ELIMINATION REACTIONS OF ALKYL HALIDES, ALCOHOLS, AND RELATED COMPOUNDS

8.1. When an alcohol molecule is heated with a strong acid such as H₂SO₄ or H₃PO₄, dehydration (loss of water) takes place to produce the most stable alkene that can be formed. Any one of the hydrogen atoms attached to the carbon atoms adjacent to the one bearing the OH group can be removed to form the double bond. Alkene stability follows these general trends:

- more highly substituted > less highly substituted
- trans > cis and (E) > (Z)
- endocyclic (inside the ring) > exocyclic (outside the ring)

In rings with fewer than nine atoms, a double bond can exist as only one isomer (the bonds that are in the ring are cis). In an acyclic compound, both (E) and (Z) isomers are likely with the (E) isomer normally predominant.

![Diagram](a)

b.

![Diagram](b)

8.2. As noted in the solution to Exercise 8.1, a molecule of water is eliminated when an alcohol is heated with strong mineral acid. Any of the hydrogen atoms attached to the carbon atoms adjacent to the one bearing the OH group can be removed to form the double bond. The major product in this exercise is the one with the most highly-substituted double bond, compound A, below.

![Diagram](c)
8.3. The amount of heat evolved during hydrogenation of an alkene double bond is inversely proportional to the stability of the double bond undergoing addition. Stability follows the following order: tetrasubstituted > trisubstituted > disubstituted > monosubstituted. Also:
- trans > cis
- (E) > (Z)
- endocyclic (inside the ring) > exocyclic (outside the ring)

8.4. For compounds that have an exocyclic double bond, the attached alkenyl group is treated as any substituent. Its name is made by appending the suffix “ylidene” to the name of the corresponding alkyl group root (eth ⇒ ethylidene; prop ⇒ propylidene, and so on). When the exocyclic double bond has only one carbon atom outside the ring, the substituent name is “methylen.” An exocyclic double bond is sometimes required to be classified as (E) or (Z), too

a. This compound has seven carbon atoms in the ring, and there are no double or triple bonds within the ring. The root word is cycloheptane.

The exocyclic double bond is connected to a single carbon atom, so the substituent is “methylen,” and its point of attachment defines C1 of the ring. A chlorine atom is attached at C2, which has the (S) configuration. The name of this molecule is (S)-2-chloro-1-methylenecycloheptane.

b. This compound has five carbon atoms in the ring, and there are no double or triple bonds within the ring. The root word is cyclopentane.

The exocyclic double bond is connected to a two-carbon fragment, so the substituent is “ethylen.” The name of this molecule is ethylenecyclopentane.

c. This compound has six carbon atoms in the alicyclic ring, and there are no double or triple bonds within the ring. The root word is cyclohexane.

The principal functional group (alcohol) defines C1 of the ring. The exocyclic double bond is connected to a carbon atom that bears the phenyl ring, so the substituent is “benzylen.” The double bond has the (E) geometry, so the name of this molecule is (E)-3-benzylenecyclohexanol.

8.5. The dehydrohalogenation reaction of the 2′ alkyl halide shown in this exercise proceeds via the E2 pathway: The substrate is an alkyl halide that has a proton attached adjacent to the carbon atom bearing the leaving group, and the reaction conditions include strong base and heat. An E2 reaction requires that the proton to be removed is anti to the leaving group.
8.5. (continued)

Start with the given conformation, and then rotate the carbon atom on the right side of the molecule through the various angles. A staggered conformation is required so that the substituents are anti to each other.

The conformation having the proton and leaving group anti (shown in the box directly above) is the one that undergoes the E2 reaction. In this conformation, the proton is removed by base, which causes the movement of electrons that displace the leaving group. The product is the (Z) alkene.

8.6. The reaction in this exercise proceeds by an E2 pathway: The substrate is an alkyl halide that has protons attached to the carbon atoms adjacent to the one with a leaving group, and the reaction conditions include strong base and heat. The E2 reaction of a bromocyclohexane derivative requires that the proton and leaving group be trans to one another as well as diaxial. Therefore, the given substrate must first undergo a ring flip so that the reactive groups assume the proper orientation (shown in color, below right).

After the correct orientation is achieved, the axial proton is removed by base, which causes the movement of electrons that displace the leaving group.

8.7. As shown in the solution to Exercise 8.6, you first have to look at the possible conformations that orient the H and Br atoms in the axial positions trans to each other. For the cis-1-bromo-4-tert-butylcyclohexane molecule, the most stable conformation already has the bromine atom in the axial position. Recall that the tert-butyl group is always equatorial (Section 3.3c). Elimination is therefore facile.
8.7. (continued)

For the trans isomer, a ring flip has to occur first in order to place the bromine atom in the axial position. The tert butyl group prevents a ring flip from happening, however, so a less stable boat conformation has to form so that the reaction can proceed. Energy is required to create this boat conformation, so the overall transformation—the E2 reaction—proceeds more slowly than it does for the cis isomer.

8.8. The course of dehydration can be different under acidic and basic conditions, as illustrated by the reactions in this exercise. If an alcohol molecule is first converted to its alkyl sulfonate ester derivative, a base can be used for the elimination process, which provides more control of stereochemistry (and sometimes regiochemistry) because the proton and leaving group must be anti. This fact accounts for the possible formation of the less stable alkene isomer under E2 conditions.

When dehydration is carried out under acid conditions, a carbocation is formed, so besides elimination, rearrangements of the carbon framework can occur. Shown below is the direct elimination reaction (no rearrangement).

Even when rearrangement occurs, as shown in the following equation (step R), the E isomer is formed.
8.9. When a vicinal dihaloalkane is treated with strong base, an alkyne forms if there are also two hydrogen atoms attached to the same carbon atoms. The base in this exercise also deprotonates the carboxylic acid groups (shown with dashed arrows in step 1a). Sulfuric acid is added in the second step to protonate the carboxylate groups, which yields the neutral diacid product.

8.10. The conjugate base of the acid reagent is bromide ion, which can react with the respective carbocation centers or with a proton attached adjacent to the respective carbocations, which leads to formation of a π bond in each case. As in Exercise 8.8, either carbocation leads to formation of the same alkene product when elimination occurs.

8.11. Follow the procedures illustrated in Examples 8.3–8.5.

a. The starting compound is a 3° alkyl sulfonate ester and the reagent is a strong base. The elimination pathway will therefore predominate. The substitution product will not be observed to an appreciable extent in this reaction.

\[
\begin{align*}
\text{CH}_3 & \quad \text{SO}_{2}\text{CH}_3 \\
\quad & \quad \text{NaOCH}_3 \\
\quad & \quad \text{DMSO} \\
\end{align*}
\]
b. The starting compound is a 1° alcohol, and the reagent is a strong mineral acid with a good nucleophile as its conjugate base. The substitution product will predominate.

\[
\text{OH} \quad \xrightarrow{\text{HI}, \Delta} \quad \text{I} \quad + \quad \text{CH}_2=\text{CH}_2
\]

c. The starting compound is a 3° alkyl halide, and the reagent is a weak base in a protic solvent. These conditions are ideal for the \( S_n1 \) pathway. Some elimination product will be formed because the \( S_n1 \) and \( E1 \) mechanisms are linked. If elimination were desired, a strong base would have been used as the reagent.

\[
\text{Br} \quad \xrightarrow{\text{CH}_3\text{SH}, \text{CH}_2\text{OH}} \quad \text{SCH}_3 \quad + \quad \text{CH}_2=\text{CH}_2
\]

\text{major}

8.12. All of the elimination reactions shown in Table 8.3 require the presence of a basic site in the enzyme that catalyzes the reaction. If the substrate is an alcohol, then an acid site is needed to provide a proton that makes the \( \text{OH} \) group a better leaving group. Each of last two entries has a good leaving group already present, although the phosphate group may pick up a proton to make it a better one.
8.13. Follow the procedures outlined in the solution to Exercise 1.18.

\[
\begin{align*}
\text{1-Pentene} & \quad \text{2-Methyl-1-butene} & \quad \text{3-Methyl-1-butene} \\
\text{cis-2-Pentene} & \quad \text{trans-2-Pentene} & \quad \text{2-Methyl-2-butene}
\end{align*}
\]

8.14. Follow the procedures given in the solution to Exercise 8.1. If one isomer will predominate, its structure is shown below in color.

a. The trans isomer will predominate.

\[
\begin{align*}
\text{OH} & \quad \rightarrow \quad \text{trans-3-Heptene} + \text{cis-3-Heptene} \\
\end{align*}
\]

b. The trisubstituted alkene will predominate.

\[
\begin{align*}
\text{OH} & \quad \rightarrow \quad \text{2-Methyl-2-pentene} + \text{2-Methylpentene}
\end{align*}
\]

c. Only one alkene can form in the six-membered ring. The name of the product derives from the parent compound naphthalene.

\[
\begin{align*}
\text{OH} & \quad \rightarrow \quad \text{1,2-Dihydronaphthalene} + \text{Naphthalene}
\end{align*}
\]

8.15. Dehydrohalogenation reactions proceed via the E2 pathway: The substrate is an alkyl halide with protons attached to the carbon atom(s) adjacent to the one bearing the leaving group, and the reaction conditions include strong base and heat. An E2 reaction requires that the proton to be removed is anti to the leaving group. Therefore, the conformations of the starting compound need to be drawn in some cases to check the stereochemical relationships. If protons are attached to more than one carbon atom adjacent to the one with the leaving group, then more than one product is likely to form. Draw each possible product with a double bond and then choose the one that is most stable (the criteria are listed in the solution to Exercise 8.1).
8.15. (continued)

a. Elimination of HX from a molecule with the halogen atom at C1 yields the terminal alkene.

\[
\text{Br} \quad \xrightarrow{\text{KOH, ethanol}} \quad \text{1-Hexene}
\]

b. Elimination of HX from a cycloalkyl halide having the halogen atom attached to a 3\text{o} carbon atom gives the endocyclic cycloalkane preferentially.

\[
\text{Br} \quad \xrightarrow{\text{KOH, ethanol}} \quad \text{Methylene cyclohexane} + \text{1-Methylcyclohexene, major}
\]

c. Elimination of HX from a cycloalkyl halide with the halogen atom attached to a 2\text{o} carbon atom gives an endocyclic cycloalkene. The chair conformations of the starting compound should be drawn to make certain that a proton is in the axial position on the adjacent carbon atom(s). Formation of the more highly-substituted alkene will predominate if more than one isomer can form.

\[
\text{Br} \quad \xrightarrow{\text{KOH, ethanol}} \quad \text{1-Methylcyclohexene, major} + \text{3-Methylcyclohexene}
\]

d. Elimination of HX from an unsymmetrical alkyl halide having the halogen atom attached to a 2\text{o} carbon atom can give multiple products that are structural isomers. The major product has the most highly-substituted double bond and the (E) or trans geometry.

\[
\xrightarrow{\text{KOH, ethanol}} \quad \text{1-Butene} + \text{trans-2-Butene, major} + \text{cis-2-Butene}
\]

e. Elimination of HX from an alkyl halide having the halogen atom attached to a 2\text{o} carbon atom can give multiple products. The major one has the most highly-substituted double bond and the (E) or trans geometry. In this case, the iodine atom is attached to the middle carbon atom, which eliminates the possibility that structural isomers will form.

\[
\xrightarrow{\text{KOH, ethanol}} \quad \text{trans-3-Heptene, major} + \text{cis-3-Heptene}
\]

8.16. Questions about rates of competing reactions require that you consider the possible conformations in which a molecule can exist. An elimination reaction carried out under basic conditions requires an anti relationship between the hydrogen atom to be removed and the leaving group. The most stable conformation of (1R,2R)-1-bromo-1,2-diphenylpropane has the H and Br atoms gauche to one another.
8.16. (continued)

To undergo elimination, this isomer undergoes rotation to a less stable conformation in which the phenyl rings are gauche. Because elimination occurs through a conformation other than the most stable one, the reaction will be slowed.

rotation about the carbon-carbon bond

On the other hand, the most stable conformation of the (1S,2R) isomer has the bromine and hydrogen atoms in the anti orientation already, which is ideal for the E2 reaction. Therefore, it reacts much more rapidly than the (1R,2R) isomer does.

8.17. Follow the procedures given in the solution to Exercise 8.3. For the compounds in part (d.), the double bond stability is related to ring size. The more strained the ring is, the less stable the double bond is because its angles deviate from the ideal angle of 120°. The six-membered ring is the most stable of the ones shown, therefore it evolves the least amount of heat during hydrogenation.

a. 

- dissubstituted exocyclic
- dissubstituted endocyclic
- trisubstituted
- tetrsubstituted

b. 

- monosubstituted
- dissubstituted geminal
- dissubstituted (E)
- trisubstituted

c. 

- dissubstituted exocyclic
- dissubstituted endocyclic
- trisubstituted exocyclic
- trisubstituted endocyclic

d. 

less heat evolved
(more stable double bond)
8.18. Acid-catalyzed dehydration reactions occur via formation of a carbocation intermediate after protonation of the hydroxyl group (step 1) and dissociation of a water molecule (step 2). Recall that a carbocation may rearrange, which is what occurs during this transformation [step R below]. Elimination of a proton from the carbon atom adjacent to the more stable 3° carbocation produces the endocyclic double bond, which is more stable than its exocyclic isomer.

8.19. Elimination reactions that occur under basic conditions are not normally subject to rearrangement processes. All that is required is the presence of a good leaving group and the use of strong base. To convert an OH group to a good leaving group, prepare the alkyl sulfonate ester, and then use base to promote elimination via the E2 pathway.

8.20. To decide what role a reagent plays in a given reaction, classify the transformation according to its fundamental type. If substitution occurs, the reagent is considered to be a nucleophile. A reagent is acting as a base if the reaction involves elimination or a proton transfer process.

a. The following is an E2 reaction, so methoxide ion functions as a base.

b. The following is a Sn2 reaction, so methoxide ion is a nucleophile.

c. The following is a proton transfer process, so methoxide ion is acting as a base.
8.21. The mechanism involved in the conversion of an acid chloride to a ketene follows the same course as any E2 process. The base triethylamine reacts with a proton attached to the carbon atom adjacent to the one bonded to chlorine. Displacement of the Cl⁻ leaving group generates the double bond.

\[
\text{Et}_3\text{N}^+ \quad \text{CH}_3
\]

8.22. The mechanism for this elimination reaction is similar to the mechanism observed for dehydrohalogenation reactions. The base (methoxide ion) reacts with the hydrogen atom attached to the carbon atom adjacent to nitrogen, which bears the leaving group, acetate ion. Displacement of acetate ion generates the carbon-nitrogen triple bond.

\[
\text{OAc}^- \quad \text{CH}_3 \quad \text{ON}^+ \quad \text{R-CN} + \text{CH}_3\text{OH} + \text{AcO}^- 
\]

8.23. Substitution reactions occur when a substrate molecule has a good leaving group attached to a carbon atom with \(sp^3\)-hybridization, and a good nucleophile is also present. An S_n2 process occurs with 1° and many 2° substrates. A chiral center attached to the leaving group undergoes inversion of configuration. The S_n1 reaction occurs most readily with 3° substrates (and 2° substrates in solvolysis processes). The stereoechemical outcome of an S_n1 reaction is racemization.

Elimination reactions occur when a substrate molecule has a good leaving group attached to a carbon atom with \(sp^3\)-hybridization, and a strong base is also present. The E2 process occurs with all types of alkyl halides and alkyl sulfonate esters. The E2 process requires that the leaving group and the proton on an adjacent carbon atom are anti to each other in terms of the molecule's conformation. The E1 mechanism accompanies the S_n1 mechanism, especially when the base is a poor nucleophile.

a. In this reaction, a 2° bromocyclohexane derivative is treated with strong base in a protic solvent, so the E2 reaction takes place. For this mechanism, both the Br and H atoms must be anti and axial, so a ring flip occurs before elimination takes place.

\[
\text{H} \quad \text{H} \quad \text{Br} \quad \text{H} \quad \text{H} \quad \text{Br} \quad \text{KOH, EtOH, } \Delta 
\]

b. The leaving group in this substrate molecule is attached to a carbon atom with \(sp^3\)-hybridization and the nucleophile is only a moderate base, so no reaction takes place.

\[
\text{Br} \quad \text{KCN, DMF, } \Delta \quad \text{N.R.} 
\]

c. This reaction is a substitution process that results in opening of an epoxide ring. The nucleophile (azide ion) can react at either carbon atom because the degree of substitution at each is the same.

The configuration of the carbon atom at which the nucleophile reacts is inverted, and the configuration of the other carbon atom is retained. The starting material is meso, which is not optically active, so the product must be racemic (overall mixture not optically active).
8.23. (continued)

d. In this reaction, a primary, benzylc alkyl chloride is treated with a strong basic nucleophile. There is no proton on the carbon adjacent to the one with the leaving group, so elimination cannot occur. Substitution therefore takes place.

\[
\text{meso} \quad \overset{\text{HN}_3}{\longrightarrow} \quad \overset{\text{H}_2\text{C}}{\text{(S)}} \overset{\text{H}}{\text{O}} \overset{\text{H}}{\text{(R)}} \overset{\text{H}}{\text{N}}_3 + \overset{\text{H}_2\text{C}}{\text{(R)}} \overset{\text{H}}{\text{O}} \overset{\text{H}}{\text{(S)}} \overset{\text{H}}{\text{N}}_3
\]

(e) In this reaction, a 3\(^\circ\) alcohol is treated with strong acid having a poorly nucleophilic conjugate base. The E1 mechanism occurs to give the more stable alkene, which has an endocyclic double bond.

\[
\text{HO} \quad \overset{\text{H}_3\text{PO}_4, \Delta}{\longrightarrow} \quad \overset{\text{achiral}}{\text{H}}
\]

f. In this reaction, a 2\(^\circ\) alcohol is treated with strong acid that has a good nucleophile as its conjugate base, so substitution most likely occurs. If this process were meant to be an elimination process, then a reagent such as sulfuric or phosphoric acid would have been employed.

\[
\text{-OH} \quad \overset{\text{HBr}}{\longrightarrow} \quad \overset{\text{achiral}}{\text{H}}
\]

g. In this reaction, a 2\(^\circ\) alcohol is first converted to its mesylate derivative, which reacts in the same manner as a 2\(^\circ\) alkyl halide. The use of strong base in a protic solvent leads to elimination via the E2 pathway. Because there are several protons attached to the carbon atoms adjacent to the one with the leaving group, the most stable double bond will be formed. Therefore, the disubstituted alkene with the (E) geometry is produced.

\[
\text{OH} \quad \overset{1. \text{CH}_3\text{SO}_2\text{Cl, NEt}_3}{\longrightarrow} \quad \overset{\text{achiral}}{\text{OH}} \quad \overset{2. \text{KOH, EtOH, } \Delta}{\longrightarrow} \quad \overset{\text{achiral}}{\text{CH}_3\text{SO}_2\text{Cl}}
\]

h. In this reaction a 2\(^\circ\) alcohol is treated with phosphorus tribromide, a reagent used for substitution reactions to convert an alcohol to a bromoalkane.

\[
\text{HO} \quad \overset{\text{PBr}_3, \Delta}{\longrightarrow} \quad \overset{\text{achiral}}{\text{Br}}
\]

i. In this reaction, a 2\(^\circ\) alcohol is treated with sodium hydride, which generates the corresponding alkoxide ion in step 1. This species is a nucleophile and replaces the iodine atom in 1-iodopropane via the Sn2 pathway. This is an example of the Williamson ether synthesis.

\[
\text{OH} \quad \overset{1. \text{NaH, DMF}}{\longrightarrow} \quad \overset{\text{repetition}}{\text{1-CH}_3\text{CH}_2\text{CH}_3} \overset{2. \text{CH}_3\text{CH}_2\text{CH}_2\text{I}}{\longrightarrow} \quad \overset{\text{OH}}{\text{H}_3\text{C}}\overset{\text{O-CH}_2\text{CH}_2\text{CH}_3}{\text{CH}_2\text{CH}_3}
\]
8.23. (continued)

In this reaction, a 3° alkyl bromide is treated with strong base, so the E2 reaction occurs. The Br and H atoms in the starting compound must be anti, but the product is achiral and symmetrical at one end, so no geometric isomers exist. Because there are several protons beta to leaving group, the most highly substituted double bond that can form is generated.

8.24. The reaction coordinate diagram for the dehydration of tert-butyl alcohol reflects the mechanism of the reaction, which is shown below: (1) protonation of the OH group, (2) dissociation of a water molecule, and (3) removal of a proton to form the double bond. The reaction coordinate diagram should therefore have maxima that correspond to the activation barriers for the three steps.

- Step 1 is an acid-base equilibrium that lies in the direction of the protonated alcohol, which is a weaker acid than sulfuric acid. This first step has a small free energy of activation.
- Step 2 has a large free energy of activation because this step leads to formation of the high-energy carbocation intermediate; it is the slow step in the transformation.
- Step 3 has a small free energy of activation because the carbocation will react quickly to form product or to regenerate the protonated alcohol.
- The free energy of the reaction, $\Delta G^\circ$, is the difference between the energies of the reactants and products.

8.25. If an alkene is to be prepared by an E2 reaction from an organohalide, then possible starting materials are conceptualized by adding a hydrogen atom to one end of the double bond, and a bromine atom to the other end in each of the two possible orientations (the added atoms are shown in color in the following structures).

Once you have identified the possible starting materials (make certain to consider stereoisomers, especially for cyclic compounds), draw structures for the alkenes that will be formed and decide which isomer is expected to be the major one. The best starting compounds are shown in boxes.
8.25. (continued)
a. The best way to prepare 1-methylcyclohexene via dehydrohalogenation starts with either 1-bromo-1-methylcyclohexane or cis-1-bromo-2-methylcyclohexane.

\[
\begin{align*}
\text{1-Methylcyclohexene} & \xrightarrow{\text{KOH, ethanol}} \text{major} \\
\text{cis-1-Bromo-2-Methylcyclohexane} & \xrightarrow{\text{KOH, ethanol}} \text{major} \\
\text{1-Bromo-1-Methylcyclohexane} & \xrightarrow{\text{KOH, ethanol}} \text{major}
\end{align*}
\]

b. The best way to prepare \textit{trans}-5-methoxy-2-pentene via dehydrohalogenation starts with 4-bromo-1-methoxypentane as the starting material.

\[
\begin{align*}
\text{trans-5-Methoxy-2-pentene} & \xrightarrow{\text{KOH, ethanol}} \text{major} \\
\text{4-Bromo-1-Methoxypentane} & \xrightarrow{\text{KOH, ethanol}} \text{major, } 50:50
\end{align*}
\]

c. The best way to prepare \textit{(E)}-3-methyl-3-heptene via dehydrohalogenation starts with 4-bromo-3-methylheptane as the starting material.

\[
\begin{align*}
\text{(E)-3-Methyl-3-heptene} & \xrightarrow{\text{KOH, ethanol}} \text{major} \\
\text{4-Bromo-3-Methylheptane} & \xrightarrow{\text{KOH, ethanol}} \text{major}
\end{align*}
\]
8.26. Follow the procedures outlined in the solution to Exercise 8.23.

a. In this reaction, a 2'-alcohol is first converted to its tosylate derivative, so it will react in the same manner as a 2'-alkyl halide. The use of strong base in a protic solvent implies elimination via the E2 pathway. The leaving group and the proton to be removed must be anti to each other, and both must be in axial positions. Therefore, the disubstituted double bond is formed.

b. In this reaction, a 2'-bromoalkane is treated with strong base, so the E2 reaction takes place. The product with the most stable double bond [disubstituted and (E)] is formed.

c. In this reaction, a 3'-alcohol is treated with strong acid that has a poorly nucleophilic conjugate base, so the E1 mechanism occurs. Elimination gives the most stable alkene possible, which is tetrasubstituted.

d. In this reaction, a 2'-alcohol is treated with strong acid that has a good nucleophile as its conjugate base, so substitution occurs. There are no protons on the carbon atoms adjacent to the alcohol group, so elimination cannot occur anyway.

e. In this reaction a 3'-alkyl bromide is treated with a good nucleophile that is also a weak base. A protic solvent is used so the SN1 pathway is indicated. The chiral center in this molecule is not attached to the leaving group, so its configuration is not affected.

f. In this reaction, a 1'-alcohol is first treated to form its mesylate derivative. Azide ion is a good nucleophile and DMF is an aprotic solvent, so the SN2 mechanism is likely. The chiral center in this molecule is not attached to the leaving group, so its configuration is not affected.
8.26. (continued)

g. In this reaction, a 3'- alcohol is treated with strong acid that has a poorly nucleophilic conjugate base, so the E1 mechanism occurs. Rearrangement can also take place (see Exercise 8.18 for a similar example). Two isomers are formed. An exocyclic double bond is less stable than an endocyclic one, but in this case, the exocyclic double bond is tetrasubstituted, so it may form to an appreciable extent.

\[
\begin{array}{c}
\text{OH} \quad \xrightarrow{\text{H}_2\text{SO}_4, \Delta} \quad \text{both achiral}
\end{array}
\]

h. In this reaction a vicinal dichloroalkane is treated with very strong base; a proton is also attached to each carbon atom, so two E2 reactions occur to produce the corresponding alkyne.

\[
\begin{array}{c}
\text{Cl} \quad \text{Cl} \quad \xrightarrow{\text{NaNH}_2, \text{THF}, \Delta} \quad \text{achiral}
\end{array}
\]

i. In this reaction, a 2'- chlorocyclohexane derivative is treated with strong base, so the E2 reaction takes place. The Cl and H are already anti and diaxial, so elimination occurs to form the trisubstituted double bond.

\[
\begin{array}{c}
\text{Cl} \quad \text{H} \quad \xrightarrow{\text{KOH, EtOH, } \Delta} \quad \text{achiral}
\end{array}
\]

j. In this reaction, a 2'' alkyl bromide is treated with an excellent nucleophile in an aprotic solvent, so the S$_2$2 mechanism is likely. The carbon atom bearing the leaving group is chiral, so inversion of its configuration occurs. The stereochemistry of the other chiral carbon atom is not affected, so its configuration is retained.

\[
\begin{array}{c}
\text{(R)} \quad \text{(R)} \quad \xrightarrow{\text{NaI, acetone}} \quad \text{inversion} \quad \text{retention}
\end{array}
\]

8.27. In an exercise such as this, the first step is to summarize the given information by constructing a flow chart.

\[
\begin{array}{c}
\text{A optically active} \\
\text{CH}_3\text{O}^-, \text{DMF} \quad 25 \degree \text{C}
\end{array}
\]

\[
\begin{array}{c}
\text{D optically active} \\
\text{D' not optically active}
\end{array}
\]

\[
\begin{array}{c}
\text{not optically active}
\end{array}
\]

\[
\begin{array}{c}
\text{B not optically active}
\end{array}
\]

\[
\begin{array}{c}
\text{1. MsCl, NEt}_3, \text{CH}_2\text{CH}_2
\end{array}
\]

\[
\begin{array}{c}
\text{2. KOH, ethanol, } \Delta
\end{array}
\]

\[
\begin{array}{c}
\text{1. NaH, DMF}
\end{array}
\]

\[
\begin{array}{c}
\text{2. CH}_3\text{I}
\end{array}
\]

\[
\begin{array}{c}
\text{C not optically active}
\end{array}
\]

\[
\begin{array}{c}
\text{H}_2\text{O, methanol} \quad 35 \degree \text{C}
\end{array}
\]
8.27. (continued)

Consider what structures are possible for any compound in the scheme for which you have structural information (if there are too many possibilities, you may have to ignore this step).

In this exercise, we can draw five structures for compound A. 1-Bromo-3-phenylpropane, I, and 2-bromo-2-phenylpropane, IV, cannot be optically active so we can eliminate them from further consideration.

Next, evaluate the reactions according to the specified conditions. The conversion of A to B is an E2 process; A to C is an Sn1 process; C to B is an E2 reaction; and A to D is an Sn2 reaction. Compound V is a primary alkyl bromide, which will not react via the Sn1 pathway needed to convert A to C. Therefore, we remove it from further consideration.

We now draw the structures of the compounds that will be formed via the given reactions from the two remaining candidates, II and III. We see that the structures of these compounds match the properties for A through D given in the exercise. Compound III is probably a better choice because the solvolysis reaction (A to C) occurs under relatively mild conditions, and a benzylic substrate is more likely to react at 35 °C than a simple secondary alkyl halide. (The squiggly bond in the structures shown below denotes that the stereochemistry is unspecified and the compound is racemic, hence not optically active.)

8.28. We can choose reagents for the given reactions by classifying the type of mechanism that is involved. The mechanism in turn is deduced by classifying the reaction type and considering the stereochemistry of the transformation.

a. This is an elimination reaction that starts with an alcohol, and the alkene product shown in the exercise is the most stable of three possibilities. Strong acid can be used under E1 conditions. The alcohol can also be converted to its alkyl sulfonate ester derivative and subjected to E2 conditions (strong base). Either choice is satisfactory.
8.28. (continued)

b. This is an elimination reaction that forms an alkyne from a vicinal dihaloalkane. A very strong base is required.

\[
\begin{align*}
\text{Br} & \quad \text{NaNH}_2, \text{THF}, \Delta \\
\text{Br} & \quad \text{NaSCH}_3, \text{DMF}
\end{align*}
\]

c. This is an elimination reaction that starts with a 3° alkyl halide so E2 conditions (strong base) will work.

\[
\begin{align*}
\text{Br} & \quad \text{KOH, ethanol, } \Delta \\
\text{OH} & \quad \text{NaSCH}_3, \text{DMF}
\end{align*}
\]

d. This is a substitution reaction that starts with a 2° alcohol and proceeds with inversion of configuration at the carbon atom bearing the OH group. Therefore, the OH group first has to be converted to a good leaving group with retention of configuration (formation of its tosylate or mesylate derivative). Then, S_N2 conditions are applied (strong nucleophile, aprotic solvent).

\[
\begin{align*}
\text{OH} & \quad 1. \text{TsCl, pyridine} \\
\text{OH} & \quad 2. \text{NaSCH}_3, \text{DMF}
\end{align*}
\]

e. This is an elimination reaction that starts with an alcohol molecule and produces an alkene product that is the less stable of two possibilities. Therefore E2 conditions are needed to control the stereochemistry. The alcohol is first converted to its alkyl sulfonate ester derivative, which is then subjected to treatment with strong base.

\[
\begin{align*}
\text{CH}_3 & \quad 1. \text{MsCl, NEt}_3, \text{CH}_2\text{CH}_2 \\
\text{CH}_3 & \quad 2. \text{KOH, ethanol, } \Delta
\end{align*}
\]

f. This is an elimination reaction that starts with an alcohol molecule and produces an alkene product that is the more stable of two possibilities. Strong acid is required because E2 conditions would yield the product shown in part (e.), directly above.

\[
\begin{align*}
\text{CH}_3 & \quad \text{H}_3\text{PO}_4, \Delta \\
\text{CH}_3 & \quad
\end{align*}
\]