and because fluoride ion is a weak enough base to dissociate without prior protonation.

These reactions are repeated twice more to give the final product. Finish this mechanism on your own.

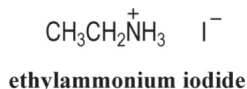


# Chapter 9

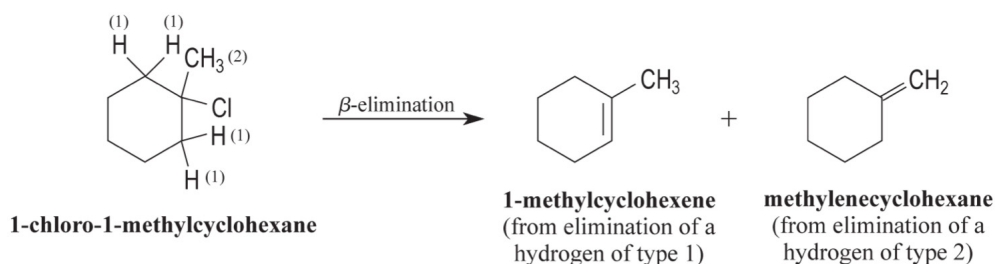
## The Chemistry of Alkyl Halides

### Solutions to In-Text Problems

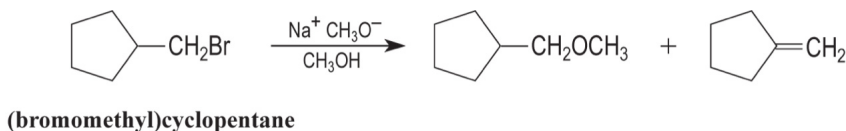
- 9.1 (b) The product is ethylammonium iodide.



- 9.2 (b) As in part (a), because there are two types of  $\beta$ -hydrogens, two alkenes can be formed:



- 9.3 (b) Methyl iodide,  $\text{H}_3\text{C}-\text{I}$ , can form only a substitution product, dimethyl ether,  $\text{H}_3\text{C}-\text{O}-\text{CH}_3$ .  
(d) (Bromomethyl)cyclopentane can form one substitution product and one elimination product.



- 9.4 (b) Because iodide ion is a weaker base than chloride ion, the equilibrium lies to the left.  
(d) Because methoxide ion is a much stronger base than chloride ion, the equilibrium lies to the right.
- 9.5 (b) The reaction is first order overall, and first order in alkyl halide. The rate constant has the dimensions of  $\text{sec}^{-1}$ .
- 9.6 (b) We transform Eq. 9.22c to get the difference between the standard free energies of activation.

$$\Delta G_A^{\ddagger} - \Delta G_B^{\ddagger} = 2.30RT \log \left( \frac{k_B}{k_A} \right) = (5.71) \log(450) = 15.2 \text{ kJ mol}^{-1}$$

Therefore, reaction A has the higher  $\Delta G^{\ddagger}$  by  $15.2 \text{ kJ mol}^{-1}$ .

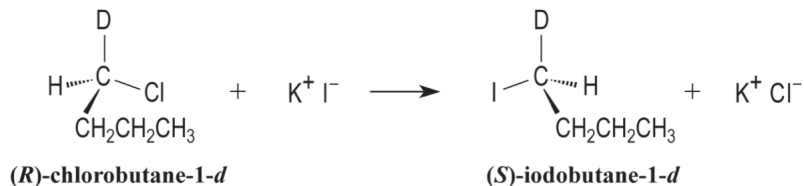
- 9.9 Because the  $\text{S}_{\text{N}}2$  mechanism involves a molecule of alkyl halide and a molecule of nucleophile in a bimolecular reaction, the expected rate law is second order, first order in alkyl halide and first order in cyanide:

$$\text{rate} = k[\text{C}_2\text{H}_5\text{Br}][\text{CN}^-]$$

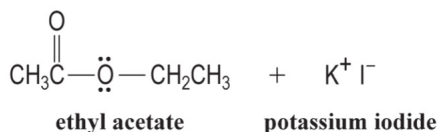
- 9.11 There is more than enough sodium cyanide to react with both the acid HBr and the alkyl halide. Therefore, the products are sodium bromide (NaBr, 0.2 M, half from the reaction with HBr and half from the reaction with ethyl bromide), "ethyl cyanide" (propionitrile,  $\text{CH}_3\text{CH}_2\text{CN}$ , 0.1 M), and unreacted sodium cyanide (0.8 M). However, 0.1

$M$  NaBr is formed instantaneously, and the rest of the NaBr as well as the nitrile are formed much more slowly, because Brønsted acids reacts much more rapidly with bases than alkyl halides.

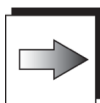
- 9.12 The reaction is an  $S_N2$  reaction with inversion of configuration. Because the relative priorities of the groups attached to the asymmetric carbon are not changed, the product has the  $S$  configuration.



- 9.14 (a) The products of the  $S_N2$  reaction between potassium acetate and ethyl iodide:

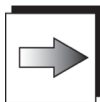


- (b) Potassium acetate is a better nucleophile in acetone because ethanol is a protic solvent and reduces the nucleophilicity of potassium acetate by hydrogen-bond donation. Consequently, potassium acetate in acetone reacts more rapidly with ethyl iodide than a solution of the same nucleophile in ethanol.
- 9.17 (a) The stepwise process involves formation of a methyl cation, which is very unstable. The instability of this cation, by Hammond's postulate, raises the energy of the transition state and retards the reaction. The concerted mechanism avoids formation of this high-energy intermediate.
- (b) A tertiary alkyl halide such as *tert*-butyl bromide,  $(\text{CH}_3)_3\text{C}-\text{Br}$ , can undergo the stepwise mechanism, because ionization gives a relatively stable tertiary carbocation—in this case,  $(\text{CH}_3)_3\text{C}^+$ . This lowers the energy of the transition state (by Hammond's postulate). Section 9.6 describes this mechanism.
- 9.19 (b) The hydration rate of the deuterium-substituted styrene should differ very little, if at all, from that of styrene itself, because the deuteriums are not transferred in the rate-limiting step.



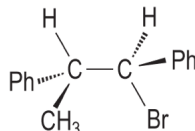
A small effect of isotopic substitution occurs in this case because of the differential effect of deuterium and hydrogen on the rehybridization of carbon in the transition state. (The carbon bearing the deuteriums rehybridizes from  $sp^2$  to  $sp^3$  in the rate-limiting step.) However, this effect on rate amounts to only a few percent. Effects of this sort are called *secondary deuterium isotope effects*.

- 9.20 (b) Reasoning identical to that used in part (a) shows that the alkene formed has the  $E$  configuration. (We leave it to you to draw the appropriate structures.)

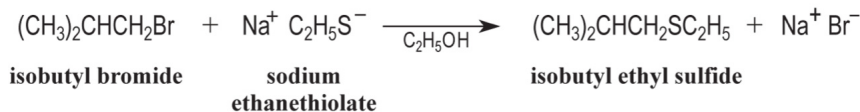


In a stereospecific reaction with a given stereochemistry—*anti*-elimination, in this case—diastereomeric starting materials must give diastereomeric products.

- 9.21 In a stereospecific reaction with a given stereochemistry—*anti*-elimination, in this case—a diastereomeric product requires a diastereomeric starting material (either enantiomer). The easiest path to the answer is to convert the starting material in Eq. 9.40a into its diastereomer by the interchange of any two groups at one of the carbons. Either the following compound or its enantiomer would give the product of  $E$  configuration.

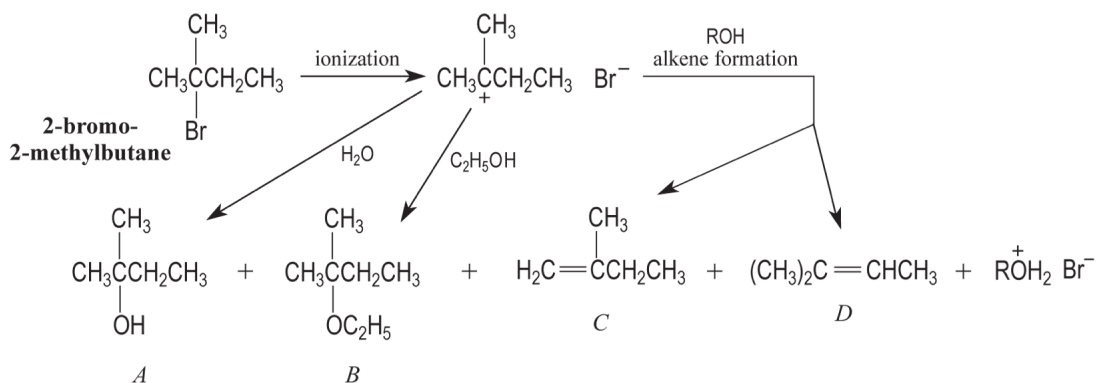


- 9.22 (b) In this case, the nucleophile is the conjugate base of ethanethiol, sodium ethanethiolate. Although a polar aprotic solvent could be used, ethanol would probably be the most convenient solvent (for solubility reasons). Because the nucleophile is from the third period, the reaction would occur at a convenient rate in a protic solvent; hence, experimental convenience determines the choice of solvent. The nucleophile would be easily formed from ethanethiol with one equivalent of sodium ethoxide, as shown in Eq. 8.13, text p. 357.

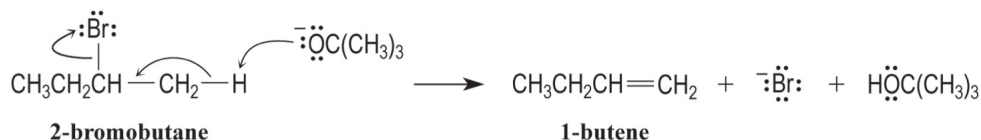


- 9.24 Because  $\alpha$ -substitution in the base promotes a greater proportion of elimination, the order is  $C > A > B$ .

- 9.25 (b) This tertiary alkyl halide will undergo the  $\text{S}_{\text{N}}1$ -E1 process to give substitution products that result from the Lewis acid-base association reactions of both water and ethanol, respectively, with the carbocation intermediate; and this carbocation can lose a  $\beta$ -proton to solvent (water or ethanol, abbreviated ROH below) to form two alkenes. Of the two alkenes, *D* will be formed in greater amount because it has a greater number of alkyl substituents at the double bond.

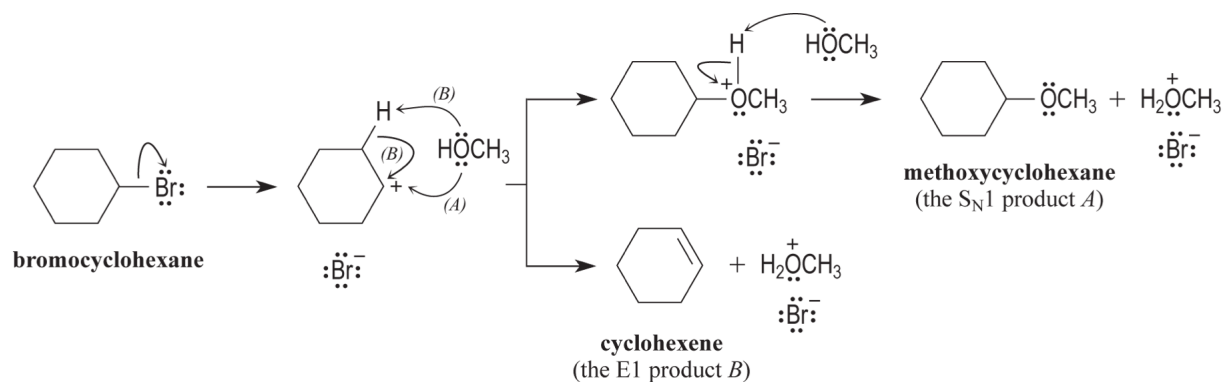


- 9.28 (b) A less stable carbocation, by the same reasoning as in part (a), should have a shorter lifetime; a greater fraction will not last past the ion-pair stage, which reacts with the solvent by inversion.
- 9.29 (b) 2-Bromobutane is a secondary alkyl halide, and potassium *tert*-butoxide is a strong, highly branched base. Entry 7 of Table 9.7 covers this case. Thus, the E2 reaction is the major process that occurs. Two possible alkenes, 1-butene and 2-butene, can form. Either or both can be considered as correct answers. A significant amount of 1-butene is formed because the large base molecule reacts at the least sterically hindered hydrogen.

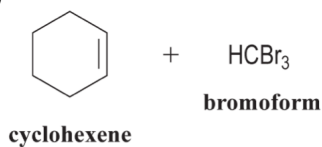


We leave it to you to show the formation of the 2-butenes.

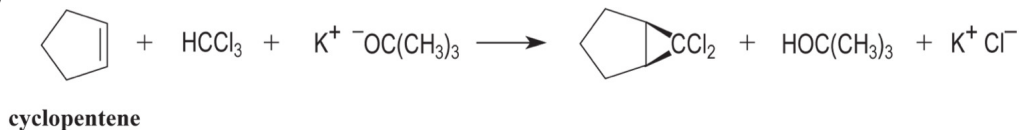
- (d) Bromocyclohexane is a secondary alkyl halide; methanol is a polar, protic solvent; and there is no strong base present. Entry 9 of Table 9.7 covers this situation; both  $\text{S}_{\text{N}}1$  product *A* and E1 product *B* are formed.



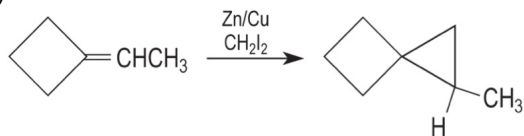
9.30 (a)



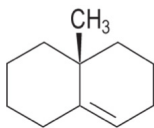
9.31 (a)



9.32 (b)

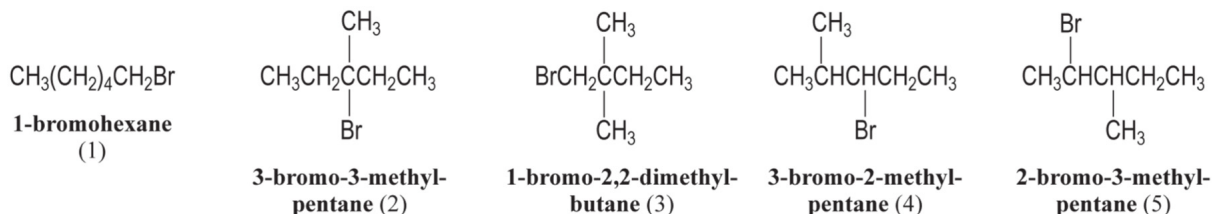


9.33 (b) Cyclopropane formation occurs at the face of the ring opposite to the methyl group for steric reasons.



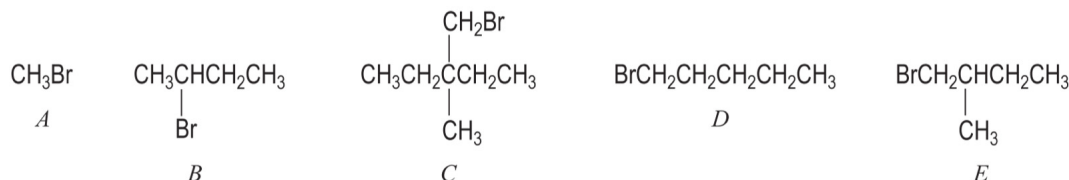
### Solutions to Additional Problems

9.34 The first step in any problem that requires structures is to draw the structures:



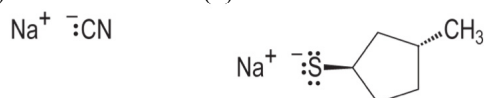
- (b) Compound (5) can exist as diastereomers because it has two asymmetric carbons.  
 (d) Compound (3) is least reactive to sodium methoxide in methanol because it cannot undergo a  $\beta$ -elimination—it has no  $\beta$ -hydrogens—and the three  $\beta$ -substituents make it virtually unreactive in the  $\text{S}_{\text{N}}2$  reaction, much like neopentyl bromide.  
 (f) Compound (2) will give an E2 but no  $\text{S}_{\text{N}}2$  reaction with sodium methoxide in methanol.  
 (h) Compound (2) will give the fastest  $\text{S}_{\text{N}}1$  reaction because it is the only tertiary alkyl halide.

9.38 The first thing to do is to draw out the structures.

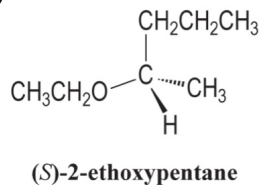


The order of increasing  $\text{S}_{\text{N}}2$  reaction rates is  $C < B < E < D < A$ . Alkyl halides with three  $\beta$ -substituents (*C*) are virtually unreactive in  $\text{S}_{\text{N}}2$  reactions. Secondary alkyl halides with no  $\beta$ -substituents (*B*) react more slowly than primary alkyl halides with two  $\beta$ -substituents (*E*), and the latter react more slowly than unbranched primary alkyl halides (*D*). Methyl halides (*A*) react most rapidly.

9.39 (b) (d)



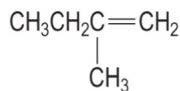
9.40 (a)



9.41 (b)

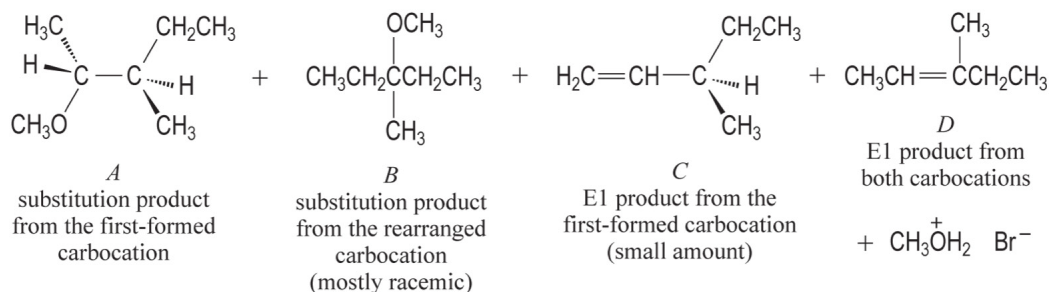


(d)



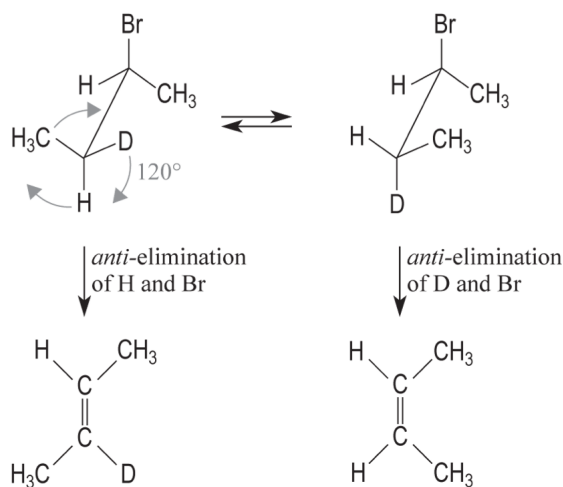
9.43 Allow the appropriate alkoxide,  $(\text{CH}_3)_3\text{CCH}_2\text{O}^- \text{Na}^+$ , to react with ethyl iodide,  $\text{CH}_3\text{CH}_2\text{I}$ . Using sodium ethoxide with neopentyl bromide,  $(\text{CH}_3)_3\text{CCH}_2\text{Br}$ , won't work; why?

9.45 (b) The reaction conditions favor a solvolysis reaction, which occurs by an  $\text{S}_{\text{N}}1\text{-E}1$  mechanism accompanied by rearrangement.

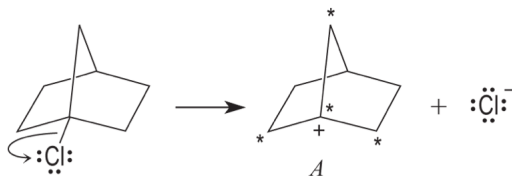


The  $\text{S}_{\text{N}}1$  product *A*, derived from the Lewis acid–base association reaction of solvent with the first-formed carbocation, should have largely inverted configuration at carbon-2, because the carbocation will be a backside-solvated ion pair; this carbocation will react faster with the solvent molecule than the bromide ion is replaced by a second solvent molecule. (See Fig. 9.13, text p. 419.) The stereochemistry of carbon-3 is unaffected. The substitution product *B*, derived from the rearranged tertiary carbocation, should be mostly racemic, although the exact stereochemical outcome is difficult to predict exactly. Compounds *C* and *D* are E1 products. The stereochemistry at carbon-3 of alkene *C* is the same as in the starting alkyl halide. Alkene *D* should be the major alkene product because it has the larger number of substituents on the double bond.

- 9.46 (b) Proceed the same way as in part (a). Because the starting materials are diastereomers, the products must also be diastereomers if the elimination is anti.



- 9.48 If this compound were to undergo solvolysis, it would have to form carbocation *A*:

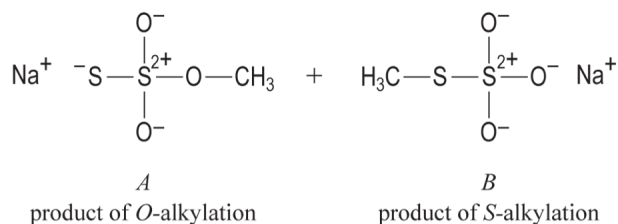


As a model will verify, the four asterisked carbons cannot become coplanar because of the constraints of the bicyclic ring system. Yet  $\text{sp}^2$  hybridization requires trigonal-planar geometry. Remember: *hybridization and geometry are connected*. If a molecule can't achieve the geometry for a given hybridization, then that hybridization will not occur. Because  $\text{sp}^2$  hybridization is the lowest-energy hybridization for a carbocation, the inability to achieve this hybridization raises the energy of the carbocation.

But that's not all. Solvation of the carbocation can only occur from one side, because the back side of the electron-deficient carbon is blocked by part of the ring system. The absence of effective solvation, then, also raises the energy of this carbocation. Any solvolysis reaction involving such an unstable carbocation is slow.



- 9.49 (b) The scheme in part (a) shows that complexation of the cation by the crown ether is essential for the reaction to occur, because this is the only way to obtain the dissolved anion. Because [18]-crown-6 does not bind the smaller lithium cation—it is selective for the larger potassium cation—lithium fluoride is not solubilized by the crown ether, and is therefore unreactive whether the crown ether is present or not.
- 9.52 (a) The thiosulfate dianion contains two types of nucleophilic atoms: the anionic oxygen and the anionic sulfur. Hence, alkylation could occur at the oxygen or the sulfur:

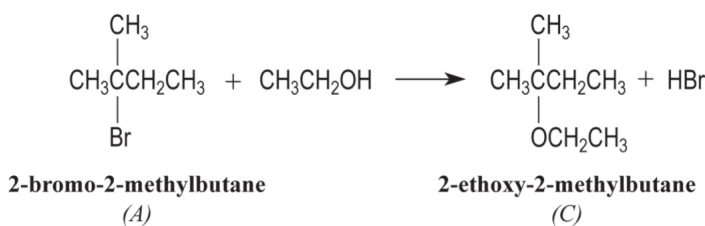


- (b) In a hydrogen-bonding solvent such as methanol, the more weakly basic atom is the better nucleophile. (The principle is the same as in the solution to Problem 9.51.) Hence, product *B* is the major one observed. (What solvent change could you make to obtain more of product *A*?)
- 9.54 The reaction between methyl iodide and sodium ethoxide is an  $\text{S}_{\text{N}}2$  process that has the following rate law:

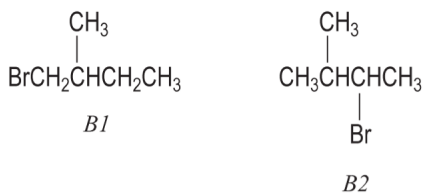
$$\text{rate} = k[\text{CH}_3\text{I}][\text{CH}_3\text{CH}_2\text{O}^-]$$

This means that the rate of the reaction depends on the concentration of the nucleophile. In the first case, the nucleophile concentration changes during the reaction from 0.1 *M* to 0 *M*; in the second case, the nucleophile concentration changes from 0.5 *M* to 0.4 *M*. In the second case, the reaction is faster because the concentration of the nucleophile is higher at all times during the reaction. However, in either case, there is sufficient nucleophile present to react completely with the alkyl halide. If we wait long enough, the yield of the reaction will be the same in either case.

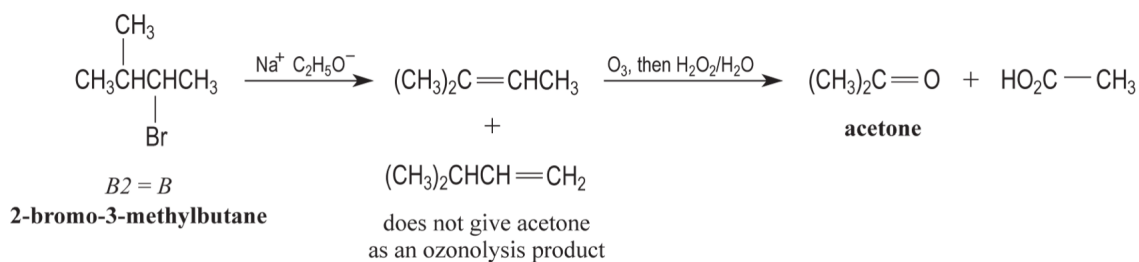
- 9.59 The fact that protonolysis reactions of the corresponding Grignard reagents give the same hydrocarbon indicates that the two compounds have the same carbon skeleton. The conditions of ethanol and no added base are  $\text{S}_{\text{N}}1$  conditions. Since compound *A* reacts rapidly to give a solution containing bromide ion, it must be an alkyl halide that readily undergoes an  $\text{S}_{\text{N}}1$  reaction, and therefore it is probably a tertiary alkyl bromide. Because the two alkyl halides give the same ether, the product from compound *B* must be formed in a rearrangement. The only tertiary alkyl halide with the formula  $\text{C}_5\text{H}_{11}\text{Br}$  is 2-bromo-2-methylbutane, and this is therefore compound *A*:



Two possible alkyl halides with the same carbon skeleton as *A* could rearrange in respective  $\text{S}_{\text{N}}1$  reactions to give the same carbocation, and hence the same ether product, as *A*; these are labeled *B1* and *B2* below. (An  $\text{S}_{\text{N}}1$  reaction of *B1* would be very slow, if it occurred at all.)

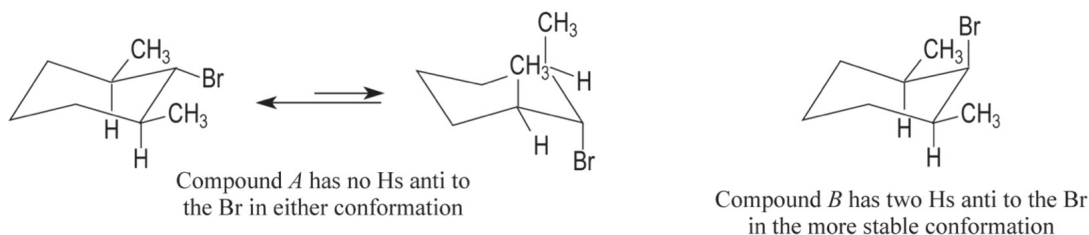


However, only *B2* can react in an E2 reaction with sodium ethoxide to give an alkene that furnishes acetone as one of its ozonolysis products:



Consequently, compound *B2* is compound *B*, 2-bromo-3-methylbutane.

- 9.62 Compound *A* has no conformation in which the  $\beta$ -hydrogens and the bromine are anti, whereas in compound *B*, the  $\beta$ -hydrogens are anti to the bromine in the more stable conformation (shown). For this reason, compound *B* should more readily undergo the E2 reaction.

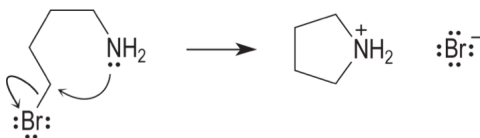


- 9.68 The reaction of butylamine with 1-bromobutane is a typical  $\text{S}_{\text{N}}2$  reaction. (Bu— = the butyl group =  $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2$ ):

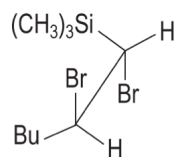


This mechanism is consistent with the second-order rate law, because the rate law requires one molecule of amine and one molecule of alkyl halide in the transition state.

The second reaction is also a nucleophilic substitution reaction, but, because it is intramolecular (that is, the nucleophile and carbon at which it reacts are part of the same molecule), the reaction is first-order.

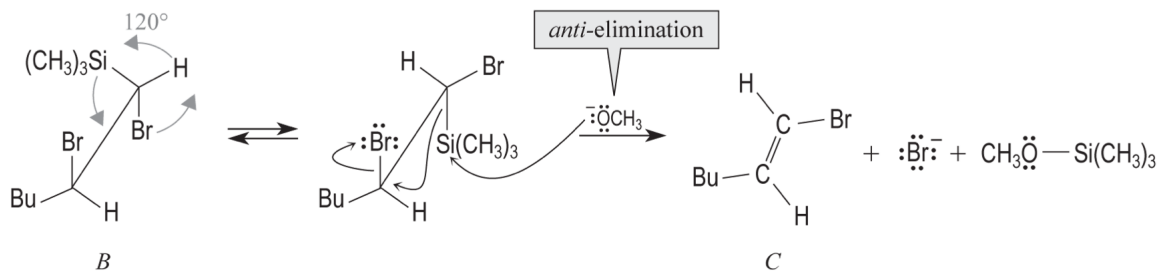


- 9.70 (a) Bromine addition to alkenes is anti; consequently, the stereochemistry of compound *B* is as follows:



(racemate)

- (b) Draw the structure of compound *B* in a conformation in which the butyl (Bu) group and the Br that remains after the elimination are on opposite sides of the molecule, because this is the way they are in the alkene product. This shows that the trimethylsilyl group and the bromine are anti; consequently, the elimination shown is an *anti*-elimination.



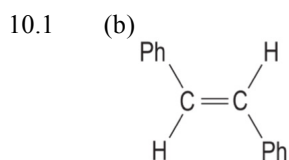
- (c) Diastereomeric starting materials must give diastereomeric products if the stereochemistry of the two reactions remains the same. The *E* stereoisomer of compound *A* therefore would give the diastereomer of compound *B* (as the racemate), and the subsequent elimination would give the *Z* stereoisomer of compound *C*. This can be shown by the analysis used in parts (a) and (b) with the positions of the trimethylsilyl group and the hydrogen interchanged.



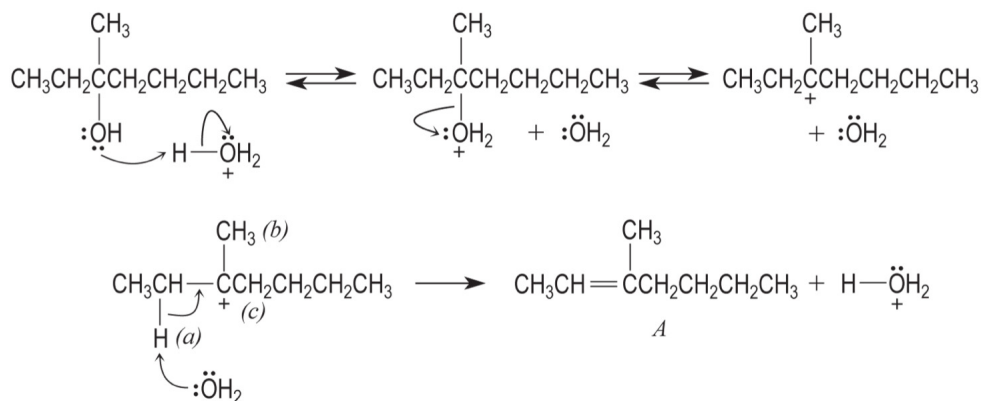
# Chapter 10

## The Chemistry of Alcohols and Thiols

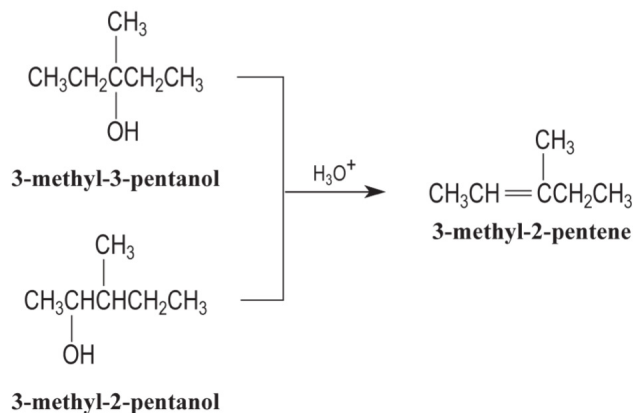
### Solutions to In-Text Problems



- 10.2 The OH group of the alcohol is protonated in a Brønsted acid–base reaction to form the conjugate acid of the alcohol. This loses water to form a carbocation in a Lewis acid–base dissociation reaction. Finally, in a Brønsted acid–base reaction, water acts as a Brønsted base to remove a  $\beta$ -proton from the carbocation, which acts as a Brønsted acid, to give the alkene. The formation of product *A* by removal of proton (*a*) is shown here; the formation of products *B* and *C* occurs in an analogous manner by removal of  $\beta$ -protons (*b*) and (*c*), respectively.

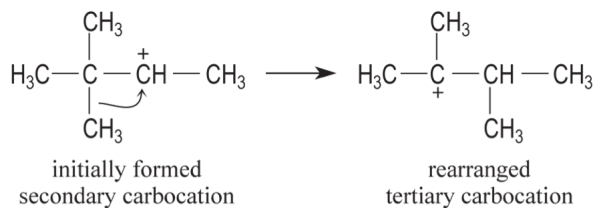


- 10.5 (b) Both 3-methyl-3-pentanol and 3-methyl-2-pentanol should give 3-methyl-2-pentene as the major product. The tertiary alcohol 3-methyl-3-pentanol should dehydrate more rapidly.

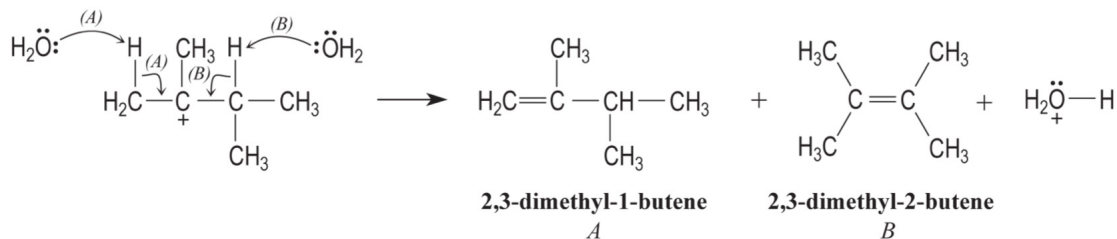


- 10.6 (a) Protonation of the OH group and loss of water as shown in several of the previous solutions, as well as in Eqs. 10.3a–b on p. 437 of the text, gives a secondary carbocation. As the text discussion of Eq. 10.6 suggests,

the mechanism involves a rearrangement of the initially formed secondary carbocation to a more stable tertiary carbocation.

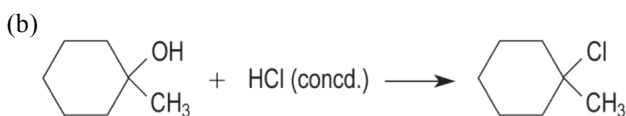


Loss of the two possible  $\beta$ -protons gives the two alkene products.



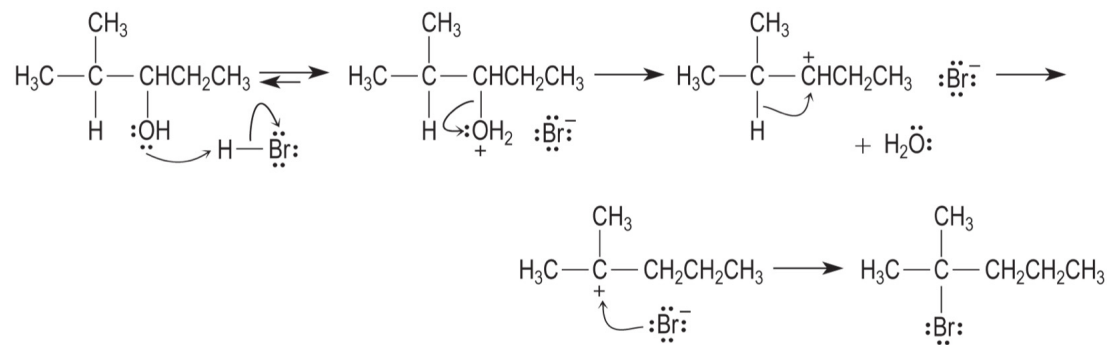
- (b) Rearrangement occurs because a more strained secondary carbocation is converted into a less strained, and therefore more stable, secondary carbocation.

10.8



10.9

This reaction involves a carbocation rearrangement. We use HBr as the acid, although, because water is generated as a product,  $\text{H}_3\text{O}^+$  could also be used.

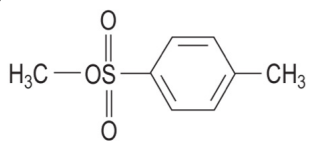


The product in part (c) results from a carbocation rearrangement.

10.10

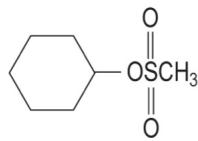
- (b) The product is  $\text{I}-\text{CH}_2\text{CH}_2\text{CH}_2-\text{I}$ .  
 (d) The compound, neopentyl alcohol, is a primary alkyl alcohol and cannot react by the  $\text{S}_{\text{N}}1$  mechanism; and it has too many  $\beta$ -substituents to react by the  $\text{S}_{\text{N}}2$  mechanism. Consequently, there is no reaction.

10.11 (b)



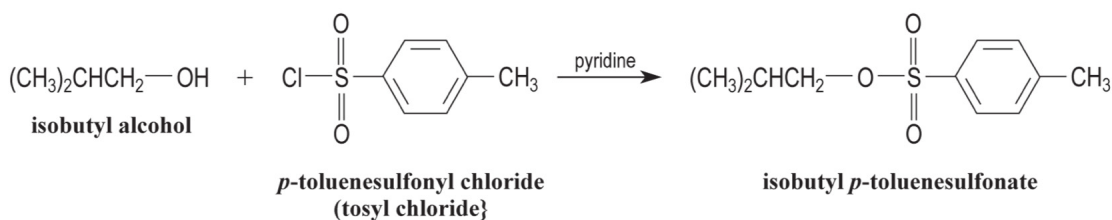
**methyl *p*-toluenesulfonate**  
(methyl tosylate)

(d)

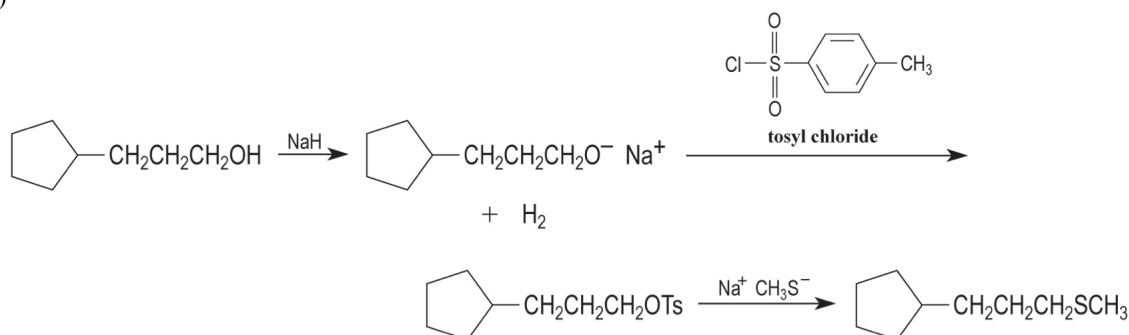


**cyclohexyl mesylate**  
(cyclohexyl methanesulfonate)

10.12 (b)

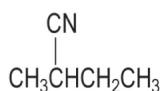


10.13 (b)

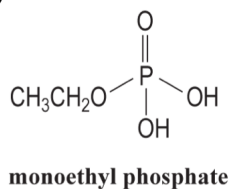


Although a polar aprotic solvent would accelerate the last step, it would probably work in an alcohol solvent. The nucleophile,  $\text{CH}_3\text{S}^-$ , can be generated by allowing the thiol  $\text{CH}_3\text{—SH}$  to react with one equivalent of sodium ethoxide in ethanol.

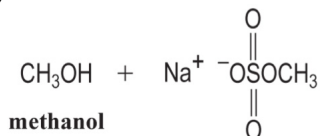
10.14 (a) Cyanide ion displaces the tosylate ester formed in the first step.



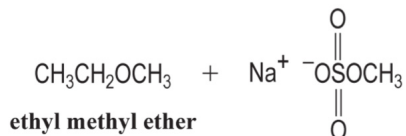
10.15 (b)



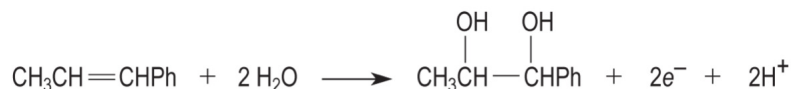
10.16 (b)



(c)



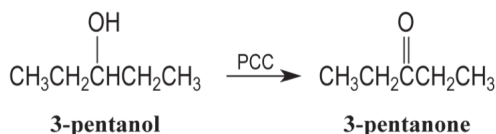
- 10.18 (b) Eq. 10.26 of the text shows that the nucleophilic reaction of the bromide ion on the reactive intermediate occurs by a concerted ( $S_N2$ ) substitution reaction. Therefore, the reaction should occur with inversion of stereochemistry, and the product would then be (*S*)-2-bromopentane. The  $S_N2$  reaction occurs at an acceptable rate on a secondary carbon in the absence of  $\beta$  substituents. In addition, the reaction is fast because the leaving group is a *very* weak base. However, it is possible that some  $S_N1$  mechanism could occur; this is hard to predict. To the extent that the  $S_N1$  reaction occurs, some racemization might also take place.
- 10.19 (b) The simplest method for effecting the conversion shown is to treat the alcohol with thionyl chloride and pyridine. Conversion of the alcohol to a sulfonate ester and treatment of the ester with sodium chloride in a polar aprotic solvent would also work, but involves more steps.
- (d) Because a carbocation intermediate and hence rearrangements are a distinct possibility if this alcohol is exposed to acidic reagents such as HBr, the sulfonate ester method should be used. Thus, treat the alcohol with tosyl chloride and pyridine, and treat the resulting tosylate with sodium bromide in a polar aprotic solvent. This type of solvent suppresses carbocation formation. Also,  $PBr_3$  often gives satisfactory results with unbranched secondary alcohols.
- 10.21 (b) The conversion of toluene into benzoic acid is a six-electron oxidation.
- (c) The oxidation of a secondary alcohol to a ketone is a two-electron oxidation.
- (e) The dihydroxylation of an alkene by  $KMnO_4$  is a two-electron oxidation.
- (g) The addition of HBr to an alkene is neither an oxidation nor a reduction. (One carbon of the alkene is formally oxidized and the other is reduced by the same amount.)
- 10.22 (e) The half-reaction of Problem 10.21, part (e):



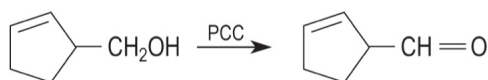
- 10.23 (b) This is an oxidation–reduction reaction; the organic compound is reduced, and the  $^-AlH_4$  is oxidized.
- (c) This is an oxidation–reduction reaction; the alkene is oxidized, and the  $Br_2$  is reduced.
- 10.25 The oxidation state of *each* Cr in  $Cr_2O_7^{2-}$  is +6, and it changes to +3 in  $Cr^{3+}$ . Therefore, six electrons are gained per mole of dichromate. Two electrons are lost in the oxidation of ethanol to acetaldehyde. To reconcile electrons lost and electrons gained, three molecules of ethanol are oxidized by one of dichromate; or, it takes one-third mole of dichromate to oxidize one mole of ethanol. We leave it to you to prove this point (if necessary) by balancing the complete reaction.
- 10.26 (b) On the assumption that sufficient PCC has been added, both primary alcohols are oxidized:



- 10.27 (b) This compound (3-pentanone) can be prepared by a PCC oxidation of the corresponding alcohol, 3-pentanol. (Aqueous dichromate could also be used.)



- (d) This aldehyde can be prepared by a PCC oxidation of the corresponding alcohol.



- 10.29 (b) Hydrogens *a* and *b* are constitutionally equivalent and enantiotopic. (The analysis of this case is essentially identical to the analysis of the  $\alpha$ -hydrogens of ethanol; see Eq. 10.49, text p. 466.)

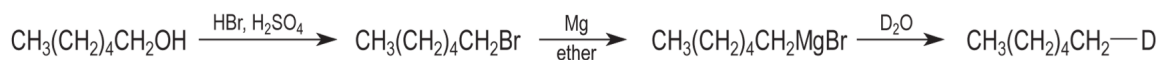


- (e) Replacing  $H^a$  and  $H^b$  in turn with a “circled H” shows that these hydrogens are constitutionally equivalent and diastereotopic, as are  $H^c$  and  $H^d$ .  $H^a$  and  $H^c$  are constitutionally equivalent and enantiotopic, as are  $H^b$  and  $H^d$ . Finally,  $H^a$  and  $H^d$  are constitutionally equivalent and Diastereotopic, as are  $H^b$  and  $H^c$ .

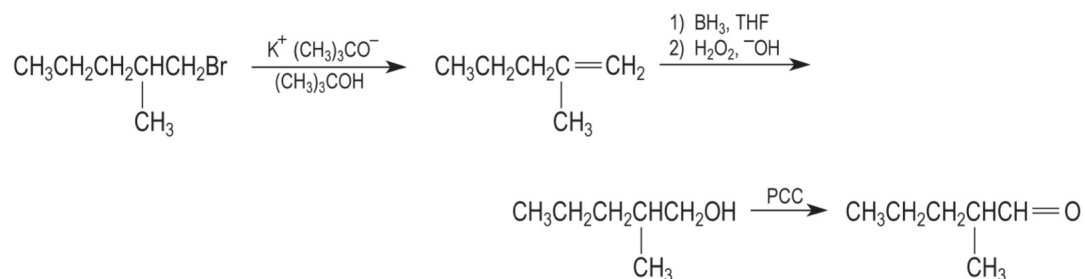
10.30 (b) Because deuterium is delivered, the  $\alpha$ -carbon of the resulting ethanol bears two deuteriums—that is, the product is  $\text{CH}_3\text{CD}_2\text{OH}$ —and it therefore has no asymmetric carbon; hence, the molecule is achiral.

10.31 (b) This is a 2-electron oxidation, because a hydrogen (which contributes  $-1$  to the oxidation number of sulfur) is replaced by an OH (which contributes  $+1$ ).

10.33 (b) The deuterium-containing alkane can be prepared by protonolysis of a Grignard reagent in  $\text{D}_2\text{O}$ ; the Grignard reagent can be prepared from an alkyl halide; and the alkyl halide can be prepared from an alcohol.



- (d) The aldehyde can be prepared by oxidation of a primary alcohol; the required primary alcohol can be prepared by hydroboration–oxidation of an alkene; and the required alkene can be prepared by an E2 reaction of a primary alkyl halide using a branched base.



10.34 (b) The final target is to enter college. The step prior to this is to pay your tuition. The step prior to this is to obtain the money for the tuition. The steps prior to this might be ...

1. Ask your parents.
2. Get a loan.
3. Get a temporary job.
4. Win the lottery.

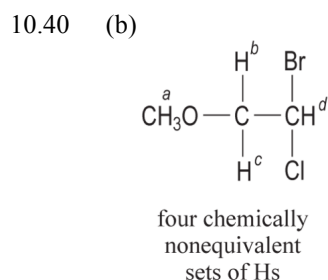
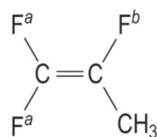
Each of these possibilities then suggests courses of action. For example, possibility 2 requires you to make an appointment at the bank. Possibility 3 requires you to buy a newspaper or to look online at classified advertising ... and so on.

## Solutions to Additional Problems

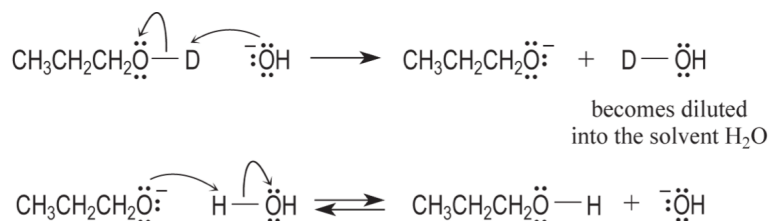
- 10.36 (a)  $(\text{CH}_3)_3\text{CCl}$  (b) no reaction (c)  $(\text{CH}_3)_2\text{C}=\text{CH}_2$  (d) no reaction (e)  $(\text{CH}_3)_3\text{CO}^- \text{K}^+$   
+  $\text{H}_2$
- (f)  $(\text{CH}_3)_3\text{COMs} + \text{pyridinium}^+ \text{Cl}^-$  (g)  $(\text{CH}_3)_2\text{C}=\text{CH}_2 + \text{Na}^+ \text{OMs}^-$  (h)  $(\text{CH}_3)_2\text{C}=\text{CH}_2 + \text{K}^+ \text{Cl}^-$   
+  $(\text{CH}_3)_3\text{COH}$



- 10.39 (b) Fluorines *a* are constitutionally equivalent and diastereotopic; fluorines *a* are constitutionally nonequivalent to fluorine *b*.

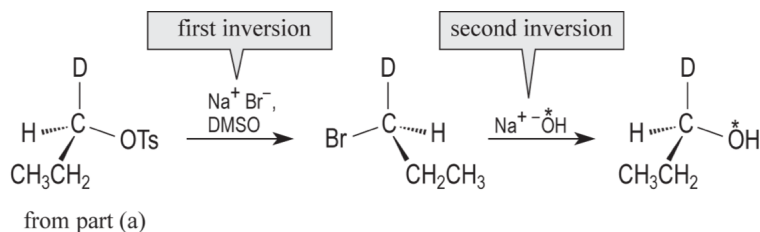


- 10.42 (a) This exchange occurs essentially through a series of Brønsted acid–base reactions. As shown below, once the deuterium is incorporated into the solvent, it is significantly diluted, so that its probability of reaction with the alkoxide is very small. In addition, such a reaction is retarded by a significant primary deuterium isotope effect and competes less effectively with the corresponding reaction of water.

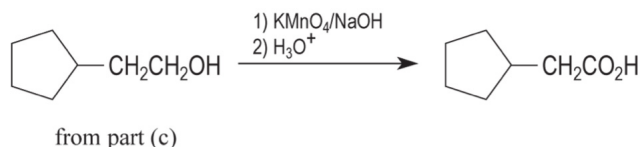


- (b) To prepare  $\text{CH}_3\text{CH}_2\text{CH}_2\text{—OD}$  from  $\text{CH}_3\text{CH}_2\text{CH}_2\text{—OH}$ , use the same reaction with  $\text{D}_2\text{O}/\text{NaOD}$  as the solvent.
- 10.43 (b) This reaction is a two-electron reduction.  
(d) This reaction is a two-electron oxidation.

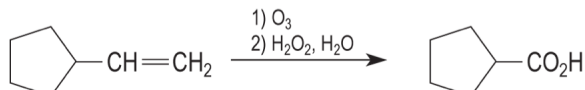
- 10.44 (b) In this case, convert the alcohol into a bromide using a method that involves an inversion of configuration. (Either  $\text{PBr}_3$  or the two-step alcohol  $\rightarrow$  tosylate  $\rightarrow$  alkyl bromide sequence shown below will work.) Then, in a second inversion step, displace the bromide with  $^{\text{O}18}\text{H}^-$  to provide the alcohol with the desired configuration.



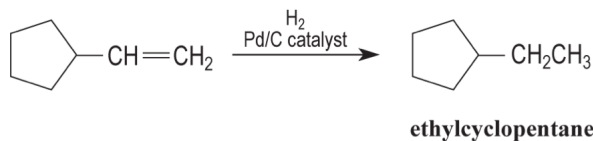
- 10.45 (b)



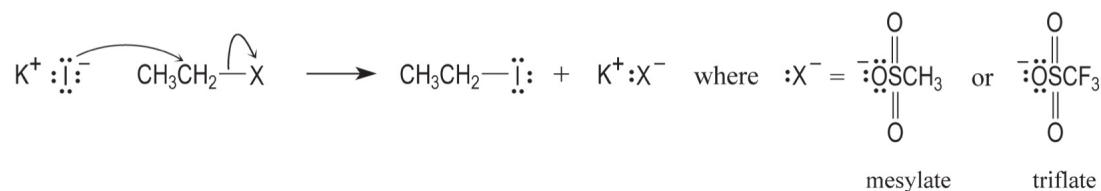
- (d) In this part, we have to “throw away” a carbon; ozonolysis comes to mind:



- (e)



- 10.46 (a) The sulfonate ester serves as a leaving group in either case:

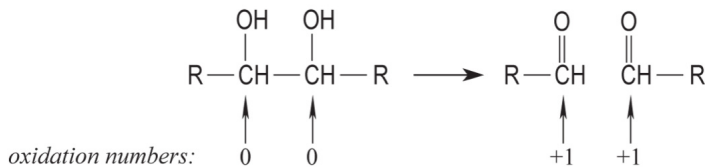


- (b) The triflate anion is a weaker base than the mesylate anion because the *polar effect* of the fluorines stabilizes the negative charge in the triflate anion and thereby lowers the  $\text{p}K_{\text{a}}$  of the conjugate sulfonic acid. (See Sec. 3.6C of the text.)
- (c) The principle to apply is that the better leaving group is the weaker base. This is true because the leaving group is accepting a negative charge and breaking a covalent bond in both the Brønsted acid–base reaction with a base and an electron-pair displacement ( $\text{S}_{\text{N}}2$ ) reaction with a nucleophile. The polar effect of the fluorines should operate in the same way on both processes, because the processes are so similar.

- 10.48 The oxidation of a secondary alcohol to a ketone is a 2-electron oxidation. [See the solution to Problem 10.21(c).] In the process,  $\text{CrO}_3$ , a form of  $\text{Cr(VI)}$ , is converted into  $\text{Cr}^{3+}$ , a form of  $\text{Cr(III)}$ ; hence the chromium half-reaction is a 3-electron reduction. Therefore,  $2/3$  mole of  $\text{CrO}_3$  is required to oxidize 1 mole of the alcohol.

The molecular mass of the alcohol is 116; therefore,  $10.0 \text{ g} = 0.0862 \text{ mole}$ . Consequently,  $(0.667)(0.0862) = 0.0575 \text{ mole}$  of  $\text{CrO}_3$  is required for the oxidation. The molecular mass of  $\text{CrO}_3 = 100$ ; therefore,  $5.75 \text{ g}$  of  $\text{CrO}_3$  is required for the oxidation.

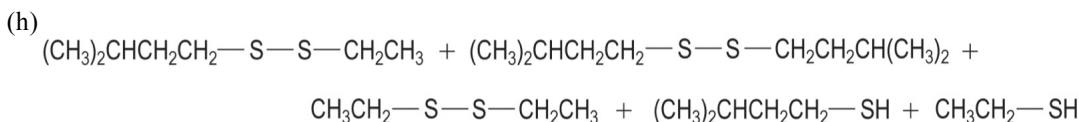
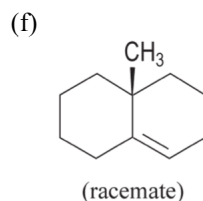
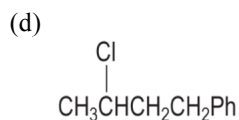
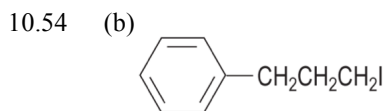
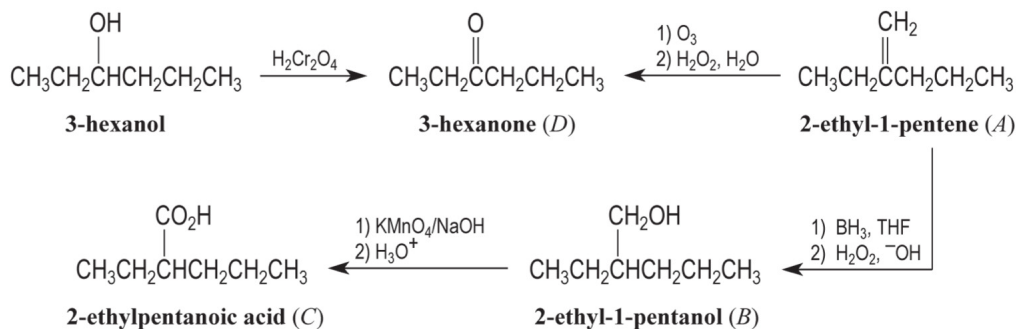
- 10.50 (a) The glycol is oxidized. This follows from the fact that a bond to carbon is replaced by a bond to oxygen at each carbon of the glycol. The other participant in the reaction, periodate ( $\text{IO}_4^-$ ) must therefore be reduced. Indeed, the ionic product iodate ( $\text{IO}_3^-$ ) contains one less oxygen bound to the iodine.
- (b) The number of electrons involved in the oxidation half-reaction is determined from the oxidation numbers of the carbons that change:



The number of electrons lost is  $[(+1) + (+1)] - [0 + 0] = +2$ . (This result could also be determined from a balanced half-reaction.)

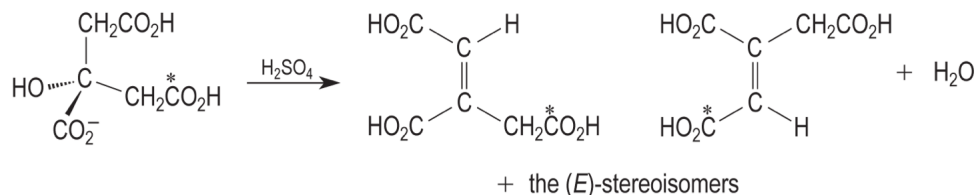
The iodine can be assigned an oxidation number of +7 in periodate and +5 in iodate. How do we know this? Assign +2 to every oxygen because oxygen is divalent and presumably has two bonds to the iodine. (See the top of text p. 456 for a similar case.) Assign a -1 for every negative charge. Hence, the reduction of periodate is a two-electron reduction. (You can verify this with a balanced half-reaction.) Another way to reach the same conclusion is to note that one mole of periodate is required per mole of diol. Because the diol undergoes a two-electron oxidation, periodate must undergo a two-electron reduction.

- (c) From the balanced equation, shown in the problem, 0.1 mole of periodate is required to oxidize 0.1 mole of the diol.
- 10.52 The reactivity data and the molecular formula of *A* indicate that compound *A* is an alkene with one double bond. The identity of compound *D* follows from the oxidation of 3-hexanol; it can only be 3-hexanone (see following equation). It is given that 3-hexanone is an ozonolysis product of alkene *A* (along with  $\text{H}-\text{CO}_2\text{H}$  (formic acid), not shown in the following equation). Since alkene *A* has seven carbons and one double bond, and 3-hexanone has six carbons, the carbon of alkene *A* not accounted for by 3-hexanone must be part of a  $=\text{CH}_2$  group. Therefore, the identity of alkene *A* is established as 2-ethyl-1-pentene. The identities of compounds *B* and *C* follow from the reactions of *A*.

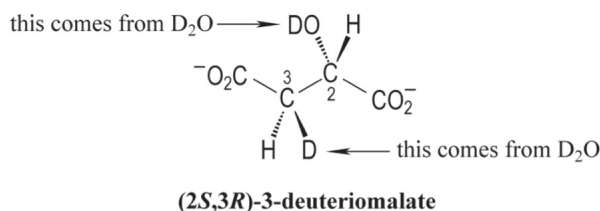


- 10.57 The two branches of citrate at the central carbon are *enantiotopic*. Hence, they are chemically distinguishable to a chiral catalyst such as an enzyme. Evidently, the difference is such that the dehydration occurs into the unlabeled branch, as shown in Fig. P10.57.

One difference in  $\text{H}_2\text{SO}_4$  solution is that the carboxylate groups are not ionized, but this is not the key difference. The point of the problem is that an achiral laboratory reagent will not make the distinction between enantiotopic groups. Hence, equal amounts of dehydration should occur into each branch, and there is no reason to expect exclusively the *Z* stereochemistry observed in the product of the enzyme-catalyzed reaction.

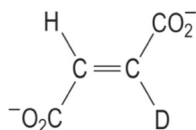


- 10.58 First, draw the *2S,3R* stereoisomer of the product so that the stereochemistry of the addition can be deduced.



Only a malate stereoisomer with the *2S* configuration will dehydrate; if the enzyme is stereospecific in one direction, it must be stereospecific in the other. (See Eqs. 7.29a–b, text p. 300.) The pro-*R* hydrogen at carbon-3 comes from the solvent; if the reaction had been run in  $\text{H}_2\text{O}$ , this would be a hydrogen. This is an *anti*-addition; we leave it to you to confirm this point. (See Problem 7.52(a), text p. 318.)

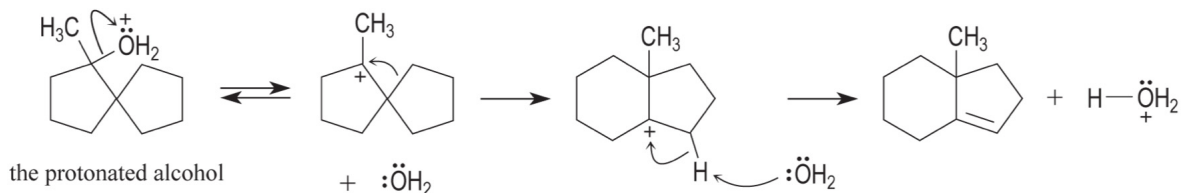
- (b) The fumarate stereoisomer obtained in this reaction is the same as in part (a).



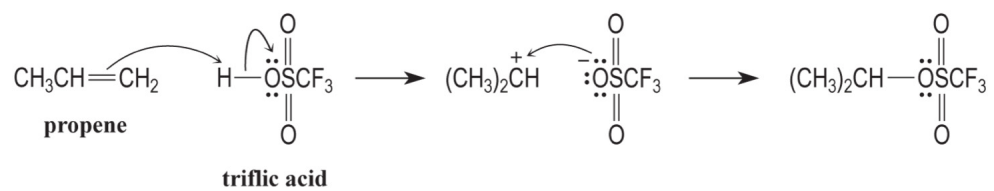
**(*E*)-2-deuteriofumarate**

The same comments apply to the dynamic reversal of the reaction; the starting material, to the extent that it remains at equilibrium, will be a mixture of the *2S,3S* and *2S,3R* diastereomers, and the deuterium will not wash out.

- 10.61 (b) The carbocation rearrangement in this mechanism also involves a ring expansion. In this case, a tertiary carbocation is converted into another tertiary carbocation.



- (d) This is an addition to the alkene that is conceptually similar to hydration or  $\text{HBr}$  addition. Trifluoromethanesulfonic acid (triflic acid), a strong acid, protonates the alkene double bond to give a carbocation, which then undergoes a Lewis acid–base association reaction to give the product.



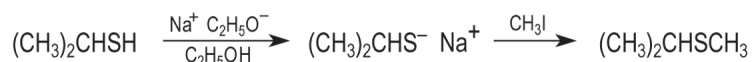
# Chapter 11

## The Chemistry of Ethers, Epoxides, Glycols, and Sulfides

### Solutions to In-Text Problems

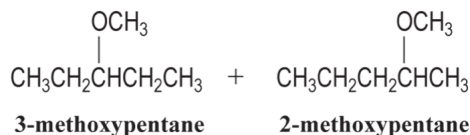
- 11.1 (b) A thiolate ion, formed by reaction of NaOH with the thiol, is alkylated by allyl chloride to give  $\text{H}_2\text{C}=\text{CH}-\text{CH}_2-\text{S}-\text{CH}_3$  (allyl methyl sulfide) +  $\text{Na}^+ \text{Cl}^-$ . NaOH is a strong enough base to form the thiolate anion, but would not be strong enough to form the conjugate base of an alcohol.
- (d) Neopentyl halides and sulfonate esters do not undergo  $\text{S}_{\text{N}}2$  reactions at room temperature; furthermore, they do not undergo  $\beta$ -elimination because there are no  $\beta$ -hydrogens. Thus, no reaction occurs.

- 11.2 (b)



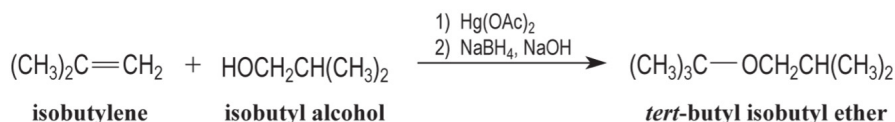
The alternative synthesis, reaction of the methanethiolate ion with isopropyl bromide, is less desirable because secondary alkyl halides react more slowly than methyl halides and give some elimination products.

- 11.5 Because each carbon of the alkene double bond has one alkene substituent, there is no strong preference for the reaction of methanol at either carbon of the resulting mercurinium ion. Consequently, two constitutional isomers of the product ether are formed.



(The same result would be obtained regardless of the stereochemistry of the alkene starting material.)

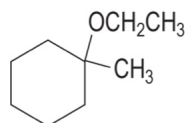
- 11.6 (b) Isobutylene (2-methylpropene) is subjected to alkoxymercuration in isobutyl alcohol, and the resulting organomercury compound is reduced with  $\text{NaBH}_4$ .



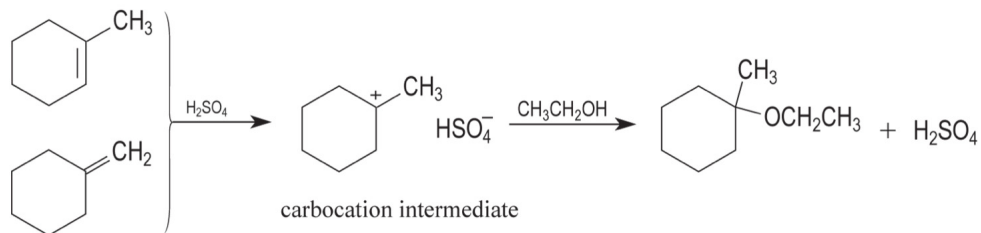
- 11.7 If we start with two primary alcohols, ROH and R'OH, we would expect them to have similar basicities and similar nucleophilicities. Each alcohol could react with each protonated alcohol. Consequently, three possible products would be formed: R—O—R, R'—O—R, and R'—O—R'. None of the alcohols would be formed in very high yield, and separation of the products could be quite laborious.

The reason we can let a *tertiary* alcohol react with a primary alcohol to give an unsymmetrical ether is that the tertiary alcohol forms a carbocation in acidic solution *much* faster than either it or the primary ether react by the  $\text{S}_{\text{N}}2$  mechanism; and, once the carbocation is formed, it is rapidly consumed by its Lewis acid–base association reaction with the large excess of primary alcohol that is present.

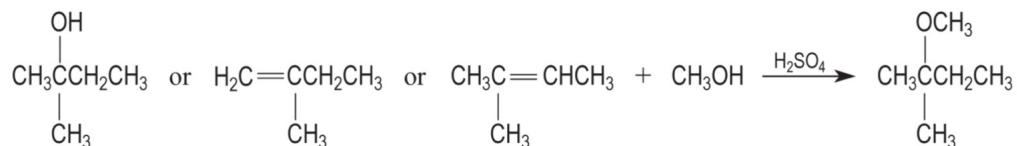
- 11.8 (b) The carbocation formed from the tertiary alcohol reacts with ethanol to give the following ether:



- 11.9 (b) Use the same approach as in part (a):



- 11.10 (b) Because this is an ether with one tertiary alkyl group and one methyl group, it can be prepared by dehydration of the tertiary alcohol in the presence of methanol, or by acid-catalyzed addition of methanol to either of two possible alkenes.



2-methyl-2-butanol

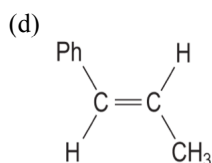
2-methyl-1-butene

2-methyl-2-butene

2-methoxy-2-methylbutane

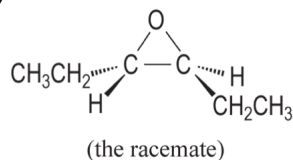
- (d) Dibutyl ether,  $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ , is a symmetrical ether that can be prepared by the acid-catalyzed dehydration of 1-butanol,  $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}$ .

- 11.11 (b)  $(\text{CH}_3)_2\text{C}=\text{CH}_2$



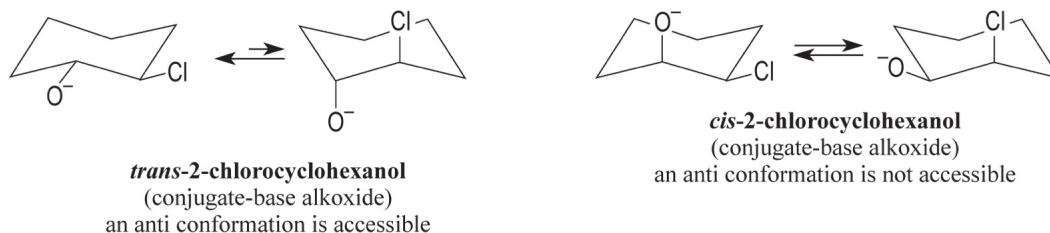
In part (b), the stereochemistry of the product and the net *syn*-addition dictate the stereochemistry of the alkene starting material.

- 11.12 (a)



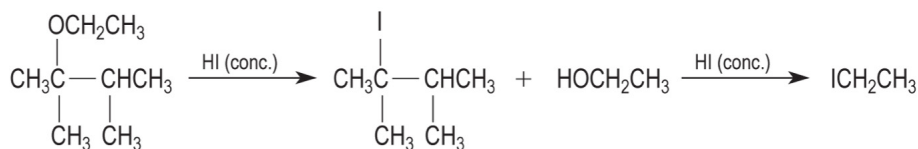
- 11.14 As in the solution to Problem 11.13, the alkoxide oxygen and the halogen leaving group must be anti in the transition state. This anti relationship is possible in a chair conformation only in the reaction of the *trans* stereoisomer (see Eq. 11.22 on text p. 492). In the *cis* stereoisomer, such an anti relationship is not possible. Because the *cis* stereoisomer cannot achieve the appropriate transition-state conformation for epoxide formation, it is unreactive.





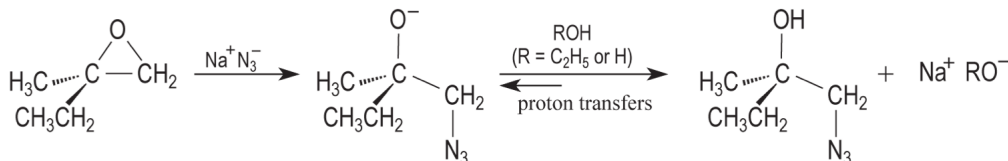
- 11.15 (b) Because alcohols react with HI to give alkyl iodides, the initially formed 1-butanol would be expected to give 1-iodobutane.
- (d) As indicated in the solution for part (c), acidic cleavage of tertiary ethers occurs by the  $S_N1$  mechanism. As in part (c), the protonated ether reacts to give the *tert*-butyl cation and methanol. Loss of a  $\beta$ -proton from the cation gives 2-methylpropene; although this can protonate to regenerate the *tert*-butyl cation, the conditions of the reaction (distillation of low-boiling compounds) drives the volatile alkene from the reaction mixture as it is formed.

- 11.16 (b) This tertiary ether reacts rapidly by a carbocation ( $S_N1$ ) mechanism to give, initially, the tertiary iodide and ethanol. The ethanol subsequently reacts more slowly to give ethyl iodide.

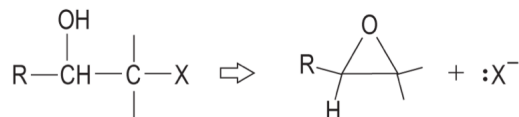


**2-ethoxy-2,3-dimethylbutane**

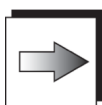
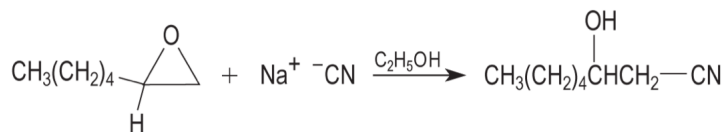
- 11.17 (b)



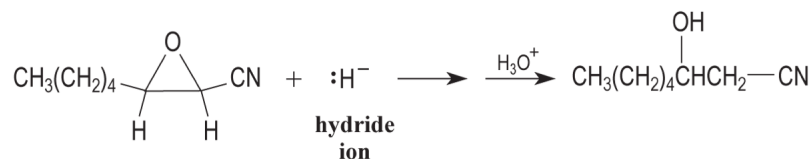
- 11.18 The strategy in this problem is to let the —OH group originate from the epoxide oxygen. In the starting material, this oxygen must be attached to the same carbon as the —OH group in the product as well as to an adjacent carbon; the nucleophile becomes attached to the adjacent carbon. To summarize:



- (b)



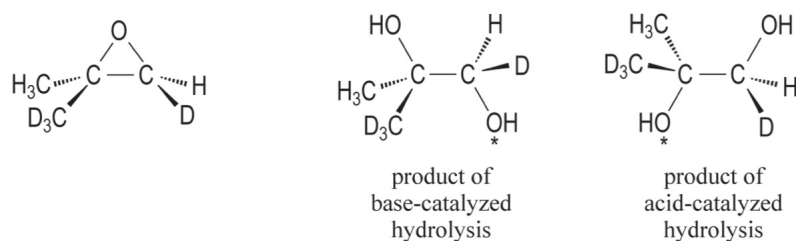
The strategy outlined above suggests another possibility:



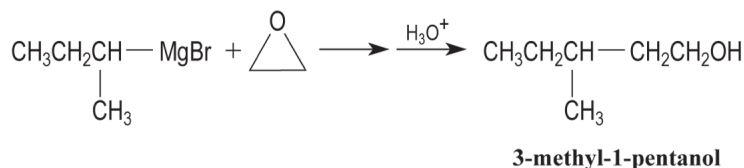
If you came up with this idea, you are reasoning correctly. However, every good idea has to be tempered by practical reality. In this case, the strategy will not work because the most common source of nucleophilic hydride,  $\text{LiAlH}_4$  (lithium aluminum hydride), also reacts with the cyano (CN) group.

11.19 (b) The enantiomer of the epoxide in part (a) gives the enantiomer of the product formed in part (a), (3*R*,4*S*)-4-methoxy-3-hexanol. (Verify this by writing the mechanism.)

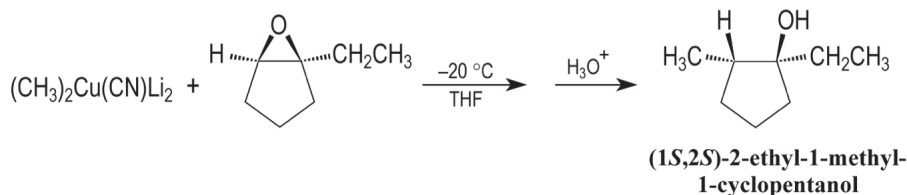
11.20 (b) Inversion of configuration would occur at the carbon of the epoxide (or protonated epoxide) at which the nucleophilic reaction occurs. (The nucleophilic oxygen is labeled with an asterisk.)



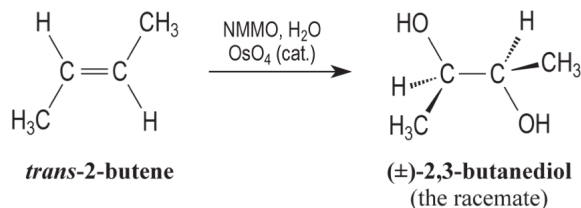
11.21 (a)



(c)



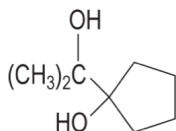
11.23 (b)



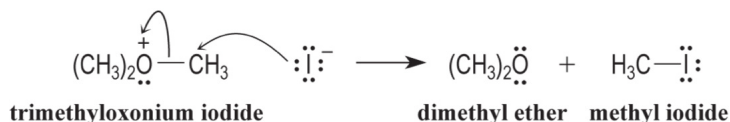
11.24 (a) The alkene required is 4-ethoxy-1-butene,  $\text{CH}_3\text{CH}_2\text{OCH}_2\text{CH}_2\text{CH}=\text{CH}_2$ .

11.26 (b) The products are phenylacetaldehyde,  $\text{PhCH}_2=\text{O}$ , and formaldehyde,  $\text{O}=\text{CH}_2$ .

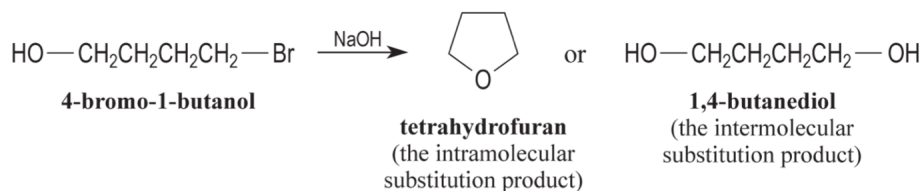
11.27 (a)



11.28 Because iodide ion is a good nucleophile and the trimethyloxonium ion is an excellent alkylating agent, alkylation of the iodide ion occurs to give dimethyl ether and methyl iodide.

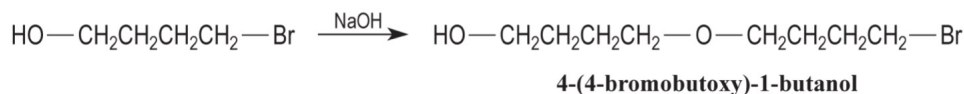


11.30 The intramolecular product tetrahydrofuran results from an internal nucleophilic substitution reaction of the alkoxide on the alkyl halide. The intermolecular product 1,4-butanediol results from the  $S_N2$  reaction of hydroxide ion with the alkyl halide.



To form the cyclic product tetrahydrofuran,  $\text{OH}^-$  must react with the alcohol to ionize it; the conjugate base anion of the alcohol then cyclizes in an *internal* substitution reaction. In contrast, to form 1,4-butanediol,  $\text{OH}^-$  must react with the alkyl halide in an  $S_N2$  reaction. Ionization reactions are much faster than  $S_N2$  reactions; and once the ionization has occurred, the cyclization, because it is intermolecular, is *much* faster than the  $S_N2$  reaction between hydroxide and the alkyl halide. Hence, tetrahydrofuran would be the major product.

Another reasonable *intermolecular* possibility you may have considered is following:

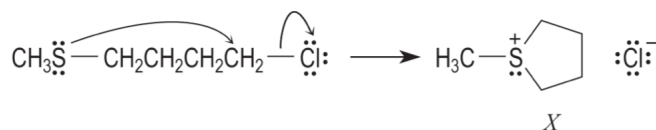


To form this product, ionized 4-bromobutanol must react with the alkyl halide “end” of another molecule of 4-bromobutanol in an  $S_N2$  reaction. Because such a reaction is bimolecular, the intramolecular reaction of the same ion to give tetrahydrofuran is *much* faster.

11.31 (b) Throwing a fistful of variously colored spaghetti onto a table has a considerably greater entropy change; a condition of greater randomness is created than if the spaghetti is sorted into variously colored piles.

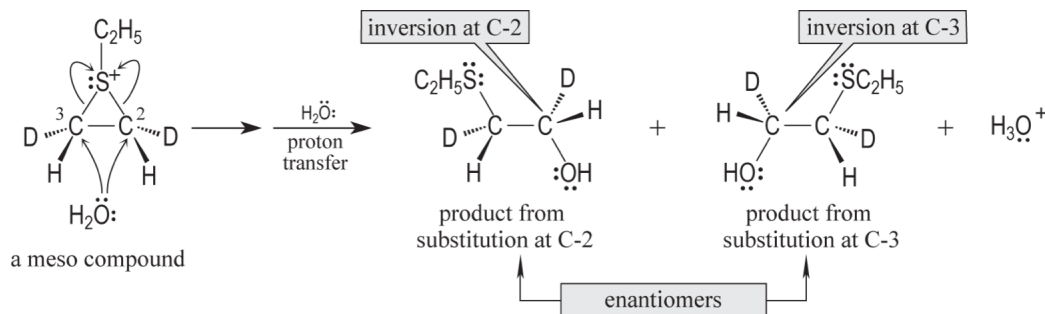
11.33 (b) The first reaction is a bimolecular reaction, whereas the second is an intramolecular reaction. Forming the transition state of the first reaction requires “freezing” the translation of one molecule relative to the other, whereas forming the transition state of the second reaction requires no freezing of translations. Because the bond changes in the two reactions are about the same, we suspect that the second reaction will be much faster because its  $\Delta S^\ddagger$  is less negative (or more positive).

11.35 (a) The sulfur can serve as a nucleophile in an intramolecular nucleophilic substitution reaction. The product is a cyclic sulfonium salt.



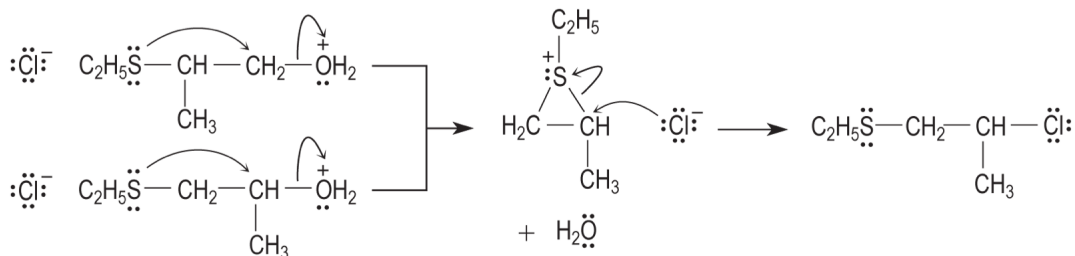
- (b) The assumption is that the reaction of water with the starting sulfide occurs at about the same rate as it does with 1-chlorohexane. If so, then the relative rate of the intramolecular reaction above and the competing intermolecular  $S_N2$  reaction of water with the same compound is 21, as given in the problem. A calculation very similar to the one in Study Problem 11.5, text p. 514, shows that  $k_1/k_2 = (21)(20 M) = 420 M$ . This is the proximity effect.

- 11.36 An analysis identical to the one shown in Study Problem 11.6, text pp. 516–517, results in the following episulfonium ion, which is the diastereomer of the one shown in Eq. 11.68b.



In this case, however, the episulfonium ion is meso and therefore achiral. The nucleophilic reactions of water at C-2 and C-3 give enantiomers, which must be formed in identical amounts.

- 11.39 The two reactions proceed through a common episulfonium ion intermediate that results from an intramolecular substitution of the protonated OH group by the sulfur.

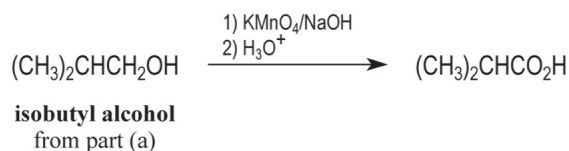


Evidently, the nucleophilic reaction of the chloride ion with this intermediate takes place at the carbon with the methyl substituent. Because the same intermediate is formed in both reactions, the product is the same.

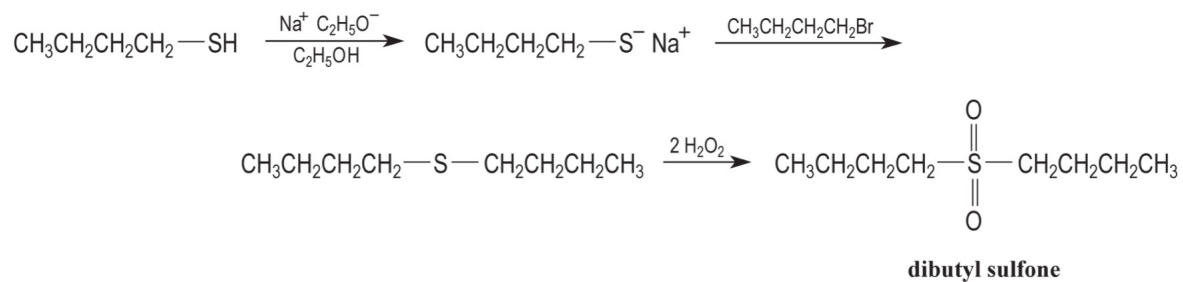


A separate question is why the chloride ion should react only at the more branched carbon. The cyclic intermediate is much like a protonated epoxide; hence, the nucleophilic reaction of chloride ion occurs at the more branched carbon for the same reason it does in a protonated epoxide. (See discussion of Eq. 11.33b on text p. 498.).

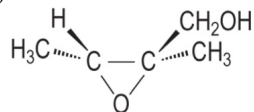
- 11.40 (b) Oxidize the isobutyl alcohol, which is obtained in the hydroboration–oxidation reaction in part (a).



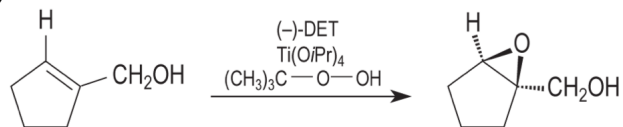
- (c) The sulfone must be obtained by oxidation of dibutyl sulfide; and the sulfide is obtained from the  $S_N2$  reaction of the thiolate conjugate base of 1-butanethiol with 1-bromobutane.



11.41 (b)



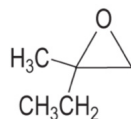
11.42 (a)



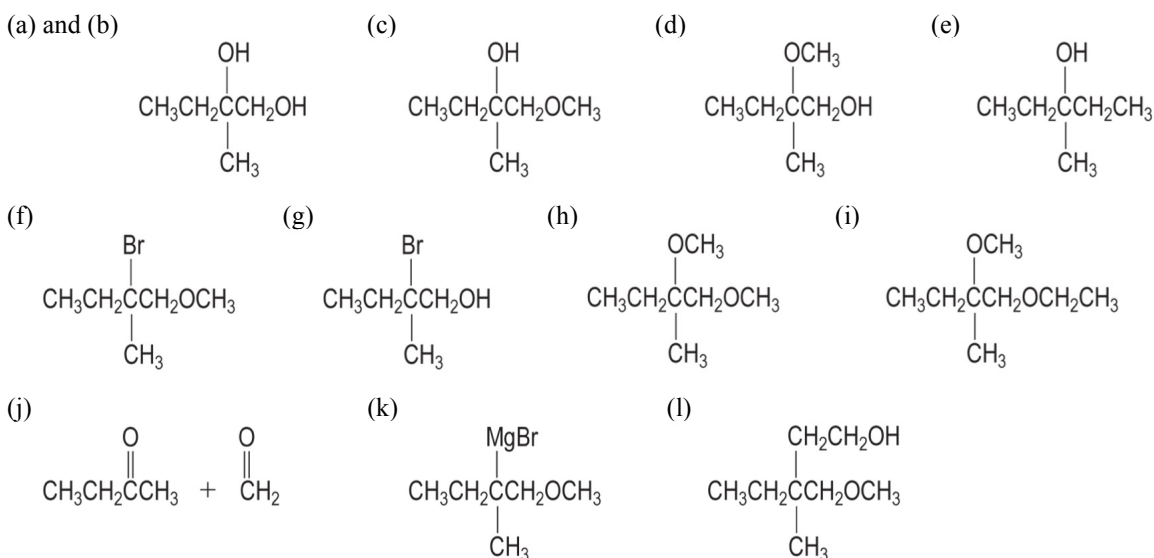
11.43 (b) The same phenomenon would be observed with (–)-DET, because the catalyst is enantiomeric to the one formed from (+)-DET and the alkene is not chiral; hence, the same energetics should apply.

### Solutions to Additional Problems

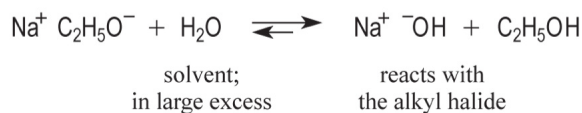
- 11.44 (b) Any ether containing only methyl or primary alkyl groups is a correct answer. Two of several possible examples are  $\text{CH}_3\text{O}(\text{CH}_2)_7\text{CH}_3$  (methyl octyl ether, or 1-methoxyoctane) and  $\text{CH}_3(\text{CH}_2)_3\text{O}(\text{CH}_2)_4\text{CH}_3$  (butyl pentyl ether, or 1-butoxypentane).
- (d) Dipropyl ether ( $(\text{CH}_3\text{CH}_2\text{CH}_2)_2\text{O}$ ), would give propyl bromide as the only alkyl halide.
- (f) 1-Butene,  $\text{H}_2\text{C}=\text{CHCH}_2\text{CH}_3$ , gives racemic 1,2-butanediol with either reagent.
- (h) A correct answer must be an alkene that gives a glycol that cannot exist as diastereomers. The alkene 1-hexene ( $\text{H}_2\text{C}=\text{CHCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ ) is one such compound.
- 11.46 It is assumed that the starting material is racemic. As an additional exercise, you should consider the stereochemical course of the reactions if the starting material is a single enantiomer.



2-ethyl-2-methyloxirane

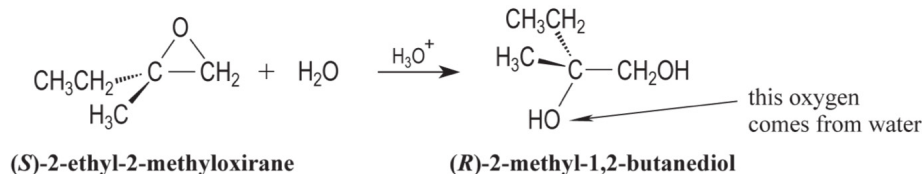


- 11.48 The first reaction, opening of the epoxide, should occur most rapidly, because the epoxide is considerably more strained than tetrahydrofuran. It is the ring strain that causes epoxide opening to be so fast.
- 11.49 (b) 1-Pentanol, the alcohol, is fairly soluble in water, whereas the ether is not. Alternatively, the alcohol evolves  $\text{H}_2$  when treated with  $\text{NaH}$  or  $\text{Na}$ , or evolves methane ( $\text{CH}_4$ ) when treated with the Grignard reagent  $\text{CH}_3\text{MgBr}$ ; the ether, which has no  $\text{O}-\text{H}$  group, does not.
- 11.51 (a) Sodium ethoxide reacts with water to give ethanol and sodium hydroxide. Although the  $\text{p}K_a$  values of water and ethanol are similar, water is present in excess because it is the solvent, and the equilibrium therefore favors sodium hydroxide. Consequently, the alcohol  $(\text{CH}_3)_2\text{CHCH}_2\text{CH}_2\text{OH}$  rather than the ether will be formed as the major substitution product.

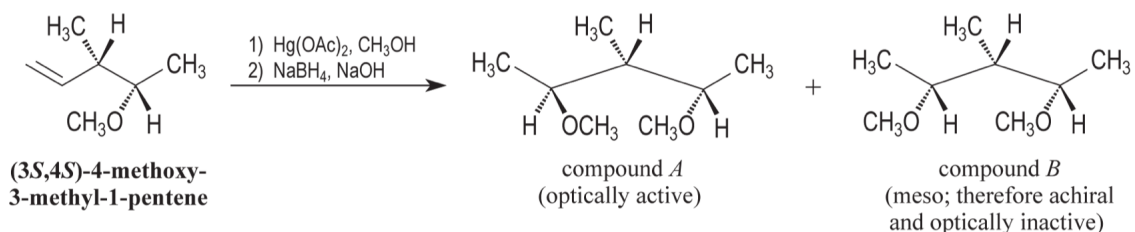


Another problem is that the alkyl halide is insoluble in water. This insolubility makes any reaction that does occur very slow because the concentration of alkyl halide is limited to the very small amount that will dissolve. Changing the solvent to ethanol would solve all of these problems.

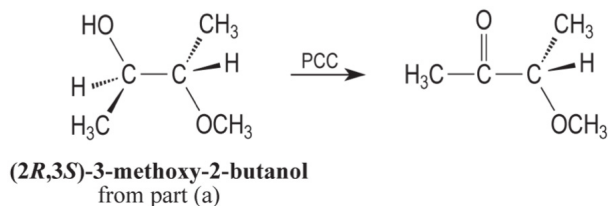
- 11.55 In this reaction the nucleophile (water) reacts at the protonated epoxide at the more substituted carbon with inversion of stereochemical configuration.



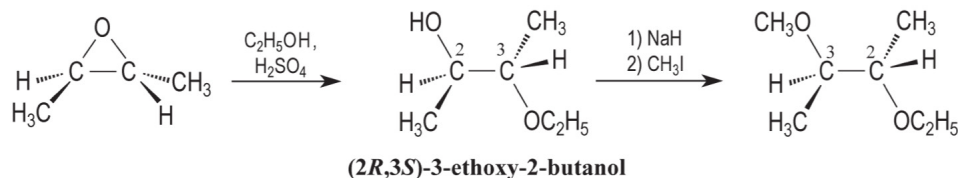
- 11.57 As a result of this reaction, carbon-2 becomes asymmetric, and diastereomers are formed corresponding to the two possible configurations of this carbon. The product with the *S* configuration at carbon-2 (compound *A*) is optically active; however, the other product (compound *B*) is a meso compound, and hence, is optically inactive.



- 11.62 (b) Carbon-3, the asymmetric carbon, has the *S* configuration, which is the same configuration that carbon-3 has in the product of part (a). Consequently, oxidation of the alcohol product of part (a) gives the desired compound:

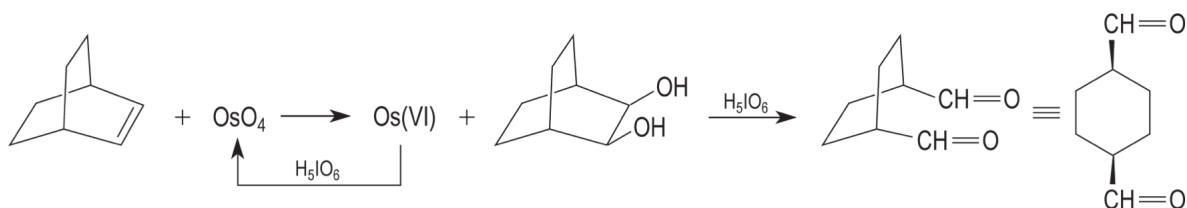
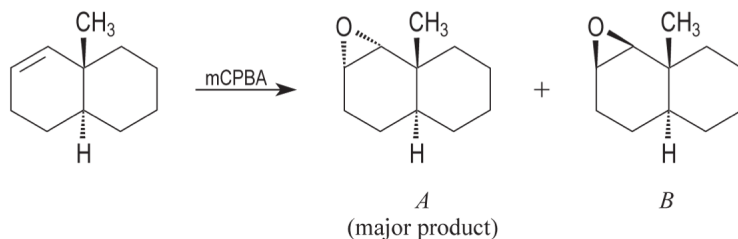


- (d) Because the carbon bearing the ethoxy group is the one that must be inverted, use the ring-opening reaction in part (a), except substitute ethanol for methanol. Then carry out the Williamson synthesis used in part (c) with methyl iodide instead of ethyl iodide.

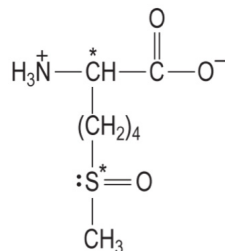


Don't be confused by the fact that the carbon numbering changes because of numbering conventions. Thus, carbon-2 in the alcohol becomes carbon-3 in the product, and vice versa.

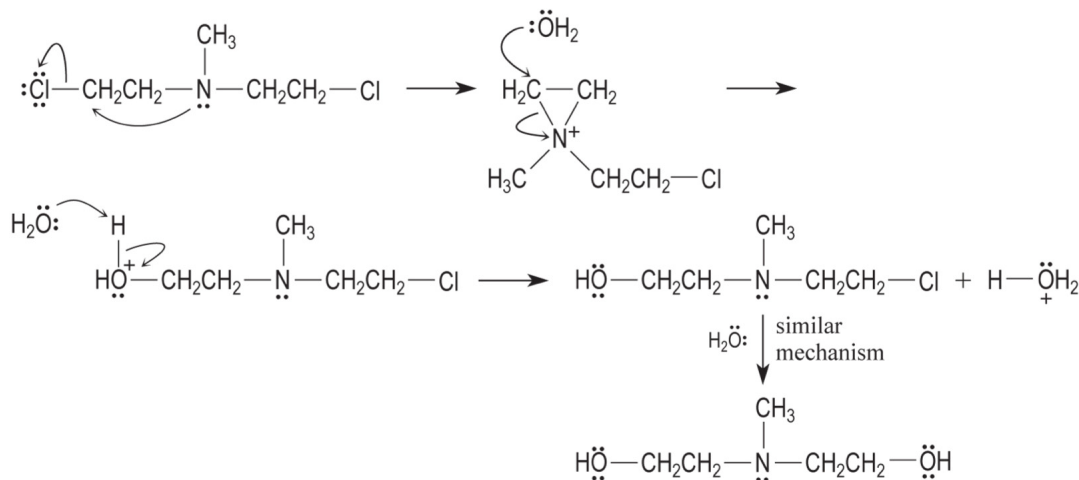
11.64 (b)

11.65 The mCPBA reacts at the side of the alkene  $\pi$  bond that involves the less severe van der Waals repulsions.(b) The face of the ring on the *same side* of the methyl group is blocked; hence, reaction occurs at the opposite face.

11.67 Because sulfur in a sulfoxide does not undergo inversion, it is an asymmetric atom. Because there are two asymmetric carbons in methionine (asterisks in the structure below), methionine sulfoxide can exist as diastereomers. (See the solution to Problem 11.66.)

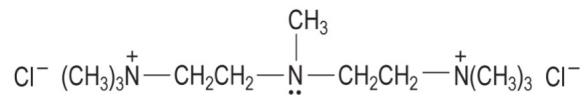


methionine sulfoxide

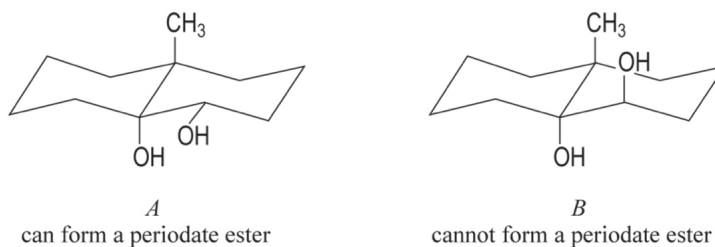
11.70 (a) The rate acceleration suggests a mechanism involving neighboring-group participation. The product of this reaction results from the net substitution of the chlorines by  $\text{—OH}$  groups to give a diol. The mechanism for the first substitution is shown below in detail; you should write the mechanism for the second.



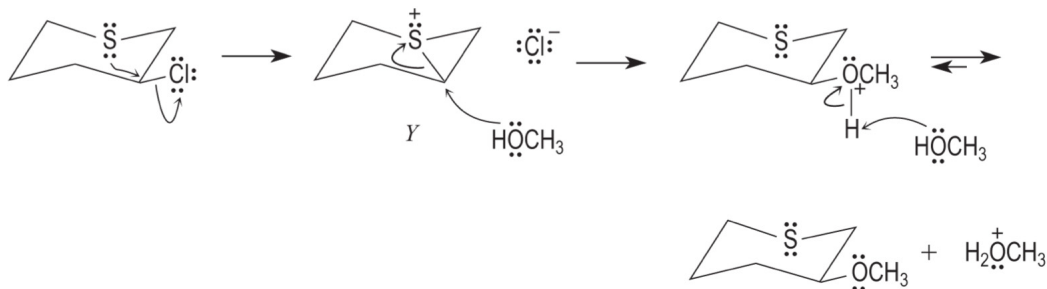
- (b) The reaction of mechlorethamine with an amine  $R_3N:$  follows a similar pattern in which the amine rather than water serves as the ultimate nucleophile. The final product is



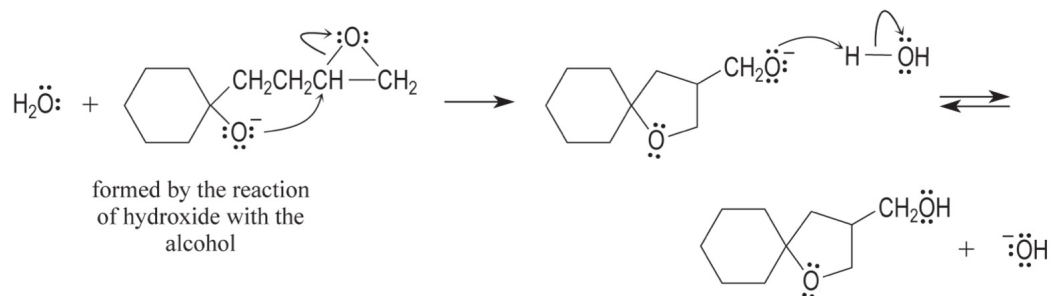
- 11.71 (b) Compound *B* is locked into a conformation in which the two hydroxy groups are trans-diaxial; consequently, this compound cannot be oxidized for the same reason that compound *A* cannot be oxidized in part (a).



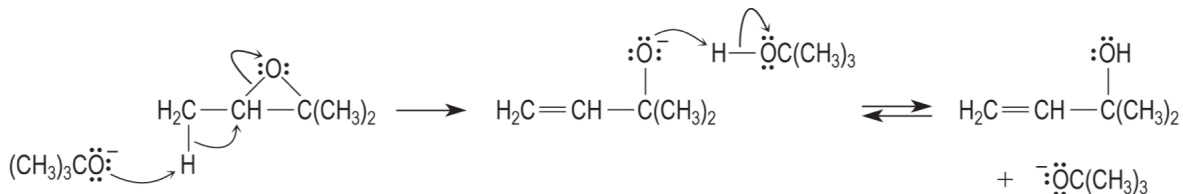
- 11.73 (b) The substitution with retention of configuration suggests a neighboring-group mechanism involving a bicyclic episulfonium ion *Y*.



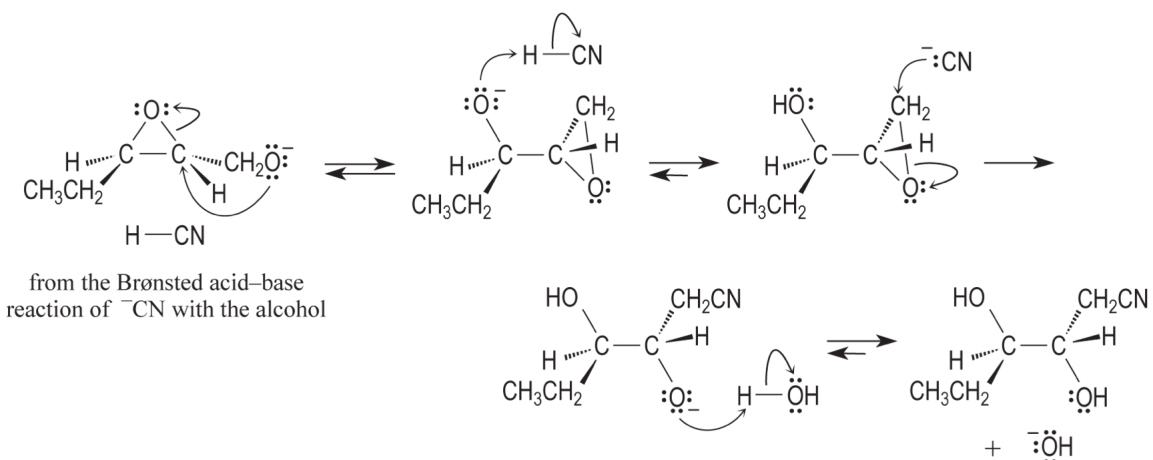
- 11.75 (b) The alkoxide, formed by ionization of the alcohol OH group, opens the epoxide intramolecularly. The hydroxide catalyst is regenerated by protonation of the resulting alkoxide ion.



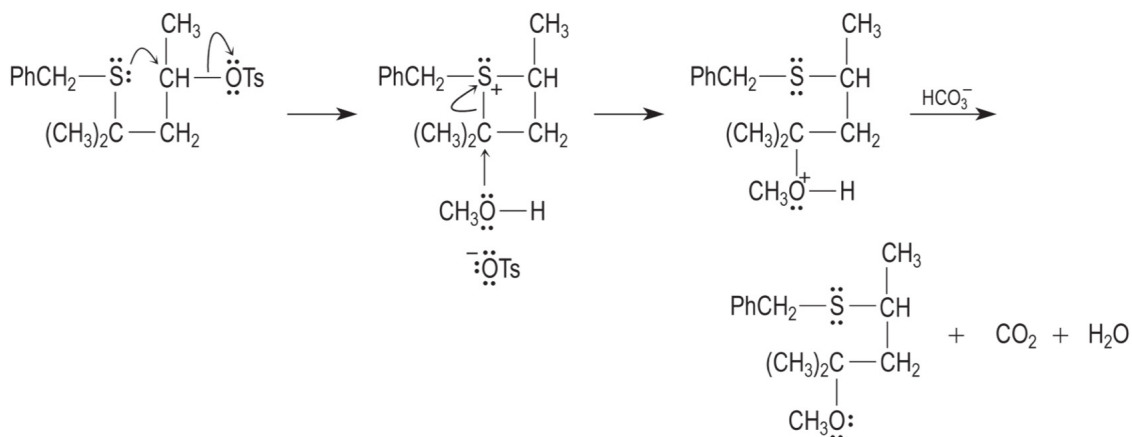
- (d) The epoxide chemistry in this chapter has focused on ring-opening substitution reactions; however, you have learned that elimination competes with substitution. Thus, this reaction is an E2-like elimination reaction in which either of the two distinguishable  $\beta$ -hydrogens is removed and the epoxide oxygen serves as a leaving group. The mechanism for the formation of the major alkene product is shown below; the minor product is formed by an essentially identical mechanism involving the other  $\beta$ -hydrogen. Substitution (that is, nucleophilic ring-opening) evidently does not occur because of the van der Waals repulsions that would result in the transition state of such a reaction between the alkyl branches of the base and those of the epoxide.



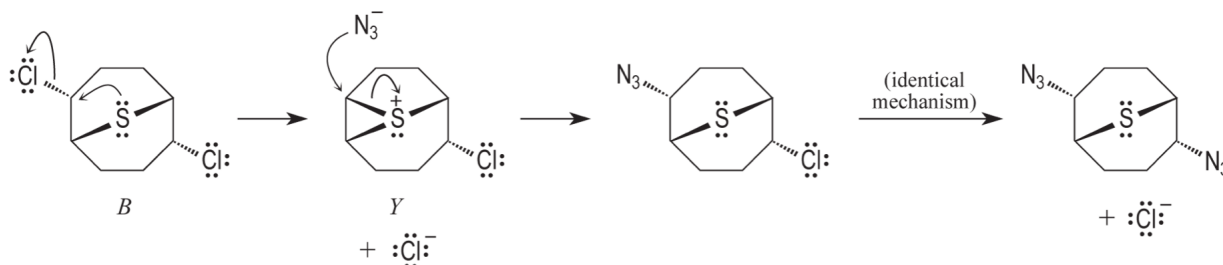
- (f) The key to this mechanism is to notice that inversion of configuration has occurred at carbon-2, and the cyanide ion has reacted at carbon-1. The formation of another epoxide by neighboring-group participation with inversion of configuration at C-2 is followed by reaction of the cyanide ion as a nucleophile at C-1, which is the less substituted carbon of the epoxide. (The rearrangement of one epoxide to another by the intramolecular reaction is called the *Payne rearrangement*.)



- (g) This appears to be a relatively rare instance of neighboring-group participation involving a four-membered ring. The ring is opened by the nucleophilic reaction of methanol at the more substituted carbon.



- 11.76 (b) The substitution with retention of stereochemical configuration suggests that neighboring-group participation has taken place. The first substitution involves the formation of episulfonium ion *B* from part (a) with loss of chloride ion under the rather extreme conditions. This ion is opened by the azide ion.



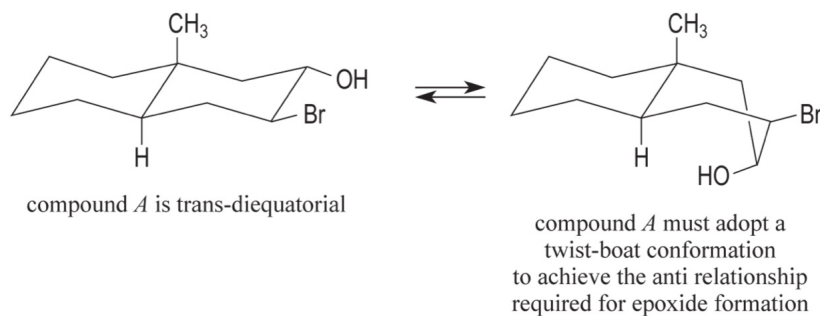
The second substitution occurs by an essentially identical mechanism.

- 11.78 As illustrated by Eq. 11.22 on text p. 492, and as discussed in the solution to the previous solution, the  $\text{O}^-$  and  $\text{Br}$  groups must be able to assume a trans-diaxial arrangement in the transition state for backside substitution to occur.

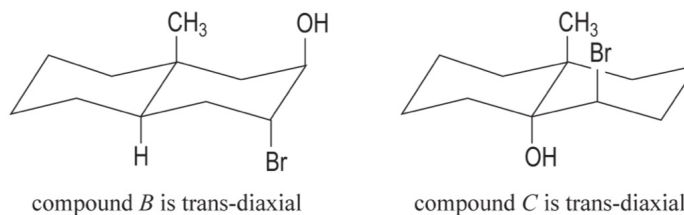
Immediately we rule out compound *D*, as the  $\text{OH}$  and  $\text{Br}$  groups are cis.

The  $\text{OH}$  and  $\text{Br}$  groups in compounds *A*–*C* are trans. Because all of the compounds shown are trans-decalin derivatives, they cannot undergo the chair flip. Hence, the  $\text{OH}$  and  $\text{Br}$  groups could be trans-diequatorial or trans-diaxial. Examine each one in turn.

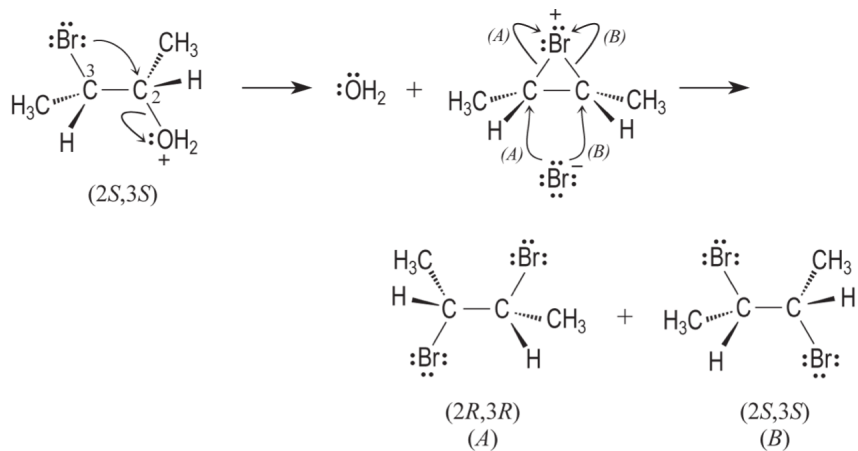
Compound *A* must assume a twist-boat conformation in order to undergo epoxide formation by backside substitution. Because this conformation, and hence the transition state of the reaction, has a very high energy, epoxide formation is likely to be very slow.



The remaining two bromohydrins *B* and *C* have trans-diaxial arrangements and thus react readily:



- 11.79 (b) The similar reaction of the  $2S,3S$  stereoisomer gives a meso bromonium ion, which is achiral. Reactions of bromide ion at the two carbons give respectively  $(2S,3S)$ - and  $(2R,3R)$ -2,3-dibromobutane in equal amounts—that is, the racemate.



# Chapter 12

## Introduction to Spectroscopy. Infrared Spectroscopy and Mass Spectrometry

### Solutions to In-Text Problems

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- 12.1 (b) Apply Eq. 12.1 and include the conversion factor  $10^{-10} \text{ m } \text{\AA}^{-1}$ .

$$\nu = \frac{3.00 \times 10^8 \text{ m sec}^{-1}}{(4800 \text{ \AA})(10^{-10} \text{ m } \text{\AA}^{-1})} = 6.25 \times 10^{14} \text{ sec}^{-1}$$

- 12.2 (b) Multiply the frequency obtained in the solution to Problem 12.1(b) times Planck's constant:

$$E = h\nu = (3.99 \times 10^{-13} \text{ kJ sec mol}^{-1})(6.25 \times 10^{14} \text{ sec}^{-1}) = 249 \text{ kJ mol}^{-1}$$

- 12.3 (a) The energy of X-rays is greater than that of any visible light, including blue light. (In fact, the energy is so much greater that prolonged exposure to X-rays is harmful.)

- 12.4 (b) Apply Eq. 12.7b on text p. 541:

$$\lambda = \text{wavelength} = (1 \times 10^4 \text{ } \mu\text{m cm}^{-1}) \div 1720 \text{ cm}^{-1} = 5.81 \text{ } \mu\text{m}$$

- 12.6 Using Eq. 12.8 on text p. 541, convert the wavenumber to a frequency, which is the "times per second" equivalent of wavelength or wavenumber.

$$\nu = c\tilde{\nu} = (3 \times 10^{10} \text{ cm sec}^{-1})(2143 \text{ cm}^{-1}) = 6.43 \times 10^{13} \text{ sec}^{-1}$$

- 12.8 Take the ratio of two equations like Eq. 12.13 on text p. 547, one for the C—H bond, and the other for the C—D bond. Everything cancels except the wavenumbers and the square roots of the masses.

$$\frac{\tilde{\nu}_D}{\tilde{\nu}_H} = \sqrt{\frac{m_H}{m_D}}$$

or

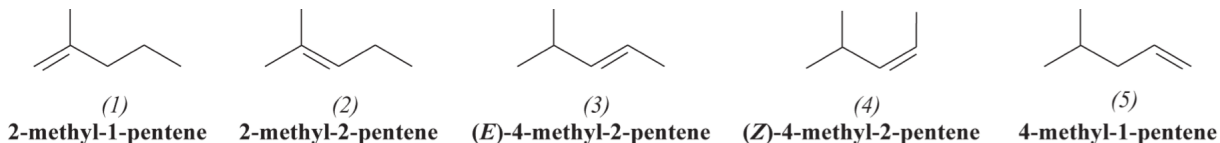
$$\tilde{\nu}_D = \tilde{\nu}_H \sqrt{\frac{m_H}{m_D}} = (3090 \text{ cm}^{-1}) \sqrt{\frac{1}{2}} = 2185 \text{ cm}^{-1}$$

In fact, C—D vibrations appear in the IR at lower energy than the corresponding C—H vibrations (to the right in conventional IR spectra).

- 12.9 (b) Active. The C=O dipole is increased by the stretch because its length changes. Recall (Eq. 1.4, text p. 11) that dipole moment is proportional to length.  
(d) Inactive. The zero dipole moment of this alkyne is not changed by stretching the triple bond.

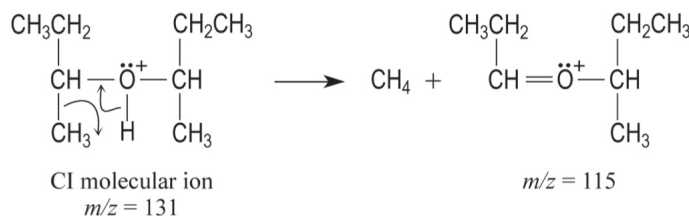
- (f) Active. The dipole moment of the molecule is due mostly to the bond dipole of the C—Cl bond, which is the only bond in the molecule with significant polarity. Increasing the length of this bond dipole will increase the dipole moment of the molecule.

12.10 The carbon skeleton of the hydrogenation product defines the following alkenes as possibilities.



The strong  $912$  and  $994\text{ cm}^{-1}$  C—H bending absorptions are very close to the standard values of  $910$  and  $990\text{ cm}^{-1}$ , which are typical of  $\text{—CH=CH}_2$  groups. Therefore compound *A* is (5). The weak or absent C=C stretching absorption in the  $1660\text{--}1670\text{ cm}^{-1}$  region suggest that the candidates for *B*, *C*, and *E* are compounds (2), (3), and (4). The strong  $967\text{ cm}^{-1}$  C—H bending absorption is the definitive absorption for trans alkenes. Therefore, compound *E* is (3). Compound *C* must be the cis alkene (4), from the C—H bending absorption at  $714\text{ cm}^{-1}$ , because the C—H bending absorption for cis alkenes occurs at lower wavenumber than the C—H bending absorption of other alkene types. The  $1650\text{ cm}^{-1}$  C=C stretching absorption as well as the  $885\text{ cm}^{-1}$  C—H bending absorption point to (1) as the structure of compound *D*. This leaves only compound *B* unassigned, and it must therefore have structure (2). Its C—H bending absorption is consistent with this assignment.

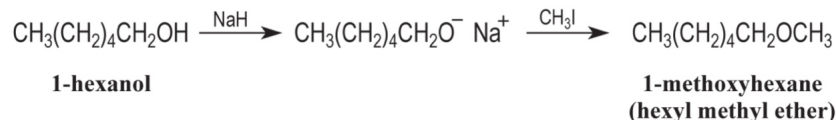
- 12.13 The two C—O bonds of an ether can undergo both symmetrical and unsymmetrical stretching vibrations; each of these normal vibrational modes has an associated infrared absorption. (These vibrations are described on the first two lines of Fig. 12.8 on text p. 549.)
- 12.16 Assume the molecular ion (base) peak at  $m/z = 50$  has an abundance of 100%. This peak is due to molecules that contain  $^{12}\text{C}$ ,  $^1\text{H}$ , and  $^{35}\text{Cl}$ . The  $M + 1$  peak is due to molecules that contain either  $^{13}\text{C}$ ,  $^1\text{H}$ , and  $^{35}\text{Cl}$  or  $^{12}\text{C}$ ,  $^2\text{H}$ , and  $^{35}\text{Cl}$ . The intensity of the  $M + 1$  peak due to  $^{13}\text{C}$  relative to the base peak is  $(0.0111/0.989) = 1.12\%$ , and the relative intensity due to  $^2\text{H}$  is  $3(0.00015)/(0.99985) = 0.0004$ , or  $0.04\%$ . Hence, the  $M + 1$  peak at  $m/z = 51$  is due almost entirely to molecules that contain  $^{13}\text{C}$ ,  $^1\text{H}$ , and  $^{35}\text{Cl}$ , but we'll include the contribution of  $^2\text{H}$  for completeness. Because there is one carbon, the intensity of the  $m/z = 51$  peak is  $1.16\%$  ( $1.12\% + 0.04\%$ ). The  $M + 2$  peak at  $m/z = 52$  is due almost entirely to  $^{12}\text{C}$ ,  $^1\text{H}$ , and  $^{37}\text{Cl}$ ; according to Table 12.3, the ratio of this peak to the base peak should be  $0.2423/0.7577 = 0.320$ , or  $32\%$ . (This peak has a contribution from molecules that contain  $^{13}\text{C}$ ,  $^2\text{H}$ , and  $^{35}\text{Cl}$  equal to  $3 \times (0.0111/0.989)(0.00015/0.99985) = 0.00017\%$  that can be ignored). Finally, there is a peak at  $M + 3$ , or  $m/z = 53$ , which is due to molecules that contain either  $^{13}\text{C}$ ,  $^1\text{H}$ , and  $^{37}\text{Cl}$  or to  $^{12}\text{C}$ ,  $^2\text{H}$ , and  $^{37}\text{Cl}$ . The contribution of  $^2\text{H}$  is only  $0.0004$ . Thus, the relative abundance from the simultaneous presence of  $^{13}\text{C}$  and  $^{37}\text{Cl}$  is  $(0.0112)(0.320) = 0.00358$ , or  $0.36\%$ . This peak is almost negligible.
- 12.18 When the molecule contains only C, H, and O, odd-electron ions have even mass, and even-electron ions have odd mass. Therefore, (a) and (d) are even-electron ions, and (b) and (c) are odd-electron ions.
- 12.20 (b) Inductive cleavage at either side of the oxygen would give a primary carbocation. With di-*sec*-butyl ether, in contrast, a secondary carbocation is formed by inductive cleavage. Because of the greater stability of secondary carbocations, more inductive cleavage occurs in the fragmentation of di-*sec*-butyl ether.
- 12.21 (b) The same process occurs, except that 16 mass units—that is, methane—is eliminated.



### Solutions to Additional Problems

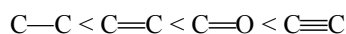
12.23 The intensity of an infrared absorption is affected by (1) the number of absorbing groups and (2) the size of the dipole moment change when the molecule undergoes the bond vibration. The number of absorbing groups, in turn, depends on (1) the number of groups of interest within a given molecule and (2) the concentration of molecules in the sample.

12.24 (b) Carry out a Williamson ether synthesis. Confirm the reaction by observing loss of the O—H stretch of the alcohol in the 3200–3400  $\text{cm}^{-1}$  region of the IR spectrum, and by intensification of the C—O stretching absorption.



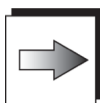
12.27 Only spectrum (2) has the C=C stretching absorption near 1640  $\text{cm}^{-1}$  and the high-wavenumber shoulder at about 3050  $\text{cm}^{-1}$  for the alkene C—H stretching absorption; this is therefore the spectrum of compound *A*, and spectrum (1) is the spectrum of compound *B*.

12.29 The solution to the previous problem noted the correlation between bond dissociation energies and IR absorption frequencies. Triple bonds are clearly stronger than double bonds, which are stronger than single bonds. The question is which of the two double bonds is stronger. Table 5.3 on text p. 213 shows that the bond dissociation energy of a C=C double bond is 728  $\text{kJ mol}^{-1}$ , and that of a C=O double bond is 749  $\text{kJ mol}^{-1}$ . On this basis, the C=O bond is predicted to absorb at higher frequency. (This is realized in practice; typical C=O absorptions occur in the 1710  $\text{cm}^{-1}$  region, whereas C=C absorptions occur in the 1650  $\text{cm}^{-1}$  region.) In summary, then, the order of increasing bond strengths and increasing IR absorption frequencies is:



12.31 The two stretching vibrations of the nitro group correspond to the symmetrical and unsymmetrical stretching modes.

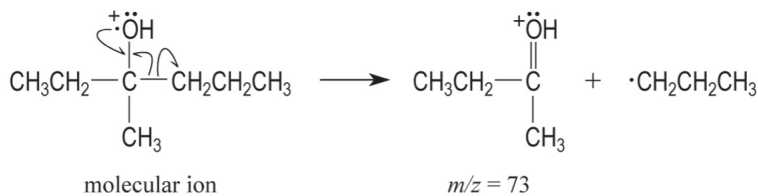
12.33 (a) Both compounds have the same absorptions, except that the absorptions of compound *C* in Fig. P12.33 are displaced to lower frequency, an observation that implies a higher mass for the absorbing group; see the discussion of the mass effect associated with Eq. 12.13 on text p. 547. In particular, a peak at 3000  $\text{cm}^{-1}$  in compound *D*, undoubtedly a C—H stretching absorption, is displaced to 2240  $\text{cm}^{-1}$  in compound *C*. Hence, compound *C* is  $\text{CDCl}_3$ .



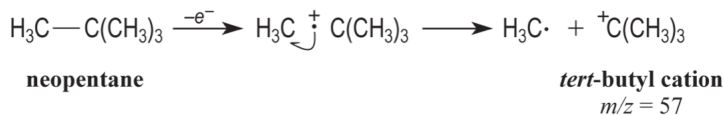
Eq. 12.13 on text p. 547 gives the quantitative basis of the mass effect. If the force constants of C—H and C—D bonds are nearly the same (and they are), then the ratio of stretching frequencies of these two bonds should be equal to the square root of the ratios of the mass terms. Eq. 12.13 predicts a ratio of  $\sqrt{2} = 1.414$ ; the more exact equation, Eq. 12.10 (text p. 546), predicts a ratio of 1.36. The actual ratio,  $(3000/2240) = 1.34$ , is very close to this prediction.

(b) The two compounds could be distinguished by mass spectrometry by the masses of their parent ions. Both  $\text{CHCl}_3$  and  $\text{CDCl}_3$  have four molecular ions. (Why four? See Table 12.3, text p. 562.) Each molecular ion peak of  $\text{CDCl}_3$  lies at one unit higher mass than the corresponding molecular ion peak of  $\text{CHCl}_3$ .

12.34 (b) Loss of a propyl radical from the molecular ion of 3-methyl-3-hexanol (molecular mass = 116) by  $\alpha$ -cleavage mechanism similar to that in part (a) gives a fragment with  $m/z = 73$ .

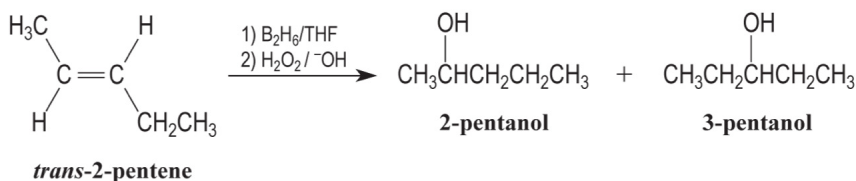


- (d) Fragmentation of neopentane at any one of its four carbon-carbon bonds gives a methyl radical and the *tert*-butyl cation, which has the correct mass:



- 12.35 (b) Loss of 18 mass units could indicate loss of H<sub>2</sub>O. (See the solution to Problem 12.34(c) for an example of such a loss.)

- 12.37 First ask what products are expected from the reaction. Two constitutional isomers, both with molecular mass = 88, are anticipated:

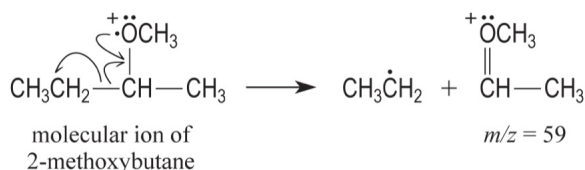


Spectrum (b) is consistent with 3-pentanol; the base peak at  $m/z = 59$  corresponds to loss of CH<sub>3</sub>CH<sub>2</sub>—, and there are two ethyl groups in this compound that could be lost by  $\alpha$ -cleavage. Spectrum (a) has a base peak at  $m/z = 45$  that corresponds to loss of 43 units (a propyl group). 2-Pentanol has a propyl branch that could be lost as a radical by  $\alpha$ -cleavage.



When unknown compounds come from a chemical reaction, use what you know about the reaction as a starting point for postulating structures.

- 12.38 (b) 2-Methoxybutane, molecular mass = 88, can lose either a methyl group (15 mass units) or an ethyl group (29 mass units) by  $\alpha$ -cleavage. Such losses would give rise to peaks at  $m/z = 73$  and  $m/z = 59$ , respectively. The ethyl group is lost preferentially because of the relative stability of the ethyl versus the methyl radical.



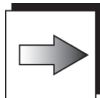
- 12.40 Follow the procedure used in the solution to Problem 12.39, except that the relative abundances are those of the chlorine isotopes.

	Cl #1	Cl #2	
$m/z = 84$	35	35	relative probability = $(0.7577)^2 = 0.574$
$m/z = 86$ }	35	37	relative probability = $(0.7577)(0.2423) = 0.184$
	37	35	relative probability = $(0.2423)(0.7577) = 0.184$
			total relative probability <span style="float: right;">0.368</span>
$m/z = 88$	37	37	relative probability = $(0.2423)^2 = 0.059$



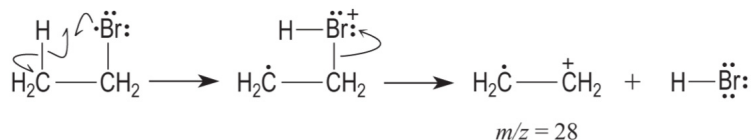
Taking the peak at  $m/z = 84$  as 100%, the ratios of the peaks are 100%, 64.1%, and 10.3%, respectively.

- 12.41 (b) The abundance of the  $M + 1$  peak relative to the  $M$  peak is  $2.5/37$ , or 0.068. At 0.011 per carbon, this accounts for six carbon atoms, or 72 mass units. It is given that the remaining mass is due to hydrogen. Therefore the formula is  $C_6H_{10}$ .



The use of isotopic peaks was once important in determining formulas. However, this has been supplanted by the use of *exact masses*, discussed on text p. 569. Typically, a formula of each peak is provided to the investigator as part of the output of a typical mass spectrometer. The use of exact masses was made possible by the advent of high-resolution mass spectrometers.

- 12.42 (b) The ion with  $m/z = 108$  is the molecular ion containing the lighter bromine isotope, and it is formed by the process shown in part (a).  
 (d) The ion with  $m/z = 79$  is the bromine cation formed from the molecular ion containing the lighter bromine isotope, and it is formed by the mechanism shown in part (c).  
 (f) The ion with  $m/z = 28$  is an odd-electron ion formed from the molecular ion by hydrogen transfer followed by loss of  $HBr$ :



- 12.43 The presence of an odd number of nitrogens in a molecule containing, as the other atoms, any combination of C, H, O, and halogen reverses the odd-electron/even-electron mass correlations in Sec. 12.6C on text p. 563 because such a molecule must have an odd molecular mass. (Molecules containing no nitrogen or an even number of nitrogens have even molecular masses.)
- (c) A fragment ion of odd mass containing a single nitrogen must be an odd-electron ion.



# Chapter 13

## Nuclear Magnetic Resonance Spectroscopy

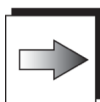
### Solutions to In-Text Problems

- 13.1 (b) Use the same equation and solve for **B**:

$$\nu = 900 \times 10^6 \text{ Hz} = \frac{\gamma_{\text{H}}}{2\pi} \mathbf{B} = \frac{26,753 \text{ rad gauss}^{-1} \text{ sec}^{-1}}{2\pi \text{ rad}} \mathbf{B}$$

Solving,

$$\mathbf{B} = 211,373 \text{ gauss}$$



Because  $\nu$  and **B** are proportional, we could also have used the result of the last part and multiplied the value of **B** in the last part by the ratio of frequencies (= 900 MHz/500 MHz).

- 13.2 (b) Following the procedure used in part (a),

$$\mathbf{B}_b - \mathbf{B}_{\text{TMS}} = (10^{-6})(3.35 \text{ ppm})(\mathbf{B}_0) = 0.24 \text{ gauss}$$

- 13.3 The greater the chemical shift, the *less shielded* are the protons. Therefore, the protons at  $\delta$  5.5 are least shielded, and those at  $\delta$  1.3 are the most shielded.

- 13.5 (a) Subtract the two chemical shifts in ppm and apply Eq. 13.1. That is,

$$\text{chemical-shift difference} = \delta_2 - \delta_1 = \frac{\Delta\nu}{\nu_0} = \frac{45}{60} = 0.75 \text{ ppm}$$

- (b) Using the procedure from part (a) gives

$$\text{chemical-shift difference} = 45/300 = 0.15 \text{ ppm.}$$

- 13.6 Parts (a)–(c) are answered in the text discussion that follows the problem (p. 587).

- (d) Because Si is more electropositive (less electronegative) than any of the other atoms in the table, hydrogens near the Si are *more shielded*. Because chemical shift decreases with increased shielding, this means that  $(\text{CH}_3)_4\text{Si}$  has a smaller chemical shift. A derivative  $(\text{CH}_3)_x\text{M}$ , in which M is an element more electropositive than Si, should have a negative chemical shift.  $(\text{CH}_3)_2\text{Mg}$  and  $(\text{CH}_3)_4\text{Sn}$  are two of several possible correct answers.

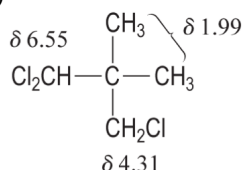
- 13.7 (a) The order is  $C < B < A$ . The protons of methylene chloride (dichloromethane,  $\text{CH}_2\text{Cl}_2$ ) have the greatest chemical shift, because chlorine is more electronegative than iodine. The chemical shift of methylene iodide is greater than that of methyl iodide because two iodines have a greater chemical shift contribution than one.

- 13.8 (b) Because protons  $\text{H}^a$  and  $\text{H}^b$  are constitutionally nonequivalent, their chemical shifts are different.  
(d) Because protons  $\text{H}^a$  and  $\text{H}^b$  are enantiotopic, their chemical shifts are identical.

- 13.9 The question asks essentially how many chemically nonequivalent sets of protons there are in each case.

- (b) This compound has two chemically nonequivalent sets of protons; hence, its NMR spectrum consists of two resonances.

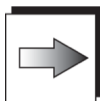
13.10 (b)



- 13.12 (b) The  $(\text{CH}_3)_3\text{CBr}$  impurity in  $\text{CH}_3\text{I}$  is more easily detected, because a given mole fraction of  $(\text{CH}_3)_3\text{CBr}$  gives a resonance that is three times as strong as the resonance for the same amount of  $\text{CH}_3\text{I}$ , as the solution to part (a) of this problem demonstrated.

13.13 In the following discussions, the integral is not mentioned. It corresponds to the number of protons under observation in each case.

- (b) The protons of the  $\text{ClCH}_2-$  group would be a doublet at  $\delta 4.2$  or higher. The protons of the  $-\text{CHCl}_2$  group would be a triplet at considerably greater chemical shift. This chemical shift would be similar to, and probably somewhat greater than, the chemical shift of the  $-\text{CHCl}_2$  protons in part (a). (The greater shift would be caused by the  $\beta$  chlorine.)
- (d) This compound, 1,3-dimethoxypropane, should have three resonances. The methylene resonances for the boldfaced protons  $\text{CH}_3\text{OCH}_2\text{CH}_2\text{CH}_2\text{OCH}_3$  should be a triplet in the  $\delta 3.5$  region, because there are two neighboring protons. The central  $-\text{CH}_2-$  should be a quintet (a five-line pattern), because there are four neighboring protons. This would normally be in the  $\delta 1.0$  region, but should appear at somewhat greater chemical shift, perhaps around  $\delta 1.8$ , because of the  $\beta$ -oxygens. The methyl groups should be one large singlet near  $\delta 3.2$ .
- (f) The spectrum of this compound consists of two singlets. The  $-\text{CH}_2-$  resonance occurs at a chemical shift greater than  $\delta 4.2$  (because of the  $\beta$ -chlorine), and the methyl groups should appear in the  $\delta 0.7$ – $1.7$  region, probably towards the higher end because of the chlorines.



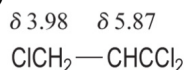
More precise estimates of chemical shift can be made using the methods discussed in Further Exploration 13.1 on p. 259 of the Study Guide and Solutions Manual.

- 13.14 There are four possibilities for the spin of three neighboring equivalent protons  $b$ ; these are shown in the following table. There are three ways in which two spins can be the same. This table shows that the resonance for protons  $a$  would be split by the three protons  $b$  into a quartet whose lines are in the intensity ratio 1:3:3:1.

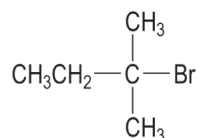
	$b$ protons											
	1	2	3	1	2	3	1	2	3			
	all (+)			two (+), one (-)			one (+), two (-)			all (-)		
spin combinations	$+\frac{1}{2}$	$+\frac{1}{2}$	$+\frac{1}{2}$	$+\frac{1}{2}$	$+\frac{1}{2}$	$-\frac{1}{2}$	$+\frac{1}{2}$	$-\frac{1}{2}$	$-\frac{1}{2}$	$-\frac{1}{2}$	$-\frac{1}{2}$	$-\frac{1}{2}$
	$+\frac{1}{2}$	$-\frac{1}{2}$	$+\frac{1}{2}$	$-\frac{1}{2}$	$+\frac{1}{2}$	$+\frac{1}{2}$	$-\frac{1}{2}$	$+\frac{1}{2}$	$-\frac{1}{2}$	$-\frac{1}{2}$	$-\frac{1}{2}$	$-\frac{1}{2}$
		$-\frac{1}{2}$	$+\frac{1}{2}$	$+\frac{1}{2}$	$-\frac{1}{2}$	$-\frac{1}{2}$	$+\frac{1}{2}$	$-\frac{1}{2}$	$+\frac{1}{2}$			

- 13.15 (b) This candidate would also be expected to have *eight* nonequivalent sets of protons. (Can you find them all?) This would also not show two triplets, and there should be four methoxy singlets (three if the two diastereotopic ones accidentally overlapped), but certainly not two.

13.16 (b)

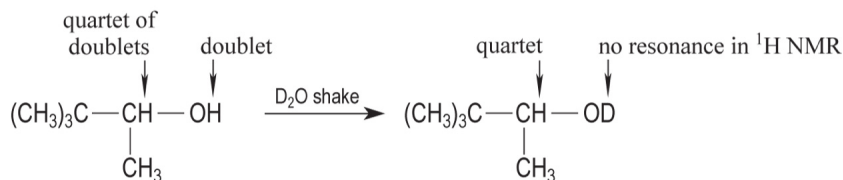


- 13.20 (a) Because protons  $H^b$  and  $H^c$  are diastereotopic, they are chemically nonequivalent; therefore, counting the methyl group, there are four chemically nonequivalent sets of protons. The methyl group is split into a doublet by  $H^a$ . The resonance for proton  $H^a$  is split into a quartet by the methyl protons, and each line of this quartet is split into a triplet by  $H^b$  and  $H^c$ , to give a “quartet of triplets,” or twelve lines, for proton  $H^a$ . (The triplet is the result of two overlapping doublets with  $J_{ab} = J_{ac}$ ; see Fig. 13.11 on text p. 606 for a related case.) Because  $H^b$  and  $H^c$  are diastereotopic, they absorb at different chemical shifts. Proton  $H^b$  is split by proton  $H^a$  into a doublet, and each line of this doublet is split into another doublet by  $H^c$ . Therefore, proton  $H^b$  is a doublet of doublets, or four equally intense lines. The same is true of  $H^c$ —its resonance will be four equally intense lines at a slightly different chemical shift from the resonance of  $H^b$ . Several of these patterns may overlap to create a very complex-looking spectrum.
- 13.21 (a) Compound *B*, from the chemical shifts, has no hydrogens  $\alpha$  to the bromine. Hence, this is a tertiary alkyl halide. We see two methyl singlets and an ethyl quartet, which determine the structure.



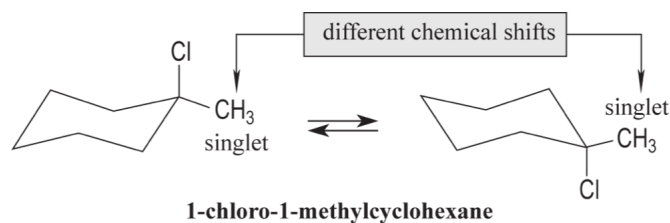
2-bromo-2-methylbutane

- 13.23 (b) Assuming that in the absence of  $\text{D}_2\text{O}$ , the sample is very dry, the spectrum of 1,2,2-trimethyl-1-propanol would change as follows as the result of a  $\text{D}_2\text{O}$  shake:

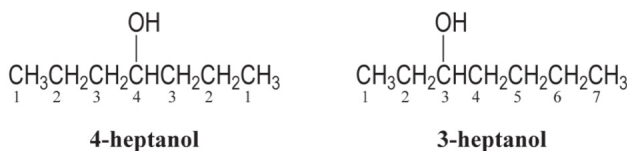


(A “quartet of doublets” can also be referred to as a “doublet of quartets.”)

- 13.26 The spectrum of ethyl chloride would resemble that of ethyl bromide (Fig. 13.6, text p. 596). It would consist of a typical ethyl pattern—a triplet (for the  $\text{CH}_3$ ) and a quartet (for the  $\text{CH}_2$ ), except that the quartet for the  $\text{CH}_2$  in the ethyl chloride spectrum would be at a somewhat greater chemical shift than it is in ethyl bromide. In ethyl fluoride, the resonance of the methyl group would be a *triplet of doublets*. (Splitting by the  $\text{CH}_2$  group gives three lines; each of these are split into two by the fluorine for a total of six.) The resonance of the  $\text{CH}_2$  group would be a *doublet of quartets*. (Splitting by the fluorine gives a widely spaced doublet; each line of the doublet is split into a quartet by the  $\text{CH}_3$  group.) The chemical shift of the  $\text{CH}_2$  resonance in ethyl fluoride would be expected to be somewhat greater than that of the  $\text{CH}_2$  group in ethyl chloride.
- 13.27 (a) The unknown is *tert*-butyl alcohol,  $(\text{CH}_3)_3\text{C}-\text{OH}$ . Notice the absence of an  $\alpha$ -proton.
- 13.29 The resonance for the methyl group at room temperature is a singlet. When the temperature is lowered, the resonance of this methyl group should consist of two singlets, one for the conformation of 1-chloro-1-methylcyclohexane in which the methyl group is axial, and one for the conformation in which the methyl group is equatorial. The relative integrals of the two singlets will be proportional to the relative amounts of the two conformations. Because chlorine and methyl are about the same size, there should be about equal amounts of the two conformations.

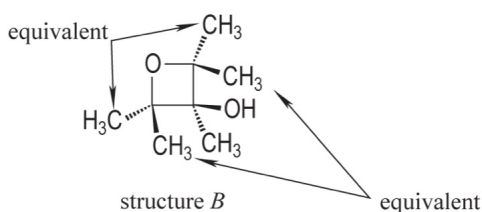


- 13.30 Because of its symmetry, 4-heptanol has only four chemically nonequivalent sets of carbons, and hence its spectrum consists of four lines, and is therefore spectrum 1. All of the carbons of 3-heptanol are chemically nonequivalent; hence, the  $^{13}\text{C}$  NMR spectrum of this compound consists of seven lines, and is therefore spectrum 2. The following structures show equivalent carbons with the same numbers.



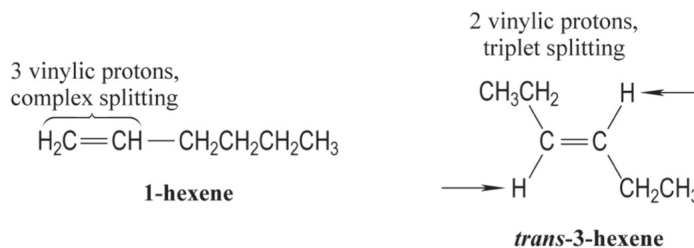
- 13.32 (b) This compound should have a  $^{13}\text{C}$  NMR spectrum with three lines, as observed. Furthermore, the attached hydrogen ratio is also consistent with this structure. What is *not* consistent, however, is the chemical shift information. The  $\delta$  112.9 resonance suggests a carbon bound to *more than one* oxygen. In this structure, no carbon is bound to more than one oxygen, whereas in the correct structure, the methine (CH) carbon is bound to three oxygens.
- 13.34 It would be easy to believe that the methyl groups of *A* could account for the twelve-proton singlet at  $\delta$  1.22, and the two OH groups for the two-proton exchangeable resonance at  $\delta$  1.96; but this leaves no hydrogens to account for the  $\delta$  1.57 resonance. In other words, structure *A* has two nonequivalent sets of hydrogens, whereas the NMR spectrum indicates at least three. Structure *A* also has two nonequivalent sets of carbons, whereas the  $^{13}\text{C}$  NMR spectrum indicates three.

Structure *B* is ruled out by its molecular formula, which is  $\text{C}_8\text{H}_{16}\text{O}_2$ . But the NMR spectrum is also not consistent with structure *B*, which should have two methyl singlets, each integrating for  $6H$ , and one methyl singlet integrating for  $3H$ , along with one exchangeable OH proton. Although it would have the required three resonances, the integration ratio (6:3:1) is different from that observed (12:4:2 or 6:2:1). This difference is well within the ability of the spectrometer to differentiate. But the  $^{13}\text{C}$  NMR is even more definitive. Structure *B* has five nonequivalent sets of carbons, whereas the  $^{13}\text{C}$  NMR spectrum indicates three sets. Even if the methyl resonances overlapped accidentally, which is unlikely, the attached-hydrogen analysis for *B* would predict no carbon with two attached protons.

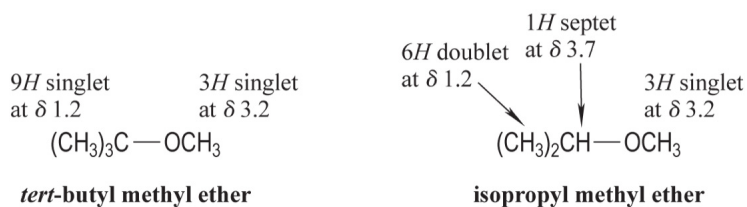


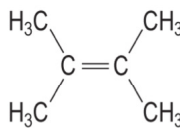
### Solutions to Additional Problems

- 13.36 (b) Only 1-hexene will have a complex vinylic proton absorption that integrates for 25% of the total absorption (that is, 3 protons); the vinylic proton absorption of *trans*-3-hexene will consist of a triplet integrating for 17% of the total absorption (that is, 2 protons).



- (d) The spectrum of *tert*-butyl methyl ether consists of two singlets; that of isopropyl methyl ether contains a singlet for the methoxy group, but a more complex doublet-septet pattern for the isopropyl group.



- 13.38 (b)  **2,3-dimethyl-2-butene**
- (d)  $(\text{CH}_3)_3\text{C}-\text{CH}_2-\text{C}(\text{CH}_3)_3$   
**2,2,4,4-tetramethylpentane**

- 13.39 (b) The compound is cyclopentane. (2,3-Dimethyl-2-butene would not be a bad answer; see the solution to Problem 13.38b. However,  $\delta$  1.5 is somewhat low for a chemical shift of the allylic methyl groups.)

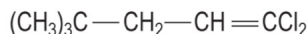


**cyclopentane**

- (f) First, convert the integrals into actual numbers of hydrogens:

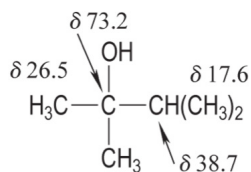
$$\delta 1.07 (9H, s); \delta 2.28 (2H, d, J = 6 \text{ Hz}); \delta 5.77 (1H, t, J = 6 \text{ Hz}).$$

The compound has one degree of unsaturation and a *tert*-butyl group. This, plus the requirement for two chlorines and a partial structure  $\text{CH}_2-\text{CH}$  required by the splitting leaves only the following possibility:



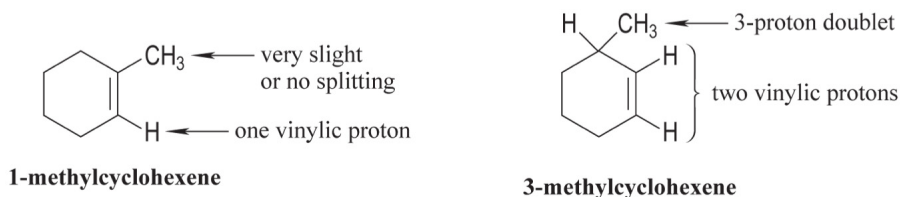
**1,1-dichloro-4,4-dimethyl-1-pentene**

- (h) The compound is  $\text{F}_3\text{C}-\text{CH}_2-\text{I}$  (1,1,1-trifluoro-2-iodoethane). The splitting of the protons is caused by the fluorines.
- (j) The  $\text{D}_2\text{O}$  exchange indicates an alcohol, which must be tertiary, because of the absence of a resonance in the  $\delta$  3–4 region. The  $^{13}\text{C}$  NMR spectrum indicates that there are four nonequivalent sets of carbons. The doublet-septet pattern indicates an isopropyl group, and the 6-proton singlet indicates two methyl groups. The compound, with assigned  $^{13}\text{C}$  NMR chemical shifts, is

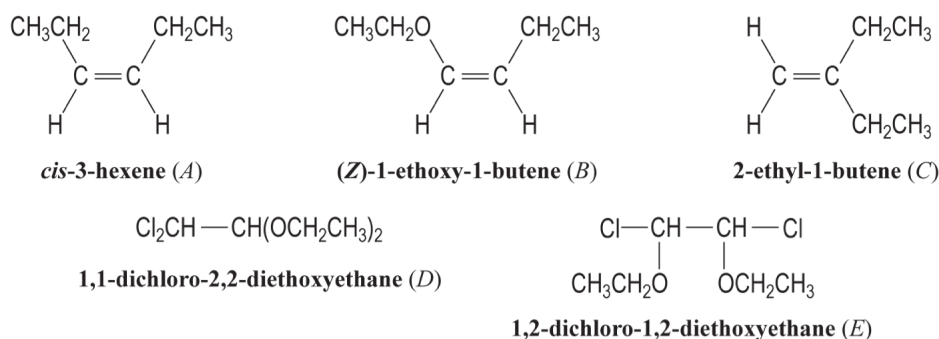


2,3-dimethyl-2-butanol

- 13.41 The most obvious difference is that the spectrum of 1-methylcyclohexene should show *one* vinylic proton and a three-proton singlet (neglecting any allylic splitting); whereas the spectrum for 3-methylcyclohexene should show *two* vinylic protons and a three-proton doublet.



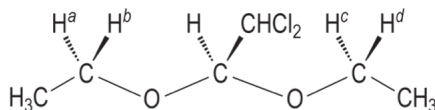
- 13.42 (b) All methyl groups are homotopic; all methine carbons are homotopic; and all methylene carbons are homotopic. (Prove this by a substitution test if this isn't clear.) Each carbon of one type is constitutionally nonequivalent to all carbons of other types. Consequently, the  $^{13}\text{C}$  NMR spectrum of this compound should consist of three resonances.
- 13.43 (a) The NMR spectrum of the first compound,  $(\text{CH}_3)_2\text{CH}-\text{Cl}$  (isopropyl chloride), should consist of the doublet-septet pattern characteristic of isopropyl groups, with the doublet at about  $\delta$  1.2 and the septet at about  $\delta$  3.7. The NMR spectrum of the deuterium-substituted analog,  $(\text{CH}_3)_2\text{CD}-\text{Cl}$ , should consist of a singlet at essentially the same chemical shift as the doublet in the first compound. (The splitting between H and D nuclei on adjacent carbons is nearly zero.)
- 13.45 The spectrum shows at least four nonequivalent sets of protons in the ratio 1:1:4:6. Let's see how the possible structures stack up against this analysis.



Compounds A–C are ruled out immediately. The vinylic hydrogens in A would be a single triplet. In compound B, there would be two methyl triplets and a more complex splitting for the two vinylic hydrogens. In compound C, the vinylic hydrogens would be a singlet (neglecting allylic splitting). The two methine hydrogens of D would definitely give a pair of doublets at fairly high chemical shift, as observed. The two methine hydrogens of E are completely equivalent and would give a singlet as the absorption at greatest chemical shift. Therefore, compound E is ruled out, and compound D is the remaining possibility.

As to the complexity of the  $\delta$  3.7 resonance, the two  $\text{CH}_2$  hydrogens in either ethyl group on both D and E are *diastereotopic*, and hence, chemically nonequivalent. For example, in the case of D,





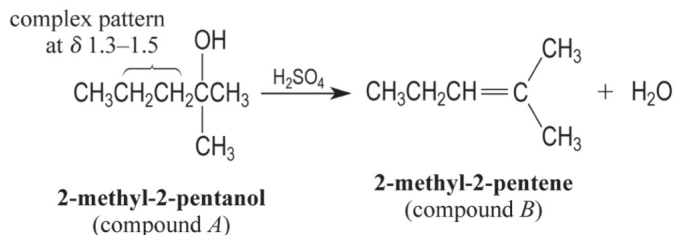
$H^a$  and  $H^b$  are diastereotopic;  $H^c$  and  $H^d$  are also diastereotopic. On the other hand,  $H^a$  is enantiotopic to  $H^c$ , and  $H^b$  is enantiotopic to  $H^d$ . (You should verify these statements by a substitution test.) Therefore,  $H^a$  and  $H^c$  are chemically equivalent, as are  $H^b$  and  $H^d$ . But  $H^a$  and  $H^b$  are chemically *nonequivalent*, as are  $H^c$  and  $H^d$ . Hence, there are *five* nonequivalent sets of hydrogens. It is perhaps not surprising that the chemical shifts of the diastereotopic protons are not very different, because their chemical environments are very similar.

Let's now consider the splitting patterns of these diastereotopic protons. We've already said that  $H^a$  and  $H^b$  occur at slightly different chemical shifts. This would account for two absorptions. Each of these is split into a doublet by the other to give four lines. Each of these is split into a quartet by the neighboring methyl group. This gives  $4 \times 4 = 16$  lines. Because  $H^c$  is chemically equivalent to  $H^a$ , and  $H^d$  is chemically equivalent to  $H^b$ , the analysis is complete. You can actually see all sixteen lines for these diastereotopic hydrogens in the spectrum.

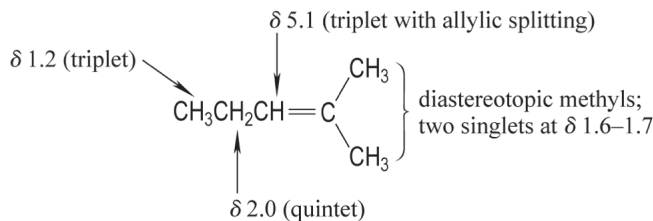
- 13.47 (b) The reason the  $^{13}\text{C}$  NMR spectrum of  $\text{CDCl}_3$  is a 1:1:1 triplet is the same reason that the proton NMR spectrum of  $^+\text{NH}_4$  is a 1:1:1 triplet [see part (a)]: deuterium, like nitrogen, can have spins of +1, 0, and -1, and deuterium splits  $^{13}\text{C}$  resonances just as it splits proton signals.
- 13.48 The IR spectrum and the  $\text{D}_2\text{O}$  shake results indicate that compound *A* is an alcohol, and the absence of a resonance in the  $\delta$  3–4 region indicates that the alcohol is tertiary. Treatment of compound *A* with  $\text{H}_2\text{SO}_4$  yields a compound *B*, which, from its  $\delta$  5.1 resonance in its NMR spectrum, is evidently an alkene. Evidently, the reaction with  $\text{H}_2\text{SO}_4$  is a dehydration. If so, the molecular mass of 84 for compound *B* means that compound *A* has the molecular mass of compound *B* plus 18 (the molecular mass of  $\text{H}_2\text{O}$ ). Hence, the molecular mass of *A* is  $84 + 18 = 102$ .

Now let's turn to the integral for compound *A*. The integrals (from high to low shift) are in the approximate ratio 1:4:6:3. Let's adopt the hypothesis that the O—H proton accounts for 1*H*. If so, then compound *A* contains 14 hydrogens, and its formula is  $\text{C}_6\text{H}_{14}\text{O}$ , which gives the molecular mass of 102 hypothesized above. Why couldn't the alcohol have a formula  $\text{C}_7\text{H}_{14}\text{O}$ ? Because this would give the wrong molecular mass.

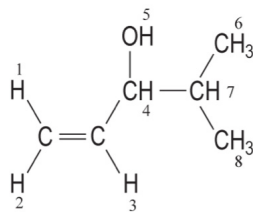
In the NMR of compound *A*, the singlet at  $\delta$  1.2 integrates for 6*H*. This can only be two methyl groups. The triplet just below  $\delta$  1.0 integrates for 3*H*, and, from its splitting, corresponds to a  $\text{CH}_3\text{CH}_2$ — group. However, the methylene protons in this group must be split by other protons because they are not a simple quartet. The following structure would account for the complex splitting at  $\delta$  1.4, as well as the other facts:



The dehydration would then give compound *B* shown above. In the NMR of this compound we expect a single vinylic proton split into a triplet, and this is what is observed at  $\delta$  5.1. (Some additional, very small, allylic splitting is also observed.) The NMR spectrum of compound *B* is rationalized as follows:



- 13.52 (a) As always, we first draw the structure:



**4-methyl-1-penten-3-ol**

The proton NMR spectrum of 4-methyl-1-penten-3-ol should contain eight sets of absorptions because the compound contains eight chemically nonequivalent sets of protons (numbered 1–8 in the preceding structure). Notice that protons 1 and 2 are diastereotopic and therefore chemically nonequivalent, as are protons 6 and 8.

- (b) Because all carbons are chemically nonequivalent, 4-methyl-1-penten-3-ol should have six carbon resonances in its  $^{13}\text{C}$  NMR spectrum. (Notice that the carbons of methyl groups 6 and 8 in the structure shown in part (a), like the protons of these groups, are diastereotopic.)
- 13.53 (b) Following a  $\text{D}_2\text{O}$  shake, the resonance of proton 1 should disappear; and the resonance of protons 2 should be the same as it is in the wet sample—that is, a triplet.

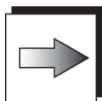
- 13.57 Shielding decreases chemical shift. Because a “naked” proton is completely *unshielded* by electrons, its chemical shift should be very large, and it should feel the full effect of the applied field. Because the range of proton chemical shifts within organic compounds extends to about 11–12 ppm (Fig. 13.4 on text p. 588), we expect the chemical shift of a “naked” proton to be even greater than this. Hence, the first answer,  $\delta > 8$ , is the correct one.

- 13.59 (b) Use Eq. 13.15 on text p. 622 with  $\gamma_n = \gamma_{\text{electron}} = 17.6 \times 10^6 \text{ radians gauss}^{-1} \text{ sec}^{-1}$ , and  $\mathbf{B}_0 = 3400 \text{ gauss}$ . We obtain

$$\nu_{\text{electron}} = \frac{\gamma_{\text{electron}} \mathbf{B}_0}{2\pi} = \frac{17.6 \times 10^6 \text{ rad gauss}^{-1} \text{ sec}^{-1}}{2\pi \text{ rad}} (3400 \text{ gauss}) = 9.5 \times 10^9 \text{ sec}^{-1} \approx 10^{10} \text{ Hz}$$

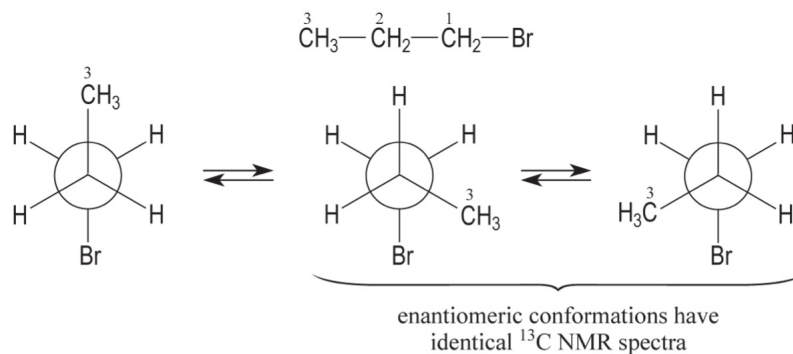
Fig. 12.2 on text p. 539 shows that a frequency of  $10^{10}$  Hz is in the microwave region of the electromagnetic spectrum. Indeed, ESR instruments employ microwave radiation to detect the magnetic resonance of electrons.

- 13.60 (b) The two lines at low temperature have different intensities because the diastereomers are present in different amounts. The intensity of each resonance is proportional to the amount of the conformation of which it is characteristic. *A priori*, if the conformations are equally probable, the resonance of the conformations with the gauche methyl groups should be twice as strong as that of the conformation with anti methyls. The actual intensities will likely differ from this 2:1 ratio in accordance with the relative stabilities of the conformations.



This answer should have been included in the Study Guide and Solutions Manual. It has been placed in the Errata and is also included here for completeness.

13.61 Number the carbons and view the Newman projection about the C1–C2 bond, with carbon-2 nearer the observer:



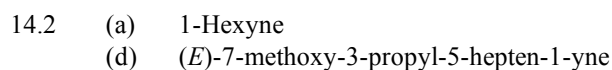
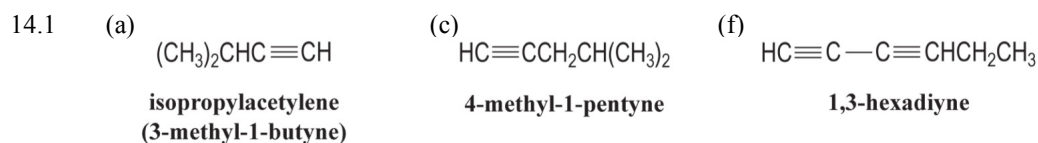
Assuming the spectrum is proton-decoupled, we would expect to see three resonances—one for each of the carbons—at room temperature. On cooling the sample, we would see two sets of three resonances. One set is due to the two enantiomeric conformations, and the other set is due to the remaining conformation. The largest chemical-shift change should be in the resonance for carbon-3, because its proximity to the bromine changes between the conformations. Smaller changes would be anticipated for carbons 1 and 2.



# Chapter 14

## The Chemistry of Alkynes

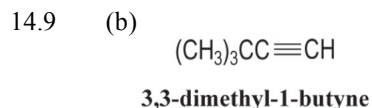
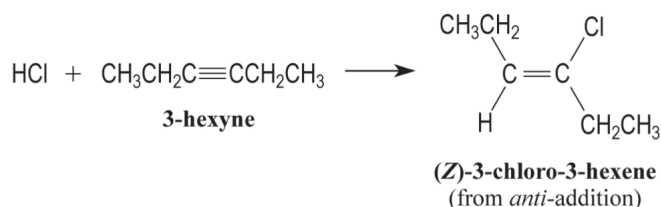
### Solutions to In-Text Problems



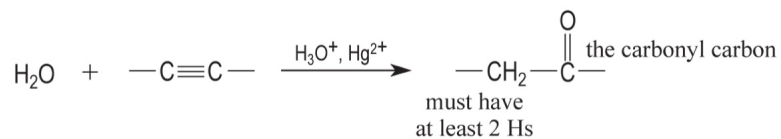
14.3 (b) Cyclodecyne is much more stable than cyclohexyne (and in fact can be isolated), because the distance of 4.1 Å referred to in part (a) can be bridged by six carbons with reasonable bond lengths and bond angles.

14.6 The proton NMR spectrum of propyne should consist of two resonances. Evidently, the two happen to have the same chemical shift of  $\delta$  1.8, which is in fact a reasonable chemical shift for both acetylenic and propargylic protons.

14.8 The product is (*Z*)-3-chloro-3-hexene:

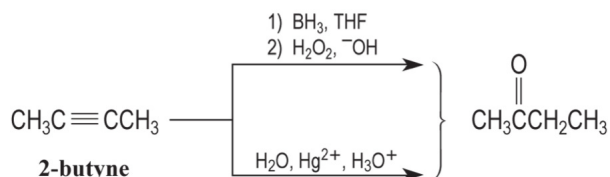


14.10 (b) Hydration can only be used to prepare ketones that have at least two hydrogens on the carbon  $\alpha$  (that is, adjacent) to the carbonyl carbon:

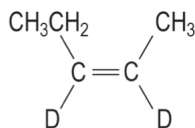


The ketone shown does not fulfill this requirement.

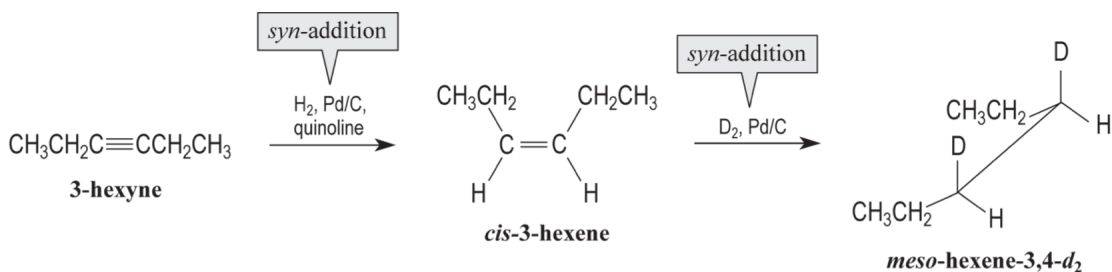
14.12 (b) Because it is symmetrical, 2-butyne gives the same product in the two reactions:



- 14.13 (b) The product is the alkane octane,  $\text{CH}_3(\text{CH}_2)_6\text{CH}_3$ .  
 (d) The product is the alkene that results from *syn*-addition of  $\text{D}_2$ :

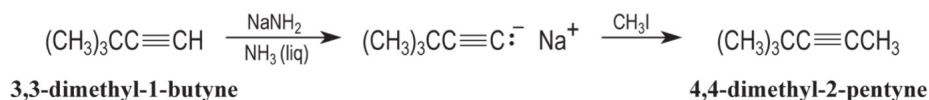


- 14.14 (b) The first reaction is a *syn*-addition that gives *cis*-3-hexene; the second is another *syn*-addition that gives *meso*-hexane-3,4- $d_2$ .

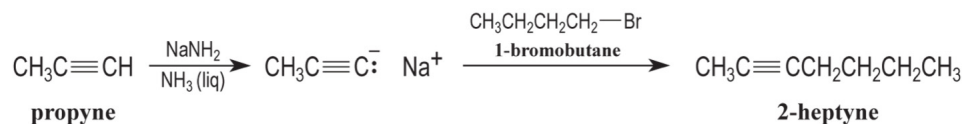


- 14.17 (a) The  $\text{p}K_a$  of ammonia is about 35 (which indicates the basicity of the amide ion), and that of an alkyne acetylenic hydrogen is about 25 (Eq. 14.20, text p. 663). Use the method described in Eq. 3.25b, text p. 104, to find that the  $K_{\text{eq}}$  for Eq. 14.22 is about  $10^{+10}$ . With the  $\text{p}K_a$  of an alkane taken as 55, the  $K_{\text{eq}}$  for the reaction of the amide base with an alkane is about  $10^{-20}$ .  
 (b) As the calculation in part (a) shows, the reaction of sodium amide with an alkane is quite unfavorable. For that reason, this base cannot be used to form the conjugate-base anions of alkanes.
- 14.18 (a) This is an  $\text{S}_{\text{N}}2$  reaction of the anion with ethyl iodide to give 2-pentyne,  $\text{CH}_3\text{C}\equiv\text{CCH}_2\text{CH}_3$ , plus sodium iodide,  $\text{Na}^+ \text{I}^-$ .  
 (d) Sodium acetylide reacts with both alkyl halide groups to give a 1,8-nonadiyne,  $\text{HC}\equiv\text{C}(\text{CH}_2)_5\text{C}\equiv\text{CH}$ , plus two equivalents of sodium bromide,  $\text{Na}^+ \text{Br}^-$ .

- 14.20 The preparation involves the reaction of 3,3-dimethyl-1-butyne with sodium amide, then with methyl iodide.

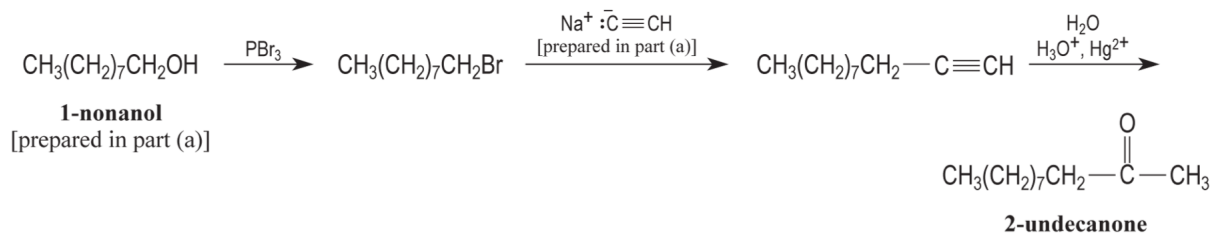


- 14.22 As in the solution to Problem 14.21, either alkyl group can be introduced by the reaction with an alkyl halide. The alternative to Eq. 14.28 is to use the acetylenic anion derived from propyne followed by alkylation with 1-bromobutane.



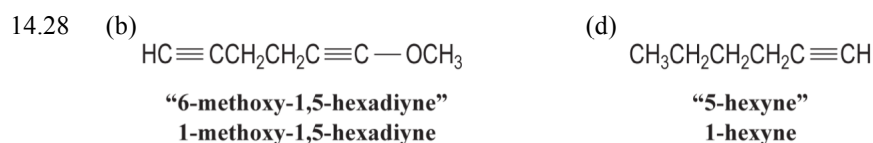
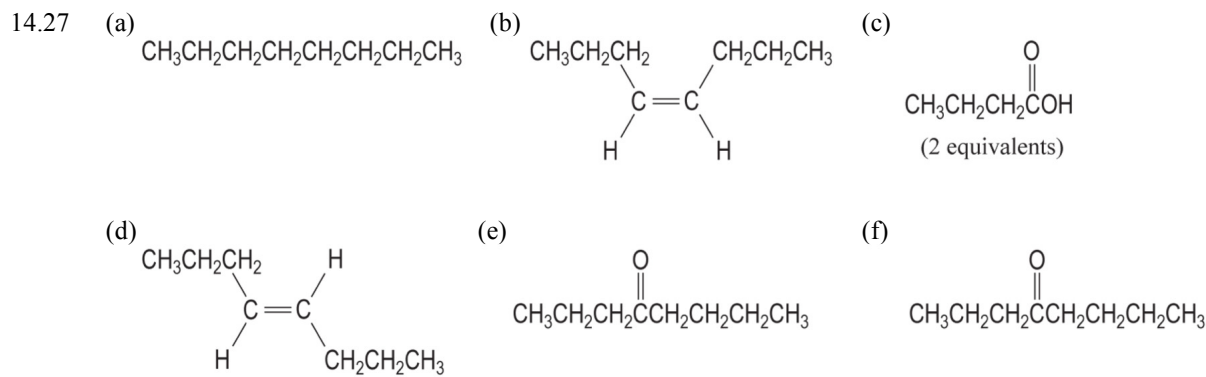
However, the reaction shown in Eq. 14.28 is probably superior because  $\text{CH}_3\text{Br}$  is the more reactive alkyl halide.

- 14.23 (b) A synthesis of 2-undecanone from compounds containing five or fewer carbons:

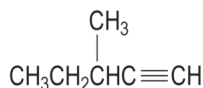


- 14.25 Catalytic hydrogenation with a Lindlar catalyst should bring about hydrogenation of the alkyne to a cis-alkene group without affecting the existing alkene.

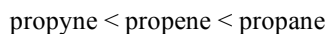
## Solutions to Additional Problems



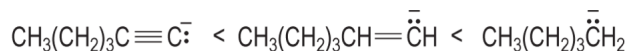
14.29 (b) Either the cis or the trans isomer of the cyclopropane derivative in part (d) is a satisfactory answer. Another is



14.30 (b) Hybridization affects the lengths of C—C bonds in the same way that it affects the lengths of C—H bonds. Therefore, the lengths of C—C bonds increase in the following order:



14.31 (b) Because alkynes are more acidic than alkenes, which are more acidic than alkanes, the acetylenic anion is less basic than the vinylic anion, which is less basic than the alkyl anion. Thus, the basicity order is

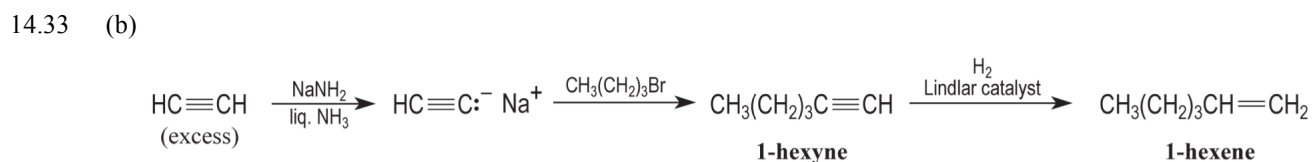


14.32 (b) Only the 1-alkyne should react with  $\text{C}_2\text{H}_5\text{MgBr}$  to release a gas (ethane).

(d) Forget about chemical tests; propyne is a gas and 1-decyne is a liquid at room temperature.



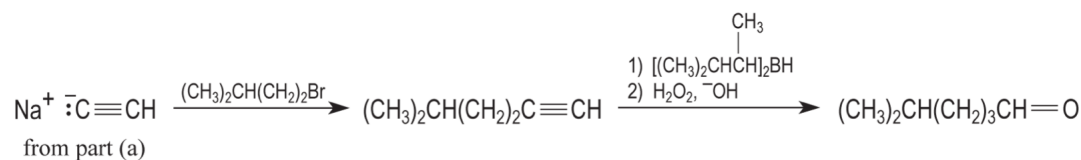
How would you know this? You know that *propane* is a gas, right? (It is used instead of natural gas in rural areas for heating or in barbecue grills as a fuel for cooking.) You also know that the presence of a double or triple bond has little effect on the physical properties of hydrocarbons. Thus, propyne is a gas also.



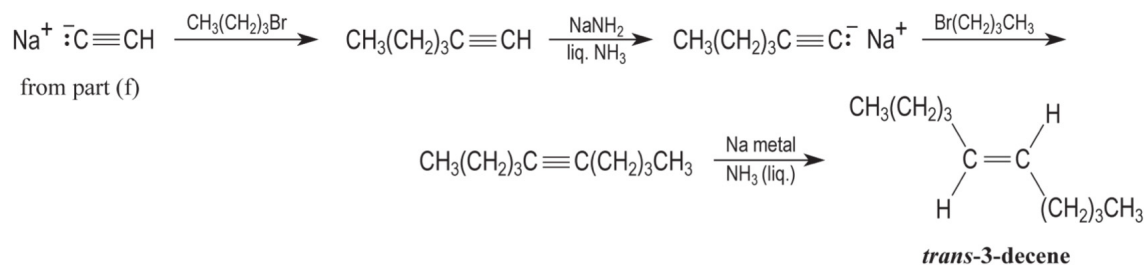
(d) 1-Hexyne was prepared in part (b).



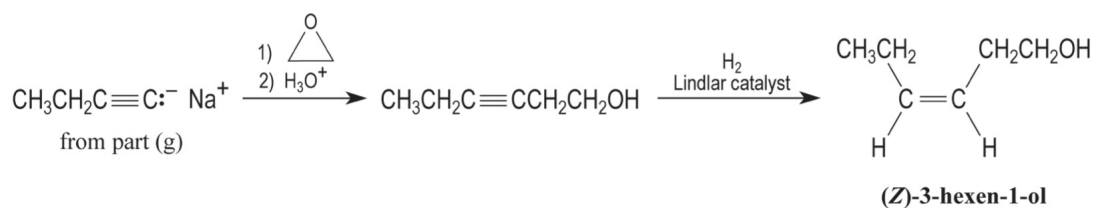
(f)



(h)



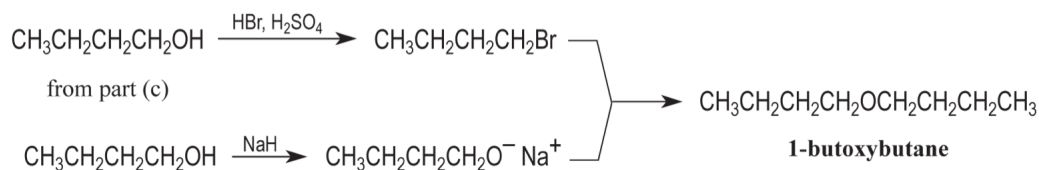
(j)



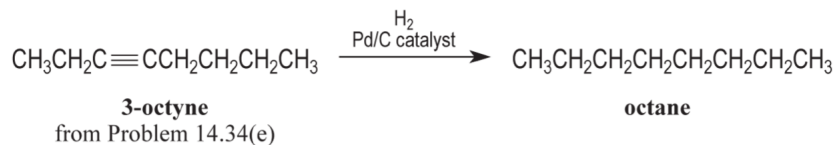
14.34 (b)



(d)

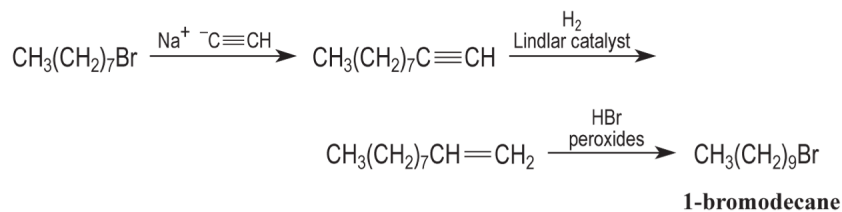


(f)

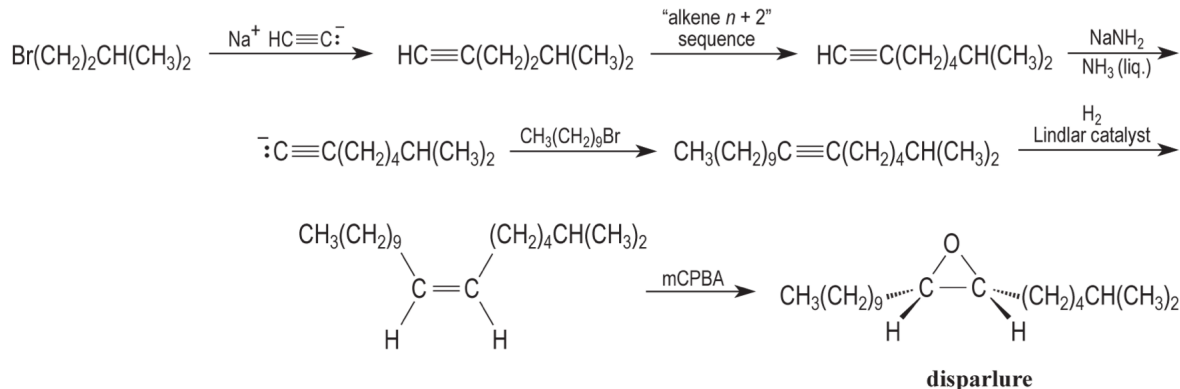


14.37 This problem is similar to the previous one. Disparlure is a *cis*-epoxide, which can be prepared by epoxidation of a *cis*-alkene. (Recall that this reaction proceeds with retention of stereochemistry; Sec. 11.2A.) The *cis*-alkene can be prepared by hydrogenation of an alkyne.

First prepare 1-bromodecane from 1-bromo-octane, which was prepared in the solution to Problem 14.36.



Next, alkylate sodium acetylide with 1-bromo-3-methylbutane (isoamyl bromide). Apply the alkyne  $n + 2$  sequence described in the previous solution, alkylate the conjugate base of the resulting alkyne with 1-bromodecane, hydrogenate, and form the epoxide to complete the synthesis.

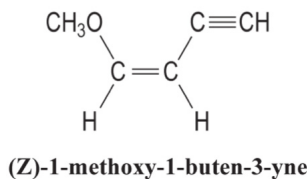


- 14.38 (b) The “anionic carbon” of one Grignard reagent acts as a base toward the C—H bond of the other.

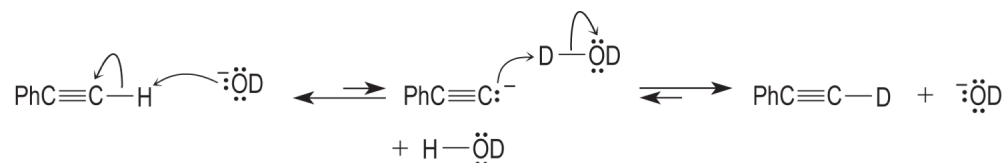


An excess of acetylene, by Le Châtelier’s principle, drives the equilibrium to the left.

- 14.40 (b) The IR data suggest a 1-alkyne, and this diagnosis is confirmed by the formation of a gas (ethane) when the compound is treated with  $\text{C}_2\text{H}_5\text{MgBr}$ . The three-proton  $\delta$  3.41 singlet suggests a methoxy group. The structure is 3-methoxypropyne,  $\text{HC}\equiv\text{CCH}_2\text{OCH}_3$ .
- (d) The IR data suggest a 1-alkyne. The presence of a methoxy group is indicated by the three-proton singlet at  $\delta$  3.79. There is one additional degree of unsaturation; because three carbons are already accounted for, the unsaturation must be in the remaining two. Consequently, there is a double bond. Cis stereochemistry is suggested by the small 6-Hz coupling constant between the vinylic protons. (See Table 13.3 on text p. 614.) The splitting suggests that one of the vinylic protons ( $\delta$  4.52) is also coupled to an acetylenic proton. The chemical shift of the other vinylic proton ( $\delta$  6.38) suggests that it is  $\alpha$  to the methoxy oxygen. All of these data conspire to give the following structure:

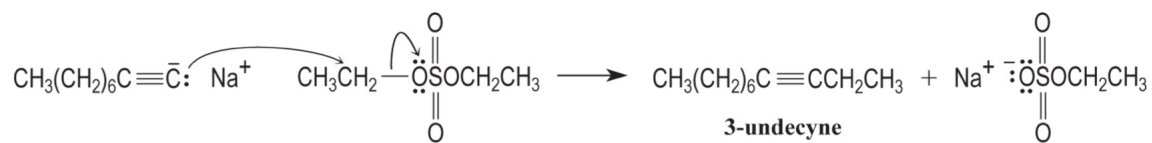


- 14.41 (b) Assuming that all resonances for chemically nonequivalent carbons are separately observable, 1-hexyne,  $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{C}\equiv\text{CH}$ , should have a CMR spectrum consisting of six resonances; 4-methyl-2-pentyne,  $(\text{CH}_3)_2\text{CHC}\equiv\text{CCH}_3$ , should have a CMR spectrum consisting of five, because two of the methyl groups are chemically equivalent.
- 14.42 (b) This mechanism consists of two successive Brønsted acid–base reactions.



14.43 The ozonolysis results define compound *B* as 1,5-hexadiene.  $\text{H}_2\text{C}=\text{CHCH}_2\text{CH}_2\text{CH}=\text{CH}_2$ . Because compound *B* is produced by hydrogenation of compound *A*, and because *two equivalents* of  $\text{H}_2$  must be added to compound *A* ( $\text{C}_6\text{H}_6$ ) to give compound *B* ( $\text{C}_6\text{H}_{10}$ ), compound *A* must be 1,5-hexadiyne,  $\text{HC}\equiv\text{CCH}_2\text{CH}_2\text{C}\equiv\text{CH}$ .

- 14.45 (a) The Grignard reagent converts 1-hexyne into the acetylenic Grignard reagent; see Eq. 14.23 on text p. 664. Protonolysis of the Grignard reagent by  $\text{D}_2\text{O}$  gives  $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{C}\equiv\text{CD}$  as the final product.
- (c) 1-Octyne is converted into its conjugate-base acetylide ion with  $\text{NaNH}_2$ . This ion is alkylated by diethyl sulfate to give 3-undecyne.





# Chapter 15

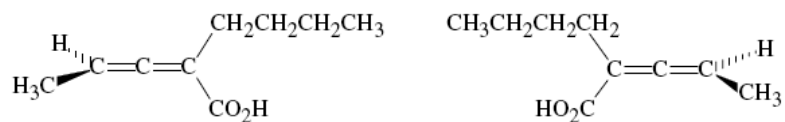
## Dienes, Resonance, and Aromaticity

### Solutions to In-Text Problems

- 15.2 The delocalization energy is the energy of each MO times the number of electrons in that MO, minus the same energy for three ethylenes:

$$\text{delocalization energy} = 2(1.80\beta) + 2(1.25\beta) + 2(0.44\beta) - (3)(2)(1.00\beta) = 0.98\beta$$

- 15.5 (a) The two enantiomers of an allene:



- (b) Because enantiomers have specific rotations of equal magnitudes and opposite signs, the other enantiomer has a specific rotation of  $+30.7^\circ$ .

- 15.6 (b) The calculation is identical to that in part (a) with different numbers:

$$E = \frac{hc}{\lambda} = \frac{(3.99 \times 10^{-13} \text{ kJ s mol}^{-1})(3.00 \times 10^8 \text{ m s}^{-1})}{250 \times 10^{-9} \text{ m}} = 479 \text{ kJ mol}^{-1}$$

(The corresponding value in  $\text{kcal mol}^{-1}$  is 114.)

- 15.7 (b) Use Eq. 15.1 on text p. 685 with  $(I_0/I) = 2$ . Thus,  $A = \log(2) = 0.30$ .

- 15.8 The piece with greater absorbance transmits less of the incident radiation. Therefore, the thick piece of glass has greater absorbance.

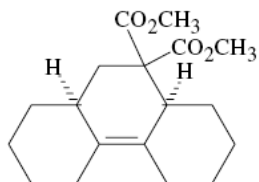
- 15.9 (b) The absorbance of the isoprene sample in Fig. 15.5 on text p. 684 at 235 nm is 0.225. With the concentration determined from part (a), Beer's law gives  $A = 0.225$  absorbance units  $= \epsilon(7.44 \times 10^{-5} \text{ mol L}^{-1})(1 \text{ cm})$ , or  $\epsilon = 3.02 \times 10^3$  absorbance units  $\text{L mol}^{-1} \text{ cm}^{-1}$ . Another way to determine the extinction coefficient at a different wavelength is based on the fact that the ratio of absorbances at different wavelengths equals the ratio of the extinction coefficients. Hence, the extinction coefficient at 235 nm is

$$\epsilon_{235} = \epsilon_{225} \frac{A_{235}}{A_{225}} = (10,750 \text{ absorbance units L mol}^{-1} \text{ cm}^{-1}) \left( \frac{0.225 \text{ absorbance units}}{0.800 \text{ absorbance units}} \right)$$

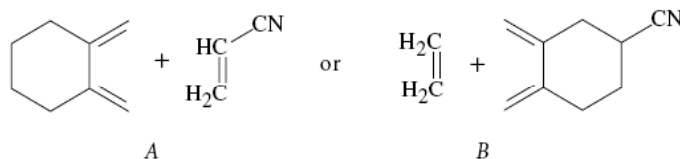
or  $\epsilon_{235} = 3.02 \times 10^3 = 3023$  absorbance units  $\text{L mol}^{-1} \text{ cm}^{-1}$ .

- 15.10 (a) The two alkyl substituents contribute +10 nm to the base  $\lambda_{\text{max}}$  of 217 for a predicted  $\lambda_{\text{max}}$  value of 227 nm.

15.11 (b)

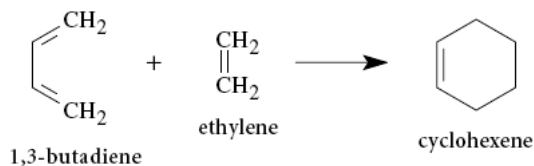


15.12 (a) An analysis like that employed in Study Problem 15.1 (text p. 692) suggests two possibilities.

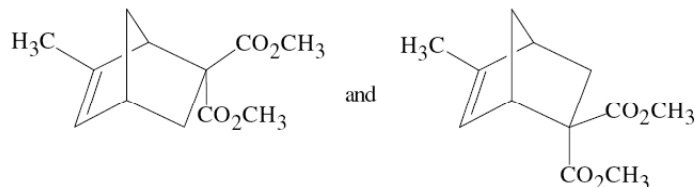
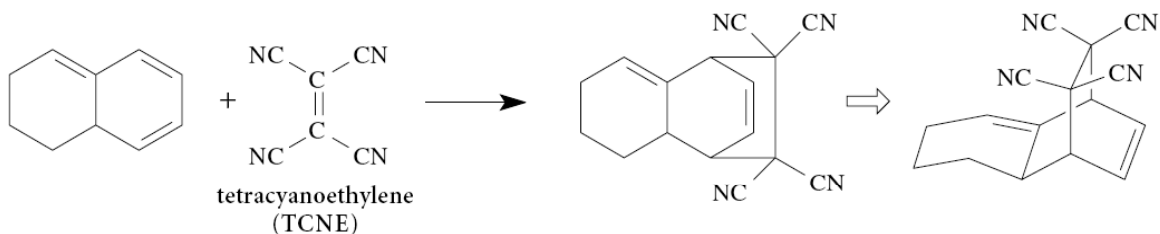


Pair *A* is preferred because, in many cases, the most reactive dienophiles are those with conjugated electronegative substituents. But if your answer was pair *B*, you have analyzed the problem correctly.

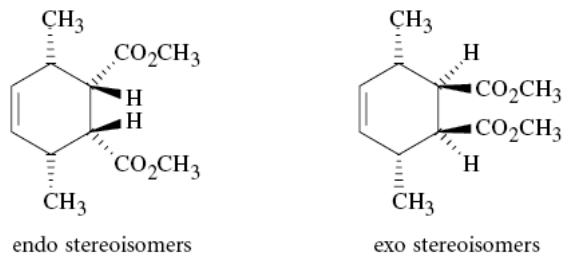
15.13 (a) With 1,3-butadiene as the diene and ethylene as the dienophile, the product would be cyclohexene.



15.14 (b) As in part (a), two possible orientations of the diene and dienophile lead to the following two possible constitutional isomers:

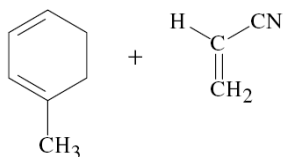
15.16 The triene contains two diene units with one double bond common to both. The dienophile reacts with the diene unit that is locked in an *s-cis* conformation.

15.17 (b) The two products correspond to the two possibilities in Eq. 15.14 on text p. 699. They result from addition of the diene at either of the two faces of the alkene (or the alkene at either of the two faces of the diene).

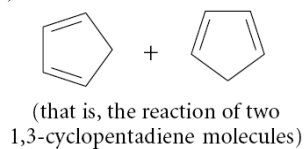


Notice that both stereoisomers result from *syn*-addition. In other words, there are *two* possible modes of *syn*-addition.

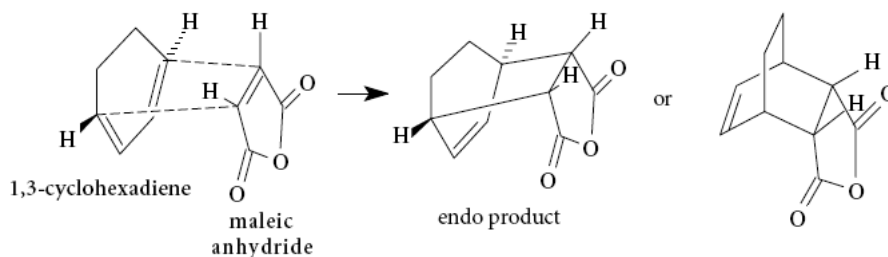
15.18 (b)



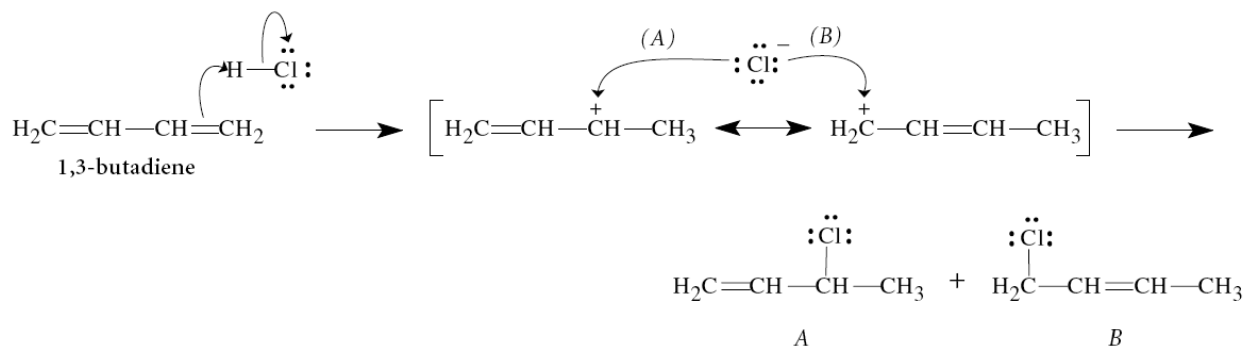
(d)



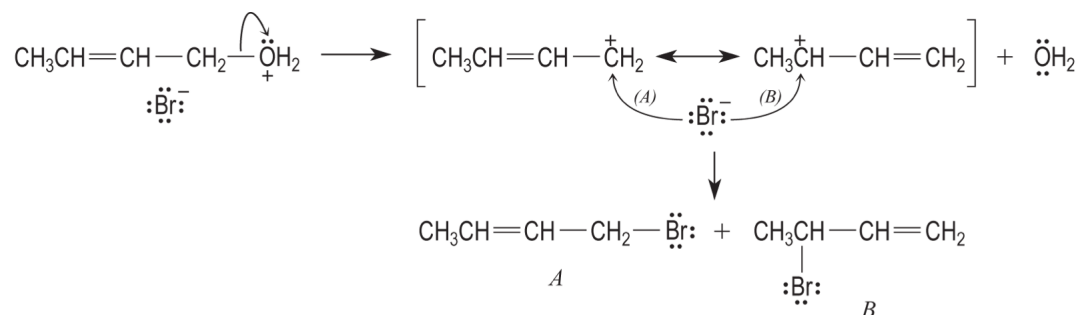
15.20 We'll use a diagram like the one in the solution to Problem 15.19:



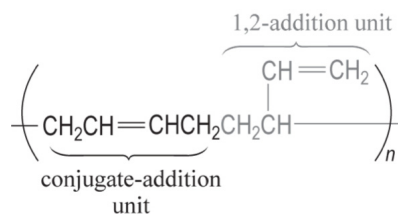
15.21 (a) The carbocation intermediate in the addition of HCl has two sites of electron deficiency, either of which can undergo a Lewis acid–base association reaction with the chloride ion.



15.22 (b) An allylic carbocation intermediate undergoes a Lewis acid–base association reaction with bromide ion at the two sites of electron deficiency.



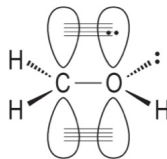
- 15.26 The structure of polybutadiene if every other unit of the polymer resulted from 1,2-addition:



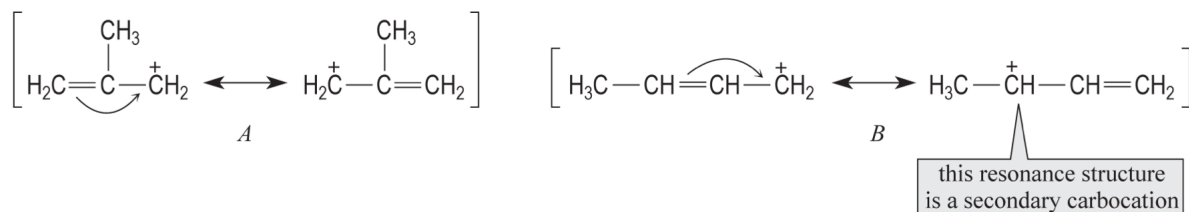
- 15.27 (b) The second structure is more important because every atom has an octet; however, the first structure has some importance because it assigns positive charge to the more electropositive atom, carbon.



- 15.28 The electron-deficient carbon has an empty  $2p$  orbital that overlaps with a filled  $2p$  orbital on the oxygen. The other oxygen electron pair in an  $sp^2$  orbital.

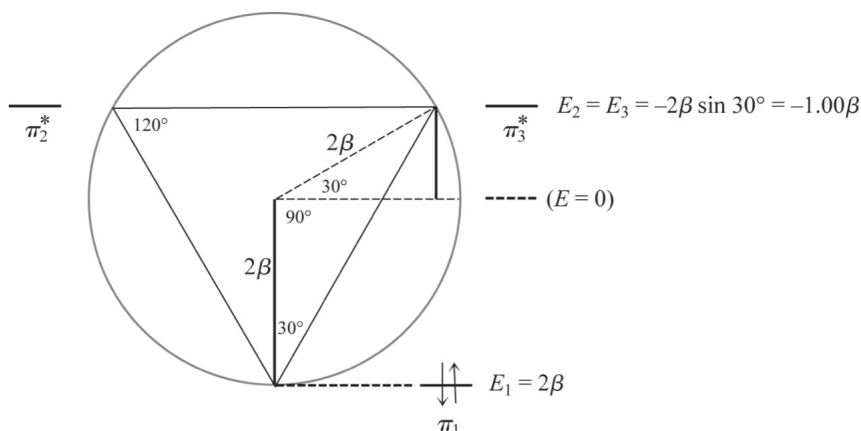


- 15.29 (c) Both ions have two resonance structures. However, the ion on the right (ion B below) is more stable because one of its resonance contributors is a secondary carbocation, whereas both contributors for the ion on the right (ion A below) are primary carbocations.



- 15.31 (b) The Frost circle construction for the cyclopropenyl cation is as follows:

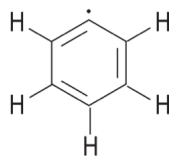




This cation contains two  $\pi$  electrons, which both occupy the bonding MO  $\pi_1$ . From Fig. 15.9, text p. 703, the  $\pi$ -electron energy of the allyl cation is  $2(1.41\beta) = 2.82\beta$ . The energy of cyclopropenyl is  $4.0\beta$ . (Remember,  $\beta$  is a negative number.) The extra stabilization,  $1.18\beta$ , is the contribution of aromaticity. (This does not take into account the destabilizing contribution of ring strain.)

- 15.34 An aromatic compound *cannot* have a single unpaired electron as part of its  $\pi$ -electron system, because the number of  $\pi$ -electrons required for aromaticity,  $4n + 2$ , must be an even number; a single unpaired electron would result in an odd number of electrons.

However, a free radical could certainly be aromatic if the unpaired electron were not part of the  $\pi$ -electron system. An example is the *phenyl radical*, which could be formed conceptually by abstraction of a hydrogen atom from benzene:



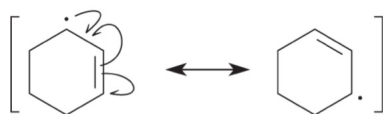
phenyl radical

However, in such a radical, the unpaired electron itself does not contribute to the aromatic stability because it is not part of the  $4n + 2$   $\pi$ -electron system.

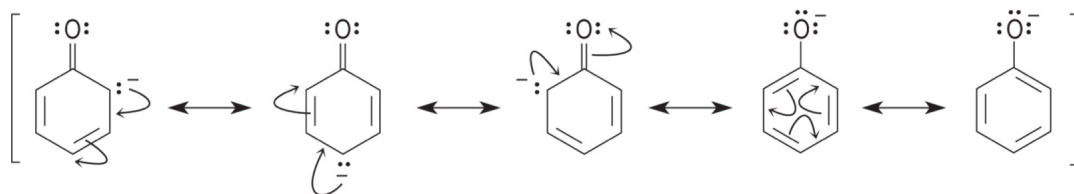
- 15.35 (b) This ion contains  $4n$ , not  $4n + 2$ ,  $\pi$  electrons, and is therefore not aromatic.  
 (d) Isoxazole is aromatic. Each double bond contributes two electrons to the  $\pi$ -electron system. One electron pair on the oxygen is also part of the  $\pi$ -electron system, but the other electron pair on the oxygen is not. (See the solution to Problem 15.33.) The electron pair on the nitrogen is vinylic and, like the electron pair in pyridine, it is not part of the  $\pi$ -electron system.  
 (f) This compound is not aromatic because it has  $4n$  rather than  $4n + 2$   $\pi$  electrons. The empty  $p$  orbital on boron, although part of the  $\pi$ -electron system, contributes no electrons.
- 15.37 Compounds (b) and (f) contain  $4n$   $\pi$  electrons and are in principle antiaromatic.

### Solutions to Additional Problems

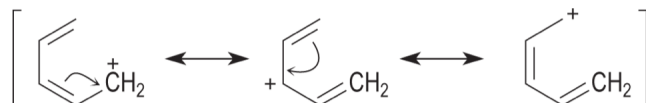
- 15.38 (b) The structures are identical; they are of equal importance.



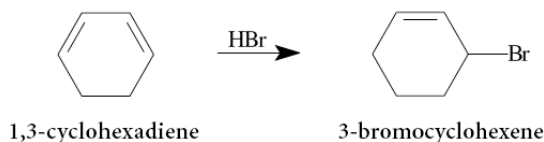
- (d) The fourth and fifth structures are most important because they are aromatic and because they have the negative charge on the most electronegative atom.



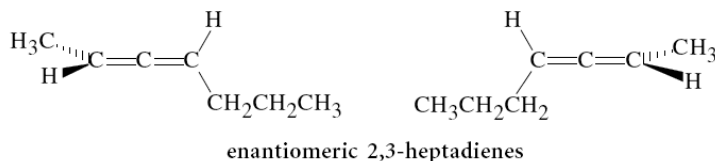
- (f) The second structure is somewhat more important because it places electron deficiency (and positive charge) on a secondary carbon. (The first and third structures are identical, although only one of the carbons is written out explicitly.)



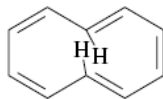
- 15.40 1,3-Cyclohexadiene gives 3-bromocyclohexene by either 1,2- or 1,4-addition of HBr.



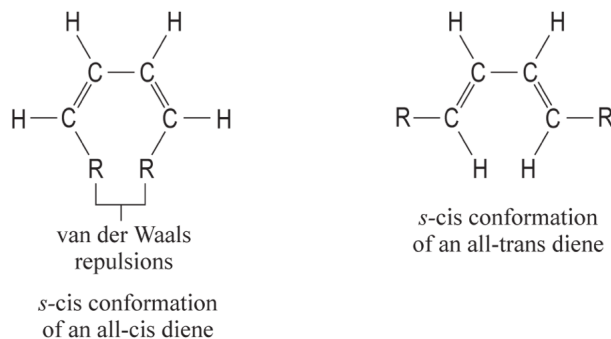
- 15.41 (a) Since the perpendicular relationship is necessary for chirality of a cumulene, allenes, as well as other cumulenes with an even number of cumulated double bonds, can be chiral. Indeed, 2,3-heptadiene is a chiral allene, and therefore exists as a pair of enantiomers that can in principle be separated by an enantiomeric resolution.



- 15.42 (b) This radical has three  $\pi$  electrons: two from the double bond and one from the unpaired electron. It is therefore not aromatic.
- (d) This anion has ten  $\pi$  electrons: two from each of the four double bonds and two from the anionic carbon. It is likely to be aromatic.
- 15.44 Severe van der Waals repulsions between the inner hydrogens (shown in the following structure) force the compound out of planarity. These van der Waals repulsions are so great in the planar conformation that not even aromaticity can compensate for the resulting destabilization.

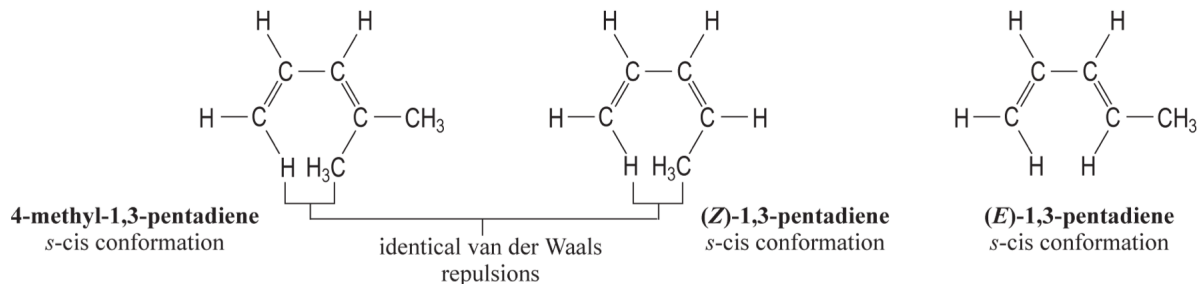


- 15.45 (b) *Heats of formation:*  $3 < 1 < 2$ . *Reasons:* Compound (3) is most stable because it is aromatic. Compound (1) is more stable than compound (2) because conjugated alkenes are more stable than isomeric alkynes.
- 15.46 (b) The first compound has three alkyl substituents on conjugated double bonds; the second compound has two. Hence, the  $\lambda_{\max}$  of the first compound should be about 5 nm greater than the  $\lambda_{\max}$  of the second.
- (d) The first compound has three conjugated double bonds, whereas the second compound has two; one double bond is not conjugated with the other two. Hence, the first compound should have a considerably greater  $\lambda_{\max}$  than the second.
- 15.48 The color of  $\beta$ -carotene is due to its chromophore of extensively conjugated double bonds. Catalytic hydrogenation would result in addition of hydrogen to these double bonds; hence, catalytic hydrogenation of a  $\beta$ -carotene sample would convert it from a red-orange conjugated alkene into a colorless alkane.
- 15.50 Although mycomycin has no asymmetric carbons, it does contain stereocenters: the outer carbons of the allene unit. Evidently, mycomycin is one enantiomer of this chiral allene. The chirality of certain allenes is discussed in Sec. 15.1C on text p. 682.)
- 15.52 The analysis in Eqs. 15.9a–b on text p. 654 shows that the *s-cis* conformations of dienes with *cis* double bonds are destabilized by van der Waals repulsions, whereas the *s-cis* conformations of dienes with *trans* double bonds do not suffer the same repulsions.



These van der Waals repulsions also destabilize the transition states of Diels–Alder reactions, which require *s-cis* conformations of the reacting dienes. Because the diene in the problem undergoes the Diels–Alder reaction under mild conditions, it is probably the all-trans diene.

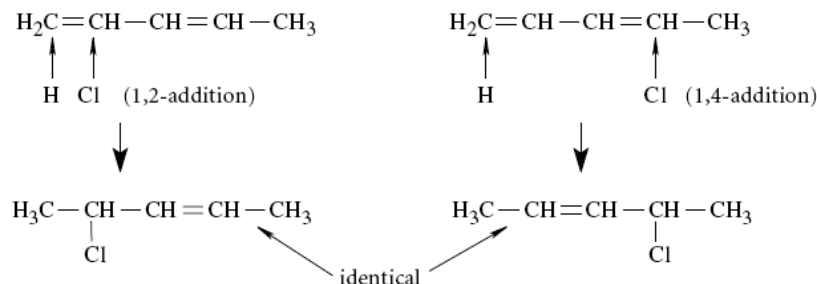
- 15.54 The answer to this problem lies in the *s-cis* conformations of the three dienes, which are as follows:



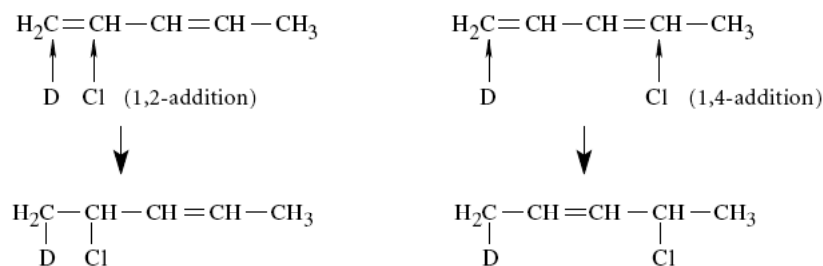
The reactivities of these three dienes in the Diels–Alder reactions correlates nicely with the accessibility of their *s-cis* conformations. (Remember, the transition state of the Diels–Alder reaction involves the *s-cis* conformation of

the diene.) The van der Waals repulsions shown above destabilize the *s*-cis conformations of both 4-methyl-1,3-pentadiene and (*Z*)-1,3-pentadiene to the same extent because the interacting groups are identical. Hence, their reactivity is reduced by about the same amount relative to that of (*E*)-1,3-pentadiene, whose *s*-cis conformation has no such repulsions.

- 15.56 (a) The 1,2- and 1,4-addition products formed in the reaction of 1,3-pentadiene and HCl are identical if we assume that all double bonds retain their *E* stereochemistry.



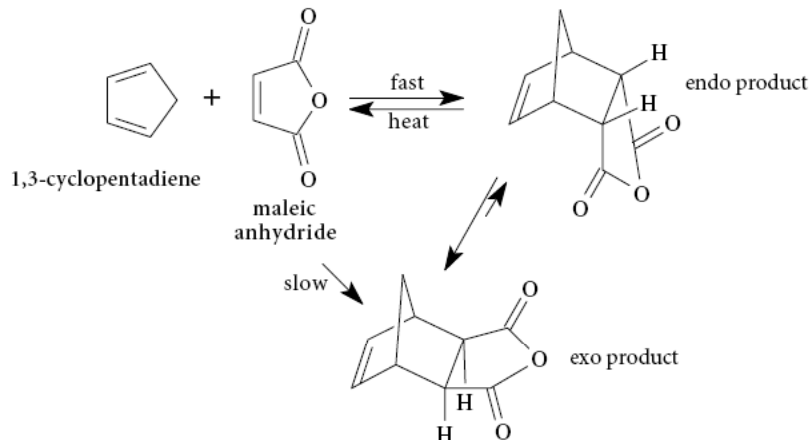
- (b) There can be no preference for 1,2- versus 1,4-addition on the basis of the product stability, because, as shown in part (a), the products are the same. The problem is that we can't tell one mode of addition from the other! The use of D—Cl, however, solves this problem. The use of deuterium allows us to distinguish between the hydrogen that has added and the ones that were originally in the diene.



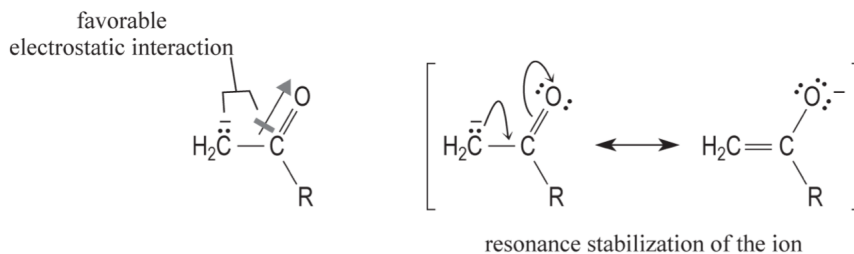
The two products are different, if only subtly so. The isotope has a negligible effect on product stability.

- (c) According to the text, the product of 1,2-addition is preferred, and it is shown in the solution to part (b). In fact, this was observed experimentally. The actual ratio is about 70:30 in favor of 1,2-addition. (How would we tell one product from the other?) This experiment, reported in 1979 by J. E. Nordlander of Case Western Reserve University, established clearly that product stability has nothing to do with the kinetic preference. The arguments in the text are the only reasonable alternative.

- 15.58 (a) The transformations involved in the reaction between 1,3-cyclopentadiene and maleic anhydride:

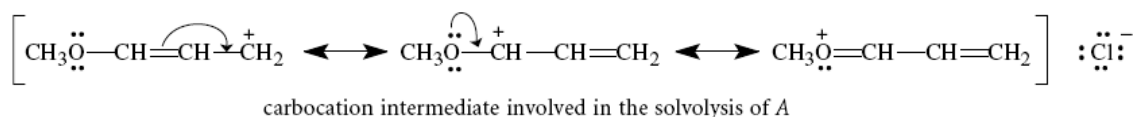






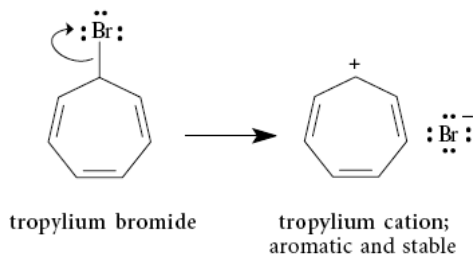
Recall (Sec. 3.6, text p. 113) that stabilization of a conjugate base increases the acidity of its conjugate acid.

- 15.66 Compound *A* should react much more rapidly because the carbocation intermediate (shown below) has three important resonance contributors. In particular, an unshared pair of electrons on the oxygen can be delocalized in this cation; in the solvolysis of the other compound, the unshared pairs on oxygen have no resonance interaction with the positive charge in the carbocation.

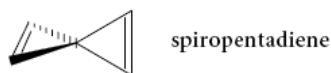


By Hammond's postulate, the reaction involving the more stable carbocation intermediate is faster.

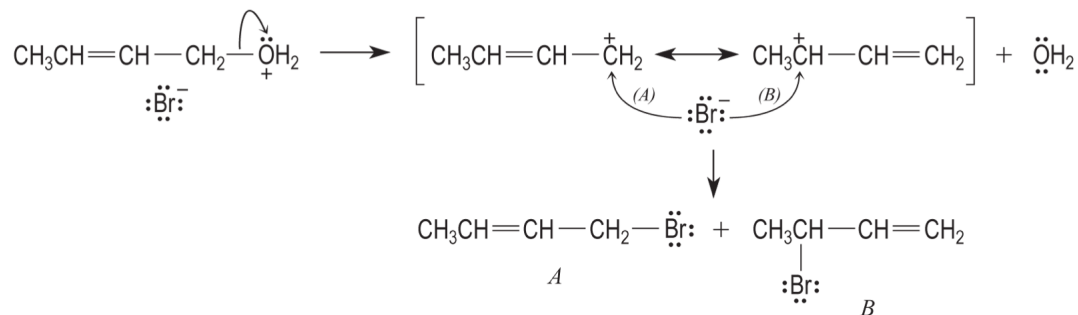
- 15.68 This compound behaves like a salt because it *is* a salt. Tropylium bromide ionizes readily to bromide ion and the *tropylium cation*, which, because it has a continuous cycle of six ( $4n + 2$ ,  $n = 1$ )  $\pi$  electrons, is aromatic, very stable, and very easily formed.



- 15.72 The structure of spiro[3.3]heptane is shown below; it undergoes a Diels-Alder reaction with two molar equivalents of 1,3-cyclopentadiene. Spiropentadiene is unstable because of its great ring strain. Although cyclopropane rings are retained in the product, they contain less ring strain than cyclopropene rings. (Why?)



- 15.73 (a) The mechanism below is shown beginning with the protonated alcohol, which is formed under the strongly acidic conditions.

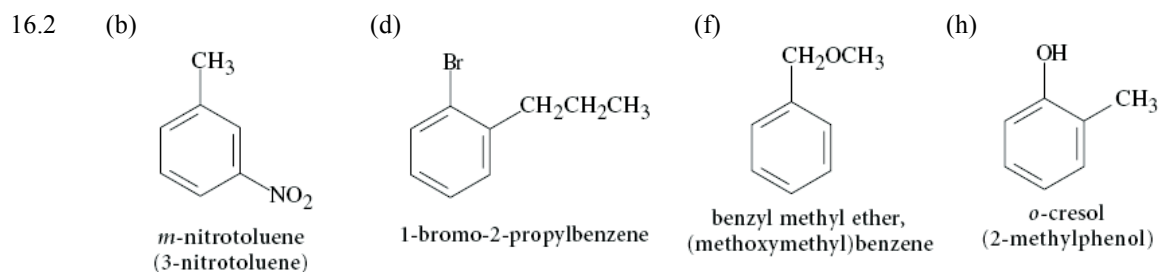


# Chapter 16

## The Chemistry of Benzene and Its Derivatives

### Solutions to In-Text Problems

- 16.1 (b) *o*-Diethylbenzene or 1,2-diethylbenzene  
(d) 2,4-Dichlorophenol  
(f) Benzylbenzene or (phenylmethyl)benzene (also commonly called diphenylmethane)



16.3 Add about 25 °C per carbon relative to toluene (110.6 °C; see text p. 743):

- (b) propylbenzene: 161 °C (actual: 159 °C)

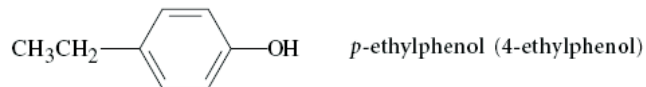
16.4 The aromatic compound has NMR absorptions with greater chemical shift in each case because of the ring current (Fig. 16.2, text p. 745).

- (b) The chemical shift of the benzene protons is at considerably greater chemical shift because benzene is aromatic and 1,4-cyclohexadiene is not.

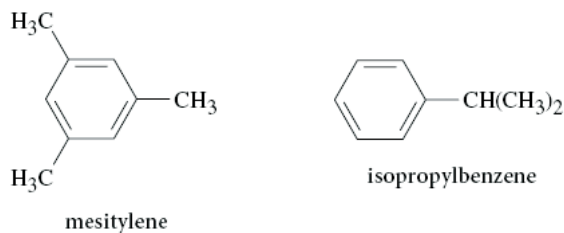
16.6 (b) Among other features, the NMR spectrum of 1-bromo-4-ethylbenzene has a typical ethyl quartet and a typical para-substitution pattern for the ring protons, as shown in Fig. 16.3, text p. 747, whereas the spectrum of (2-bromoethyl)benzene should show a pair of triplets for the methylene protons and a complex pattern for the ring protons. If this isn't enough to distinguish the two compounds, the integral of the ring protons relative to the integral of the remaining protons is different in the two compounds.



16.7 (b) The IR spectrum indicates the presence of an OH group, and the chemical shift of the broad NMR resonance ( $\delta$  6.0) suggests that this could be a phenol. The splitting patterns of the  $\delta$  1.17 and  $\delta$  2.58 resonances show that the compound also contains an ethyl group, and the splitting pattern of the ring protons shows that the compound is a para-disubstituted benzene derivative. The compound is *p*-ethylphenol.

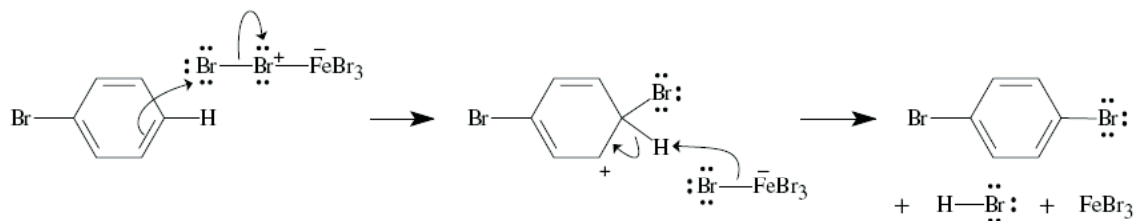


- 16.9 Count the resonances. Mesitylene has three resonances; isopropylbenzene has six.

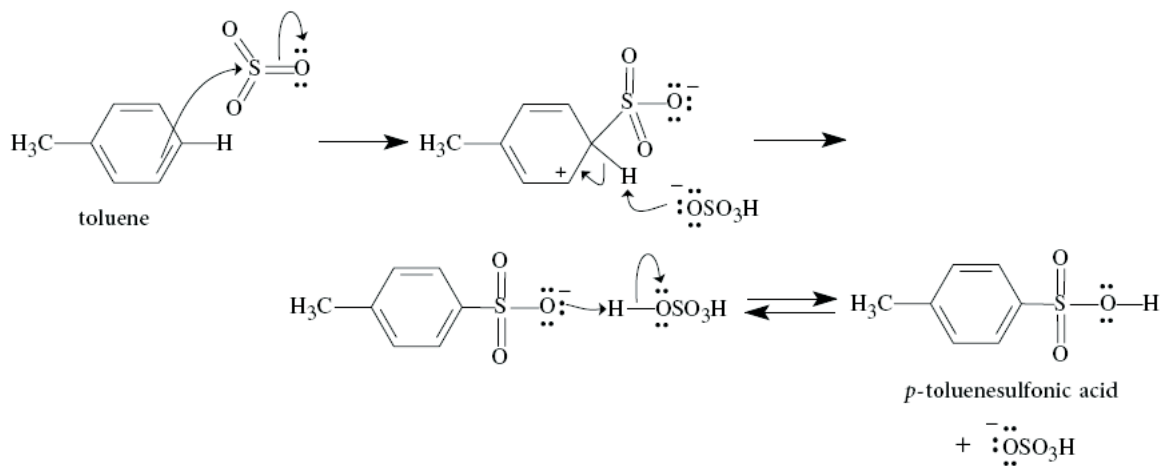


- 16.11 Because styrene has a double bond in conjugation with the ring and ethylbenzene does not, styrene has a greater  $\lambda_{\max}$  in its UV spectrum.

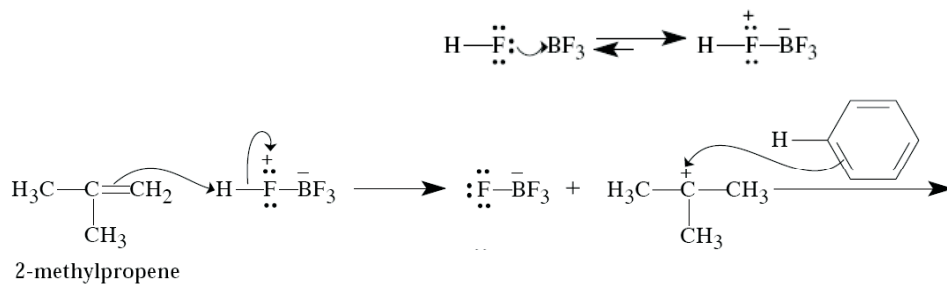
- 16.12 Apply the steps shown in Eqs. 16.6–16.7 on text p. 752 to the para position of bromobenzene.



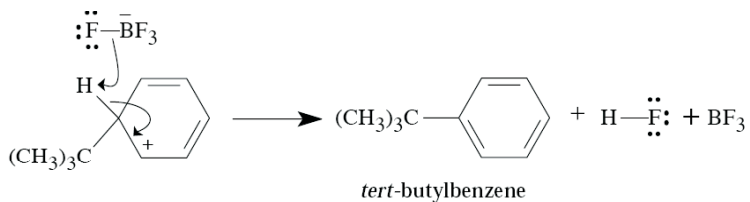
- 16.14 Apply the sulfonation mechanism shown in Eq. 16.13 on text p. 756 to the para position of toluene.



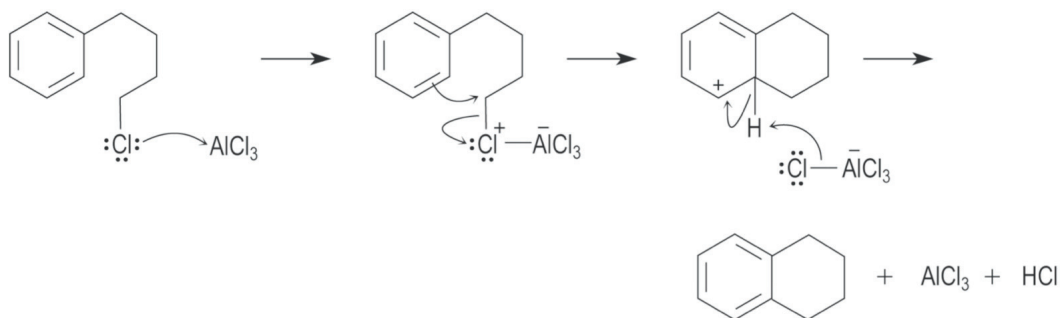
- 16.16 The product is *tert*-butylbenzene. The role of the Lewis acid  $\text{BF}_3$  is to promote the ionization of HF. The mechanism of the reaction is as follows:



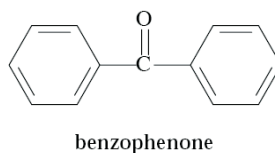




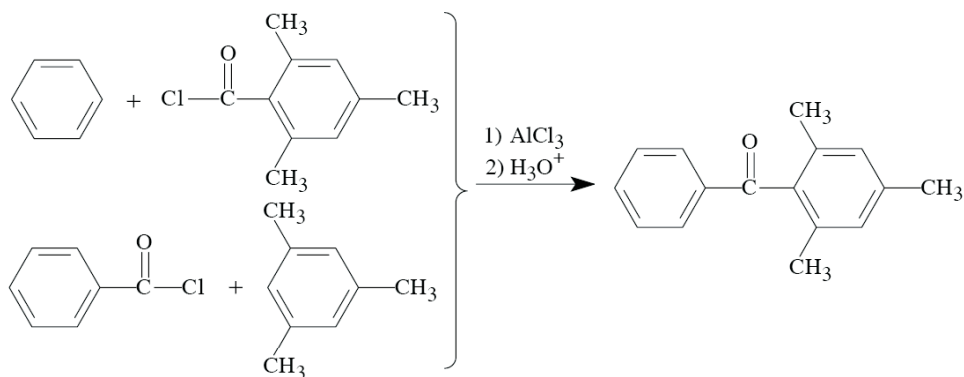
- 16.17 (b) This is another example of an intramolecular Friedel-Crafts reaction—in this case, one that forms a six-membered ring.



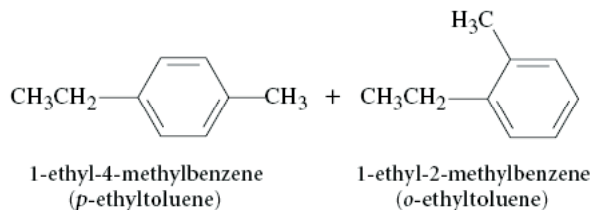
- 16.18 (b)



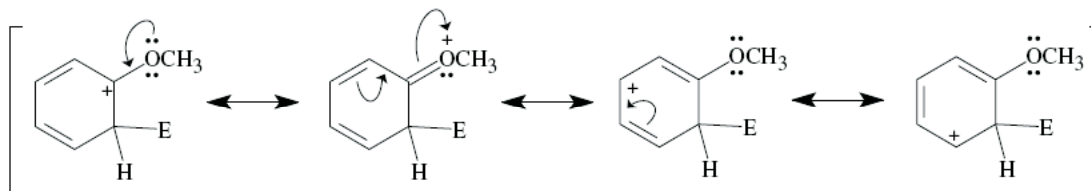
- 16.19 The two possible Friedel-Crafts reactions:



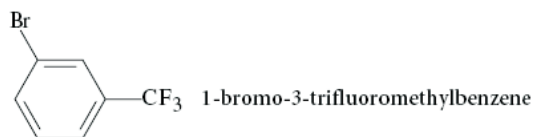
- 16.21 (b) Table 16.2 indicates that alkyl groups are ortho, para-directing groups, and the ethyl group is a typical alkyl group:



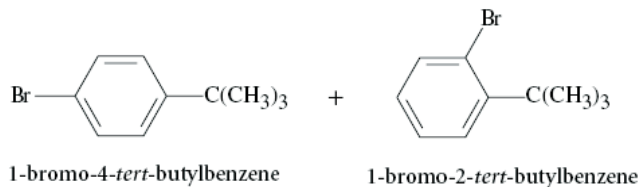
- 16.22 Let  $E^+$  be a general electrophile. The four resonance structures of the carbocation intermediate that results from reaction of  $E^+$  at the position ortho to the methoxy group of anisole are as follows:



- 16.24 (b) The three strong carbon-fluorine bond dipoles result in substantial positive charge on the carbon of the  $CF_3$  group; consequently, this is a meta-directing group.



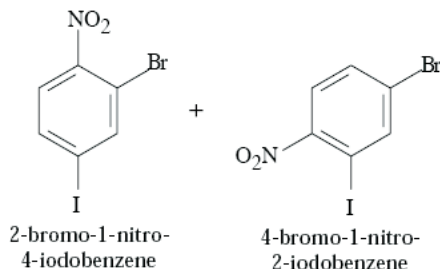
- (d) The *tert*-butyl group, like all other alkyl groups, is an ortho, para-directing substituent.



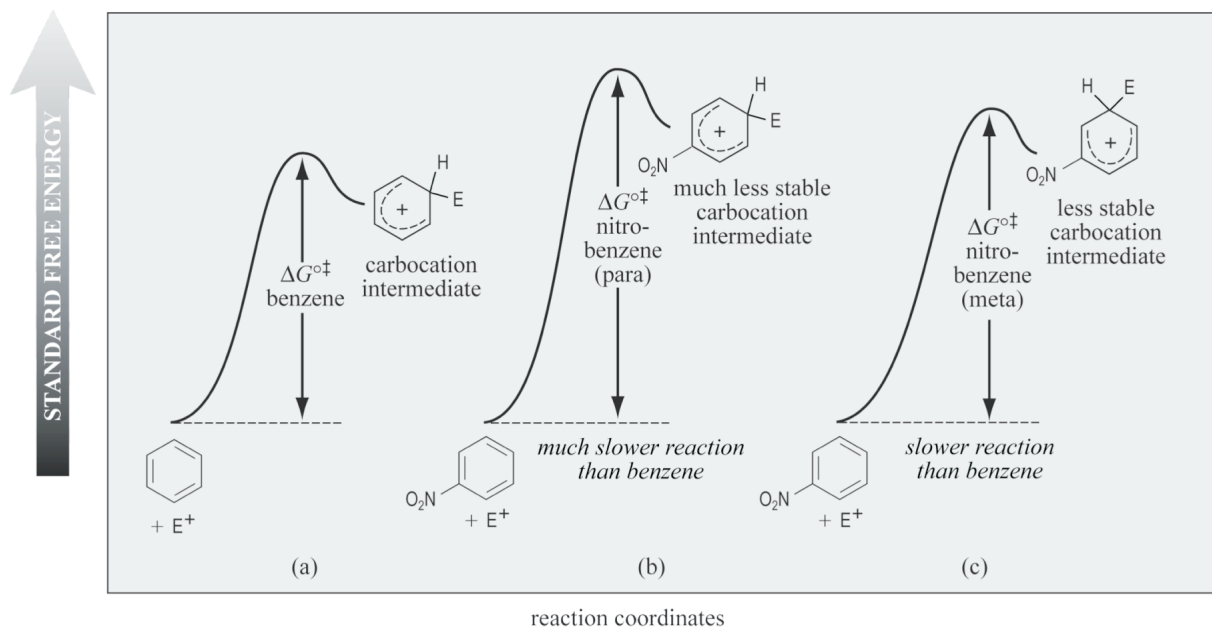
- 16.25 (b) The reaction-free energy profiles for electrophilic substitution of benzene, nitrobenzene at the meta position, and nitrobenzene at the para position are shown in Fig. IS16.1. Notice that nitrobenzene is less reactive than benzene because the nitro group is a deactivating substituent. Notice also that meta-substitution reactions on nitrobenzene are faster than para-substitution reactions because the nitro group is a meta-directing group.

- 16.27 Bromination of *N,N*-dimethylaniline is faster because nitrogen has an unshared electron pair that can stabilize the carbocation intermediate by resonance. As in the case of oxygen, the electron-withdrawing polar effect of nitrogen is much less important than its electron-donating resonance effect.

- 16.28 (b) As in part (a), each substituent is an ortho, para-directing group. Two products satisfy the directing effects of both groups.

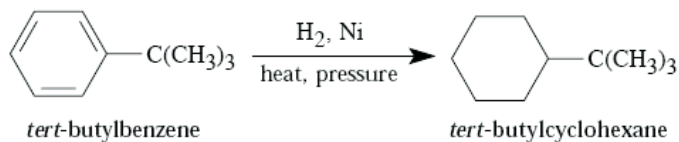


- 16.29 (b) The order is anisole < toluene < chlorobenzene. Chlorobenzene requires the harshest conditions because chlorine is a deactivating group. Anisole requires the mildest conditions because the methoxy group is more activating than the methyl group of toluene. (See Table 16.2 on text p. 763.)



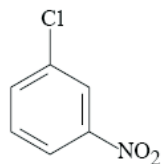
**Figure IS16.1** Reaction-free energy profiles to accompany the solution to Problem 16.25(b)

- 16.31 (b) Hydrogenate *tert*-butylbenzene, which, in turn, is prepared by Friedel–Crafts alkylation as shown in Eq. 16.18 on text p. 758 or by the reaction shown in the solution to Problem 16.16.



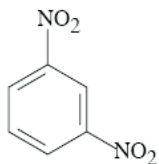
## Solutions to Additional Problems

16.33 (a)



1-chloro-3-nitrobenzene

(b)

1,3-dinitrobenzene or  
*m*-dinitrobenzene

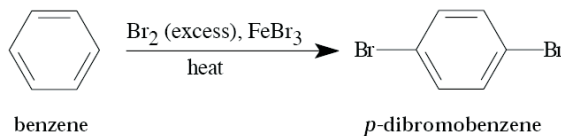
- (c) No electrophilic aromatic substitution reaction takes place. Friedel–Crafts acylation does not take place on any benzene derivative less reactive than the halobenzenes. In fact, nitrobenzene can be used as an inert solvent for Friedel–Crafts acylation.

16.37 Ethylbenzene has a three-proton triplet and, at somewhat greater chemical shift, in the benzylic proton region, a two-proton quartet. *p*-Xylene has a six-proton singlet in the benzylic region. Styrene, Ph—CH=CH<sub>2</sub>, has no protons in the benzylic region.

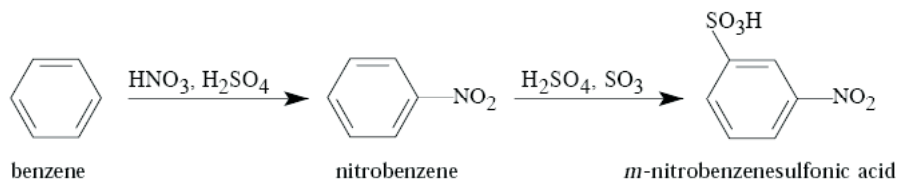
16.38 (b) Fig. 16.2 on text p. 745 shows that aromatic protons located in the plane of the ring and outside of the ring experience an augmented local field and thus a greater chemical shift. However, in the region above and below the ring, the induced field has the opposite direction, and consequently protons located in this region experience a reduced local field and thus a smaller chemical shift. Such is the case with the methyl group in the problem; the local field at this group is so small that its resonance occurs at nearly 1.7 ppm *smaller* chemical shift than that of TMS.

16.40 In each synthesis that involves substitution on a benzene derivative that contains an ortho, para-directing group, only the product resulting from para substitution is shown.

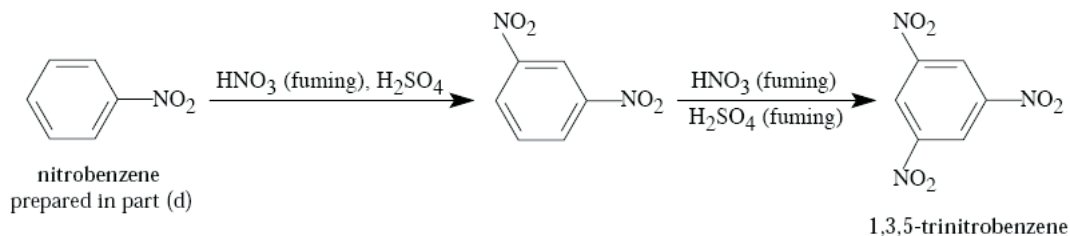
(b)



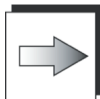
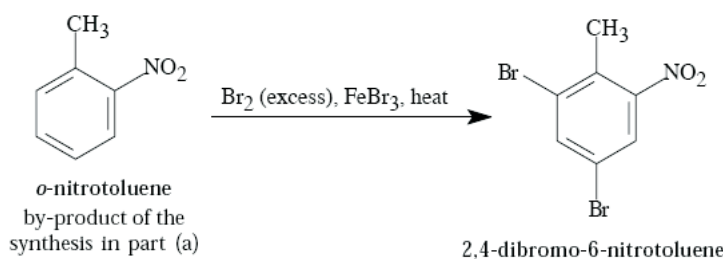
(d)



(f)

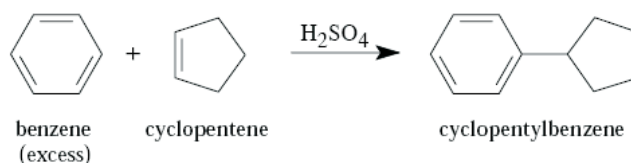


(h)



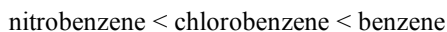
Nitration of toluene actually gives more ortho isomer than para isomer of toluene, and the two nitrotoluene isomers are readily separated by fractional distillation. (See text p. 768.) *o*-Nitrotoluene is a good starting material for a number of ortho-substituted benzene derivatives.

(j)

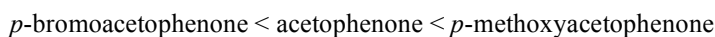


Cyclopentanol may be substituted for cyclopentene in this synthesis, or chlorocyclopentane and  $\text{AlCl}_3$  catalyst may be used instead of cyclopentene and  $\text{H}_2\text{SO}_4$ . Note that each of these possible starting materials serves as a source of the same carbocation, the cyclopentyl cation.

- 16.41 (b) The reactivity order follows from the relative activating effects of the substituents. (See the last column of Table 16.2 on text p. 763.)

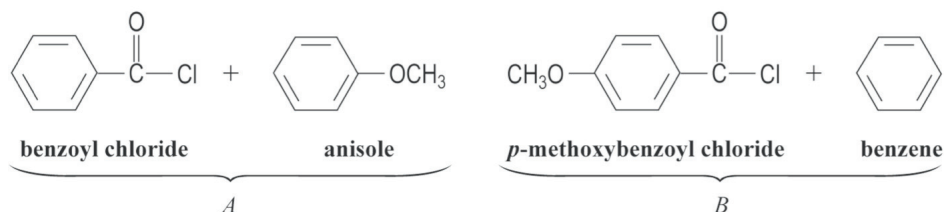


- (d) The reactivity order follows from the relative activating effects of the substituents. (See the last column of Table 16.2 on text p. 763.)



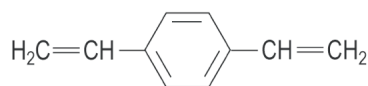
- 16.43 The reactivity order is  $A < B < D < C$ . Compound *C* is most reactive because the substituent has an unshared electron pair that can be used to stabilize the intermediate carbocation by resonance. Compounds *B* and *D* have alkyl substituents, which stabilize carbocations; however, the alkyl group of compound *B* contains a positively charged group that would interact unfavorably with a carbocation, offsetting the stabilizing effect of the alkyl carbon. Compound *A* has a positively charged, electronegative substituent attached directly to the ring that would interact most unfavorably with the carbocation. (See the solution to Problem 16.42b.) Compounds *C* and *D* undergo bromination at the ortho and para positions; compound *A* undergoes bromination at the meta position; and the position of substitution in compound *B* depends on the balance of the stabilizing effect of the alkyl group and the destabilizing effect of the positive charge. (In fact, this compound brominates in the ortho and para positions.)

- 16.45 The two possibilities are the acylation of anisole by benzoyl chloride (pair *A*), or the acylation of benzene by *p*-methoxybenzoyl chloride (pair *B*). Because the methoxy group activates electrophilic substitution at the *ortho* and *para* positions, the Friedel-Crafts reaction of pair *A* should occur under the milder conditions.



(Both reactions would work, however; and the use of pair *B* avoids the possibility of *ortho* substitution, although, with the Friedel–Crafts reaction, this does not generally occur to a great extent.)

- 16.47 Any compound must have an unsaturation number of 6 and must contain a benzene ring.



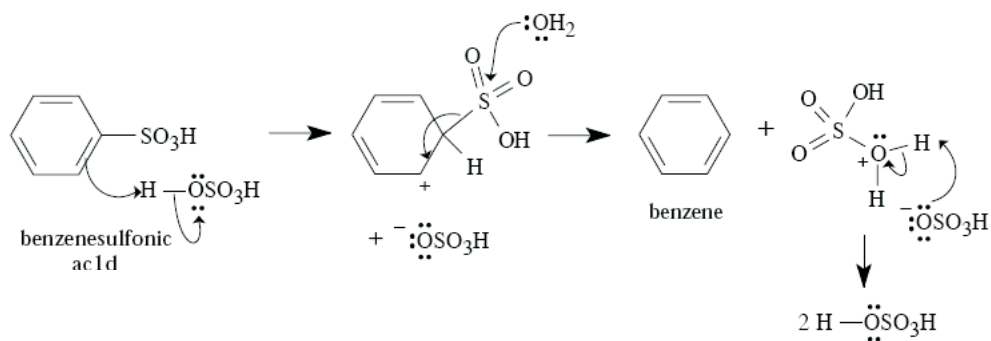
*p*-divinylbenzene



structures such as this without a benzene ring would hydrogenate to *cis*-1,4-diethylcyclohexane

Structures such as the one on the right that do not contain a benzene ring do not meet the criterion, because they would undergo hydrogenation of the ring double bonds.

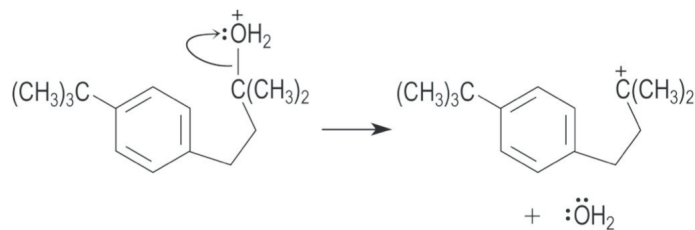
- 16.50 Run the electrophilic aromatic substitution reaction in reverse.



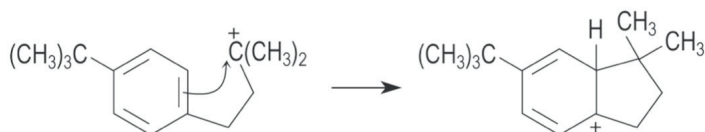
There are several variations on this mechanism. For example,  $\text{SO}_3\text{H}$  could be lost from the carbocation intermediate to give protonated  $\text{SO}_3$  (that is,  $^+\text{SO}_3\text{H}$ ; see Problem 16.13 on text p. 756) which could react with water to give  $\text{SO}_3$  (sulfur trioxide) and  $\text{H}_3\text{O}^+$ . Sulfur trioxide reacts vigorously with water to give  $\text{H}_2\text{SO}_4$  (sulfuric acid). The important aspect of the mechanism is the protonation of the ring and loss of a species which would serve as an electrophile in the reverse reaction.

- 16.52 (a) and (b)

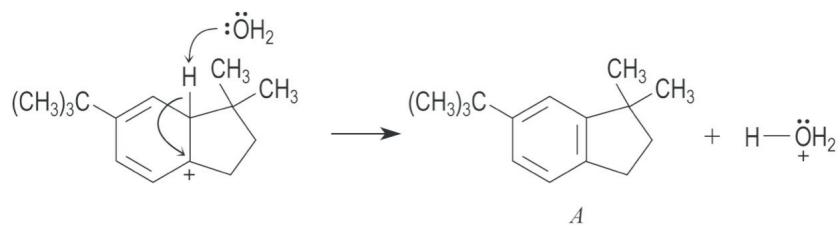
*Generation of the electrophile:* The electrophile is the carbocation generated by protonation of the alcohol oxygen and loss of water.



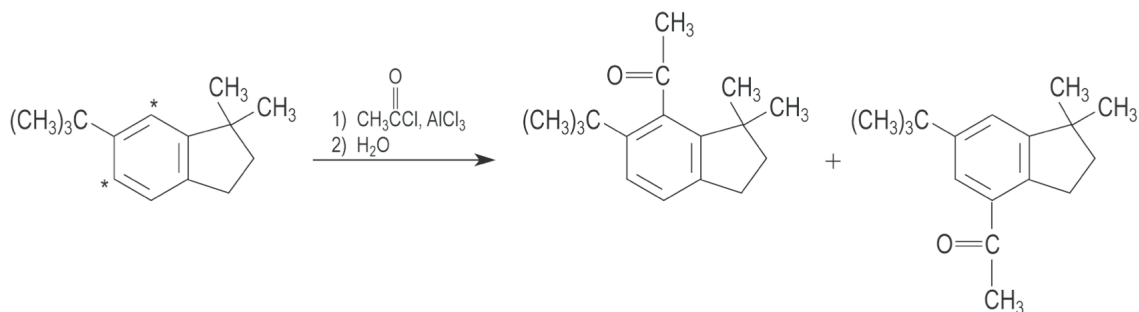
*A Lewis acid–base association reaction of the benzene  $\pi$  electrons with the electrophile to generate another carbocation:*



*Loss of a  $\beta$ -proton to the Brønsted base  $\text{H}_2\text{O}$  to form the new aromatic compound:*

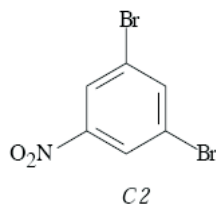
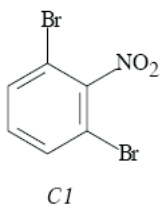


- (c) The aromatic ring of compound *A* has three alkyl substituents. Two of them—the *tert*-butyl group and one of the ring bonds—direct substitution by their electronic effects to the positions indicated by the asterisk:

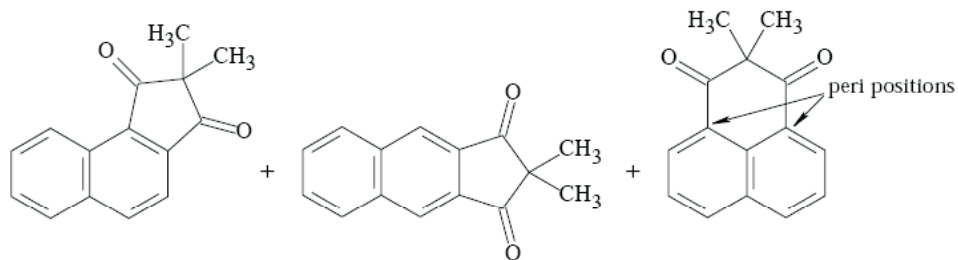


Electrophilic substitution might have occurred at either of these positions to give either or both of the compounds shown in the foregoing equation. Both of these positions, however, are ortho to the very large *tert*-butyl group, and one of them is ortho to *two* highly branched groups. For steric reasons substitution cannot occur at these very congested positions. Hence, it occurs at the remaining position. Note that ring position meta to alkyl substituents are not deactivated; they are simply less activated than positions that are ortho and para to alkyl substituents. Furthermore, the remaining ring position is activated by one alkyl substituent.

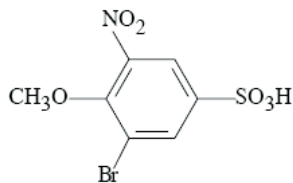
- 16.58 (c) The following two products derived from nitration of compound *C* were probably formed in smallest amount. In the formation of compound *C1*, the nitro group and the two bromines are involved in severe van der Waals repulsions; and the formation of compound *C2* satisfies the directing effect of neither bromine substituent.



- 16.59 (b) The formula indicates that successive electrophilic aromatic substitution reactions have occurred; the product is triphenylmethane,  $\text{Ph}_3\text{CH}$ .
- (d) Comparison of the formula of the product to that of naphthalene shows that one molar equivalent of the acylating agent has been introduced. Since there is no chlorine in the product, the reaction must involve a double acylation of the naphthalene ring by both ends of the acid chloride. The only way that this can occur with the formation of rings of reasonable size is for the acylation to occur across ortho positions of one benzene ring, or across the peri positions, which are the two positions on either side of the ring junction. These three possibilities account for the three products:

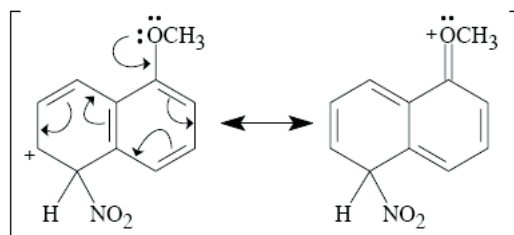


- (g) The nitro group is directed by both substituents to the position ortho to the methoxy group, and the bromine in the second reaction is directed to the other position ortho to the methoxy group.

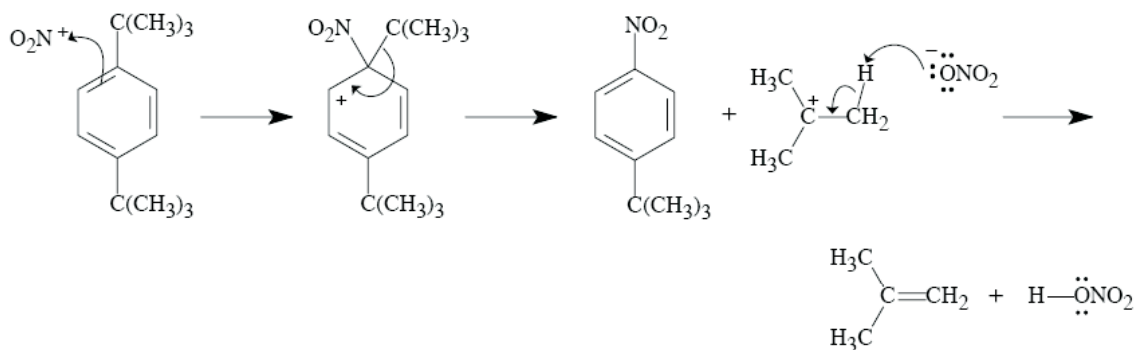


3-bromo-4-methoxy-5-nitrobenzenesulfonic acid

- 16.60 (b) When nitration occurs at carbon-5, the unshared electrons of the oxygen can be used to stabilize the carbocation intermediate by resonance; consequently, nitration at carbon-5 of 1-methoxynaphthalene is faster than nitration of naphthalene itself.



- 16.64 In this reaction a *tert*-butyl cation is lost rather than a proton from the carbocation intermediate. The electrophile, a nitronium ion  $^+\text{NO}_2$ , is generated by the mechanism shown in Eqs. 16.11a–d on text p. 755.



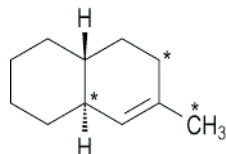


# Chapter 17

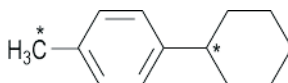
## Allylic and Benzylic Reactivity

### Solutions to In-Text Problems

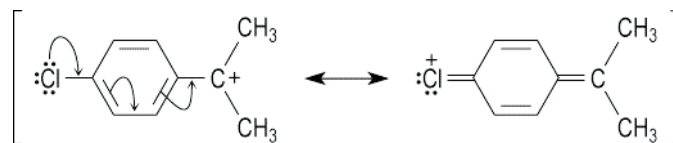
- 17.1 (b) The allylic carbons are indicated with an asterisk (\*).



- 17.2 (b) The benzylic carbons are indicated with an asterisk (\*).



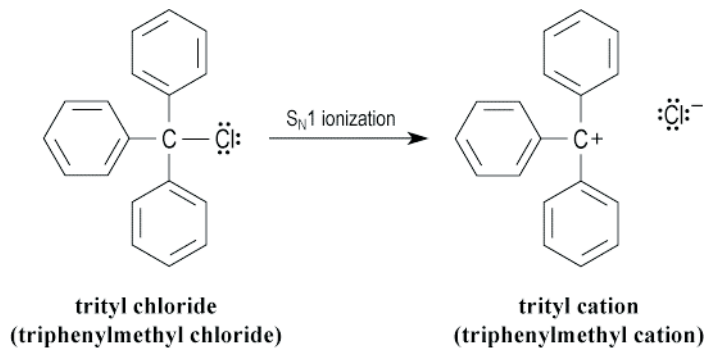
- 17.3 (b) The reactivity order is (2) < (3) < (1). The S<sub>N</sub>1 reaction of compound (2) is slowest because the polar effect of the meta-chloro substituent destabilizes the intermediate carbocation. The reaction of compound (3) is faster because the resonance effect of the *para*-chloro group partially offsets its polar effect.



carbocation intermediate in the solvolysis of compound (3)

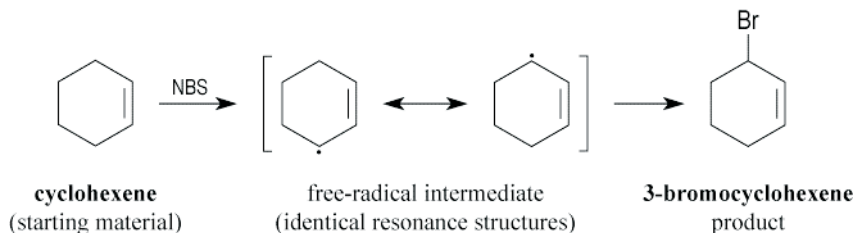
Compound (1) reacts most rapidly because the carbocation intermediate is not destabilized by the deactivating polar effect of a chloro substituent, which outweighs its resonance effect.

- 17.5 The carbocation formed when trityl chloride ionizes, the *trityl cation* (Ph<sub>3</sub>C<sup>+</sup>), is stabilized by delocalization of electrons from *all three* phenyl rings. This carbocation has more resonance structures than the carbocations formed from the other alkyl halides in the table, and is thus so stable that the transition state leading to its formation also has very low energy; consequently, it is formed very rapidly.

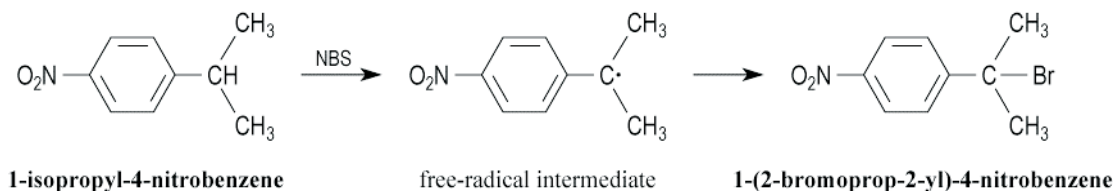


- 17.6 The number of products depends on (1) whether all of benzylic or allylic positions are equivalent, and (2) whether the resonance structures of the free-radical intermediate are identical.

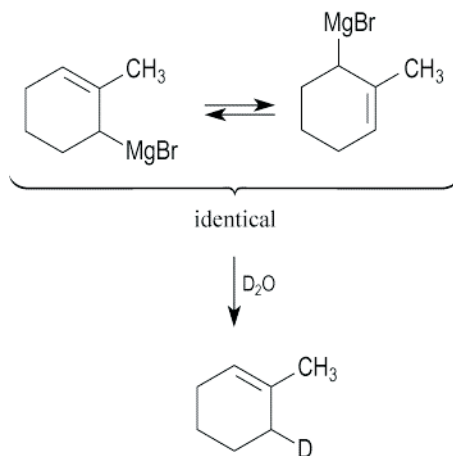
- (a) All allylic positions of cyclohexene are chemically equivalent, and the two resonance structures are identical. Hence, only one allylic bromination product is possible.



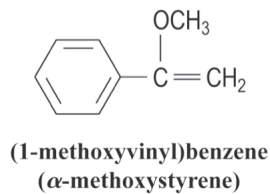
- (e) A benzylic hydrogen is abstracted from the isopropyl group rather than a hydrogen of the two methyl groups because a more stable benzylic free-radical intermediate is obtained.



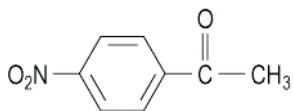
- 17.7 (b) Because the two Grignard reagents in rapid equilibrium are identical, only one product is obtained:



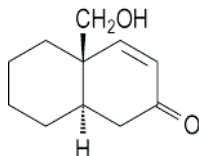
- 17.8 (b) The benzylic proton is abstracted;  $\beta$ -elimination gives a vinylic ether.



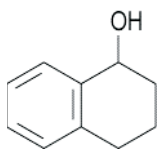
- 17.10 (b)



- (d)

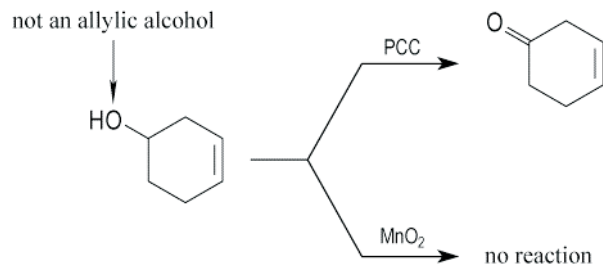


17.11 (b)

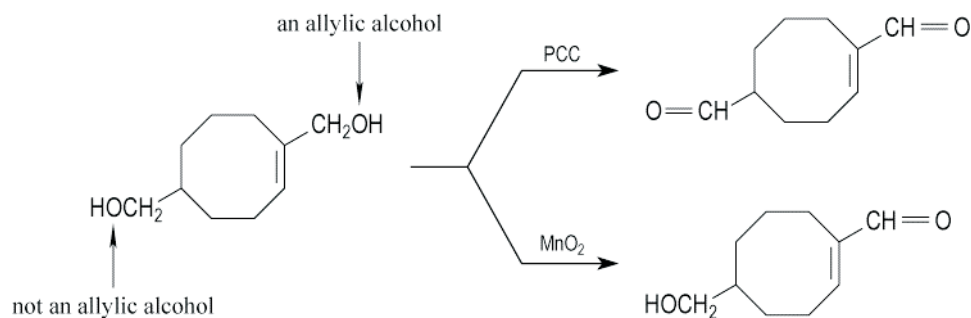


17.12 PCC oxidizes all primary alcohols to aldehydes and all secondary alcohols to ketones;  $\text{MnO}_2$  oxidizes only allylic or benzylic alcohols (primary alcohols to aldehydes and secondary alcohols to ketones).

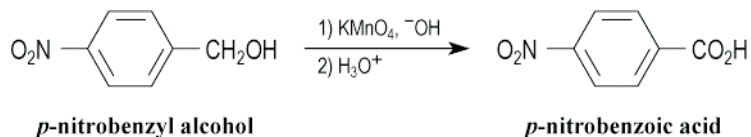
(b)



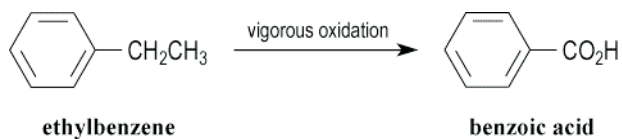
(d)



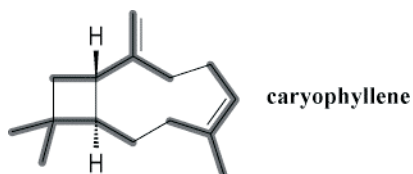
17.13 (a)



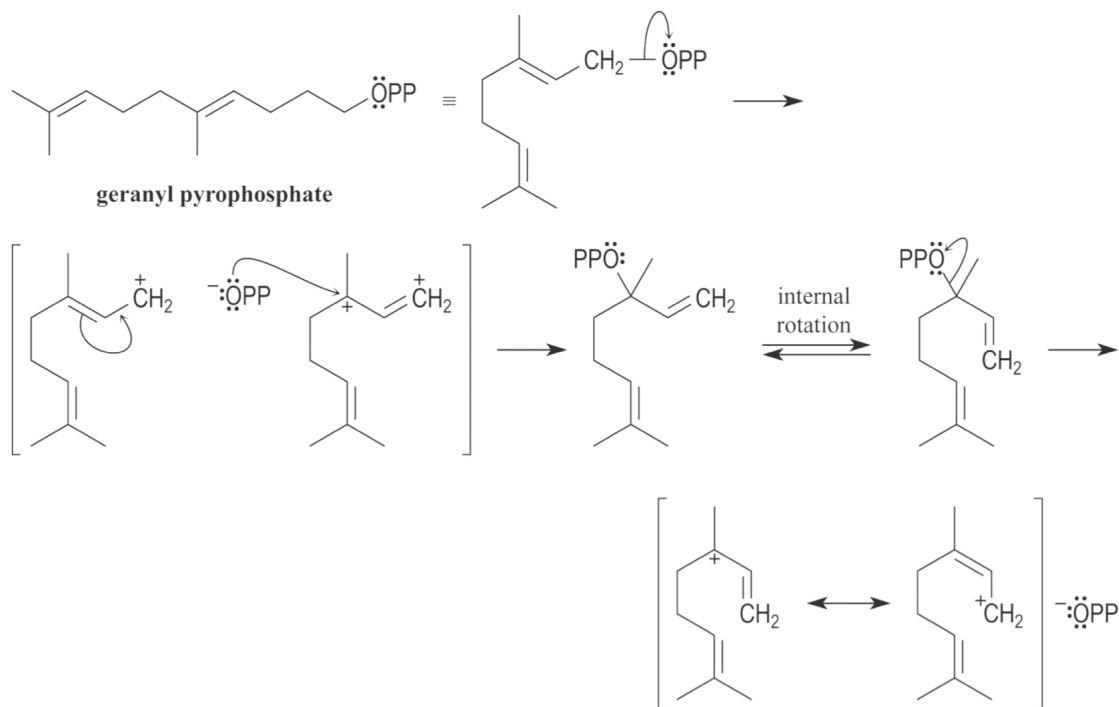
17.14 (b) Because one carbon is lost as a result of the oxidation, and because the benzene ring accounts for all four degrees of unsaturation, compound *B* must be ethylbenzene.



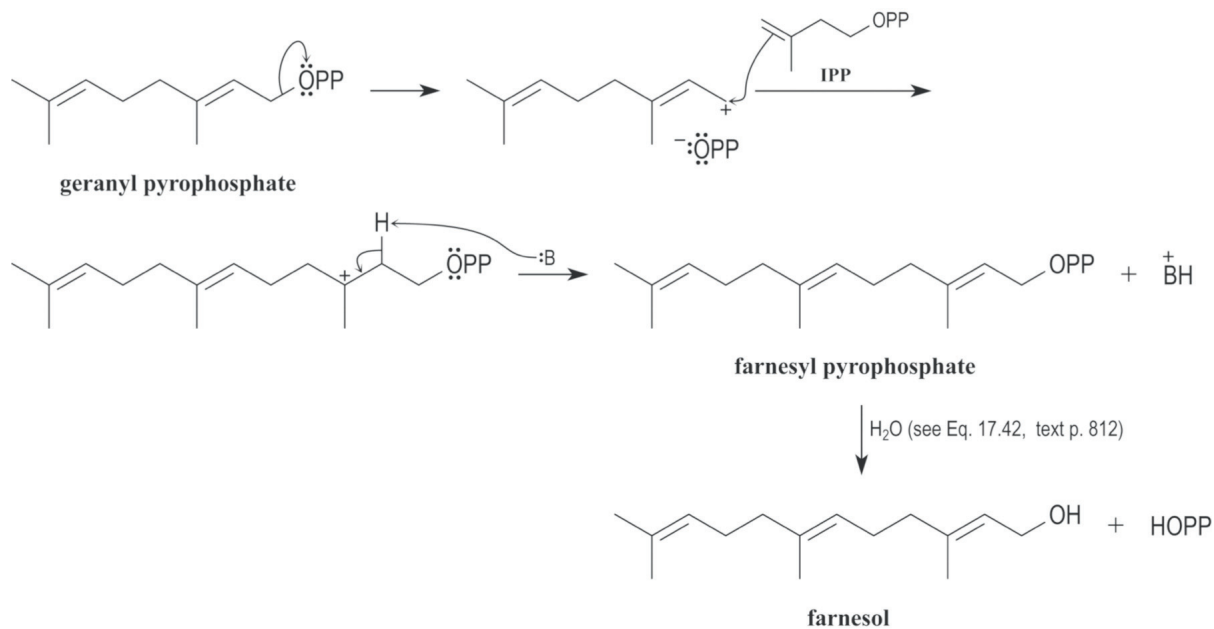
17.15 (b) Caryophyllene is a sesquiterpene because it contains three isoprene skeletons, which are shown as heavy bonds.



- 17.16 (b) Ionization of geranyl pyrophosphate is followed by reaction with the pyrophosphate anion on the other electron-deficient carbon of the resonance-stabilized carbocation; rotation about a single bond is followed by ionization of pyrophosphate to give the desired carbocation.

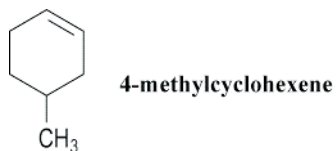


- 17.17 (b) Geranyl pyrophosphate is converted into farnesyl pyrophosphate by a mechanism exactly analogous to the one shown in Eq. 17.38 on text p. 765. Then farnesyl pyrophosphate hydrolyzes to farnesol; see text Eq. 17.39.

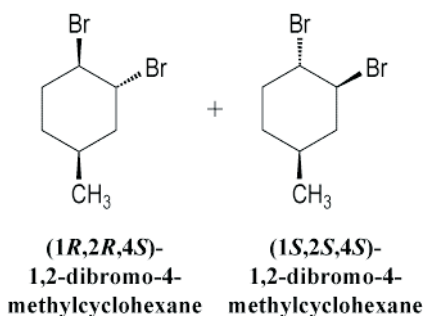


## Solutions to Additional Problems

17.19 The structure of the starting material is:

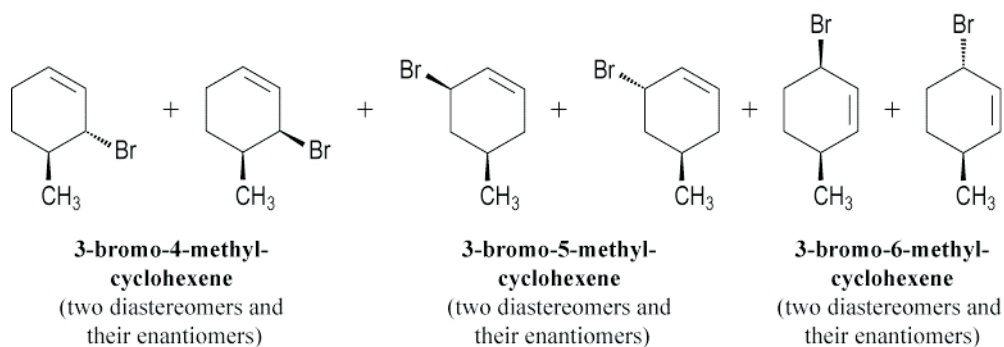


(a)

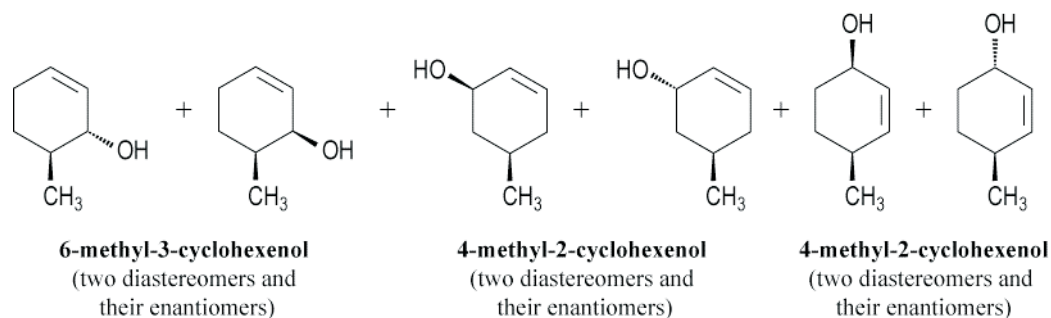


(and their enantiomers)

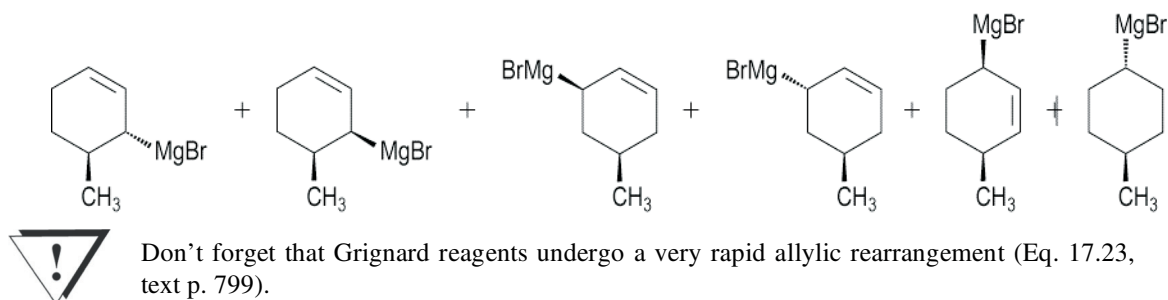
(b)



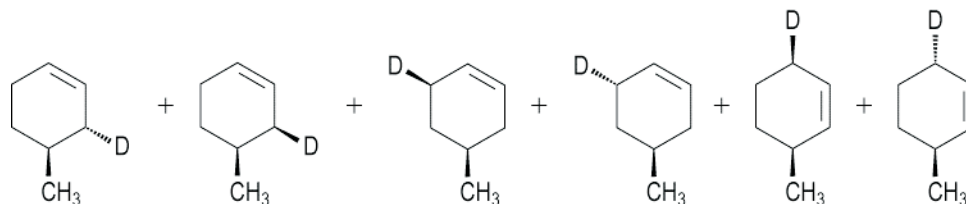
(c)



(d) As in the previous parts, all four stereoisomers of each compound are formed.



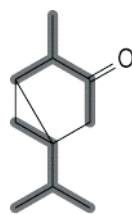
- (e) As in the previous part, all four stereoisomers of each compound are formed.



17.20 Compound (d) is a terpene. The isoprene skeleton is shown with heavy bonds.

- (b) Compound (b) is not a terpene.

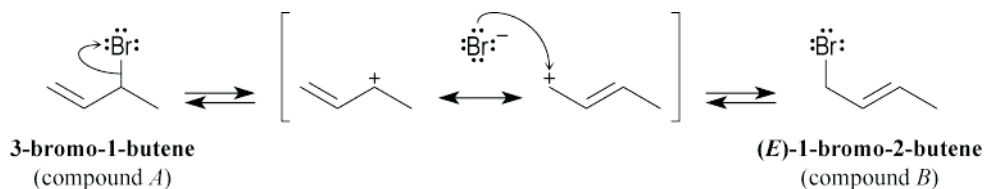
- (d) Compound (d) is a terpene. The isoprene skeleton is shown with heavy bonds.



**b-thujone**

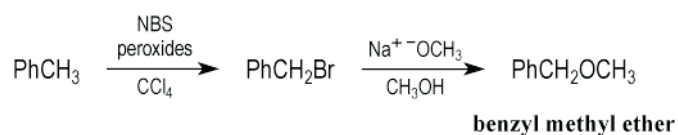
- (f) Compound (f) is not a terpene.

- 17.23 (a) The allylic-rearrangement product *B* [(*E*)-1-bromo-2-butene] could be formed by ionization to a carbocation and bromide ion followed by reaction with the bromide ion on the other electron-deficient carbon.  
 (b) The curved-arrow notation is shown in the following scheme.

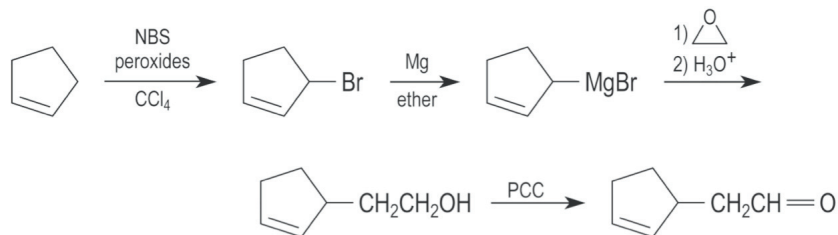


- (c) Compound *B*, the rearrangement product, is favored at equilibrium because it has the double bond with the greater number of alkyl branches.

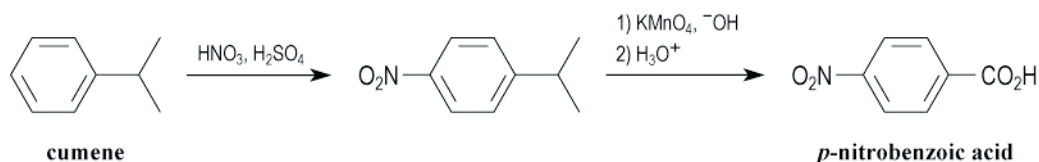
- 17.24 (a)



(d)

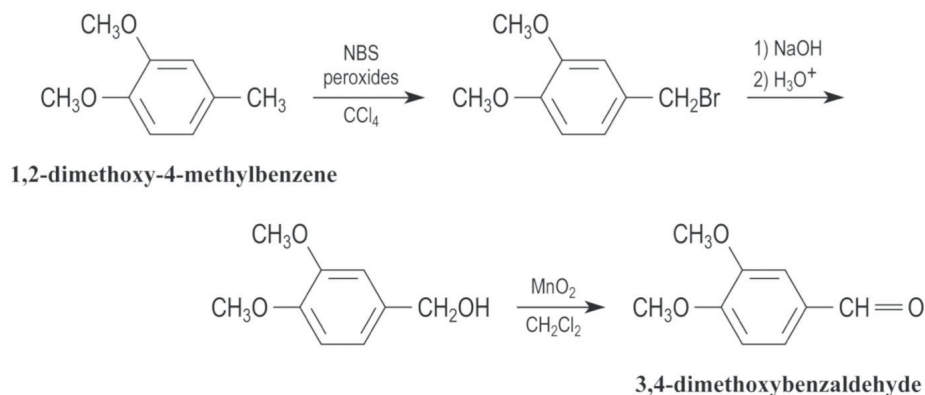


(f)

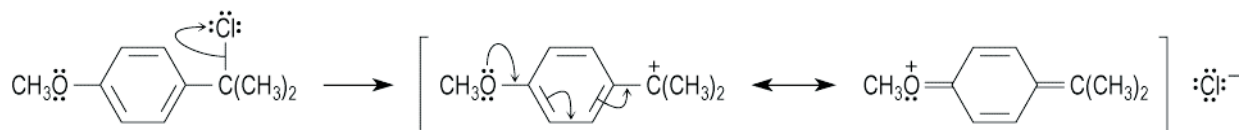


Compare the solutions to parts (e) and (f) and notice how reversing the sequence of the oxidation and nitration steps brings the directing effects of different substituents into play during nitration.

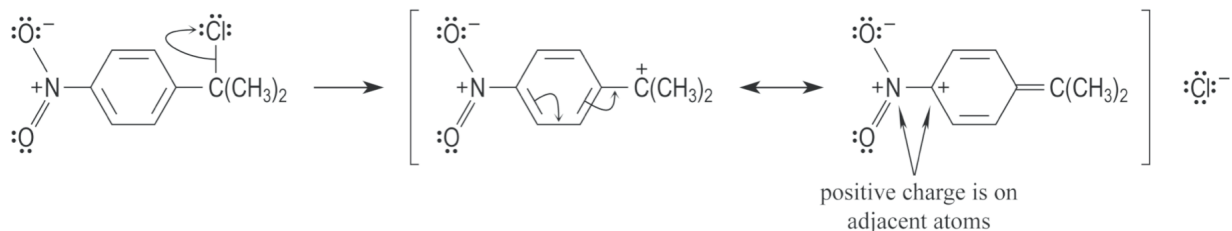
(g)



- 17.25 The compounds that give the most stable carbocation intermediates are the ones that undergo the most rapid solvolysis. This problem deals with the effect of substituent on the stability of the carbocation intermediate. The key is to analyze the balance of resonance and polar substituent effects just as you would for electrophilic aromatic substitution. The order of increasing reactivity is (4) < (1) < (3) < (2). Thus, compound (2) reacts most rapidly because the carbocation intermediate is stabilized by the *electron-donating resonance effect* of the *p*-methoxy substituent:

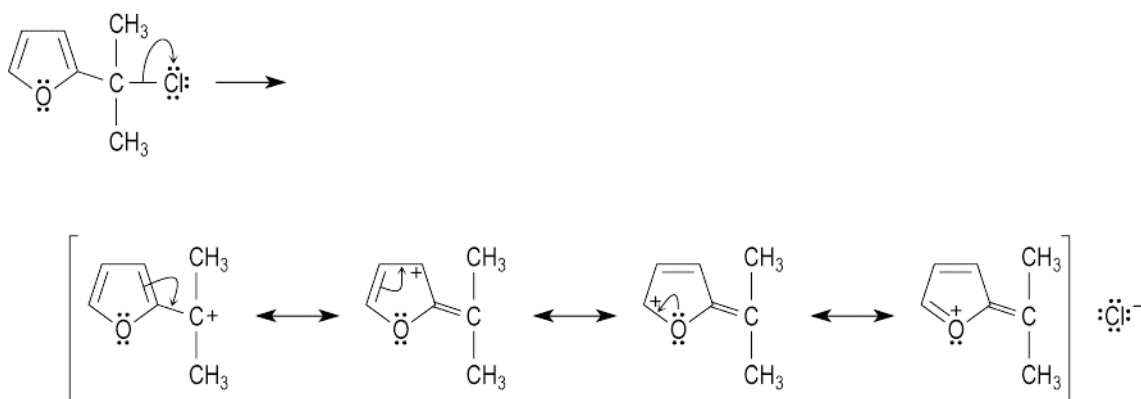


As in electrophilic substitution, the resonance effect of the *p*-methoxy group strongly outweighs its electron-withdrawing polar effect. In compound (3), there is a similar resonance effect; however, the polar effects of halogen substituents outweigh their resonance effects. Consequently, compound (3) reacts more slowly. The nitro group exerts no resonance effect in the carbocation intermediates derived from compounds (1) and (4); the question is then whether its polar effect is stronger from the meta or para position. As in electrophilic aromatic substitution, a *para*-nitro group destabilizes a carbocation intermediate more than a *meta*-nitro group because, in a *para*-nitro carbocation, positive charge is on adjacent atoms:



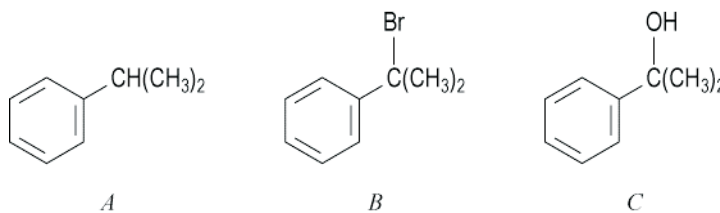
In the *meta*-nitro carbocation, positive charge does *not* reside on adjacent atoms. Consequently, the *meta*-nitro carbocation is more stable (or perhaps we should say *less unstable*) than the *para*-nitro carbocation, and *m*-nitro-*tert*-cumyl chloride solvolyzes more rapidly than *p*-nitro-*tert*-cumyl chloride.

- 17.28 The solution to this problem, like the previous three solutions, hinges on an analysis of the relative stabilities of the carbocation intermediates involved in the  $S_N1$  reactions of the two compounds. The carbocation intermediate in the solvolysis of compound *A* is resonance-stabilized:



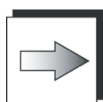
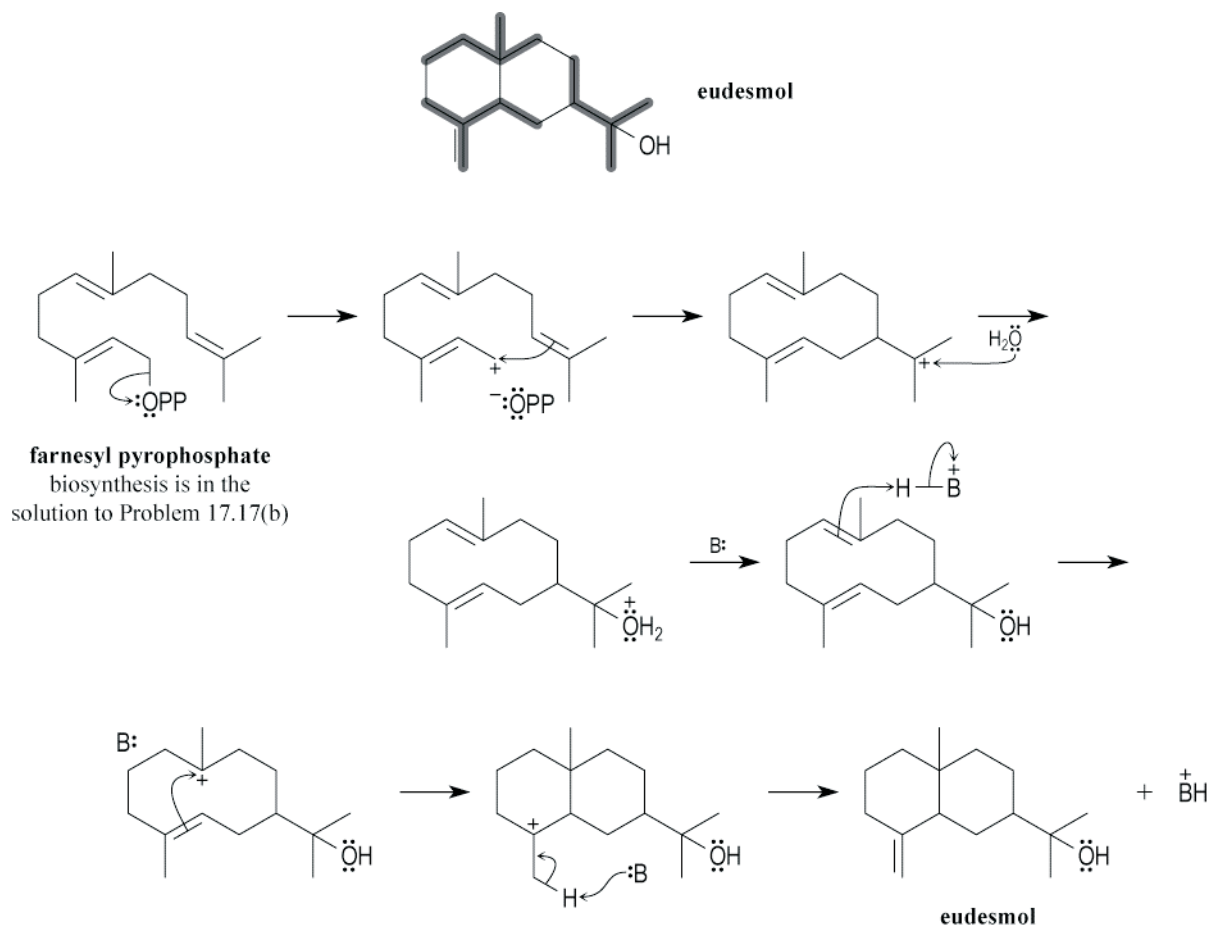
The carbocation intermediate involved in the solvolysis of compound *B* is not resonance-stabilized, and in fact is somewhat destabilized by the electron-withdrawing polar effect of the oxygen. The greater stability of the carbocation derived from compound *A* results in a greater solvolysis rate.

- 17.29 The fact that benzoic acid is obtained by chromic acid oxidation shows that all compounds contain a monosubstituted benzene ring. The NBS reaction is a benzylic bromination, and the alcohol produced by solvolysis of the resulting bromide must be tertiary, since it cannot be oxidized with  $CrO_3$  and pyridine. The structures of compound *A*, *B*, and *C* are therefore as follows:

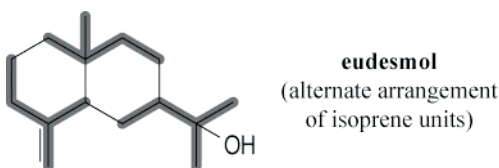


- 17.34 First analyze the relationship of the isoprene skeletons. Then use steps like the ones shown in Eqs. 17.40–17.42, text pp. 812, to assemble the parts from IPP and DMAP. Start with farnesyl pyrophosphate, the biosynthesis of which is shown in the solution to Problem 17.17(b), text p. 813. Note that B: = a base.



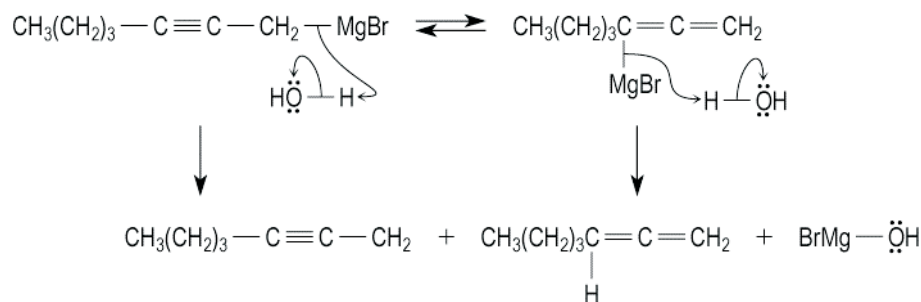


A different arrangement of isoprene units in eudesmol can also be envisioned:

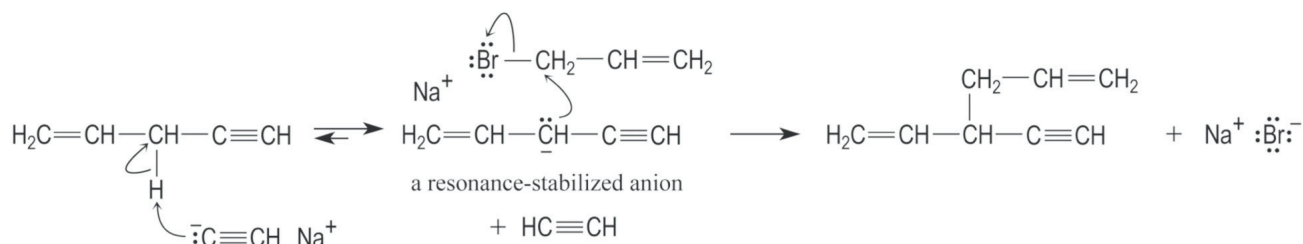


A biosynthetic scheme based on this arrangement would be an equally correct answer. An isotope-labeling experiment would be required to distinguish between the two arrangements.

- 17.36 (a) Although the conjugate-base anion of 1,4-pentadiene is doubly allylic and resonance-stabilized, the conjugate-base anion of 1,3-cyclopentadiene is in addition aromatic. (See text p. 726 for a discussion of this case.) Consequently, much less energy is required for the ionization of 1,3-cyclopentadiene, and its  $pK_a$  is therefore much lower. (The  $pK_a$  difference between these two compounds is estimated to be 10–15 units.)
- 17.38 (a) Propargylic Grignard reagents, like allylic Grignard reagents, are an equilibrium mixture of two constitutional isomers. Each reacts with  $H_2O$ .

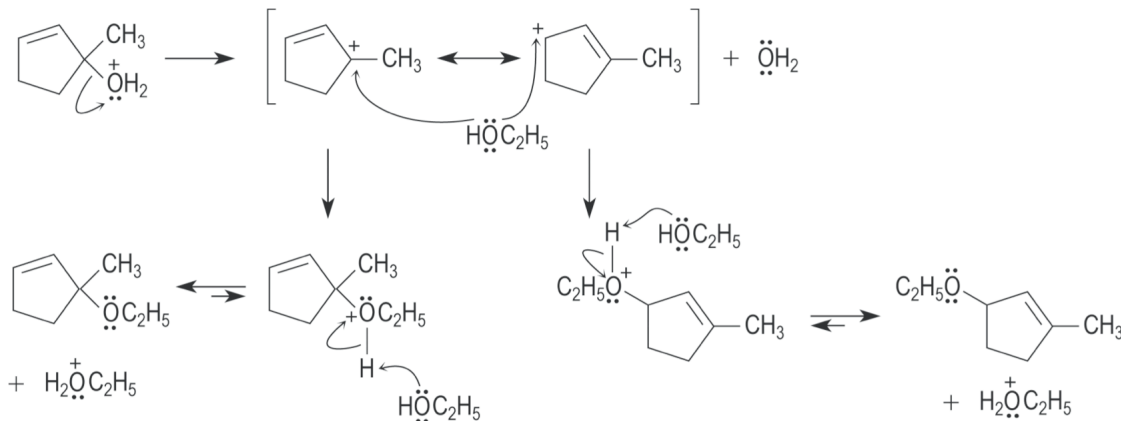


- (c) A hydrogen on the central carbon is more acidic than an acetylenic hydrogen because the conjugate-base anion resulting from removal of the central hydrogen is both allylic and propargylic, and is therefore doubly resonance-stabilized. The conjugate-base anion is alkylated by allyl bromide.

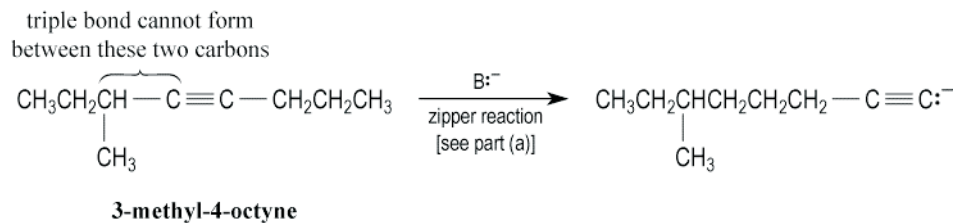


In the resonance structures of the anion intermediate, the negative charge is delocalized to two other carbons. (Draw these structures.) While the mechanism above shows why the indicated product is reasonable, it does not explain why products derived from the other possible resonance structures are not observed (or reported).

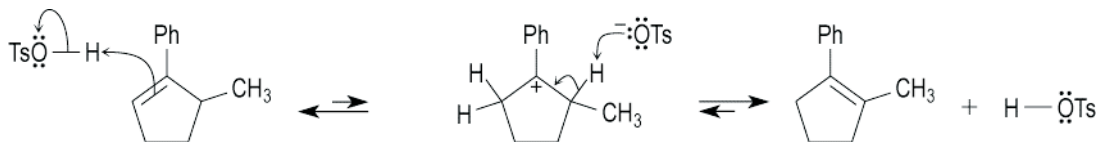
- (d) Protonation of the alcohol and loss of water give an allylic carbocation that can react with ethanol at either of two electron-deficient carbons to give a mixture of two constitutionally isomeric ethyl ethers. The following mechanism begins with the protonated alcohol.



- 17.39 (b) The question is whether the triple bond migrates to the end of the carbon chain nearer to the methyl branch or to the end of the chain farther from the methyl branch. Once we consider the mechanism shown in part (a), the answer becomes clear. The migration of the triple bond occurs *away* from the methyl branch, because the mechanism of the reaction requires a stepwise migration of the triple bond, and a triple bond cannot form at a carbon that bears a branch because a carbon have no more than four bonds.



- 17.41 The equilibrium lies to the right because the double bond has four alkyl substituents whereas, in the starting material, it has three. Recall that alkyl substitution at double bonds is a stabilizing effect (Sec. 4.5B, text pp. 144–146). The mechanism involves simply protonation of the double bond to give the benzylic cation and loss of a proton to give the product.



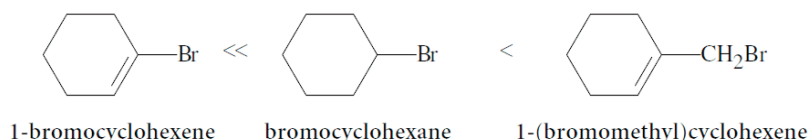


# Chapter 18

## The Chemistry of Aryl Halides, Vinyl Halides, and Phenols. Transition-Metal Catalysis

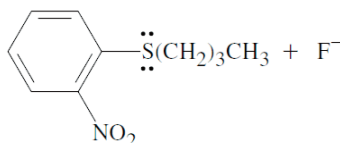
### Solutions to In-Text Problems

- 18.1 (b) 1-Bromocyclohexene, a vinylic halide, does not react by the  $S_N2$  mechanism; 1-(bromomethyl)cyclohexene, an allylic halide, reacts most rapidly. (See text Sec. 17.4, text p. 802.)



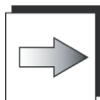
- 18.3 (b) The reactivity order is  $B \ll C < A$ . The reaction of compound *B* is slowest because vinylic halides are virtually inert in  $S_N1$  reactions; and the reaction of compound *A* is fastest because its ionization gives a resonance-stabilized allylic carbocation.

- 18.4 (b) The product results from nucleophilic aromatic substitution by the thiolate group:



- 18.5 (b) The second compound, *p*-fluoronitrobenzene, reacts most rapidly because only in the reaction of this compound is the intermediate Meisenheimer complex stabilized by resonance interaction of an unshared electron pair with the nitro substituent.

- 18.7 (b) The PPh<sub>3</sub> ligands are L-type ligands; hence, there are no X-type ligands, and, because the charge on Pd is 0, the oxidation state of Pd is 0.

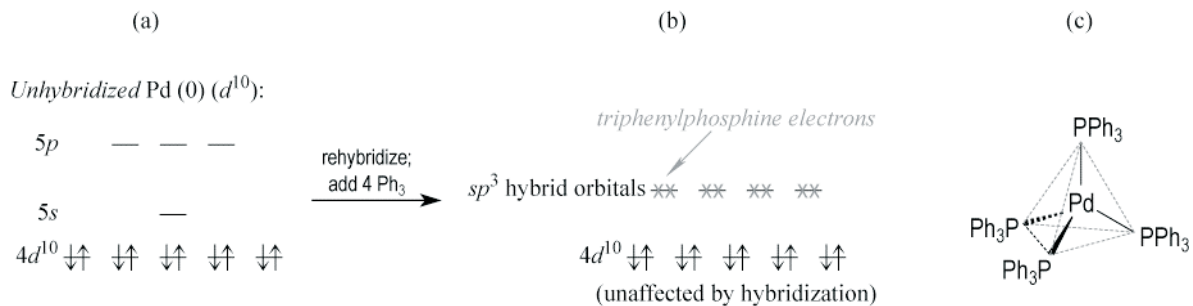


You might be wondering about the prefix *tetrakis* in the name of this complex. The prefixes *bis*, *tris*, and *tetrakis* are used as numerical prefixes instead of *di*, *tri*, and *tetra* when the group that is enumerated itself contains multiple substituents. Thus, the ligand triphenylphosphine has three phenyl groups on the phosphorus (thus the prefix *tri* in the name of this ligand). There are four triphenylphosphine ligands—thus the prefix *tetrakis*.

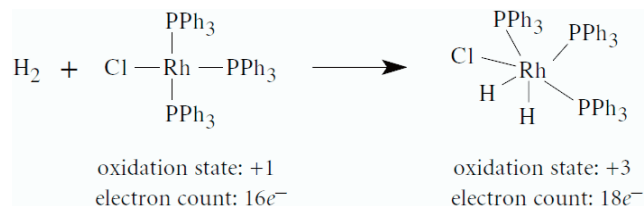
- 18.9 (b) Pd has ten valence electrons in the neutral atom. There are no charges and no X-type ligands in the complex; hence, this is a  $d^{10}$  complex. Using Eq. 18.24, text p. 836, with an oxidation state of 0, we get the same answer.

- 18.11 Neutral iron (Fe) has 8 electrons. Because CO is an L-type ligand, it is counted twice in the electron count. We simply solve for  $x$  in  $8 + 2x = 18$  and obtain  $x = 5$ . Fe(CO)<sub>5</sub>, or pentacarbonyliron(0), is in fact a stable complex that can be purchased commercially.

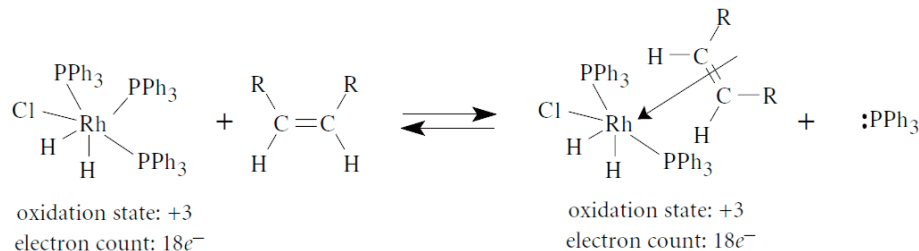
- 18.13 (b) Triphenylphosphine (PPh<sub>3</sub>) is an L-type ligand. If we strip the four PPh<sub>3</sub> ligands from the Pd (palladium), a Pd (0) atom remains. From Fig. 18.3 on text p. 832, Pd has 10 valence electrons. This is exactly the number needed to fill all of the 4d orbitals with two electrons each. This leaves four valence orbitals—the 5s and the 5p orbitals—empty. These are hybridized to form more directed orbitals. (This situation is exactly like carbon hybridization in methane, except that we are using orbitals from period 5.) Hybridize one 5s and three 5p orbitals gives four sp<sup>3</sup> hybrid orbitals, which, as we know from methane, are directed to the corners of a regular tetrahedron. Each of these empty orbitals accepts a pair of electrons from a PPh<sub>3</sub> ligand. Thus, the Pd(PPh<sub>3</sub>)<sub>4</sub> complex is tetrahedral.



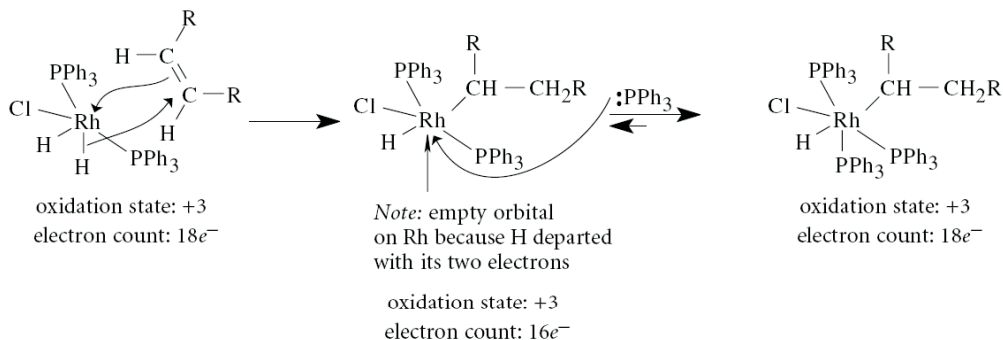
- 18.15 (a) Oxidative addition of H<sub>2</sub> to the catalyst:



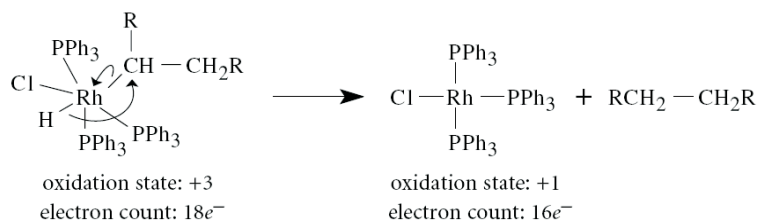
Ligand substitution of one PPh<sub>3</sub> by the alkene:



1,2-Insertion of the alkene into an Rh—H bond and addition of the previously expelled PPh<sub>3</sub>:



*Reductive elimination of the product to regenerate the catalyst:*



18.16 The steps in Eq. 18.42b, text p. 846, of the text are numbered for reference.

*Step 1:*

Fundamental process: oxidative addition

Oxidation state of Pd starting catalyst ( $\text{PdL}_2$ ): 0

Electron count of Pd in the starting catalyst:  $14e^-$ . (Note that neutral Pd is a 10-electron atom.)

Oxidation state of Pd in the product: +2

Electron count of Pd in the product:  $16e^-$

*Step 2: (From here on, the reactant has the same properties as the product of the previous step.)*

Fundamental process: ligand substitution

Oxidation state of Pd in the product: +2

Electron count of Pd in the product:  $16e^-$

*Step 3:*

Fundamental process: 1,2-ligand insertion

Oxidation state of Pd in the product: +2

Electron count of Pd in the product:  $14e^-$

*Step 4:*

Fundamental process:  $\beta$ -elimination

Oxidation state of Pd in the product: +2

Electron count of Pd in the product:  $16e^-$

*Step 5:*

Fundamental process: ligand dissociation

Oxidation state of Pd in the product: +2

Electron count of Pd in the product:  $14e^-$

*Step 6:*

Fundamental process: ligand association

Oxidation state of Pd in the product: +2

Electron count of Pd in the product:  $16e^-$

*(Steps 5 and 6 together result in a ligand substitution.)*

Step 7:

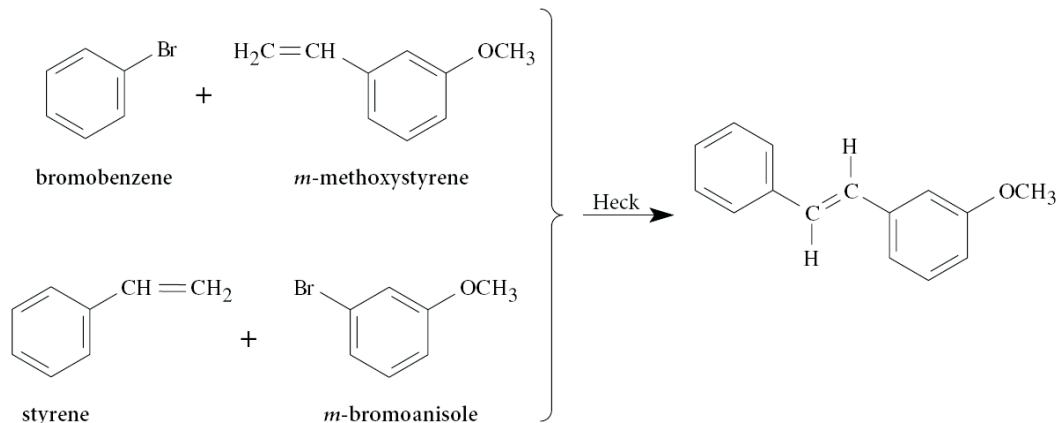
Fundamental process: reductive elimination

Oxidation state of Pd in the product: 0

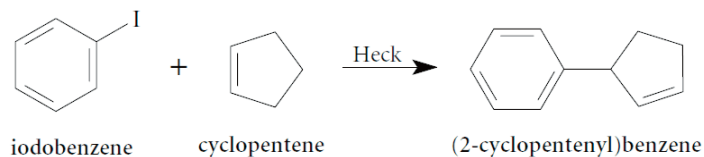
Electron count of Pd in the product:  $14e^-$

(The catalyst is regenerated in this step.)

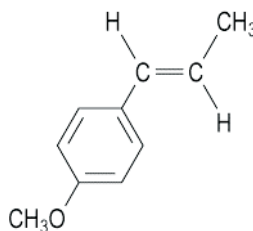
- 18.18 Either aryl substituent could originate from the aryl halide or from the alkene. Remember, if the alkene substituent is aryl (as in these cases), substitution occurs mainly at the less branched carbon.



- 18.20 This is essentially like the cyclohexene case given in Eq. 18.43 (text p. 846) and subsequent discussion.

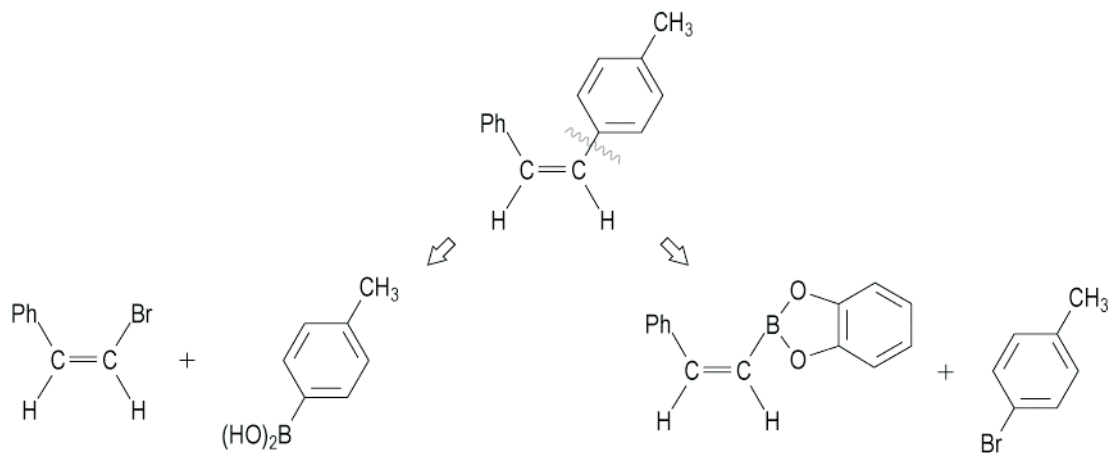


- 18.21 (b) As illustrated in Eq. 18.48, text p. 849, Suzuki coupling occurs with retention of the alkene stereochemistry.

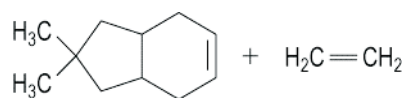


- 18.23 Start by breaking the compound at the bond between the aryl ring and the alkene; then place a bromine atom (Br) on one of the cleaved fragments and a boronic acid [ $B(OH)_2$ ] or catecholborane (see Eq. 18.50, text p. 849) on the other:

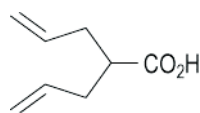




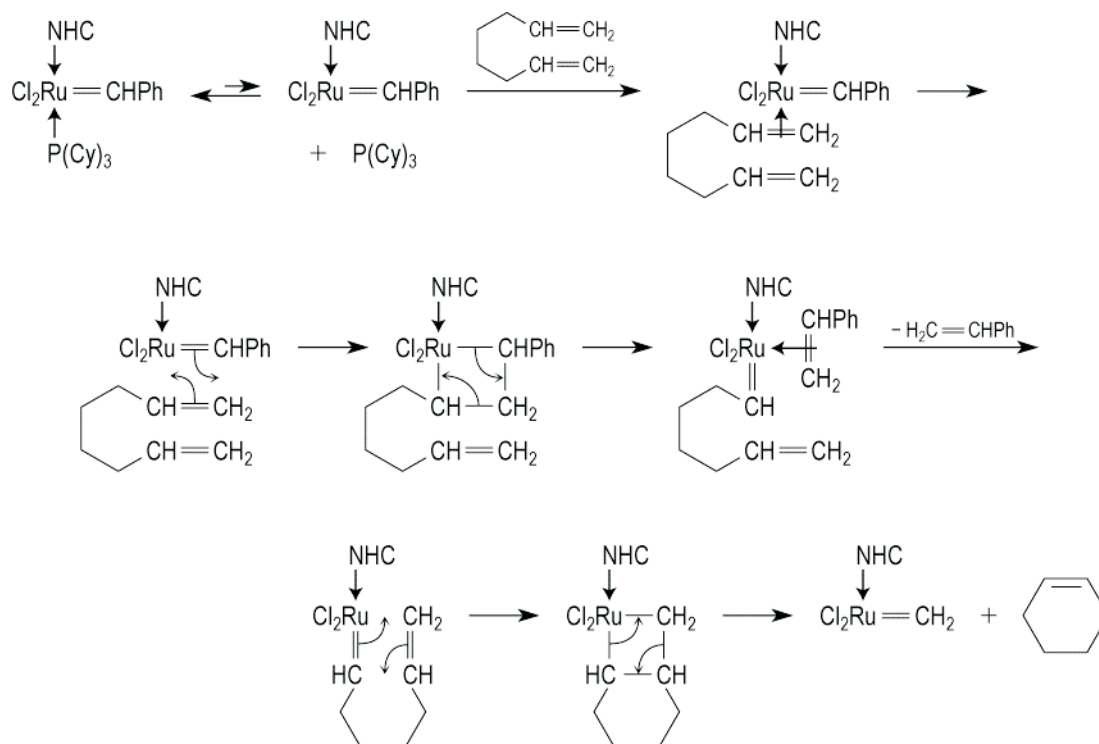
18.26 (b)



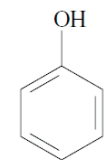
18.27 (b)



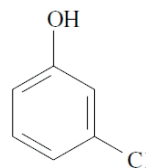
18.28



- 18.30 (b) *Meta*-chlorophenol is more acidic because the conjugate-base anion, *m*-chlorophenoxide, is stabilized by the electron-withdrawing polar effect of the chloro substituent. The actual  $pK_a$  values are

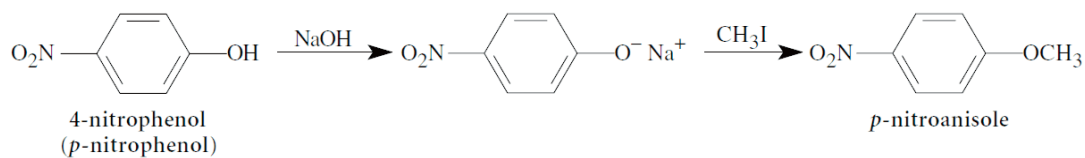


phenol  
 $pK_a = 9.95$

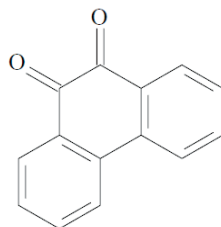


*m*-chlorophenol  
 $pK_a = 9.02$

- 18.31 (a)

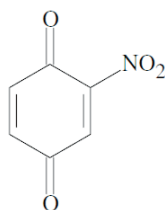


- 18.34 (a)

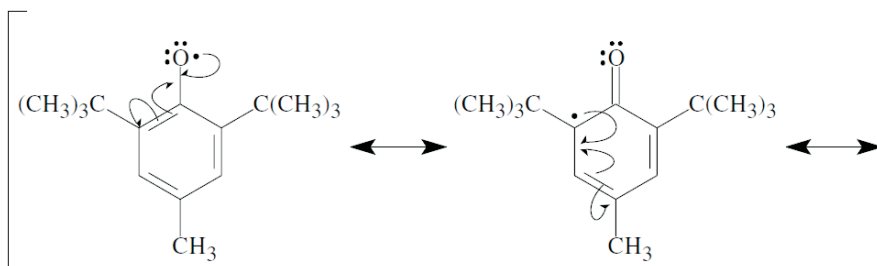


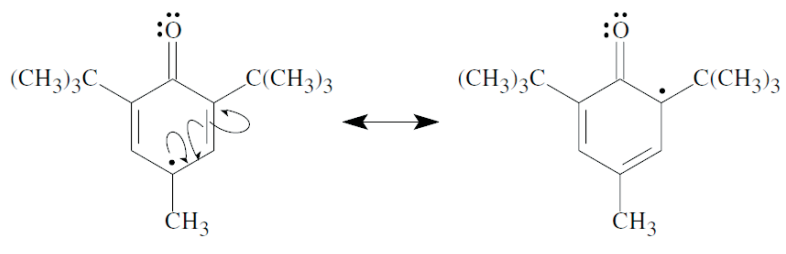
9,10-phenanthraquinone  
(an *o*-quinone)

- 18.35 (a) A *para*-quinone is formed as in Eq. 18.69, text p. 862; the nitro group is unaffected.

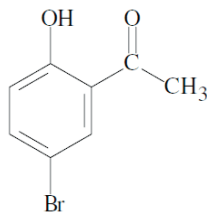


- 18.36 (b) As in part (a), the phenolic hydrogen atom is abstracted because a resonance-stabilized radical is formed.

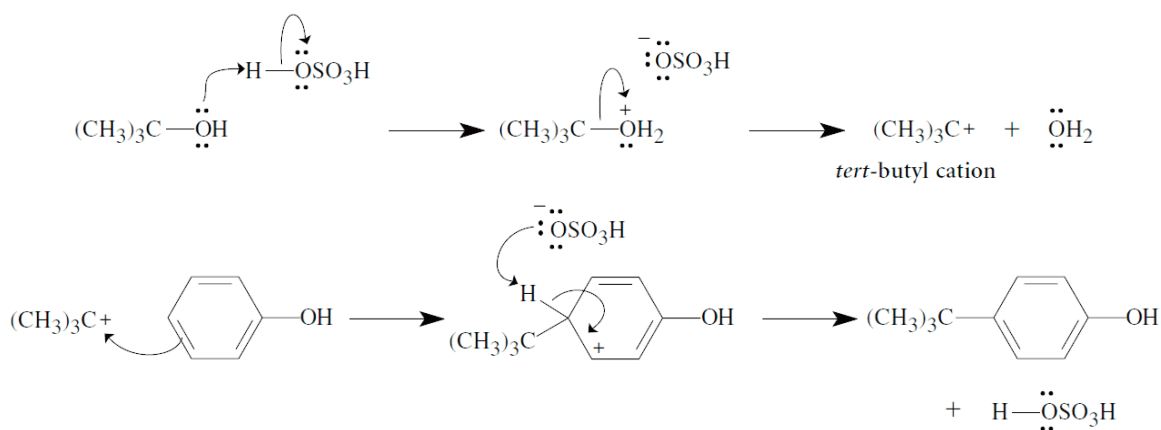




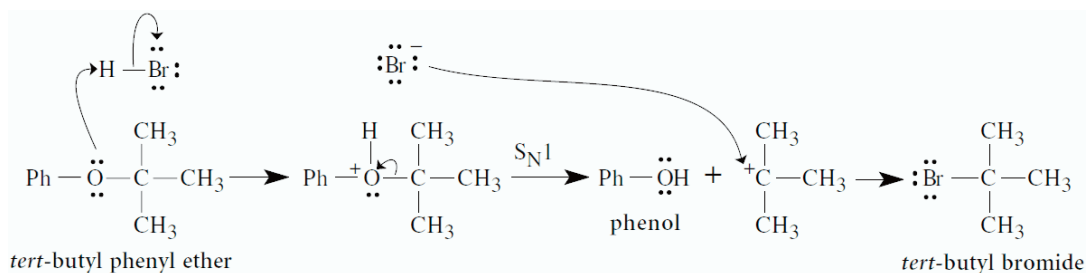
18.38 (c)



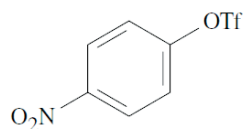
18.39 The electrophile is the *tert*-butyl cation, which is formed by protonation of the alcohol and the Lewis acid–base dissociation of water.



18.40 (b) Diphenyl ether does not cleave with hot, concentrated HBr, because such a cleavage would require either an  $S_N1$  reaction or an  $S_N2$  reaction at a phenyl–oxygen bond; as this section of the text shows, such reactions do not occur. In contrast, *tert*-butyl phenyl ether cleaves by an  $S_N1$  mechanism involving protonation of the oxygen and loss of phenol to form a *tert*-butyl cation, which undergoes a Lewis acid–base association reaction with bromide ion to form *tert*-butyl bromide.

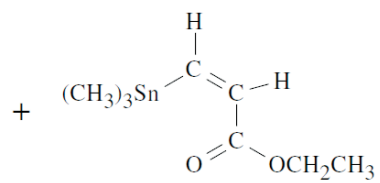


18.42 The triflate derivative of *p*-nitrophenol and the (*Z*)-stereoisomer of the appropriate trimethylstannyl derivative would be required.



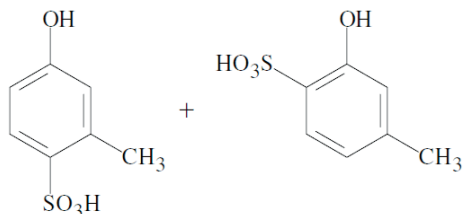
*p*-nitrophenyl triflate

(prepared from *p*-nitrophenol  
and triflic anhydride; Eq. 18.88, text p. 872)

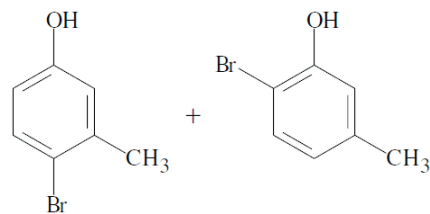


## Solutions to Additional Problems

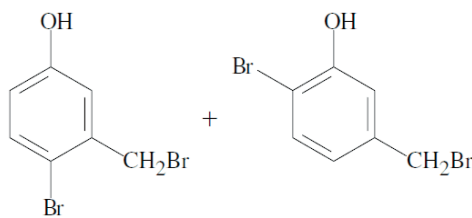
18.45 (a)



(b)



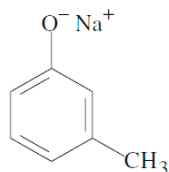
(c) Both benzylic bromination and ring bromination take place; see Eq. 18.75, text p. 867.



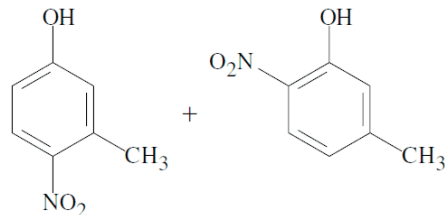
(d)

no reaction

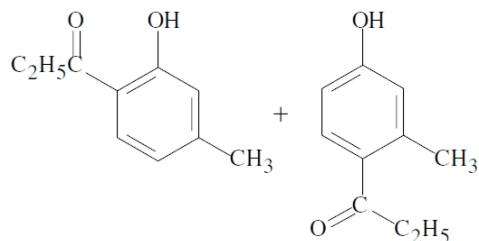
(e)



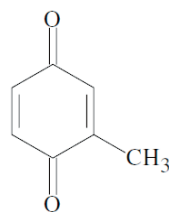
(f)



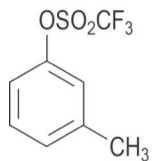
(g)



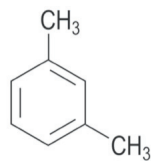
(h)



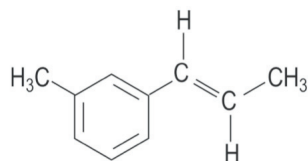
(i)



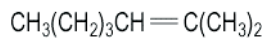
(j)



(k)

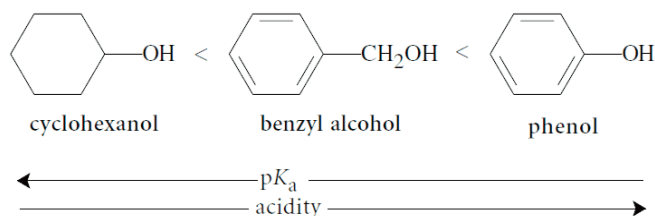


18.46 (b)

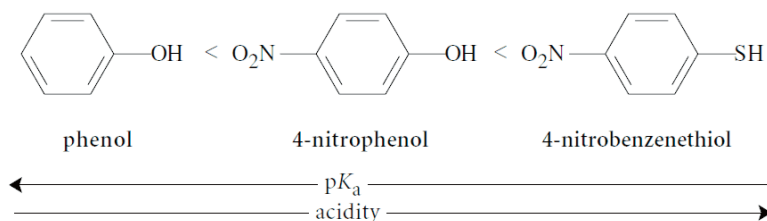
**2-methyl-2-heptene**

18.47 (b)

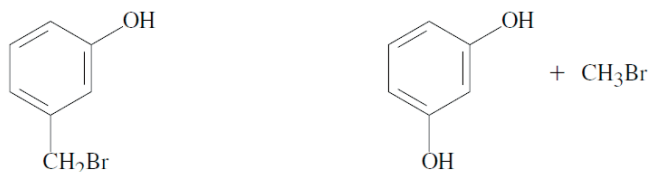
Phenol is most acidic because its conjugate-base anion is stabilized by both the polar and resonance effects of the phenyl group. The conjugate-base anion of benzyl alcohol is stabilized by the polar effect of the phenyl group. The conjugate-base anion of cyclohexanol has none of these stabilizing contributions. The acidity order is



- (d) 4-Nitrophenol is more acidic than phenol (see text p. 859), and benzenethiols are more acidic than phenols (element effect.) The acidity order is

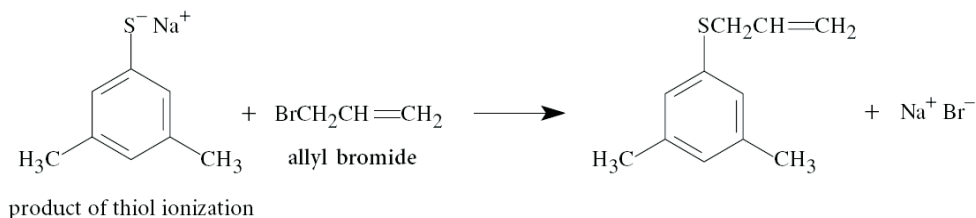


- 18.52 The phenol group is unaffected in both compounds (except for a small amount of protonation of the phenol oxygen); the alcohol and ether groups react.



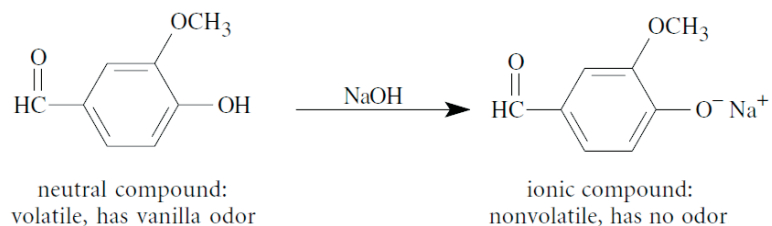
- 18.54 Sodium ethoxide converts the thiol completely into its conjugate-base thiolate ion.

- (a) The thiolate ion is alkylated. (Remember from Sec. 17.4, text p. 802, that allyl bromide is a particularly reactive alkylating agent.)

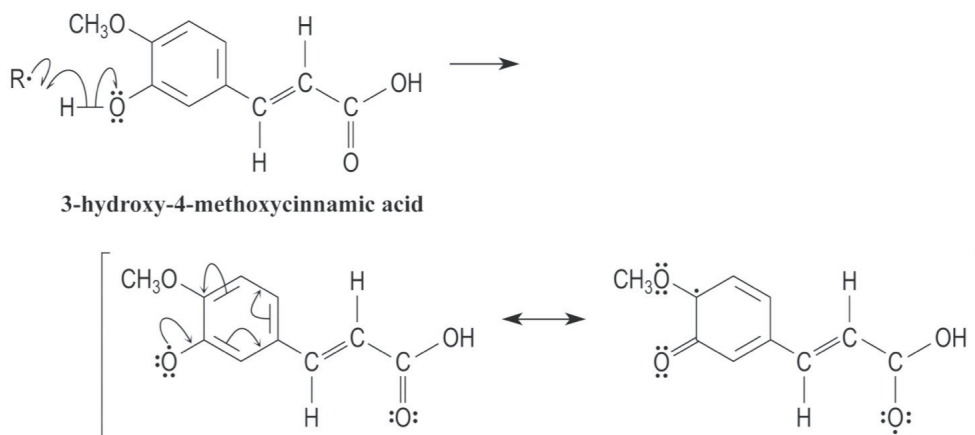


- (b) No further reaction of the thiolate occurs because bromobenzene, an aryl halide, is inert to nucleophilic substitution and elimination reactions. (Sec. 18.1, text p. 823.)

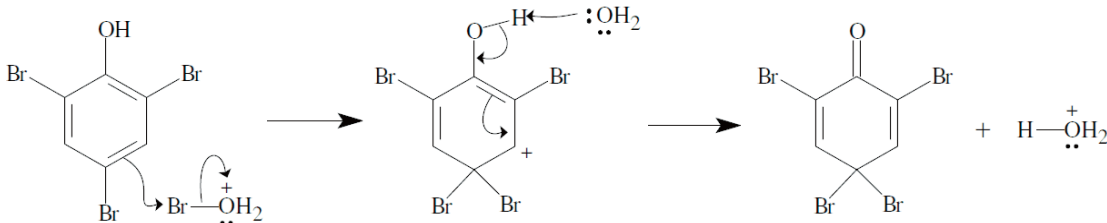
- 18.57 It is the *un-ionized* form of vanillin that has the typical odor. In NaOH solution, the phenol group of vanillin ionizes to its conjugate-base phenoxide ion; because vanillin is no longer present, and because ionic compounds such as the conjugate-base phenoxide are not volatile, the odor disappears. (A compound has to be volatile—that is, it must have a significant vapor pressure—to enter the gas phase and thus reach the nostrils.) Acidification of the solution brings about protonation of the phenoxide and regeneration of vanillin and, hence, the characteristic odor.



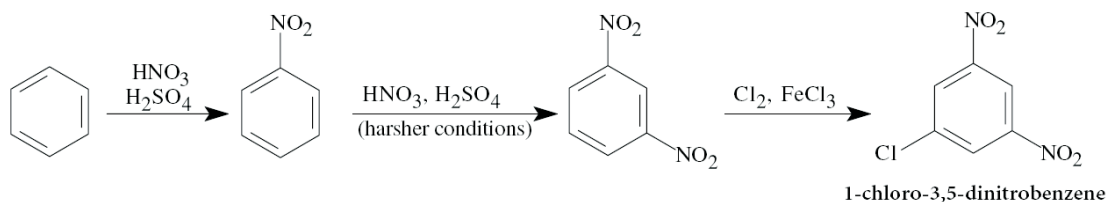
- 18.59 (a) Because the  $S_N2$  reaction requires approach of the nucleophile from the backside of the C—Br bond, and because this would require approach of the nucleophile along the axis of the triple bond, the  $S_N2$  reaction is impossible.
- (b) 1-Haloalkynes cannot undergo an  $S_N1$  reaction. Such a reaction would require that a carbocation be formed at an  $sp$ -hybridized carbon. Yet carbocations optimally require  $sp^2$  hybridization, which, in turn, requires trigonal planar geometry. An alkyne carbon cannot achieve this geometry because its three bonds are connected to the same atom. Hence, the  $sp^2$  hybridization required for carbocation formation is impossible.
- 18.60 (b) No. The phenolic group is meta to the alkene and carboxylic acid groups and the radical that is formed from proton abstraction cannot delocalize to the alkene and carboxylic acid groups.



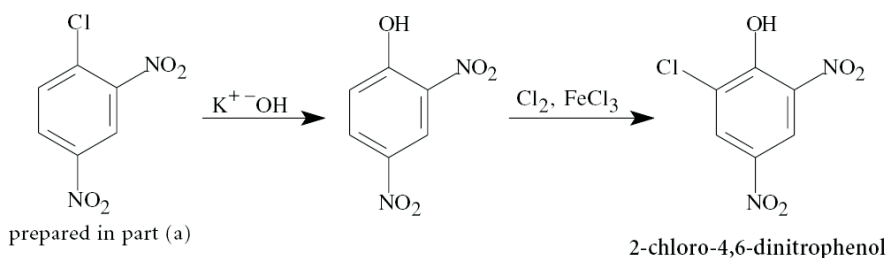
- 18.62 By loss of a proton from the hydroxy group, the carbocation intermediate becomes the neutral compound that precipitates. (Formation of the electrophile is shown in Eq. 18.77, text p. 868.)



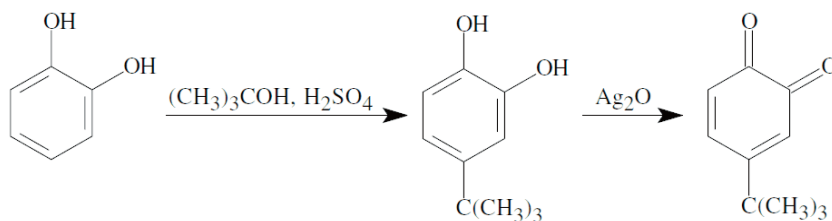
- 18.64 (b)



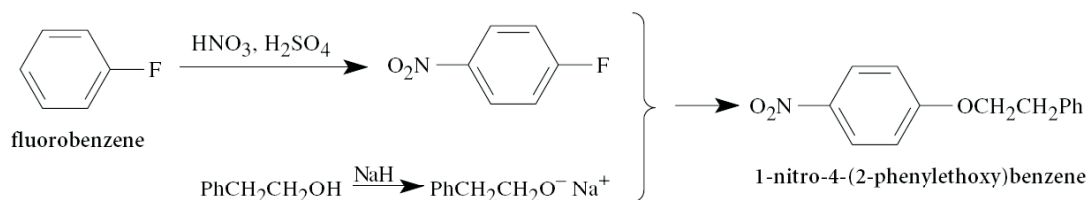
- (e)



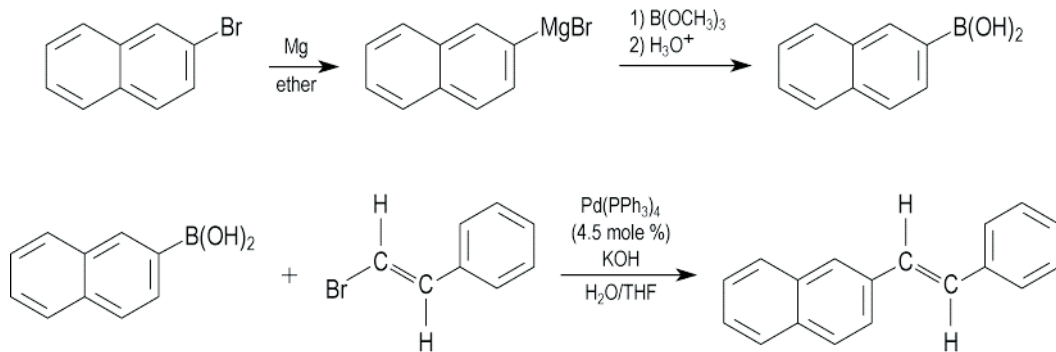
(g)



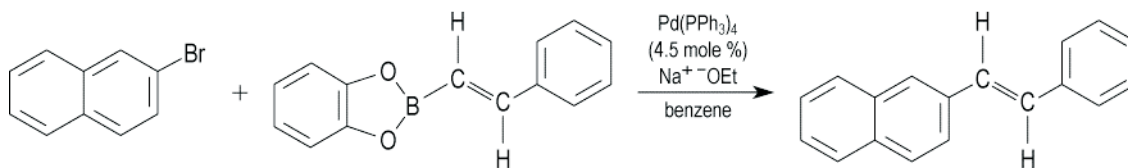
(i)



(k) First, prepare the Grignard reagent from the aryl bromide, and use it to prepare the corresponding aryl boronic acid. Couple the resulting aryl boronic acid with (*E*)-1-bromo-2-phenylethene in the presence of a Pd(0) catalyst and aqueous base (Suzuki coupling).



Alternatively, couple the aryl bromide with (*E*)-1-catecholboranyl-2-phenylethene in the presence of a Pd(0) catalyst, sodium ethoxide, and a non-aqueous solvent (Suzuki coupling)—water would hydrolyze the catecholboranyl reagent.

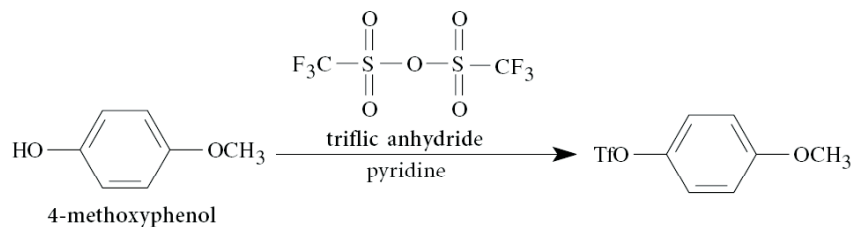


(m) First, prepare the Grignard reagent from the alkyne, and use it to prepare the corresponding stannane.

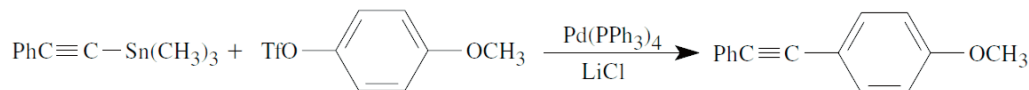


Next, prepare the triflate of the phenol.

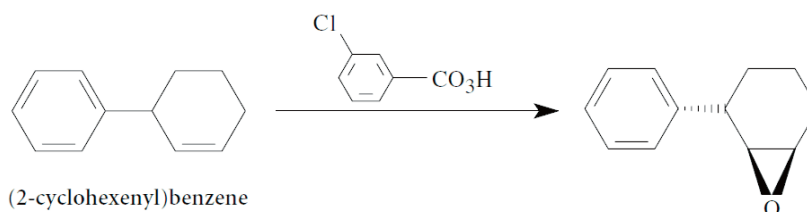




Finally, couple the triflate and the stannane in a Stille reaction.

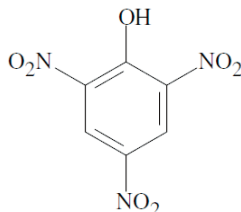


- (o) Start with (2-cyclohexenyl)benzene, which is prepared from iodobenzene and cyclohexene by a Heck reaction as shown in Eq. 18.43, text p. 846.

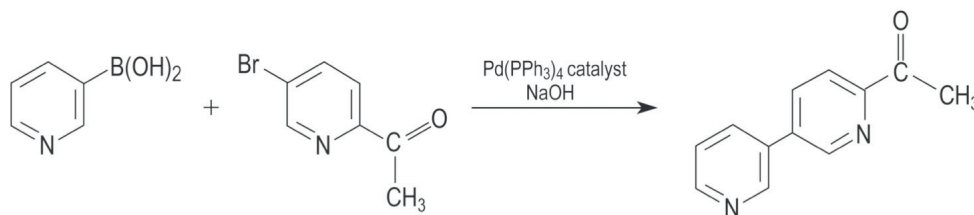


It is reasonable to suppose that epoxidation will occur at the face of the ring opposite to that occupied by the bulky phenyl group. (As noted in the problem, the product is a racemate because the reagents are achiral.)

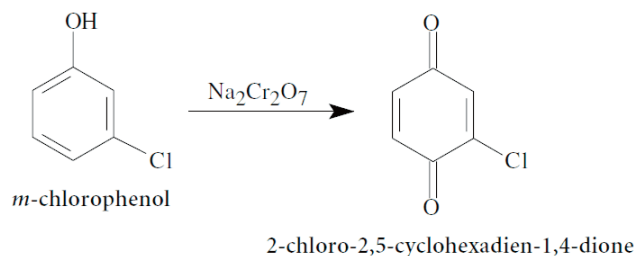
- 18.65 (b) The product is formed by a nucleophilic aromatic substitution reaction in which chloride is displaced by hydroxide ion. The product is ionized by  $\text{OH}^-$  present in the reaction mixture; addition of acid ( $\text{H}_3\text{O}^+$ ) forms the neutral phenol.



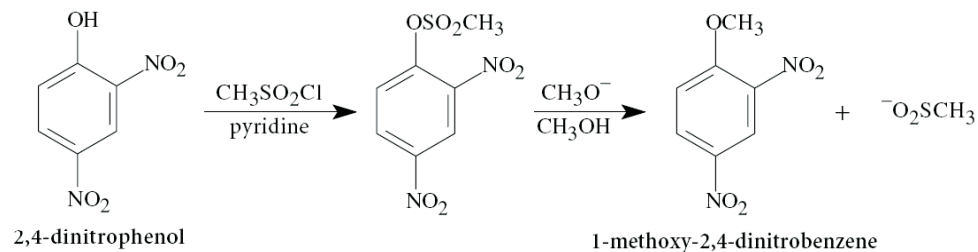
- (d) No reaction occurs under the mild conditions.  
 (e) This is a Suzuki coupling reaction in which pyridine derivatives are used instead of benzene derivatives.



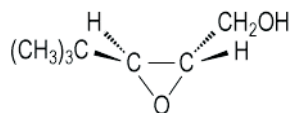
- (k) Oxidation occurs to give the quinone.



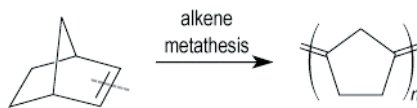
- (l) The methanesulfonate derivative of 2,4-dinitrophenol undergoes a nucleophilic substitution reaction in which the methanesulfonate group is displaced by methoxide.



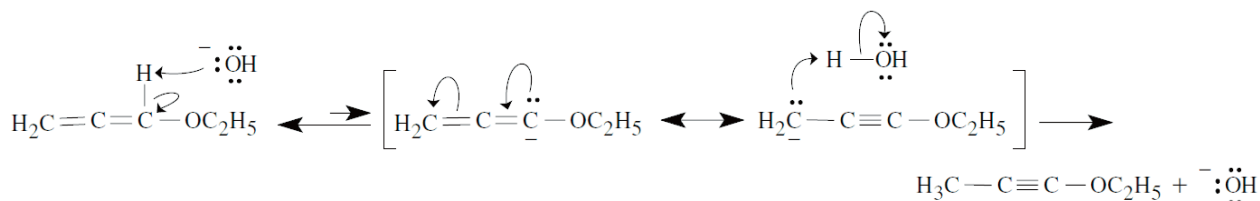
- (o) Alkene metathesis produces the more stable *trans* alkene; asymmetric epoxidation (see Sec. 11.10, text p. 522) produces the epoxide shown (see Eq. 11.74a, text p. 523, for an equivalent reaction).



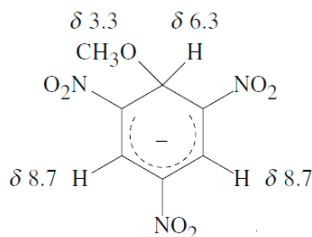
18.66 (b)



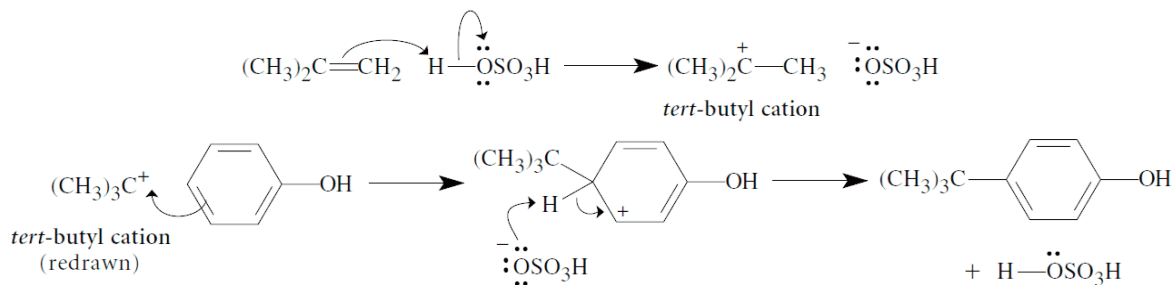
- 18.68 The basic principle needed to understand the results is that elimination is most rapid when it occurs with *anti* stereochemistry. In the first reaction, *anti*-elimination leads to the observed product. In the second reaction, formation of the alkyne requires a slower *syn*-elimination; hence, another process can compete, namely, elimination of a methyl hydrogen and the bromine to form the allene. In the first reaction, elimination of the methyl hydrogen to form the allene is a slower process because allenes are not so stable as alkynes. The transition state for elimination is destabilized by its allene-like character. (The methyl hydrogens are approximately as acidic as the vinylic hydrogens because they are allylic.) It is also possible that the allene is the only product formed in the second reaction and that the alkyne is formed by a base-catalyzed isomerization of the allene:



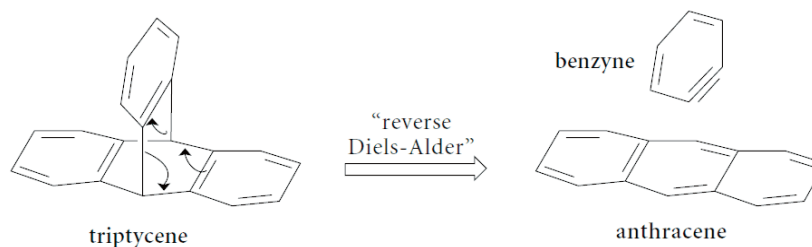
- 18.70 The spectrum is consistent with the formation of an anionic intermediate—a stable Meisenheimer complex. (The dotted lines symbolize resonance delocalization of the negative charge.) If you draw out the resonance structures for this ion, you will see that charge is delocalized to the carbons bearing the nitro groups, and it can also be delocalized into the nitro groups. However, charge is *not* delocalized to the other carbons. Hence, the protons on these carbons do not show the smaller chemical shift that would be expected if there were high electron density on these carbons.



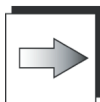
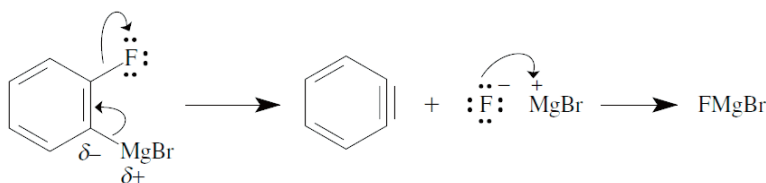
- 18.73 (b) Protonation of 2-methylpropene gives the *tert*-butyl cation, which serves as the electrophile in an electrophilic aromatic substitution reaction.



- 18.77 Deduce the structure of the “very interesting intermediate” by mentally imagining a “reverse Diels–Alder” reaction of triptycene that yields anthracene and the intermediate, which is benzyne:

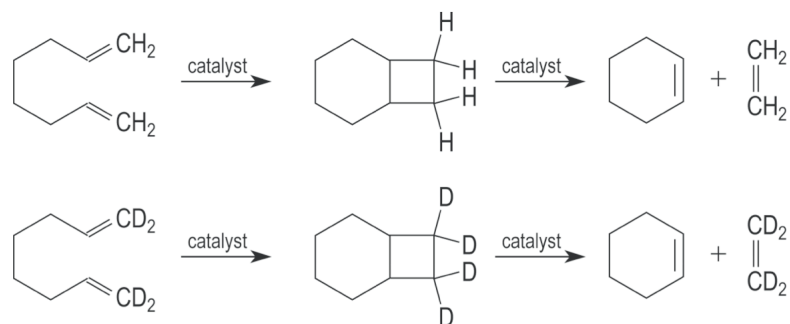


The Grignard reagent has carbanion character, and this “carbanion” is a strong base. Elimination of the weaker base fluoride gives benzyne:

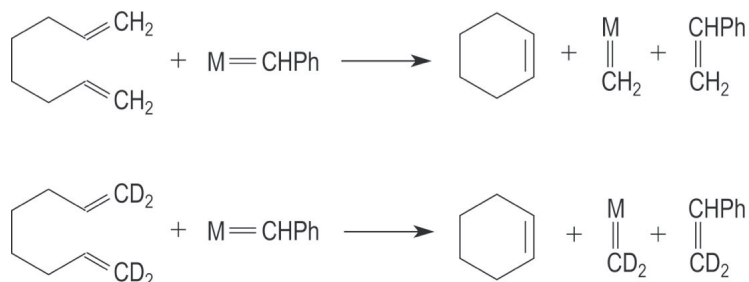


Because alkynes require linear geometry, it is difficult to incorporate them into six-membered rings. Therefore, benzyne is highly *strained* and, although it is a neutral molecule, it is very unstable. (Benzyne is about  $205 \text{ kJ mol}^{-1}$  ( $49 \text{ kcal mol}^{-1}$ ) more unstable than an ordinary alkyne.) Indeed, benzyne has been too reactive to isolate except at temperatures near absolute zero. (See also the solution to Problem 18.76 in the Study Guide and Solutions Manual.)

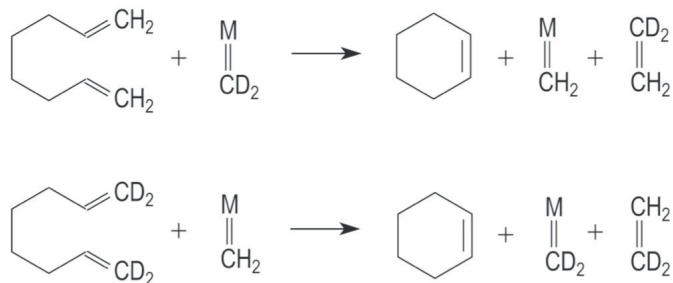
- 18.81 (b) The pairwise mechanism can only give ethylene and ethylene- $d_4$ , because at no point in the mechanism does one of the  $\text{CH}_2$  (or  $\text{CD}_2$ ) groups become detached from its parent molecule:



To see the results of the metallacycle mechanism, note that  $M=CH_2$  and  $M=CD_2$  (where  $M$  = the ruthenium and its ligands) are formed in the first catalytic cycle. (We leave it to you to fill in the details.)



Now, ethylene- $d_2$  can form in *two ways*: by the reaction of  $M=CH_2$  with the  $d_4$ -diene starting material, or by the reaction of  $M=CD_2$  with the undeuterated diene:



However, ethylene- $d_4$  can form in only one way—the reaction of  $M=CD_2$  with the  $d_4$ -diene starting material; and ethylene- $d_0$  can form in only one way—the reaction of  $M=CH_2$  with the undeuterated diene starting material. Consequently, the formation of ethylene- $d_2$  enjoys a two-fold statistical advantage, and the ratio of the three ethylenes is therefore  $H_2C=CH_2 : H_2C=CD_2 : D_2C=CD_2 = 1 : 2 : 1$ . The result of this very elegant experiment was that the three ethylenes were formed in this statistical ratio.

- 18.85 Whether the nucleophile occurs in biological systems or in the laboratory, nucleophilic substitution does not occur on aryl derivatives (see Sec. 18.1, text p. 823) unless the ring is activated by electron-withdrawing groups (such as carbonyl groups or nitro groups) that stabilize the Meisenheimer complex in nucleophilic aromatic substitution. (See Sec. 18.4, text p. 828.) Furthermore, both fluoride and cyanide are fairly strong bases (see Table 3.1, text p. 103) and are therefore very poor leaving groups.

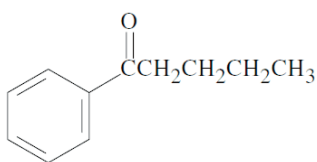
# Chapter 19

## The Chemistry of Aldehydes and Ketones.

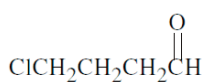
### Addition Reactions

#### Solutions to In-Text Problems

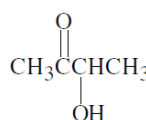
19.1 (b)



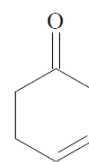
(d)



(e)



(g)

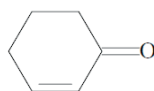


19.2

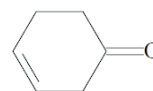
- (a) 2-Propanone  
(d) (*E*)-3-Ethoxy-2-propenal  
(f) 4,4-Dimethyl-2,5-cyclohexadienone

19.3

- (b) 2-Cyclohexenone has a lower carbonyl stretching frequency because its two double bonds are conjugated.



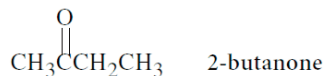
2-cyclohexenone  
has conjugated double bonds



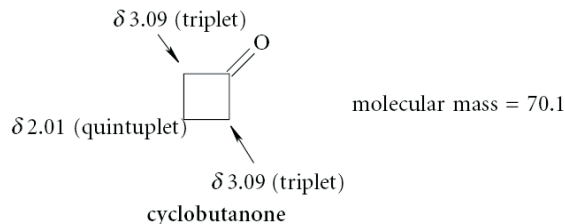
3-cyclohexenone

19.4

- (b) The compound is 2-butanone:

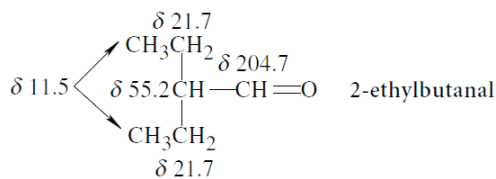


- (c) The high frequency of the carbonyl absorption suggests a strained ring. (See Eq. 19.4, text p. 897.) In fact, cyclobutanone matches the IR stretching frequency perfectly and the NMR fits as well:

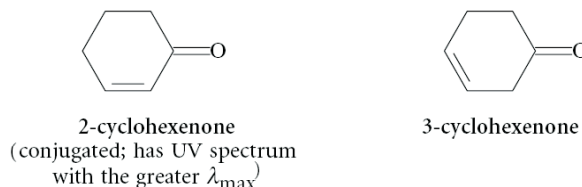


19.6

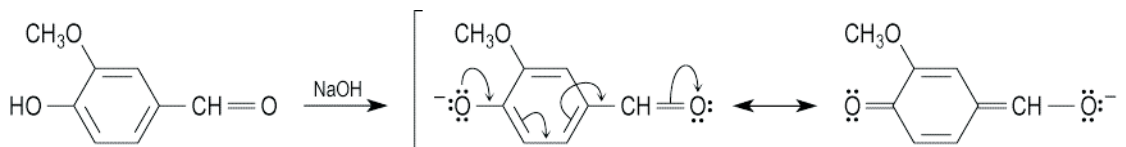
The structure and CMR assignments of 2-ethylbutanal are shown below. The two methyl groups are chemically equivalent, and the two methylene groups are chemically equivalent; all carbons with different CMR chemical shifts are chemically nonequivalent.



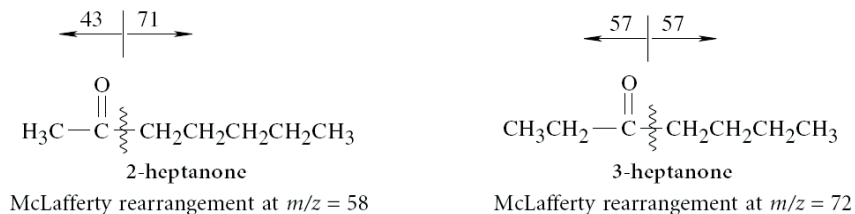
- 19.7 (a) The double bonds in 2-cyclohexenone are conjugated, but the double bonds in 3-cyclohexenone are not. Consequently, 2-cyclohexenone has the UV spectrum with the greater  $\lambda_{\text{max}}$ .



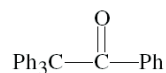
- 19.9 Compound *A*, vanillin, should have a  $\pi \rightarrow \pi^*$  absorption at a greater  $\lambda_{\text{max}}$  when dissolved in NaOH solution because the resulting phenolate can delocalize into the carboxaldehyde group; the resulting phenolate from compound *B*, isovanillin, on the other hand, can only delocalize in the aromatic ring.



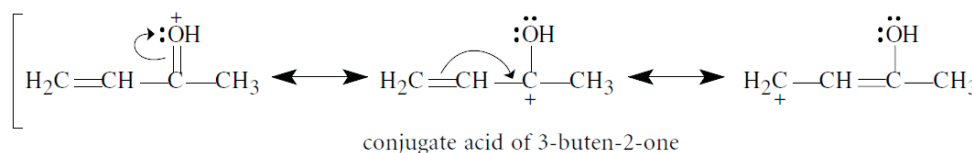
- 19.11 The mass spectrum of 2-heptanone should have major peaks at  $m/z = 43$  (from  $\alpha$ -cleavage), 71 (from inductive cleavage), and 58 (from McLafferty rearrangement). The mass spectrum of 3-heptanone should have a major peak resulting from both inductive cleavage and  $\alpha$ -cleavage at  $m/z = 57$  and a major peak resulting from McLafferty rearrangement at  $m/z = 72$ . Notice that the position of the even-mass, odd-electron ion is a major distinguishing feature. We leave it to you to draw out these fragmentations.



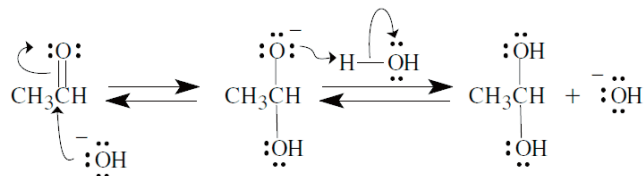
- 19.13 (b) The reaction is exactly like the one shown in Study Problem 19.2 on text p. 905 with phenyl instead of methyl substituents. The product is the following ketone:



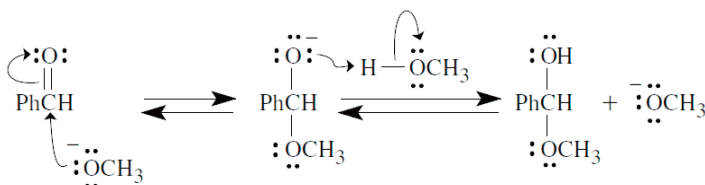
- 19.14 (b) The conjugate acid of 3-buten-2-one has more important resonance structures than the conjugate acid of 2-butanone and is therefore more stable relative to unprotonated ketone than the conjugate acid of 2-butanone. Greater stability of the conjugate acid means that the ketone is more basic.



- 19.15 (a) The mechanism of the hydroxide-catalyzed hydration of acetaldehyde:

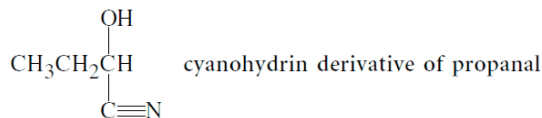


- 19.16 (b) The methoxide-catalyzed addition of methanol to benzaldehyde is very similar to the hydroxide-catalyzed hydration mechanism (Problem 19.15a):



(See the discussion starting at the bottom of text p. 909.) We typically invoke as a base the conjugate base of whatever acid is involved in the mechanism. Thus, if  $\text{H}_3\text{O}^+$  is involved in a mechanism, its conjugate base ( $\text{H}_2\text{O}$ ) acts as the base. We would not invoke both  $\text{H}_3\text{O}^+$  and  $\text{OH}^-$  in the same mechanism because a strong acid and a strong base cannot coexist in solution.

- 19.17 The data in Table 19.2, text p. 911, of the text show that hydration of benzaldehyde is less than 0.01 times as favorable as hydration of an unconjugated aliphatic aldehyde such as acetaldehyde. The assumption that the same principles apply to cyanohydrin formation leads to the prediction that propanal should have the greater proportion of cyanohydrin at equilibrium. The structure of this cyanohydrin is as follows:

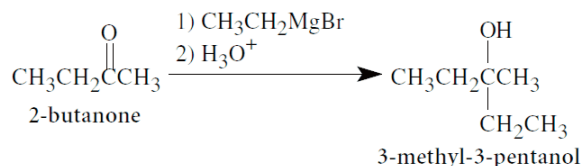


- 19.19 We use the same principles to predict reactivity that we use to predict relative equilibrium constants. The more prone a carbonyl compound is to form an addition product, the more reactive it is.
- (b) The first compound, 2,3-butanedione, is more reactive, because the partial positive charge on one carbonyl destabilizes the molecule by its repulsive interaction with the partial positive charge on the other. (See Problem 19.18, text p. 913, for a similar situation.)

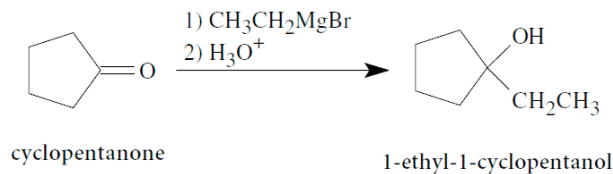
- 19.20 (b)
- $$\text{CH}_3\overset{\text{O}}{\parallel}\text{CCH}_2\text{CH}_3$$
- 2-butanone

- 19.22 In each case, ethyl bromide,  $\text{CH}_3\text{CH}_2\text{Br}$ , reacts with Mg to give ethylmagnesium bromide,  $\text{CH}_3\text{CH}_2\text{MgBr}$ , which is then allowed to react as shown below.

(b)

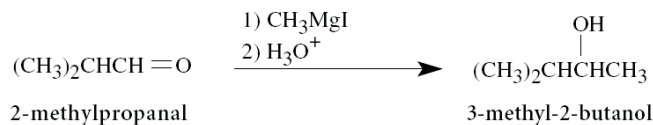


(f)

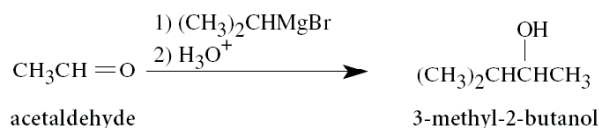


19.23 Either alkyl group bound to the  $\alpha$ -carbon of the alcohol can in principle originate from the Grignard reagent.

Synthesis #1:

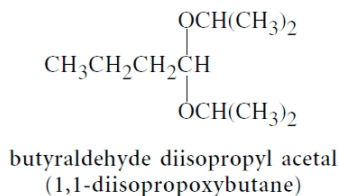


Synthesis #2:



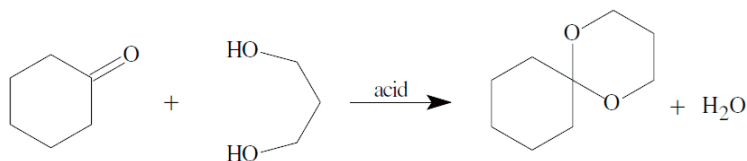
In synthesis #1, the Grignard reagent is prepared by the reaction of  $\text{CH}_3\text{I}$  (methyl iodide) and Mg in dry ether; in synthesis #2, the Grignard reagent is prepared from the similar reaction of  $(\text{CH}_3)_2\text{CH}-\text{Br}$  (isopropyl bromide) and Mg.

19.24 (b)

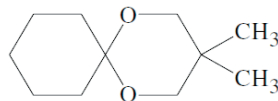


19.25 A diol reacts with a ketone to form a cyclic acetal.

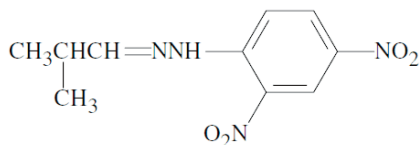
(b)



19.26 (b) When five- and six-membered rings can be formed, diols generally react with aldehydes and ketones to give cyclic acetals, and this case is no exception:

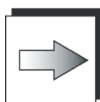
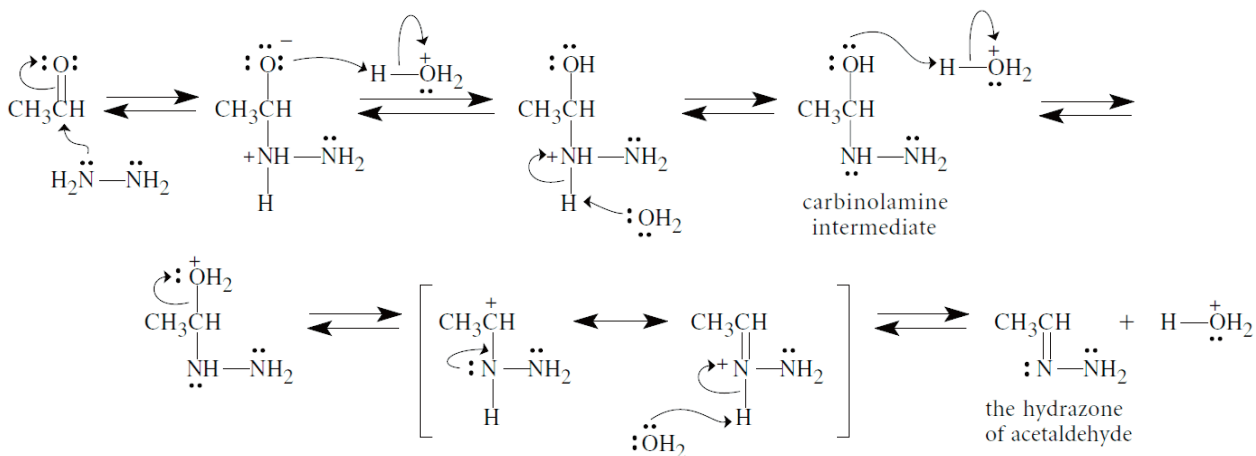


19.28 (b)

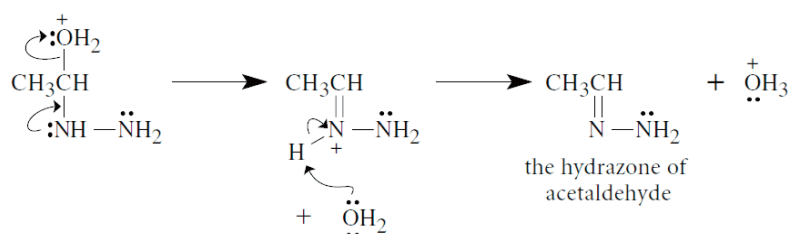




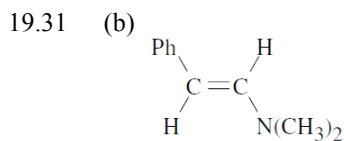
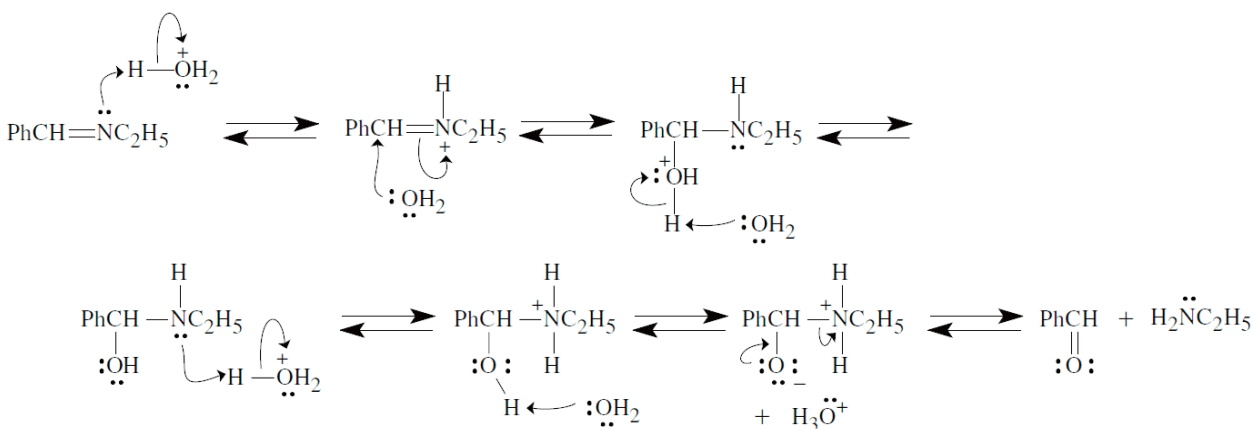
- 19.29 First, the carbinolamine intermediate is formed. This intermediate then undergoes acid-catalyzed dehydration to give the hydrazone. (Be sure to consult Study Guide Link 19.7 on p. 436 of the Study Guide and Solutions Manual.)



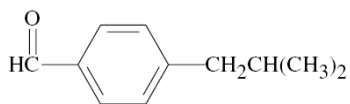
Note that it is equally appropriate to write the loss of water and formation of the carbon-nitrogen double bond as one step, thus avoiding the necessity of drawing resonance structures:



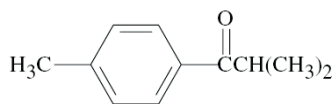
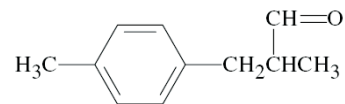
- 19.30 Imine hydrolysis is the reverse of imine formation. Therefore, retrace the steps of imine formation as illustrated in the solution to Problem 19.29, starting with the imine and working backwards to the aldehyde and the amine.



- 19.32 Any compound with a carbonyl group on any of the prospective alkyl carbons could in principle serve as a starting material. (The answer is restricted to compounds containing only one carbonyl group.)

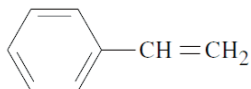


4-isobutylbenzaldehyde

*p*-methylisobutyrophenone

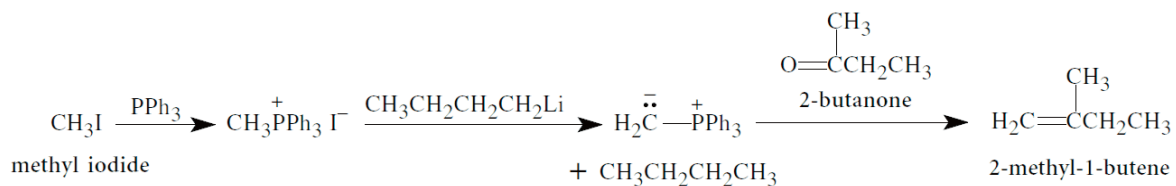
2-methyl-3-(4-methylphenyl)propanal

19.34 (b)

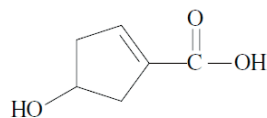


styrene

19.35 (b)



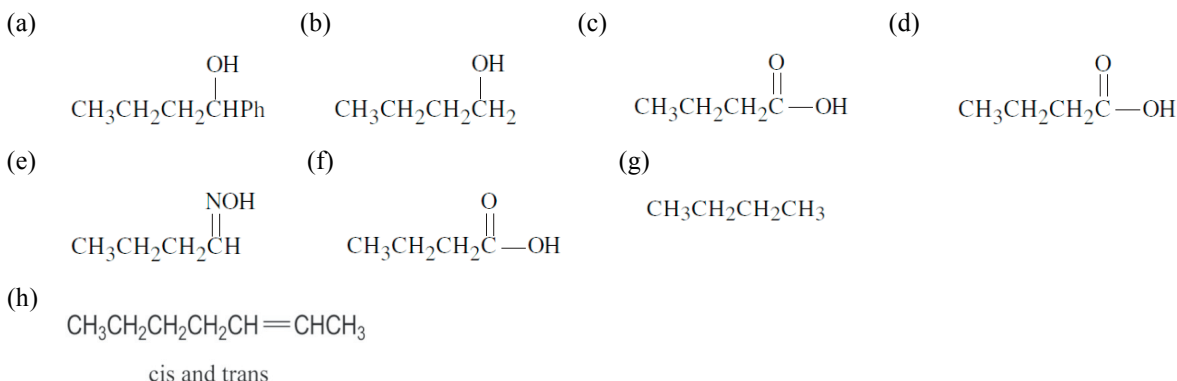
19.37 Silver(I) oxide oxidizes the aldehyde selectively to the following carboxylic acid:



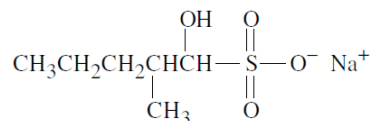
4-hydroxy-1-cyclopentenecarboxylic acid

### Solutions to Additional Problems

19.39 Only organic products are shown.

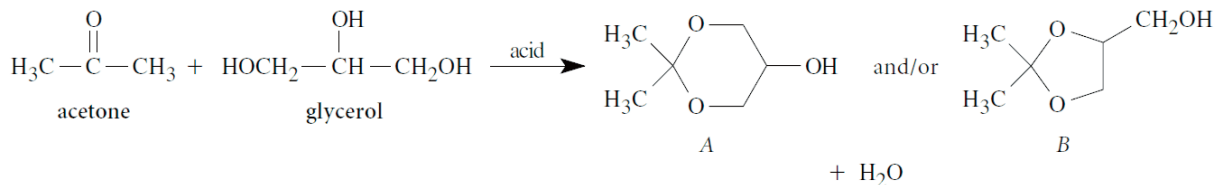


19.40 (c) The bisulfite addition product of 2-methylpentanal:



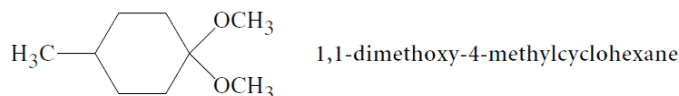
19.41 (b) Both cis and trans isomers of the alkene  $\text{PhCH}=\text{CHCH}_3$  [(1-propenyl)benzene, also known as  $\beta$ -methylstyrene] are formed.

19.43 (a) Glycerol has three hydroxy groups. Two possible cyclic acetals can be formed; one (*A*) contains a six-membered ring, and the other (*B*) contains a five-membered ring.

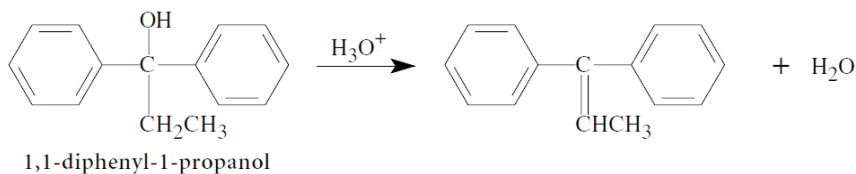


(b) Only compound *B* is chiral, and for this reason only compound *B* can be resolved into enantiomers; hence, compound *B* is the observed compound.

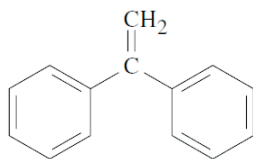
19.45 (b) The reaction is a straightforward dimethyl acetal formation.



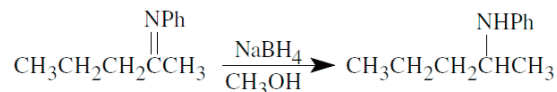
(e) This is a Grignard addition to the ketone to give a tertiary alcohol that subsequently dehydrates under the acidic conditions to an alkene. Whether the dehydration occurs depends on the acid concentration and whether the conditions are designed to remove water.



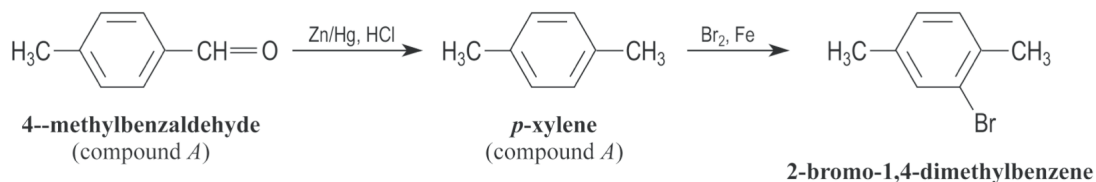
(f) This is a Wittig reaction.



- 19.46 (b) An initially formed imine reacts with sodium borohydride to form an amine. (Although this reaction is discussed in Sec. 23.7B, text p. 1133, the product follows directly from the hint.)

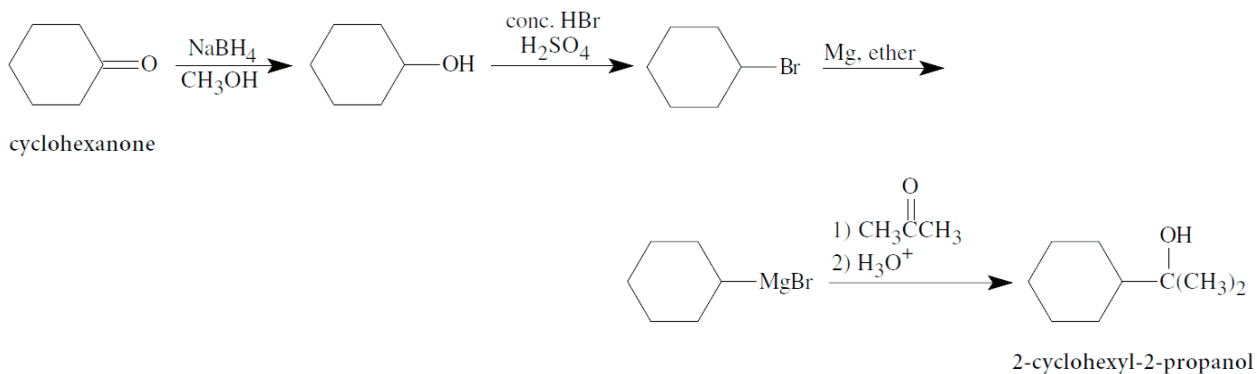


- 19.48 The data indicate that compound *A* is a benzene derivative with an additional degree of unsaturation. Its reactivity in the Clemmensen reduction and the formation of a xylene suggests that it has two substituents on a benzene ring, one of which is a methyl group and one of which is an aldehyde. Only *p*-methylbenzaldehyde would give, after Clemmensen reduction, a compound (*p*-xylene) that in turn gives, because of its symmetry, one and only one monobromination product, 2-bromo-1,4-dimethylbenzene.

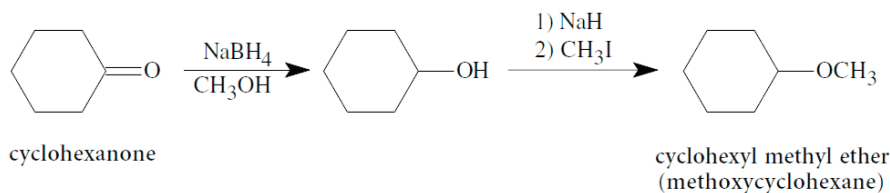


- 19.49 As always, bear in mind that there is often more than one acceptable synthesis that fits the parameters given.

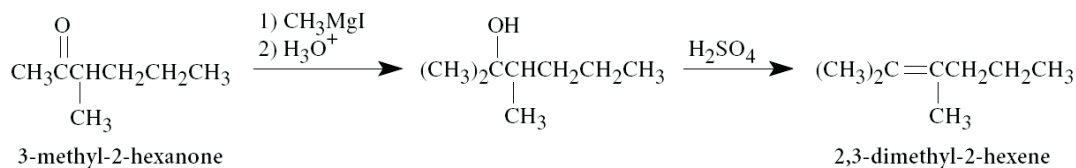
(b)



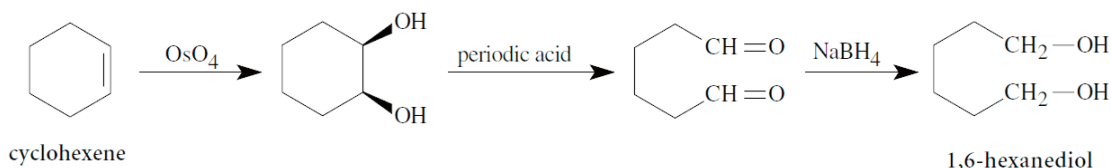
(c)



(e)

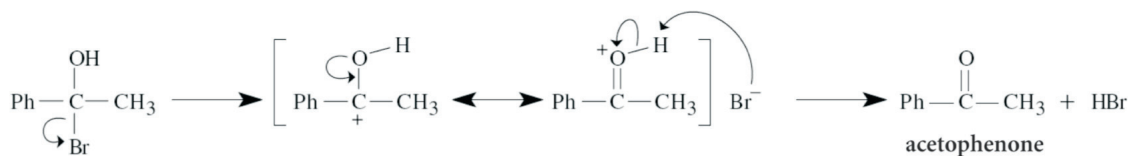


(i)

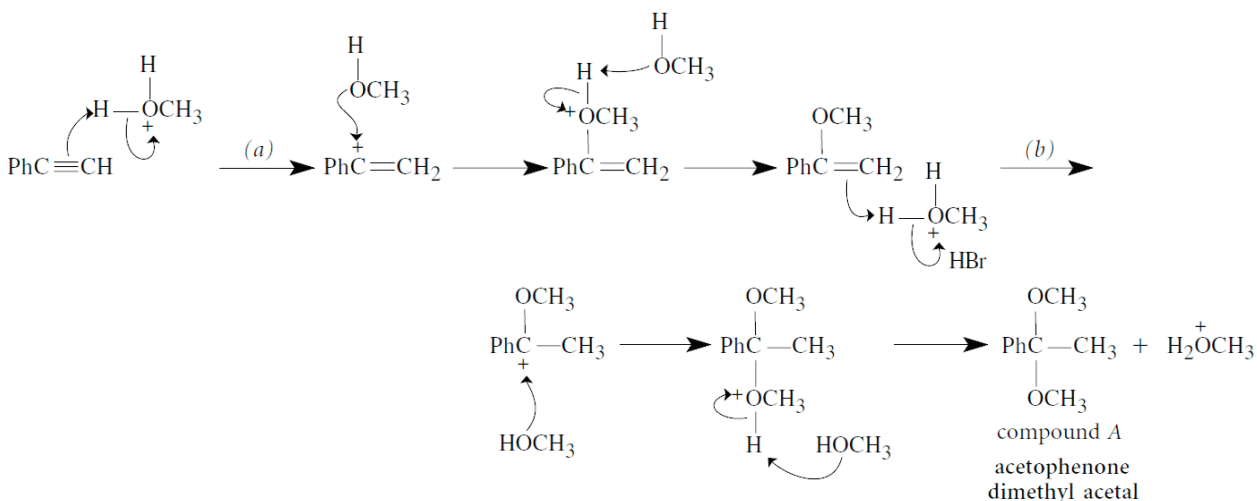


Ozonolysis could also be used to prepare the dialdehyde.

- 19.50 (a) An Lewis acid–base dissociation of the bromide—essentially an  $S_N1$  reaction—gives an  $\alpha$ -hydroxy carbocation, which is, by resonance, also the conjugate acid of acetophenone. Deprotonation by bromide ion gives the ketone and HBr.

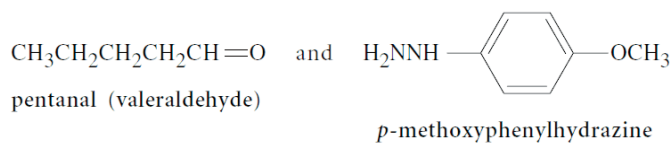


- 19.51 The molecular formula of compound *A* shows that two equivalents of methanol are added to the alkyne. The fact that the product hydrolyzes to acetophenone indicates that the two methoxy groups of compound *A* are on the same carbon, that is, that compound *A* is an acetal.



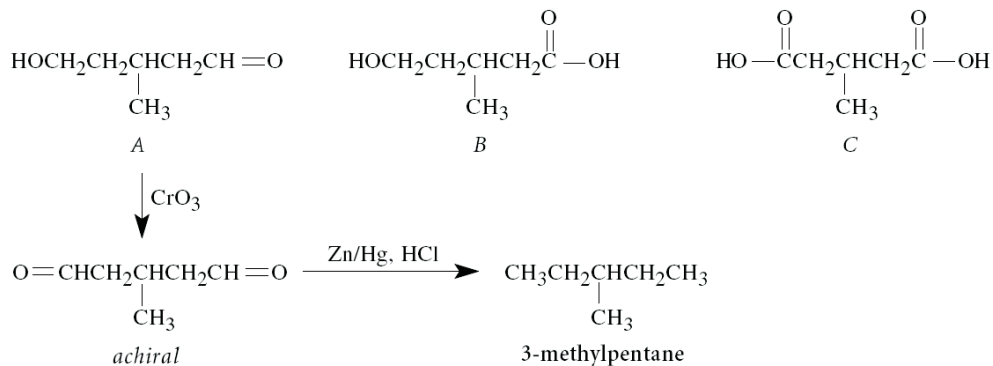
In the step labeled (a), the acid  $\text{CH}_3\text{OH}_2^+$  is used to protonate the alkyne because it is the major acidic species present when  $\text{H}_2\text{SO}_4$  is dissolved in methanol (just as  $\text{H}_3\text{O}^+$  is the major acidic species present when  $\text{H}_2\text{SO}_4$  is dissolved in water). Protonation occurs on the terminal carbon because it gives a carbocation that is benzylic and therefore resonance-stabilized. In the step labeled (b), protonation again occurs on the terminal carbon because the resulting carbocation is resonance-stabilized by electron donation from both the benzene ring and the neighboring oxygen.

19.53 (a)

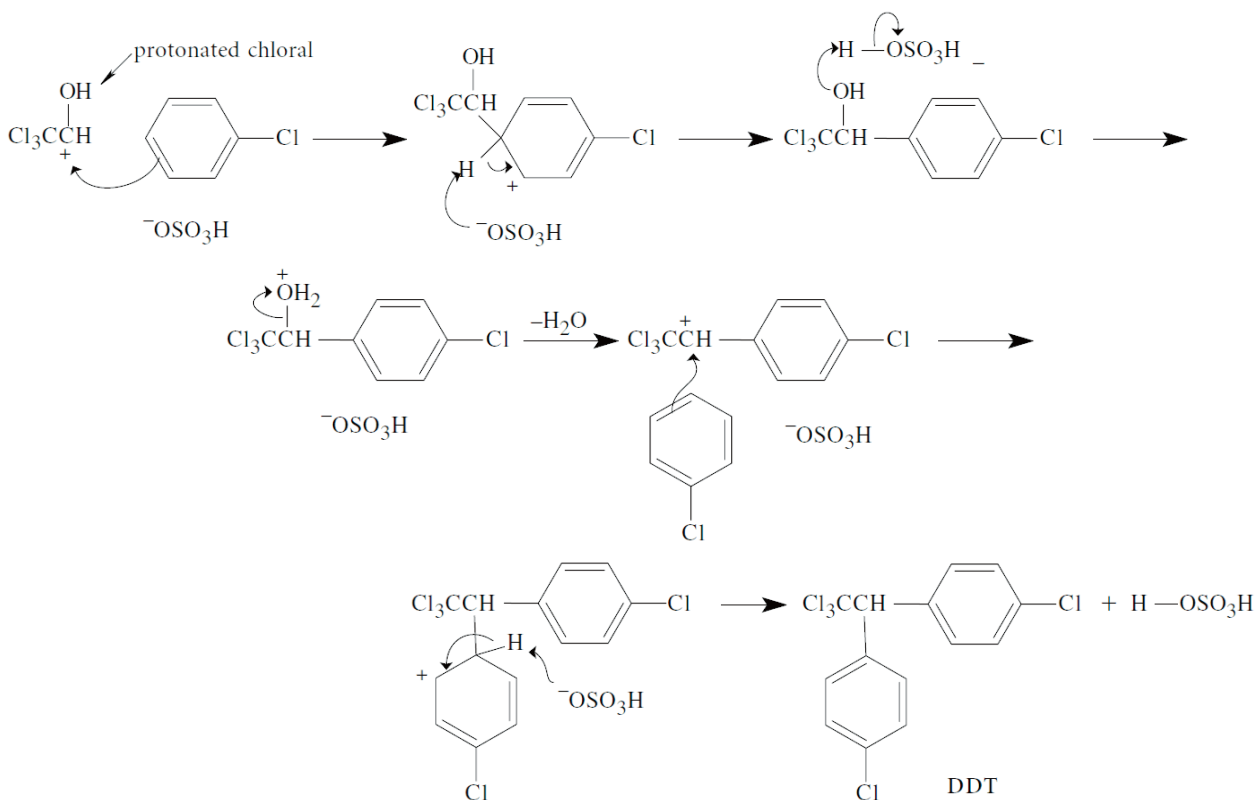


- 19.55 Compound *A* is an aldehyde because it is oxidized with  $\text{Ag}(\text{I})$ . Because there is no additional unsaturation, the remaining oxygen is accounted for by either an alcohol or an ether functional group. Because Clemmensen reduction of the  $\text{CrO}_3$  oxidation product gives a compound without oxygens, the  $\text{CrO}_3$  oxidation product of *A* must

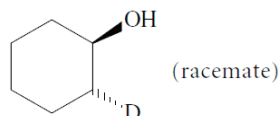
be a keto aldehyde or a dialdehyde. Because compound *A* is oxidized to a dicarboxylic acid by  $\text{H}_2\text{CrO}_4$ , it must contain a primary alcohol; hence, its  $\text{CrO}_3$  oxidation product must be a dialdehyde. Compound *A*, then, is a chiral hydroxy aldehyde that is oxidized by  $\text{CrO}_3$  to an achiral dialdehyde. The Clemmensen reduction product shows that all compounds have the carbon skeleton of 3-methylpentane. The compounds with this carbon skeleton that fit all the data are the following.



- 19.56 The mechanism below begins with the protonated aldehyde chloral, which serves as a carbocation electrophile in the ring alkylation of chlorobenzene. The resulting product, an alcohol, dehydrates under the acidic conditions to give another carbocation that alkylates a second chlorobenzene molecule and thus forms the product.

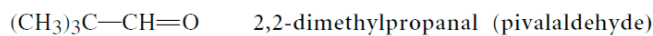


- 19.58 (a) In this case,  $\text{LiAlD}_4$  serves as a source of nucleophilic isotopic hydride (deuteride); deuteride opens the epoxide with inversion of configuration.

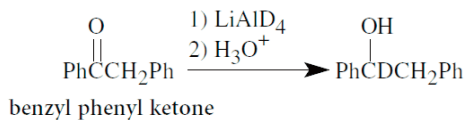


19.59 (a) Thumbs wants a Grignard reagent to react selectively with a ketone in the presence of an aldehyde. Because aldehydes are more reactive than ketones, the aldehyde, not the ketone, will react most rapidly.

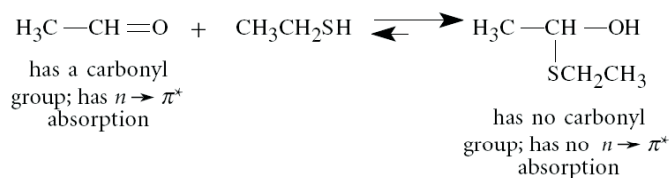
19.62 (b) The NMR spectrum indicates the presence of a *tert*-butyl group and an aldehyde. The compound is



19.65 (b) Allow benzyl phenyl ketone to react with  $\text{LiAlD}_4$ .



19.66 (b) The  $n \rightarrow \pi^*$  absorption is characteristic of the carbonyl group. This absorption disappears because a reaction occurs in which the carbonyl group is converted into another group that does not have this absorption. This reaction is addition of ethanethiol to give the sulfur analog of a hemiacetal:



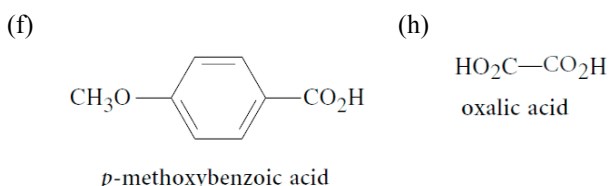
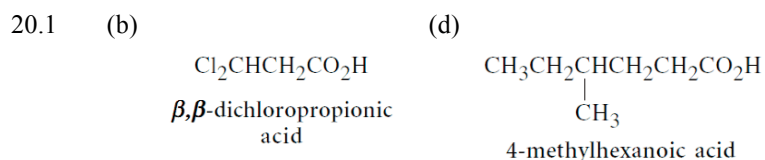




# Chapter 20

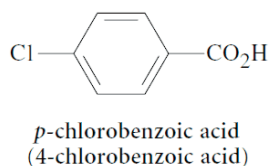
## The Chemistry of Carboxylic Acids

### Solutions to In-Text Problems

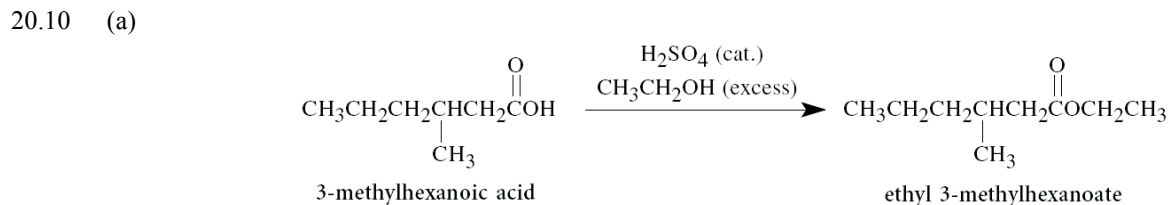
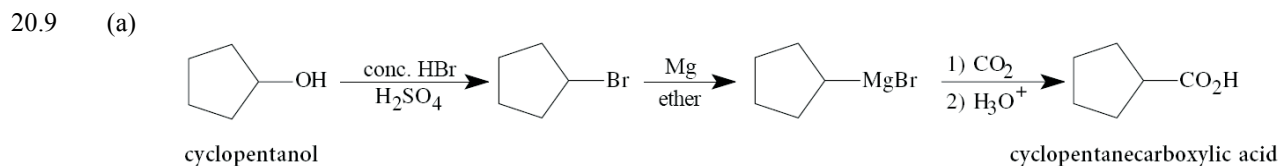


- 20.2 (b) 9-Methyldecanoic acid (common:  $\omega$ -methylcapric acid). Note that the term  $\omega$  (*omega*, the last letter of the Greek alphabet) is used in common nomenclature for a branch at the end of a carbon chain.
- (d) 2,4-Dichlorobenzoic acid
- (f) Cyclopropanecarboxylic acid

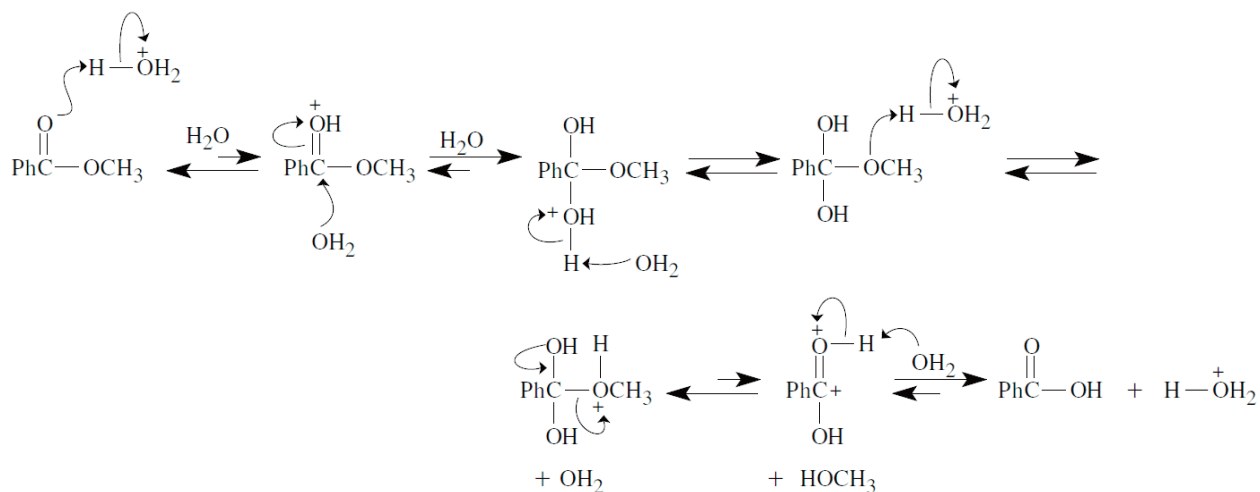
- 20.5 The NMR data indicate a *para*-substituted benzoic acid derivative; given this deduction, the *para* substituent must be a chlorine.



- 20.8 Extract an ether solution of the two compounds with an aqueous solution of  $\text{NaHCO}_3$ ,  $\text{Na}_2\text{CO}_3$ , or  $\text{NaOH}$ . The acid will ionize and its conjugate-base anion will dissolve in the aqueous layer as the sodium salt; *p*-bromotoluene will remain in the ether layer. After isolating the aqueous layer, acidify it with concentrated  $\text{HCl}$ ; neutral *p*-bromobenzoic acid will precipitate.

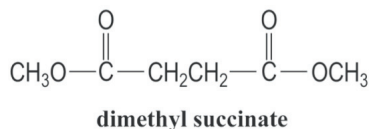


- 20.11 (a) Follow the reverse of the steps shown in Eqs. 20.18a–c, text pp. 966–967, with R— = Ph—.

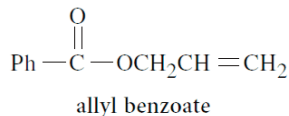


- (b) To favor ester hydrolysis rather than ester formation, use a large excess of water as solvent rather than an alcohol. By Le Châtelier's principle, this drives the carboxylic acid–ester equilibrium toward the carboxylic acid.

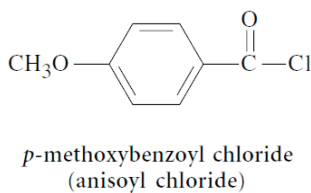
- 20.13 (b)



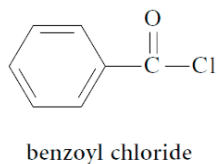
- (d)



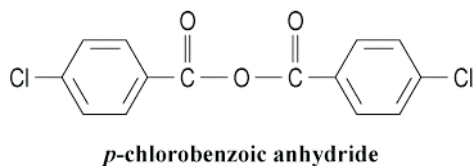
- 20.15 (b)



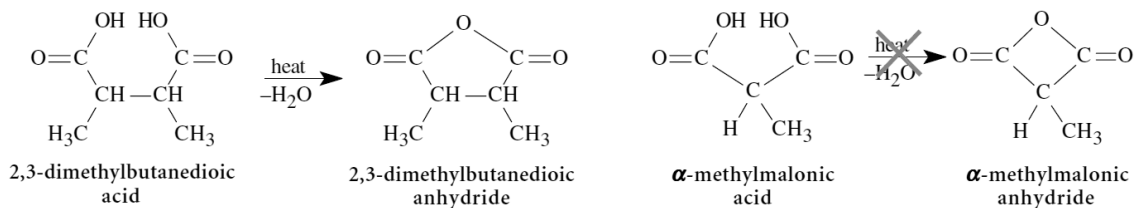
- 20.16 (b)



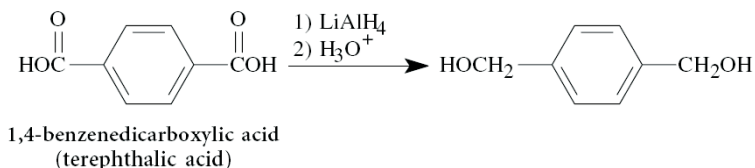
- 20.18 (b)



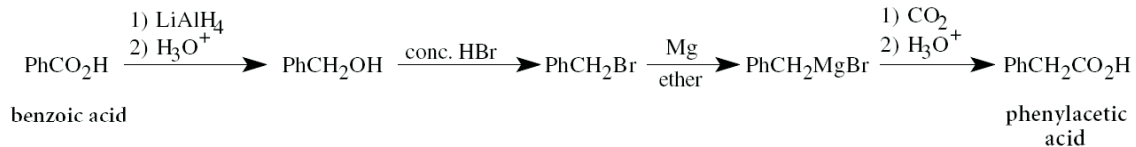
- 20.19 (b) On heating, 2,3-dimethylbutanedioic acid forms a cyclic anhydride containing a five-membered ring. Because a cyclic anhydride of  $\alpha$ -methylmalonic acid would contain a very strained four-membered ring, it is not formed on heating.



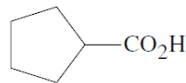
- 20.20 (b) 1,4-Benzenedicarboxylic acid (terephthalic acid) is a compound with the formula  $C_8H_6O_4$  that gives the indicated diol on treatment with  $LiAlH_4$  followed by protonolysis.



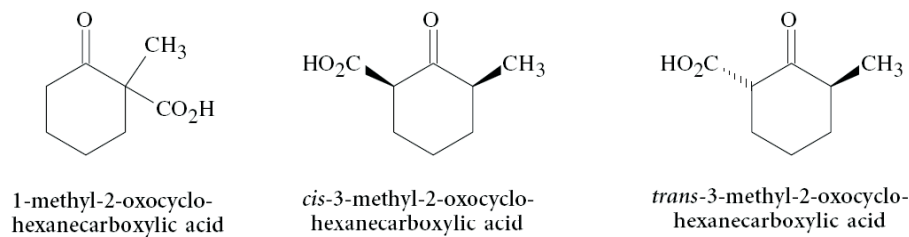
- 20.21 (a) This synthesis requires the addition of one carbon. Follow the general scheme in Study Problem 20.2, text p. 975.



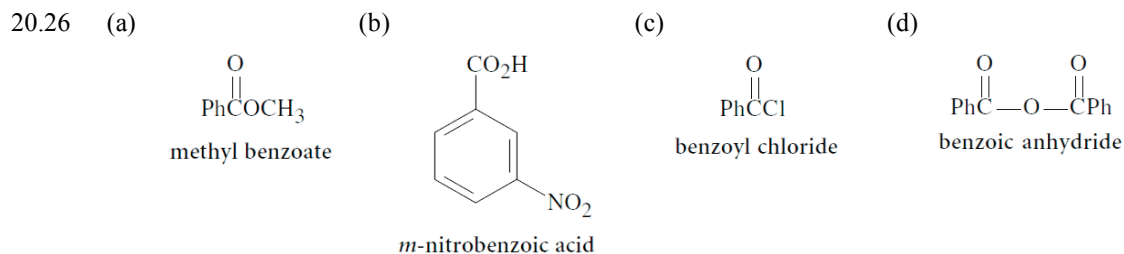
- 20.22 (b) The compound decarboxylates; it is a disubstituted malonic acid in which the two  $\alpha$  substituents are joined within a ring. The net effect is the replacement of the carboxy group by a hydrogen.



- 20.23 The following  $\beta$ -keto acids (and their enantiomers) will decarboxylate to give 2-methylcyclohexanone:



## Solutions to Additional Problems



- 20.28 (b) First, calculate the number of millimoles of succinic acid (see Table 20.1, text p. 950) in 100 mg of succinic acid:

$$\text{mmol succinic acid} = \frac{100 \text{ mg succinic acid}}{118.10 \text{ mg succinic acid (mmol succinic acid)}^{-1}} = 0.847$$

Using the facts that sodium hydroxide reacts with the carboxylic acid groups and that succinic acid has two dicarboxylic acid groups per molecule, calculate the millimoles of carboxylic acid groups present in the sample:

$$\text{mmol carboxylic acid} = \frac{2 \text{ mmol carboxylic acid}}{\text{mmol succinic acid}} \times 0.847 \text{ mmol succinic acid} = 1.69$$

Finally, calculate the volume 0.1 M NaOH required for the neutralization:

$$\text{mL of NaOH} = \frac{1 \text{ mL of NaOH}}{0.1 \text{ mmol of NaOH}} \times \frac{1 \text{ mmol of NaOH}}{1 \text{ mmol of carboxylic acid}} \times 1.69 \text{ mmol of carboxylic acid} = 16.9$$

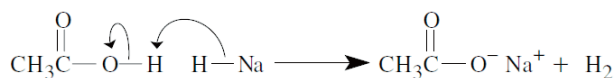
- 20.29 (b)



- (d)



- (f)



- 20.31 As the chain length becomes larger the distance between the two carboxy groups becomes greater. Because polar effects decrease with distance, the polar effect is negligible when the chain length is great, and the two  $pK_a$  values are nearly equal. (However, they are not *exactly* equal; for an explanation, see the icon comment following the solution to Problem 3.43 on p. 43 of Study Guide and Solutions Manual.)

- 20.34 Use Eq. 20.7c, text p. 959. (This equation is sometimes called the Henderson–Hasselbalch equation.) Let the ratio  $[\text{RCO}_2\text{H}]/[\text{RCO}_2^-]$  given in the problem be  $r$ . Rearranging Eq. 20.7c, and noting that  $\log(1/r) = -\log r$ ,

$$\text{pH} = pK_a - \log r$$

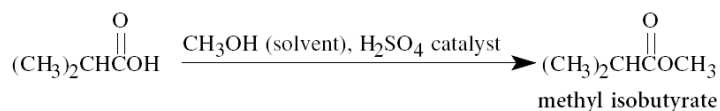
- (a) When  $r = 1/3$ ,  $\text{pH} = 4.76 - \log(1/3) = 5.24$ .  
 (b) When  $r = 3$ ,  $\text{pH} = 4.76 - \log 3 = 4.28$ .  
 (c) When  $r = 1$ ,  $\text{pH} = 4.76 - \log 1 = 4.76$ .



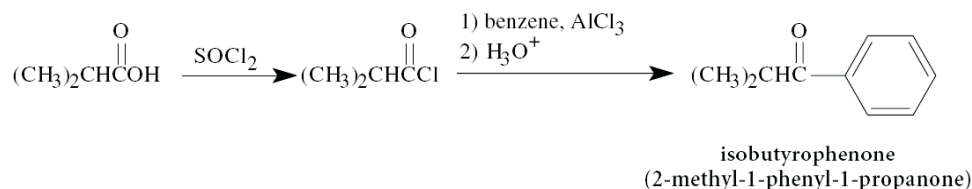
Many students confuse  $pK_a$ , which is a property of a compound, with pH, which is a property of the solution in which the compound is dissolved. The  $pK_a$  is a constant property of an acid that does not vary with concentration; the pH, as text Eq. 20.7c shows, depends on the relative concentrations of the acid and its conjugate base. (See Study Guide Link 3.4, on p. 31 of the Study Guide and Solutions Manual.) As the calculation in this problem is designed to illustrate, the pH equals the  $pK_a$  when the concentrations of an acid and its conjugate base are identical. When the concentration of the conjugate acid is greater, the pH is less than the  $pK_a$ ; when the concentration of the acid is less, the pH is greater than the  $pK_a$ .

- 20.35 (b) Use the result in part (a). When acetic acid is the solvent, the most acidic species that can exist is the *conjugate acid* of acetic acid (that is, protonated acetic acid; see structure in Eq. 20.8, text p. 960, with  $R- = H_3C-$ ), which has a  $pK_a$  of about  $-6$  (text p. 960). Table 3.1 on text p. 103 gives the  $pK_a$  of HBr as  $-8$  to  $-9.5$ . Consequently, the HBr–acetic acid system has an effective  $pK_a$  of about  $-6$ . In aqueous solution, HBr is dissociated to give  $H_3O^+$ , the conjugate acid of water, which has a  $pK_a$  of  $-1.7$ ; therefore the effective  $pK_a$  of aqueous HBr is  $-1.7$ . Hence, HBr in acetic acid is far more acidic than HBr in water because of the greater acidity of the conjugate acid of acetic acid, the solvent.

- 20.37 (b)

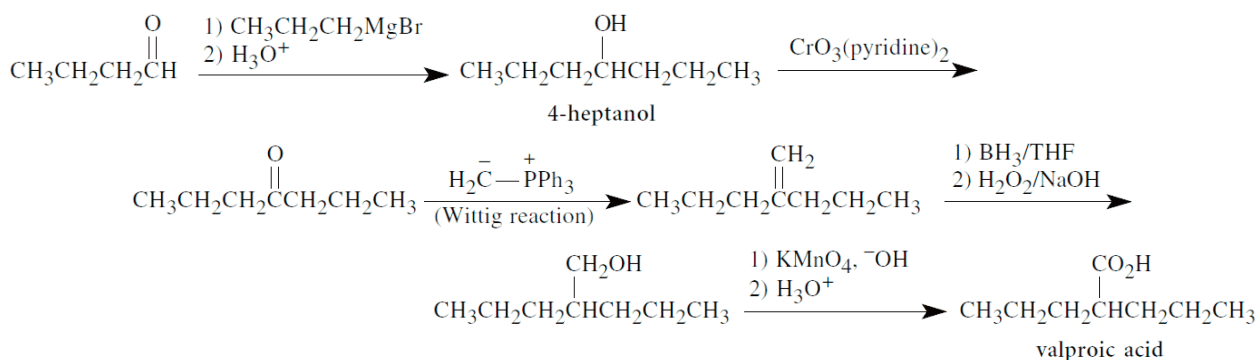


- (d)

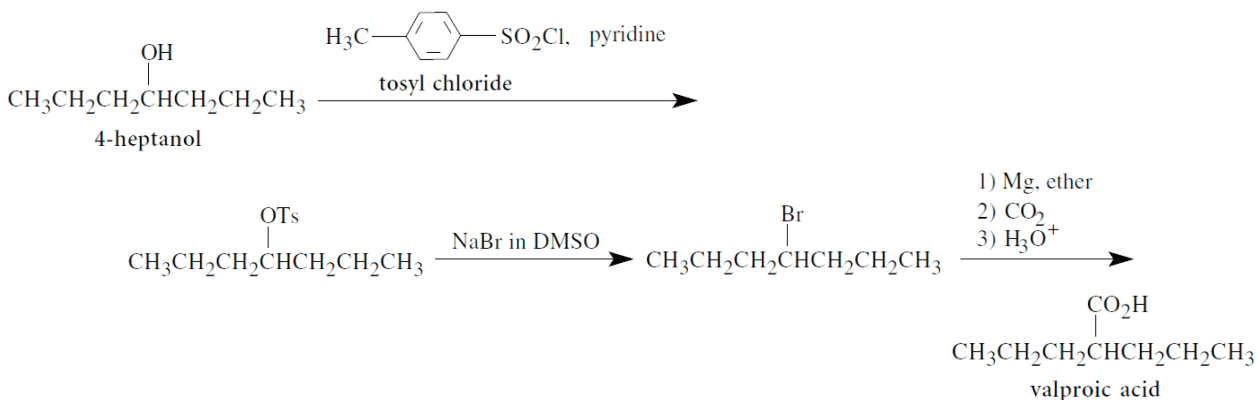


- 20.39 (a) The substitutive name of valproic acid is 2-propylpentanoic acid.  
 (b) The common name of valproic acid is  $\alpha$ -propylvaleric acid.  
 (c) A number of syntheses are possible. Here are two:

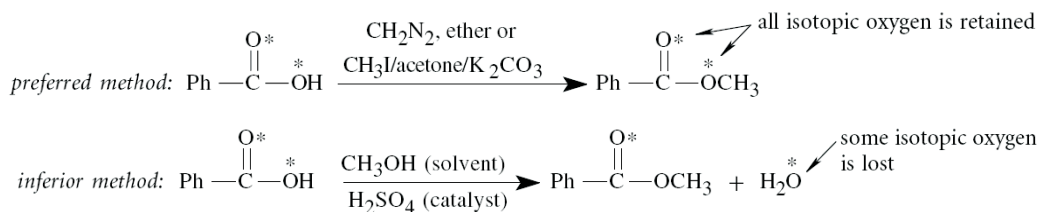
*Synthesis #1:*



Synthesis #2:

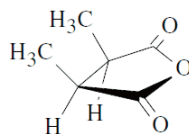


- 20.41 Use a method that does not involve loss of oxygen from benzoic acid. Thus, acid-catalyzed esterification should not be used, because, as Eq. 20.18c on text p. 967 shows, this method results in cleavage of the bond between the carbonyl carbon and the carboxylate oxygen. Esterification with either diazomethane or methyl iodide and  $\text{K}_2\text{CO}_3$  would be the preferred method because, as the discussion in Sec. 20.8B, text p. 968, shows, these methods do not involve loss of oxygen. ( $\text{O}^* = {}^{18}\text{O}$ )



- 20.43 The essence of this solution is to determine the ionization state of penicillin-G at the different pH values. The principles involved are discussed in the solution to Problem 20.34. Because penicillin G is a carboxylic acid, its  $\text{pK}_a$  should be in the 3–5 range. Because the pH of blood, 7.4, is considerably higher than the  $\text{pK}_a$  of the drug, penicillin-G is ionized in blood. Because the pH of stomach acid is lower than the  $\text{pK}_a$  of penicillin-G, the penicillin is largely un-ionized in stomach acid. Because carboxylate ions are generally more soluble in aqueous solution than un-ionized carboxylic acids, penicillin-G is more soluble in blood than it is in stomach acid.

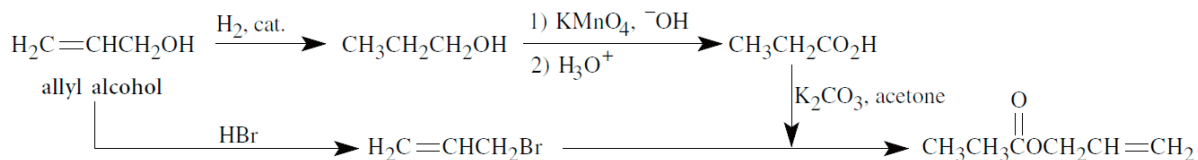
- 20.45 (b)

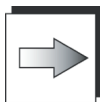


*meso*- $\alpha,\beta$ -dimethylsuccinic anhydride

Notice the *cis* relationship of the methyl groups. (The anhydride with *trans* methyl substituents would be formed from *racemic*  $\alpha,\beta$ -dimethylsuccinic acid).

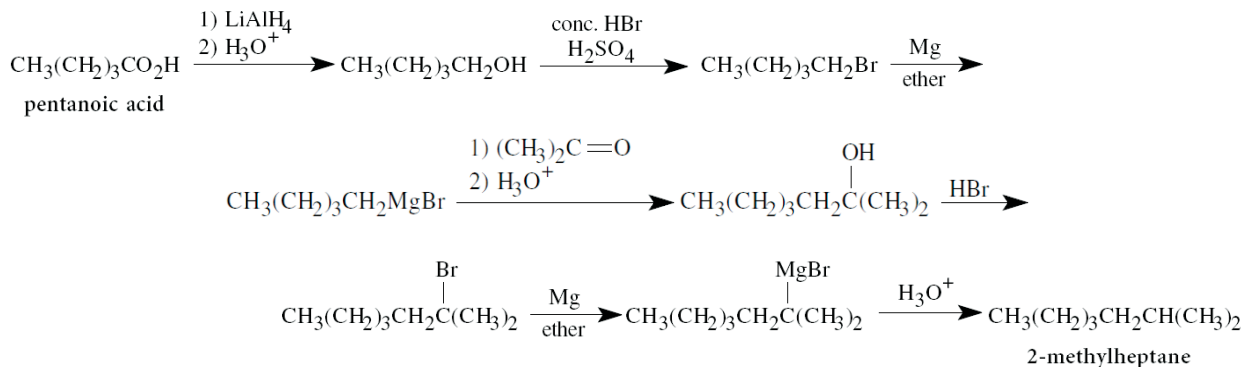
- 20.46 (b)



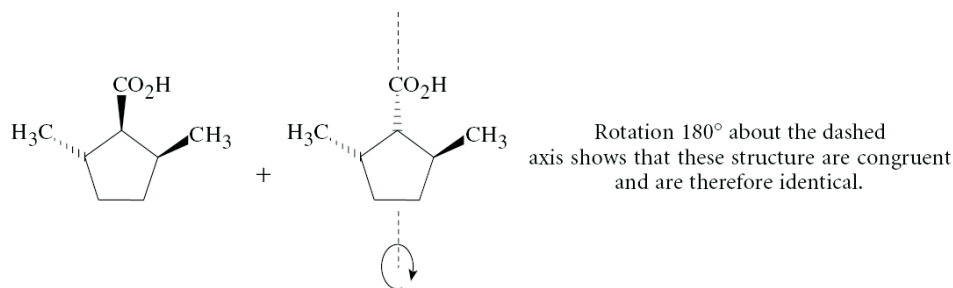


Acid-catalyzed esterification of propionic acid (prepared as shown above) with allyl alcohol could also be used, but this reaction would require an excess of allyl alcohol.

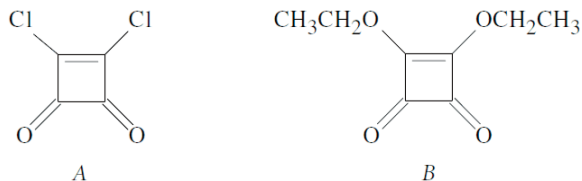
(c)



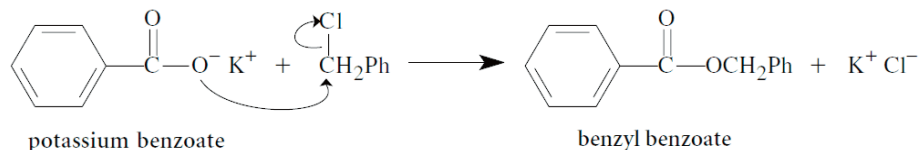
- 20.47 (b) The question is whether loss of the different carboxy groups gives rise to the same compound or to different compounds. Draw the two possible structures and determine whether they are different or identical. In fact, the two are identical; therefore, only one product is formed when compound *B* decarboxylates.



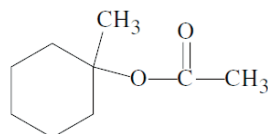
- 20.48 (c) The reactions of squaric acid with a number of reagents are analogous to the corresponding reactions of carboxylic acids. Thus, reaction with  $\text{SOCl}_2$  results in the formation of the “di-acid chloride” *A*; and reaction with ethanol and an acid catalyst results in formation of the “di-ester” *B*.



- 20.49 (b) The KOH converts benzoic acid into its conjugate-base benzoate anion, which is alkylated by benzyl chloride to give benzyl benzoate.

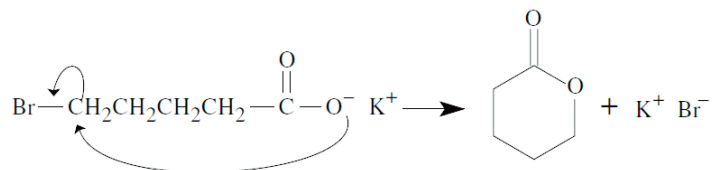


- (d) This is an oxymercuration-reduction reaction in which acetic acid rather than water serves as the nucleophile that opens the mercurinium ion. (See the solution to Problem 5.35(c) on pp. 92–93 of Study Guide and Solutions Manual.)

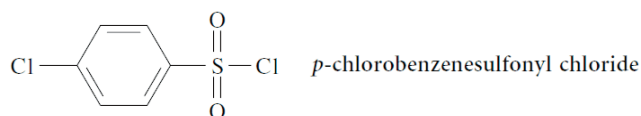


1-methylcyclohexyl acetate

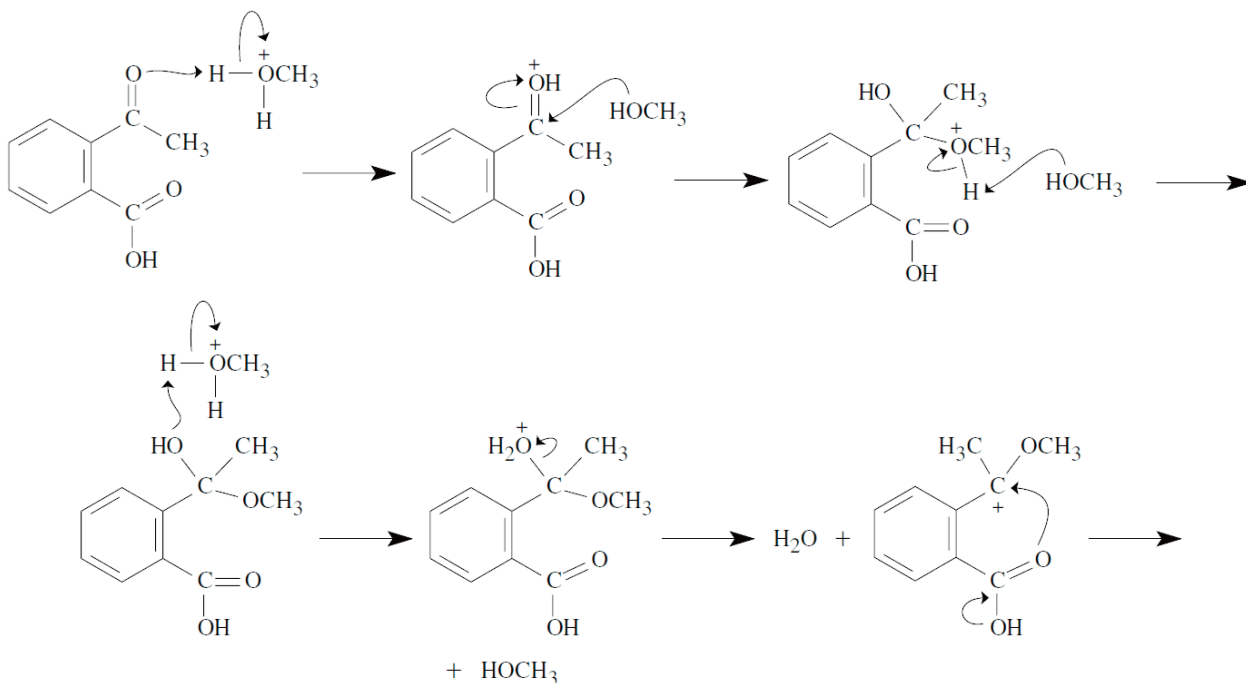
- (f) This is an intramolecular variation of the esterification shown in Eq. 20.22, text p. 969. In this case, potassium carbonate converts the carboxylic acid into its conjugate-base potassium carboxylate, which is then intramolecularly alkylated to form the cyclic ester (lactone).



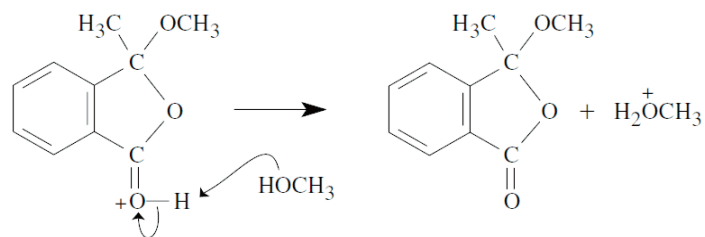
- (h) Chlorosulfonation of chlorobenzene gives electrophilic aromatic substitution at the para position. (See Eq. 20.28a–b on text p. 972.)



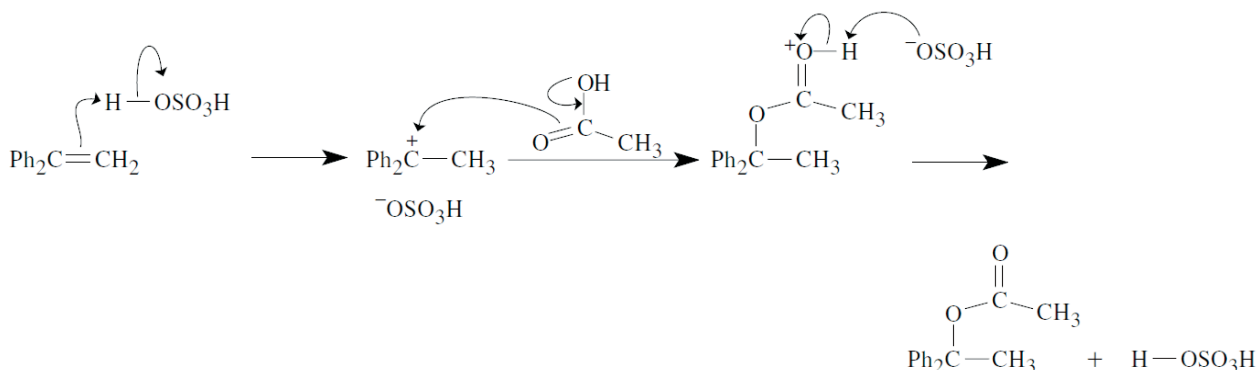
- 20.51 (b) The mechanism is much like that for acetal formation, except that the carboxy group rather than a second alcohol molecule reacts with the  $\alpha$ -alkoxy carbocation intermediate. (Recall that many intramolecular reactions that form small rings are faster than related intermolecular reactions; see Sec. 11.7A–B, text p. 510.)



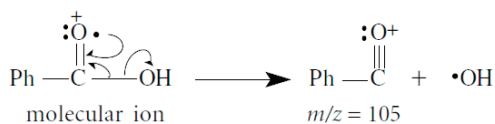




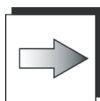
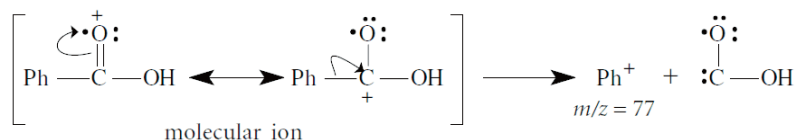
- (d) The pattern is much like that in the solution to part (c), except that acetic acid rather than carbon monoxide reacts with the carbocation intermediate.



- 20.52 (b) The molecular mass of benzoic acid is 122; therefore, the  $m/z = 105$  peak in its mass spectrum represents a mass loss of 17 units, which corresponds to loss of an  $\text{—OH}$  group. This loss can occur by an  $\alpha$ -cleavage mechanism.

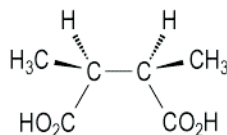


The  $m/z = 77$  peak corresponds to a phenyl cation, which can be lost by inductive cleavage at the other side of the carboxy group.



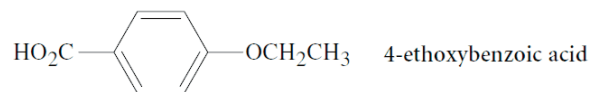
You may recall that aryl cations are very unstable. (See Fig. 18.2, text p. 827.) The high electron energies involved in mass spectroscopy enable the formation of such intermediates that would ordinarily not form in solution.

- 20.53 (b) The meso stereoisomer would have  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra that are almost identical to that of *A*. Because it is a diastereomer of *A*, it has a different melting point.



*meso*-2,3-dimethylbutanedioic acid

- 20.55 (b) The IR spectrum indicates the presence of a carboxylic acid, and the NMR indicates the presence of an ethoxy group ( $-\text{OCH}_2\text{CH}_3$ ) and a *para*-disubstituted benzene ring. The compound is 4-ethoxybenzoic acid.

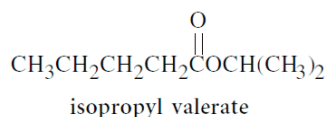


# Chapter 21

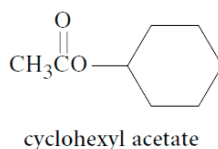
## The Chemistry of Carboxylic Acid Derivatives

### Solutions to In-Text Problems

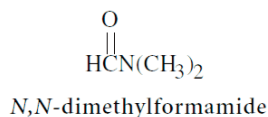
21.1 (b)



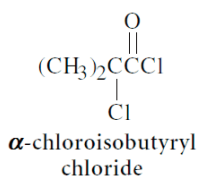
(d)



(e)

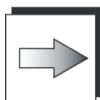


(h)

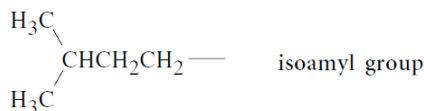


21.2

- (a) butanenitrile (common: butyronitrile)  
(c) isopentyl 3-methylbutanoate (*common*: isoamyl isovalerate)

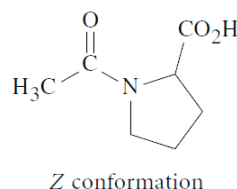
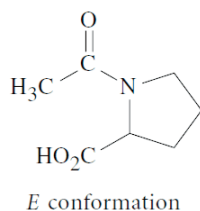


The *isoamyl* group is the same as an isopentyl or 3-methylbutyl group:

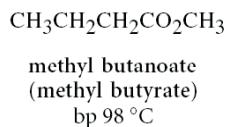
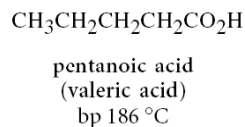


(d) *N,N*-dimethylbenzamide

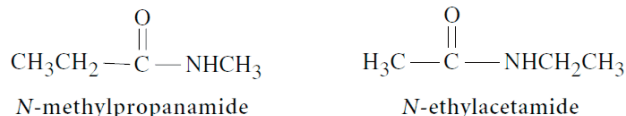
21.3 The *E* and *Z* conformations of *N*-acetylproline:



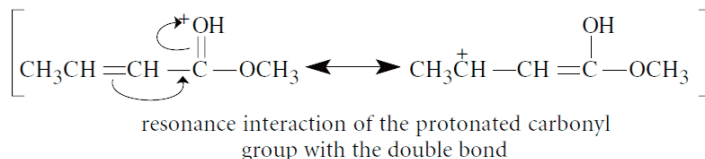
21.5 As shown by the data above the problem, a carboxylic acid has a higher boiling point than an ester because it can both donate and accept hydrogen bonds within its liquid state; hydrogen bonding does not occur in the ester. Consequently, pentanoic acid (valeric acid) has a higher boiling point than methyl butanoate. Here are the actual data:



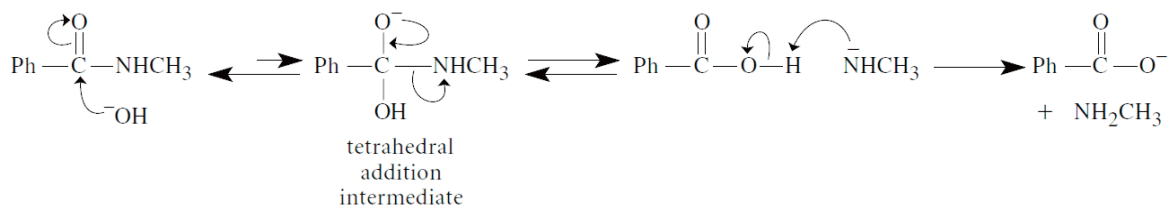
- 21.7 (a) The carbonyl absorption of the ester occurs at higher frequency, and only the carboxylic acid has the characteristic strong, broad O—H stretching absorption in 2400–3600  $\text{cm}^{-1}$  region.
- (d) In *N*-methylpropanamide, the *N*-methyl group is a doublet at about  $\delta$  3. *N*-Ethylacetamide has no doublet resonances. In *N*-methylpropanamide, the  $\alpha$ -protons are a quartet near  $\delta$  2.5. In *N*-ethylacetamide, the  $\alpha$ -protons are a singlet at  $\delta$  2. The NMR spectrum of *N*-methylpropanamide has no singlets.



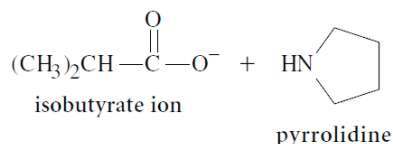
- 21.9 (a) The first ester is more basic because its conjugate acid is stabilized not only by resonance interaction with the ester oxygen, but also by resonance interaction with the double bond; that is, the conjugate acid of the first ester has one more important resonance structure than the conjugate acid of the second. (See Problem 19.14(b), text p. 906, and its solution for a similar situation.)



- 21.10 (b) The mechanism of the base-promoted hydrolysis of *N*-methylbenzamide is essentially a saponification mechanism analogous to that shown for esters in Eq. 21.9a–b, text p. 1005.



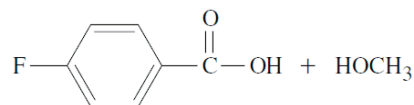
- 21.11 (a) The hydrolysis products consist of the conjugate base of the carboxylic acid and an amine:



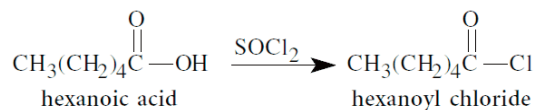
- 21.12 *Resonance effects:* The application of the resonance effect for predicting the relative rates of acid-catalyzed ester and amide hydrolyses is exactly the same as it is for the corresponding base-promoted hydrolyses. (See Eq. 21.26, text p. 1013, and Eq. 21.28, text p. 1014, and the discussion on text pp. 1012–1014.)

*Leaving-group basicities:* In the acid-catalyzed hydrolysis of an ester, the leaving group is an alcohol; in the acid-catalyzed hydrolysis of an amide, the leaving group is ammonia or an amine. Alcohols are much weaker bases (conjugate-acid  $\text{p}K_{\text{a}} = -2$  to  $-3$ ) than amines or ammonia (conjugate-acid  $\text{p}K_{\text{a}} = 9$ – $10$ ). Because weaker bases are better leaving groups, esters should hydrolyze more rapidly, and they do.

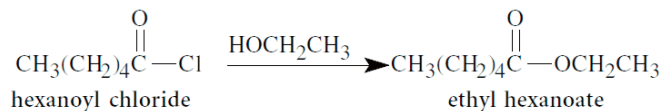
- 21.14 (b) This is an ordinary ester saponification followed by acidification.



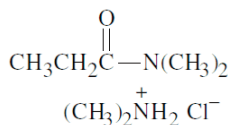
- 21.15 First, prepare the acid chloride from hexanoic acid:



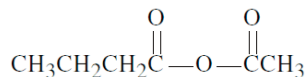
(a) To prepare the ester, allow the acid chloride to react with ethanol:



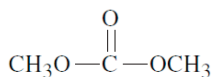
21.16 (a)



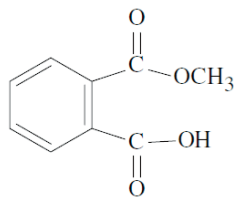
(d)



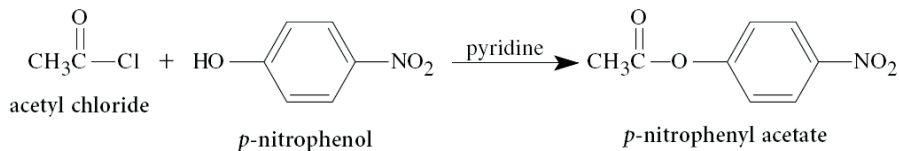
(f)



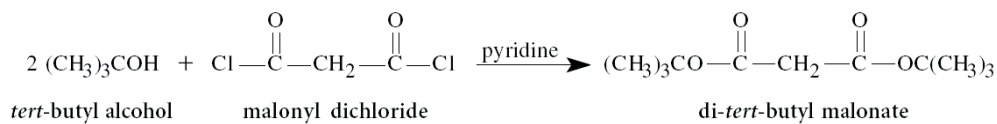
(h)



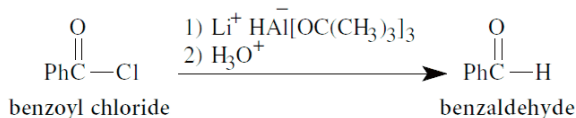
21.18 (b)



(d)

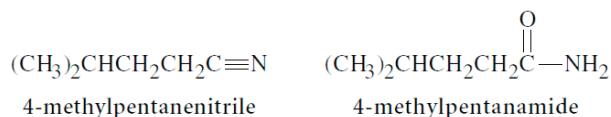


21.19 (a) Carry out one of the reductions in Sec. 21.9D, text p. 1027:

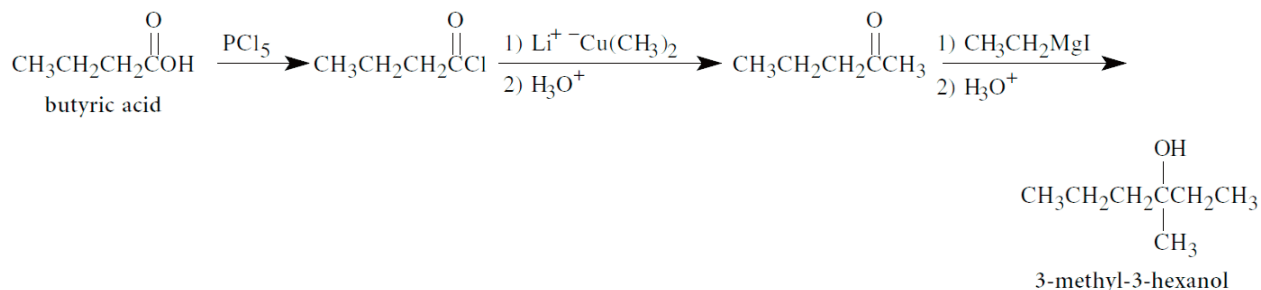


21.20 (a)  $\text{PhCH}_2\text{CH}_2\text{NH}_2$

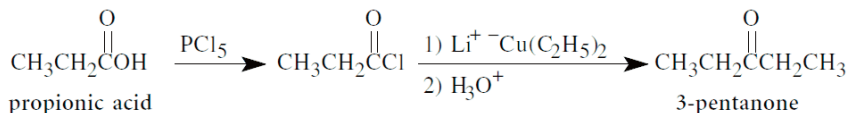
21.21 Among the compounds that would give  $(\text{CH}_3)_2\text{CHCH}_2\text{CH}_2\text{CH}_2\text{NH}_2$  as the result of  $\text{LiAlH}_4$  reduction are the following:



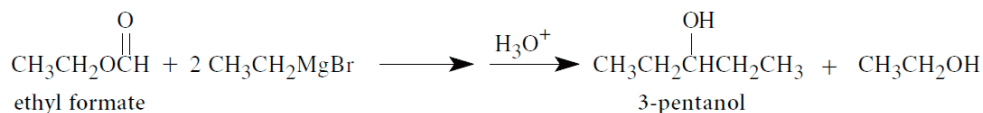
21.23 (b)



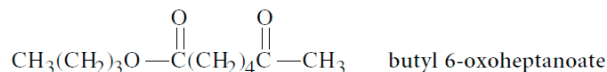
(d)



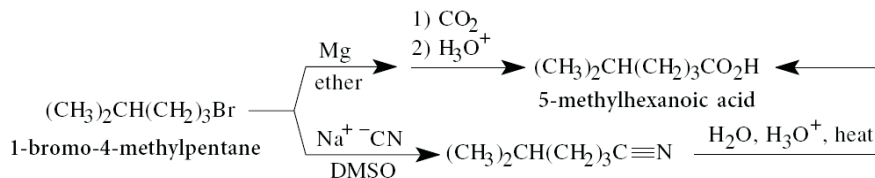
21.24 (b) The reaction of a Grignard reagent with ethyl formate gives a secondary alcohol in which the two alkyl groups at the  $\alpha$ -carbon are identical.



21.25 (b) Because only the acid chloride reacts, the product is the following keto ester:

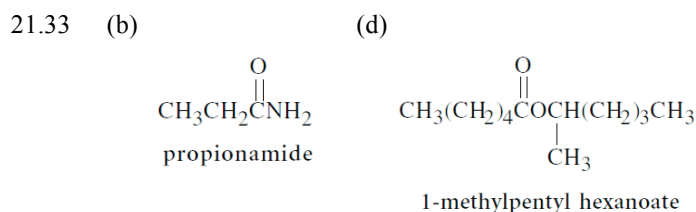
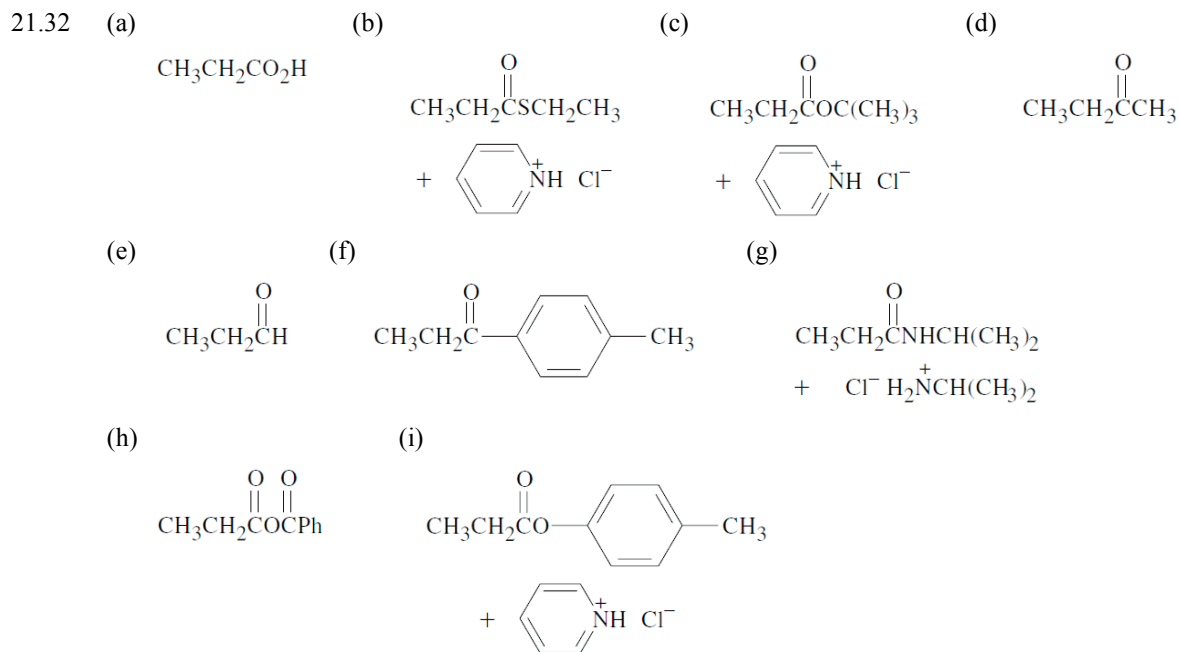


21.26 The first method involves carbonation of the corresponding Grignard reagent; the second involves hydrolysis of the nitrile.

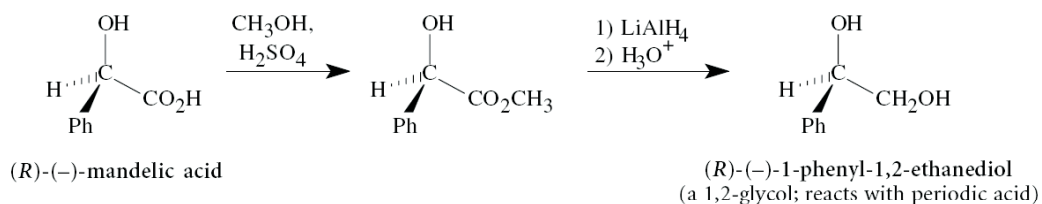


21.29 Process (a) is catalytic hydrogenation. Because furan is aromatic, high pressure and/or heat might be required. Process (b) is ether cleavage with HCl and ZnCl<sub>2</sub> (or other acidic catalyst) and heat. Process (c) consists of the S<sub>N</sub>2 reactions of cyanide ion with the dichloride. Process (d) is catalytic hydrogenation or LiAlH<sub>4</sub> reduction followed by protonolysis. Process (e) is nitrile hydrolysis with aqueous acid and heat. Finally, process (f) is to mix the amine and the carboxylic acid and heat (Eq. 21.70, text p. 1034), or to form the di-acid chloride and allow it to react with the amine.

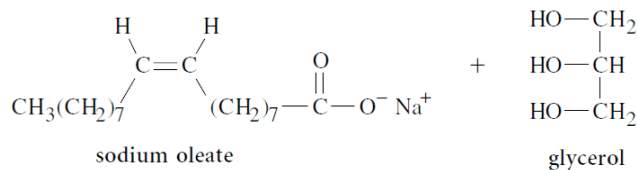
## Solutions to Additional Problems



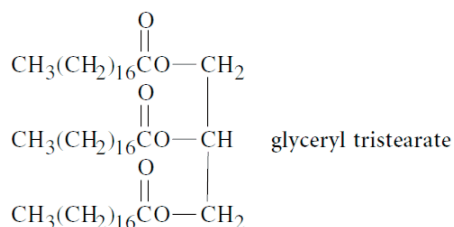
21.35 The product is (*R*)-(-)-1-phenyl-1,2-ethanediol. Notice that the asymmetric carbon is unaffected by these transformations.



21.38 (a) In aqueous base the ester groups are saponified to give glycerol (1,2,3-propanetriol) and three equivalents of sodium oleate, the sodium salt of oleic acid.

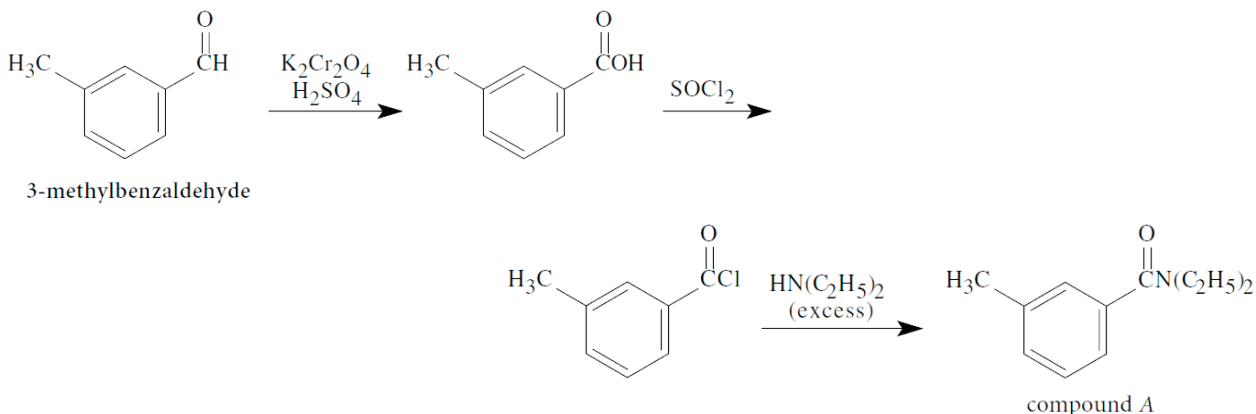


(b) The structure of glyceryl tristearate:

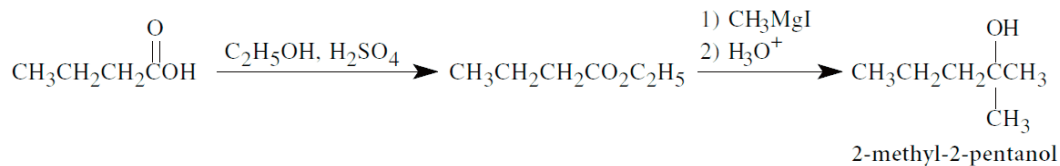


Because unsaturated fats are oils and saturated fats are solids, glyceryl trioleate is a liquid, whereas the product of hydrogenation is a solid. In fact, glyceryl trioleate is a major component of olive oil, whereas glyceryl tristearate is a major component of lard.

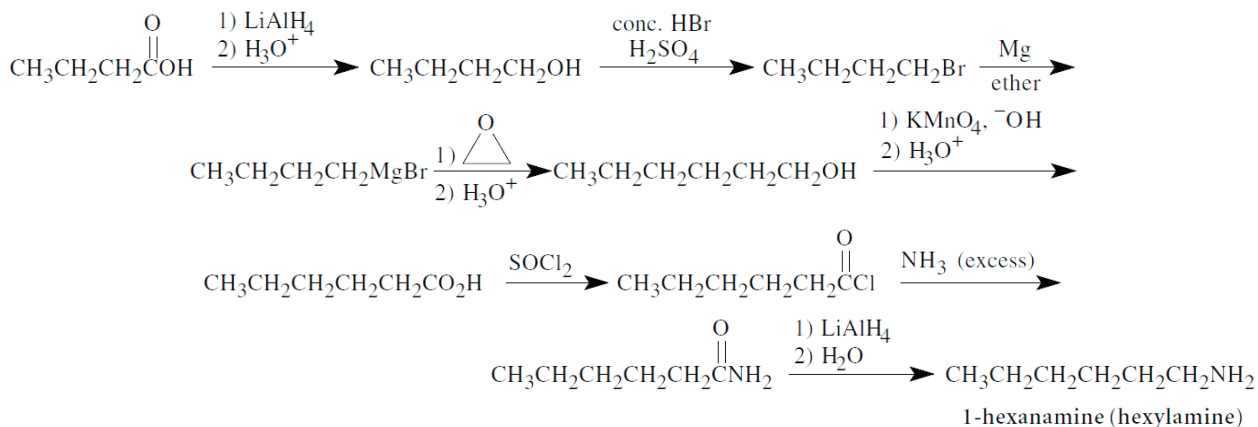
21.39 (a)



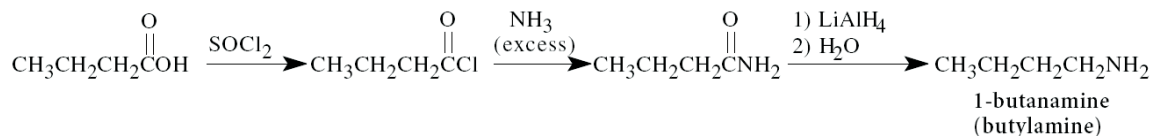
21.40 (b)



(d)

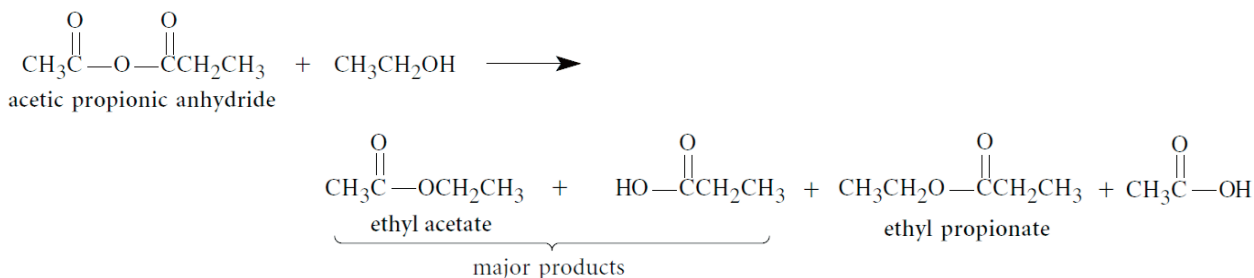


(f)



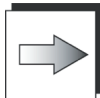


- 21.42 Because the two carbonyl groups of the anhydride are not equivalent, two different products are possible; each corresponds to reaction with the ethanol at a different carbonyl group. Because ethyl propionate has a higher molecular mass than ethyl acetate, ethyl propionate should have the higher boiling point. Since it is given that the ester with the lower boiling point is formed in greater amount, then ethyl acetate is the major product.



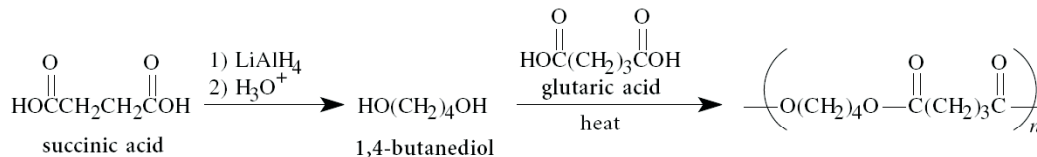
- 21.43 Carboxylate salts are less reactive than esters in nucleophilic acyl substitution reactions for two reasons. First, resonance stabilization of carboxylate salts is particularly important because carboxylates have two identical, important resonance structures; see Eq. 20.4 on text p. 957. Resonance stabilization of esters is less important because one resonance structure separates charge; see the structures in Eq. 21.28, text p. 1014. Because resonance stabilization reduces reactivity, carboxylates are less reactive than esters.

The second and major reason that carboxylate salts are less reactive is that they contain no leaving group. The oxygen anion of the carboxylate, in order to serve as a leaving group, would have to depart as an oxide ion,  $\text{O}_2^-$ . This very basic leaving group is unprecedented in the usual reactions of organic chemistry.

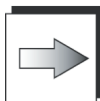
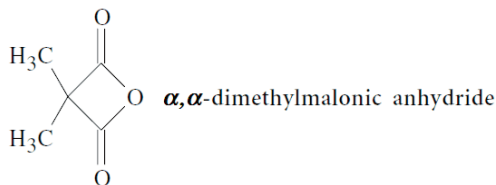


Reactions such as  $\text{LiAlH}_4$  reduction that occur on carboxylate salts might at first glance appear to involve oxide ions as leaving groups. In such reactions, however, the “oxygen anion” is bonded to another species that allows the oxygen to serve as a leaving group. (See the details in Further Exploration 20.4 on p. 479 of the Study Guide and Solutions Manual.)

- 21.45 (b) The preparation of this polyester requires heating 1,4-butanediol with glutaric acid.  
(Alternatively, the di-acid chloride of glutaric acid could be mixed with 1,4-butanediol.)



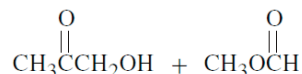
- 21.47 The high-frequency IR absorption and the reaction with water to give a dicarboxylic acid suggest that this compound is the anhydride of  $\alpha,\alpha$ -dimethylmalonic acid. The formation of a half ester in the reaction with methanol also supports the hypothesis that this compound is an anhydride.



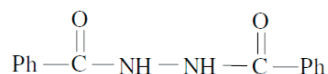
In most cases cyclic anhydrides show two carbonyl stretching absorptions. Can you think of a reason why this particular anhydride shows only one? (*Hint*: See Study Problem 12.2 on text p. 551.) Is the missing carbonyl absorption at lower or higher frequency than the one that is observed at  $1820 \text{ cm}^{-1}$ ? (*Hint*: See Table 21.3, text p. 996, and extrapolate from the absorptions of six- and five-membered cyclic anhydrides.)

- 21.50 (a) This is a reprise of Problem 10.59 on text pp. 480–481, which is answered on p. 209 of the Study Guide and Solutions Manual. The very weak acid HCN is not significantly dissociated. Consequently, the solution is insufficiently acidic to effect protonation of the —OH group of the alcohol. This protonation is necessary to convert this group into a good leaving group. Furthermore, there is virtually no cyanide ion ( $\text{C}\equiv\text{N}^-$ ) present, and hence virtually no nucleophile to displace the —OH group.
- (b) First of all, an excess of an alcohol is generally required to drive acid-catalyzed esterification to completion. However, even if some of the adipic acid is converted into its ester, there is no reason why this monoester would not be essentially as reactive as adipic acid itself, and the reaction mixture would ultimately contain a mixture of adipic acid, its monomethyl ester, and its dimethyl ester. The yield of the desired monoester would be poor, and it would have to be separated from both the di-ester and the unreacted adipic acid.
- (c) There is no reason why acetic acid should form an anhydride only with benzoic acid, and vice-versa; substantial amounts of acetic anhydride and benzoic anhydride should also be obtained. If all the reactions were totally random, the desired unsymmetrical anhydride would be formed in a maximum of 50% yield.
- (d) The hydroxide ion reacts *much* more rapidly with the O—H proton of the phenol than it does with the ester. (See Study Guide Link 20.1 on p. 473 of the Study Guide and Solutions Manual for a discussion of this point.) Consequently, the one equivalent of hydroxide is consumed by this reaction, and no base is left to saponify the ester.
- (e) Several functional groups in the  $\beta$ -lactam molecule are more reactive toward acid hydrolysis than the amide indicated. Because esters are more reactive than amides, the acetate ester will undoubtedly also hydrolyze under the reaction conditions. The  $\beta$ -lactam ring itself is an amide, and because hydrolysis of this amide relieves substantial ring strain, this amide should also hydrolyze more rapidly. Once the  $\beta$ -lactam hydrolyzes, the resulting enamine also should hydrolyze readily in acid, and the N—C—S linkage is also unstable toward hydrolysis in the same sense that an acetal is unstable. With so many faster competing processes, Klutz has no hope for a selective reaction.

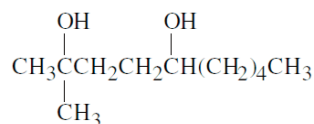
- 21.52 (b) Transesterification of the formate ester occurs.



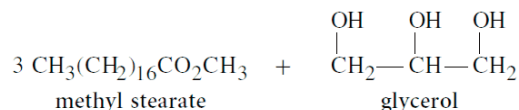
- (d) Both amino groups are acylated by the excess of the acid chloride.



- (g) The Grignard reactions of lactones are much like those of esters, except that the alcohol displaced by the nucleophilic acyl substitution reaction remains as part of the same molecule.

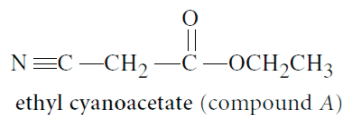


- (i) Lithium aluminum hydride reacts with acid chlorides in the same way that it reacts with esters, only faster. The product is  $(\text{CH}_3)_3\text{CCH}_2\text{OH}$  (2,2-dimethyl-1-propanol).
- (k) Transesterification occurs to give three equivalents of methyl stearate and one of glycerol.

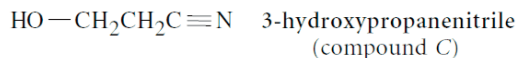


- 21.54 (a) The odd molecular mass indicates the presence of an odd number of nitrogens, and the hydroxamate test and the IR carbonyl absorption at  $1733 \text{ cm}^{-1}$  indicate the presence of an ester. The IR absorption at  $2237 \text{ cm}^{-1}$  indicates a nitrile. The triplet–quartet pattern in the NMR spectrum clearly indicates that compound *B* is an

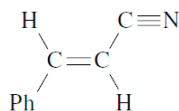
ethyl ester. Subtracting the masses of all the atoms accounted for leaves 14 mass units, the mass of a  $\text{CH}_2$  group. Compound *A* is ethyl cyanoacetate.



- (c) The odd molecular mass indicates the presence of nitrogen. The IR spectrum indicates the presence of both a nitrile and an alcohol. The broad,  $\text{D}_2\text{O}$ -exchangeable resonance at  $\delta$  3.4 in the NMR spectrum confirms the presence of an O—H group, and the pair of triplets indicates a  $-\text{CH}_2\text{CH}_2-$  group. Compound *C* is 3-hydroxypropanenitrile ( $\beta$ -hydroxypropionitrile).

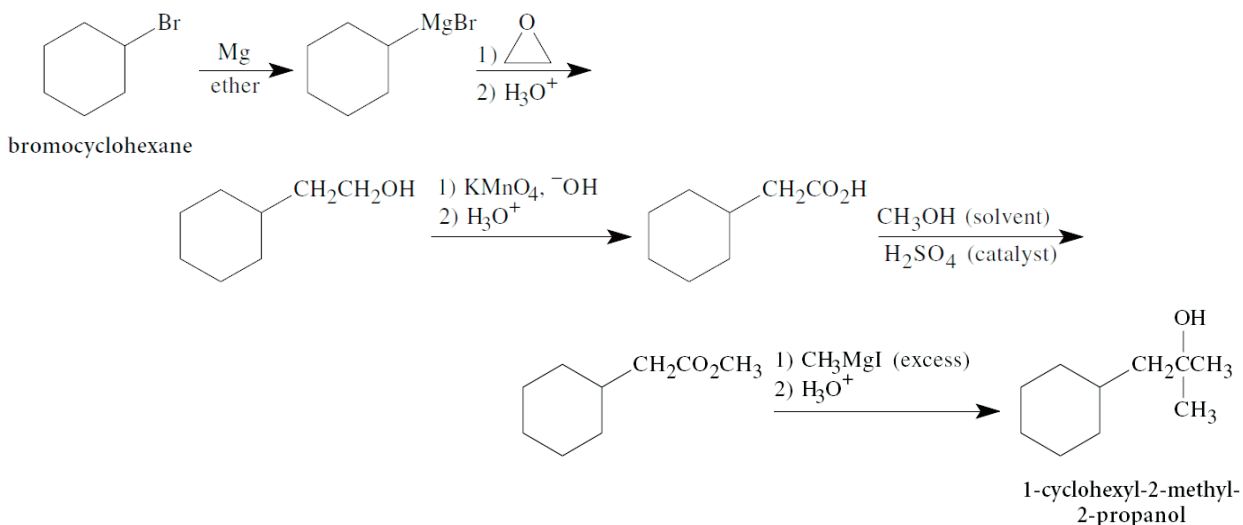


- (e) The mass spectrum shows an odd mass, which indicates the presence of nitrogen. The IR spectrum could indicate the presence of a nitrile, although, if so, the  $\text{C}\equiv\text{N}$  absorption is about  $50\text{ cm}^{-1}$  lower in frequency than the  $\text{C}\equiv\text{N}$  absorption of an ordinary nitrile. The IR spectrum also indicates a trans alkene. The UV spectrum indicates extensive conjugation. This shift of the nitrile IR absorption is similar to that observed with conjugated carbonyl groups, and it suggests that the nitrile group is conjugated with the double bond. The NMR shows resonances for 7 protons. The large splitting in the resonances at  $\delta$  5.85 and  $\delta$  7.35 confirms the presence of the trans alkene. Evidently, the apparent singlet at  $\delta$  7.4 corresponds to five protons, that is, to a monosubstituted benzene ring. Compound *E* is (*E*)-3-phenylpropenenitrile.

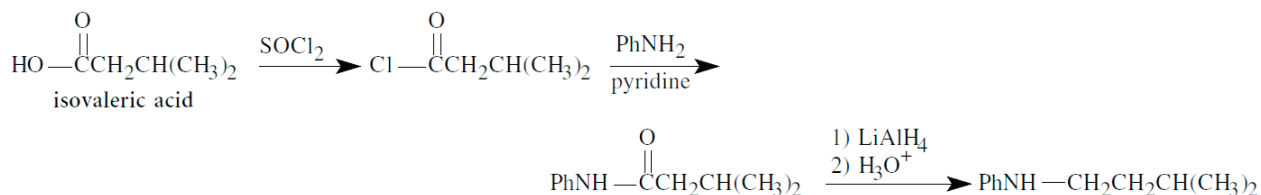


(*E*)-3-phenylpropenenitrile  
(compound *E*)

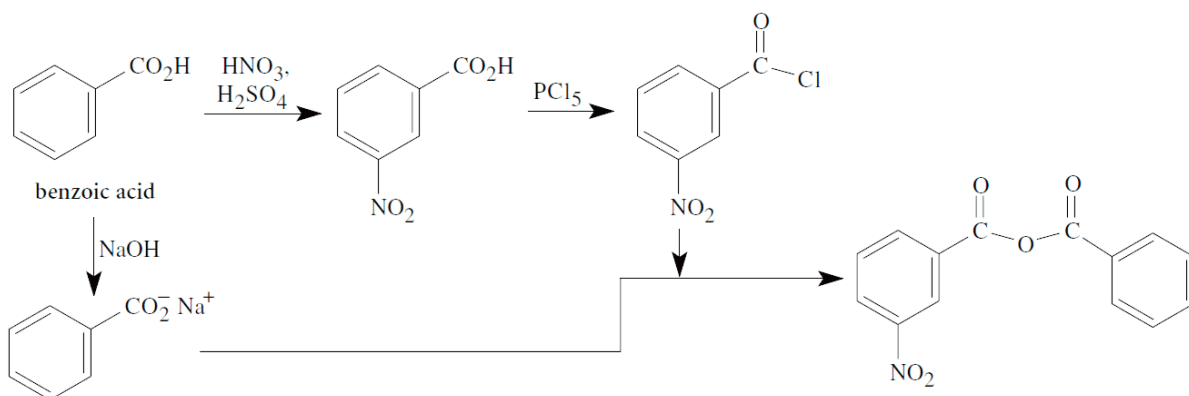
21.55 (b)



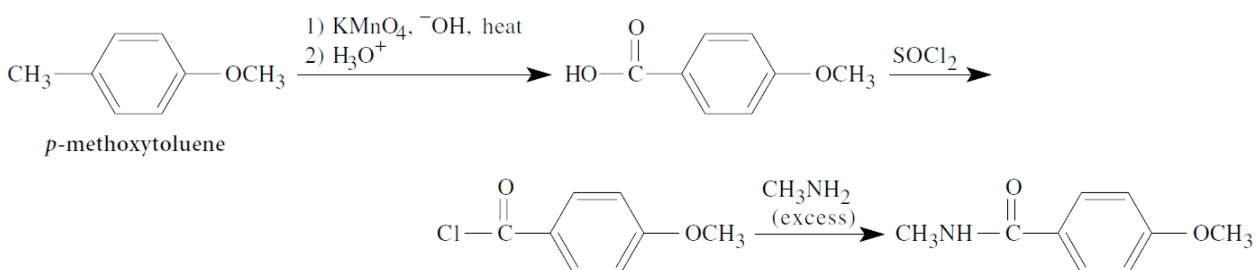
(d)



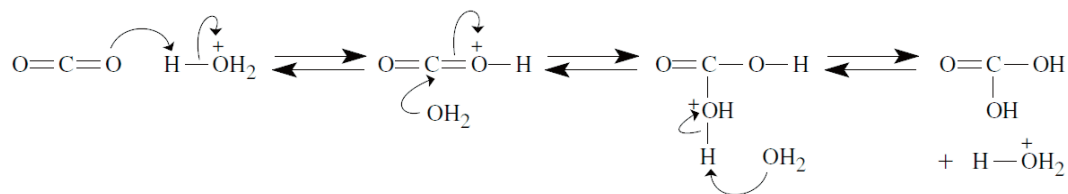
(g)



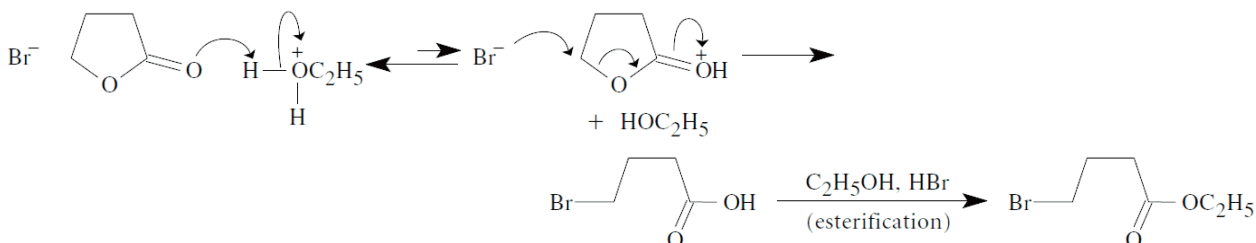
(i)



- 21.56 (a) The reversible hydration of carbon dioxide to carbonic acid is an acid-catalyzed addition of water that is mechanistically identical to the hydration of aldehydes and ketones shown in Eq. 19.18a–b, text pp. 909–910.

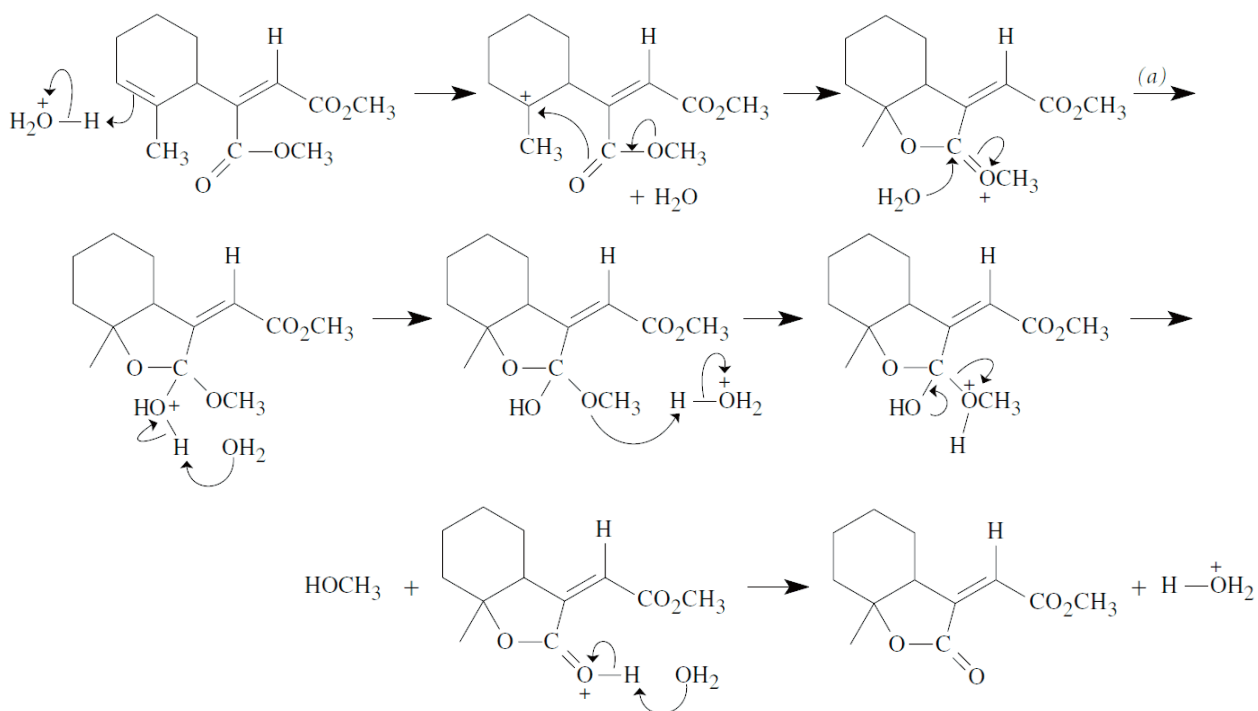


- (c) Protonation of the carbonyl oxygen produces a good leaving group which is displaced by bromide ion. The carboxy group is then esterified by the usual mechanism (Eqs. 20.18a–c, text pp. 966–7).

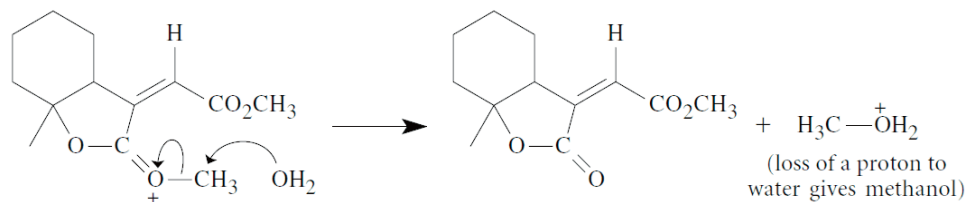


An alternative reasonable mechanism involves transesterification of the lactone by ethanol to give a hydroxy ester, followed by conversion of the alcohol to a bromide by an acid-catalyzed  $\text{S}_{\text{N}}2$  reaction. (See Eqs. 10.11a–b, text p. 441.) However, it is likely that the mechanism shown above is the correct one, because the equilibrium between lactone and hydroxy ester is likely to strongly favor the lactone, and because a protonated carboxy group is an excellent leaving group.

- (e) Protonation of the ring double bond gives a tertiary carbocation that reacts with the carbonyl oxygen of the ester to give the lactone.

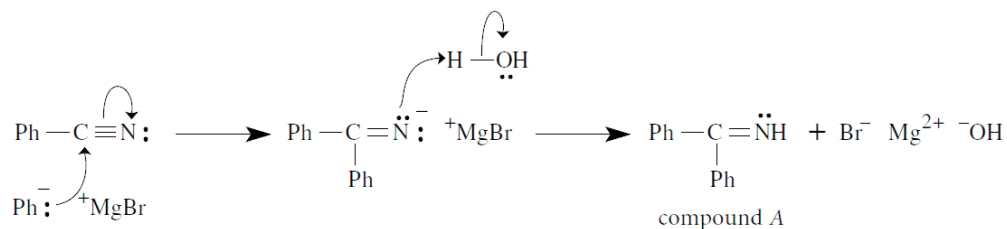


As an alternative to step (a) and the subsequent steps in the foregoing mechanism, water could react with the methyl group:

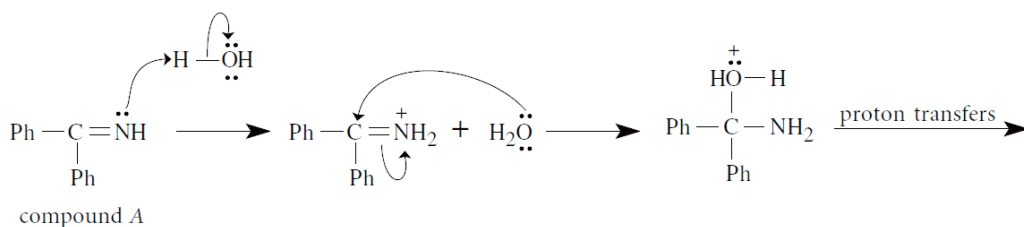


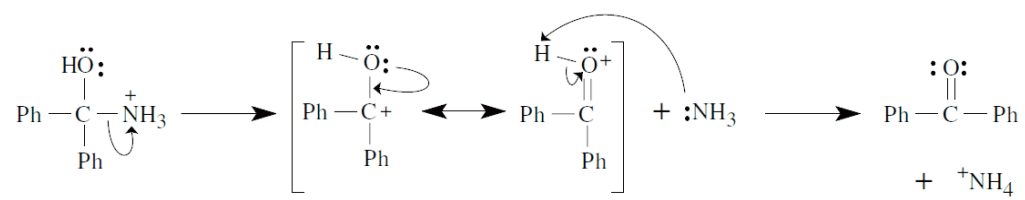
How might carrying out the reaction in  $^{18}\text{O}$ -water enable one to distinguish between these two mechanisms?

- 21.57 Addition of the Grignard reagent to the carbon–nitrogen triple bond is expected by analogy with carbonyl-group reactions. The product *A* is an imine.



This imine hydrolyzes in acidic solution to benzophenone:



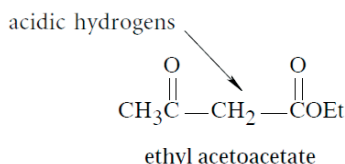


# Chapter 22

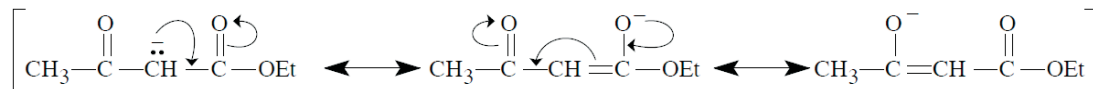
## The Chemistry of Enolate Ions, Enols, and $\alpha,\beta$ -Unsaturated Carbonyl Compounds

### Solutions to In-Text Problems

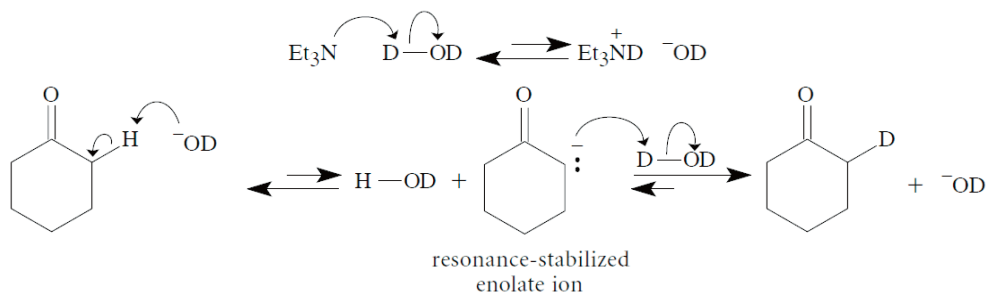
- 22.1 (b) The acidic hydrogens are the  $\alpha$ -hydrogens on the carbons between the two carbonyl groups. (—OEt = ethoxy group = —OCH<sub>2</sub>CH<sub>3</sub>.)



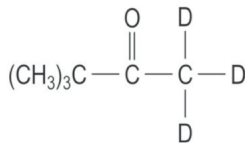
The reason that these hydrogens are particularly acidic is that the conjugate-base enolate ion is stabilized by the polar effects and resonance effects of two carbonyl groups, whereas the conjugate-base enolate ion of an ordinary ester is stabilized by the corresponding effects of only one carbonyl group. The resonance structures of the conjugate-base enolate ion of ethyl acetoacetate are as follows:



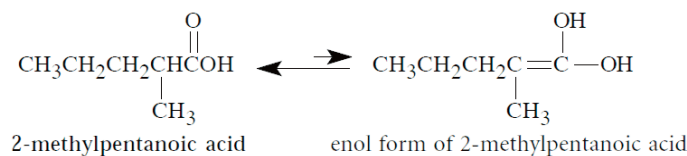
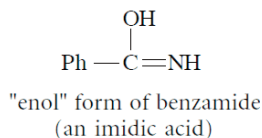
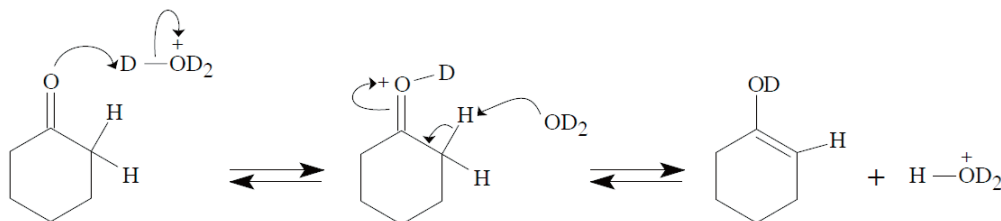
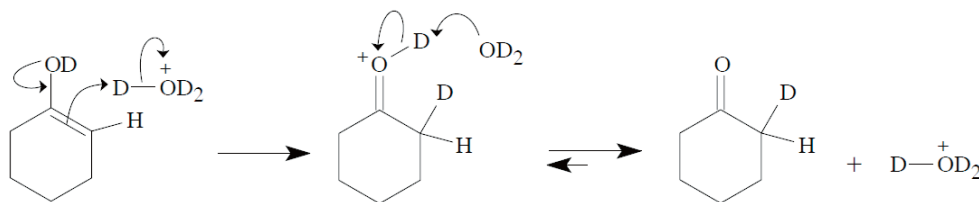
- 22.3 A mechanism for replacement of one hydrogen in the reaction of Eq. 22.6, text p. 1051, is shown in the following equation. (The mechanisms for replacement of the others are identical.) Only the  $\alpha$ -hydrogens are replaced because the enolate ion is the only carbanion stable enough to be formed. The carbanion intermediates required in a similar mechanism for the replacement of the hydrogens other than the  $\alpha$ -hydrogens are not resonance-stabilized.



- 22.6 (b) All  $\alpha$ -hydrogens are exchanged for deuterium. (The methyl hydrogens of the *tert*-butyl group are not  $\alpha$ -hydrogens.)



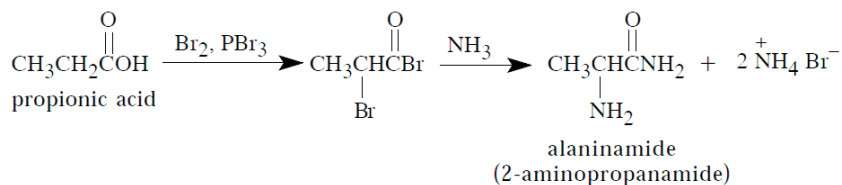
22.7 (b)

(c) Benzaldehyde,  $\text{PhCH}=\text{O}$ , has no enol forms because it has no  $\alpha$ -hydrogens.22.9 (b) The "enol" form of an amide that has a carbon–nitrogen double bond is called an *imidic acid*; see Eq. 21.20b, text p. 1009. Notice that this particular amide cannot enolize toward the  $\alpha$ -carbon because it has no  $\alpha$ -hydrogens on that carbon.22.11 (b) The enol is formed by the mechanism shown in Eq. 22.17b on text p. 1056, except that  $\text{D}_3\text{O}^+$  is the acid. This results in the "washout" of one  $\alpha$ -hydrogen into the large excess of deuterated solvent.Protonation of the double bond by  $\text{D}_3\text{O}^+$  gives a deuterium at the  $\alpha$ -position. Replacement of one  $\alpha$ -hydrogen by deuterium is shown; the mechanism for replacement of the other  $\alpha$ -hydrogens is identical.

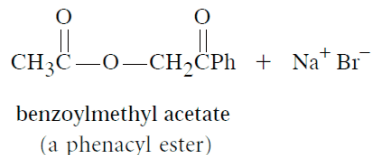
22.13 (b) Because the rate of ketone halogenation is independent of the halogen concentration, the rates of halogenation of the same ketone with two different halogens are also independent of halogen concentration and therefore independent of the identity of the halogen itself. In fact, the rate in both cases is the rate of enolization, as in part (a). The two processes are compared at the same acid concentration because the enolization process is acid-catalyzed (Eq. 22.24, text p. 1058).

22.14 In part (b), benzophenone does not halogenate because it cannot form an enolate ion (it has no  $\alpha$ -hydrogens), and the aromatic rings are deactivated by the carbonyl group toward electrophilic halogenation.22.16 (b) The  $\alpha$ -bromo acid bromide is formed first. Then ammonia reacts as a nucleophile with it in both an acyl substitution reaction to give the amide, and in an  $\text{S}_{\text{N}}2$  reaction at the  $\alpha$ -carbon to give the  $\alpha$ -amino amide of the  $\alpha$ -amino acid alanine.

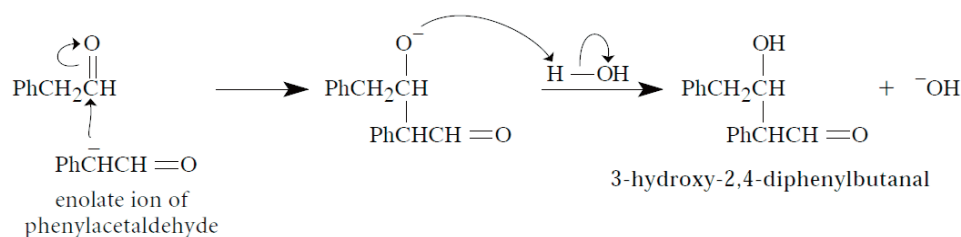




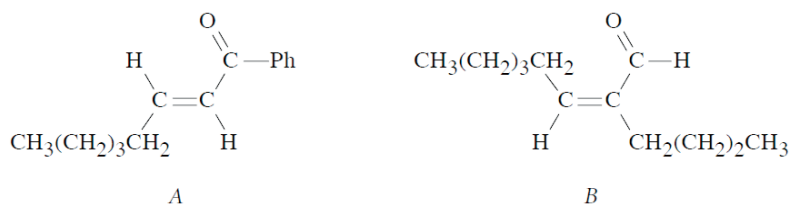
- 22.17 (b) The base acetate ion displaces the  $\alpha$ -bromine to give a compound that is an example of a *phenacyl ester*.



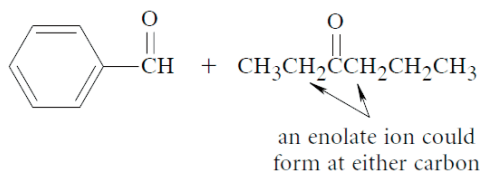
- 22.19 (a) The aldol addition reaction of phenylacetaldehyde:



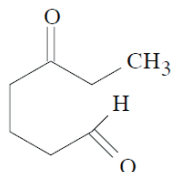
- 22.20 (b) As in part (a), the enolate ion of the ketone adds to the aldehyde carbonyl group to give product *A* because aldehyde carbonyl groups are more reactive than ketone carbonyl groups. It is also likely that aldol condensation of two molecules of hexanal will occur to give product *B*.



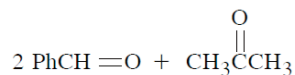
- 22.22 (b) The product shown would require the following starting materials. However, since the enolate ion required for the synthesis is only one of two that could form, at least two isomeric products are possible of which the desired product is only one. The desired product would therefore be formed as one component of a mixture of isomers.



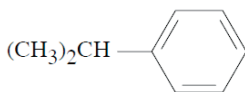
- (d) This product is the result of an intramolecular reaction of a ketone enolate and an aldehyde carbonyl group; hence, its synthesis from the following starting material is reasonable.



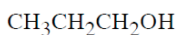
- (f) This is a reaction of two equivalents of benzaldehyde with one of acetone. Because an aldehyde without  $\alpha$ -hydrogens is involved, the reaction is a reasonable example of the Claisen–Schmidt condensation.



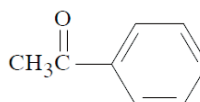
22.24 (b)



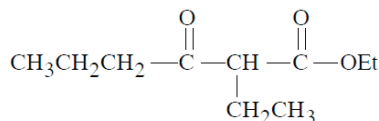
(d)



(f)

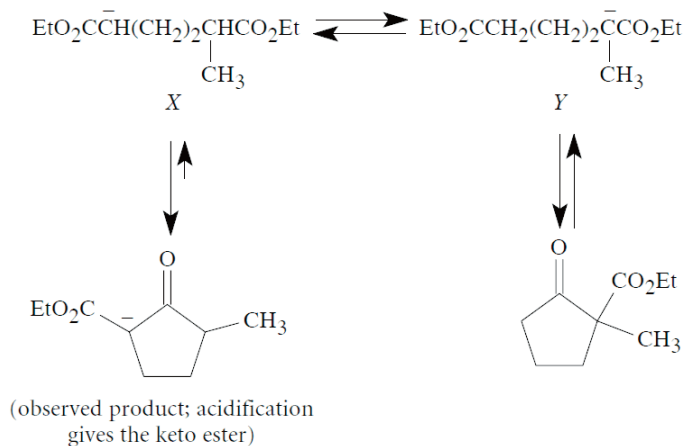


22.25 (b)

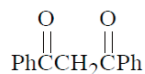


ethyl 2-ethyl-3-oxohexanoate

- 22.27 (b) Use reasoning similar to that used in solving part (a). Two possible enolate ions, *X* and *Y*, can form; the product derived from ion *X* is ultimately observed because only this product is formed irreversibly by ionization.

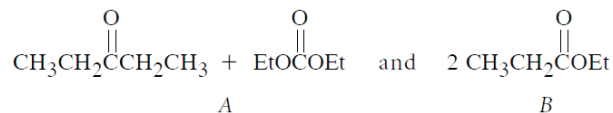


22.28 (b)



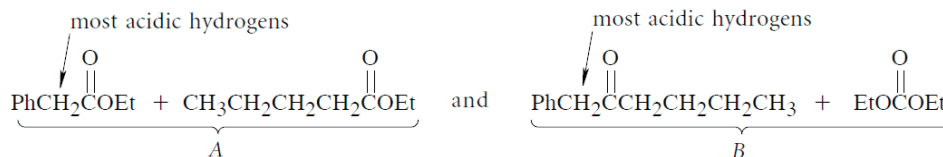
Ethanol is a by-product.

- 22.29 (b) The two possible sets of starting materials are as follows:



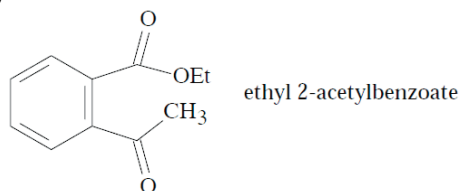
Either set would work. In set *A*, a large excess of diethyl carbonate must be used. (See Eq. 22.58, text p. 1077, and the discussion that follows.) However, set *B* would be more convenient because only one ester is required as a starting material and because we would not have to separate the product from an excess of starting material, as in set *A*.

- (d) The two possible sets of starting materials are as follows:

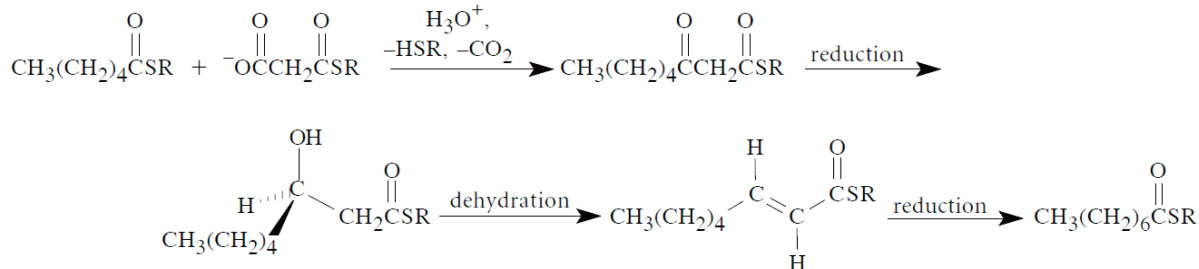


Set *A* consists of two esters with  $\alpha$ -hydrogens; four different products are possible. Furthermore, the  $\alpha$ -hydrogens of ethyl phenylacetate are considerably more acidic than those of ethyl valerate (why?); therefore, the major product is likely to be derived from the enolate ion formed at this position, but this is not the desired product. In set *B*, there are two sets of  $\alpha$ -hydrogens, but the hydrogens that are  $\alpha$  to the phenyl ring are considerably more acidic (why?). Unfortunately, the desired product is *not* derived from the enolate ion formed at this position. Hence, both sets of starting materials are unsatisfactory. In summary, the desired product cannot be made by a Claisen condensation.

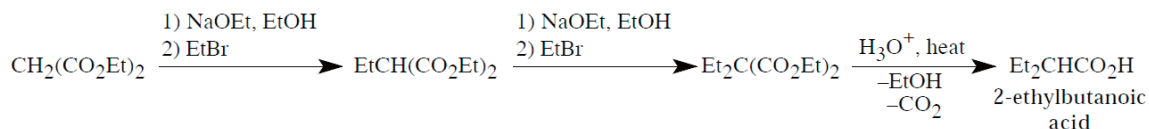
22.30 (b)



22.31 Follow the pattern in Eqs. 22.63c–d, text p. 1083.

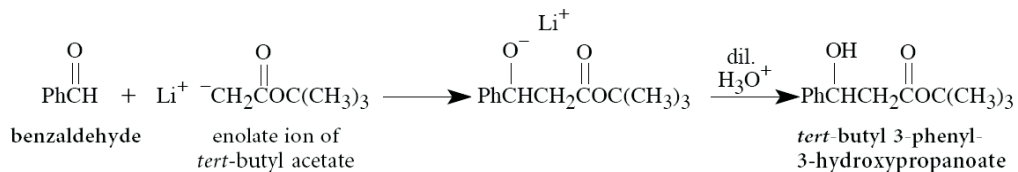


22.33 (b) 2-Ethylbutanoic acid can be prepared by a malonic ester synthesis:

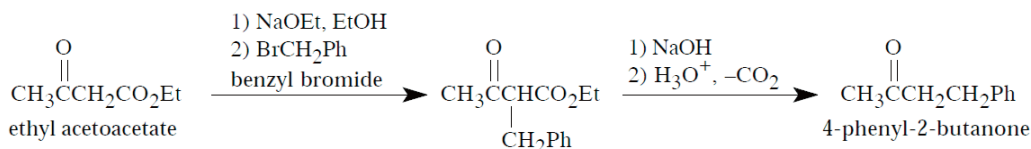


22.35 (a) Recall Sec. 18.1, text p. 823, where the four reasons for the lack of reactivity of aryl halides under  $\text{S}_{\text{N}}2$  conditions is discussed. Firstly, the relatively high energy of the transition state required for the conversion of an  $sp^2$ -hybridized carbon into an  $sp$ -hybridized carbon (about  $21 \text{ kJ mol}^{-1}$  or  $5 \text{ kcal mol}^{-1}$ ) that must occur in an  $\text{S}_{\text{N}}2$  reaction at an aryl carbon. Secondly, the nucleophile, in this case the conjugate-base enolate of diethyl malonate, must approach the carbon–bromine bond in the plane of the phenyl ring, which would result in significant van der Waals repulsions (a steric effect) of both the nucleophile and the phenyl ring. Thirdly, the nucleophile must also approach the carbon–bromine bond through the plane of the phenyl ring, which is impossible. And fourthly, because the carbon at which substitution occurs would have to undergo stereochemical inversion, the reaction would necessarily yield a benzene derivative containing a twisted and highly strained double bond.

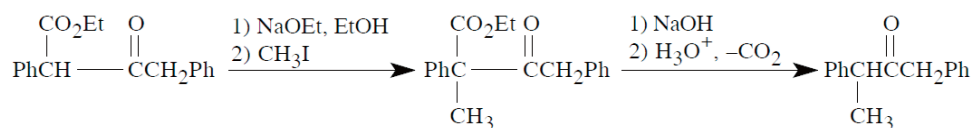
22.37 (b) By the same logic used in part (a), the  $\beta$ -hydroxy ester is formed.



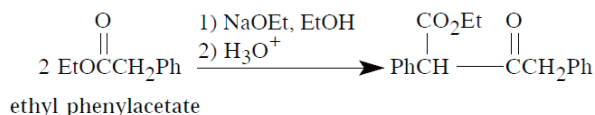
22.39 (b)



22.40 (b)



The starting  $\beta$ -keto ester is prepared by a Claisen condensation of ethyl phenylacetate:



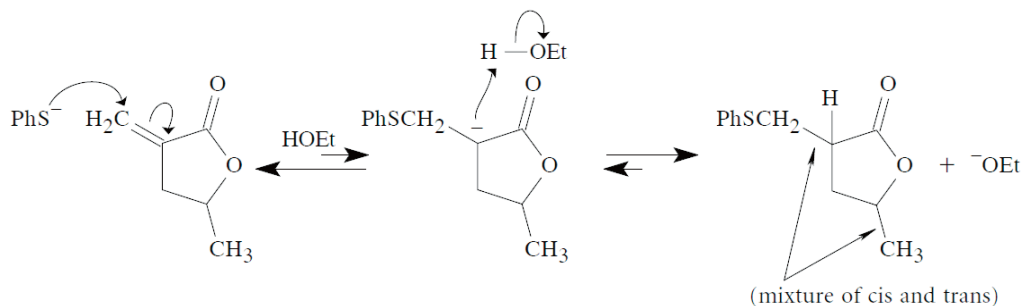
22.42 (b)

(d)



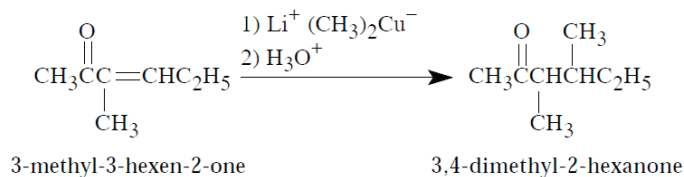
In part (d), saponification occurs instead of conjugate addition because saponification is an *irreversible* nucleophilic acyl substitution reaction.

22.43 (b) This is a conjugate addition of the benzenethiolate anion to the carbon-carbon double bond. The benzenethiolate nucleophile,  $\text{PhS}^-$ , is formed by the reaction of benzenethiol,  $\text{PhSH}$ , with  $^- \text{OEt}$ . A mixture of diastereomers is formed because the final protonation step can occur from the same face as the methyl group or from the face opposite the methyl group.

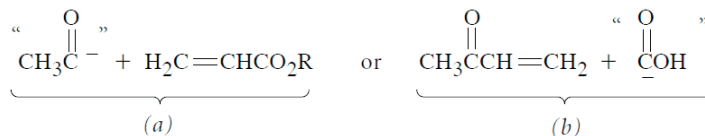


22.44 (b) The nucleophile must be a species that can be converted into a carboxymethyl ( $\text{HO}_2\text{CCH}_2-$ ) group. Because the nucleophile ends up as a “substituted acetic acid,” the conjugate-base enolate ion of diethyl malonate can serve as species  $X$ . Addition of  $X$  to the ester gives compound  $D$ . All ester groups of  $D$  are hydrolyzed and one of the resulting carboxy groups is decarboxylated when  $D$  is heated in aqueous acid.



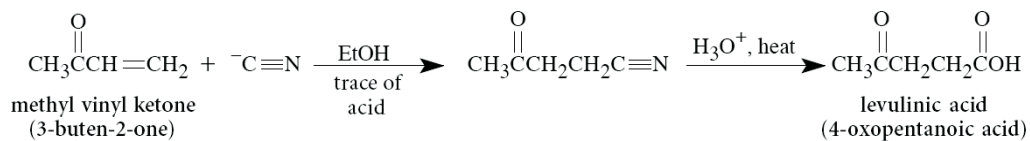


- (d) An analysis similar to that in Study Problem 22.7, text p. 1104, suggests the following possibilities:



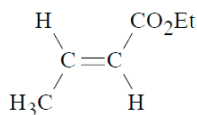
A practical equivalent for the anion in (a) might be an acetylide anion,  $^-\text{CCH}$ . The resulting acetylene could then be hydrated to the desired ketone. Unfortunately, acetylenic cuprate reagents do not work in conjugate additions because the acetylenic ligands do not transfer from the copper. Nevertheless, if you came up with this possibility, you are analyzing the problem with considerable sophistication.

Anion (b) does have a simple practical equivalent: the cyanide ion:

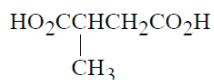


### Solutions to Additional Problems

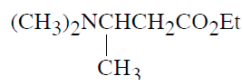
22.51 The structure of the starting material is

ethyl *trans*-2-butenoate

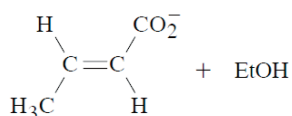
(a)



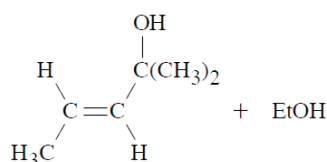
(b)



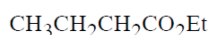
(c)



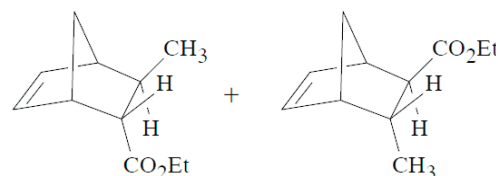
(d)



(e)



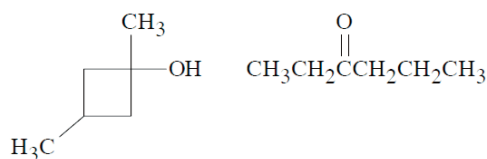
(f)



(both compounds are racemates)

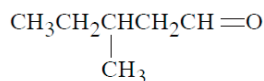
As in Problem 22.50(h), text p. 1106, the  $\alpha,\beta$ -unsaturated ester in part (f) serves as a Diels–Alder dienophile.

22.52 (b)

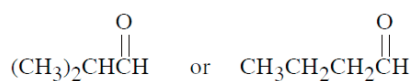


(two of several possibilities)

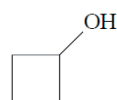
(d)



22.53 (b)

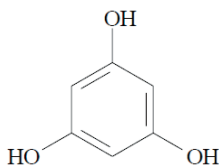


(d)

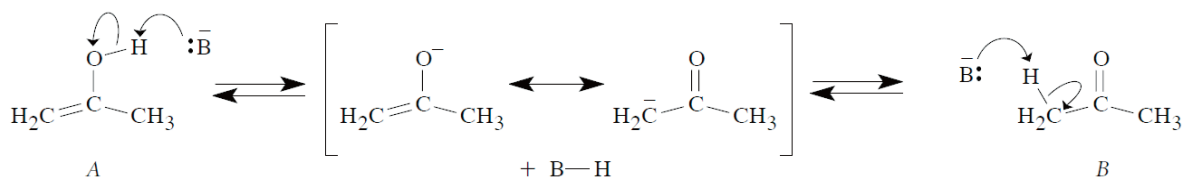


(one of several possibilities)

22.54 (b) This compound, 1,3,5-cyclohexanetrione, exists as its “triene-triol” isomer phloroglucinol because the latter is aromatic.

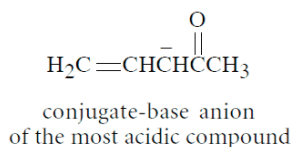
1,3,5-benzenetriol  
(phloroglucinol)

22.56 (a) Removal of the O—H proton from *A* and a C—H proton from *B* gives conjugate-base anions that are resonance structures and therefore identical. ( $\text{B}^-$  = a general base.)

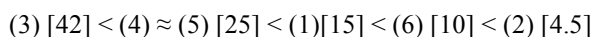


- (b) Because the ketone is more stable than its enol, more energy must be expended for it to ionize. Consequently, the ketone is less acidic. The logic is similar to that used in the solution to Problem 22.55(b).

- 22.57 (b) The first compound is more acidic because the conjugate-base anion (see following structure) has the greater number of resonance structures. It is stabilized by resonance interaction with both the carbon-carbon double bond and the carbonyl group. The two possible enolate ions of the second compound lack the resonance interaction with a carbon-carbon double bond.

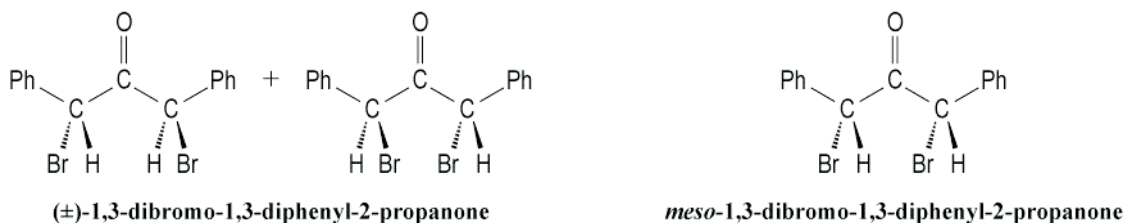


- 22.58 The order of increasing acidity (decreasing  $pK_a$ ) is as follows. [Approximate  $pK_a$  values are in brackets.]

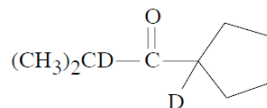


Toluene is much less acidic than phenol, and amides are much less acidic than carboxylic acids (element effect). The  $pK_a$  values of 1-alkynes and esters are very similar (about 25). The remaining rankings require knowledge of approximate  $pK_a$  values. The point of this problem is that it is very important to know the typical  $pK_a$  values of organic compounds because so much of organic reactivity is based on acid-base principles.

- 22.60 The dibromo derivative is a mixture of diastereomers: the ( $\pm$ )-diastereomer (that is, the racemate) and the meso diastereomer.



- 22.63 (b) The two  $\alpha$ -hydrogens are acidic enough to be replaced. These hydrogens are shown as deuteriums in the following structure.



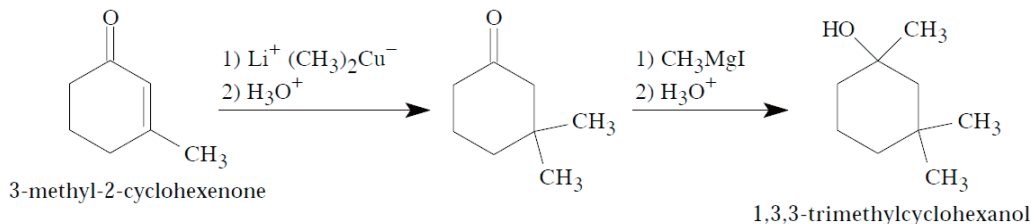
- 22.64 (b) The analogous isomerization of compound C cannot occur because there is no  $\alpha$ -hydrogen at the ring junction. Only the removal of an acidic hydrogen at a ring junction could lead to isomerization, and the hydrogen at the other carbon of the ring junction is not acidic enough to ionize under the conditions given.

- 22.67 (b) Tropone is unusually basic because its conjugate acid is an aromatic carbocation.

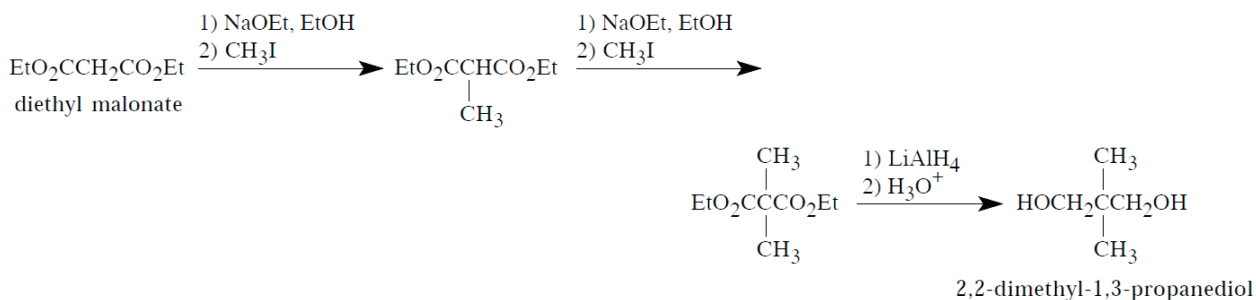




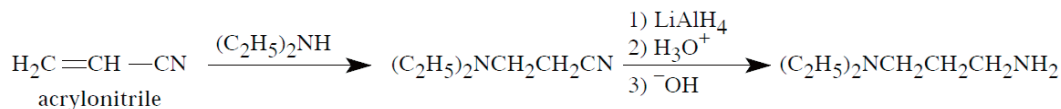
22.75 (b)



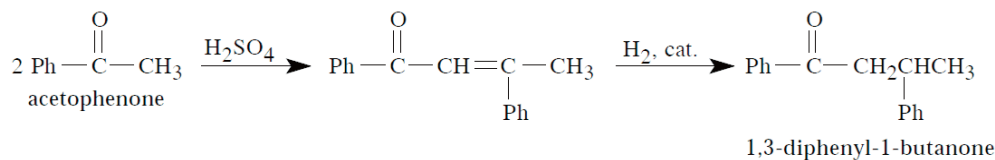
(d)



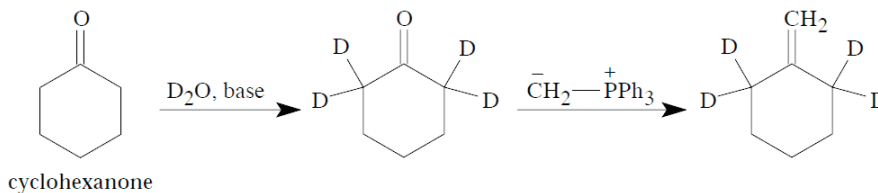
(f)



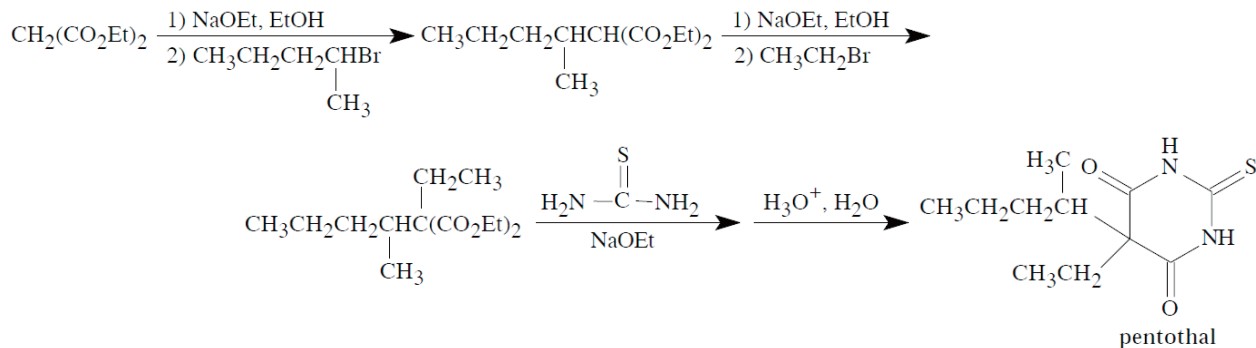
(h)



(j)

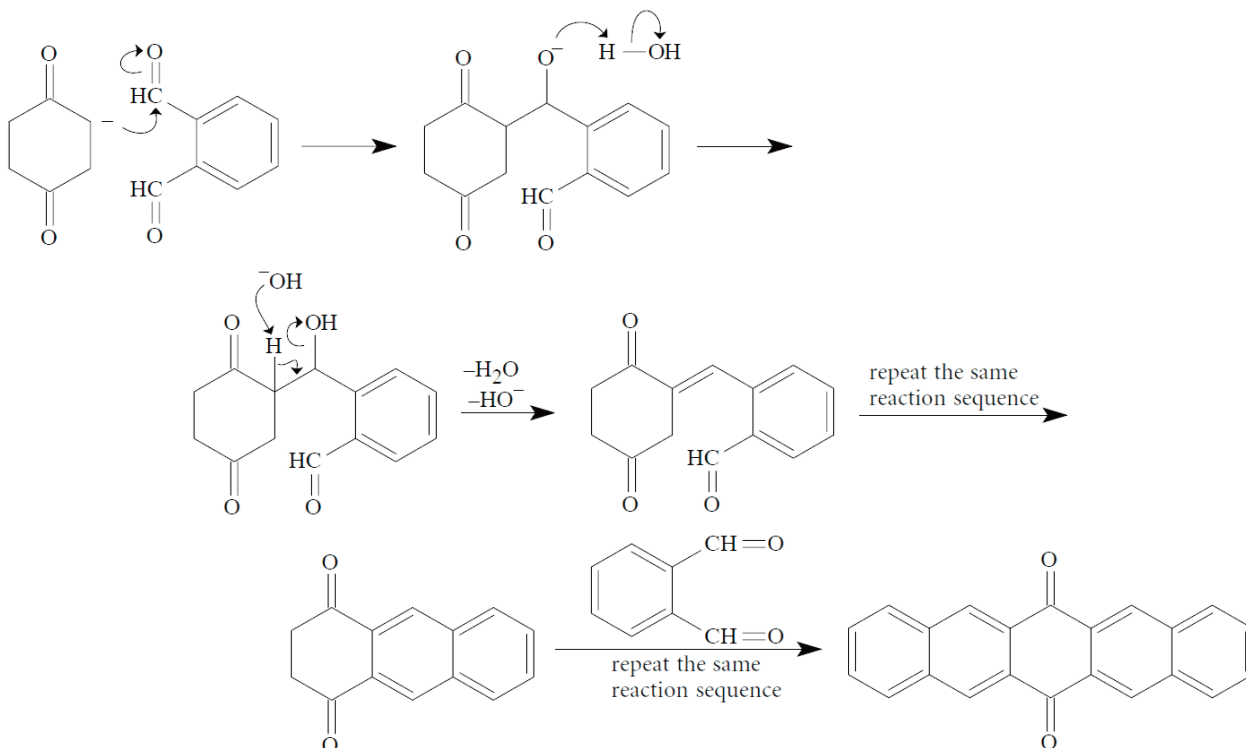


22.78 The synthesis of pentothal involves, first, preparation of the substituted malonic ester derivative, and then condensing it with thiourea, the sulfur analog of urea.

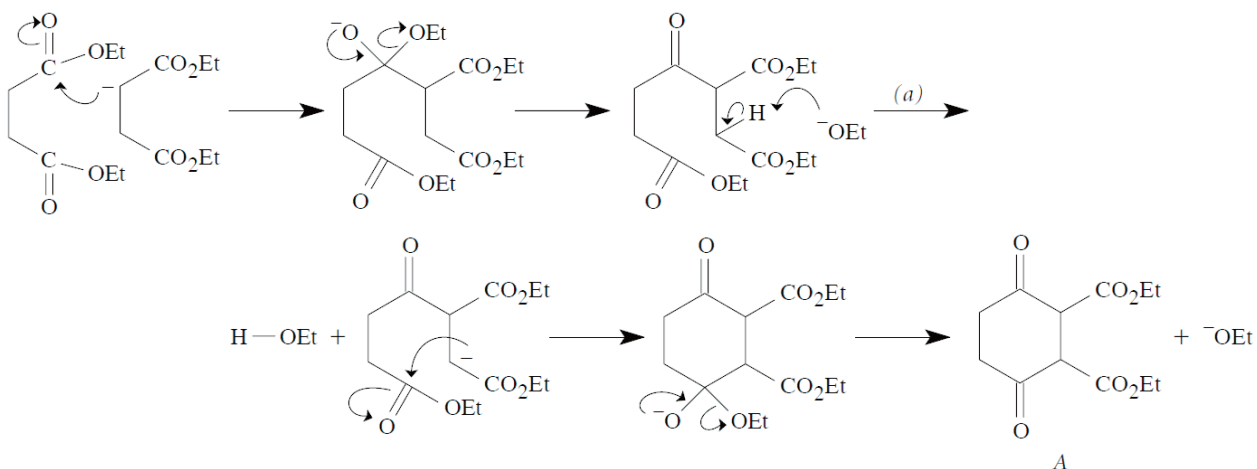


22.80 (b) This reaction is crossed aldol condensation followed by an intramolecular crossed aldol condensation followed by the same sequence with another molecule of dialdehyde. The following mechanism begins with

the conjugate-base enolate ion of the diketone. Although the dehydration step is shown for brevity as a concerted process, it probably involves an enolate-ion intermediate. (See Eq. 22.44, text p. 1065.)

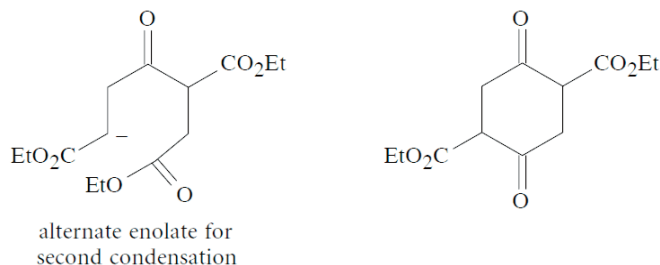


- (d) This is a double Claisen condensation followed by hydrolysis and decarboxylation of the ester groups. The mechanism below begins with the conjugate-base enolate ion of the diester.



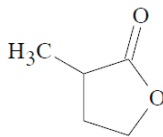
Compound *A* forms a conjugate-base enolate ion under the basic conditions but is regenerated when acid is added. Hydrolysis of the two ester groups and decarboxylation of the resulting  $\beta$ -keto acid groups give the product. In the step labeled (*a*), the hydrogen that is removed is not the most acidic hydrogen in the molecule. (Which hydrogen is most acidic?) However, removal of the most acidic hydrogen does not lead to the observed product. Removal of the hydrogen shown, although occurring less frequently, leads rapidly to product.

Note also that the second condensation reaction could involve the reaction of a different enolate ion with a different ester group so that the  $\beta$ -keto ester shown on the right would be formed:

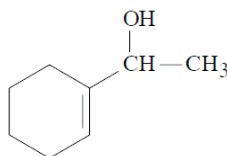


Ester hydrolysis and decarboxylation of this compound would also give the observed product.

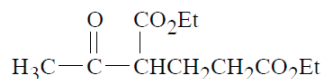
- 22.81 (b) The lactone, a cyclic ester, can form an enolate ion, and this ion is alkylated by methyl iodide. (The structure of  $\gamma$ -butyrolactone is given on text p. 988.)



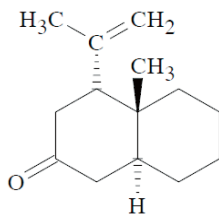
- (d) Lithium aluminum hydride reduces the carbonyl group to an alcohol.



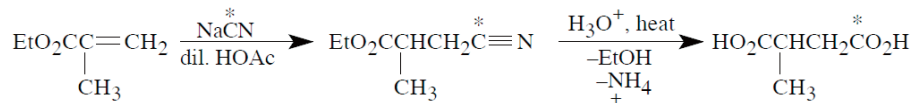
- (f) This is a Michael addition in which the conjugate-base enolate ion of acetoacetic ester is the nucleophile.



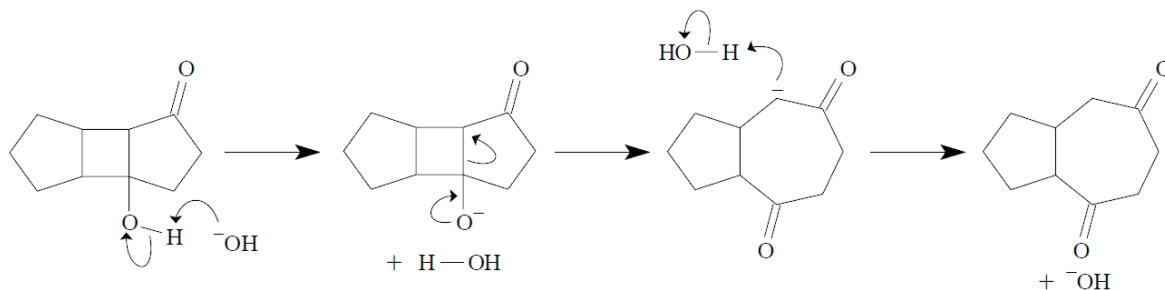
- (h) This is a conjugate addition of the magnesium organocuprate reagent. Assume that the isopropenyl group (the group delivered from the organocuprate reagent) enters trans to the angular methyl group to avoid van der Waals repulsions.



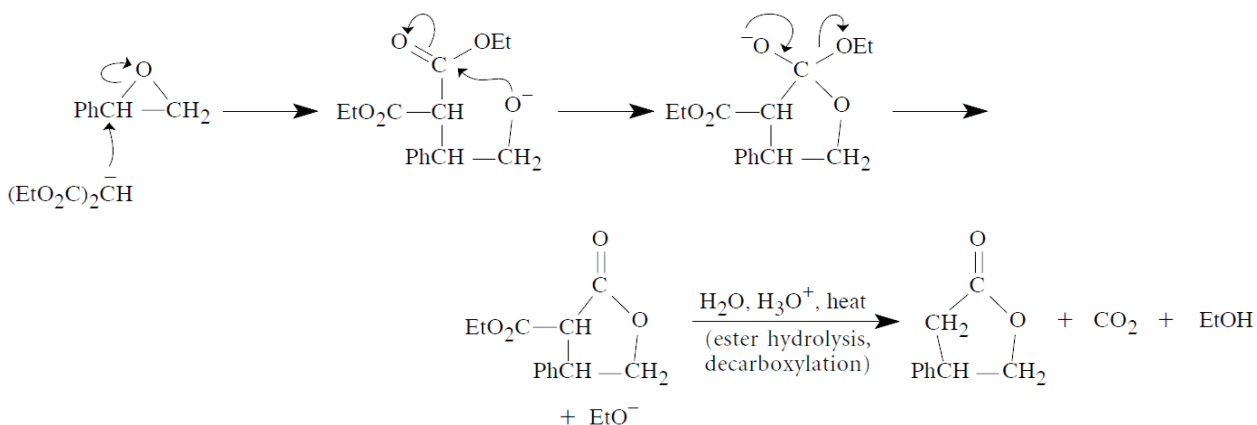
- 22.82 (b) Take the same approach as in part (a), but with a different ester.



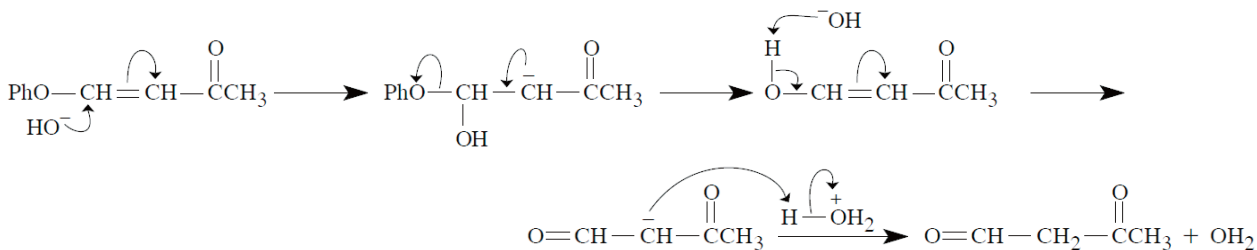
- 22.83 (b) The starting material is a  $\beta$ -hydroxy ketone. Ionization of the hydroxy group followed by the reverse of an aldol addition gives the product. The reaction is driven by relief of strain in the four-membered ring.



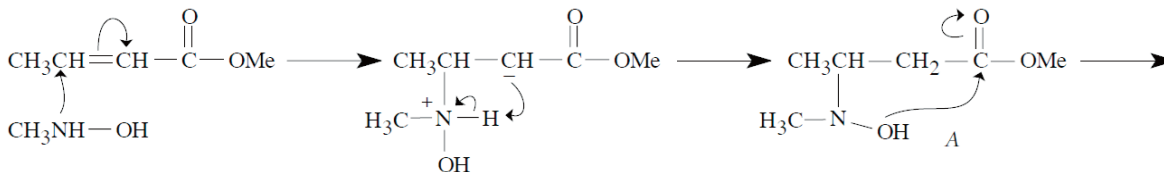
- 22.84 (b) The conjugate-base anion of diethyl malonate serves as the nucleophile in an epoxide-opening reaction. Normally, epoxide opening under basic conditions involves reaction with the nucleophile at the less branched carbon. In this case, however, reaction also occurs at the more branched carbon because it is benzylic and therefore activated toward nucleophilic substitution. (Only reaction at the benzylic carbon is shown below; reaction at the other carbon occurs by a similar mechanism.) The resulting alkoxide undergoes intramolecular transesterification to give a lactone; hydrolysis and decarboxylation of the remaining ester give the product. The lactone does not hydrolyze because the equilibrium favors lactone formation when five- and six-membered rings are involved; see Eqs. 21.12–21.13 on text p. 1007.

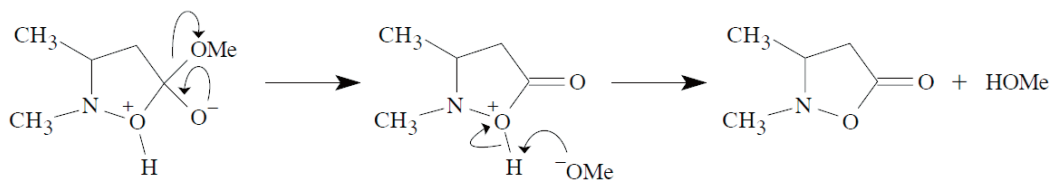


- (e) This mechanism is much like that in part (d), except that basic conditions are involved in all steps but the last.

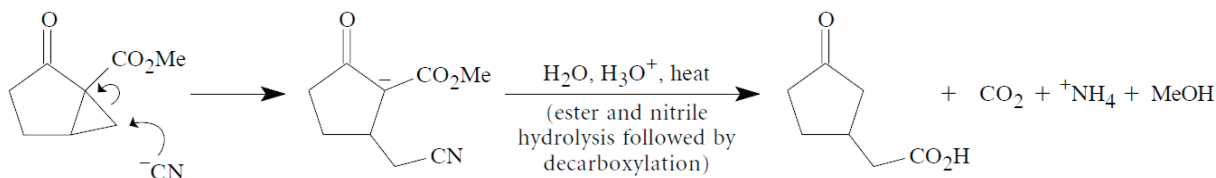


- (g) Conjugate addition with the nitrogen as a nucleophile gives compound *A*, which undergoes intramolecular transesterification. Alternatively, transesterification could occur first followed by conjugate addition.

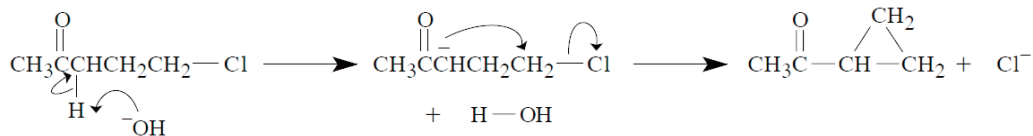




- (j) This reaction is a “conjugate addition” of cyanide ion on a cyclopropane. Notice that reaction at the least branched carbon of the cyclopropane occurs and that the immediate product of ring opening is a very stable anion. Heating in acid protonates this anion, hydrolyzes the ester and nitrile groups, and decarboxylates the resulting  $\beta$ -keto acid.



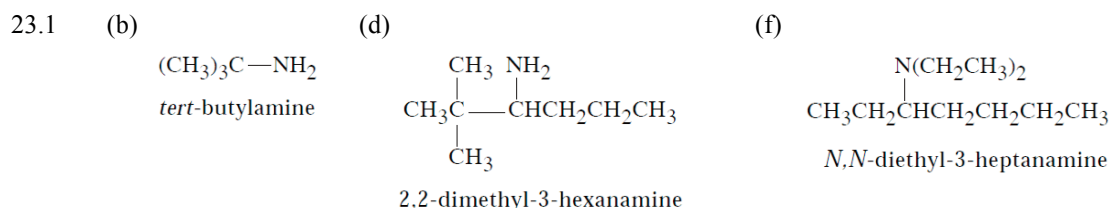
- 22.85 (b) One of the two possible conjugate-base enolate ions undergoes an intramolecular nucleophilic substitution reaction to give the cyclopropane. Although the other enolate is undoubtedly also formed, its cyclization would lead to a different product. In addition, the enolate that leads to product is the more stable enolate (why?) In any case, the enolate ion shown evidently reacts more rapidly.



# Chapter 23

## The Chemistry of Amines

### Solutions to In-Text Problems



- 23.2 (b) *N,N*-Dimethyl-*p*-nitroaniline (common), or 1-dimethylamino-4-nitrobenzene  
(c) Dicyclohexylamine (common), or *N*-cyclohexylcyclohexanamine

- 23.3 (b) Apply the principle used in part (a). The order of increasing carbon–nitrogen bond length is

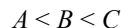


Compound *B* has a true carbon–nitrogen single bond, and hence has the longest carbon–nitrogen bond. Compound *A* has a true carbon–nitrogen double bond, and hence has the shortest carbon–nitrogen bond. The carbon–nitrogen bond of *C* has some double-bond character because of resonance interaction of the nitrogen unshared pair with the double bond. (Draw the appropriate resonance structure.) Another way to compare the C–N bond lengths of compounds *B* and *C* is to note that the C–N bond in *B* is an  $sp^3-sp^3$  single bond, whereas the C–N bond in *C* is an  $sp^2-sp^3$  single bond, and to remember that  $\sigma$  bonds with greater *s* character are shorter. (See discussion on text pp. 127 and 678.)

- 23.5 The NMR spectrum indicates the presence of only two phenyl hydrogens, and the singlet absorptions at  $\delta$  2.07 and  $\delta$  2.16 indicate the presence of chemically nonequivalent methyl groups in the ratio 2:1. Only compound (2), 2,4,6-trimethylaniline, fits the data. The two resonances at  $\delta$  2.07 and  $\delta$  2.16 correspond to the ortho and para methyl groups, respectively, and the  $\delta$  3.19 resonance to the  $-\text{NH}_2$  protons of the amine.

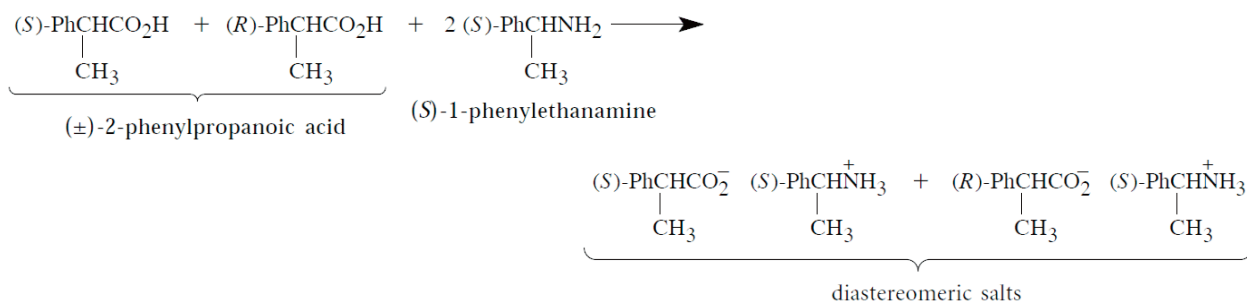
- 23.6 (a) 2,2-Dimethyl-1-propanamine (neopentylamine,  $(\text{CH}_3)_3\text{CCH}_2\text{NH}_2$ ) has a maximum of three resonances in its CMR spectrum. 2-Methyl-2-butanamine,  $\text{CH}_3\text{CH}_2\text{C}(\text{CH}_3)_2\text{NH}_2$ , should have four resonances in its CMR spectrum.

- 23.8 From Table 23.1, text p. 1123, we see that the basicity order is as follows:

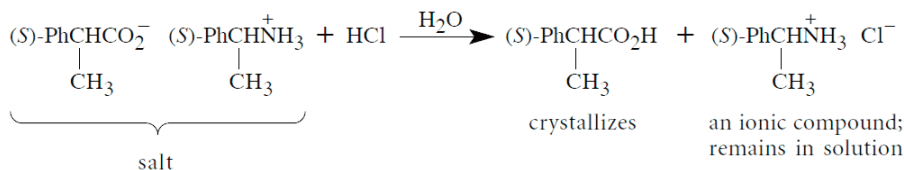


The basicities of all these amines are reduced by resonance interaction of the nitrogen unshared electron pair with the ring. The electron-withdrawing polar effect of the nitro group lowers basicity further, and resonance interaction of the nitrogen unshared pair with the *p*-nitro group stabilizes *p*-nitroaniline and lowers its basicity even more. (Resonance structures depicting this interaction are shown in the solution to Problem 23.3(a) on p. 610 of the Study Guide and Solutions Manual.)

- 23.10 Mix the racemic acid with one equivalent of the enantiomerically pure amine. (The *S* enantiomer of the amine is utilized in the equation below, but either *pure* enantiomer of the amine could be used.) The carboxylic acids will react with the amine to give a mixture of *diastereomeric* salts.

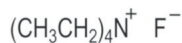


Because these salts have different properties, they can be separated by differential solubility, for example, by fractional crystallization from some solvent, probably an alcohol. After separating the salts, aqueous acid is added to each. The amine resolving agent dissolves in the aqueous acid solution (from which it can be recovered), leaving the enantiomerically pure free carboxylic acid as a solid that can be isolated by filtration and recrystallized.



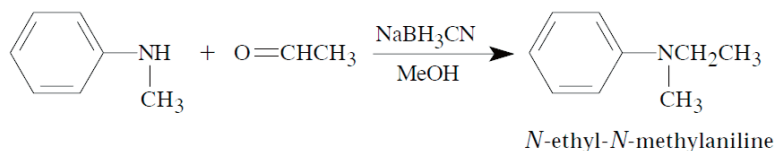
Notice that not only is amine basicity important in forming the initial salt, but also it is important in separating the amine resolving agent from the resolved carboxylic acid.

23.11 (a)

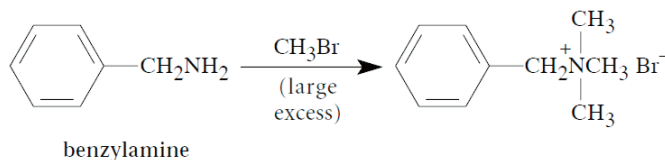


tetraethylammonium fluoride

23.14 The ethyl group could originate from acetaldehyde:

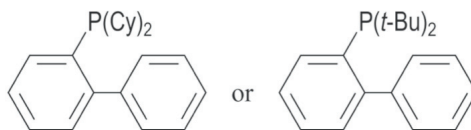


23.15 (b) Exhaustively methylate benzylamine with a large excess of methyl bromide.



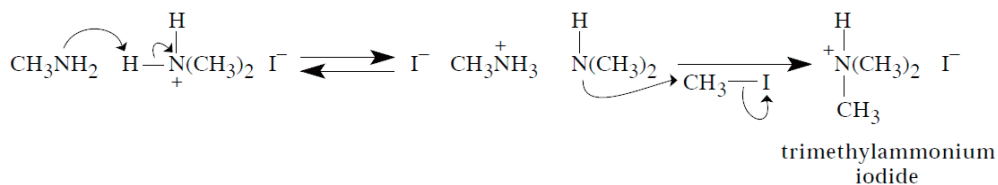
23.16 (a) Caleb has forgotten, if he ever knew, that aryl halides such as bromobenzene do not undergo  $\text{S}_{\text{N}}2$  reactions (Sec. 18.1).

(b) A Pd(0) catalyst of the type  $\text{PdL}_2$ . This reaction is discussed in Sec. 23.11C, where L is:

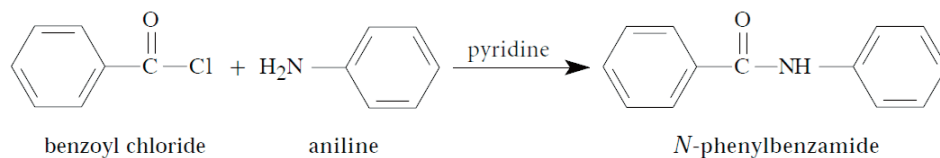


23.17 The dimethylammonium ion can lose a proton to give dimethylamine, which can then be alkylated by methyl iodide.

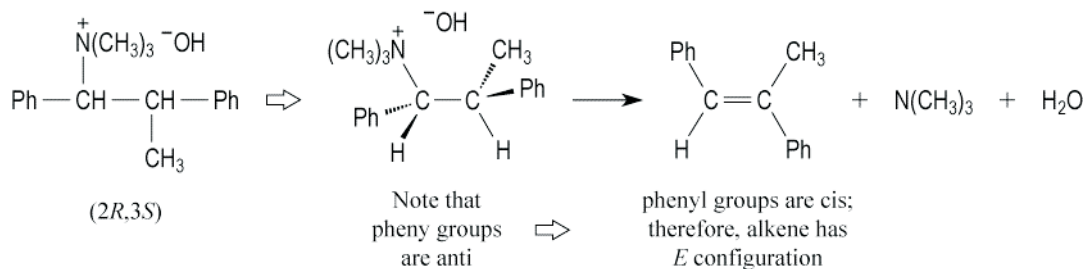




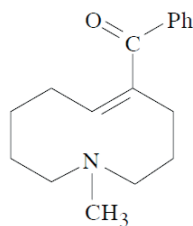
23.18 (a)



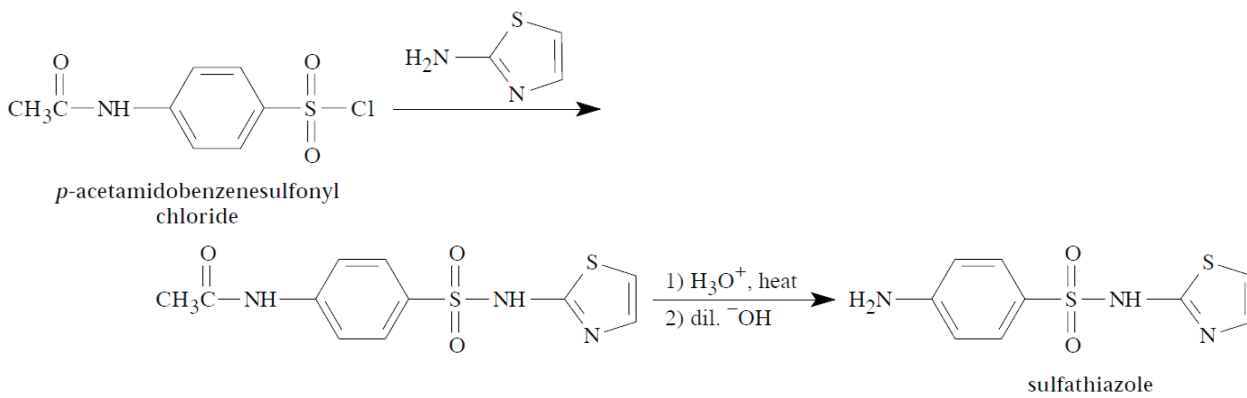
23.19 (b) Draw the molecule in a conformation in which the trimethylammonium group is anti to the  $\beta$ -hydrogen, and examine the relative positions of the phenyl groups. In this part, the alkene product must have the *E* configuration.



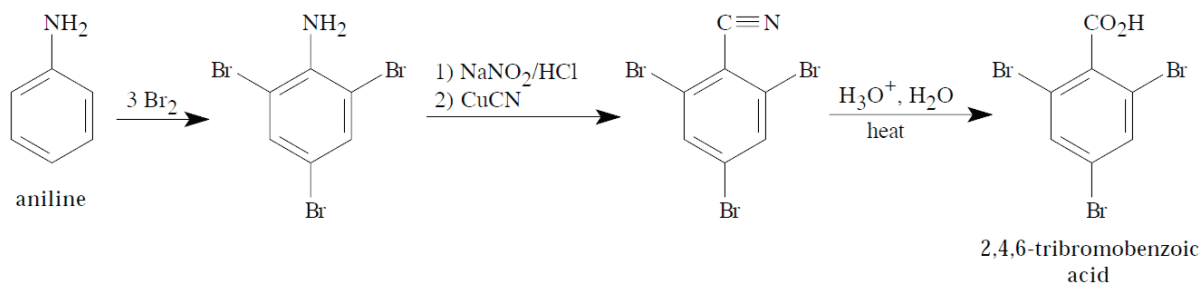
23.20 (b) The hydrogen  $\alpha$  to the carbonyl group is removed because it is considerably more acidic than the other  $\beta$ -hydrogens.



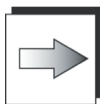
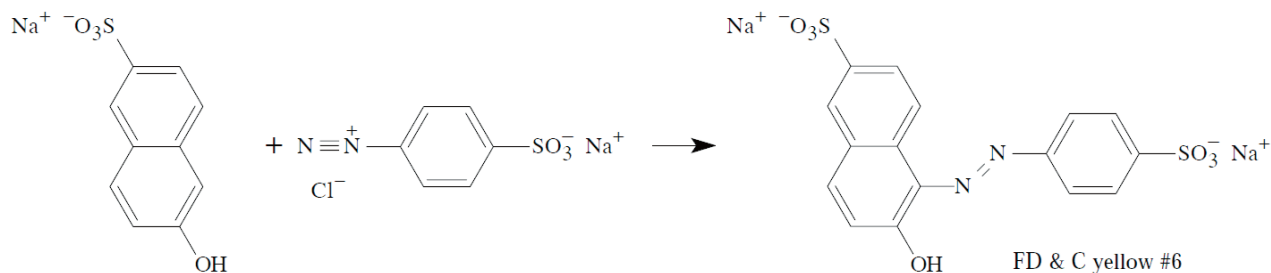
23.23 (b) Begin with *p*-acetamidobenzenesulfonyl chloride, prepared as shown in the solution to Problem 23.22, p. 614 of the Study Guide and Solutions Manual.



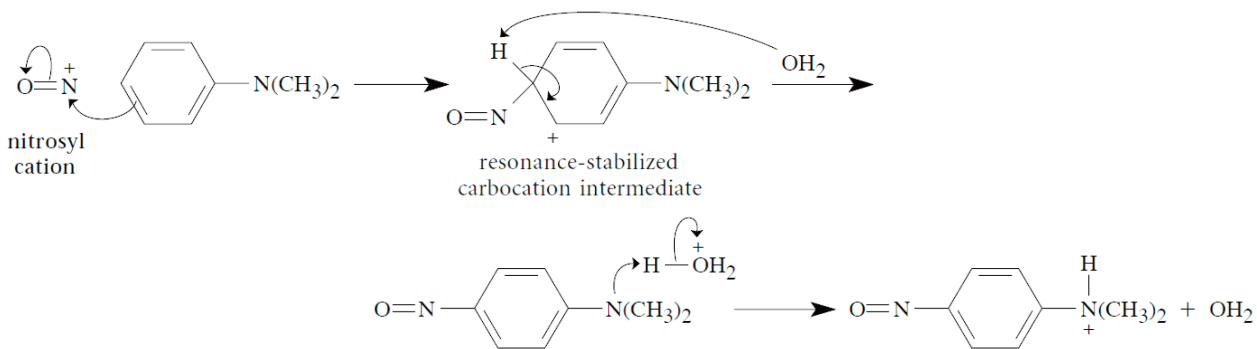
23.24 (b)



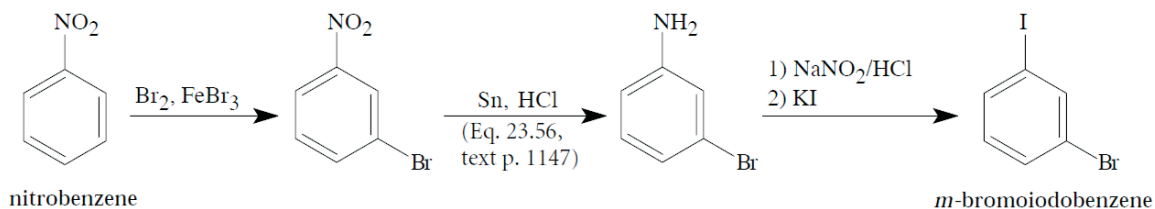
23.27 The following compounds would react to give FD &amp; C Yellow No. 6:



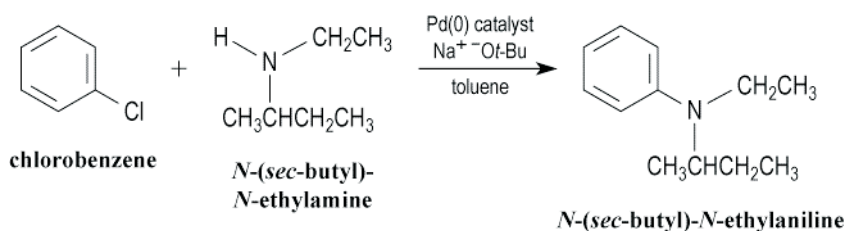
The position next to the ring junction (called the  $\alpha$ -position) in a naphthalene ring is more reactive in electrophilic substitution than the ring position one carbon removed. Hence, of the two positions "ortho" to the phenolic  $\text{—OH}$  group, the  $\alpha$ -position is the more reactive and gives the observed product.

23.28 (b) The loss of  $\text{H}_2\text{O}$  from protonated nitrous acid provides the nitrosyl cation, as shown in the solution to part (a) of this problem. This cation then serves as the electrophile in an electrophilic aromatic substitution reaction:

23.30 (b)

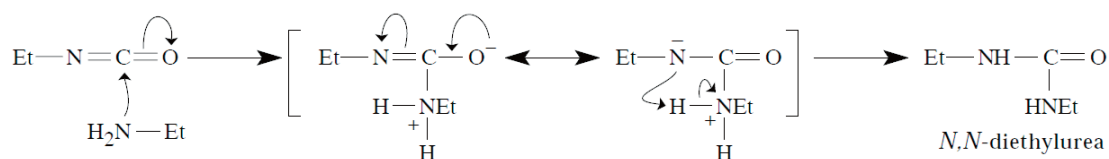


23.31 (a)

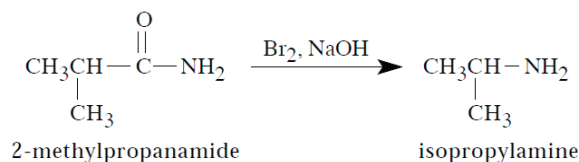


23.32 (a) *Tert*-butylamine cannot be prepared by the Gabriel synthesis because it would require that the nitrogen of phthalimide be alkylated with *tert*-butyl bromide in an  $S_N2$  reaction. Tertiary alkyl halides generally do not undergo  $S_N2$  reactions but, under basic conditions, undergo E2 reactions instead.

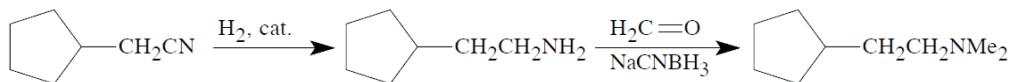
23.33 (b) The curved-arrow mechanism for the reaction of ethylamine with ethyl isocyanate to give *N,N'*-diethylurea:



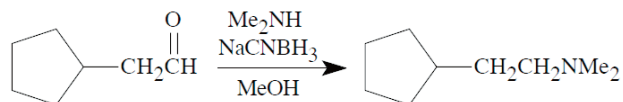
23.34 (b) In aqueous NaOH, hydroxide is the nucleophile that reacts with the isocyanate, and the resulting carbamic acid (or its salt) decarboxylates to give the corresponding amine.



23.36 (b)

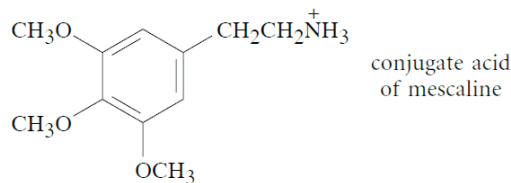


(d) One synthesis involves a reductive amination of the aldehyde:



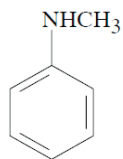
A second synthesis involves oxidation of the aldehyde to the carboxylic acid starting material of part (a) with aqueous  $\text{H}_2\text{CrO}_4$ ,  $\text{KMnO}_4$ , or other common oxidant, and then proceeding as in part (a).

23.37 (b) The most basic atom in mescaline is the amine nitrogen. Thus, the conjugate acid of mescaline has the following structure:

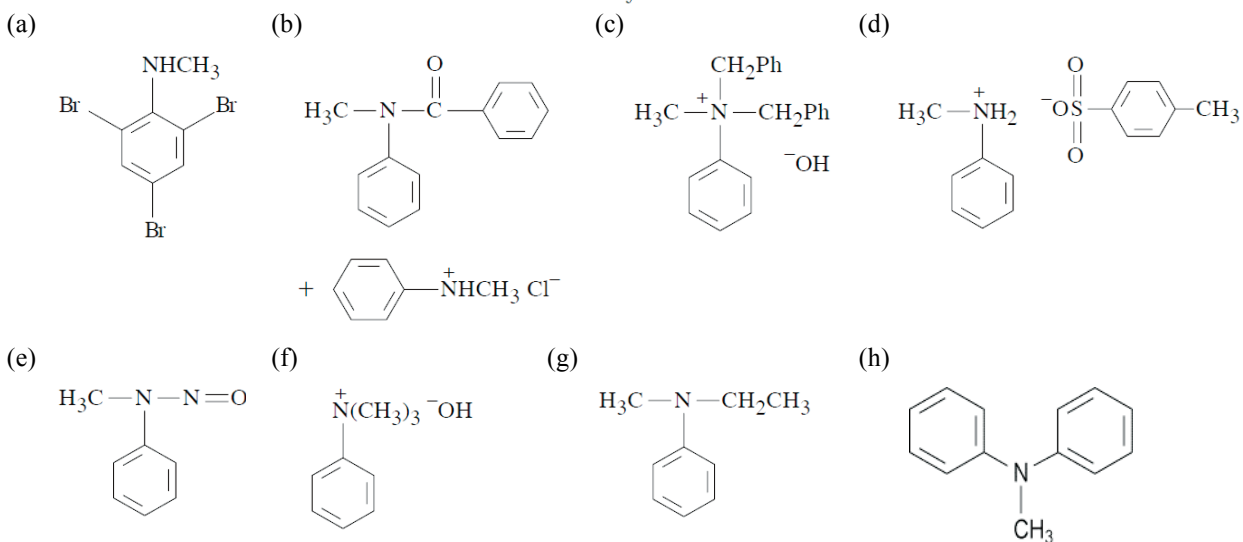


### Solutions to Additional Problems

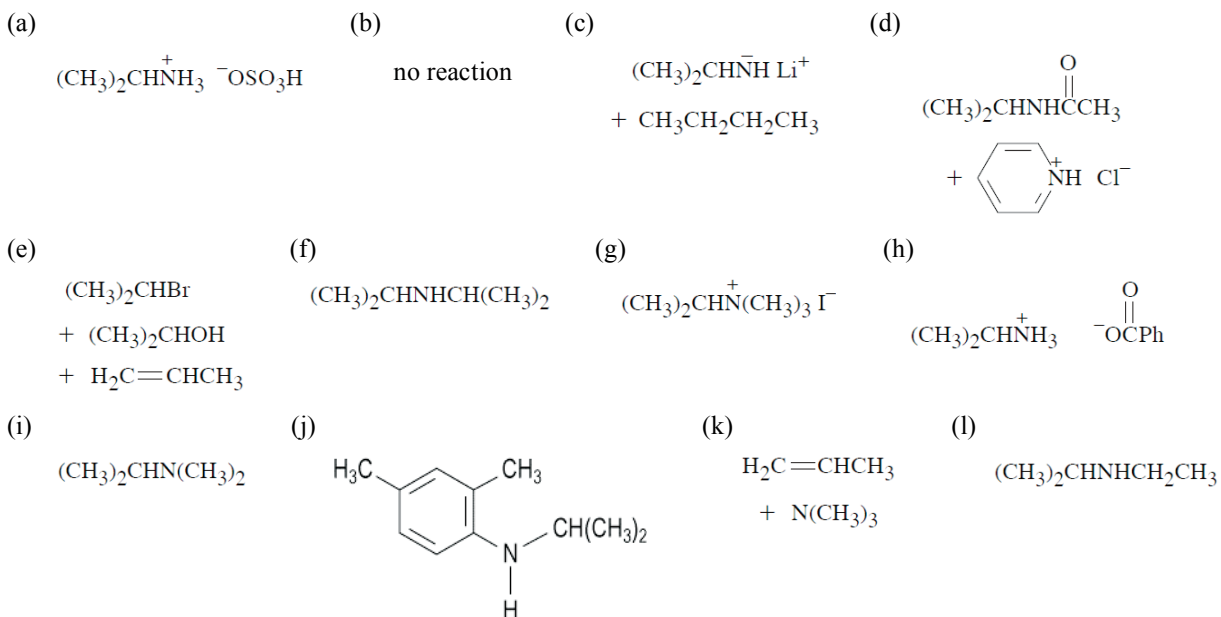
23.39 The structure of *N*-methylaniline is

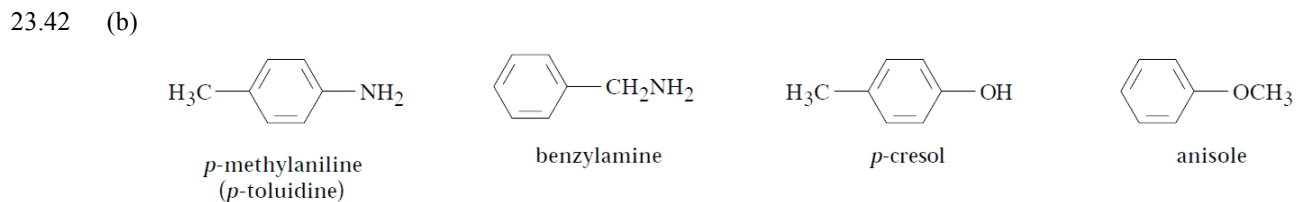
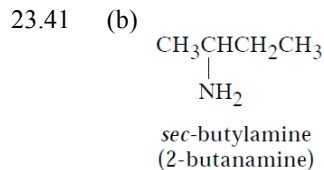


*N*-methylaniline



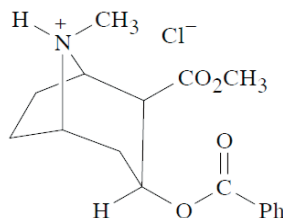
23.40 The structure of isopropylamine is  $(\text{CH}_3)_2\text{CH}-\text{NH}_2$



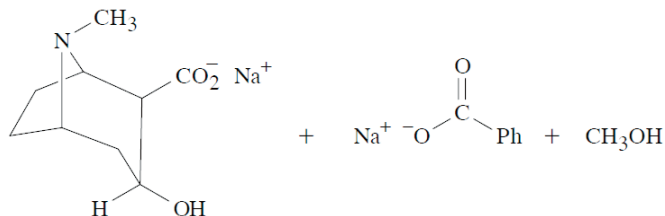


Only the two amines, *p*-methylaniline and benzylamine, are soluble (as their conjugate-acid ammonium ions) in dilute HCl. Only the phenol *p*-cresol is soluble (as its conjugate-base phenolate) in dilute NaOH solution. Anisole is soluble in neither dilute acid nor dilute base. Only benzylamine gives off a gas ( $\text{N}_2$ ) when diazotized at  $0^\circ$  with  $\text{HNO}_2$ . *p*-Methylaniline gives off  $\text{N}_2$  when the corresponding diazonium salt is heated.

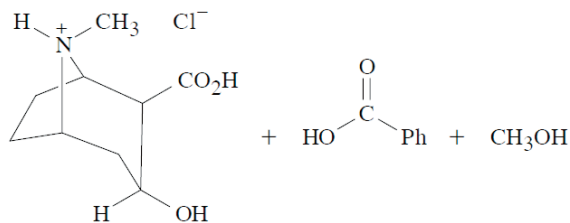
23.44 (a) In 1 M HCl solution, cocaine is protonated on its amino nitrogen.



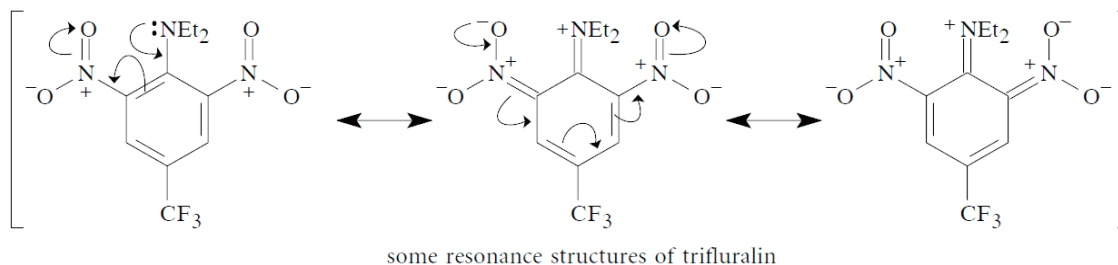
(b) Hot aqueous NaOH would bring about saponification of the ester groups:



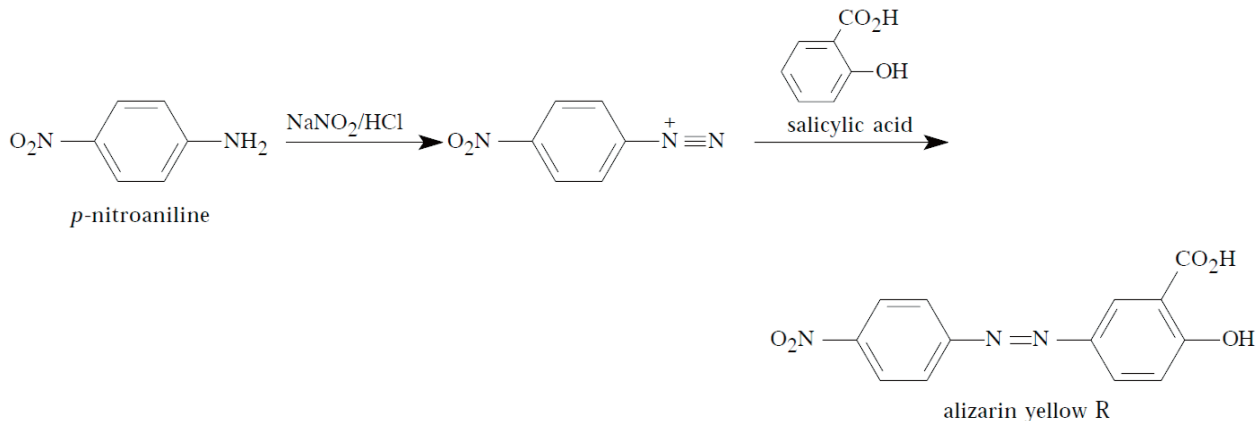
(c) Concentrated, hot aqueous HCl would protonate the amine nitrogen (as in part (a)) and would bring about hydrolysis of the two ester groups.



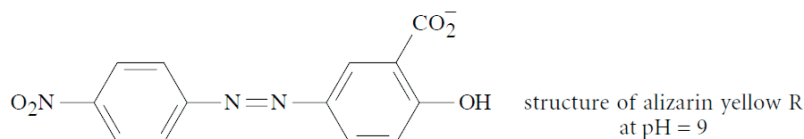
23.46 The basicity of trifluralin is much less than that of *N,N*-diethylaniline. The electron-withdrawing polar effects of both the nitro substituents and the trifluoromethyl substituent destabilize the conjugate acid of trifluralin, and resonance interaction of the nitrogen unshared electron pair with the two nitro groups stabilizes trifluralin itself; this interaction is absent in the ammonium ion. (In fact, trifluralin is not basic enough to dissolve in dilute HCl.)



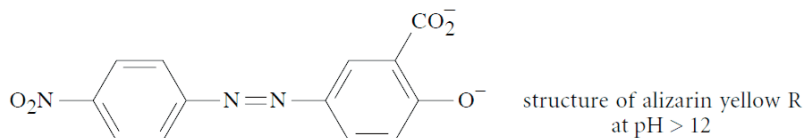
- 23.48 (a) First prepare *p*-nitroaniline from aniline as shown in Study Problem 23.4 on text p. 1138. Then diazotize this amine to give the diazonium salt. Couple the diazonium salt to salicylic acid to obtain alizarin yellow R.



- (b) From the solution to the Problem (23.47 on p. 620 of the Study Guide and Solutions Manual), or from the information in the problem, the  $pK_a$  of a protonated diazo group should be around 5. Consequently, at a pH value well above 5, the diazo nitrogens are unprotonated. The  $pK_a$  of the carboxy group should be around 4. Therefore, at pH = 9, the carboxy group should be ionized. The group that ionizes between 10 and 12 should affect the conjugated  $\pi$ -electron system because it affects the color. Since this group is not the diazo group, it must be the phenol. If the phenol has a  $pK_a$  of about 11, then at pH = 9 it is un-ionized.

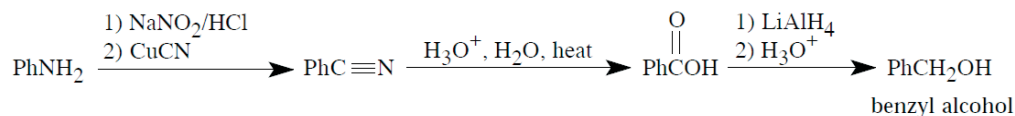


- (c) At pH > 12, both the carboxy group and the phenol are ionized. (Show the resonance structures for the delocalization of the phenolate ion throughout the  $\pi$ -electron system of the rings, the diazo group, and the *p*-nitro group. This interaction is the basis for the color change.)

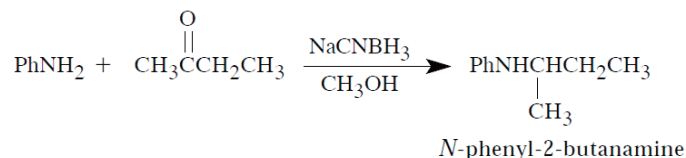


- 23.49 (b) Excess methyl iodide will form the quaternary salt  $(\text{CH}_3)_3\text{CN}^+(\text{CH}_3)_3 \Gamma^-$ ; the reaction will not stop at the secondary amine shown in the problem.
- (d) Although the aldehyde will indeed be reduced, so will the nitro group. (See Eq. 23.57 on text p. 1147.)
- (f) Amanda is attempting to carry out an  $S_N2$  reaction on a tertiary alkyl halide. Unfortunately, tertiary alkyl halides do not undergo  $S_N2$  reactions. If a reaction occurs at all, it will be the competing  $E2$  process.

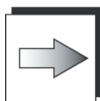
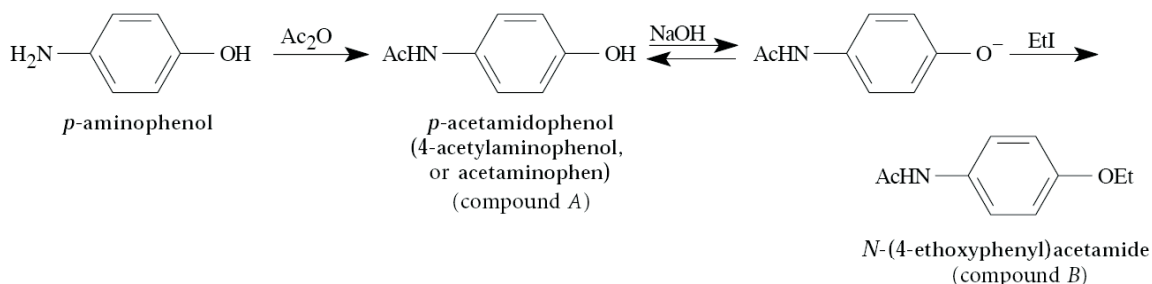
23.50 (b)



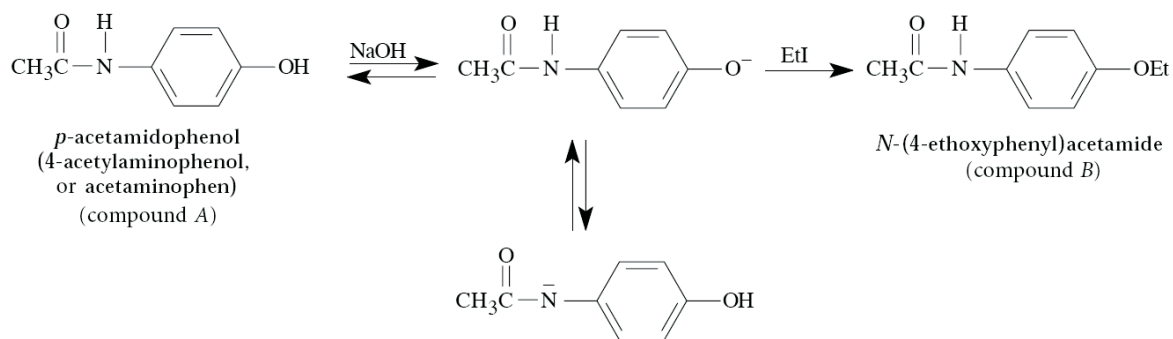
(d)



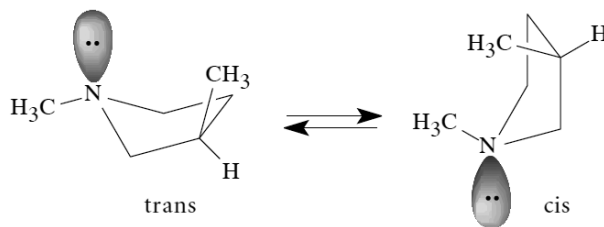
23.51 The acetic anhydride treatment acetylates either the amino group or the hydroxy group. Because the initially formed product *A* can form an ethyl ether, its —OH group is not affected in the first reaction. Consequently, compound *A* is *p*-acetamidophenol and compound *B* is its ethyl ether. This is reasonable because, so long as the hydroxy group is not ionized, the amino group is the most basic group in the molecule, and is thus the more nucleophilic group. Compound *A* dissolves in base because the hydroxy proton can ionize.



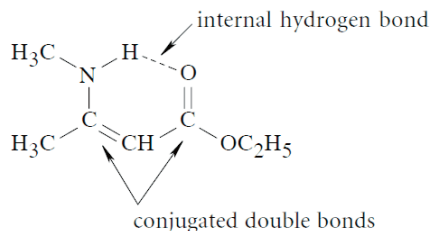
In compound *A* the acidity of the amide N—H is likely to be comparable to that of the phenol (why?). Hence, the conjugate-base anion of the phenoxide is in equilibrium with the phenoxide ion. If both ions are indeed present, evidently the conjugate base phenolate is alkylated more rapidly. Alkylation of the oxygen then pulls the equilibrium between the anions towards the phenoxide:



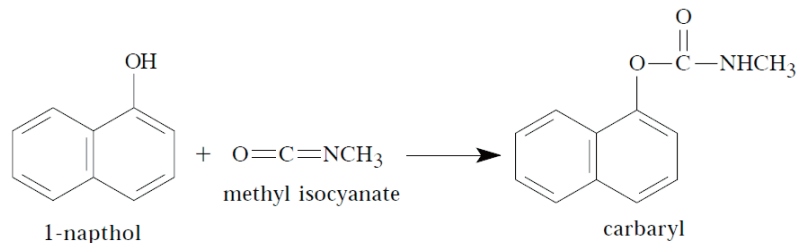
23.53 (b) *Cis*- and *trans*-1,3-dimethylpyrrolidine rapidly interconvert because all that is required for this process is amine inversion, which is very rapid.



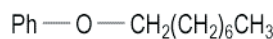
- (d) This compound exists as an enamine for the same reason that  $\beta$ -diketones exist as enols: internal hydrogen bonding and conjugation stabilize the enamine form.



- 23.55 Carbaryl can be prepared by the reaction of 1-naphthol with methyl isocyanate.

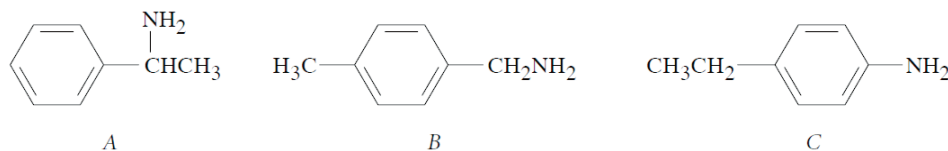


- 23.56 (a) Sodium benzenethiolate,  $\text{Na}^+ \text{PhS}^-$ , is a salt and thus soluble in water but not an organic solvent; 1-bromooctane is relatively nonpolar and thus insoluble in water. No reaction occurs initially because the two reactants cannot interact; however, with the addition of the phase-transfer catalyst tetrabutylammonium bromide,  $(\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2)_4\text{N}^+ \text{Br}^-$ , the two reactants can interact to form octyl phenyl sulfide. (See text p. 1130.)

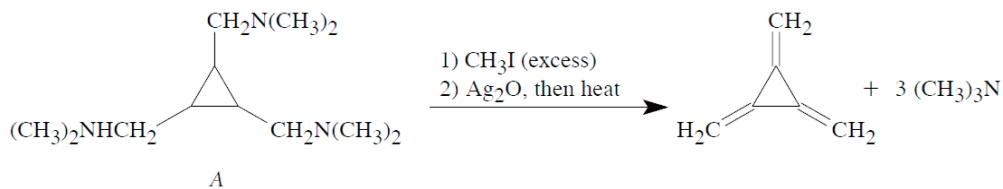


octyl phenyl sulfide

- 23.58 The oxidation data reveal that compound *A* contains a monosubstituted benzene ring, compounds *B* and *C* contain *para*-disubstituted benzene rings, and compound *C* additionally has an amino group directly attached to the ring. The  $\text{p}K_a$  of compound *C* additionally confirms that it is an aniline derivative, and the fact that compound *C*, following diazotization, requires warming to evolve a gas ( $\text{N}_2$ ) also indicates that it is an aniline derivative. Compound *A* is chiral, and furthermore, it must be the racemate, because it evidently forms diastereomeric salts with (+)-tartaric acid. Because six carbons are involved in a benzene ring, the problem is to determine how the remaining two carbons are arranged so that the resulting structures are consistent with the data. The following structures are the only reasonable possibilities:

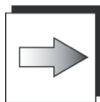
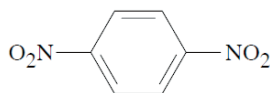


- 23.59 (c) The triamide resulting from treatment of the acid chloride is reduced with  $\text{LiAlH}_4$  to give triamine *A*, which is exhaustively methylated and then subjected to Hofmann elimination to give the product, which is an isomer of benzene.



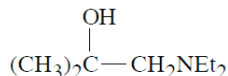


- (e) In this variation of the Sandmeyer reaction, copper(I) nitrite introduces a nitro group into the ring.

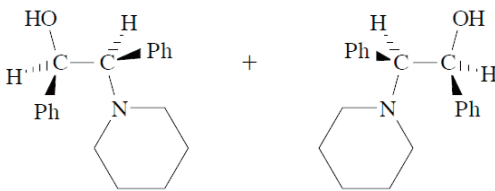


*p*-Dinitrobenzene would be very difficult to prepare by electrophilic aromatic substitution; can you see why?

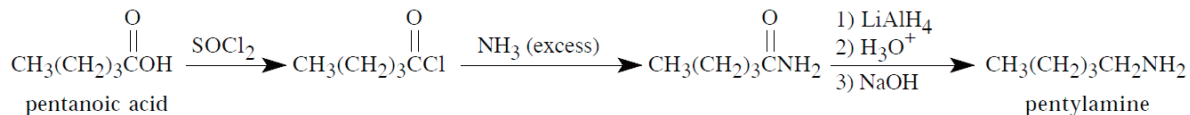
- (g) The amine reacts with the epoxide at the carbon with fewer alkyl substituents.



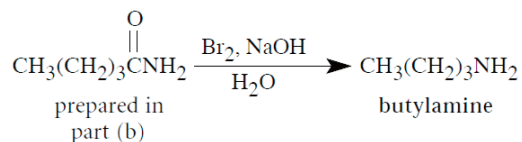
- (i) The amine reacts with the epoxide with inversion of configuration. Because both starting materials are achiral (the epoxide is the meso stereoisomer), the product is the racemate; one enantiomer results from reaction at one carbon of the epoxide, and the other enantiomer results from reaction at the other carbon.



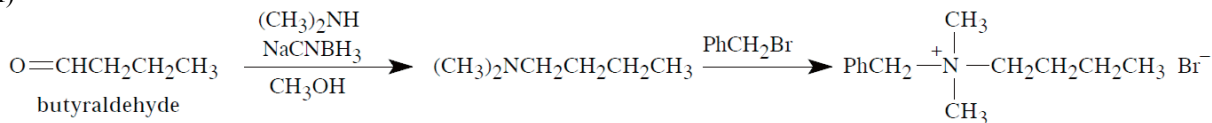
23.60 (b)



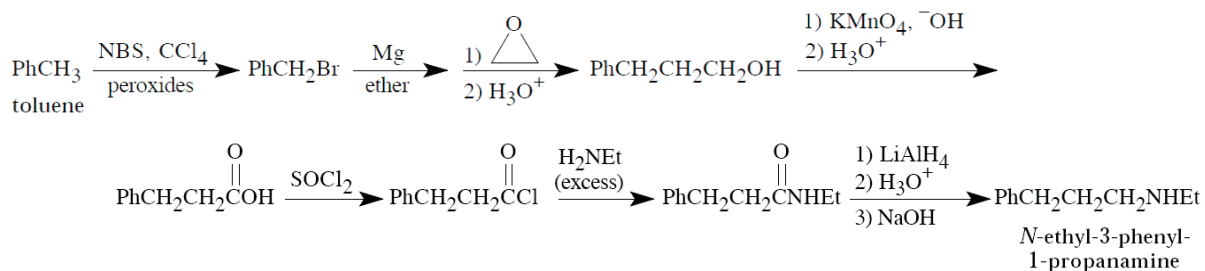
(d)



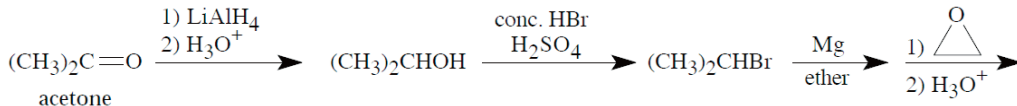
(f)

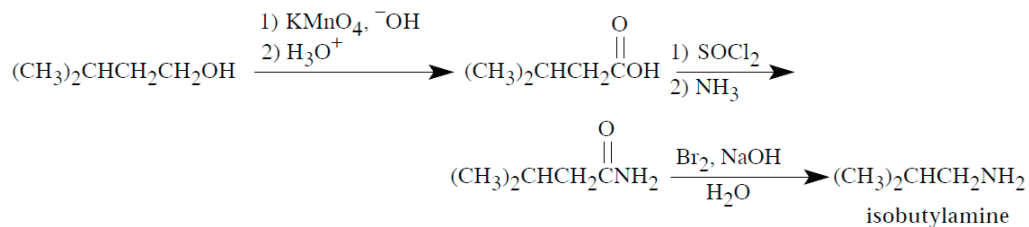


(g)

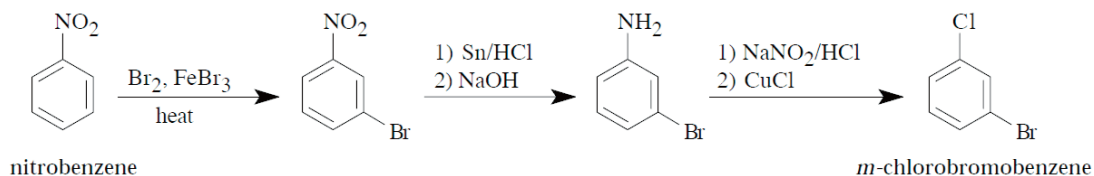


(i)

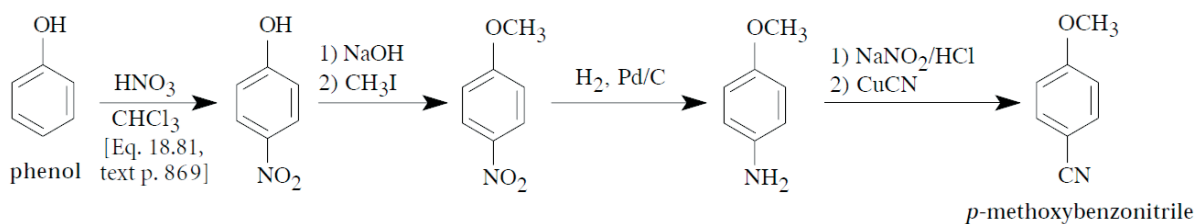




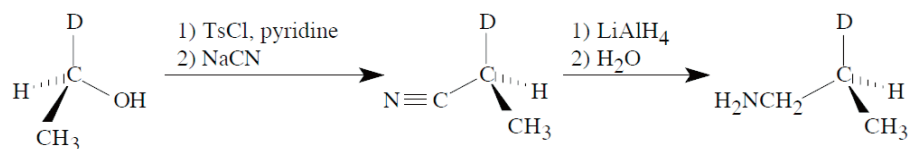
(k)



(m)

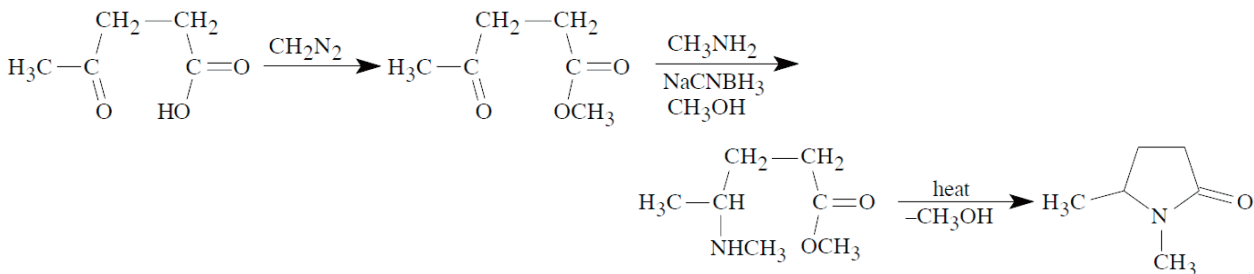


(n)

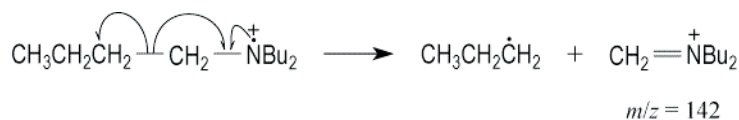


Note that the  $\text{S}_{\text{N}}2$  reaction of cyanide ion proceeds with inversion of configuration.

(o)



23.61 (b) The  $\alpha$ -cleavage of tributylamine produces a major peak at  $m/z = 142$ :



23.64 Assume that the  $\text{---NH}_2$  or  $\text{---NH}$  protons of the amine rapidly exchange, so that they are not coupled to adjacent protons on carbon.

Compound *C* should have the resonance at greatest chemical shift, because the proton  $\alpha$  to the nitrogen is also benzylic and is a methine proton. This proton should be a triplet.

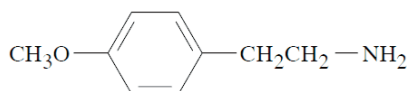
Compound *B* should have the resonance at the next greatest chemical shift, because the protons  $\alpha$  to the nitrogen are also benzylic, but are methylenes, which have smaller chemical shifts than methine protons by about

0.5–0.7 ppm. These  $\alpha$ -protons should be a singlet. The relative integrations of the  $\alpha$ -protons of *B* and *C* are different, as well.

Between compounds *A* and *D*, compound *A* has the resonance at smallest chemical shift—the methyl group, which should be a doublet. These methyl protons are neither benzylic nor  $\alpha$  to a nitrogen; thus, they should have a resonance not far from  $\delta$  1.

All of the resonances of compound *D* are in the  $\delta$  2–3.5 range. This spectrum should consist of two triplets and a singlet (plus the NH proton). Other features of these spectra might be cited as well.

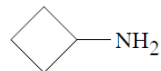
- 23.65 (a) With an unsaturation number of 4 and clear evidence for a para-substituted benzene ring (the four-proton pair of doublets centered at about  $\delta$  7), no other unsaturations are possible. The NMR indicates partial structures —OCH<sub>3</sub> and —CH<sub>2</sub>CH<sub>2</sub>—. With no other unsaturation, the nitrogen has to be an amine, and the broad, two-proton resonance near  $\delta$  1 suggests an —NH<sub>2</sub> group. The only structure that fits all the data is



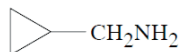
2-(4-methoxyphenyl)ethylamine  
(compound *A*)

- 23.67 (a) The chemical data indicate the presence of a primary amine. The compound has one degree of unsaturation, and the chemical shifts in the CMR are too small for any carbon to be involved in a double bond. Hence, compound *A* contains a ring, and only CH and CH<sub>2</sub> groups are present. The presence of only three resonances means that two carbons are equivalent. Compound *A* is cyclobutylamine.

Cyclopropylmethanamine is ruled out by the fact that the carbon bound to one hydrogen has the largest chemical shift and therefore must be bound to the nitrogen.

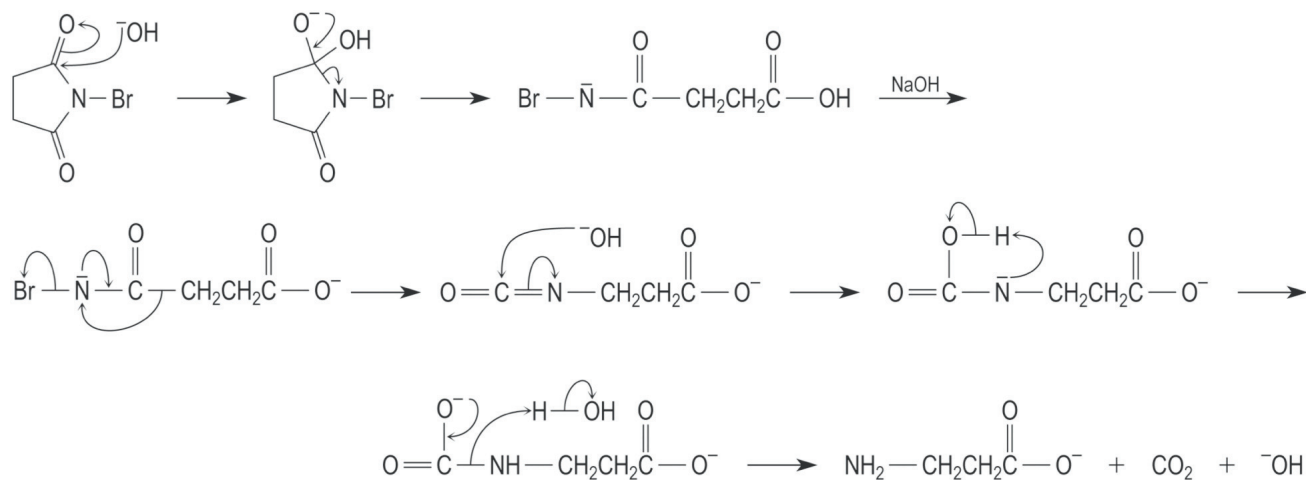


cyclobutylamine  
(compound *A*)



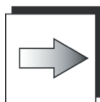
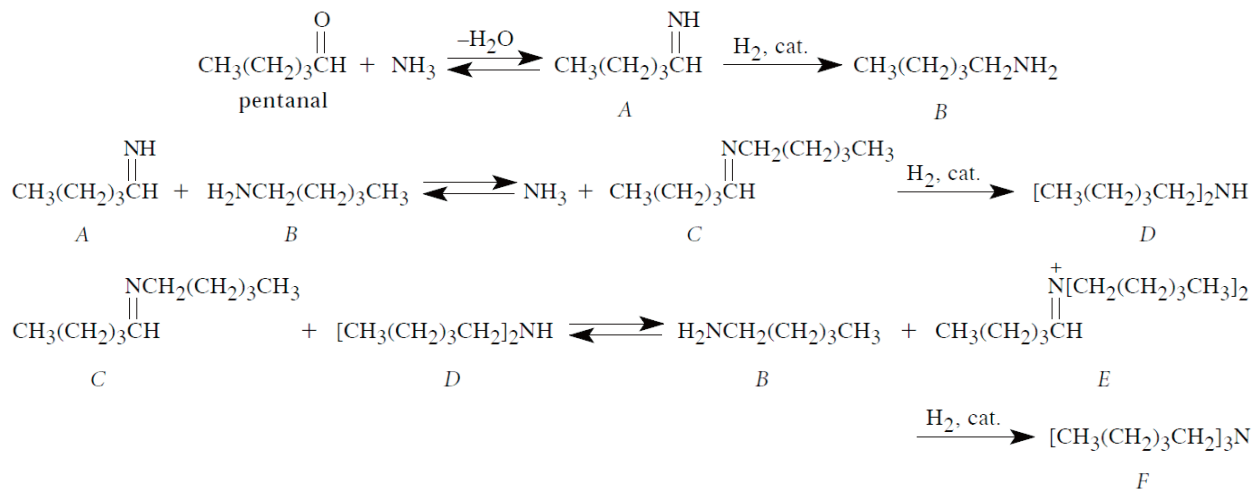
cyclopropylmethanamine  
(ruled out)

- 23.68 (b) This reaction is related to the Hofmann rearrangement. Reaction with hydroxide on the carbonyl carbon of *N*-bromosuccinimide gives an *N*-bromo anion, which undergoes a Hofmann rearrangement to the corresponding isocyanate, which in turn, hydrolyzes and decarboxylates to the amine product.



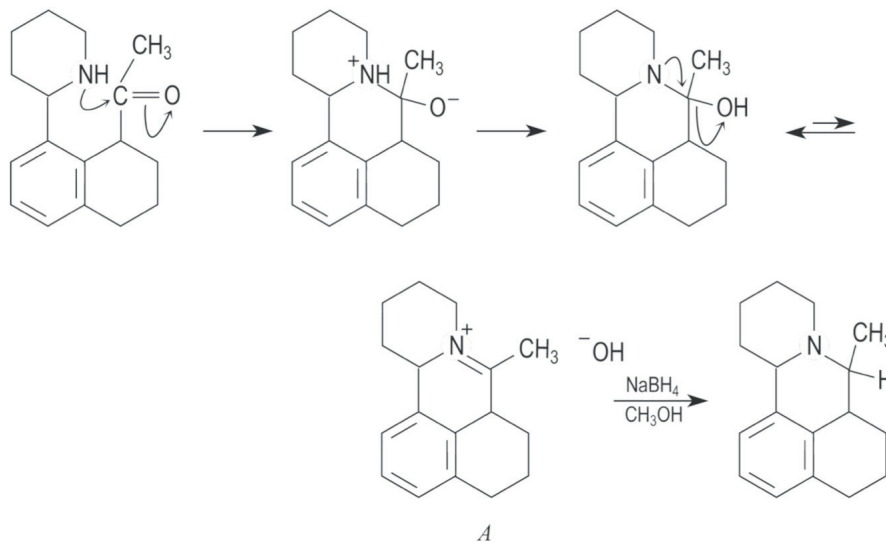
- 23.70 An intermediate in the formation of 1-pentanamine is the imine *A*. The other products arise from the fact that 1-pentanamine, *B*, can react with either the starting aldehyde, pentanal, or with imine *A* to give a new imine *C*. (Give the mechanism for this reaction.) Imine *C* can also undergo hydrogenation to the second product,

dipentylamine, *D*. Dipentylamine can also react with other imine intermediates to form iminium ion *E*, which can undergo hydrogenation to form tripentylamine *F*, the tertiary amine by-product.

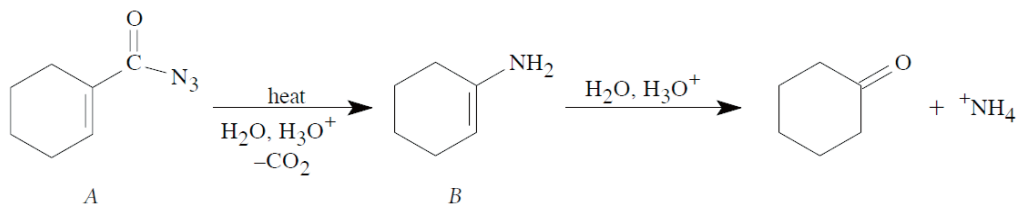


The yield of pentylamine (compound *B*) can be increased, and the amounts of the other by-products reduced, by including ammonia in the reaction mixture. Can you see why? (*Hint*: Apply Le Châtelier's principle.)

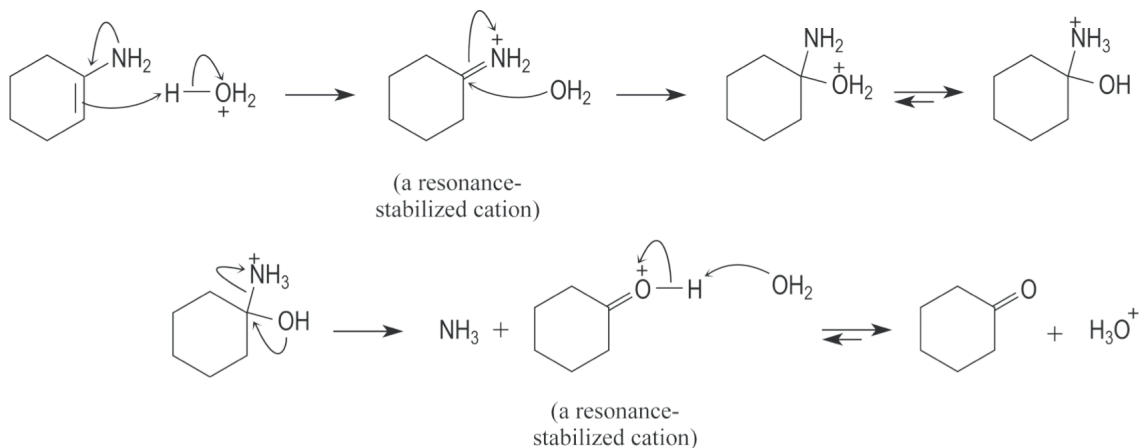
- 23.72 (b) The amine reacts intramolecularly with the carbonyl group to give a carbinolamine, which then reacts to form a cyclic iminium ion *A*, which is reduced by the sodium borohydride.



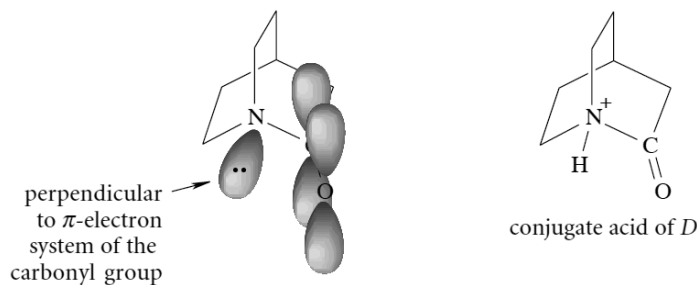
- (d) The acyl azide *A* undergoes Curtius rearrangement to an enamine *B*, which hydrolyzes under the aqueous reaction conditions to the product ketone.



The mechanism of the Curtius rearrangement is shown on text p. 1151, and the hydrolysis of the enamine occurs as follows:



- 23.74 The data show that the conjugate-acid  $pK_a$  values of a bicyclic tertiary amine *C* (which is the same as amine *C* in the previous problem) and a monocyclic tertiary amine *B* are not very different. Hence, the additional ring has no unusual effect on  $pK_a$ . The conjugate-acid  $pK_a$  of amide *A* is also fairly normal for an amide that is protonated on the carbonyl oxygen. (See Eq. 21.4b on text p. 1001.) The  $pK_a$  of amide *D*, then, is unusual. Normally, amides protonate on the carbonyl oxygen because the resulting carbocation is resonance-stabilized. In this case, however, the bicyclic structure of the ring prevents the overlap of the nitrogen unshared electron pair with the  $\pi$ -electron system of the carbonyl group. Hence, the electronic character of this nitrogen is more like that of an amine with a neighboring electron-withdrawing substituent (the carbonyl group) than it is like that of an amide. Thus, this amide behaves like an amine: it protonates on nitrogen. What about the hydrolysis rate? Recall that ordinary amides hydrolyze slowly because they are resonance-stabilized. (See Sec. 21.7E, text p. 1011.) When resonance stabilization is not present, as in the case of compound *D*, an amide hydrolyzes rapidly. In acidic solution, when the nitrogen is protonated, its hydrolysis rate is more like that of an acid chloride!



(See also the sidebar on text pp. 1002–1003 for a discussion of this case.)

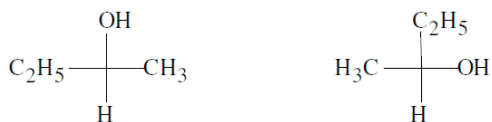


# Chapter 24

## Carbohydrates

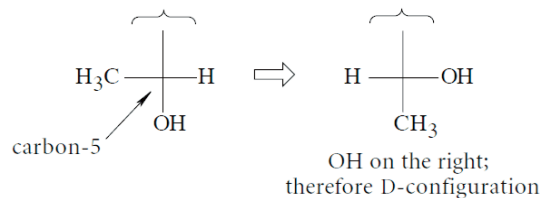
### Solutions to In-Text Problems

- 24.1 (b) The following two of the nine possible Fischer projections of (*S*)-2-butanol are related by a cyclic permutation of the ethyl, —OH, and the methyl group.

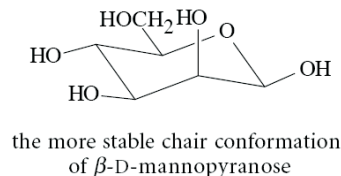
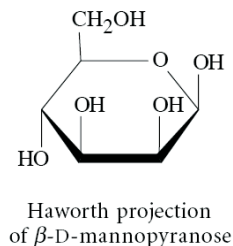
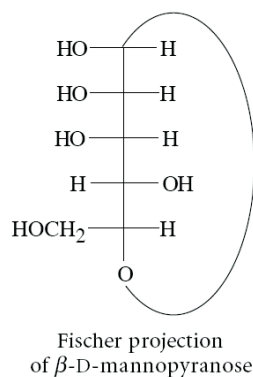


- 24.2 (b) Turning either projection 180° in the plane of the page establishes that it is identical to the other projection.

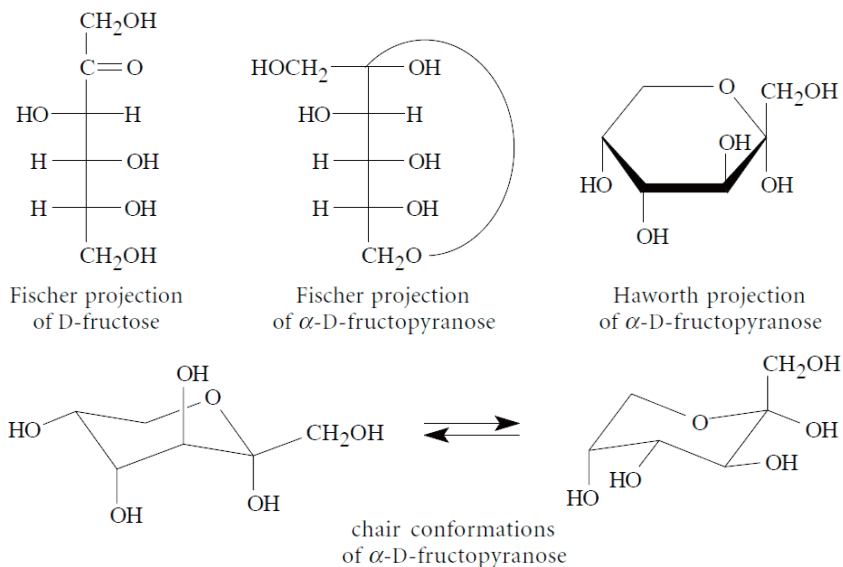
- 24.4 (a) Use a cyclic permutation to transform the given Fischer projection into a standard form in which all of the backbone carbons are in a vertical line. This will show that the —OH group on carbon-5 is on the right. Thus, this aldose has the D-configuration.



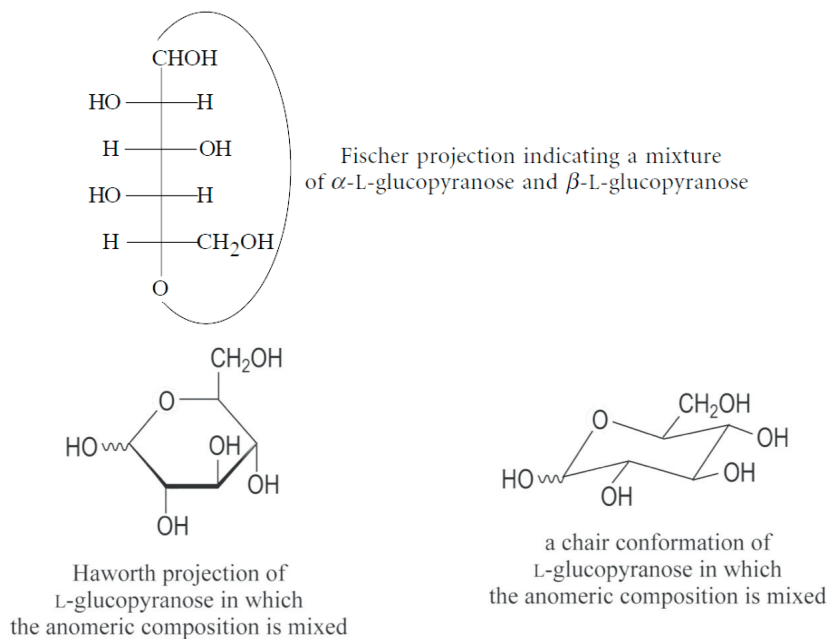
- 24.6 (b) Recognize that D-mannose is epimeric to D-glucose at carbon-2, and thus convert the β-D-glucopyranose structures on text p. 1180 to β-D-mannopyranose structures by inverting the configuration of carbon-2.



- (d) Start with the Fischer projection for D-fructose from text p. 1177.

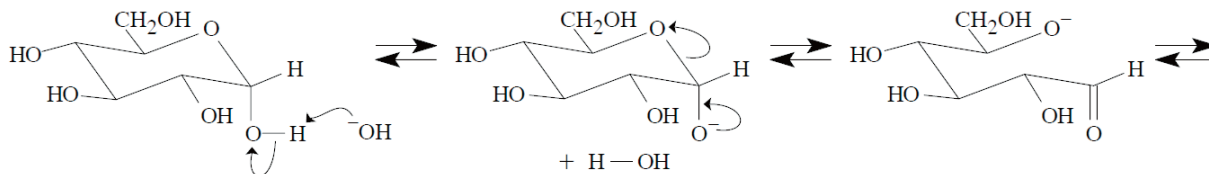


- (f) Start with the structures of  $\alpha$ -D-glucopyranose in the solution for part (e) (p. 644 of the Study Guide and Solutions Manual) and make the bond to the anomeric carbon a “squiggly bond.” (For the Fischer projection simply do not show the configuration. “Squiggly bonds” are not used in Fischer projections.)

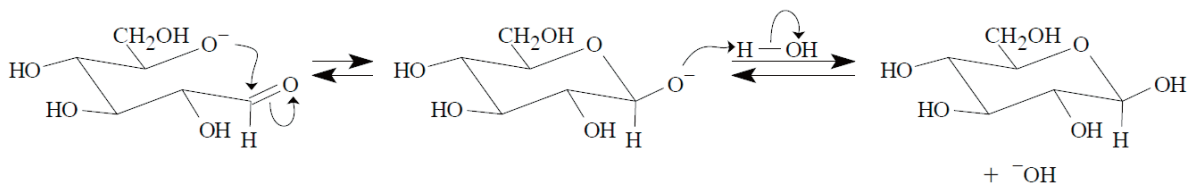


- 24.7 (b) This is the  $\beta$ -anomer of a D-hexopyranose that differs from D-glucose in its configuration at carbons 3 and 4; therefore, it is  $\beta$ -D-gulopyranose.

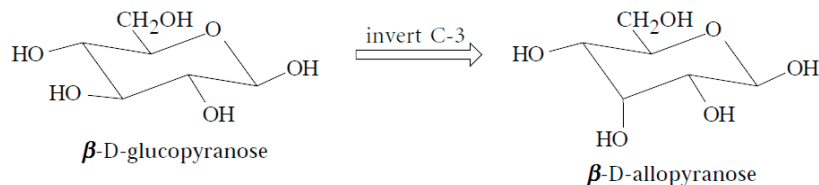
- 24.9 The mechanism for base-catalyzed mutarotation of glucose:



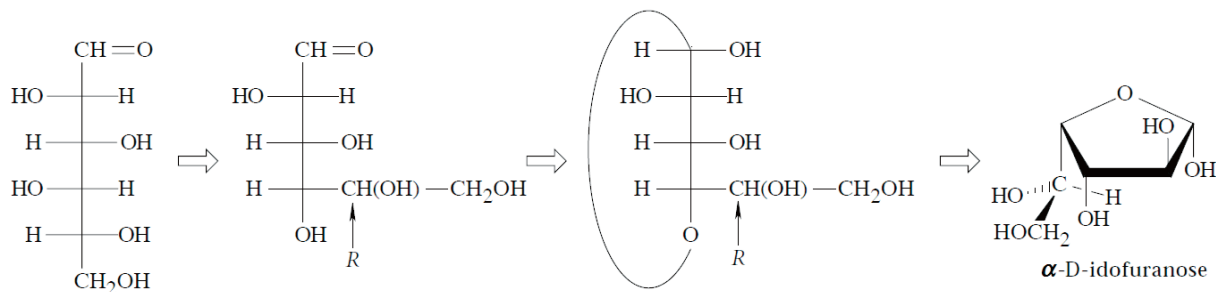




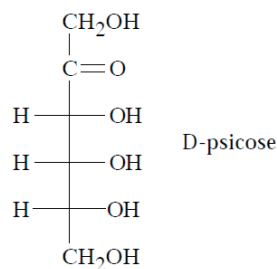
- 24.11 (a) The easiest way to do this is to consider the relationship of D-allose to D-glucose and modify the conformational representation of  $\beta$ -D-glucopyranose (in which all of the ring substituents are equatorial) accordingly. Thus, Fig. 24.3 on text p. 1174 shows that D-allose is epimeric to D-glucose at carbon-3. Consequently, configurational inversion of the  $\beta$ -D-glucopyranose structure at carbon-3 gives the desired conformational representation of  $\beta$ -D-allopyranose.



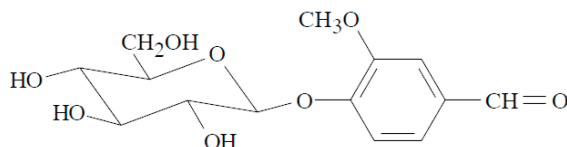
- (b) Follow the procedure in Study Problem 24.2 on text p. 1180. Note that in the second and third Fischer projections the configuration of carbon-5 cannot be represented without violating the Fischer-projection conventions. We must remember that this carbon has the *R* configuration, and this configuration must be shown explicitly in the conformational representation.



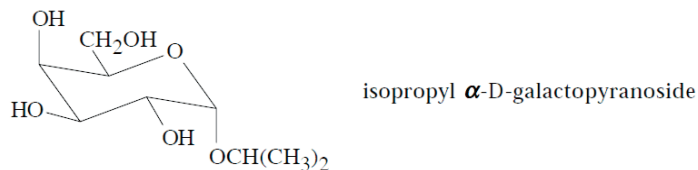
- 24.13 (b) D-Allose would be transformed by base into a mixture of D-altrose (structure in Fig. 24.3 on text p. 1174) and the ketose D-psicose.



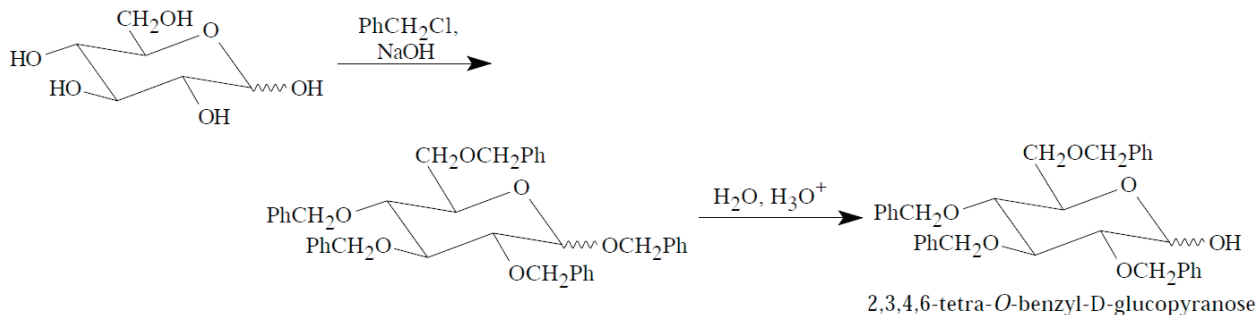
- 24.15 Because naturally occurring glycosides generally have bonds between an alcohol or phenol oxygen and the anomeric carbon of a carbohydrate, it is reasonable to propose that the  $\beta$ -D-glycoside of vanillin and glucose has the following structure:



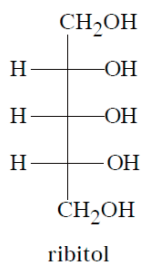
- 24.16 (b) Start with the structure of  $\alpha$ -D-galactopyranose, which is the same as  $\alpha$ -D-glucopyranose except that carbon-4 is inverted. Then substitute an isopropoxy group for the hydroxy group at the anomeric carbon.



- 24.18 (b) Alkylate all of the hydroxy groups with benzyl chloride ( $\text{PhCH}_2\text{Cl}$ ), a very reactive alkyl halide; then hydrolyze the benzyl glycoside. (Why is benzyl chloride very reactive? See Sec. 17.4, text p. 802.)

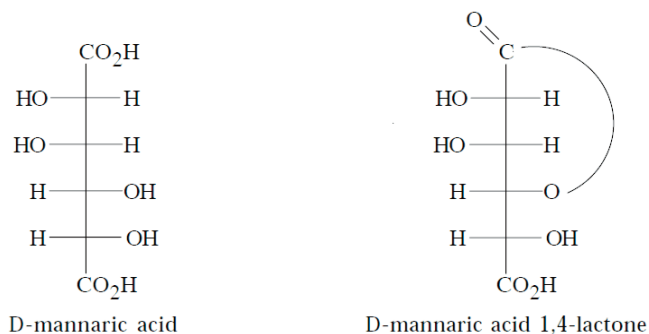


- 24.19 (b)

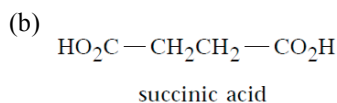


Notice that ribitol is a meso compound.

- 24.21 (b) The structure of the aldaric acid derived from oxidation of D-mannose, and the structure of its 1,4-lactone:



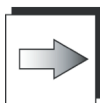
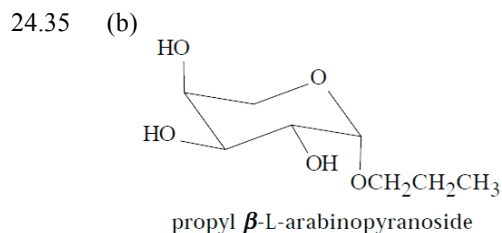
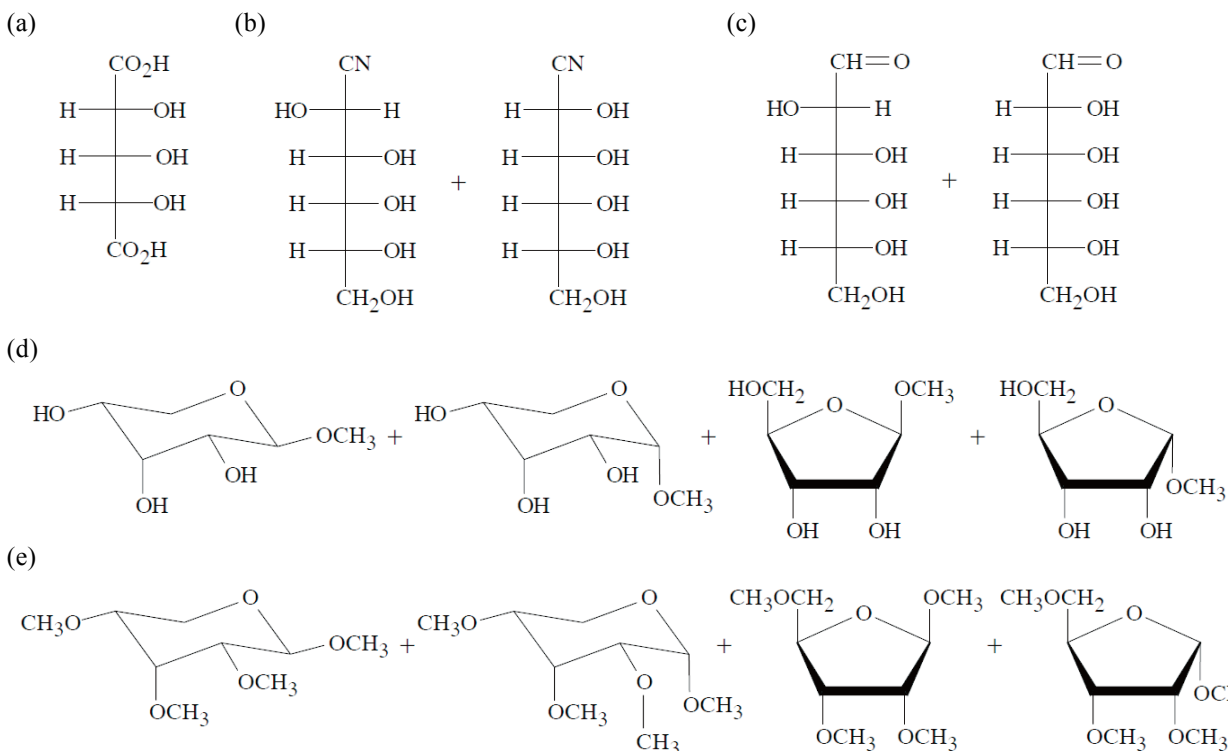
- 24.22 As is the case with carbohydrates, the primary alcohol groups are selectively oxidized by  $\text{HNO}_3$



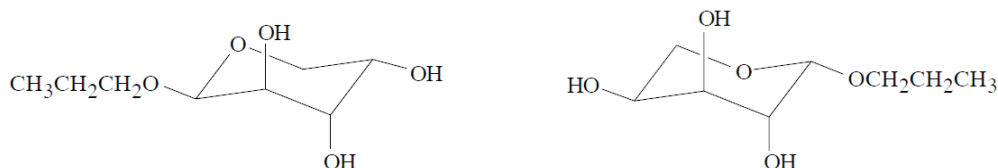
- 24.24 The discussion in the solution to Problem 24.23 (p. 647 in the Study Guide and Solutions Manual) shows that the fragment obtained from oxidation of a  $\beta$ -D-pyranoside is the *diastereomer* of the fragment obtained from oxidation of an  $\alpha$ -D-pyranoside. Diastereomers have different properties. Hence, these fragments, which can in principle be identified by their properties, including their optical rotations, can be used to determine whether the original pyranoside was  $\alpha$  or  $\beta$ . This method works not only for the methyl galactopyranosides, but for *all* pyranosides. (Periodate oxidation was used to determine the anomeric configurations of many pyranosides before modern spectroscopic tools were available, and these results have withstood the scrutiny of modern analytical methods.)
- 24.27 Compound *A* is D-gulose, because it gives the same aldaric acid as L-glucose. The fact that some aldaric acids can be derived from two different aldoses is also addressed in Problem 24.20 in the Study Guide and Solutions Manual. The same point is discussed in Study Guide Link 24.2 on p. 633 of the Study Guide and Solutions Manual. In contrast, D-idose is the only aldohexose that can be oxidized to its aldaric acid.
- 24.29 In such a case, the structure of D-(+)-glucose, indeed, the structures of *all* D-carbohydrates, would be the enantiomers of the structures shown in Fig. 24.3 on text p. 1174.
- 24.31 Because cellobiose is a dimer of D-glucose, it is hydrolyzed by aqueous acid into two molar equivalents of D-glucose.

### Solutions to Additional Problems

24.34 Note that carboxylic acids derived from carbohydrates usually exist as lactones, and aldoses exist primarily as cyclic hemiacetals. For simplicity they are represented below in their noncyclic forms.

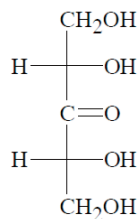


Remember that there are several valid ways to draw the chair conformations of pyranoses. Because the text probably has made you accustomed to seeing  $\beta$ -anomers with equatorial groups at carbon-1, you may be thinking that the chair conformation in the solution to part (b) shows the  $\alpha$ -anomer. However, this *is* a correct representation of the  $\beta$ -anomer. Whether the  $\beta$ -anomer has an equatorial or axial group at the anomeric carbon depends on which chair conformation you choose to draw. The following equally valid representations of a different chair conformation of the same compound do have the group at the anomeric carbon in an equatorial position.

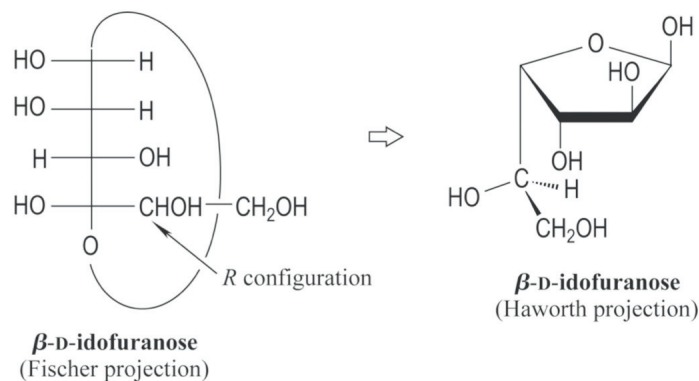


27.36 (b) This pyranose is epimeric to  $\beta$ -D-glucopyranose at carbon-3. Consult Fig. 24.4 on text p. 1174 to discover that the aldohexose epimeric to glucose at carbon-3 is allose. Therefore, this compound is  $\beta$ -D-allopyranose.

24.37 (b) An achiral ketopentose must be a meso compound:



(d) Derivation of the structure of  $\beta$ -D-idofuranose from the Fischer projection:

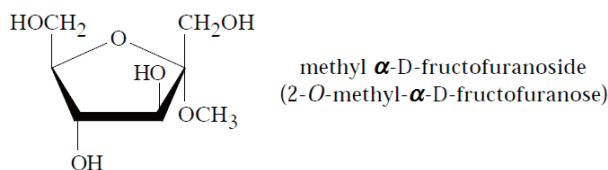


This is identical to the structure in the solution to Problem 24.11b except for the configuration at the anomeric carbon.

24.38 (b) Diastereomers and epimers

(d) Constitutional isomers

(f) The two names describe the same structure.



24.39 (b) L-Sorbose is a ketohexose, or hexulose.

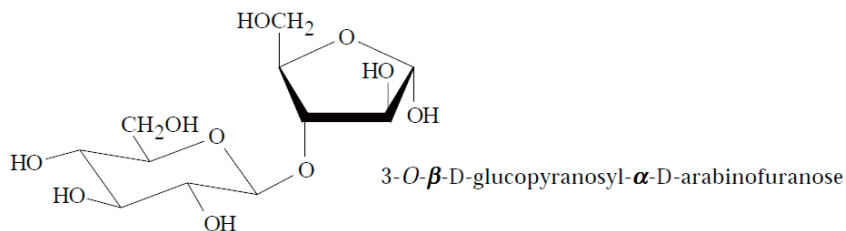
(d) L-Sorbose is not an aldohexose; it is a ketohexose, as noted in the solution to part (b).

(f) This compound is epimeric to L-sorbose at carbon-5, and thus it is not a form of L-sorbose. In fact, it is D-fructose.

(h) This structure is the enantiomer of the structure in part (g), and thus it is not a form of L-sorbose. (It is the  $\alpha$ -furanose form of D-sorbose.)

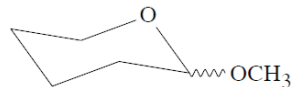
(j) This is an aldopyranose and therefore cannot be a form of L-sorbose. (It is  $\beta$ -D-glucopyranose.)

24.41 The structure of 3-O- $\beta$ -D-glucopyranosyl- $\alpha$ -D-arabinofuranose:

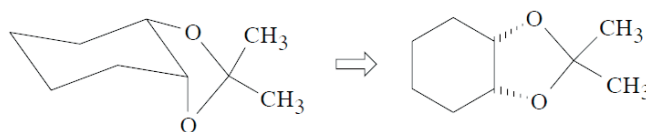


27.43 (b) D-Ribose gives the same osazone as D-arabinose because D-ribose is epimeric to D-arabinose at carbon-2.

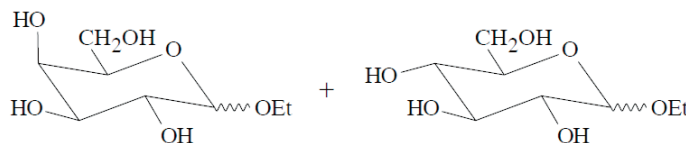
24.44 (b) Any 3- or 4-hydroxy aldehyde, like a carbohydrate, will form a cyclic acetal in acidic methanol.



(d) Cyclohexene reacts with  $\text{OsO}_4$  to give *cis*-1,2-cyclohexanediol, which forms a cyclic acetal with acetone.



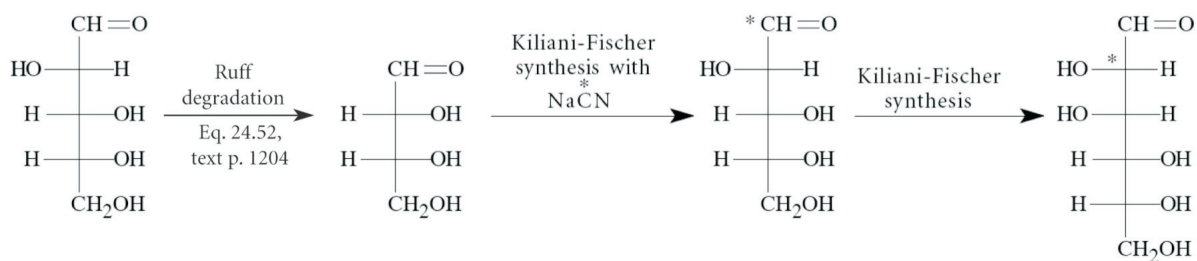
(f) Ethanolysis of the acetal linkage occurs in ethanol just as hydrolysis occurs in water. An ethyl pyranoside is also formed from the glucose residue at the reducing end of lactose.



24.45 (a) This is an isotopically labeled analog of glucose, and is prepared by the Kiliani–Fischer synthesis shown in Eqs. 24.43 and 24.44 on text p. 1198, except that radioactive sodium cyanide ( $\text{Na}^{14}\text{CN}$ ) is used instead of ordinary  $\text{NaCN}$ . In this synthesis,  $^{14}\text{C}$ -D-mannose will be a by-product.

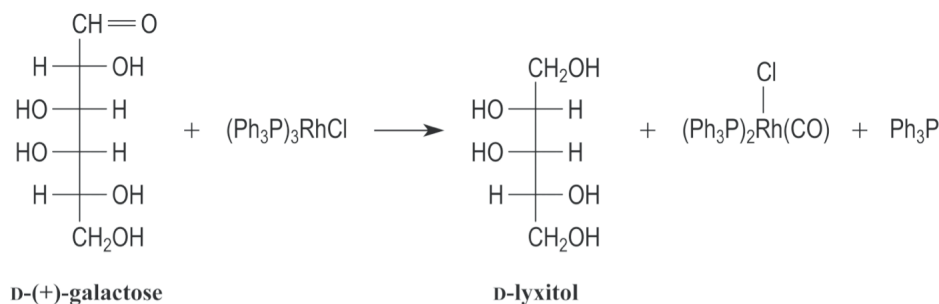
(b) This compound is prepared in the same way as the compound in (a), except that ordinary (unlabeled)  $\text{NaCN}$  is used, and the reduction is carried out with tritium-enriched hydrogen ( $^3\text{H}_2$ ). In this synthesis,  $^3\text{H}$ -D-mannose will be isolated as a by-product.

(c) The synthesis of compound (c) requires removal of an *unlabeled* carbon from D-arabinose, replacing it with a labeled carbon, and then completion of an ordinary Kiliani–Fischer synthesis to give labeled mannose. (\* =  $^{14}\text{C}$ )

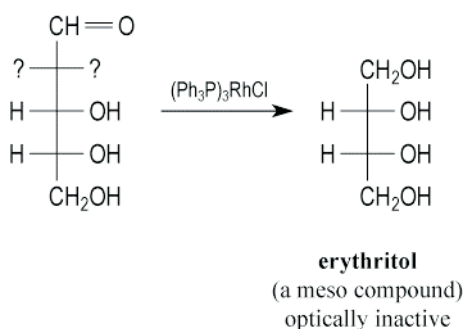


Each of the last two reactions also gives epimeric sugars—D-ribose and D-glucose, respectively—as by-products.

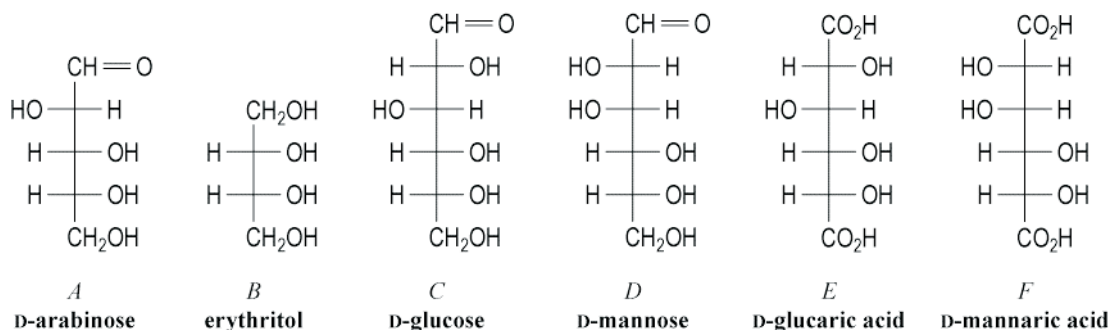
24.47 (a)



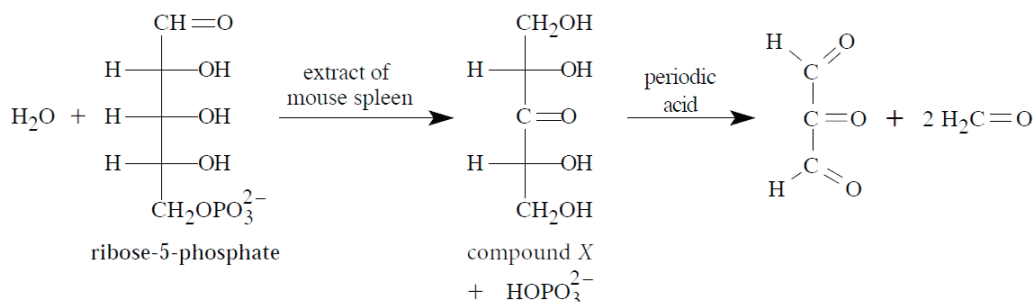
24.48 Since the product of the decarbonylation reaction is optically inactive, compound *B* must be *meso*-(2*R*,3*S*)-butane-1,2,3,4-tetraol (erythritol) in which all of the —OH groups are on the right side in the Fisher projection. Thus, the aldopentose *A* is either D-ribose or D-arabinose (see Fig. 24.3, text p. 1174).



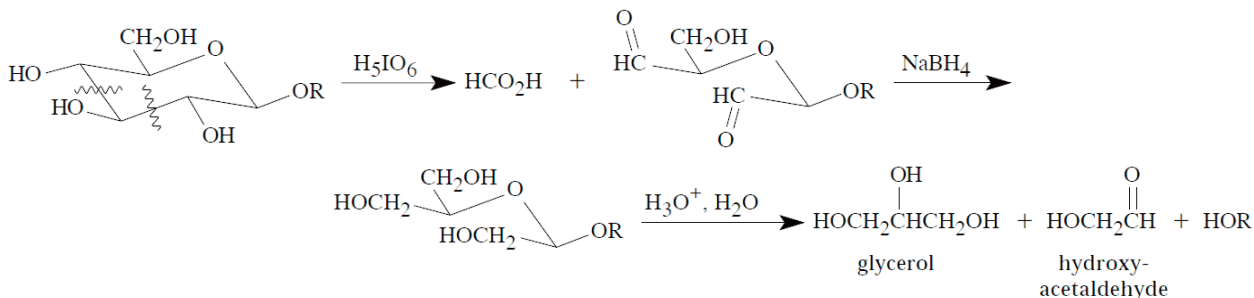
The products from the Kiliani–Fisher synthesis would then be either D-allose and D-altrose or D-glucose and D-mannose (see Fig. 24.3, text p. 1174). Since both of the products from the nitric acid oxidation are optically active, that means that D-allose could not be a product from the Kiliani–Fisher synthesis because it would produce an optically inactive aldaric acid. Thus, *A* is D-arabinose, *C* and *D* are D-glucose and D-mannose, and *E* and *F* are D-glucaric acid and D-mannaric acid. (See Eqs. 24.43–44, text p. 1198, for the Kiliani–Fisher synthesis using D-arabinose as the starting aldose.)



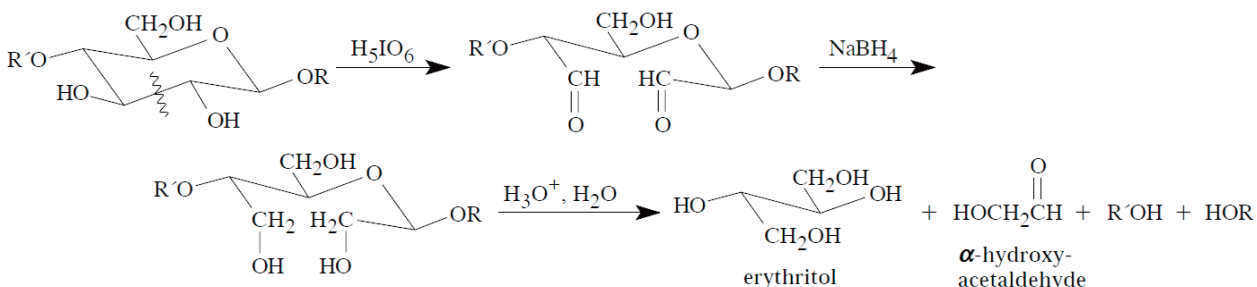
24.49 The extract of mouse spleen evidently contains enzymes that catalyze the removal of a phosphate as well as the conversion of ribose into an optically inactive isomer. Ribitol and xylitol are the alditols derived from ribose and xylose, respectively, and therefore are epimeric at carbon-3. Compound *X* has one degree of unsaturation, and, because reduction gives alcohols that are epimeric at carbon-3, compound *X* is a 3-ketopentose. The structure for *X* shown in the following transformation fits the data:



24.53 The residue at the nonreducing (“left”) end undergoes the following transformation:



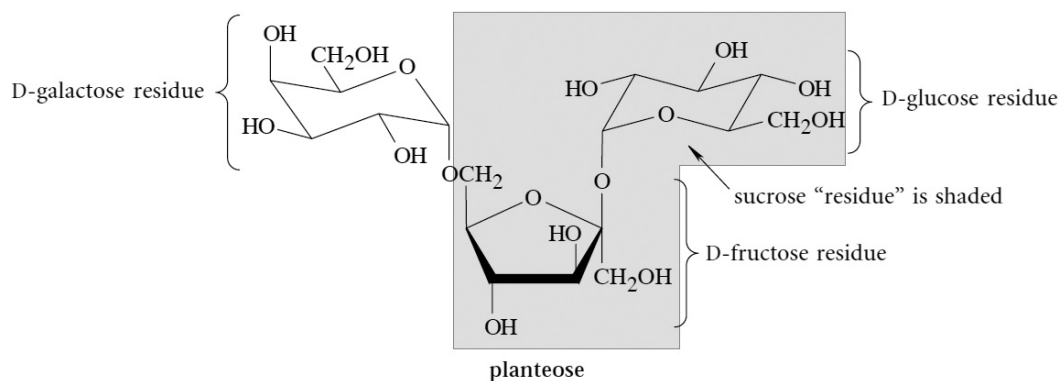
The internal residues undergo the following transformation:



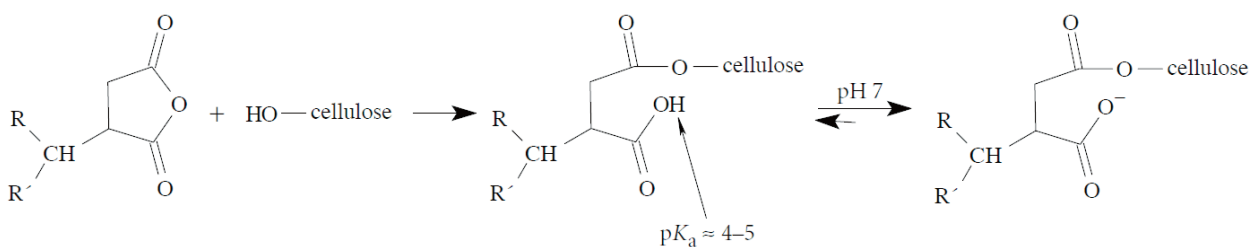
The residue at the reducing (“right”) end gives erythritol, R’OH, and two equivalents of formic acid (HCO<sub>2</sub>H). (Demonstrate this for yourself; see Eq. 24.39 on text p. 1196.) Erythritol therefore results from the cleavage reactions of all residues except for the one at the nonreducing end; and glycerol results from cleavage of that residue. Thus, glycerol is produced from one residue, and erythritol is produced from  $n - 2 + 1 = n - 1$  residues. Since  $n = 12$ , eleven moles of erythritol per mole of glycerol are formed.

24.55 The hydrolysis of planteose by almond emulsin establishes that an intact sucrose unit is connected to a galactose residue by an  $\alpha$ -galactosyl glycosidic bond. The question, then, is which oxygen of the sucrose residue is involved in the glycosidic linkage to the galactose. Methylation followed by hydrolysis provides the answer. (It will be helpful to refer to the structure of sucrose on text p. 1207.) If the fructose residue of sucrose were *not* connected to the galactose, it would have four oxygens available for methylation: the oxygens at carbons 1, 3, 4, and 6. Because the oxygen at carbon-6 is not methylated, it must be the point of attachment of the galactose residue. Hence, the structure of planteose is as follows:



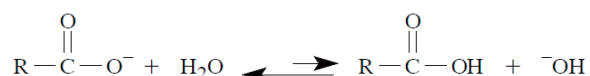


- 24.56 (a) The hydroxy groups of cellulose react with the anhydride to introduce succinate half-esters into the cellulose structure, as follows. (In these equations, HO—cellulose means any of the hydroxy groups of cellulose.)



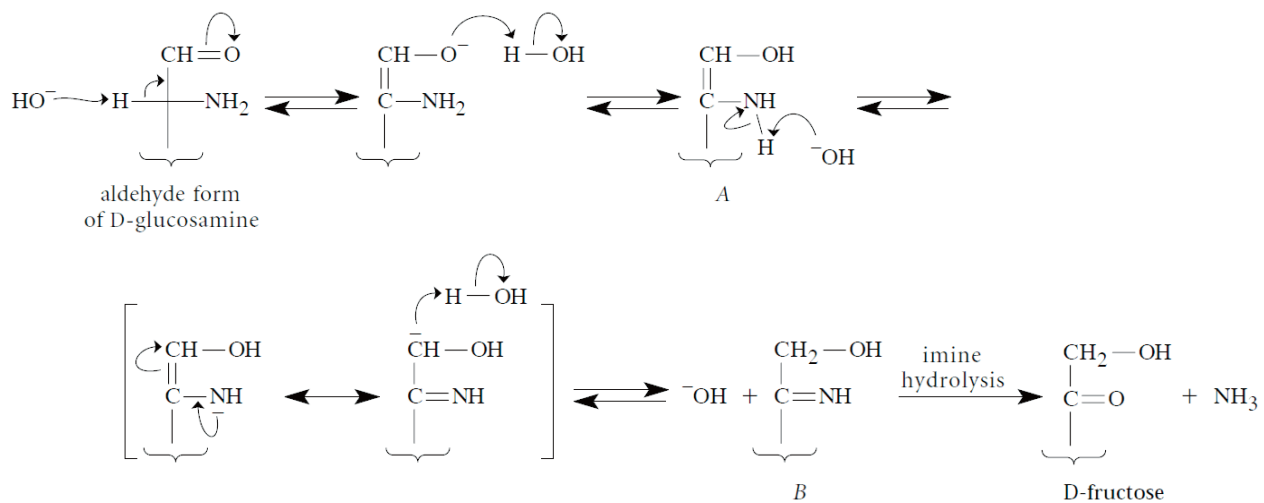
- (b) Sizing introduces a large number of alkyl groups into the cellulose structure. These resist solvation by water for the same reasons that hydrocarbons are insoluble in water; they are “hydrophobic” groups. Hence, these groups tend to resist the incorporation of solvent water into the cellulose structure. Furthermore, many of the —OH groups in the cellulose, which are hydrogen-bond donors before the reaction, become ester oxygens as a result of the reaction and therefore can no longer donate hydrogen bonds.
- (c) As the reaction in the solution to part (a) shows, the carboxylic acid groups introduced by the reaction are ionized by the pH 7 treatment because their  $pK_a$  values are well below the pH of the solution. When the paper is dried, these groups are left in their ionized state (with an appropriate counter-ion). The carboxylate groups are the slightly basic groups.

For example, when they come into contact with water, they react with water to produce a small amount of hydroxide ion:



You can use the  $pK_a$  value for the carboxylic acid and the ion-product constant of water to calculate that the pH of an aqueous solution of a carboxylic acid salt should have a pH of around 9. Hence, when the “sized” paper comes into contact with acid, the acid is neutralized by the small amount of hydroxide ion present. So many carboxylate groups are present that the hydroxide ion is immediately replenished, by Le Châtelier’s principle.

- 24.58 This transformation is essentially a Lobry de Bruyn–Alberda van Ekenstein reaction, the detailed mechanism of which is shown in Eqs. 24.22–24.23 on text pp. 1186–7. The aldehyde form of D-glucosamine is in equilibrium with a small amount of its enol *A*. This enol is also an enamine, which is in equilibrium with an imine *B*. Because imine formation is reversible in aqueous acid and base, the imine hydrolyzes to give the corresponding ketose, D-fructose, along with the by-product ammonia. Under the basic conditions, D-fructose is also in equilibrium with D-glucose and D-mannose, as shown on text p. 1186.

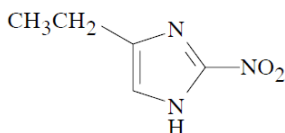


# Chapter 25

## The Chemistry of the Aromatic Heterocycles

### Solutions to In-Text Problems

25.1 (b)

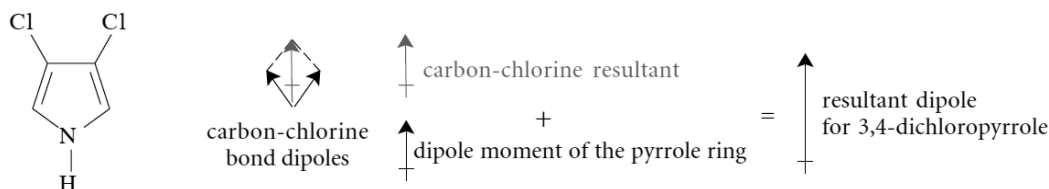


4-ethyl-2-nitroimidazole

25.2 (b) 2-Bromo-4-nitropyrrole

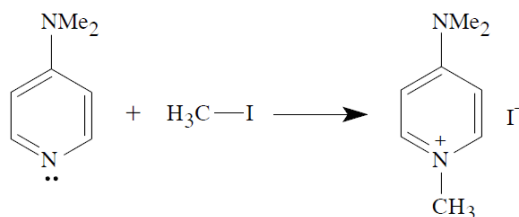
(d) 8-Methoxyquinoline

25.4 (c) Because the dipole vector of pyrrole is directed away from the nitrogen, and because the resultant of the two carbon-chlorine bond dipoles is also directed away from the nitrogen, the dipole moment of 3,4-dichloropyrrole should be greater than that of pyrrole:

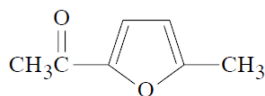


25.6 (b) Imidazole has one nitrogen that has the electronic character of the nitrogen in pyrrole, and one that is like the nitrogen in pyridine, except that it is somewhat more basic than the nitrogen of pyridine (Study Problem 25.1 on text p. 1225). Because of its basicity, imidazole can accept hydrogen bonds from water and, like pyridine, it is very soluble in water.

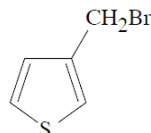
25.7 (b) Because the pyridine nitrogen is the more basic nitrogen, it is also the more nucleophilic nitrogen. Consequently, alkylation occurs on this nitrogen.



25.9 (b) This is a Friedel–Crafts acylation; both the methyl group and the ring direct substitution to the open “para” position (5-position).

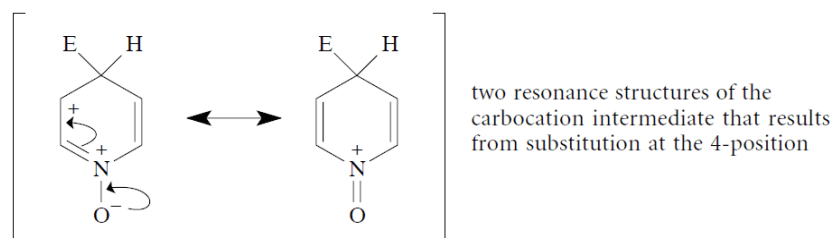


- (d) This is essentially a “benzylic” bromination: a free-radical bromination at a carbon adjacent to an aromatic ring (Sec. 17.2, text p. 793).

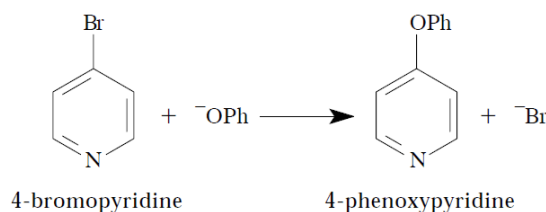


3-(bromomethyl)thiophene

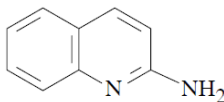
- 25.12 Substitution at the 4-position gives a carbocation that is stabilized by resonance interaction with an unshared electron pair on the oxygen. Substitution at the 3-position gives a carbocation that is not stabilized by such an interaction.



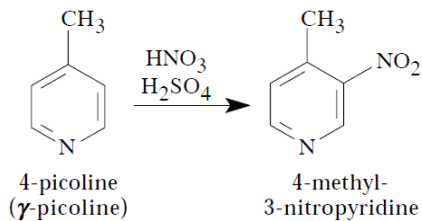
- 25.14 4-Bromopyridine undergoes nucleophilic aromatic substitution by phenolate ion. The anionic intermediate is stabilized because negative charge is delocalized onto the nitrogen, as shown in Eq. 25.42b on text p. 1238 (with  $Y = \text{Br}$ ,  ${}^{-}\text{Nuc} = {}^{-}\text{OPh}$ ). In the analogous substitution reaction of 3-bromopyridine, negative charge cannot be delocalized onto the nitrogen in the anionic intermediate; consequently, the intermediate is less stable and the reaction doesn't occur.



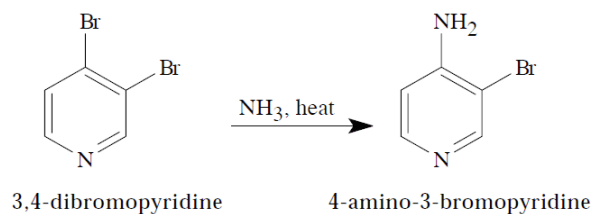
- 25.15 (b)



- 25.16 (b) In this case, the pyridine ring is nitrated on the 3-position by direct nitration.

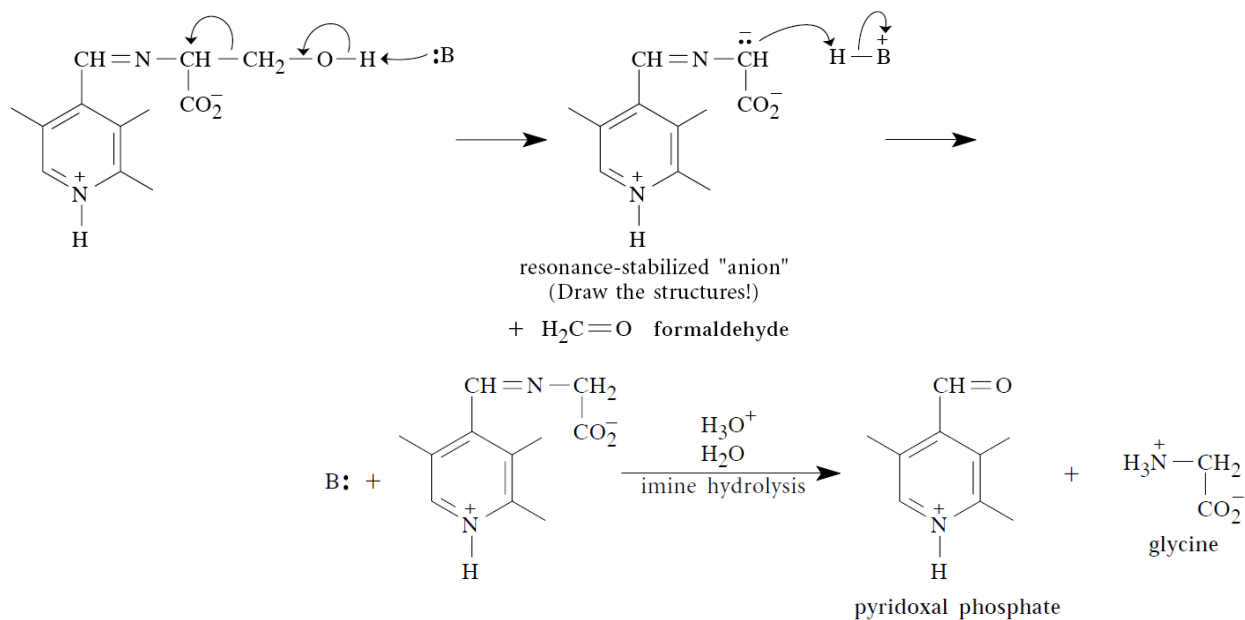


- 25.17 (b) The bromine at the 4-position is displaced by ammonia for the reasons discussed in the solution to Problem 25.14 in this supplement.

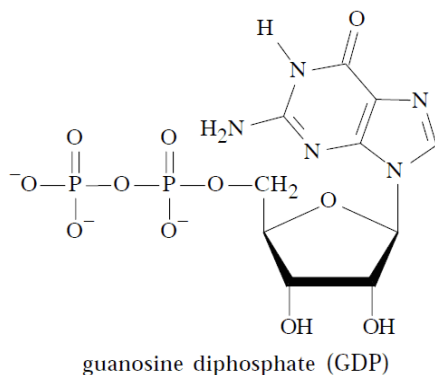


- 25.18 (b) Begin with the imine product of Eq. 25.55, text p. 1243, formed from pyridoxal phosphate and the amino group of serine. (We abbreviate the structure of pyridoxal phosphate as in the text.)

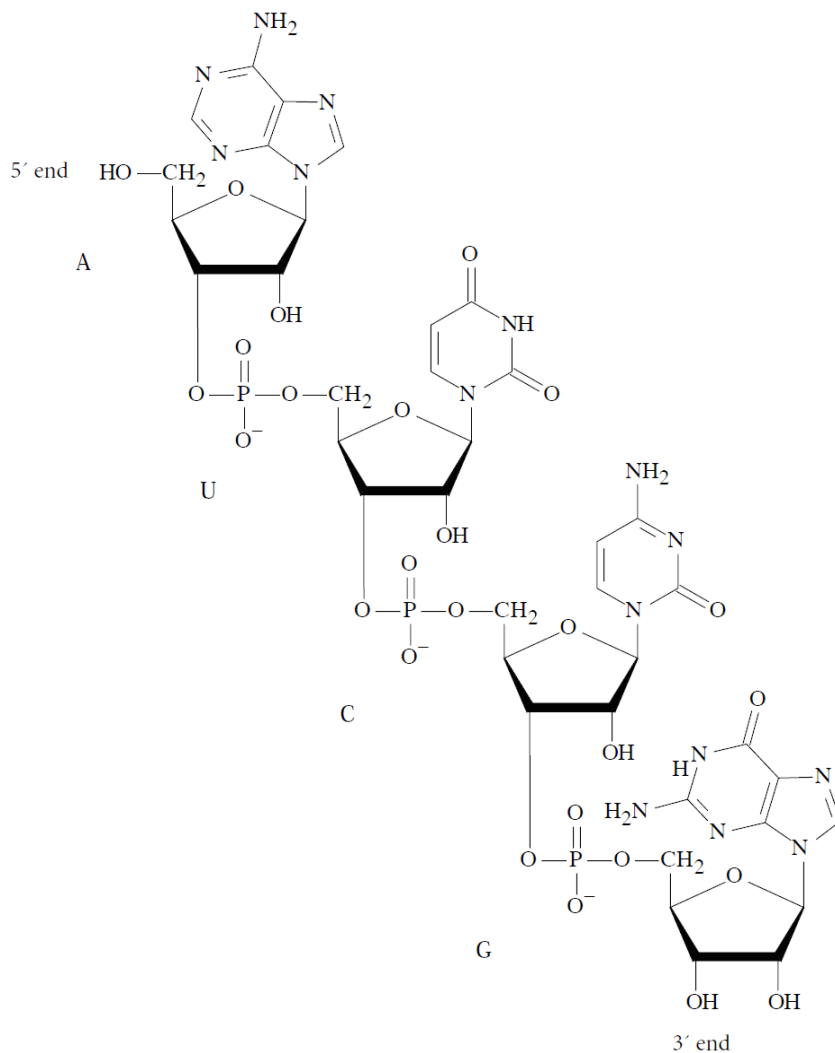
The first step is a  $\beta$ -elimination that produces formaldehyde and a resonance-stabilized "carbanion" in which the charge is essentially neutralized by delocalization of electrons onto the nitrogen of the pyridinium ring. (Be sure to show this!) This "carbanion" is then protonated to give an imine, which, in turn, hydrolyzes to glycine and pyridoxal phosphate.



- 25.20 (b)



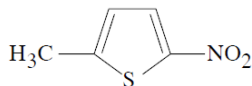
- 25.21 The structure of a tetranucleotide (a four-residue segment of RNA) with the sequence A-U-C-G is:



- 25.23 (b) Refer to Fig. 25.6(b), text p. 1251, and to Eq. 25.62 on text p. 1254. The answer to part (a) shows that *O*-methylation eliminates the hydrogen on nitrogen-3 of thymine that is involved in hydrogen bonding with nitrogen-1 of adenine. Because this hydrogen bonding is an essential part of base pairing, disruption of this hydrogen bond also disrupts base pairing.

## Solutions to Additional Problems

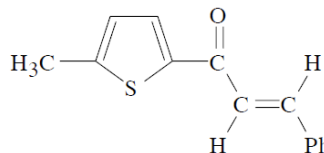
25.24 (b)



(e)

no reaction

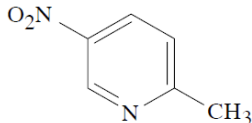
(g)



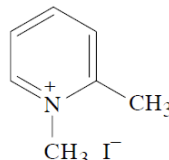
25.25 (b)

no reaction

(d)



(f)



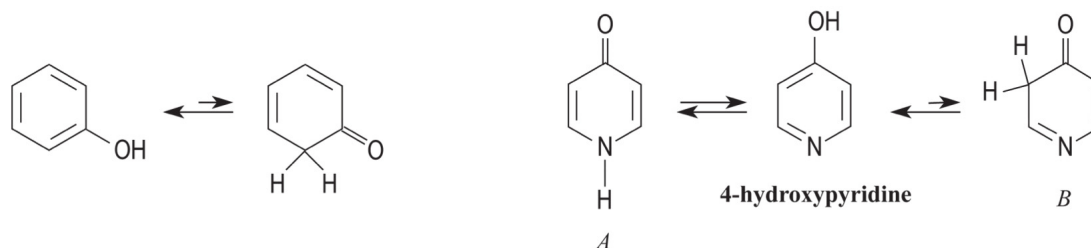
25.26 (b) The order of increasing reactivity is

benzene  $\ll$  thiophene  $<$  3-methylthiophene  $<$  2-methylfuran

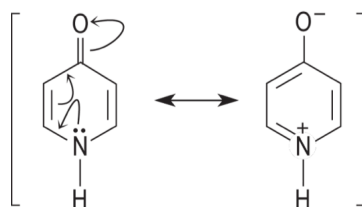
The relative reactivity of thiophene and benzene is discussed on text pp. 1228–9. Another reason that thiophene is more reactive is that it has a smaller aromatic resonance energy than benzene, and therefore it sacrifices less aromatic stabilization when reacting with electrophile. 3-Methylthiophene is more reactive than thiophene because it contains an activating substituent, the methyl group. Furan is even more reactive for reasons also discussed on text p. 1228, and 2-methylfuran is even more reactive because the methyl group is an activating substituent.

25.28 The hydroxy isomer is aromatic, and the carbonyl isomer is not. The principle to apply is that the compound with the greater resonance energy (Table 25.1, text p. 1223) has the greater amount of hydroxy isomer.

(b) Because benzene has greater aromatic stabilization (greater resonance energy) than pyridine, phenol contains the greater percentage of hydroxy isomer and 4-hydroxypyridine contains more carbonyl isomer.



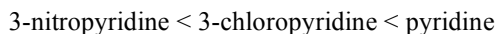
(A second carbonyl isomer of phenol, shown in Eq. 22.14 on text p. 1054, is not shown above.) Pyridine also has two carbonyl isomers; isomer *A* is undoubtedly the major one of the two because the unshared pair on nitrogen can participate in amide-like resonance:



Because the structure on the right is aromatic, this isomer of 4-hydroxypyridine is stabilized. This type of resonance is possible neither for isomer *B* nor for phenol. This is a second reason that 4-hydroxypyridine has

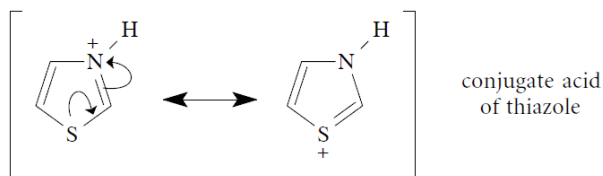
more of the carbonyl isomer than phenol. (See the similar discussion of amide resonance in 2-hydroxypyridine on text p. 1236.)

- 25.29 (b) The order of increasing basicity is



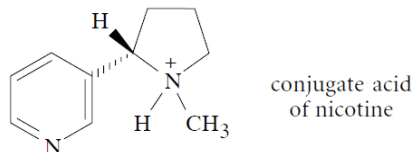
The order is a consequence of the relative polar effects of the nitro and chloro substituents, both of which are electron-withdrawing and base-weakening. As shown by the  $pK_a$  values in Table 23.1, text p. 1123, the electron-withdrawing polar effect of the nitro group on the  $pK_a$  of an ammonium ion is greater than that of the chloro group.

- (e) See Study Problem 25.1 on text p. 1225 for the structure of protonated imidazole. In the case of thiazole, an electron pair of a sulfur is involved in the resonance stabilization of the conjugate acid:

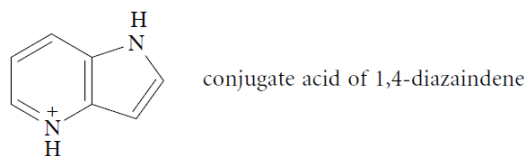


The orbitals of sulfur overlap more poorly than those of nitrogen with carbon  $2p$  orbitals because they are derived from a different quantum level; consequently, the resonance structure on the right is less important than the corresponding structure of protonated imidazole. The sulfur in thiazole is actually less electronegative than the nitrogen in imidazole, but, as in electrophilic aromatic substitution, the electron-donating resonance effect of nitrogen far outweighs its electron-withdrawing polar effect. Consequently, imidazole is considerably more basic than thiazole. (The actual conjugate-acid  $pK_a$  of imidazole is 6.95, and that of thiazole is 2.44.)

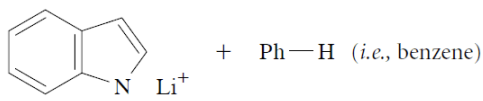
- 25.31 (b) The alkylamine group is more basic than the pyridine:



- (e) One nitrogen resembles the nitrogen of indole, which is not basic; the other resembles the nitrogen of pyridine, which is basic. Furthermore, protonation of the pyridine nitrogen gives a conjugate-acid cation that is stabilized by resonance interaction with the unshared pair on the “indole” nitrogen. (Draw the appropriate resonance structures.) In fact, the conjugate-acid  $pK_a$  of 1,4-diazaindene is 6.92, whereas the conjugate-acid  $pK_a$  of pyridine is 5.2. The greater basicity of 1,4-diazaindene reflects the resonance stabilization of its conjugate acid.

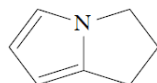


- 25.32 (b) The indole N—H is acidic enough to be removed by strong bases such as phenyllithium:

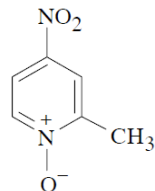




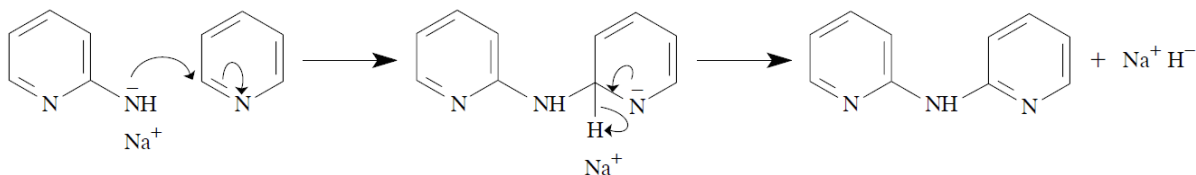
- (d) The product results from hydrogenation of the double bond that is not part of the aromatic system:



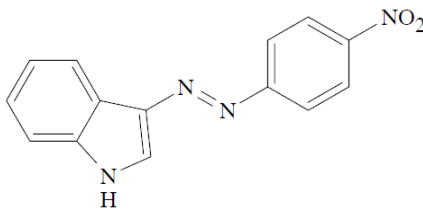
- (g) Pyridine-*N*-oxides are nitrated at carbon-4. (See Eq. 25.30, text p. 1233.) The directing effect of methyl is not strong enough to override the effect of an OH group. (Note that the *N*-oxide oxygen is protonated under the conditions of nitration; this point was not mentioned in the text.)



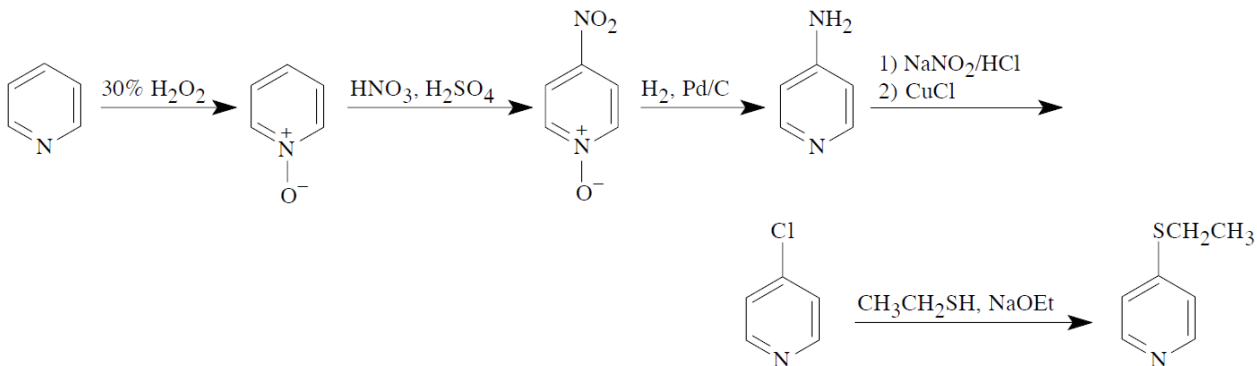
- 25.34 The conjugate-base anion of 2-aminopyridine, formed as shown in Eq. 25.33d, text p. 1235, reacts with another pyridine molecule in a Chichibabin-like reaction:



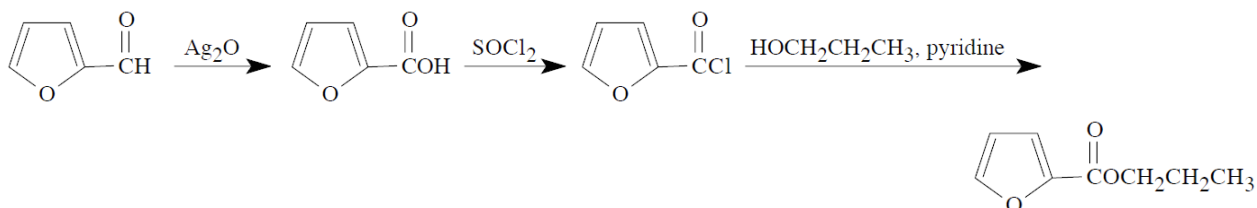
- 25.36 The *p*-nitrobenzenediazonium ion, which is formed in the diazotization reaction, acts as the electrophile in an electrophilic aromatic substitution at carbon-3 of indole:



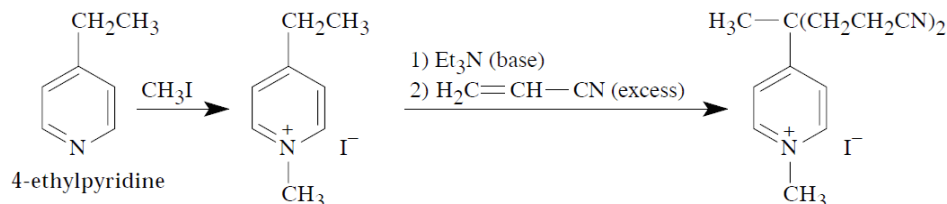
- 25.37 (b) Use the *N*-oxide to direct nitration to the 4-position. Then convert the nitrated *N*-oxide into 4-chloropyridine, which is then displaced with ethanethiolate anion.



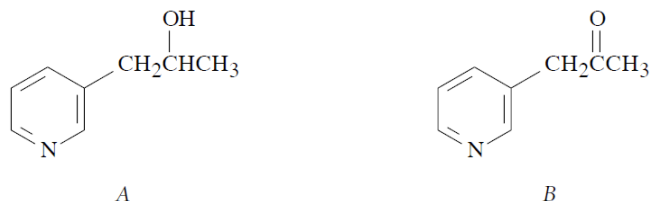
- (d) Oxidize furfural to the carboxylic acid and convert the acid into the ester. Notice that the acid chloride method of esterification is preferable to acid-catalyzed esterification with propanol because furans are somewhat sensitive to strongly acidic conditions. (See, for example, Problem 25.38, text p. 1260.)



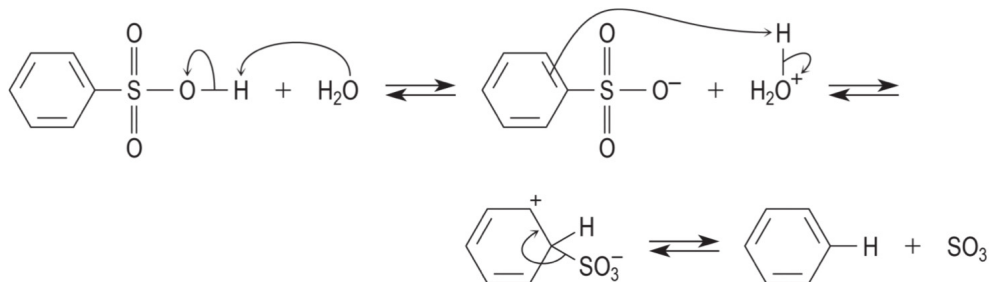
- (f) Use the enhanced “benzylic” acidity of *N*-methylpyridinium salts to form a nucleophilic anion at the benzylic carbon of the ethyl group, which is then cyanoethylated twice. (Compare to the reactions in Eqs. 25.49 and 25.50, text p. 1240. Cyanoethylation is discussed at the bottom of text p. 1093).



- 25.39 The unsaturation number of compound *A* is 4; its oxidation to nicotinic acid shows that it contains a pyridine ring with a 3-substituent. The pyridine ring accounts for all four degrees of unsaturation. Because pyridine contains five carbons, the side-chain has three carbons. Compound *A* cannot be a primary alcohol, because the oxidation product of such an alcohol would be an aldehyde, which could not have five exchangeable  $\alpha$ -hydrogens. (An aldehyde of the form  $RCH_2CH=O$  has only two  $\alpha$ -hydrogens.) Therefore, compound *A* is a secondary alcohol, and ketone *B* is its oxidation product.

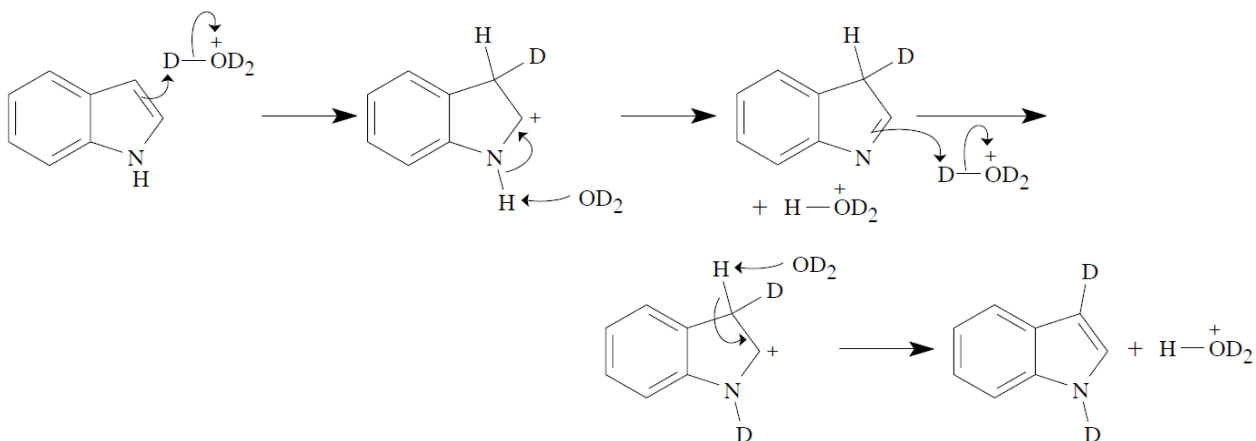


- 25.40 (a) By the principle of microscopic reversibility (see the bottom of text p. 171), the mechanism for the desulfonation of an arylsulfonic acid will be the reverse of the mechanism for sulfonation (see Eq. 16.13, text p. 756). For sulfonation to take place, a high concentration of the electrophilic agent ( $SO_3$ ) is used in the presence of  $H_2SO_4$ , a powerful acid and dehydrating agent to provide a low concentration of water. For desulfonation to take place, a high concentration of water is required to reverse the equilibrium of the reaction. ( $SO_3$  reacts with water to give  $H_2SO_4$ .)

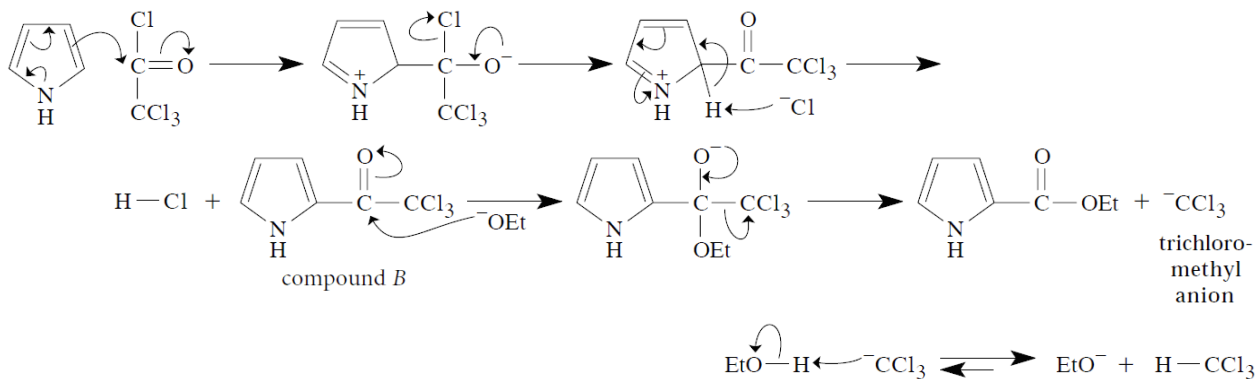


- (c) 3-Nitrothiophene cannot be made directly from thiophene because thiophene nitrates mostly in the 2-position to give 2-nitrothiophene (see Eq. 25.14, text p. 1227).

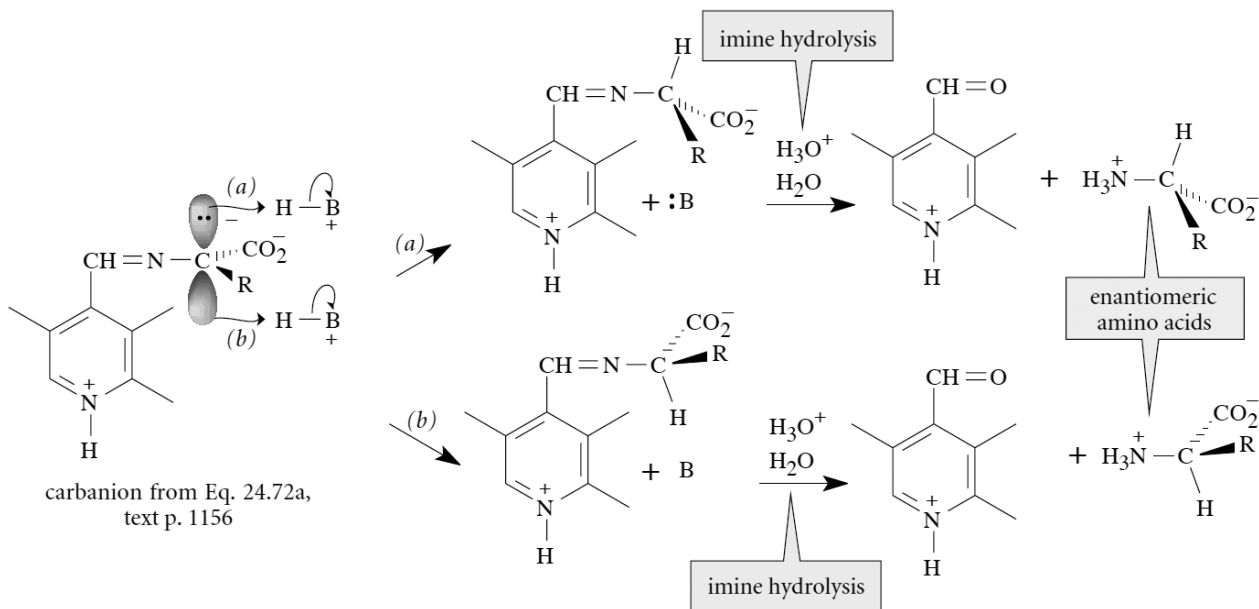
- 25.41 (b) Exchange is initiated with protonation by the deuterated acid at carbon-3 of the indole. In any exchange reaction of this sort, the experiment is set up so that there is a large excess of deuterium in the solvent; thus, the hydrogen that washes out into the solvent is swamped by the large excess of deuterium. In the last step, hydrogen is lost much more rapidly than deuterium because of the primary isotope effect (Sec. 9.5D, text p. 402). However, the relatively few molecules from which deuterium is lost are continually recycled through the mechanism until hydrogen is eventually washed out into the solvent.



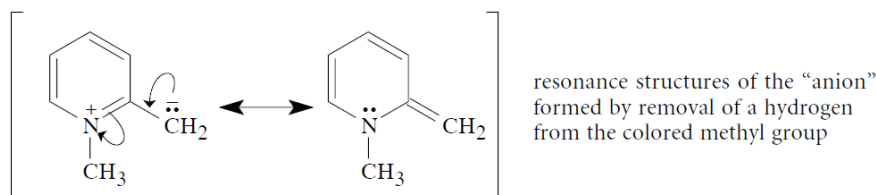
- (f) Because of the three chlorines on its  $\alpha$ -carbon, trichloroacetyl chloride is unusually reactive in nucleophilic acyl substitution reactions. (Recall that reactivity toward nucleophiles of a carbonyl compound is enhanced by electron-withdrawing substituents on the  $\alpha$ -carbon; see Sec. 19.7B, text pp. 910–912.) The  $\pi$  electrons of pyrrole are nucleophilic enough to be acylated by this acid chloride to give compound *B*. The remaining mechanistic steps are the same as the final steps of a haloform reaction (see Eq. 22.27e on text p. 1060), except that the base is ethoxide rather than hydroxide. Ethoxide displaces the trichloromethyl anion, which reacts with ethanol to give chloroform and ethoxide.



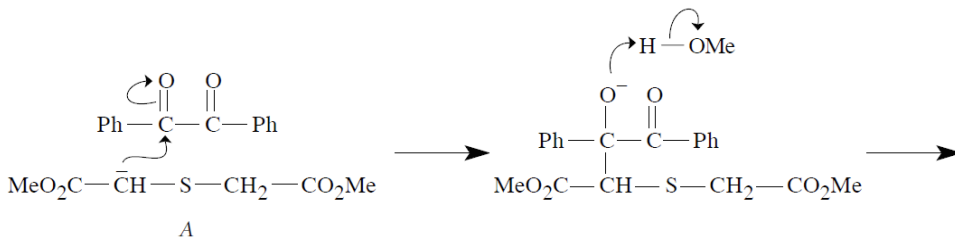
- 25.44 Form the carbanion intermediate as shown in Eqs. 25.55 and 25.56a, p. 1243 of the text. This carbanion can be protonated from either face to give enantiomers. The enantiomeric amino acids are freed by imine hydrolysis.

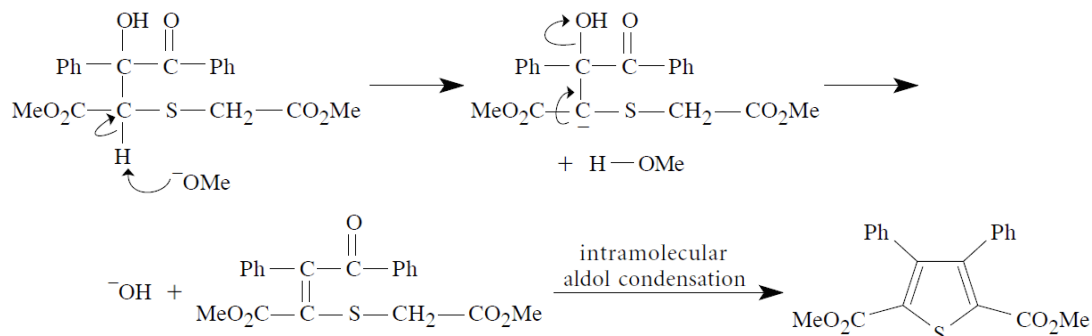


- 25.45 (b) Removal of a hydrogen from the black methyl group gives an anion that is stabilized by the polar effect of the attached positively charged nitrogen and by resonance interaction with the adjacent double bond. However, the resonance structure of this anion (draw it) delocalizes charge to a carbon atom. In contrast, removal of a hydrogen from the colored methyl group gives an “anion” which is actually a neutral compound; that is, the negative charge is delocalized to the positively charged nitrogen. Such charge neutralization is a significant stabilizing effect, and is the reason for the greater acidity of the colored hydrogen.

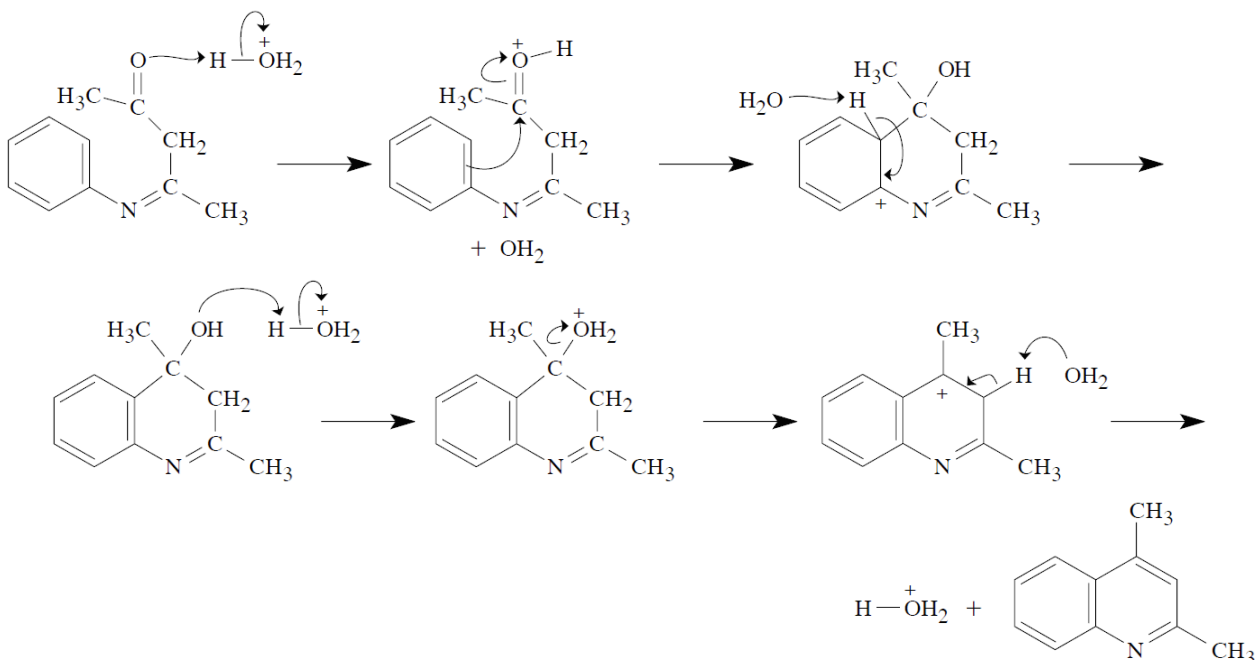


- (e) The reaction of 4-chloropyridine with ammonia is a nucleophilic aromatic substitution reaction that occurs readily because the negative charge in the addition intermediate is delocalized to the pyridine nitrogen, an electronegative atom, as shown in Eq. 25.42b, text p. 1238 (with  $\text{:Nuc} = \text{:NH}_3$  and  $\text{Y} = \text{Cl}$ ). In contrast, the negative charge in the corresponding intermediate for nucleophilic aromatic substitution of 3-chloropyridine can only be delocalized to carbon atoms. (See Eq. 25.42c, text page 1238.) As a result, 3-chloropyridine is much less reactive.
- 25.47 (b) This reaction begins as an aldol condensation between the conjugate-base enolate ion *A* of the diester and the diketone. Normally esters undergo Claisen condensations, but, because 1,2-diketones are particularly reactive (why?), the aldol condensation is observed instead. Once the two molecules are joined by the first aldol condensation, a second aldol condensation by an analogous mechanism closes the ring.

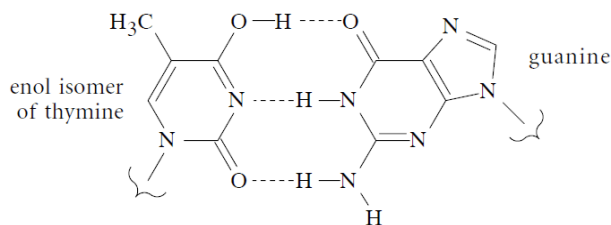




- (d) Imine formation between the amine and one of the ketone groups is followed by an intramolecular electrophilic aromatic substitution reaction in which the protonated ketone serves as the electrophile. The mechanism below begins with the imine; the mechanism of imine formation is discussed on text p. 927.

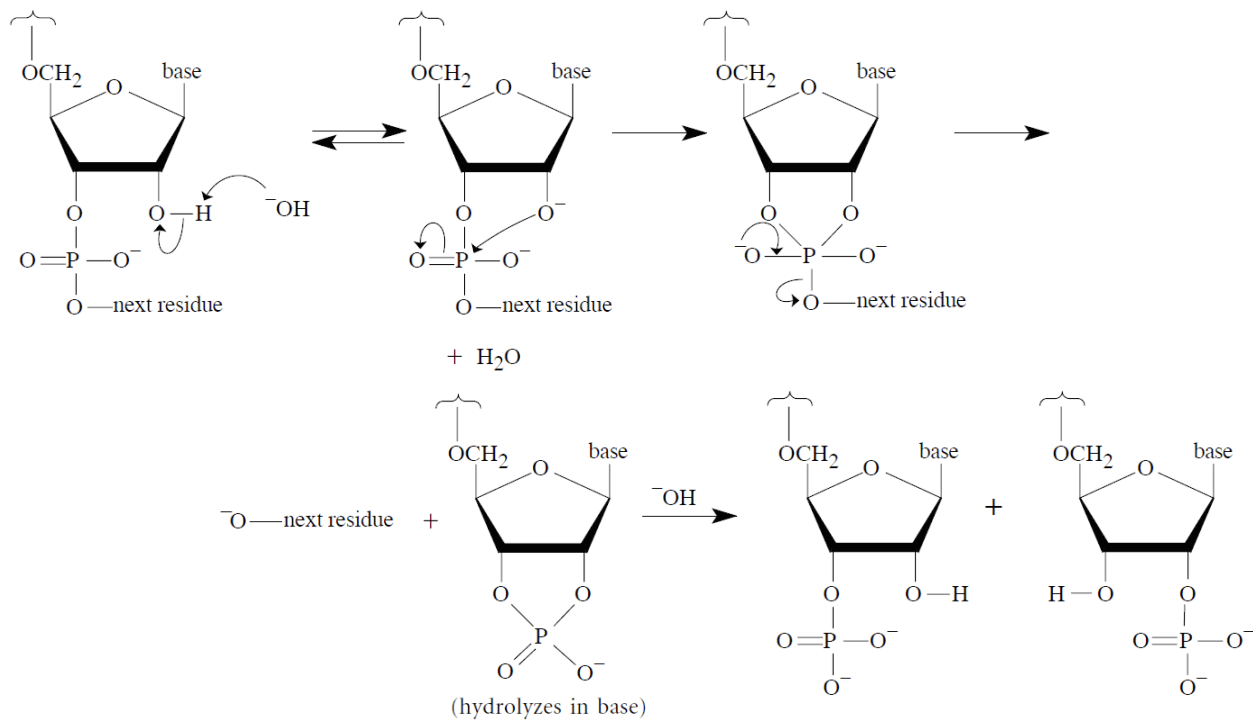


- 25.48 (b) The pairing of an enol isomer of T with G:



- 25.49 (b) The solution to part (a) leads to the conclusion that, because of the greater amount of hydrogen bonding in G-C base pairs, G-C rich DNA should have a higher melting temperature than A-T rich DNA. Hence, the human adenovirus I DNA contains the greater ratio of G + C.
- 25.51 The reaction of RNA involves ionization of the 2'-hydroxy group within each residue and reaction of the resulting alkoxide ion as a nucleophile at the neighboring phosphorus. This reaction is particularly rapid because it is intramolecular; it is an example of neighboring-group participation. (See Sec. 11.7, text p. 510.) Loss of the leaving group splits the internucleotide bond. DNA cannot undergo this reaction because the reaction depends on the

presence of the 2'-hydroxy group to act as an intramolecular nucleophile; DNA lacks this hydroxy group. (That is why it is called deoxyribonucleic acid.)



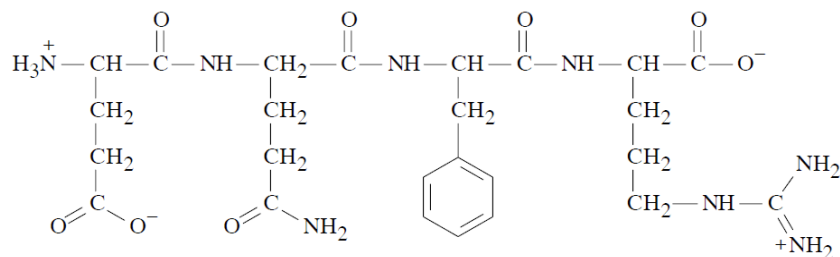
# Chapter 26

## Amino Acids, Peptides, and Proteins

### Solutions to In-Text Problems

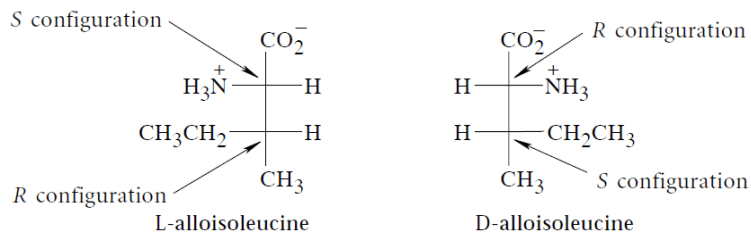
26.1 The peptide is drawn in the form that exists at neutral pH.

(b) The structure of Glu-Gln-Phe-Arg:



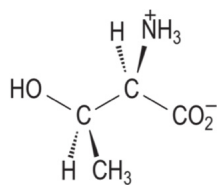
Glu-Gln-Phe-Arg  
(glutamylglutaminylphenylalanylarginine, or E-Q-F-R)

26.3 (b) L-Alloisoleucine has the 2S configuration, that is, the same configuration at the  $\alpha$ -carbon as L-leucine, but has a different configuration at the  $\beta$ -carbon. D-Alloisoleucine is the enantiomer of L-alloisoleucine.



26.4 (b) In terms of the sequence rules for determining configuration, the two carbons attached to the  $\alpha$ -carbons of cysteine or serine can be represented as C(O,O,O) and C(X,H,H), where X = S or O, respectively. When X = S (cysteine), the latter carbon receives priority. When X = O (serine), the former receives priority. Sulfur receives priority over oxygen because it has higher atomic number, and the priority is decided *at the first point of difference*. (See Sec. 4.2B, text p. 134.)

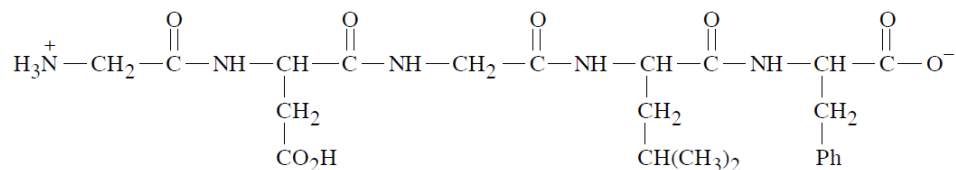
26.5 (b)



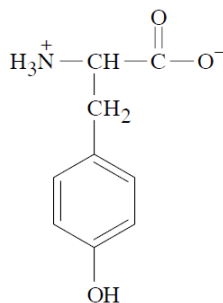
D-allothreonine

26.6 (b) In the major neutral form of G-D-G-L-F (Gly-Asp-Gly-Leu-Phe), the side-chain carboxy group of Asp is un-ionized and the carboxy-terminal carboxy group is ionized because it has the lower  $pK_a$  of the two carboxy

groups (Table 26.1, text p. 1268). This form would exist at a pH between the  $pK_a$  values of the two carboxy groups. That is, the pH at which this neutral form predominates is relatively acidic. (See Sec. 26.3B.) Notice that the major neutral form of a peptide (such as this one) may not be the form that predominates at *neutral pH*.



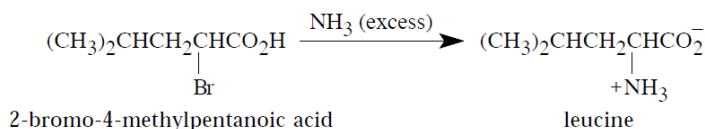
- 26.7 (a) The amino group of tyrosine can be protonated, and both the carboxy group and the phenolic O—H group can be ionized.
- (b) At pH 6, the net charge on tyrosine is zero. A pH value of 6 is below the  $pK_a$  of the conjugate acid of the amino group, and the amino group is therefore protonated; a pH value of 6 is above the  $pK_a$  of the carboxy group, which is therefore ionized; and a pH value of 6 is below the  $pK_a$  of the phenolic O—H group, which is therefore un-ionized.
- (c) The structure of tyrosine in aqueous solution at pH 6:



- 26.9 The general rule of thumb is that if the peptide contains more acidic than basic groups it is an acidic peptide; if it contains more basic than acidic groups it is a basic peptide; and if the number of acidic and basic groups are equal, the peptide is neutral. (An acidic group is a group that is in its conjugate-base form at neutral pH, such as a carboxy group; a basic group is a group that is in its conjugate-acid form at neutral pH, such as an amino group.)
- (b) This peptide contains three basic groups: the  $\alpha$ -amino group of the amino-terminal residue Leu and the side-chain amino groups of the Lys residues. The peptide contains one acidic group: the carboxy group of the carboxy-terminal Lys residue. Because the peptide contains more basic residues than acidic residues; it is a basic peptide. Its net charge at pH 6 is +2.
- (d) This peptide contains three acidic groups: the side-chain carboxy groups of the Asp and Glu residues and the carboxy group of the carboxy-terminal Ile residue. The peptide contains two basic groups: the  $\alpha$ -amino group of the amino-terminal residue Glu and the side-chain amino group of the Lys residue. Because the peptide contains more acidic residues than basic residues, it is an acidic peptide. Its net charge at pH 6 is -1.
- 26.12 At pH 6 the ion-exchange column is negatively charged because it bears strongly acidic sulfonic acid pendant groups. At this pH, the peptide Ac-Leu-Gly bears a negative charge, is repelled by the column, and will emerge first; Lys-Gly-Leu has a net charge of +1, is attracted to the column, and will emerge next; and Lys-Gly-Arg has a net charge of +2, is most strongly attracted to the column, and will emerge last.

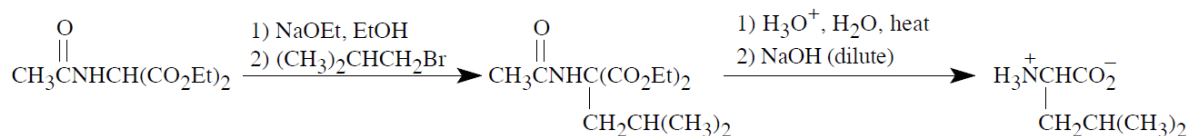
- 26.13 (b) All three methods would work in principle for leucine.

*Alkylation of ammonia:*

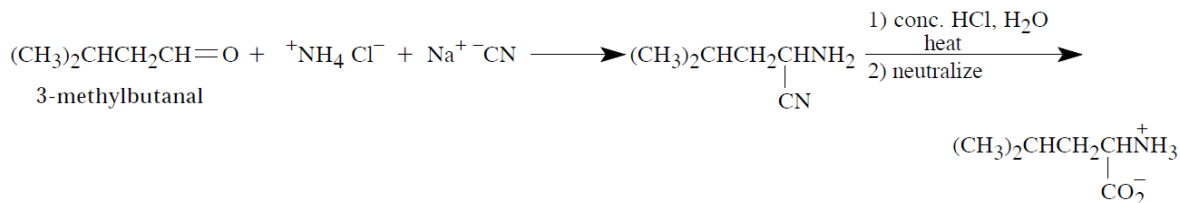




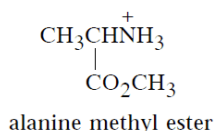
*Acetamidomalonnate method:*



*Strecker synthesis:*



- 26.14 (b) Alanine is esterified to give its methyl ester:



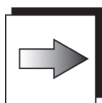
- 26.17 The box on text p. 1283 shows that solid-phase peptide synthesis requires about three synthetic steps per residue. Hence, about 300 steps are required for the synthesis of a protein containing 100 amino acid residues. If the average yield of each step is  $Y$ , then

$$Y^{300} = 0.50$$

$$300 \log Y = \log 0.50 = -0.3010$$

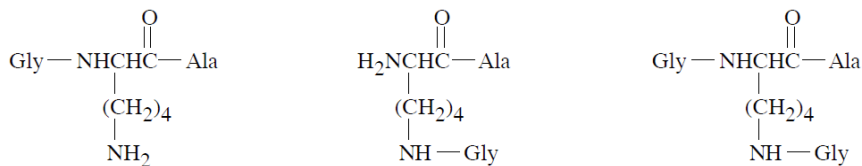
$$\log Y = -0.001003, \text{ or } Y = 0.998$$

Thus, an average yield of 99.8% per step would be required.



If you used 100 steps for your calculation, the average yield is 99.3%. Either way, the yield must be nearly perfect at each step to achieve even a 50% overall yield. Notice that, because there are so many steps, a drop of a small fraction of a percent in average yield per step has a large effect on the overall yield.

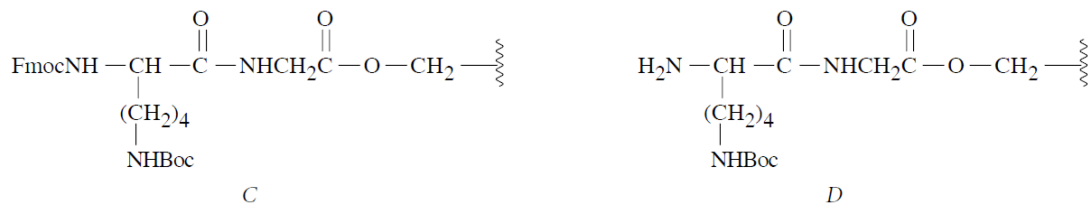
- 26.18 (b) The 20% piperidine step removes both Fmoc protecting groups. Hence, both amino groups react in subsequent acylation reactions. (The Lys residue is drawn in more structural detail for clarity.)



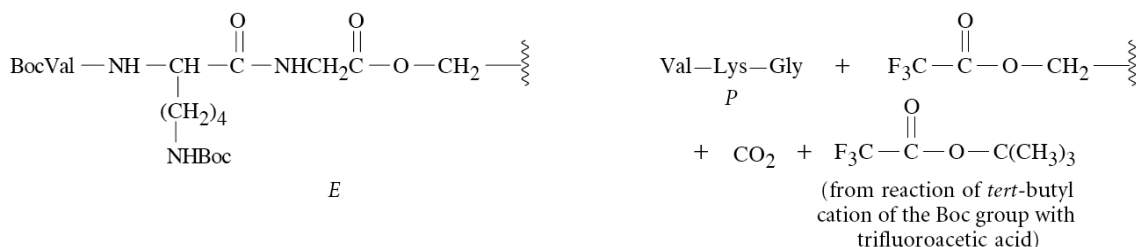
- 26.19 (a) Compound *A* results from the  $\text{S}_\text{N}2$  coupling reaction to the resin (analogous to Eq. 26.22 on text p. 1285), and compound *B* results from deprotection of *A*:



Compound *C* is the coupling product that results from coupling of the lysine derivative reacting at its carboxylic acid group with the free amino group of *B*, and compound *D* results from removal of the Fmoc protecting group, *but not the Boc group*, from compound *C*.



Compound *E* results from coupling of the carboxy terminus of Boc-Val with the free amino group of *D*. Peptide *P* results from both removal of *E* from the resin and removal of the Boc group.



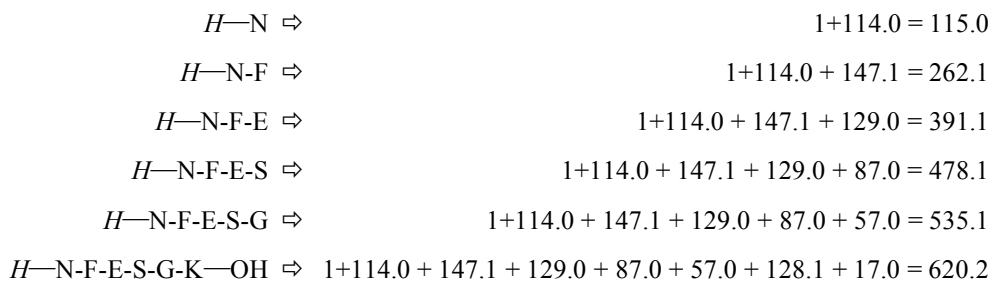
Note that the tripeptide *P* is in the di-cationic, amino-protonated form as a result of the acidic deprotection conditions. The neutral (zwitterionic) form would be obtained by neutralization.

- (b) The Boc group prevents the side-chain amino group of lysine from reacting with the carboxylic acid group of another molecule of itself under the coupling conditions. Also, it remains intact when the amino-terminal Fmoc group is removed with piperidine. The lysine side-chain thus remains protected in the subsequent coupling step as well.
- (c) Boc-Val introduces a protecting group that can be removed at the same time as the peptide is released from the resin. Use of Fmoc-Val would require an additional deprotection step with 20% piperidine.
- 26.20 (b) Glu and Gln are not differentiated by amino acid analysis because the side-chain carboxamide group of Gln, like that of Asn in part (a), is hydrolyzed; that is, Gln is converted into Glu.
- 26.21 The indole side-chain of tryptophan is very hydrocarbonlike, more so than the side chain of any other amino acid. [Recall (Sec. 25.2, text p. 1224) that pyrrole and indole are neither basic nor acidic.] Hence, we would expect to see AQC-Trp emerge on the far right of the amino acid analysis chromatogram, beyond AQC-Tyr.
- 26.23 Trypsin catalyzes the hydrolysis of peptides or proteins at the carbonyl group of arginine (R) or lysine (K) residues. Therefore, the peptide E-R-G-A-N-I-K-K-H-E-M would produce the following peptides upon trypsin-catalyzed hydrolysis:

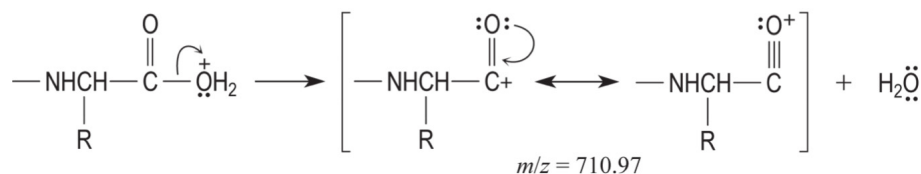
- (1) E-R
- (2) G-A-N-I-K
- (3) K
- (4) K-H-E-M
- (5) H-E-M

Peptides (2) and (4) originate by hydrolysis at the peptide bond between the two K residues. Peptides (3) that is, K, and (5) originate from hydrolysis at the peptide bond between the K and H residues to give G-A-N-I-K-K followed by hydrolysis at the C-terminal peptide bond of this peptide. However, peptide (5) does not originate from (4), because, when a lysine residue is at the amino terminus of a peptide, the hydrolysis of its peptide bond is not catalyzed by trypsin. (Trypsin is an endopeptidase.)

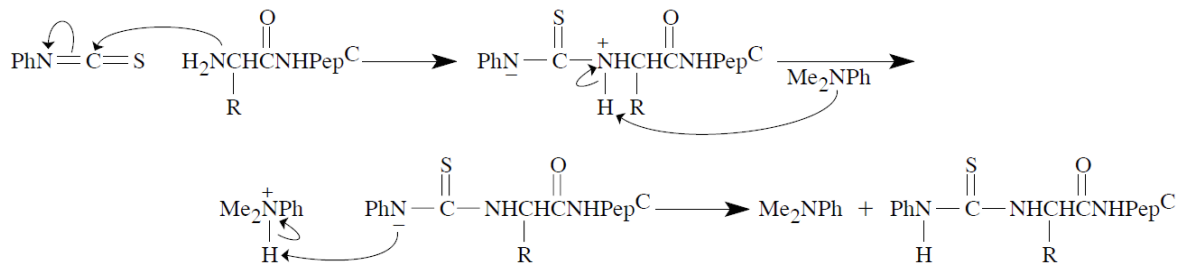
- 26.25 (a) b-Type fragmentation of the peptide N-F-E-S-G-K would produce the following  $m/z$  values. In this notation, each amino acid letter represents a residue (that is,  $\text{—NH—CHR—CO—}$ ). Therefore, the  $H\text{—}$  must be added to indicate the additional hydrogen at the amino terminus  $\text{H}_2\text{N—}$ , and one mass unit must be added to the corresponding residue mass.



- 26.26 (b) The  $M + 1$  ion (shown here protonated on the  $\text{—OH}$  group of the carboxylic acid) loses water to give an acylium ion, which is the ion of interest. Although carboxylic acids are normally protonated on the carbonyl group, the small amount of the form shown here, once formed, is very unstable.

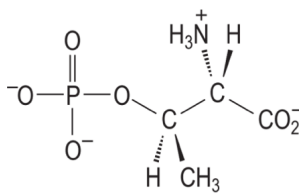


- 26.27 (a) The amino group serves as a nucleophile in an addition to the isothiocyanate.



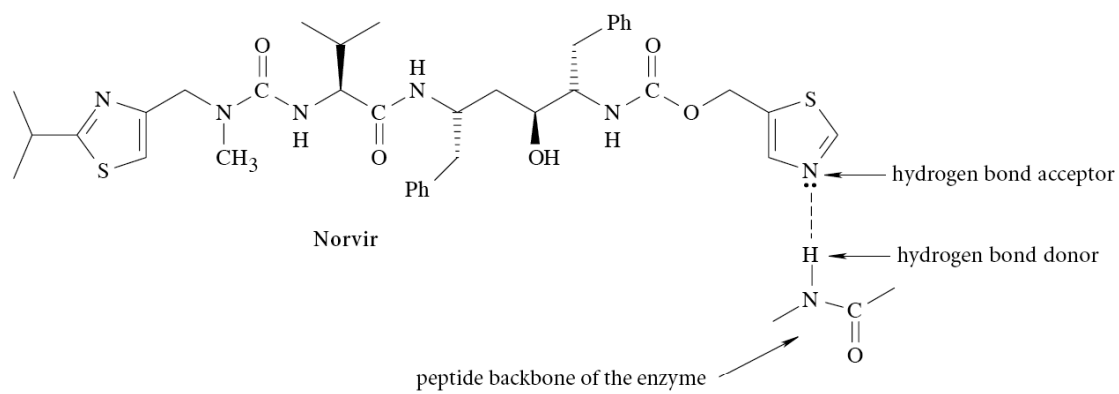
- 26.28 (a) As Eq. 26.41a on text p. 1303 as well as its mechanism in the solution to Problem 26.27(a) show, the Edman degradation depends on the presence of a free terminal amino group in the peptide. Because this group is blocked as an amide in acetylated peptides, such peptides cannot undergo the Edman degradation.

- 26.30 The compound is shown in its ionization state at  $\text{pH} = 7.4$  (physiological  $\text{pH}$ ). (Refer to the configuration of L-threonine on text p. 1271.) The configuration that is naturally occurring in proteins is assumed.



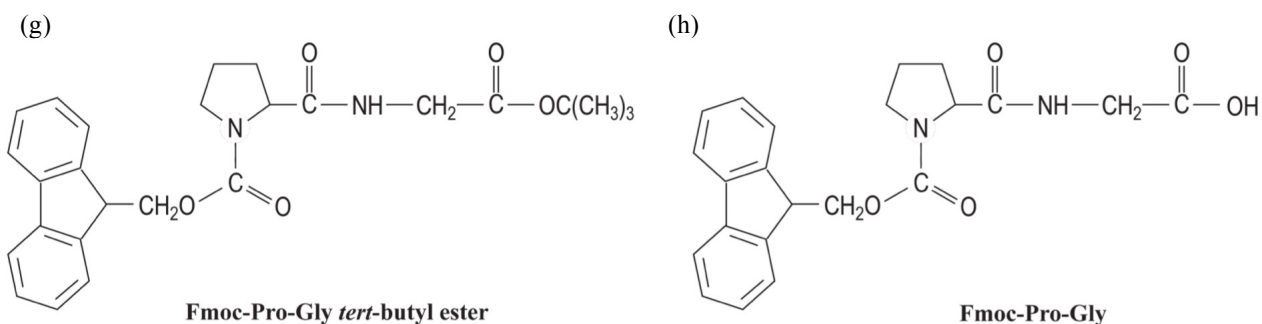
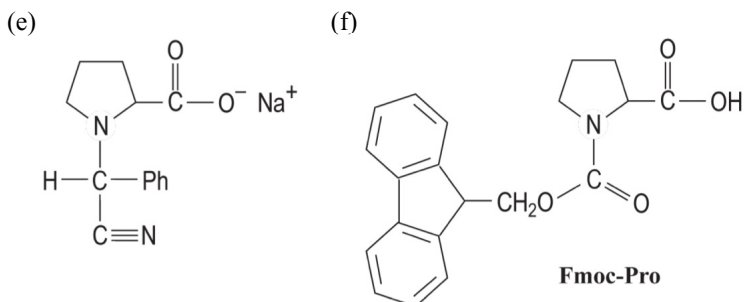
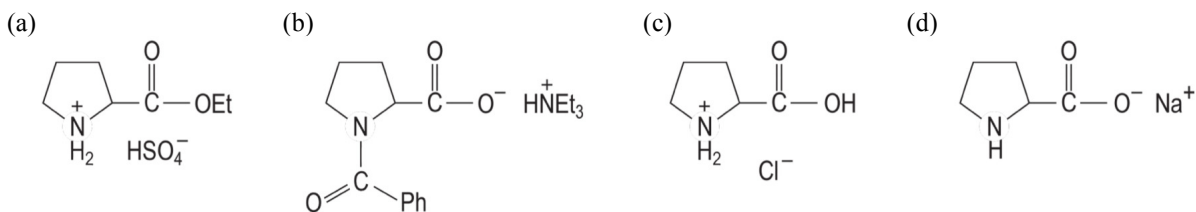
**L-phosphothreonine**

- 26.35 Although the sulfur has two unshared pairs, the nitrogen of the thiazole is like the nitrogen of pyridine or imidazole and is the most basic site on the ring; hence, it is likely to be the hydrogen-bond acceptor. An amide backbone  $\text{N—H}$  is the only hydrogen bond donor site on a peptide backbone.



### Solutions to Additional Problems

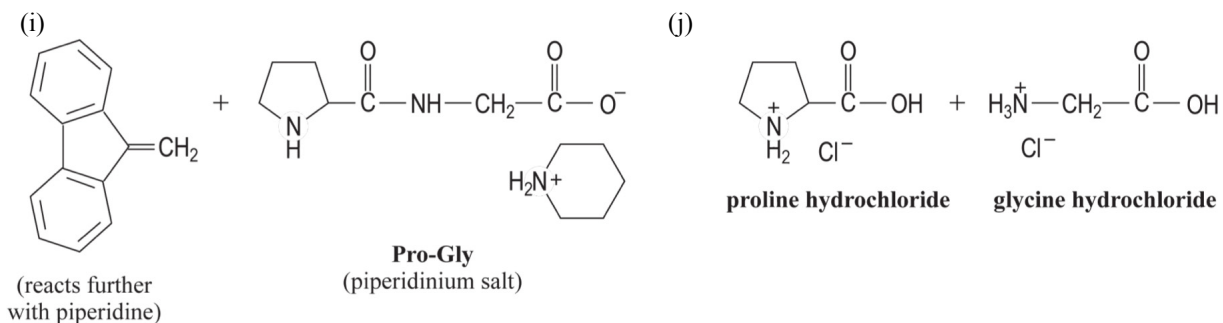
26.37 The results for proline:



**Fmoc-Pro-Gly *tert*-butyl ester**

**Fmoc-Pro-Gly**

+ *tert*-butyl trifluoroacetate



26.38 (b) The most basic amino acid is arginine. It has the highest isoelectric point.

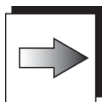
(d) Glycine is not chiral and therefore it cannot be optically active.

26.39 (b) Fmoc-Leu, once attached to the resin, must be deprotected before the subsequent coupling reaction can be expected to succeed. Polly forgot the deprotection step with 20% piperidine, which is essential for removing the Fmoc group.

26.41 Cysteic acid is essentially an aspartic acid in which the side-chain carboxy group has been substituted with a sulfonic acid group. Because sulfonic acids are more acidic than carboxylic acids, cysteic acid is expected to be

(and is) more acidic than aspartic acid. Thus, the correct answer is (1): cysteic acid has a lower isoelectric point than aspartic acid.

- 26.43 The amino-terminal residue of the peptide *P* is valine. Because dansyl-valine is obtained, the  $\alpha$ -amino group of valine must have been free in the peptide, and hence, valine must have been the amino-terminal residue. The sequence of the other residues cannot be determined from the data given.



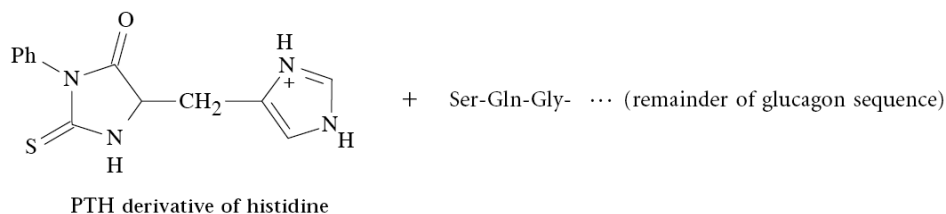
“Dansylation” is a method for determining the amino-terminal residue of a peptide.

- 26.45 (a) Trypsin should catalyze the cleavage of glucagon at Lys and Arg residues. The following five fragments are expected. (Remember that, by convention, peptides written in this way have their amino ends on the left.) We assume that all cleavages proceed to completion, although in practice intermediate cleavage fragments might be formed as well.

- (1) His-Ser-Gln-Gly-Thr-Phe-Thr-Ser-Asp-Tyr-Ser-Lys
- (2) Tyr-Leu-Asp-Ser-Arg
- (3) Arg
- (4) Ala-Gln-Asp-Phe-Val-Gln-Trp-Leu-Met-Asn-Thr
- (5) Arg-Ala-Gln-Asp-Phe-Val-Gln-Trp-Leu-Met-Asn-Thr

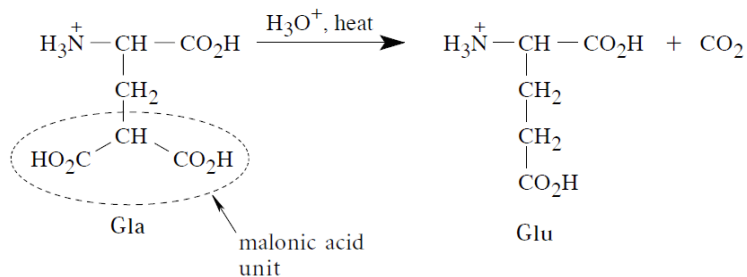
If cleavage occurs after the first Arg in the Arg-Arg sequence of glucagon, then the peptide (5) is formed, and the second Arg becomes the amino terminus of this peptide. Cleavage does not occur at the peptide bond of this Arg because trypsin is an endopeptidase. (Eq. 26.36b, text p. 1296.) If cleavage of glucagon occurs after the second Arg, then Tyr-Leu-Asp-Ser-Arg-Arg is formed. Subsequent cleavage of this peptide at the Arg-Arg bond gives (2) and (3).

- (b) The products of this Edman cleavage would be the PTH derivative of histidine along with a new peptide, which is glucagon without its amino-terminal residue.

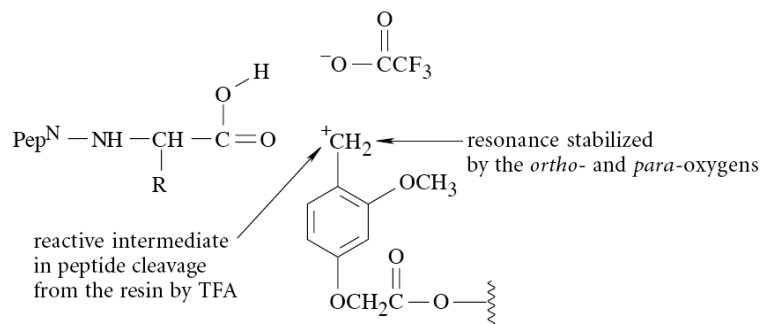


- 26.47 The presence of two amino-terminal residues suggests that either (a) insulin is an approximately equimolar mixture of two proteins, or (b) it is a single protein containing two peptide chains. In fact, the latter is correct; insulin is two polypeptide chains connected by disulfide bonds. Glycine is the amino-terminal residue of one chain, and phenylalanine is the amino-terminal residue of the other.

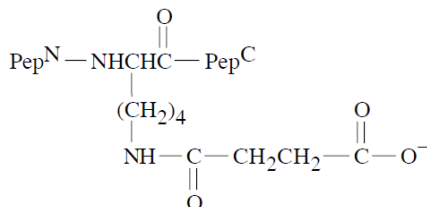
- 26.49 This amino acid is really a substituted malonic acid. When heated in acid, it, like most malonic acid derivatives, decarboxylates. In this case, the product is glutamic acid. (See Eq. 20.40, text p. 977.)



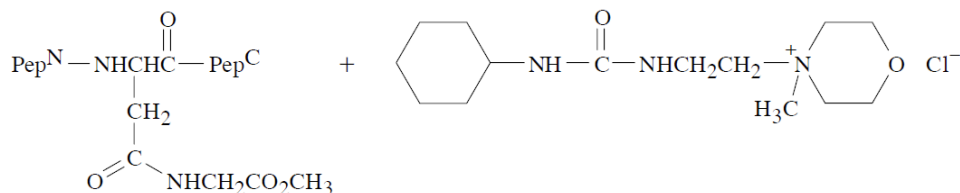
- 26.51 The principle is that a peptide with a given charge migrates to the electrode of opposite charge; a peptide with zero charge does not migrate. Because Gly-Lys is a basic peptide, it has a net positive charge at pH 6, and it therefore migrates to the cathode, the negatively charged electrode. Because Gly-Asp is an acidic peptide, it has a net negative charge at pH 6, and it migrates to the anode, the positively charged electrode. Gly-Ala is a neutral peptide; it has net zero charge at pH 6, and therefore it does not migrate.
- 26.53 Such a resin should be less effective in partitioning the amino acids with hydrocarbon side chains, because they will be “less soluble” in the resin phase. In effect, there are fewer  $\text{—CH}_2\text{—}$  groups on the resin to provide favorable interactions with the amino acid side chains. Furthermore, the amino acid side-chains would be forced to be closer to the more polar and hydrophilic resin surface, with which they might not interact as favorably. The separation should be less effective. The separation should be less effective with the C8-silica.
- 26.55 (b) Hydrogen peroxide oxidizes the disulfide bonds to sulfenic acids, then to sulfinic acids, and finally to sulfonic acids (see Fig. 10.3, text p. 472).
- 26.58 The mechanism of cleavage in trifluoroacetic acid involves a benzylic carbocation intermediate. This carbocation is resonance-stabilized not only by the *para*-oxygen, but also by the *ortho*-oxygen as well. (Draw the resonance structures.) Because the carbocation intermediate is more stable, the cleavage reaction is faster. Hence, milder conditions (lower acid concentration) can be used for the cleavage.



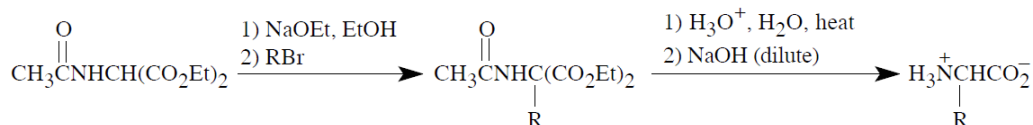
- 26.61 (b) The side-chain amino group of lysine serves as a nucleophile to open the anhydride. The resulting carboxy group is ionized at the pH of the reaction.



- (d) The carbodiimide promotes a condensation between the side-chain carboxy group of aspartic acid and the amino group of the glycine ester.

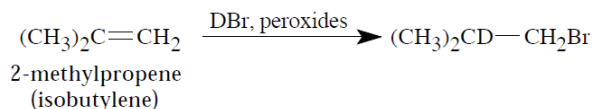


- 26.63 Every synthesis has the same final steps:



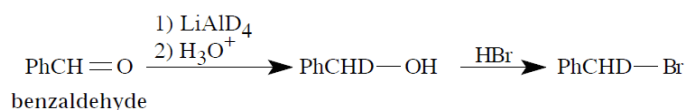
The challenge in each case is to prepare the alkyl halide R—Br from the given starting material.

(a)

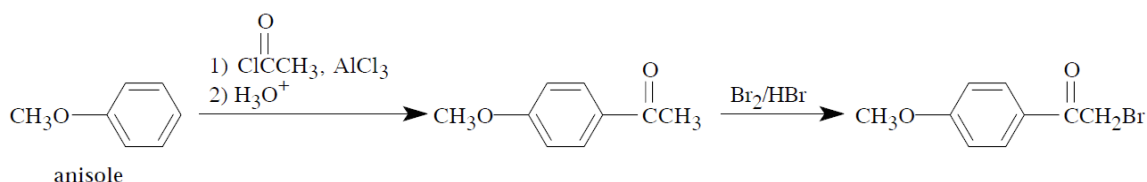


Alternatively, the same alkene could be hydroborated with  $\text{BD}_3$ , the resulting organoborane oxidized to the primary alcohol by alkaline  $\text{H}_2\text{O}_2$ , and the alcohol converted into the alkyl bromide with concentrated  $\text{HBr}$  and  $\text{H}_2\text{SO}_4$  catalyst.

(b)

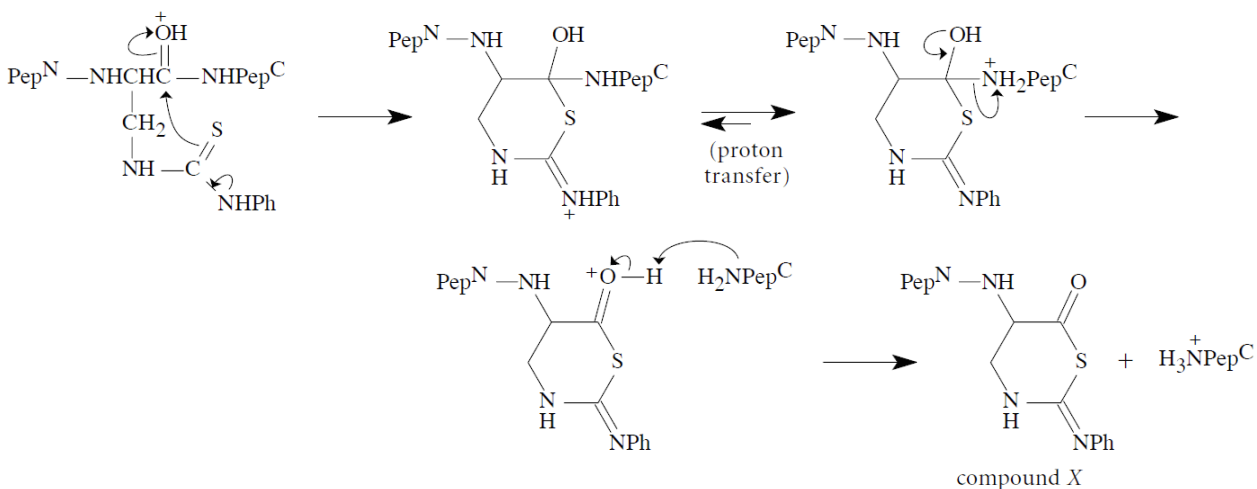


(c)



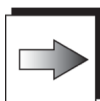
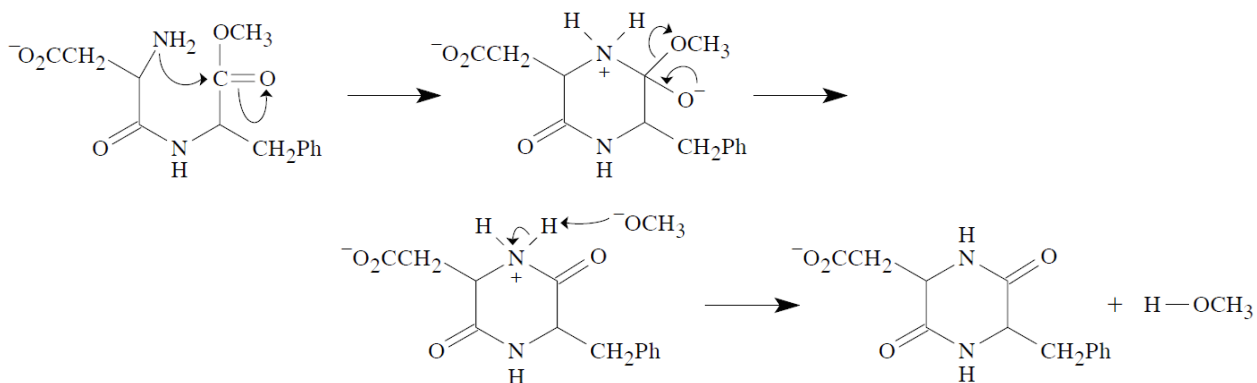
Alkylate the acetamidomalonate ion with this halide. Then, in the final hydrolysis step, use concentrated  $\text{HBr}$ , which will also cleave the methyl ether. Recall that  $\alpha$ -bromo carbonyl compounds are very reactive in  $\text{S}_{\text{N}}2$  reactions (Sec. 22.3, text p. 1042).

- 26.64 In the first step, the amine adds to the Edman reagent; for the mechanism of this reaction, see the solution to Problem 26.27(a) on p. 5 of this chapter. The sulfur of the thiourea then serves as a nucleophile to close a six-membered ring and cleave the peptide. The mechanism below begins with the product of the reaction between the Edman reagent and the peptide, which is protonated on the carbonyl oxygen by the catalyzing acid.



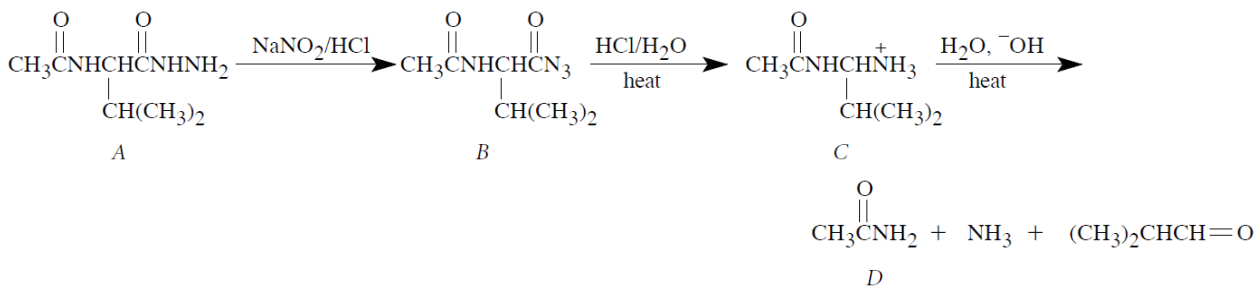
- 26.65 This reaction is an intramolecular ester aminolysis. The mechanism below begins with the conjugate base of the peptide formed by loss of a proton from the terminal amino group.



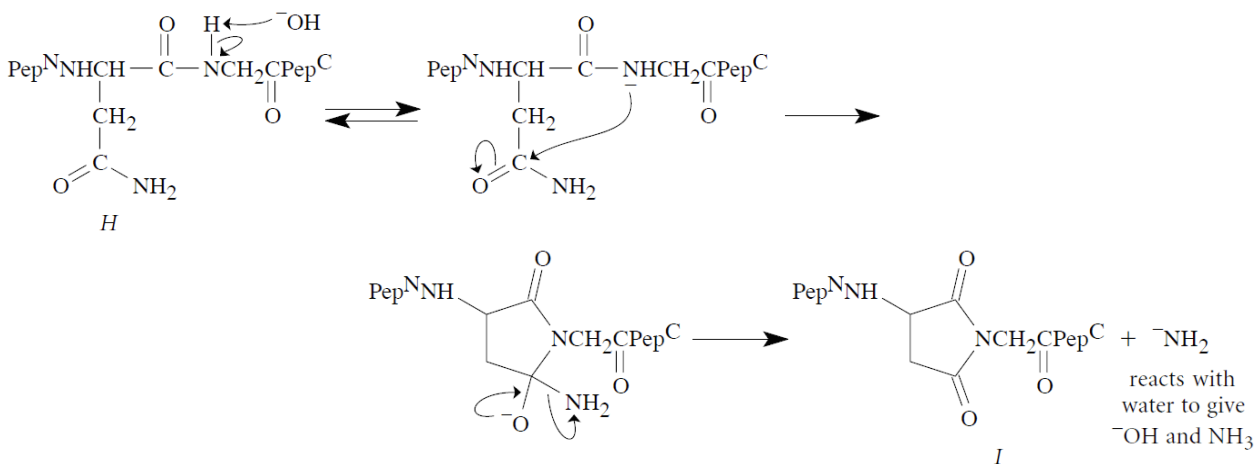


You may have noticed that diet soft drinks that go on sale in the supermarket are not quite as sweet as really fresh ones. This is because some of the sweetener has degraded by the mechanism just depicted.

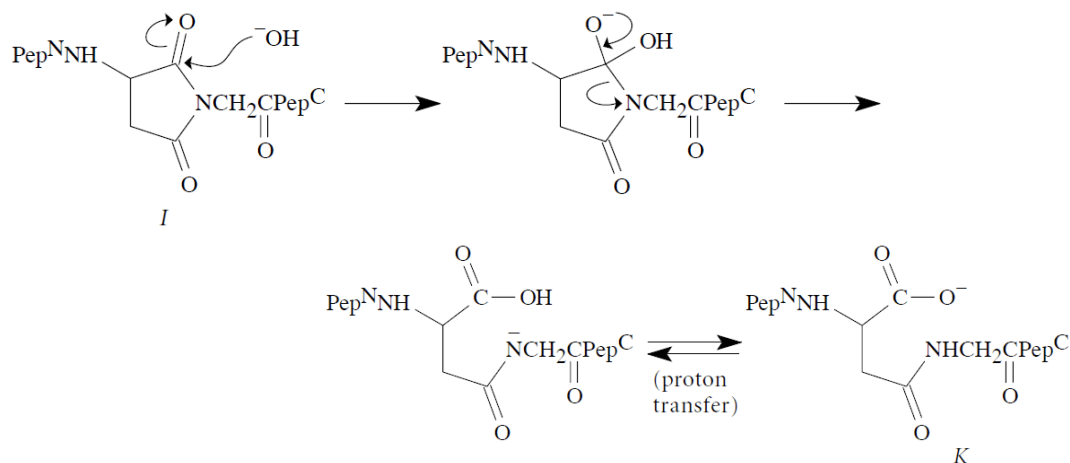
- 26.67 The chemistry is very similar to that of Problem 26.66(i), text p. 1330. Compound *A* is the hydrazide; compound *B* is the acyl azide; compound *C* is the conjugate acid of an *N*-(1-aminoalkyl)amide, which is a nitrogen analog of a hemiacetal. This hydrolyzes in base to the aldehyde shown, ammonia, and acetamide *D*. (If the conditions were harsh enough, acetamide *D* would be converted into acetate ion and ammonia. If you postulated that compound *D* is acetate ion, your answer is equally satisfactory.)



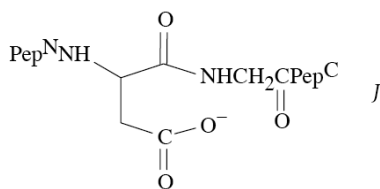
- 26.69 Peptide *I* results from intramolecular nucleophilic reaction with the conjugate-base anion of the neighboring amide bond. This occurs mostly at Asn-Gly because glycine has no carbon side chain; in residues other than glycine, the carbon side chains can cause rate-retarding van der Waals repulsions in the ring-closure step.



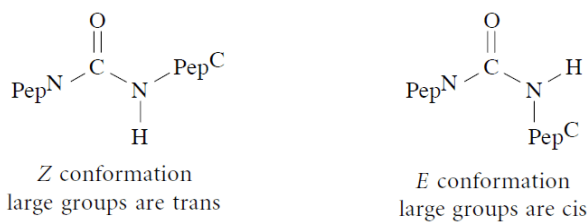
Derivative *I* is an imide, which is the nitrogen analog of an anhydride. Hydroxide can react with either carbonyl carbon of the imide ring to open the ring, thus generating either peptide *J* or peptide *K*. The mechanism for the formation of peptide *K* is as follows:



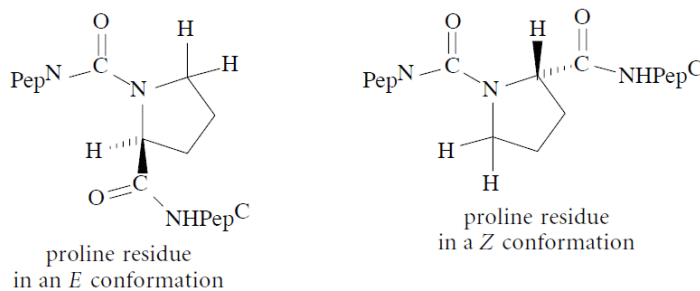
The structure of peptide *J* is as follows; you should show the mechanism for its formation.



- 26.71 (a) In the *Z* conformation, the two large groups  $\text{Pep}^{\text{N}}$  and the *N*-alkyl group  $\text{Pep}^{\text{C}}$  are trans, and thus van der Waals repulsions between these groups cannot occur. In the *E* conformation, these two groups are close enough that van der Waals repulsions can result. These raise the energy of the peptide; hence, the *Z* conformation is energetically preferred.

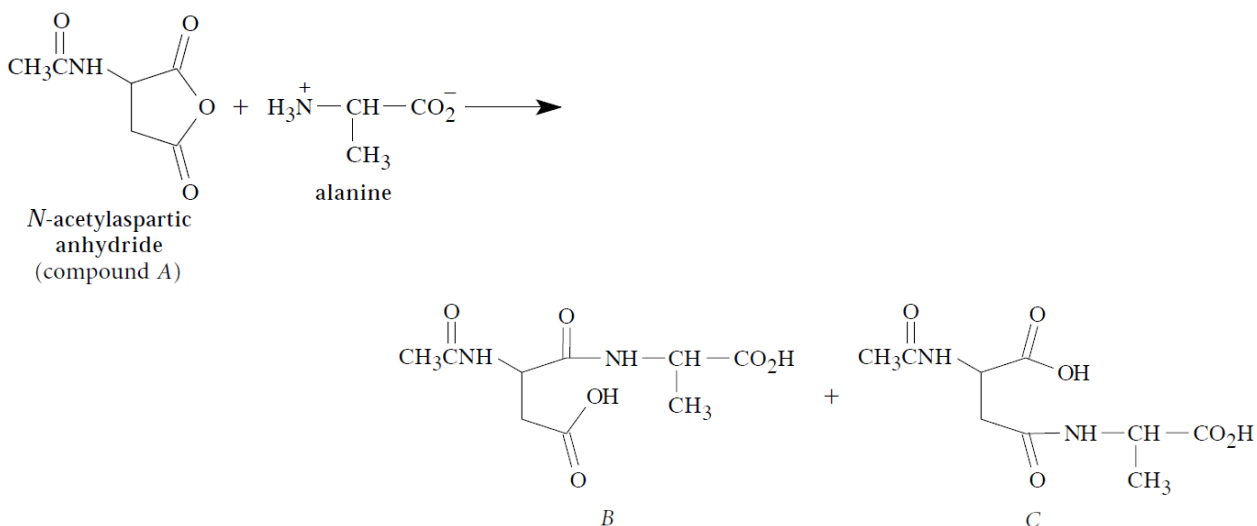


- (b) The proline nitrogen bears two *N*-alkyl groups, whereas the peptide-bond nitrogens of other residues have only one. Thus, in either the *E* or the *Z* conformation, an alkyl group is cis to the  $\text{Pep}^{\text{N}}$  group. Although the group that is cis to  $\text{Pep}^{\text{N}}$  in the *E* configuration is larger, there is a much smaller difference in energy between *E* and *Z* conformations for proline residues than there is for other residues. Hence, *E* conformations in peptide bonds are sometimes found at proline residues in proteins and peptides.

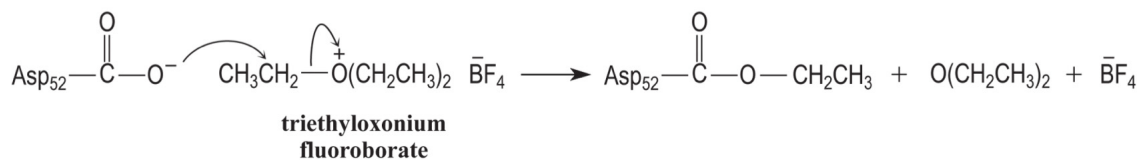


Notice that the *E* conformation of proline in a peptide forms a turn or bend in the peptide chain. Proline residues with *E* conformations are often found within turns in the three-dimensional structures of proteins.

- 26.73 The formula of compound *A* is the same as that of *N*-acetylaspartic acid minus the elements of water. Since treatment of a dicarboxylic acid with acetic anhydride is a good way to prepare a cyclic anhydride (see Eq. 20.31, text p. 973), it is reasonable to suppose that compound *A* is the cyclic anhydride of aspartic acid. When this anhydride is treated with L-alanine, the amino group of alanine can react with either of the two carbonyl groups to give either of the two isomeric peptides *B* and *C*. Both would hydrolyze to give alanine and aspartic acid (as well as acetic acid).



- 26.74 (b) (See the enzyme mechanism on p. 720 of the Study Guide and Solutions Manual.) The lysozyme reaction with triethyloxonium fluoroborate,  $\text{Et}_3\text{O}^+ \text{BF}_4^-$ , results in the formation of the ethyl ester of the carboxylate of  $\text{Asp}_{52}$ . As shown in Sec. 11.6A on text p. 508, oxonium salts are powerful alkylating agents.



The obliteration of enzyme activity could be due to either one or both of the following reasons. First, the ethyl group of the ethyl ester may block the active site between the  $\text{Asp}_{52}$  and  $\text{Glu}_{35}$  residues and thus prevent the substrate from binding. Second, the mechanism shows that the negatively charged  $\text{Asp}_{52}$  residue plays a key role in stabilizing the cationic intermediates, possibly by nucleophilic involvement. Formation of the ethyl ester eliminates the nucleophilic capability of the carboxylate group.

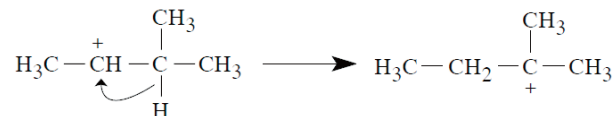


# Chapter 27

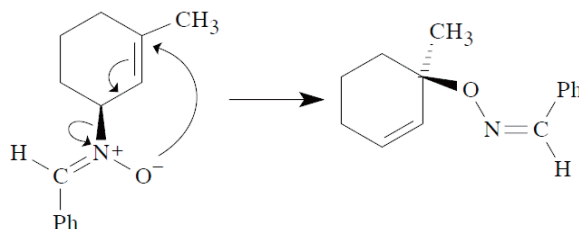
## Pericyclic Reactions

### Solutions to In-Text Problems

- 27.1 (b) This is a sigmatropic reaction; two electrons are involved.



- (d) This is a sigmatropic reaction; six electrons are involved.



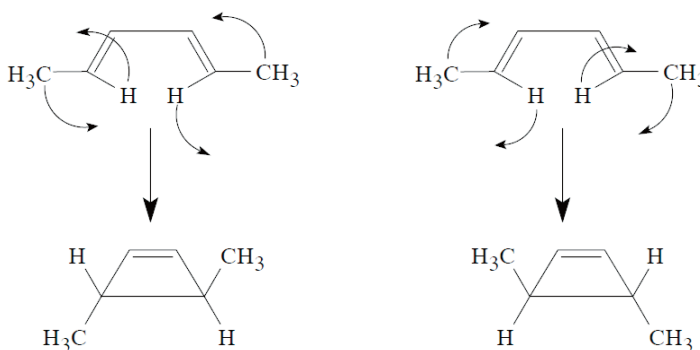
- 27.3 Because there are ten  $\pi$  electrons, there are five occupied MOs in this alkene, each containing two electrons. The MOs alternate in symmetry; the odd-numbered ones are symmetric, and the even-numbered ones are antisymmetric. Hence,  $\pi_6^*$  is antisymmetric (A); it is antibonding; and it is the LUMO and is thus one of the frontier orbitals.

- 27.5 (a) The resonance structures of the allyl radical show that the unpaired electron is shared between the terminal carbons:



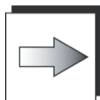
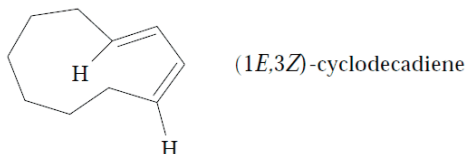
- (b) Figure 27.4, text p. 1341, shows that the unpaired electron of the allyl radical resides in the nonbonding MO, which has a node at the central carbon. The unpaired electron density therefore exists only at the carbons on either side of a node, that is, at the terminal carbons, as the resonance structures show.

- 27.7 The two different conrotatory processes are as follows: (The curved arrows indicate atomic motion, not electron flow.)



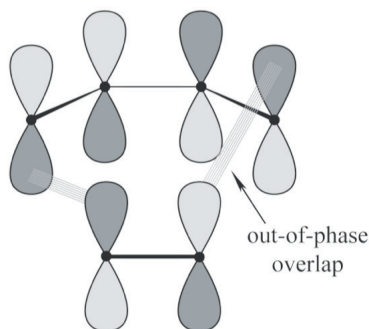
They are equally likely because they are enantiomeric; enantiomers have equal energies, and enantiomeric pathways have identical energies at all points and therefore identical rates (Sec. 7.8A, text p. 301).

- 27.9 The opening of the cyclobutene is conrotatory and therefore gives (1*E*,3*Z*)-cyclodecadiene. The trans double bond does not introduce as much strain into the large ring as was present in the starting cyclobutene.

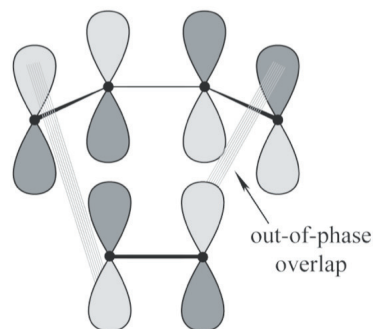


Here is one way to use models to visualize this transformation. To avoid having to build two models, construct a cyclodecane (the cyclic *alkane* with a ten-membered ring); don't worry about the missing double bond. Now connect two carbons to make a cis-fused four-membered ring. Identify the "up" hydrogens on these two carbons. Using a pencil, draw a single line across the bond that is a double bond in the starting material (even though it is a single bond in your model). Now draw two lines across each of the bonds that will become double bonds as a result of the reaction. Now break the cyclobutane ring and turn the carbons bearing the "up" hydrogens in a conrotatory manner. Examine the stereochemistry at the bonds marked with two lines; one should have an *E* configuration and the other a *Z* configuration. Voila!

- 27.11 Use the HOMO of the  $4\pi$ -electron component and the LUMO of the  $2\pi$ -electron component. The  $[4a + 2s]$  process would involve the overlap shown in (a) below. The  $[4s + 2a]$  process would involve the overlap shown in (b). In both cases an out-of-phase overlap between the  $\pi$ -electron systems is required at one end. Consequently, these processes are not allowed.

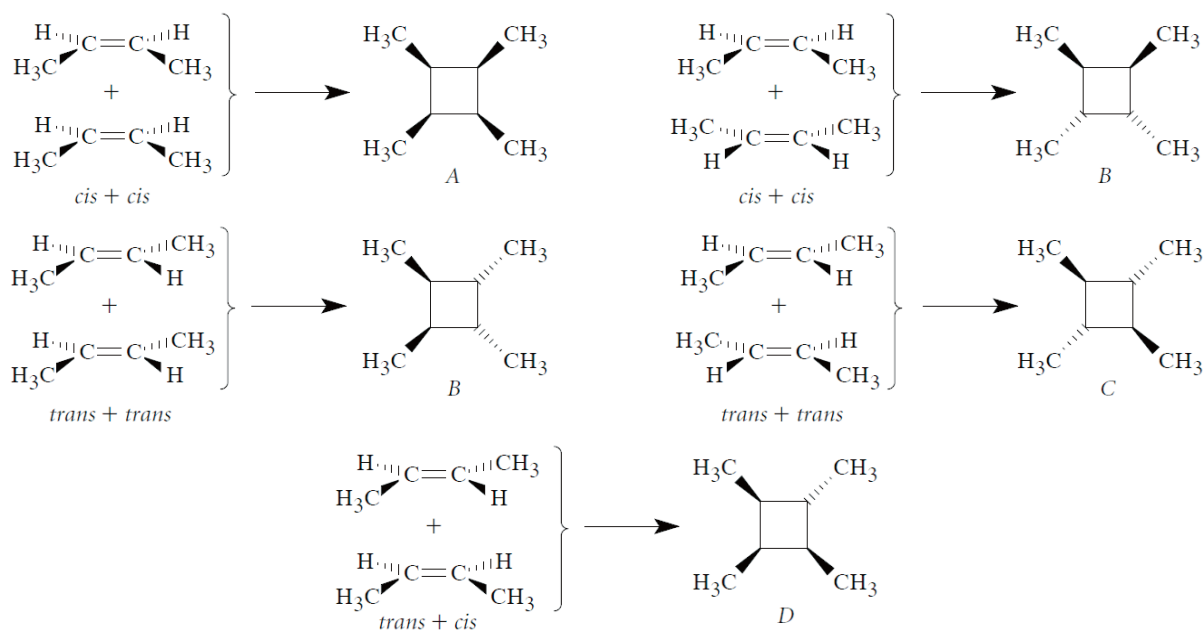
HOMO of  $4\pi$ -electron componentLUMO of  $2\pi$ -electron component

(a)  
[4*a* + 2*s*]

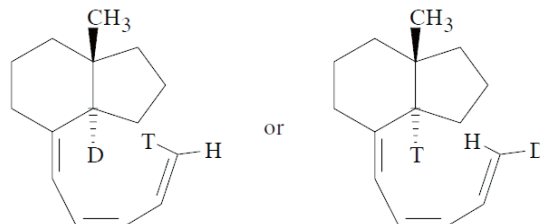
HOMO of  $4\pi$ -electron componentLUMO of  $2\pi$ -electron component

(b)  
[4*s* + 2*a*]

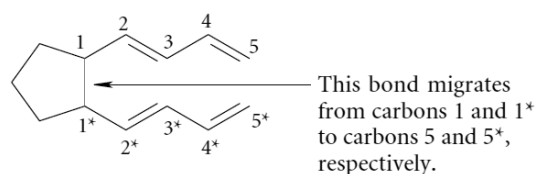
- 27.13 The four products are the diastereomeric 1,2,3,4-tetramethylcyclobutanes. Each of the pure alkene stereoisomers can undergo an allowed photochemical  $[2s + 2s]$  cycloaddition in two distinguishable ways. *Cis*-2-butene reacts to give compounds *A* and *B*; *trans*-2-butene reacts to give compounds *B* and *C*; and the mixture of *cis*- and *trans*-2-butene can give these three compounds plus a fourth, compound *D*, that results from the  $[2s + 2s]$  cycloaddition of *cis*-2-butene to *trans*-2-butene.



27.14 (b) Two other starting materials that would give the same product as in part (a):

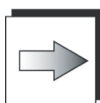
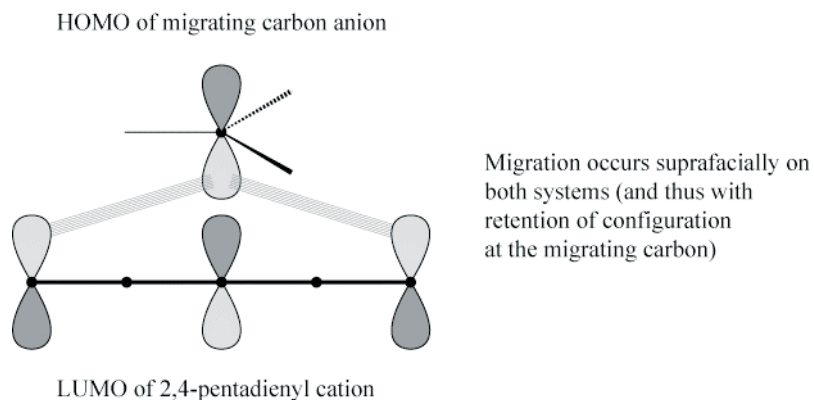


27.15 (c) This is a [5,5] sigmatropic rearrangement.



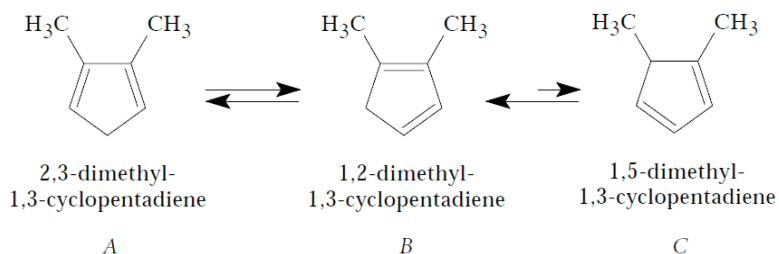
27.17 If the migration were antarafacial, the opposite stereochemical result would have been observed; that is, the 3*E* stereoisomer of the product would have the *S* configuration at the asymmetric carbon stereocenter, and the 3*Z* stereoisomer of the product would have the *R* configuration at the asymmetric carbon stereocenter. This is the result that is *not* observed.

27.18 (a) Think of the five-carbon  $\pi$ -electron system as a 2,4-pentadienyl cation, whose MOs are shown in Fig. 27.5, text p. 1342, and think of the migrating group as a carbon anion in which the unshared electron pair resides in a  $2p$  orbital. The orbitals involved in the rearrangement are the LUMO of the pentadienyl system and the HOMO of the carbon anion. The LUMO of the pentadienyl system, as shown by Fig. 27.5, is symmetric; that is, at each end of the system, the LUMO has the same phase on a given face. The HOMO of the carbon anion is simply the filled  $2p$  orbital. The migration is allowed only if the carbon anion migrates suprafacially such that each end of the pentadienyl LUMO interacts with the same lobe of the carbon anion  $2p$  orbital.

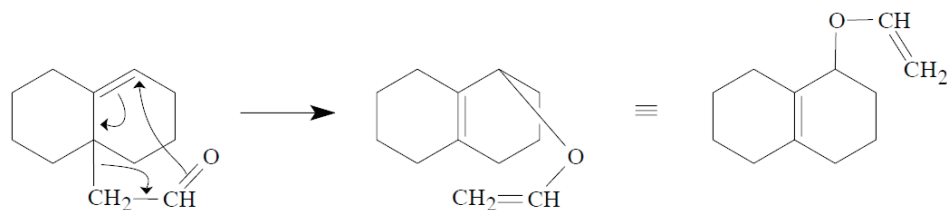


Alternatively, you can think of this problem in terms of the 2,4-pentadienyl *anion* and a methyl *cation*. The orbitals involved are now the HOMO of the anion and the LUMO of the cation. But these are the same orbitals used in the foregoing solution (only their occupancies are different); hence, the stereochemical result is the same.

- 27.19 (b) The “hydrogen walk” on 2,3-dimethyl-1,3-cyclopentadiene should proceed as shown in the following equation. Although a hydrogen that starts out on carbon-1 could migrate to four other carbons, only two of the possible products are unique. It can be argued that compounds *A* and *B* should be the predominant alkenes at equilibrium, and that compound *C* should be present in least amount. (Why? See Sec. 4.5B, text p. 144.) Remember that the selection rules have nothing to say about which compound is favored at equilibrium, only whether the equilibrium can be attained at a reasonable rate.)

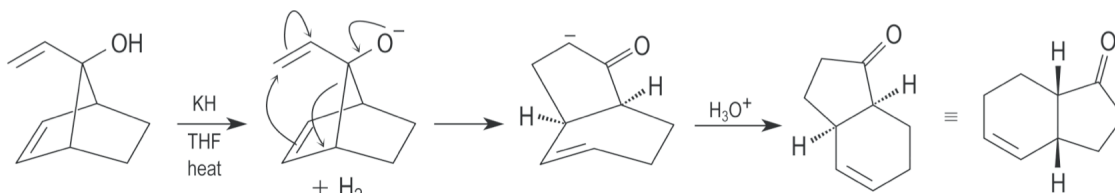


- 27.20 (b) Deduce the starting material by drawing the curved arrows for the reverse of a Claisen rearrangement:



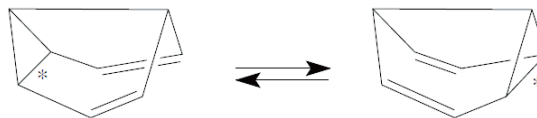
- 27.21 See Fig. 27.4, text p. 1341, for the relevant orbital diagram. The SOMOs of the two allylic radicals ( $\pi_2$ ) interact because it is these molecular orbitals that contain the unpaired electrons. Since the two orbitals are the same, they have the same symmetry, and therefore interact suprafacially on both components with positive overlap.

- 27.22 (b)

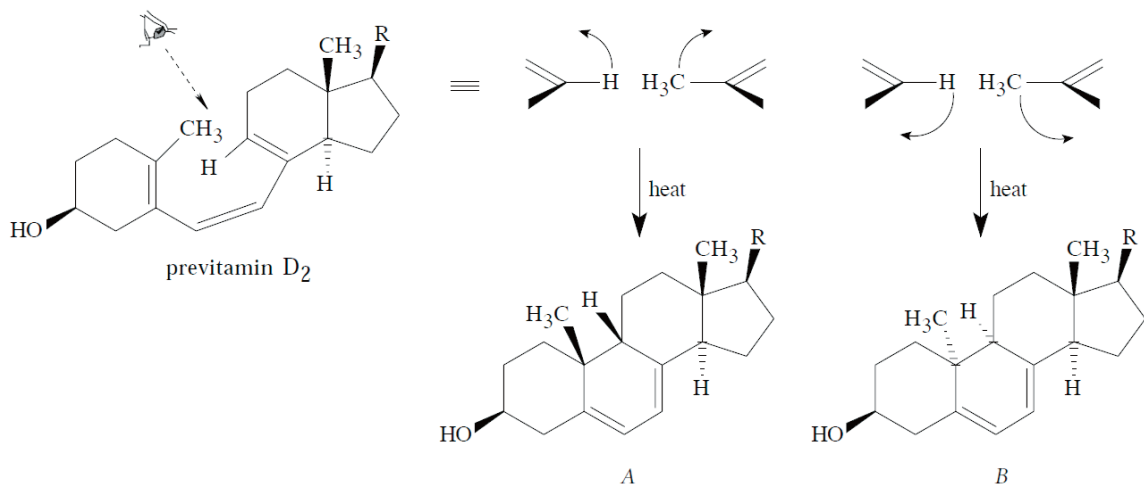




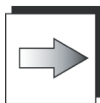
- 27.24 (a) The  $\sigma$  bond that “moves” is indicated with an asterisk (\*). It moves suprafacially on both  $\pi$  systems; [3,3] sigmatropic rearrangements are thermally allowed processes.



- 27.26 Heating should promote a disrotatory reaction; that is, the reaction should have a stereochemical course which is opposite to that of the photochemical reaction.



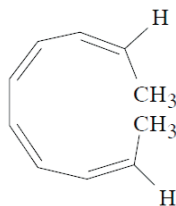
- 27.28 A [1,7] thermal sigmatropic hydrogen shift should be antarafacial. That is, a hydrogen from the methyl group migrates from a conformation in which it is “up” to the lower face of the ring, or a hydrogen from the methyl group migrates from a conformation in which it is “down” to the upper face of the ring, or both.



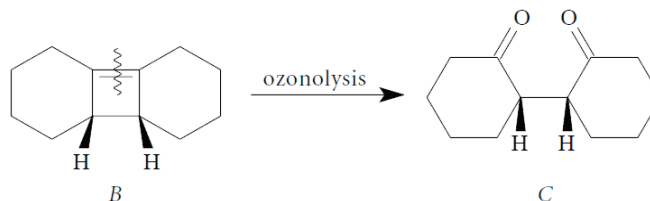
Problem 27.51 (text p. 1373) describes an effort to elucidate the stereochemistry of the previtamin D rearrangement.

### Solutions to Additional Problems

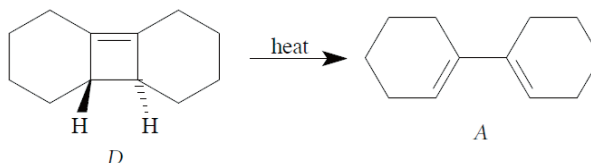
- 27.29 (b) Think of the Diels–Alder reaction as a prototype for an allowed thermal cycloaddition. If  $4n + 2$  electrons are involved, a cycloaddition is allowed thermally. If  $4n$  electrons are involved, then the thermal cycloaddition is forbidden and the photochemical cycloaddition is allowed. Therefore, a photochemical  $[8s + 4s]$  process (12 electrons) is allowed.
- 27.30 The pericyclic selection rules say *absolutely nothing* about the position of equilibrium in each case. These rules refer to *rates* of reactions, not to equilibrium constants. Other considerations must be used to decide on the position of equilibrium. The point of the problem is for you to use what you have learned about the relative energies of molecules; the molecule of lower energy is favored in each equilibrium.
- (b) The left side of the equation is favored at equilibrium because the double bonds have more alkyl branches. (Alkyl substitution stabilizes a double bond.)
- (d) The right side of the equation is favored at equilibrium because one product is aromatic and therefore particularly stable, and the other product is volatile (ethylene is a gas).
- 27.31 (b) The stereoisomer of compound *A* that also gives compound *C* on heating is the one in which both of the terminal double bonds have the *Z* configuration.



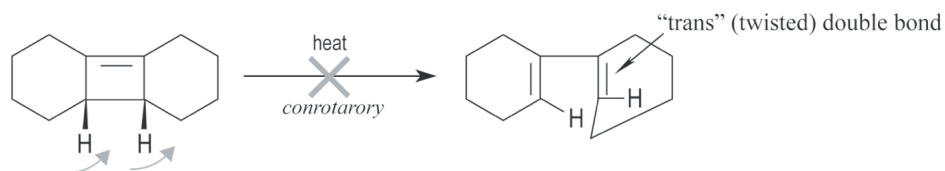
- 27.32 (b) Because a thermal suprafacial  $[1,9]$  or  $[1,13]$  methyl migration must occur with retention of configuration at the migrating carbon, the methyl group that migrates, when isotopically substituted, must have the *S* configuration in both starting material and product.
- 27.34 (a) The structure of the ozonolysis product *C* shows that compound *B* is a cyclobutene, which must be formed in a disrotatory photochemical electrocyclic reaction. This defines the stereochemistry of *B*, which, in turn, defines the stereochemistry of *C*:



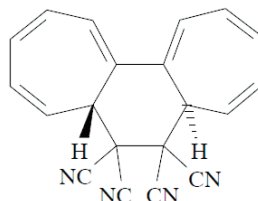
- (b) Compound *D* is the *trans*-fused stereoisomer of the cyclobutene derivative, which undergoes conrotatory opening upon heating to give compound *A*.



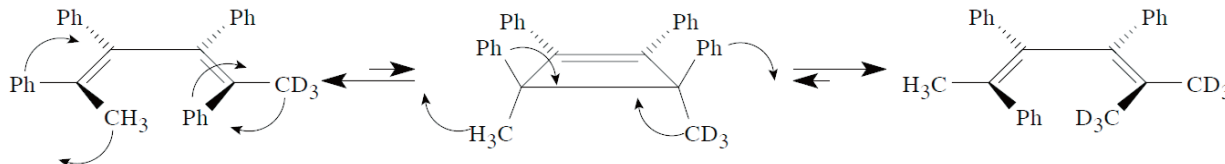
The reason that compound *B* is inert under the same conditions is that conrotatory ring opening of *B* would give a stereoisomer of *A* in which one of the cyclohexene rings would contain a *trans* double bond within a six-membered ring. This introduces so much strain that the reaction does not occur, even though it is allowed by the selection rules.



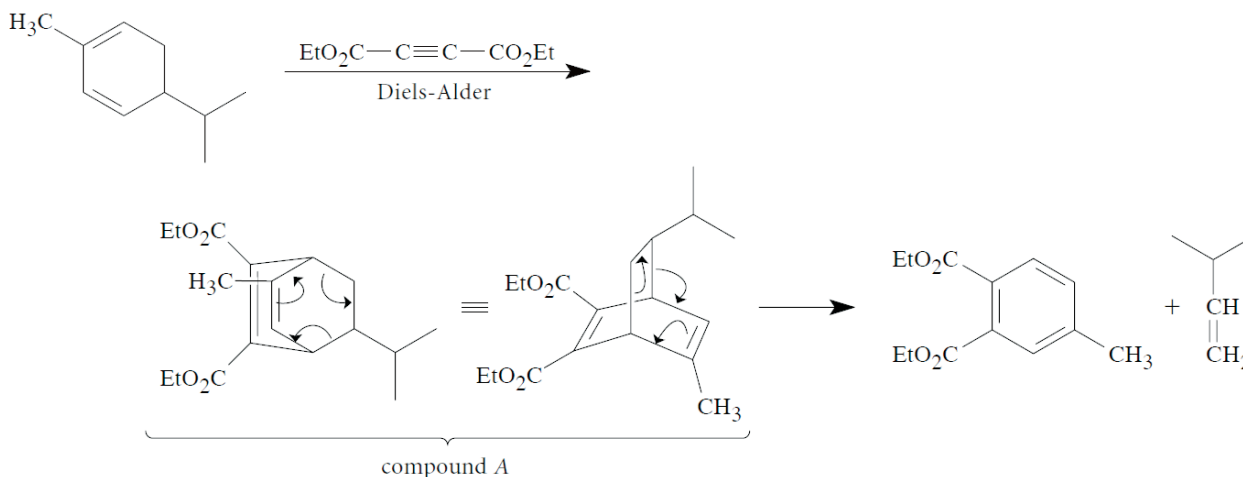
- 27.36 This cycloaddition reaction involves sixteen electrons; hence, it must be suprafacial on one component and antarafacial on the other. Thus, it must be a  $[14s + 2a]$  or a  $[14a + 2s]$  cycloaddition. The heptafulvene molecule is large enough that its  $\pi$ -electron system can twist without introducing too much strain or without losing too much  $\pi$ -electron overlap; hence, the cycloaddition is a  $[14a + 2s]$  process. In either case, the product has the following stereochemistry:



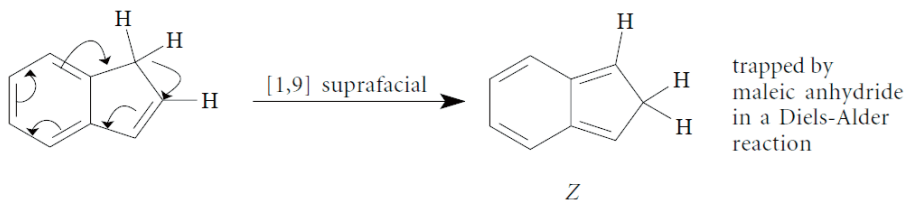
- 27.37 (a) Toluene has added stability associated with aromaticity; compound *A*, although conjugated, is not aromatic. Because any equilibrium favors the more stable compound, the added stability of toluene causes it to be strongly favored in the equilibrium.
- 27.38 (b) This reaction superficially appears to involve internal rotation about both double bonds, a process that is virtually impossible. However, a more reasonable pericyclic mechanism is available: a sequence of two conrotatory electrocyclic reactions, the first one a ring closing, and the second one a ring opening. (The curved arrows refer to the clockwise rotations of groups and not to electron flow.)



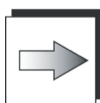
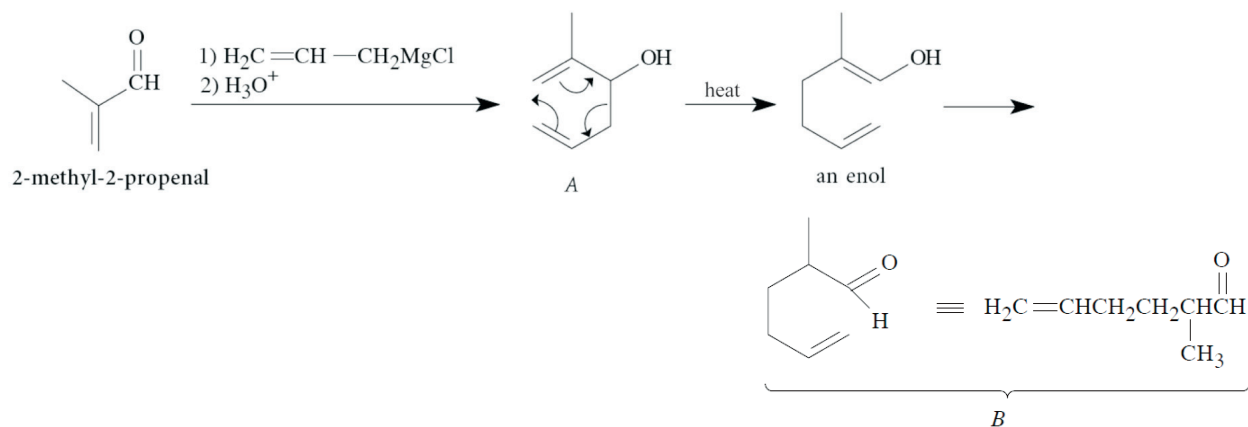
- 27.41 These transformations are very much like the last two in the solution to Problem 27.40, text p. 1370. A Diels–Alder reaction is followed by a reverse Diels–Alder reaction. The driving force for the reverse Diels–Alder is the formation of a product that is stabilized by aromaticity.



- 27.43 (c) The intermediate trapped by maleic anhydride is the tetraene *Z* formed by a [1,9] (presumably suprafacial) sigmatropic hydrogen migration.

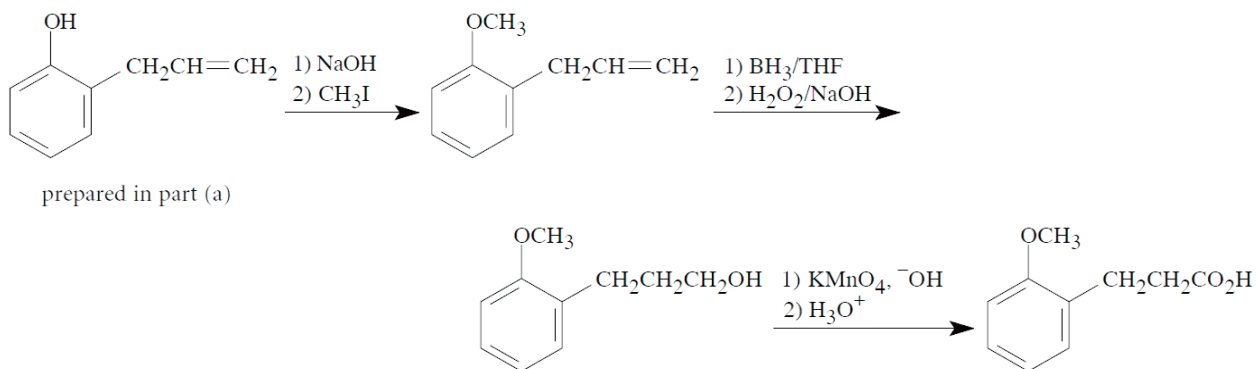


- 27.44 Compound *A* is a secondary alcohol, and the aldehyde *B* is formed from an enol intermediate (shown in parentheses) that results from a [3,3] sigmatropic (oxyCope) rearrangement.

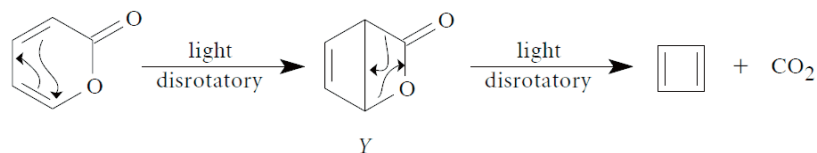


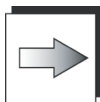
Evidently in this case the Grignard reagent undergoes mostly 1,2-addition to the  $\alpha,\beta$ -unsaturated aldehyde; none of the 1,4-addition product is formed. (See Sec. 22.10A, text p. 1101.)

- 27.46 (b) A key step in this synthesis is a Claisen rearrangement of the starting material, which is prepared in the solution to part (a)



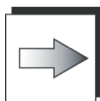
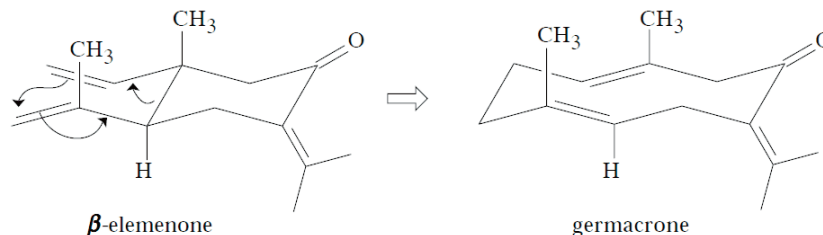
- 27.47 (b) Two successive photochemical disrotatory electrocyclic reactions account for the products.





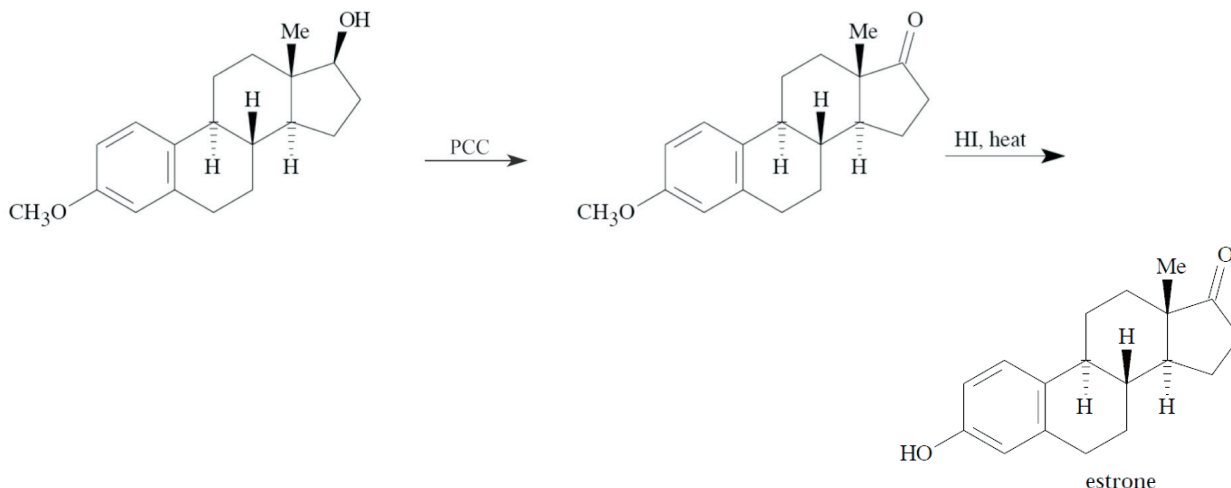
The product, the very unstable antiaromatic cyclic diene 1,3-cyclobutadiene (see text p. 729), was generated in 1972 by this sequence of reactions carried out at a temperature of 8 K in the laboratory of Professor Orville L. Chapman (1932–2004), then at Iowa State University, and later at the University of California, Los Angeles. This technique allowed the observation and characterization of 1,3-cyclobutadiene by infrared spectroscopy.

- 27.48 (b) Given that germacrone assumes a chairlike conformation in its transition state when it reacts to give  $\beta$ -elemenone, deduce the structure of germacrone by mentally reversing the Cope rearrangement.

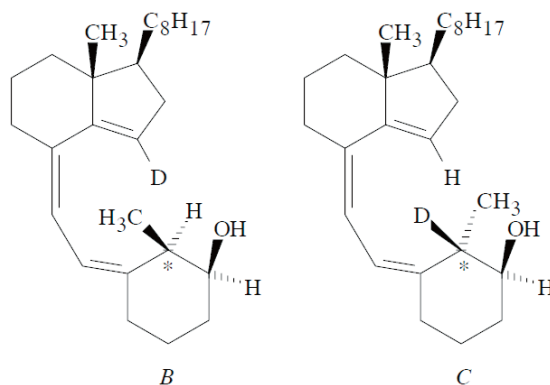


Now re-examine (or work) Problem 27.42, text p. 1370, to see why the product in that problem has *E* stereochemistry.

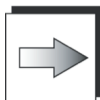
- 27.50 (b) Oxidation of the secondary alcohol and cleavage of the ether gives estrone:



- 27.51 This is a [1,7] sigmatropic rearrangement, which, according to the selection rules, should be antarafacial. (See Problem 27.28, text p. 1367, and its solution on p. 5 of this chapter.) Migration of hydrogen gives *B* and migration of deuterium gives *C*. (Presumably, the predominance of *B* is due in part to a primary isotope effect, which should favor more rapid migration of hydrogen, all things being equal.) If the rearrangements are indeed antarafacial, the stereochemistry of the products should be as follows:

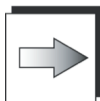


This was indeed the stereochemistry observed.



This work was carried out to adduce evidence for the stereochemistry of the previtamin D rearrangement to vitamin D (Eq. 27.39, text p. 1366). Compound A was constructed to be a “model” for previtamin D. As noted in Problem 27.28, the structure of the previtamin itself does not reveal the stereochemistry of the rearrangement.

- 27.54 (a) If the formation of benzene were concerted, it would have to be a thermal disrotatory electrocyclic ring-opening reaction involving four electrons.
- (b) The reaction that gives benzene is not allowed by the selection rules; therefore, it does not occur. In spite of the high degree of strain of Dewar benzene, and in spite of the great stability of benzene, Dewar benzene is effectively constrained to exist by the selection rules!



Prismane, or Ladenburg benzene, which is discussed on text p. 718 and 1348, is another very unstable constitutional isomer of benzene that is effectively trapped into existence because its concerted conversion into benzene would violate the selection rules for pericyclic reactions.