CHAPTER

7

Alkenes and Alkynes I

PROPERTIES AND SYNTHESIS. ELIMINATION REACTIONS OF ALKYL HALIDES

Despite being a world of seven billion people spread over seven continents, a popular but unproven theory claims that there are only six degrees of separation between each of us and every other person. In other words, we are all a friend of a friend, and so on. As strange as it might sound, organic molecules are not much different, with alkenes and alkynes being the key connectors to numerous other functional groups as well as to C—C bond-formation processes that can rapidly create molecular complexity. In truth, it rarely takes six steps to find where an alkene or alkyne may have played a role in the synthesis of a molecule; more typically, it takes only one or two steps.

IN THIS CHAPTER WE WILL CONSIDER:

- the properties of alkenes and alkynes and how they are named
- how alkenes and alkynes can be transformed into alkanes
- how to plan the synthesis of any organic molecule

[WHY DO THESE TOPICS MATTER?] At the end of the chapter, we will show how simple changes in the placement of alkene functional groups can lead to distinct properties, from the strength of the rubber in our tires to our ability to see.

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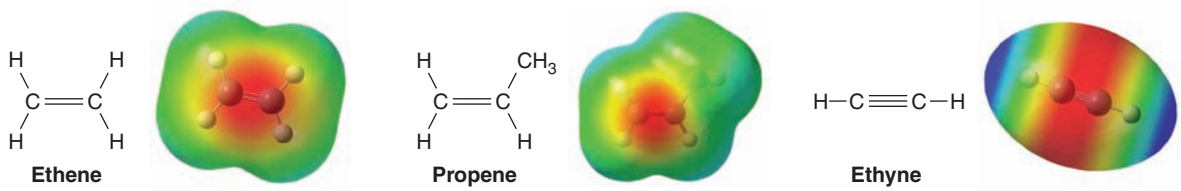
7.1 INTRODUCTION

Alkenes are hydrocarbons whose molecules contain a carbon–carbon double bond. An old name for this family of compounds that is still often used is the name **olefins**. Ethene (ethylene), the simplest olefin (alkene), was called olefiant gas (Latin: *oleum,* oil + *facere,* to make) because gaseous ethene (C_2H_4) reacts with chlorine to form $C_2H_4Cl_2$, a liquid (oil).

Hydrocarbons whose molecules contain the carbon–carbon triple bond are called alkynes. The common name for this family is **acetylenes,** after the simplest member, HC≡CH:

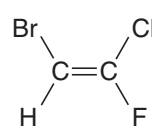


7.1A Physical Properties of Alkenes and Alkynes

Alkenes and alkynes have physical properties similar to those of corresponding alkanes. Alkenes and alkynes up to four carbons (except 2-butyne) are gases at room temperature. Being relatively nonpolar themselves, alkenes and alkynes dissolve in nonpolar solvents or in solvents of low polarity. Alkenes and alkynes are only *very slightly soluble* in water (with alkynes being slightly more soluble than alkenes). The densities of alkenes and alkynes are lower than that of water.

7.2 THE (*E*)–(*Z*) SYSTEM FOR DESIGNATING ALKENE DIASTEREOMERS

In Section 4.5 we learned to use the terms cis and trans to designate the stereochemistry of alkene diastereomers (**cis–trans isomers**). These terms are unambiguous, however, only when applied to disubstituted alkenes. If the alkene is trisubstituted or tetrasubstituted, the terms cis and trans are either ambiguous or do not apply at all. Consider the following alkene as an example:



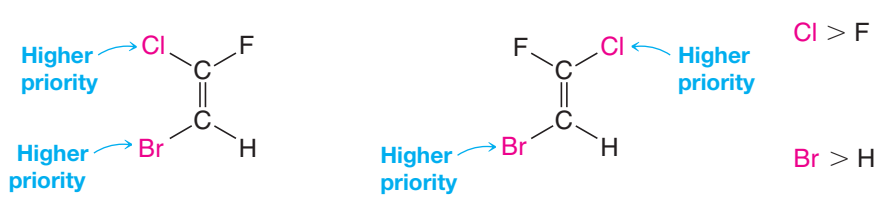
A

It is impossible to decide whether **A** is cis or trans since no two groups are the same.

A system that works in all cases is based on the priorities of groups in the Cahn–Ingold–Prelog convention (Section 5.7). This system, called the **(*E*)–(*Z*) system**, applies to alkene diastereomers of all types.

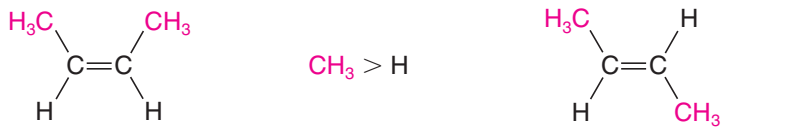
7.2A HOW TO Use The (*E*)–(*Z*) System

1. Examine the two groups attached to one carbon atom of the double bond and decide which has higher priority.
2. Repeat that operation at the other carbon atom:



(*Z*)-2-Bromo-1-chloro-1-fluoroethene **(*E*)-2-Bromo-1-chloro-1-fluoroethene**

3. Compare the group of higher priority on one carbon atom with the group of higher priority on the other carbon atom. If the two groups of higher priority are on the same side of the double bond, the alkene is designated (*Z*) (from the German word *zusammen,* meaning together). If the two groups of higher priority are on opposite sides of the double bond, the alkene is designated (*E*) (from the German word *entgegen,* meaning opposite). The following isomers provide another example.

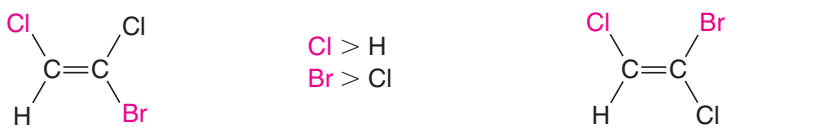


(*Z*)-2-Butene or (*Z*)-but-2-ene (*cis*-2-butene) **(*E*)-2-Butene or (*E*)-but-2-ene (*trans*-2-butene)**

SOLVED PROBLEM 7.1

The two stereoisomers of 1-bromo-1,2-dichloroethene cannot be designated as cis and trans in the normal way because the double bond is trisubstituted. They can, however, be given (*E*) and (*Z*) designations. Write a structural formula for each isomer and give each the proper designation.

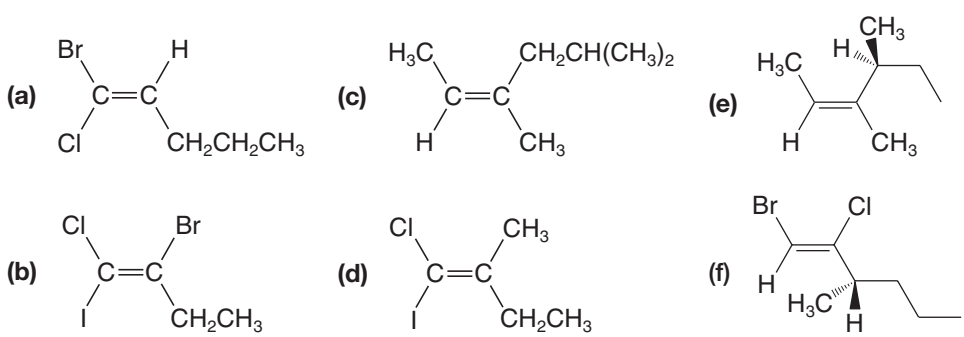
STRATEGY AND ANSWER: We write the structures (below), then note that chlorine has a higher priority than hydrogen, and bromine has a higher priority than chlorine. The group with higher priority on C1 is bromine and the group with higher priority at C2 is chlorine. In the first structure the higher priority chlorine and bromine atoms are on opposite sides of the double bond, and therefore this isomer is (*E*). In the second structure those chlorine and bromine atoms are on the same side, so the latter isomer is (*Z*).



(*E*)-1-Bromo-1,2-dichloroethene **(*Z*)-1-Bromo-1,2-dichloroethene**

PRACTICE PROBLEM 7.1

Using the (*E*)–(*Z*) designation [and in parts **(e)** and **(f)** the (*R*)–(*S*) designation as well] give IUPAC names for each of the following:



7.3 RELATIVE STABILITIES OF ALKENES

Cis and trans isomers of alkenes do not have the same stability.

- Strain caused by crowding of two alkyl groups on the same side of a double bond makes cis isomers generally less stable than trans isomers (Fig. 7.1).

This effect can be measured quantitatively by comparing thermodynamic data from experiments involving alkenes with related structures, as we shall see later.

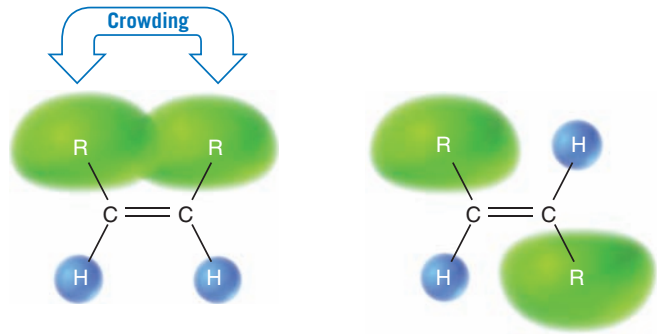
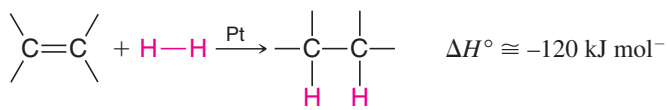


FIGURE 7.1 Cis and trans alkene isomers. The cis isomer is less stable due to greater strain from crowding by the adjacent alkyl groups.

7.3A Heat of Reaction

The addition of hydrogen to an alkene (**hydrogenation**, Sections 4.16A and 7.13) is an exothermic reaction; the enthalpy change involved is called the **heat of reaction** or, in this specific case, the **heat of hydrogenation**.



We can gain a quantitative measure of relative alkene stabilities by comparing the heats of hydrogenation for a family of alkenes that all become the same alkane product on hydrogenation. The results of such an experiment involving platinum-catalyzed hydrogenation of three butene isomers are shown in Fig. 7.2. All three isomers yield the same product—butane—but the heat of reaction is different in each case. On conversion to butane, 1-butene liberates the most heat (127 kJ mol^{-1}), followed by *cis*-2-butene (120 kJ mol^{-1}), with *trans*-2-butene producing the least heat (115 kJ mol^{-1}). These data indicate that the trans isomer is more stable than the cis isomer, since less energy is released when the trans isomer is converted to butane. Furthermore, it shows that the terminal alkene, 1-butene, is less stable than either of the disubstituted alkenes, since its reaction is the most exothermic. Of course, alkenes that do not yield the same hydrogenation products cannot be compared on the basis of their respective heats of hydrogenation. In such cases it is necessary to compare other thermochemical data, such as heats of combustion, although we will not go into analyses of that type here.

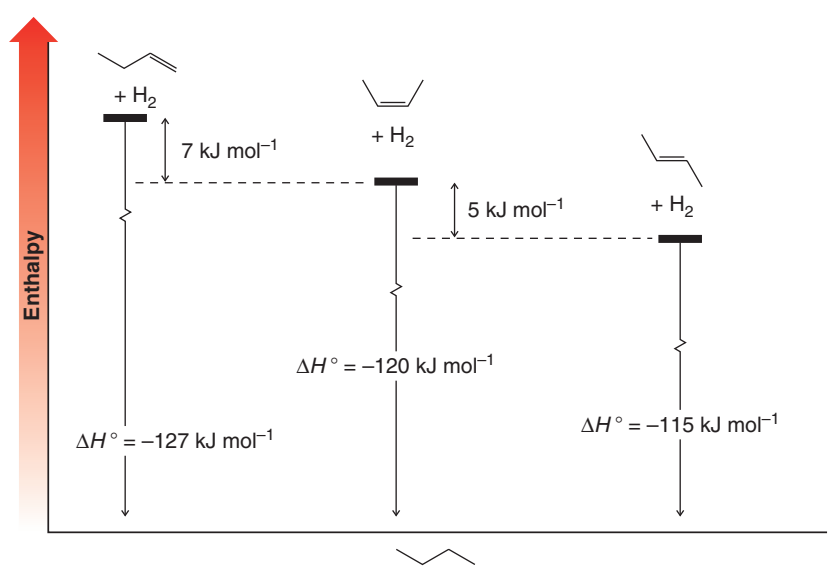


FIGURE 7.2 An energy diagram for platinum-catalyzed hydrogenation of the three butene isomers. The order of stability based on the differences in their heats of hydrogenation is *trans*-2-butene > *cis*-2-butene > 1-butene.

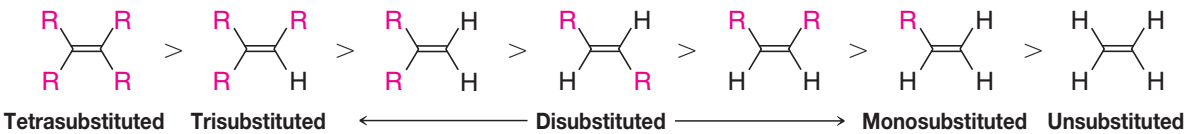
7.3B Overall Relative Stabilities of Alkenes

Studies of numerous alkenes reveal a pattern of stabilities that is related to the number of alkyl groups attached to the carbon atoms of the double bond.

- The greater the number of attached alkyl groups (i.e., the more highly substituted the carbon atoms of the double bond), the greater is the alkene's stability.

This order of stabilities can be given in general terms as follows:*

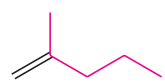
Relative Stabilities of Alkenes



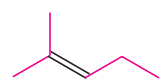
SOLVED PROBLEM 7.2

Consider the two alkenes 2-methyl-1-pentene and 2-methyl-2-pentene and decide which would be most stable.

STRATEGY AND ANSWER: First write the structures of the two alkenes, then decide how many substituents the double bond of each has.



2-Methyl-1-pentene (disubstituted, less stable)

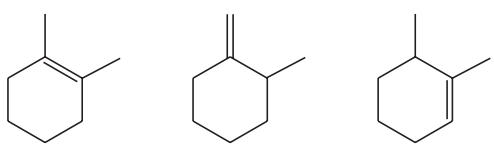


2-Methyl-2-pentene (trisubstituted, more stable)

2-Methyl-2-pentene has three substituents on its double bond, whereas 2-methyl-1-pentene has two, and therefore 2-methyl-2-pentene is the more stable.

PRACTICE PROBLEM 7.2

Rank the following cycloalkenes in order of increasing stability.



PRACTICE PROBLEM 7.3

Heats of hydrogenation of three alkenes are as follows:

2-methyl-1-butene (-119 kJ mol^{-1})
3-methyl-1-butene (-127 kJ mol^{-1})
2-methyl-2-butene (-113 kJ mol^{-1})

(a) Write the structure of each alkene and classify it as to whether its doubly bonded atoms are monosubstituted, disubstituted, trisubstituted, or tetrasubstituted. **(b)** Write the structure of the product formed when each alkene is hydrogenated. **(c)** Can heats of hydrogenation be used to relate the relative stabilities of these three alkenes? **(d)** If so, what is the predicted order of stability? If not, why not? **(e)** What other alkene isomers are possible for these alkenes? Write their structures. **(f)** What are the relative stabilities among just these isomers?

*This order of stabilities may seem contradictory when compared with the explanation given for the relative stabilities of cis and trans isomers. Although a detailed explanation of the trend given here is beyond our scope, the relative stabilities of substituted alkenes can be rationalized. Part of the explanation can be given in terms of the electron-releasing effect of alkyl groups (Section 6.11B), an effect that satisfies the electron-withdrawing properties of the sp^2-hybridized carbon atoms of the double bond.

PRACTICE PROBLEM 7.4 Predict the more stable alkene of each pair: **(a)** 2-methyl-2-pentene or 2,3-dimethyl-2-butene; **(b)** *cis*-3-hexene or *trans*-3-hexene; **(c)** 1-hexene or *cis*-3-hexene; **(d)** *trans*-2-hexene or 2-methyl-2-pentene.

PRACTICE PROBLEM 7.5 How many stereoisomers are possible for 4-methyl-2-hexene, and how many fractions would you obtain if you distilled the mixture?

7.4 CYCLOALKENES

The rings of cycloalkenes containing five carbon atoms or fewer exist only in the cis form (Fig. 7.3). The introduction of a trans double bond into rings this small would, if it were possible, introduce greater strain than the bonds of the ring atoms could accommodate.

Cyclopropene **Cyclobutene** **Cyclopentene** **Cyclohexene**

FIGURE 7.3 *cis*-Cycloalkenes.

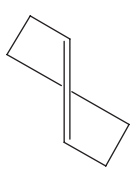


FIGURE 7.4 Hypothetical *trans*-cyclohexene. This molecule is apparently too strained to exist at room temperature.

(Verify this with handheld molecular models.) *trans*-Cyclohexene might resemble the structure shown in Fig. 7.4. There is evidence that it can be formed as a very reactive short-lived intermediate in some chemical reactions, but it is not isolable as a stable molecule.

trans-Cycloheptene has been observed spectroscopically, but it is a substance with a very short lifetime and has not been isolated.

trans-Cyclooctene (Fig. 7.5) has been isolated, however. Here the ring is large enough to accommodate the geometry required by a trans double bond and still be stable at room temperature. *trans*-Cyclooctene is chiral and exists as a pair of enantiomers. You may wish to verify this using handheld models.

Helpful Hint

Exploring all of these cycloalkenes with handheld molecular models, including both enantiomers of *trans*-cyclooctene, will help illustrate their structural differences.

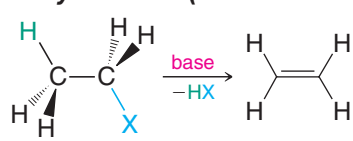
***cis*-Cyclooctene** ***trans*-Cyclooctene**

FIGURE 7.5 The cis and trans forms of cyclooctene.

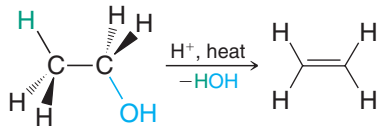
7.5 SYNTHESIS OF ALKENES VIA ELIMINATION REACTIONS

Elimination reactions are the most important means for synthesizing alkenes. In this chapter we shall study two methods for alkene synthesis based on elimination reactions: dehydrohalogenation of alkyl halides and dehydration of alcohols.

Dehydrohalogenation of Alkyl Halides (Sections 6.15, 6.16, and 7.6)



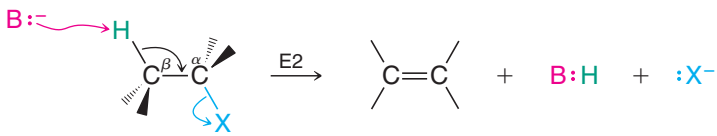
Dehydration of Alcohols (Sections 7.7 and 7.8)



7.6 DEHYDROHALOGENATION OF ALKYL HALIDES

- The best reaction conditions to use when synthesizing an alkene by **dehydrohalogenation** are those that promote an E2 mechanism.

In an E2 mechanism, a base removes a β hydrogen from the β carbon, as the double bond forms and a leaving group departs from the α carbon.



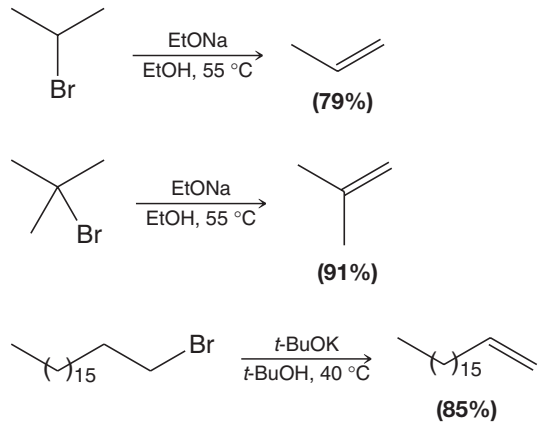
Reaction conditions that favor elimination by an E1 mechanism should be avoided because the results can be too variable. The carbocation intermediate that accompanies an E1 reaction can undergo rearrangement of the carbon skeleton, as we shall see in Section 7.8, and it can also undergo substitution by an S_N1 mechanism, which competes strongly with formation of products by an E1 path.

7.6A HOW TO Favor an E2 Mechanism

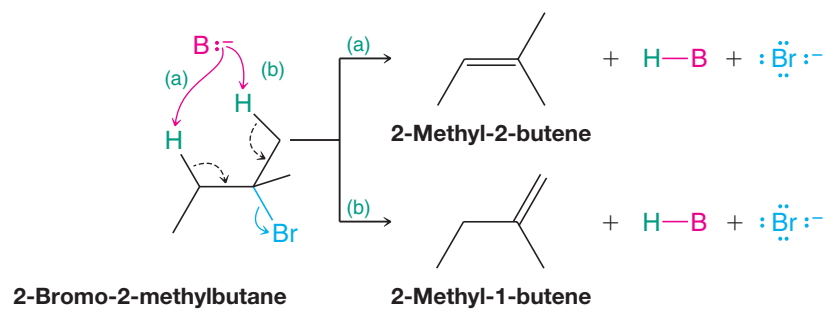
1. **Use a secondary or tertiary alkyl halide if possible.**
   Why? Because steric hindrance in the substrate will inhibit substitution.
2. **When a synthesis must begin with a primary alkyl halide, use a bulky base.**
   Why? Because the steric bulk of the base will inhibit substitution.
3. **Use a high concentration of a strong and nonpolarizable base such as an alkoxide.**
   Why? Because a weak and polarizable base would not drive the reaction toward a bimolecular reaction, thereby allowing unimolecular processes (such as S_N1 or E1 reactions) to compete.
4. **Sodium ethoxide in ethanol (EtONa/EtOH) and potassium *tert*-butoxide in *tert*-butyl alcohol (*t*-BuOK/*t*-BuOH) are bases typically used to promote E2 reactions.**
   Why? Because they meet criterion 3 above. Note that in each case the alkoxide base is dissolved in its corresponding alcohol. (Potassium hydroxide dissolved in ethanol or *tert*-butyl alcohol is also sometimes used, in which case the active base includes both the alkoxide and hydroxide species present at equilibrium.)
5. **Use elevated temperature because heat generally favors elimination over substitution.**
   Why? Because elimination reactions are entropically favored over substitution reactions (because the products are greater in number than the reactants). Hence $\Delta S°$ in the Gibbs free-energy equation, $\Delta G° = \Delta H° - T\Delta S°$ is significant, and $\Delta S°$ will be increased by higher temperature since T is a coefficient, leading to a more negative (favorable) $\Delta G°$.

7.6B Zaitsev's Rule: Formation of the More Substituted Alkene Is Favored with a Small Base

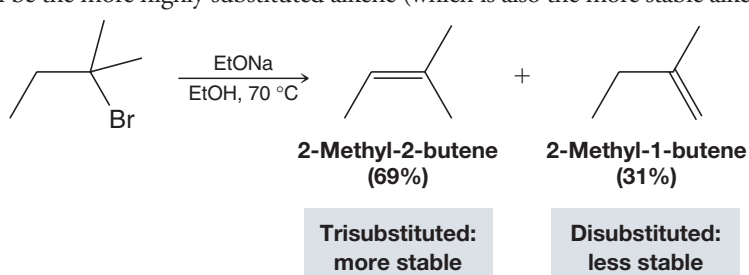
We showed examples in Sections 6.15–6.17 of dehydrohalogenations where only a single elimination product was possible. For example:



Dehydrohalogenation of many alkyl halides, however, yields more than one product. For example, dehydrohalogenation of 2-bromo-2-methylbutane can yield two products: 2-methyl-2-butene and 2-methyl-1-butene, as shown here by pathways (a) and (b), respectively:



- If we use a small base such as ethoxide or hydroxide, the major product of the reaction will be the more highly substituted alkene (which is also the more stable alkene).



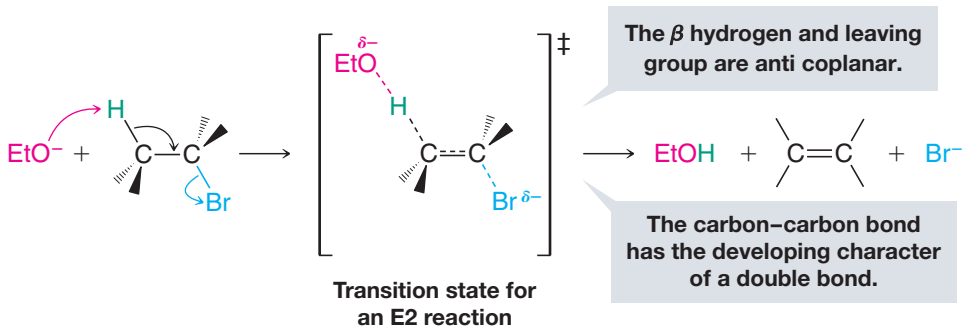
2-Methyl-2-butene is a trisubstituted alkene (three methyl groups are attached to carbon atoms of the double bond), whereas 2-methyl-1-butene is only disubstituted. 2-Methyl-2-butene is the major product.

- Whenever an elimination occurs to give the more stable, more highly substituted alkene, chemists say that the elimination follows **Zaitsev's rule**, named for the nineteenth-century Russian chemist A. N. Zaitsev (1841–1910) who formulated it. (Zaitsev's name is also transliterated as Zaitzev, Saytzeff, Saytseff, or Saytzev.)

Helpful Hint

The Zaitsev product is that which is the more stable product.

The reason for this behavior is related to the double-bond character that develops in the transition state (cf. Section 6.16) for each reaction:



The transition state for the reaction leading to 2-methyl-2-butene (Fig. 7.6) has the developing character of the double bond in a trisubstituted alkene. The transition state for the reaction leading to 2-methyl-1-butene has the developing character of a double bond in a disubstituted alkene. Because the transition state leading to 2-methyl-2-butene resembles a more stable alkene, this transition state is more stable (recall the Hammond–Leffler postulate, Fig. 6.10). Because this transition state is more stable (occurs at lower free energy), the free energy of activation for this reaction is lower and 2-methyl-2-butene is formed faster. This explains why 2-methyl-2-butene is the major product.

- In general, the preferential formation of one product because the free energy of activation leading to its formation is lower than that for another product, and therefore the rate of its formation faster, is called **kinetic control** of product formation. (See also Section 13.10A.)

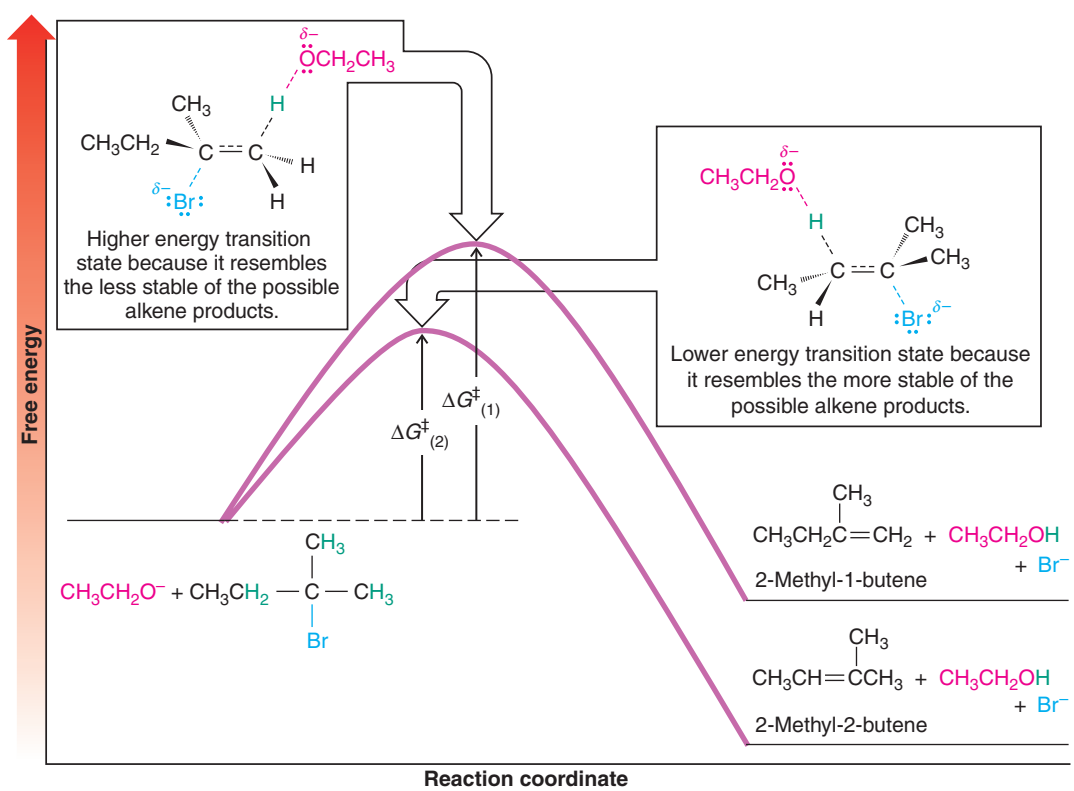
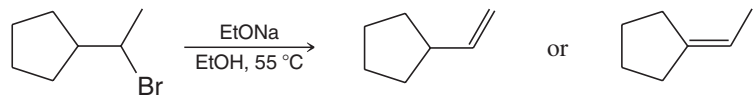


FIGURE 7.6 Reaction (2) leading to the more stable alkene occurs faster than reaction (1) leading to the less stable alkene; $\Delta G^{\ddagger}_{(2)}$ is less than $\Delta G^{\ddagger}_{(1)}$.

SOLVED PROBLEM 7.3

Using Zaitsev's rule, predict which would be the major product of the following reaction:



A **B**

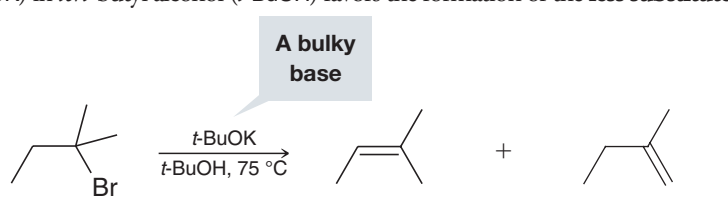
STRATEGY AND ANSWER: Alkene **B** has a trisubstituted double bond whereas the double bond of **A** is only monosubstituted. Therefore, **B** is more stable and, according to Zaitsev's rule, would be the major product.

PRACTICE PROBLEM 7.6 Predict the major product formed when 2-bromobutane is subjected to dehydrobromination using sodium ethoxide in ethanol at 55 °C.

PRACTICE PROBLEM 7.7 List the alkenes that would be formed when each of the following alkyl halides is subjected to dehydrohalogenation with potassium ethoxide in ethanol and use Zaitsev's rule to predict the major product of each reaction: **(a)** 2-bromo-3-methylbutane and **(b)** 2-bromo-2,3-dimethylbutane.

7.6C Formation of the Less Substituted Alkene Using a Bulky Base

- Carrying out dehydrohalogenations with a bulky base such as potassium *tert*-butoxide (*t*-BuOK) in *tert*-butyl alcohol (*t*-BuOH) favors the formation of the **less substituted alkene:**



2-Methyl-2-butene (27.5%) — **More substituted but formed more slowly.**

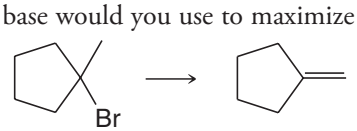
2-Methyl-1-butene (72.5%) — **Less substituted but formed faster.**

The reasons for this behavior are related in part to the steric bulk of the base and to the fact that in *tert*-butyl alcohol the base is associated with solvent molecules and thus made even larger. The large *tert*-butoxide ion appears to have difficulty removing one of the internal (2°) hydrogen atoms because of greater crowding at that site in the transition state. It removes one of the more exposed (1°) hydrogen atoms of the methyl group instead.

- When an elimination yields the less substituted alkene, we say that it follows the **Hofmann rule** (see also Section 20.12A).

SOLVED PROBLEM 7.4

Your task is the following synthesis. Which base would you use to maximize the yield of this specific alkene?



STRATEGY AND ANSWER: Here you want the Hofmann rule to apply (you want the less substituted alkene to be formed). Therefore, use a bulky base such as potassium *tert*-butoxide in *tert*-butyl alcohol.

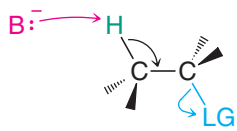
PRACTICE PROBLEM 7.8

Examine Solved Problem 7.3. Your task is to prepare **A** in the highest possible yield by dehydrobromination. Which base would you use?

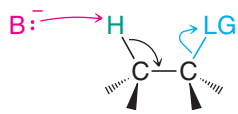
7.6D The Stereochemistry of E2 Reactions: The Orientation of Groups in the Transition State

- The five atoms involved in the transition state of an E2 reaction (including the base) must be **coplanar**, i.e., lie in the same plane.

The requirement for coplanarity of the H—C—C—LG unit arises from a need for proper overlap of orbitals in the developing π bond of the alkene that is being formed (see Section 6.16). There are two ways that this can happen:



Anti coplanar transition state (preferred)



Syn coplanar transition state (only with certain rigid molecules)

- The **anti coplanar** conformation is the preferred transition state geometry.

The **syn coplanar** transition state occurs only with rigid molecules that are unable to assume the anti arrangement. The reason: the anti coplanar transition state is staggered (and therefore of lower energy), while the syn coplanar transition state is eclipsed. Practice Problem 7.9 will help to illustrate this difference.

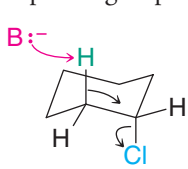
Helpful Hint

Be able to draw a three-dimensional representation of an anti coplanar E2 transition state.

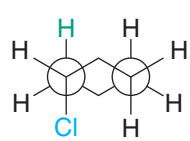
PRACTICE PROBLEM 7.9

Consider a simple molecule such as ethyl bromide and show with Newman projection formulas how the anti coplanar transition state would be favored over the syn coplanar one.

Part of the evidence for the preferred anti coplanar arrangement of groups comes from experiments done with cyclic molecules. Two groups axially oriented on adjacent carbons in a chair conformation of cyclohexane are anti coplanar. If one of these groups is a hydrogen and the other a leaving group, the geometric requirements for an anti coplanar E2 transition state are met. Neither an axial–equatorial nor an equatorial–equatorial orientation of the groups allows formation of an anti coplanar transition state. (Note that there are no syn coplanar groups in a chair conformation, either.)

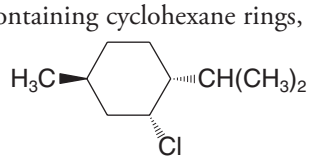


Here the β hydrogen and the chlorine are both axial. This allows an anti coplanar transition state.

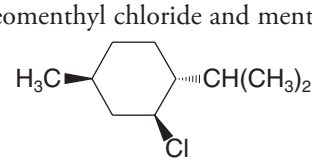


A Newman projection formula shows that the β hydrogen and the chlorine are anti coplanar when they are both axial.

As examples, let us consider the different behavior in E2 reactions shown by two compounds containing cyclohexane rings, neomenthyl chloride and menthyl chloride:



Neomenthyl chloride



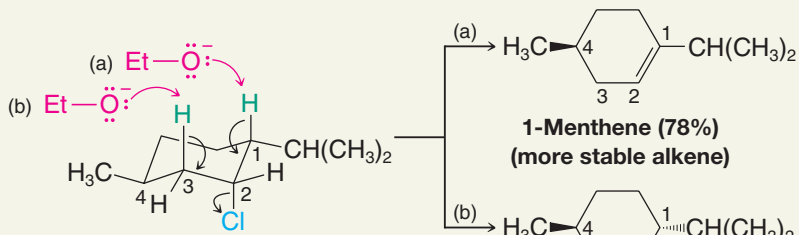
Menthyl chloride

Helpful Hint

Examine the conformations of neomenthyl chloride using handheld models.

In the more stable conformation of neomenthyl chloride (see the following mechanism), the alkyl groups are both equatorial and the chlorine is axial. There are also axial hydrogen atoms on both C1 and C3. The base can attack either of these hydrogen atoms and achieve an anti coplanar transition state for an E2 reaction. Products corresponding to each of these transition states (2-menthene and 1-menthene) are formed rapidly. In accordance with Zaitsev's rule, 1-menthene (with the more highly substituted double bond) is the major product.

A MECHANISM FOR THE REACTION — E2 Elimination Where There Are Two Axial β Hydrogens

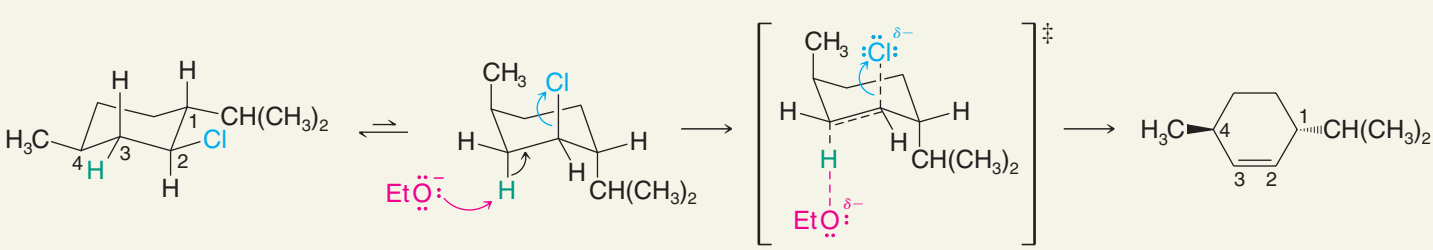


Neomenthyl chloride

Both green hydrogens are anti to the chlorine in this, the more stable conformation. Elimination by path (a) leads to 1-menthene; by path (b) to 2-menthene.

On the other hand, the more stable conformation of menthyl chloride has all three groups (including the chlorine) equatorial. For the chlorine to become axial, menthyl chloride has to assume a conformation in which the large isopropyl group and the methyl group are also axial. This conformation is of much higher energy, and the free energy of activation for the reaction is large because it includes the energy necessary for the conformational change. Consequently, menthyl chloride undergoes an E2 reaction very slowly, and the product is entirely 2-menthene because the hydrogen atom at C1 cannot be anti to the chlorine. This product (or any resulting from an elimination to yield the less substituted alkene) is sometimes called the *Hofmann product* (Sections 7.6C and 20.12A).

A MECHANISM FOR THE REACTION — E2 Elimination Where the Only Axial β Hydrogen Is from a Less Stable Conformer



Menthyl chloride (*more stable conformation*)
Elimination is not possible for this conformation because no hydrogen is anti to the leaving group.

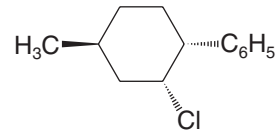
Menthyl chloride (*less stable conformation*)
Elimination is possible from this conformation because the green hydrogen is anti to the chlorine.

The transition state for the E2 elimination is anti coplanar.

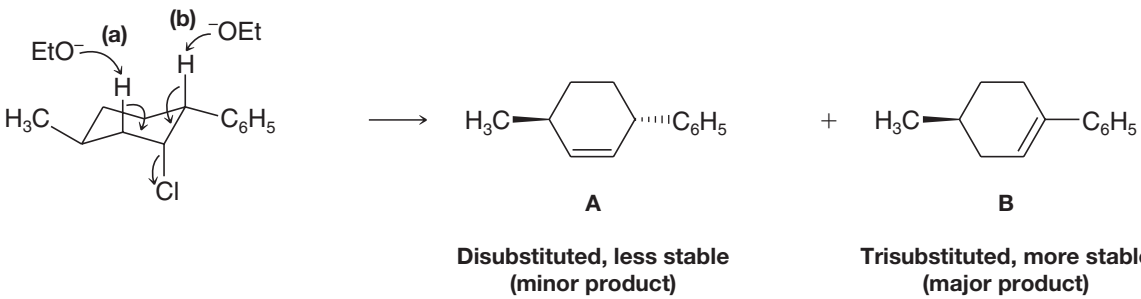
2-Menthene (100%)

SOLVED PROBLEM 7.5

Predict the major product formed when the following compound is subjected to dehydrochlorination with sodium ethoxide in ethanol.



STRATEGY AND ANSWER: We know that for an E2 dehydrochlorination to take place the chlorine will have to be axial. The following conformation has the chlorine axial and has two hydrogen atoms that are anti coplanar to the chlorine. Two products will be formed but **(B)** being more stable should be the major product.



Disubstituted, less stable (minor product)

Trisubstituted, more stable (major product)

PRACTICE PROBLEM 7.10

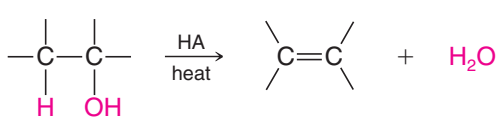
When *cis*-1-bromo-4-*tert*-butylcyclohexane is treated with sodium ethoxide in ethanol, it reacts rapidly; the product is 4-*tert*-butylcyclohexene. Under the same conditions, *trans*-1-bromo-4-*tert*-butylcyclohexane reacts very slowly. Write conformational structures and explain the difference in reactivity of these cis–trans isomers.

PRACTICE PROBLEM 7.11

(a) When *cis*-1-bromo-2-methylcyclohexane undergoes an E2 reaction, two products (cycloalkenes) are formed. What are these two cycloalkenes, and which would you expect to be the major product? Write conformational structures showing how each is formed. **(b)** When *trans*-1-bromo-2-methylcyclohexane reacts in an E2 reaction, only one cycloalkene is formed. What is this product? Write conformational structures showing why it is the only product.

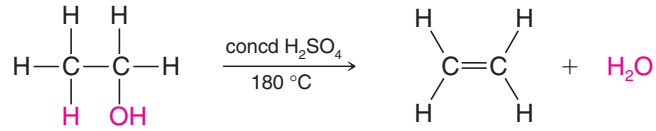
7.7 ACID-CATALYZED DEHYDRATION OF ALCOHOLS

- Most alcohols undergo **dehydration** (lose a molecule of water) to form an alkene when heated with a strong acid.



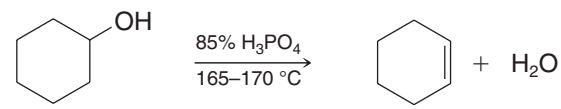
The reaction is an **elimination** and is favored at higher temperatures (Section 6.18A). The most commonly used acids in the laboratory are Brønsted acids—proton donors such as sulfuric acid and phosphoric acid. Lewis acids such as alumina (Al_2O_3) are often used in industrial, gas-phase dehydrations.

1. **The temperature and concentration of acid required to dehydrate an alcohol depend on the structure of the alcohol substrate.**
   - **(a) Primary alcohols** are the most difficult to dehydrate. Dehydration of ethanol, for example, requires concentrated sulfuric acid and a temperature of 180 °C:



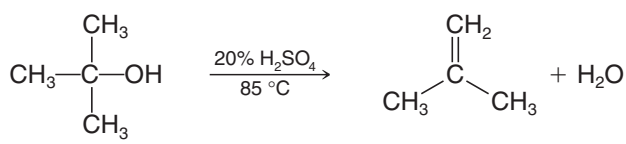
Ethanol (a 1° alcohol) **Ethene**

(b) Secondary alcohols usually dehydrate under milder conditions. Cyclohexanol, for example, dehydrates in 85% phosphoric acid at 165–170 °C:



Cyclohexanol **Cyclohexene (80%)**

(c) Tertiary alcohols are usually so easily dehydrated that relatively mild conditions can be used. *tert*-Butyl alcohol, for example, dehydrates in 20% aqueous sulfuric acid at a temperature of 85 °C:

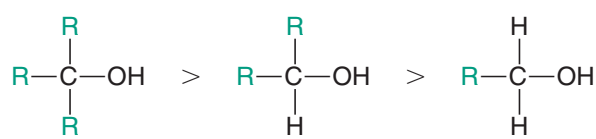


***tert*-Butyl alcohol** **2-Methylpropene (84%)**

- The relative ease with which alcohols undergo dehydration is 3° > 2° > 1°.

Helpful Hint

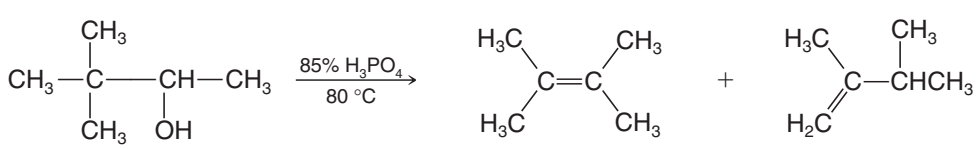
Be able to classify any alcohol as 1°, 2°, or 3°, and thereby assess its relative ease of dehydration.



3° Alcohol **2° Alcohol** **1° Alcohol**

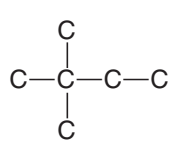
This behavior, as we shall see in Section 7.7B, is related to the relative stabilities of carbocations.

2. **Some primary and secondary alcohols also undergo rearrangements of their carbon skeletons during dehydration.** Such a rearrangement occurs in the dehydration of 3,3-dimethyl-2-butanol:

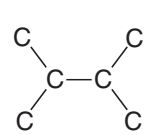


3,3-Dimethyl-2-butanol **2,3-Dimethyl-2-butene (80%)** **2,3-Dimethyl-1-butene (20%)**

Notice that the carbon skeleton of the reactant is



while that of the products is



The carbon skeleton has rearranged

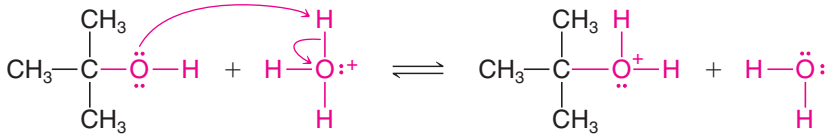
We shall see in Section 7.8 that this reaction involves the migration of a methyl group from one carbon to the next so as to form a more stable carbocation. (Rearrangements to carbocations of approximately equal energy may also be possible with some substrates.)

7.7A Mechanism for Dehydration of Secondary and Tertiary Alcohols: An E1 Reaction

Explanations for these observations can be based on a stepwise mechanism originally proposed by F. Whitmore (of Pennsylvania State University).

The mechanism is an E1 reaction in which the substrate is a protonated alcohol. Consider the dehydration of *tert*-butyl alcohol as an example:

Step 1



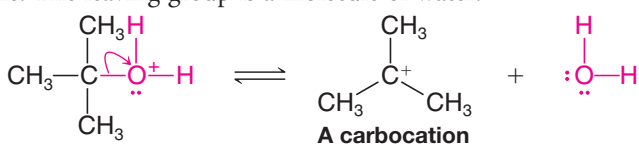
Protonated alcohol

Protonation of the alcohol

In this step, an acid–base reaction, a proton is rapidly transferred from the acid to one of the unshared electron pairs of the alcohol. In dilute sulfuric acid the acid is a hydronium ion; in concentrated sulfuric acid the initial proton donor is sulfuric acid itself. This step is characteristic of all reactions of an alcohol with a strong acid.

The presence of the positive charge on the oxygen of the protonated alcohol weakens all bonds to oxygen, including the carbon–oxygen bond, and in step 2 the carbon–oxygen bond breaks. The leaving group is a molecule of water:

Step 2



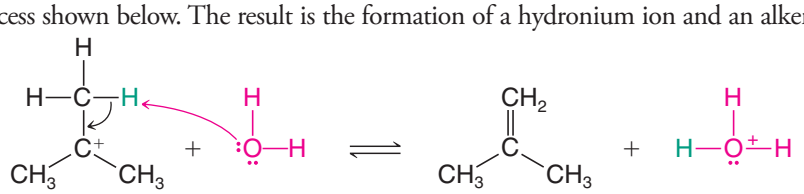
A carbocation

Departure of a water molecule

The carbon–oxygen bond breaks **heterolytically.** The bonding electrons depart with the water molecule and leave behind a carbocation. The carbocation is, of course, highly reactive because the central carbon atom has only six electrons in its valence level, not eight.

Finally, in step 3, a water molecule removes a proton from the β carbon of the carbocation by the process shown below. The result is the formation of a hydronium ion and an alkene:

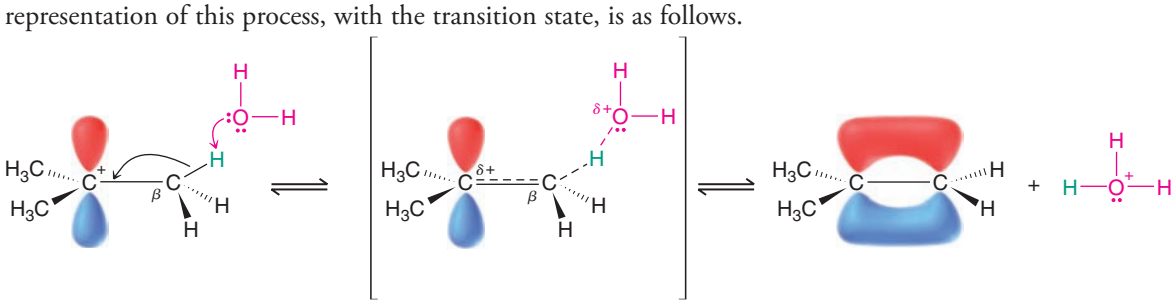
Step 3



2-Methylpropene

Removal of a β hydrogen

In step 3, also an acid–base reaction, any one of the nine protons available at the three methyl groups can be transferred to a molecule of water. The electron pair left behind when a proton is removed becomes the second bond of the double bond of the alkene. Notice that this step restores an octet of electrons to the central carbon atom. An orbital representation of this process, with the transition state, is as follows.

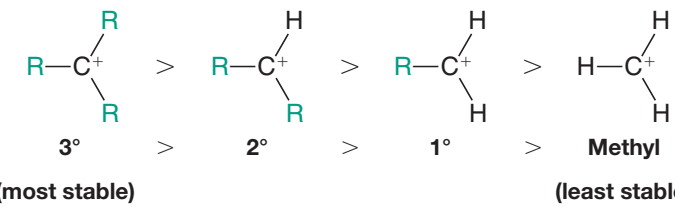


Transition state for removal of a proton from the β carbon of the carbocation

PRACTICE PROBLEM 7.12 Dehydration of 2-propanol occurs in 14 M H_2SO_4 at 100 °C. **(a)** Using curved arrows, write all steps in a mechanism for the dehydration. **(b)** Explain the essential role performed in alcohol dehydrations by the acid catalyst. [*Hint:* Consider what would have to happen if no acid were present.]

7.7B Carbocation Stability and the Transition State

We saw in Section 6.11B that the order of stability of carbocations is tertiary > secondary > primary > methyl:



In the dehydration of secondary and tertiary alcohols the slowest step is formation of the carbocation as shown in step 2 of the "A Mechanism for the Reaction" box in this section. The first and third steps involve simple acid–base proton transfers, which occur very rapidly. The second step involves loss of the protonated hydroxyl as a leaving group, a highly endergonic process (Section 6.7), and hence it is the rate-determining step.

Because step 2 is the rate-determining step, it is this step that determines the overall reactivity of alcohols toward dehydration. With that in mind, we can now understand why tertiary alcohols are the most easily dehydrated. The formation of a tertiary carbocation is easiest because the free energy of activation for step 2 of a reaction leading to a tertiary carbocation is lowest (see Fig. 7.7). Secondary alcohols are not so easily dehydrated because the free energy of activation for their dehydration is higher—a secondary carbocation is less stable. The free energy of activation for dehydration of primary alcohols via a carbocation is so high that they undergo dehydration by another mechanism (Section 7.7C).

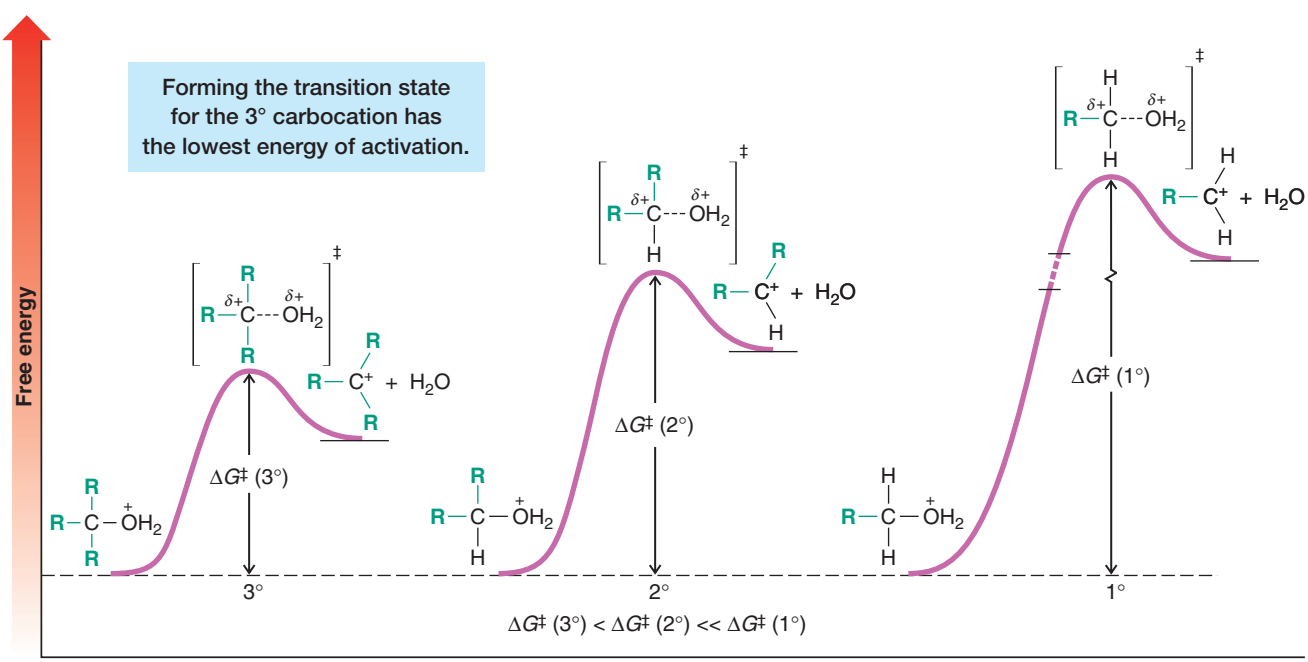
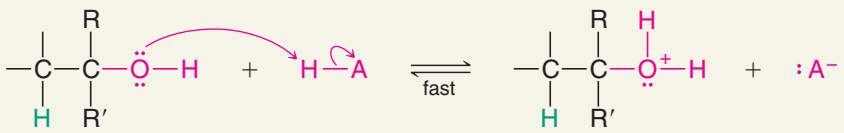


FIGURE 7.7 Free-energy diagrams for the formation of carbocations from protonated tertiary, secondary, and primary alcohols. The relative free energies of activation are tertiary < secondary ≪ primary.

A MECHANISM FOR THE REACTION — Acid-Catalyzed Dehydration of Secondary or Tertiary Alcohols: An E1 Reaction

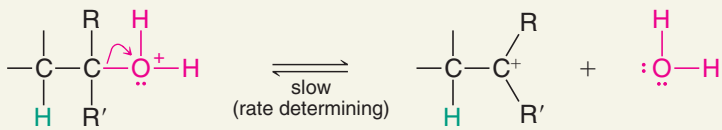
Step 1



2° or 3° Alcohol (R′ may be H) | **Acid catalyst (typically sulfuric or phosphoric acid)** | **Protonated alcohol** | **Conjugate base**

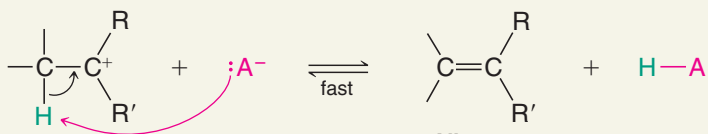
The alcohol accepts a proton from the acid in a fast step.

Step 2



The protonated alcohol loses a molecule of water to become a carbocation. This step is slow and rate determining.

Step 3



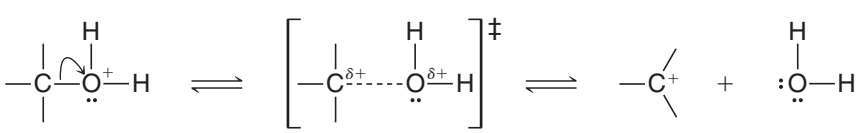
Alkene

The carbocation loses a proton to a base. In this step, the base may be another molecule of the alcohol, water, or the conjugate base of the acid. The proton transfer results in the formation of the alkene. Note that the overall role of the acid is catalytic (it is used in the reaction and regenerated).

The reactions by which carbocations are formed from protonated alcohols are all highly *endergonic*. Based on the Hammond–Leffler postulate (Section 6.13A), there should be a strong resemblance between the transition state and the carbocation in each case.

- ***The transition state that leads to the tertiary carbocation is lowest in free energy because it resembles the carbocation that is lowest in energy.***

By contrast, the transition state that leads to the primary carbocation occurs at highest free energy because it resembles the carbocation that is highest in energy. In each instance, moreover, the same factor stabilizes the transition state that stabilizes the carbocation itself: **delocalization of the charge**. We can understand this if we examine the process by which the transition state is formed:

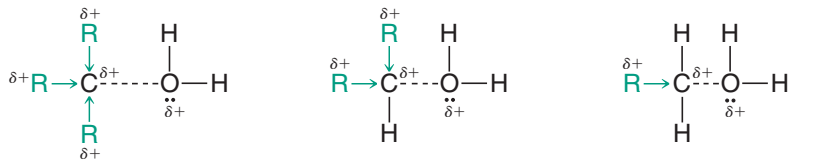


Protonated alcohol | **Transition state** | **Carbocation**

The oxygen atom of the protonated alcohol bears a full positive charge. As the transition state develops, this oxygen atom begins to separate from the carbon atom to which it is attached. The carbon atom begins to develop a partial positive charge because it is losing the electrons that bonded it to the oxygen atom. This developing positive charge ***is most effectively delocalized in the transition state leading to a tertiary carbocation because three alkyl groups are present to contribute electron density by***

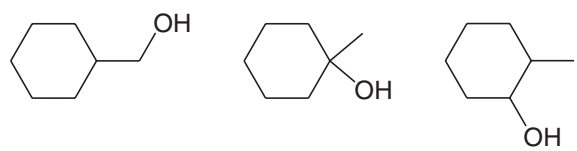
hyperconjugation (Section 6.11B) to the developing carbocation. The positive charge is less effectively delocalized in the transition state leading to a secondary carbocation (*two* electron-releasing groups) and is least effectively delocalized in the transition state leading to a primary carbocation (*one* electron-releasing group). For this reason the dehydration of a primary alcohol proceeds through a different mechanism—an E2 mechanism.

Hyperconjugative stabilization (see Figure 6.7) is greatest for a tertiary carbocation.



Transition state leading to 3° carbocation (most stable) | **Transition state leading to 2° carbocation** | **Transition state leading to 1° carbocation (least stable)**

PRACTICE PROBLEM 7.13 Rank the following alcohols in order of increasing ease of acid-catalyzed dehydration.

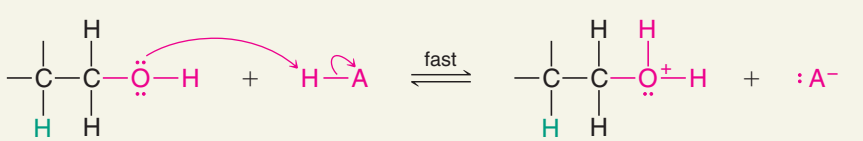


(a) **(b)** **(c)**

7.7C A Mechanism for Dehydration of Primary Alcohols: An E2 Reaction

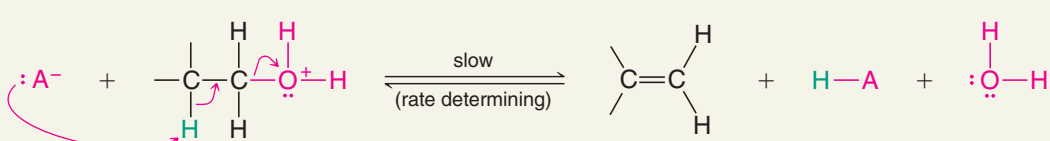
Dehydration of primary alcohols apparently proceeds through an E2 mechanism because the primary carbocation required for dehydration by an E1 mechanism is relatively unstable. The first step in dehydration of a primary alcohol is protonation, just as in the E1 mechanism. Then, with the protonated hydroxyl as a good leaving group, a Lewis base in the reaction mixture removes a β hydrogen simultaneously with formation of the alkene double bond and departure of the protonated hydroxyl group (water).

A MECHANISM FOR THE REACTION — Dehydration of a Primary Alcohol: An E2 Reaction



Primary alcohol | **Acid catalyst (typically sulfuric or phosphoric acid)** | **Protonated alcohol** | **Conjugate base**

The alcohol accepts a proton from the acid in a fast step.



Alkene

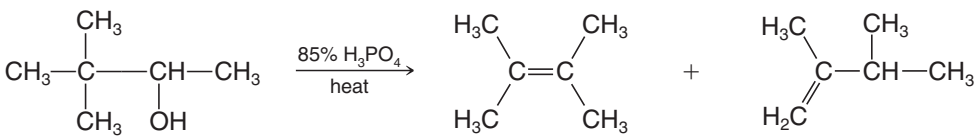
A base removes a hydrogen from the β carbon as the double bond forms and the protonated hydroxyl group departs. The base may be another molecule of the alcohol or the conjugate base of the acid.

7.8 CARBOCATION STABILITY AND THE OCCURRENCE OF MOLECULAR REARRANGEMENTS

With an understanding of carbocation stability and its effect on transition states, we can now proceed to explain the rearrangements of carbon skeletons that occur in some alcohol **dehydrations**.

7.8A Rearrangements During Dehydration of Secondary Alcohols

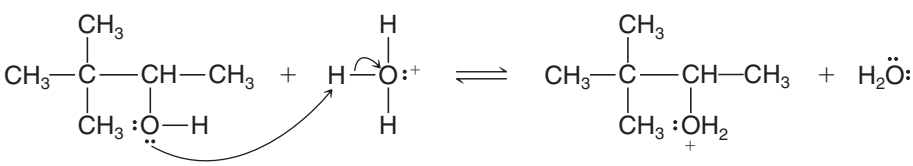
Consider again the **rearrangement** that occurs when 3,3-dimethyl-2-butanol is dehydrated:



3,3-Dimethyl-2-butanol → **2,3-Dimethyl-2-butene (major product)** + **2,3-Dimethyl-1-butene (minor product)**

The first step of this dehydration is the formation of the protonated alcohol in the usual way:

Step 1

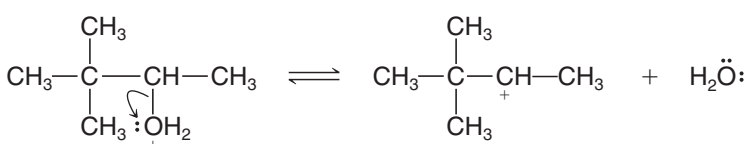


Protonation of the alcohol

Protonated alcohol

In the second step the protonated alcohol loses water and a secondary carbocation forms:

Step 2

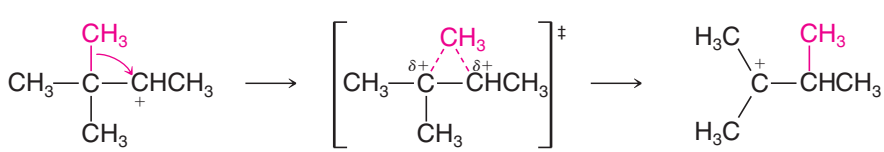


Departure of a water molecule

A 2° carbocation

Now the rearrangement occurs. ***The less stable, secondary carbocation rearranges to a more stable tertiary carbocation:***

Step 3



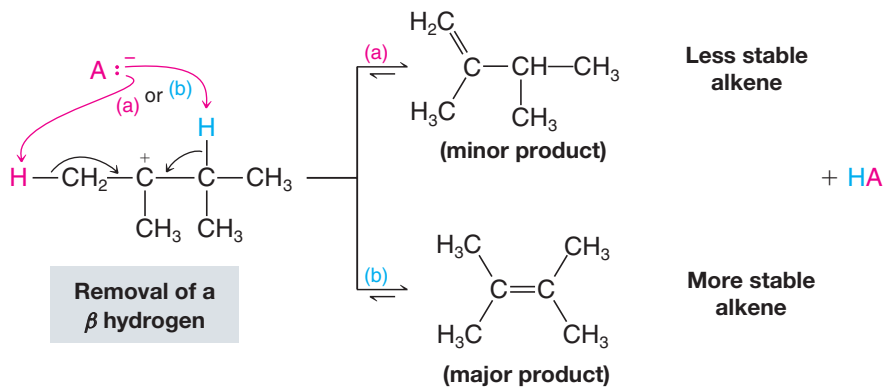
2° Carbocation (less stable) → **Transition state** → **3° Carbocation (more stable)**

Rearrangement by migration of a methyl group

The rearrangement occurs through the migration of an alkyl group (methyl) from the carbon atom adjacent to the one with the positive charge. The methyl group migrates **with its pair of electrons** (called a **methanide** shift). In the transition state the shifting methyl is partially bonded to both carbon atoms by the pair of electrons with which it migrates. It never leaves the carbon skeleton. After the migration is complete, the carbon atom that the methyl anion left has become a carbocation, and the positive charge on the carbon atom to which it migrated has been neutralized. Because a group migrates from one carbon to an adjacent one, this kind of rearrangement is also called a **1,2 shift**.

The final step of the reaction is the removal of a proton from the new carbocation (by a Lewis base in the reaction mixture) and the formation of an alkene. This step, however, can occur in two ways:

Step 4

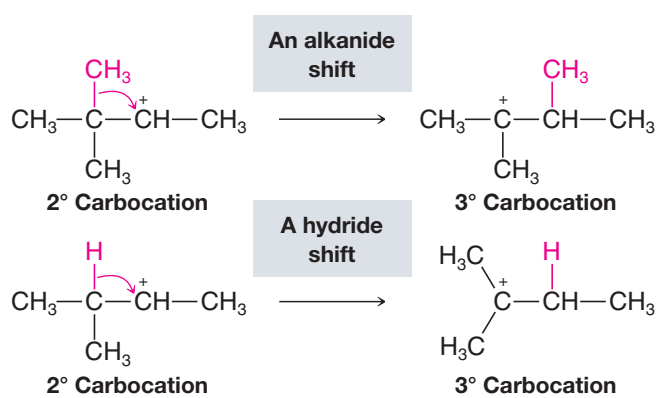


The more favored product is dictated by the stability of the alkene being formed. The conditions for the reaction (heat and acid) allow **equilibrium to be achieved** between the two forms of the alkene, and **the more stable alkene is the major product because it has lower potential energy**. Such a reaction is said to be **under equilibrium** or **thermodynamic control**. Path (b) leads to the highly stable tetrasubstituted alkene and this is the path followed by most of the carbocations. Path (a), on the other hand, leads to a less stable, disubstituted alkene, and because its potential energy is higher, it is the minor product of the reaction.

Helpful Hint
Alcohol dehydration follows Zaitsev's rule.

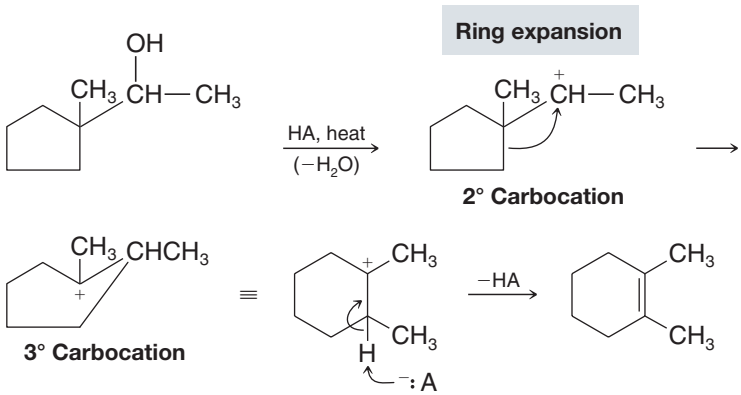
- **Formation of the more stable alkene is the general rule in acid-catalyzed dehydration of alcohols (Zaitsev's rule).**

Studies of many reactions involving carbocations show that rearrangements like those just described are general phenomena. ***They occur almost invariably when an alkanide shift or hydride shift can lead to a more stable carbocation***. The following are examples:



We shall see biological examples of alkanide (specifically methanide) and hydride migrations in "The Chemistry of … Cholesterol Biosynthesis" (online in *WileyPLUS* for Chapter 8).

Rearrangements of carbocations can also lead to a change in ring size, as the following example shows:

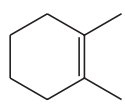


Ring expansion by migration is especially favorable if relief in ring strain occurs.

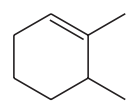
It is important to note that rearrangements to carbocations having approximately equal energy are also possible (e.g., from one secondary carbocation to another), and this can complicate the mixture of products that might be obtained from a reaction.

SOLVED PROBLEM 7.6

Explain why the major product of the dehydration above is 1,2-dimethylcyclohexene (as shown) and not 2,3-dimethyl-1-cyclohexene.



1,2-Dimethylcyclohexene (major product)



2,3-Dimethyl-1-cyclohexene (minor product)

STRATEGY AND ANSWER: We have just learned that dehydration leads mainly to the more stable alkene (when two are possible). We also know that the stability of an alkene is related to the number of alkyl groups that are attached to the carbons of the double bond. 1,2-Dimethylcyclohexene has a tetrasubstituted double bond (and is more stable), while in 2,3-dimethylcyclohexene the double bond is only trisubstituted.

PRACTICE PROBLEM 7.14

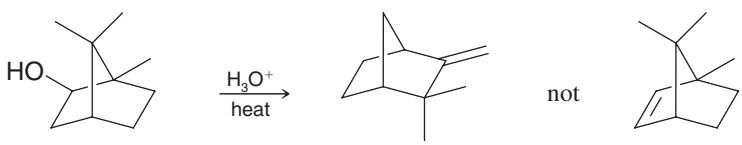
Acid-catalyzed dehydration of neopentyl alcohol, $(CH_3)_3CCH_2OH$, yields 2-methyl-2-butene as the major product. Outline a mechanism showing all steps in its formation.

PRACTICE PROBLEM 7.15

Acid-catalyzed dehydration of either 2-methyl-1-butanol or 3-methyl-1-butanol gives 2-methyl-2-butene as the major product. Write plausible mechanisms that explain these results.

PRACTICE PROBLEM 7.16

When the compound called *isoborneol* is heated with 9 M sulfuric acid, the product of the reaction is the compound called camphene and not bornylene, as one might expect. Using models to assist you, write a step-by-step mechanism showing how camphene is formed.

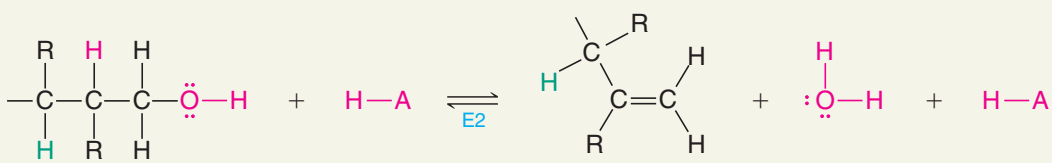


Isoborneol **Camphene** **Bornylene**

7.8B Rearrangement After Dehydration of a Primary Alcohol

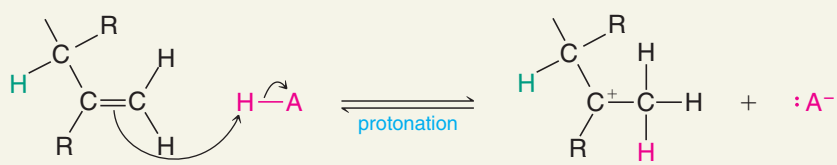
Rearrangements also accompany the dehydration of primary alcohols. Since a primary carbocation is unlikely to be formed during dehydration of a primary alcohol, the alkene that is produced initially from a primary alcohol arises by an E2 mechanism, as described in Section 7.7C. However, an alkene can accept a proton to *generate* a carbocation in a process that is essentially the reverse of the *deprotonation* step in the E1 mechanism for dehydration of an alcohol (Section 7.7A). When a terminal alkene does this by using its π electrons to bond a proton at the terminal carbon, a carbocation forms at the second carbon of the chain.* This carbocation, since it is internal to the chain, will be secondary or tertiary, depending on the specific substrate. Various processes that you have already learned can now occur from this carbocation: (1) a different β hydrogen may be removed, leading to a more stable alkene than the initially formed terminal alkene; (2) a hydride or alkanide rearrangement may occur leading to a yet more stable carbocation (e.g., moving from a 2° to a 3° carbocation) or to a carbocation of approximately equal stability, after which the elimination may be completed; or (3) a nucleophile may attack any of these carbocations to form a substitution product. Under the high-temperature conditions for alcohol dehydration the principal products will be alkenes rather than substitution products.

A MECHANISM FOR THE REACTION — Formation of a Rearranged Alkene During Dehydration of a Primary Alcohol



Primary alcohol (R may be H) — Initial alkene

The primary alcohol initially undergoes acid-catalyzed dehydration by an E2 mechanism (Section 7.7C).

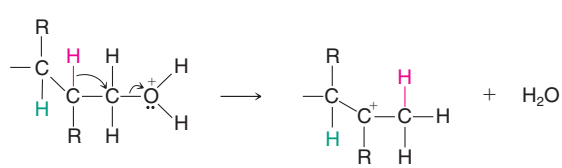


The π electrons of the initial alkene can then be used to form a bond with a proton at the terminal carbon, forming a secondary or tertiary carbocation.*

Final alkene

A different β hydrogen can be removed from the carbocation, so as to form a more highly substituted alkene than the initial alkene. This deprotonation step is the same as the usual completion of an E1 elimination. (This carbocation could experience other fates, such as further rearrangement before elimination or substitution by an S_N1 process.)

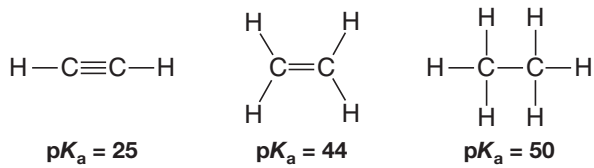
*The carbocation could also form directly from the primary alcohol by a hydride shift from its β carbon to the terminal carbon as the protonated hydroxyl group departs:



7.9 THE ACIDITY OF TERMINAL ALKYNES

The hydrogen bonded to the carbon of a terminal alkyne, called an **acetylenic hydrogen atom**, is considerably more acidic than those bonded to carbons of an alkene or alkane (see Section 3.8A). The pK_a values for ethyne, ethene, and ethane illustrate this point:

A terminal alkyne is ~10^{20} times more acidic than an alkene or alkane.



pK_a = 25 **pK_a = 44** **pK_a = 50**

The order of basicity of their anions is opposite that of their relative acidity:

Relative Basicity

$$CH_3CH_2{:}^- > CH_2{=}CH{:}^- > HC{\equiv}C{:}^-$$

If we include in our comparison hydrogen compounds of other first-row elements of the periodic table, we can write the following orders of relative acidities and basicities. This comparison is useful as we consider what bases and solvents to use with terminal alkynes.

Relative Acidity

Most acidic **Least acidic**

$$H{-}\ddot{O}H > H{-}\ddot{O}R > H{-}C{\equiv}CR > H{-}\ddot{N}H_2 > H{-}CH{=}CH_2 > H{-}CH_2CH_3$$

pK_a 15.7 **16–17** **25** **38** **44** **50**

Relative Basicity

Least basic **Most basic**

$$^-{:}\ddot{O}H < ^-{:}\ddot{O}R < ^-{:}C{\equiv}CR < ^-{:}\ddot{N}H_2 < ^-{:}CH{=}CH_2 < ^-{:}CH_2CH_3$$

We see from the order just given that while terminal alkynes are more acidic than ammonia, they are less acidic than alcohols and are less acidic than water.

SOLVED PROBLEM 7.7

As we shall soon see, sodium amide ($NaNH_2$) is useful, especially when a reaction requires a very strong base. Explain why a solvent such as methanol cannot be used to carry out a reaction in which you might want to use sodium amide as a base.

STRATEGY AND ANSWER: An alcohol has pK_a = 16–17, and ammonia has pK_a = 38. This means that methanol is a significantly stronger acid than ammonia, and the conjugate base of ammonia (the $^-NH_2$ ion) is a significantly stronger base than an alkoxide ion. Therefore, the following acid–base reaction would take place as soon as sodium amide is added to methanol.

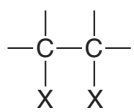
$$\underset{\substack{\text{Stronger}\\\text{acid}}}{CH_3OH} + \underset{\substack{\text{Stronger}\\\text{base}}}{NaNH_2} \xrightarrow{CH_3OH} \underset{\substack{\text{Weaker}\\\text{base}}}{CH_3ONa} + \underset{\substack{\text{Weaker}\\\text{acid}}}{NH_3}$$

With a pK_a difference this large, the sodium amide would convert all of the methanol to sodium methoxide, a much weaker base than sodium amide. (This is an example of what is called the leveling effect of a solvent.)

PRACTICE PROBLEM 7.17 Predict the products of the following acid–base reactions. If the equilibrium would not result in the formation of appreciable amounts of products, you should so indicate. In each case label the stronger acid, the stronger base, the weaker acid, and the weaker base:

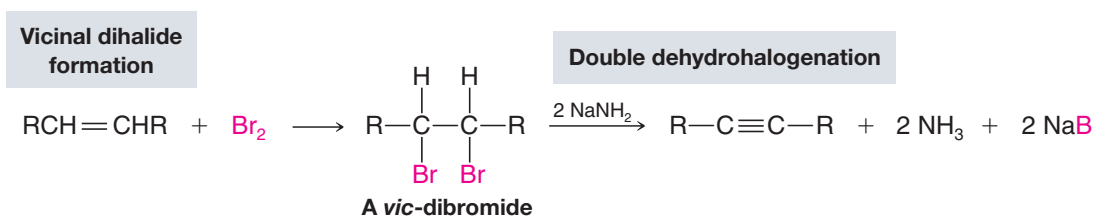
(a) $CH_3CH{=}CH_2 + NaNH_2 \longrightarrow$
(b) $CH_3C{\equiv}CH + NaNH_2 \longrightarrow$
(c) $CH_3CH_2CH_3 + NaNH_2 \longrightarrow$
(d) $CH_3C{\equiv}C{:}^- + CH_3CH_2OH \longrightarrow$
(e) $CH_3C{\equiv}C{:}^- + NH_4Cl \longrightarrow$

7.10 SYNTHESIS OF ALKYNES BY ELIMINATION REACTIONS


A *vic*–dihalide

- Alkynes can be synthesized from alkenes via compounds called vicinal dihalides.

A vicinal dihalide (abbreviated ***vic*-dihalide**) is a compound bearing the halogens on adjacent carbons (*vicinus,* Latin: adjacent). Vicinal dihalides are also called 1,2-dihalides. A vicinal dibromide, for example, can be synthesized by addition of bromine to an alkene (Section 8.1). The *vic*-dibromide can then be subjected to a double dehydrohalogenation reaction with a strong base to yield an alkyne.

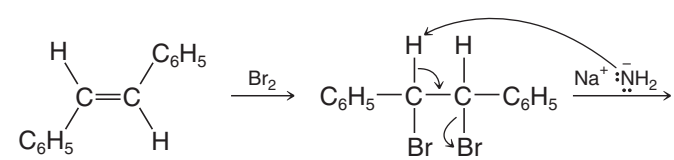


A *vic*-dibromide

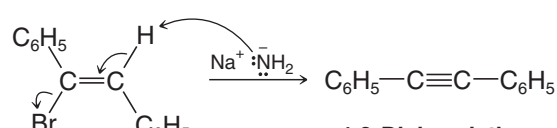
The dehydrohalogenations occur in two steps, the first yielding a bromoalkene, and the second, the alkyne.

7.10A Laboratory Application of This Alkyne Synthesis

The two dehydrohalogenations may be carried out as separate reactions, or they may be carried out consecutively in a single mixture. Sodium amide ($NaNH_2$), a very strong base, can be used to cause both reactions in a single mixture. At least two molar equivalents of sodium amide per mole of the dihalide must be used. For example, adding bromine to 1,2-diphenylethene provides the vicinal dihalide needed for a synthesis of 1,2-diphenylethyne:



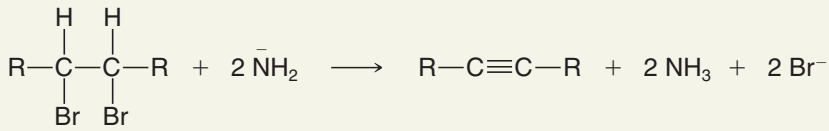
1,2-Diphenylethene



1,2-Diphenylethyne

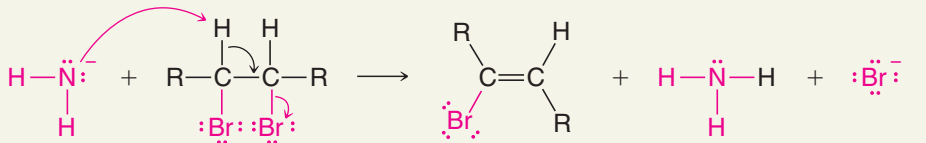
A MECHANISM FOR THE REACTION — Dehydrohalogenation of *vic*-Dibromides to Form Alkynes

Reaction



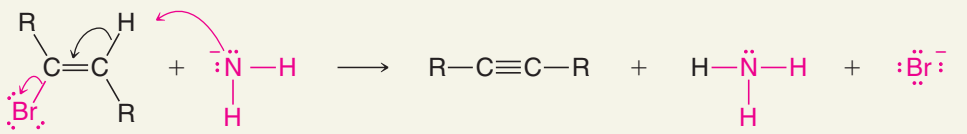
Mechanism

Step 1



The strongly basic amide ion brings about an E2 reaction.

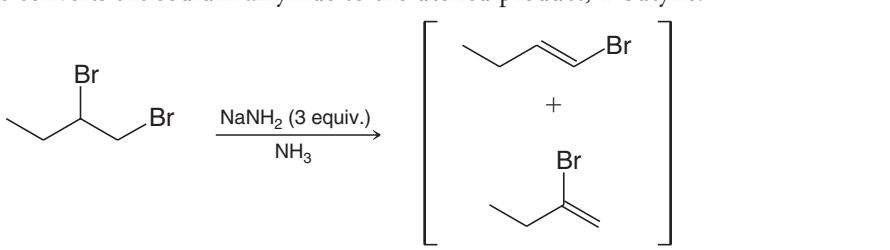
Step 2



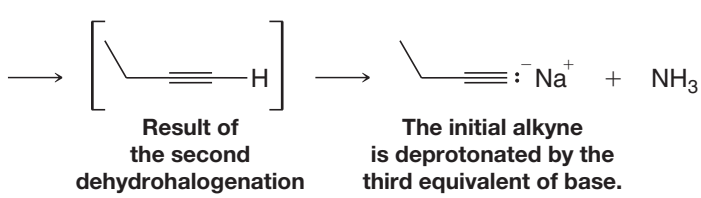
A second E2 reaction produces the alkyne.

- If the product is to be an alkyne with a triple bond at the end of the chain (a terminal alkyne) as we show in the example below, then three molar equivalents of sodium amide are required.

Initial dehydrohalogenation of the *vic*-dihalide produces a mixture of two bromoalkenes that are not isolated but that undergo a second dehydrohalogenation. The terminal alkyne that results from this step is deprotonated (because of its acidity) by the third mole of sodium amide (see Section 7.9). To complete the process, addition of ammonium chloride converts the sodium alkynide to the desired product, 1-butyne.

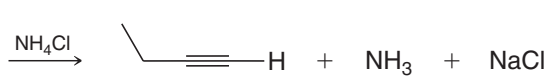


Result of the first dehydrohalogenation

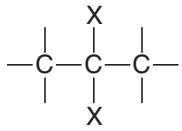


Result of the second dehydrohalogenation

The initial alkyne is deprotonated by the third equivalent of base.



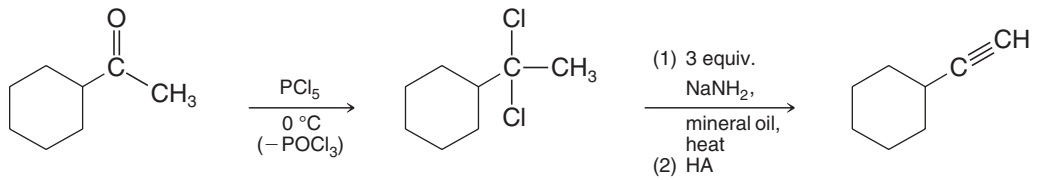
1-Butyne



A *gem*–dihalide

- **Geminal** dihalides can also be converted to alkynes by dehydrohalogenation.

A geminal dihalide (abbreviated ***gem*-dihalide**) has two halogen atoms bonded to the same carbon (*geminus,* Latin: twins). Ketones can be converted to *gem*-dichlorides by reaction with phosphorus pentachloride, and the *gem*-dichlorides can be used to synthesize alkynes.



Cyclohexyl methyl ketone | **A *gem*-dichloride (70–80%)** | **Cyclohexylacetylene (46%)**

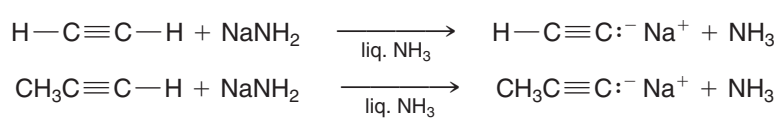
PRACTICE PROBLEM 7.18 Show how you might synthesize ethynylbenzene from methyl phenyl ketone.

PRACTICE PROBLEM 7.19 Outline all steps in a synthesis of propyne from each of the following:

(a) CH_3COCH_3
(b) $CH_3CH_2CHBr_2$
(c) $CH_3CHBrCH_2Br$
(d) $CH_3CH{=}CH_2$

7.11 TERMINAL ALKYNES CAN BE CONVERTED TO NUCLEOPHILES FOR CARBON–CARBON BOND FORMATION

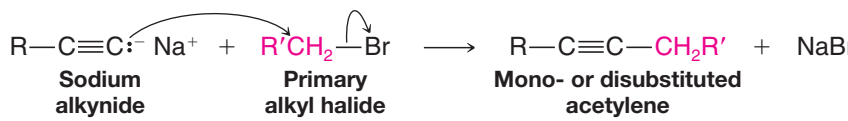
- The acetylenic proton of ethyne or any terminal alkyne (pK_a 25) can be removed with a strong base such as sodium amide ($NaNH_2$). The result is an alkynide anion.



- Alkynide anions are useful nucleophiles for carbon–carbon bond forming reactions with primary alkyl halides or other primary substrates.

The following are general and specific examples of carbon–carbon bond formation by alkylation of an alkynide anion with a primary alkyl halide.

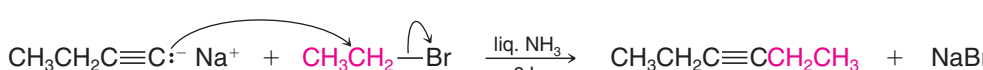
General Example



Sodium alkynide | **Primary alkyl halide** | **Mono- or disubstituted acetylene**

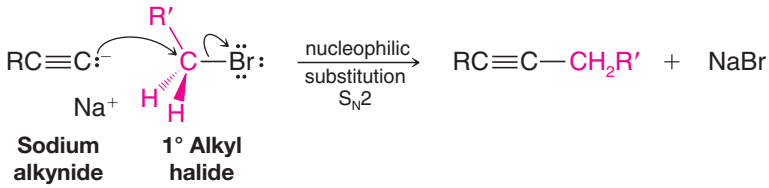
(R or R′ or both may be hydrogen.)

Specific Example



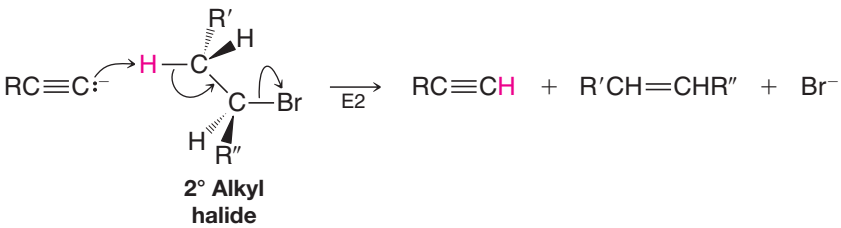
3-Hexyne (75%)

The alkynide anion acts as a nucleophile and displaces the halide ion from the primary alkyl halide. We now recognize this as an S_N2 reaction (Section 6.5).



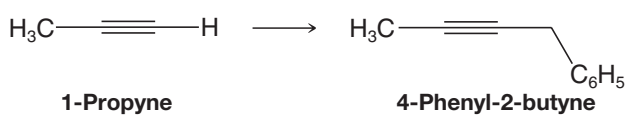
- Primary alkyl halides should be used in the alkylation of alkynide anions, so as to avoid competition by elimination.

Use of a secondary or tertiary substrate causes E2 elimination instead of substitution because the alkynide anion is a strong base as well as a good nucleophile.

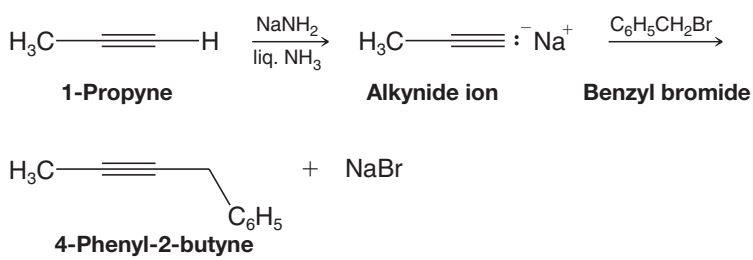


SOLVED PROBLEM 7.8

Outline a synthesis of 4-phenyl-2-butyne from 1-propyne.

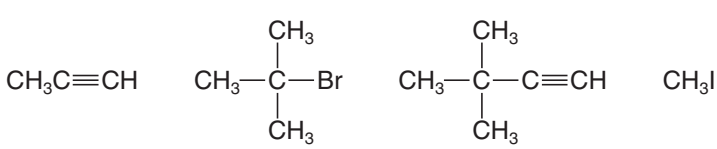


STRATEGY AND ANSWER: Take advantage of the acidity of the acetylenic hydrogen of propyne and convert it to an alkynide anion using sodium amide, a base that is strong enough to remove the acetylenic hydrogen. Then use the akynide ion as a nucleophile in an S_N2 reaction with benzyl bromide.



PRACTICE PROBLEM 7.20

Your goal is to synthesize 4,4-dimethyl-2-pentyne. You have a choice of beginning with any of the following reagents:



Assume that you also have available sodium amide and liquid ammonia. Outline the best synthesis of the required compound.

7.11A General Principles of Structure and Reactivity Illustrated by the Alkylation of Alkynide Anions

The **alkylation** of alkynide anions illustrates several essential aspects of structure and reactivity that have been important to our study of organic chemistry thus far.

1. Preparation of the alkynide anion involves simple **Brønsted–Lowry acid–base chemistry.** As you have seen (Sections 7.9 and 7.11), the hydrogen of a terminal alkyne is weakly acidic ($pK_a \cong 25$), and with a strong base such as sodium amide it can be removed. The reason for this acidity was explained in Section 3.8A.
2. Once formed, the alkynide anion is a **Lewis base** (Section 3.3) with which the alkyl halide reacts as an electron pair acceptor (a **Lewis acid**). The alkynide anion can thus be called a ***nucleophile*** (Sections 3.4 and 6.3) because of the negative charge concentrated at its terminal carbon—it is a reagent that seeks positive charge.
3. The alkyl halide can be called an ***electrophile*** (Sections 3.4 and 8.1) because of the partial positive charge at the carbon bearing the halogen—it is a reagent that seeks negative charge. Polarity in the alkyl halide is the direct result of the difference in electronegativity between the halogen atom and carbon atom.

Helpful Hint

You should pay attention to the bookkeeping of valence electrons and formal charges in the reaction shown in Fig. 7.8, just as with every other reaction you study in organic chemistry.

The electrostatic potential maps for ethynide (acetylide) anion and chloromethane in Fig. 7.8 illustrate the complementary nucleophilic and electrophilic character of a typical alkynide anion and alkyl halide. The ethynide anion has strong localization of negative charge at its terminal carbon, indicated by red in the electrostatic potential map. Conversely, chloromethane has partial positive charge at the carbon bonded to the electronegative chlorine atom. (The dipole moment for chloromethane is aligned directly along the carbon–chlorine bond.) Thus, acting as a Lewis base, the alkynide anion is attracted to the partially positive carbon of the alkyl halide. Assuming a collision between the two occurs with the proper orientation and sufficient kinetic energy, as the alkynide anion brings two electrons to the alkyl halide to form a new bond, it will displace the halogen from the alkyl halide. The halogen leaves as an anion with the pair of electrons that formerly bonded it to the carbon. This is an S_N2 reaction, of course, akin to others we discussed in Chapter 6.

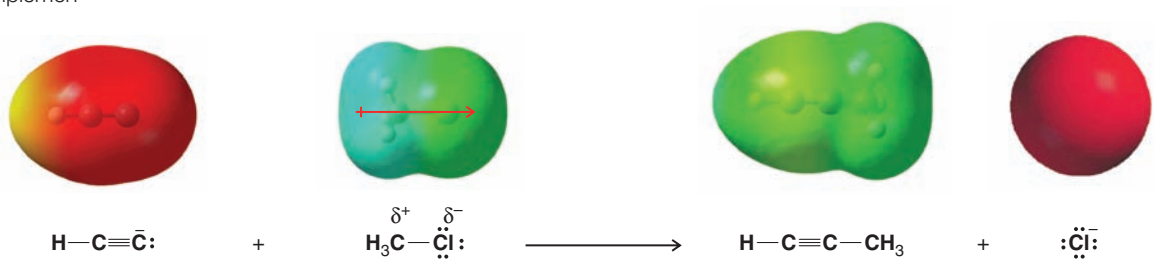


FIGURE 7.8 The reaction of ethynide (acetylide) anion and chloromethane. Electrostatic potential maps illustrate the complementary nucleophilic and electrophilic character of the alkynide anion and the alkyl halide. The dipole moment of chloromethane is shown by the red arrow.

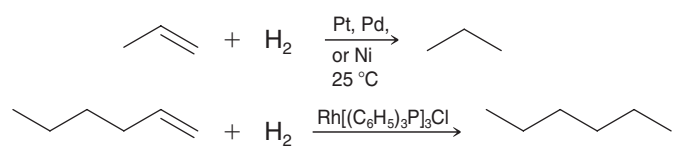
7.12 HYDROGENATION OF ALKENES

- Alkenes react with hydrogen in the presence of a variety of metal catalysts to add one hydrogen atom to each carbon atom of the double bond (Sections 4.16A, 5.10A).

Hydrogenation reactions that involve *insoluble* platinum, palladium, or nickel catalysts (Section 4.16A) proceed by **heterogeneous catalysis** because the catalyst is not soluble in the reaction mixture. Hydrogenation reactions that involve soluble catalysts occur by **homogeneous catalysis.** Typical homogeneous hydrogenation catalysts include rhodium and ruthenium complexes that bear various phosphorus and other ligands. One of the most well-known homogeneous hydrogenation catalysts is Wilkinson's catalyst, tris(triphenylphosphine)rhodium chloride, $Rh[(C_6H_5)_3P]_3Cl$ (see Special Topic G.) The following are some examples of hydrogenation reactions under heterogeneous and homogeneous catalysis:

Helpful Hint

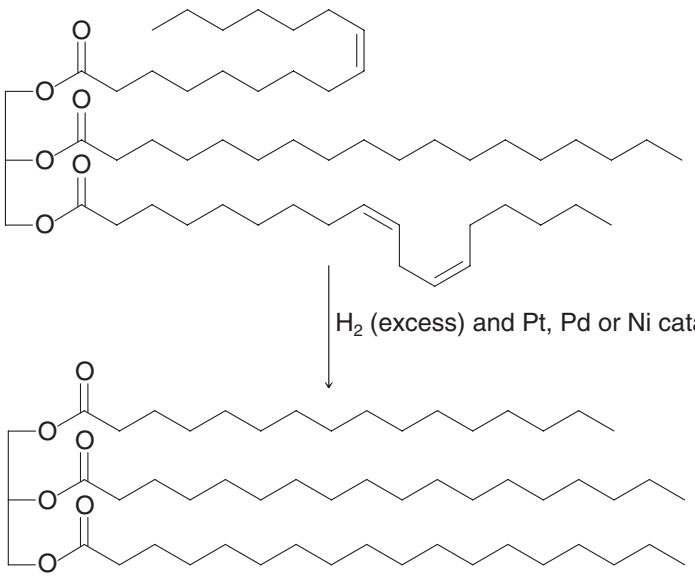
These are addition reactions.



Catalytic hydrogenation reactions, like those shown above, are a type of **addition reaction** (versus substitution or elimination), and they are also a type of reduction. This leads to a distinction between compounds that are saturated versus those that are unsaturated.

- Compounds containing only carbon–carbon single bonds (alkanes and others) are said to be **saturated compounds** because they contain the maximum number of hydrogen atoms that a given formula can possess.
- Compounds containing carbon–carbon multiple bonds (alkenes, alkynes, and aromatic compounds) are said to be **unsaturated compounds** because they contain fewer than the maximum number of hydrogen atoms possible for a given formula.

Unsaturated compounds can be **reduced** to saturated compounds by **catalytic hydrogenation**. The following example shows conversion of an unsaturated triglyceride to a saturated triglyceride (both are fats), in a catalytic hydrogenation reaction as might be done in the food industry to change the physical properties of a fat.



An unsaturated fat can be hydrogenated to form a saturated fat.

Molecules of a natural unsaturated fat can align less evenly with each other than can molecules of saturated fats due to the "kinks" from the cis double bonds in unsaturated fats. Hence intermolecular forces between unsaturated fat molecules are weaker and they have lower melting points than saturated fats. See "The Chemistry of … Hydrogenation in the Food Industry."

THE CHEMISTRY OF... Hydrogenation in the Food Industry

The food industry makes use of catalytic hydrogenation to convert liquid vegetable oils to semisolid fats in making margarine and solid cooking fats. Examine the labels of many prepared foods and you will find that they contain "partially hydrogenated vegetable oils." There are several reasons why foods contain these oils, but one is that partially hydrogenated vegetable oils have a longer shelf life.

Fats and oils (Section 23.2) are glyceryl esters of carboxylic acids with long carbon chains, called "fatty acids." Fatty acids are saturated (no double bonds), monounsaturated (one double bond), or polyunsaturated (more than one double bond). Oils typically contain a higher proportion of fatty acids with one or more double bonds than fats do. Partial hydrogenation of an oil converts some of its double bonds to single bonds, and this conversion has the effect of producing a fat with the consistency of margarine or a semisolid cooking fat.

One potential problem that arises from using catalytic hydrogenation to produce partially hydrogenated vegetable oils is that the catalysts used for hydrogenation cause isomerization of some of the double bonds of the fatty acids (some of those that do not absorb hydrogen). In most natural fats and oils, the double bonds of the fatty acids have the cis configuration. The catalysts used for hydrogenation convert some of these cis double bonds to the unnatural trans configuration. The health effects of trans fatty acids are still under study, but experiments thus far indicate that they cause an increase in serum levels of cholesterol and triacylglycerols, which in turn increases the risk of cardiovascular disease.

Photo by Lisa Gee

A product used in baking that contains oils and mono- and diacylglycerols that are partially hydrogenated.

© Jonathan Vasata/iStock photo

No (or zero%) trans fatty acids.

7.13 HYDROGENATION: THE FUNCTION OF THE CATALYST

Hydrogenation of an alkene is an exothermic reaction ($\Delta H^\circ \cong -120$ kJ mol^{-1}):

$$\text{R—CH=CH—R} + \text{H}_2 \xrightarrow{\text{hydrogenation}} \text{R—CH}_2\text{—CH}_2\text{—R} + \text{heat}$$

Although the process is exothermic, there is usually a high free energy of activation for uncatalyzed alkene hydrogenation, and therefore, the uncatalyzed reaction does not take place at room temperature. However, hydrogenation will take place readily at room temperature in the presence of a catalyst because the catalyst provides a new pathway for the reaction that involves lower free energy of activation (Fig. 7.9).

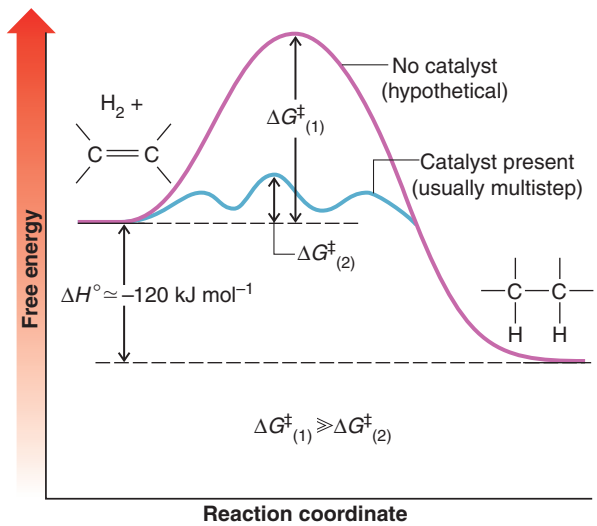
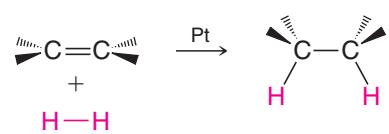


FIGURE 7.9 Free-energy diagram for the hydrogenation of an alkene in the presence of a catalyst and the hypothetical reaction in the absence of a catalyst. The free energy of activation for the uncatalyzed reaction ($\Delta G^\ddagger_{(1)}$) is very much larger than the largest free energy of activation for the catalyzed reaction ($\Delta G^\ddagger_{(2)}$). The uncatalyzed hydrogenation reaction does not occur.

Heterogeneous hydrogenation catalysts typically involve finely divided platinum, palladium, nickel, or rhodium deposited on the surface of powdered carbon (charcoal). Hydrogen gas introduced into the atmosphere of the reaction vessel adsorbs to the metal by a chemical reaction where unpaired electrons on the surface of the metal *pair* with the electrons of hydrogen (Fig. 7.10*a*) and bind the hydrogen to the surface. The collision of an alkene with the surface bearing adsorbed hydrogen causes adsorption of the alkene as well (Fig. 7.10*b*). A stepwise transfer of hydrogen atoms takes place, and this produces an alkane before the organic molecule leaves the catalyst surface (Figs. 7.10*c, d*). As a consequence, *both hydrogen atoms usually add from the same side of the molecule.* This mode of addition is called a **syn** addition (Section 7.14A):



Catalytic hydrogenation is a syn addition.

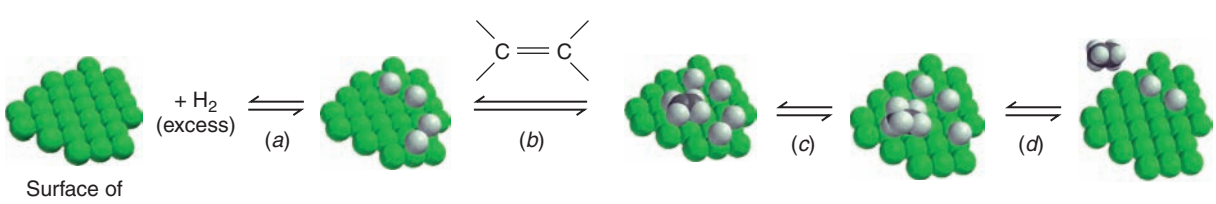
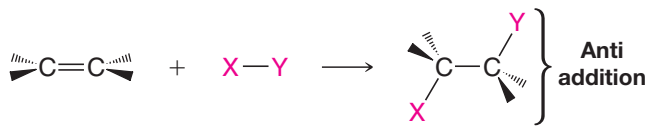


FIGURE 7.10 The mechanism for the hydrogenation of an alkene as catalyzed by finely divided platinum metal: (*a*) hydrogen adsorption; (*b*) adsorption of the alkene; (*c, d*) stepwise transfer of both hydrogen atoms to the same face of the alkene (syn addition).

7.13A Syn and Anti Additions

An addition that places the parts of the adding reagent on the same side (or face) of the reactant is called **syn addition**. We have just seen that the platinum-catalyzed addition of hydrogen (X = Y = H) is a syn addition:

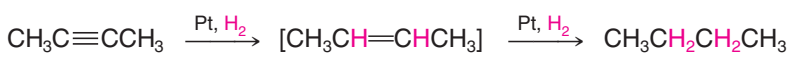
The opposite of a syn addition is an **anti addition**. An anti addition places the parts of the adding reagent on opposite faces of the reactant.



In Chapter 8 we shall study a number of important syn and anti additions.

7.14 HYDROGENATION OF ALKYNES

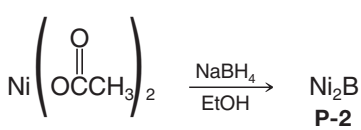
Depending on the conditions and the catalyst employed, one or two molar equivalents of hydrogen will add to a carbon–carbon triple bond. When a platinum catalyst is used, the alkyne generally reacts with two molar equivalents of hydrogen to give an alkane:



However, **hydrogenation** of an alkyne to an alkene can be accomplished through the use of special catalysts or reagents. Moreover, these special methods allow the preparation of either (*E*)- or (*Z*)-alkenes from disubstituted alkynes.

7.14A Syn Addition of Hydrogen: Synthesis of *cis*-Alkenes

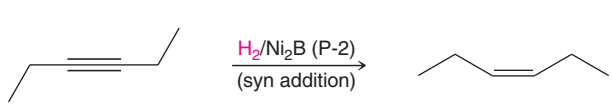
A **heterogeneous catalyst** that permits hydrogenation of an alkyne to an alkene is the nickel boride compound called P-2 catalyst. The P-2 catalyst can be prepared by the reduction of nickel acetate with sodium borohydride:



- Hydrogenation of alkynes in the presence of P-2 catalyst causes **syn addition of hydrogen**. The alkene formed from an internal alkyne has the (*Z*) or cis configuration.

The hydrogenation of 3-hexyne illustrates this method. The reaction takes place on the surface of the catalyst (Section 7.14), accounting for the syn addition:

Syn addition of hydrogen to an alkyne

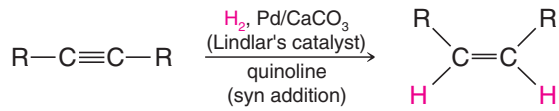


3-Hexyne

(*Z*)-3-Hexene (*cis*-3-hexene) (97%)

Other specially conditioned catalysts can be used to prepare *cis*-alkenes from disubstituted alkynes. Metallic palladium deposited on calcium carbonate can be used in this

way after it has been conditioned with lead acetate and quinoline (an amine, see Section 20.1B). This special catalyst is known as **Lindlar's catalyst**:

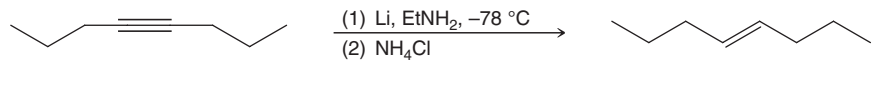


7.14B Anti Addition of Hydrogen: Synthesis of *trans*-Alkenes

- **Anti addition** of hydrogen to the triple bond of alkynes occurs when they are treated with lithium or sodium metal in ammonia or ethylamine at low temperatures.

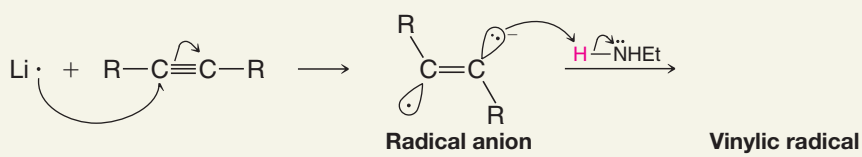
This reaction, called a **dissolving metal reduction,** takes place in solution and produces an (*E*)- or *trans*-alkene. The mechanism involves radicals, which are molecules that have unpaired electrons (see Chapter 10).

Anti addition of hydrogen to an alkyne.



4-Octyne **(anti addition)** **(*E*)-4-Octene (*trans*-4-octene) (52%)**

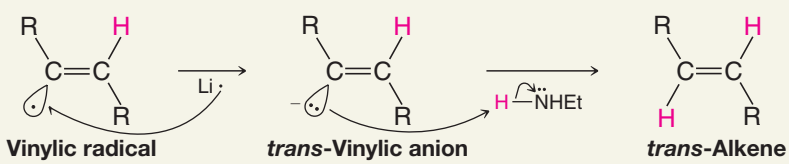
A MECHANISM FOR THE REACTION — The Dissolving Metal Reduction of an Alkyne



Radical anion **Vinylic radical**

A lithium atom donates an electron to the π bond of the alkyne. An electron pair shifts to one carbon as the hybridization states change to sp^2.

The radical anion acts as a base and removes a proton from a molecule of ethylamine.



Vinylic radical ***trans*-Vinylic anion** ***trans*-Alkene**

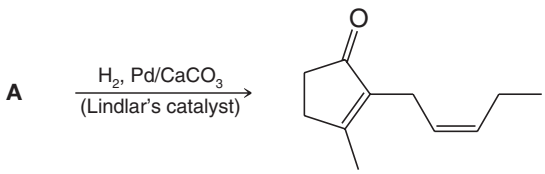
A second lithium atom donates an electron to the vinylic radical.

The anion acts as a base and removes a proton from a second molecule of ethylamine.

The mechanism for this reduction, shown in the preceding box, involves successive electron transfers from lithium (or sodium) atoms and proton transfers from amines (or ammonia). In the first step, a lithium atom transfers an electron to the alkyne to produce an intermediate that bears a negative charge and has an unpaired electron, called a **radical anion.** In the second step, an amine transfers a proton to produce a **vinylic radical.** Then, transfer of another electron gives a **vinylic anion.** It is this step that determines the stereochemistry of the reaction. The *trans*-vinylic anion is formed preferentially because it is more stable; the bulky alkyl groups are farther apart. Protonation of the *trans*-vinylic anion leads to the *trans*-alkene.

PRACTICE PROBLEM 7.21

Write the structure of compound **A**, used in this synthesis of the perfume ingredient (*Z*)-jasmone.



(*Z*)-Jasmone

PRACTICE PROBLEM 7.22

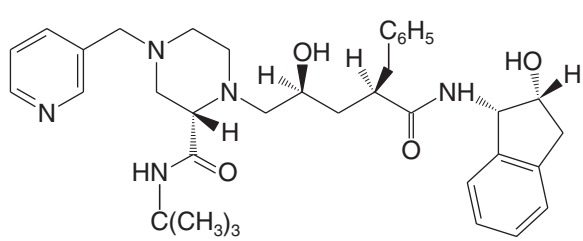
How would you convert 2-nonyne into (*E*)-2-nonene?

7.15 AN INTRODUCTION TO ORGANIC SYNTHESIS

You have learned quite a few tools that are useful for organic synthesis, including nucleophilic substitution reactions, elimination reactions, and the hydrogenation reactions covered in Sections 7.12–7.14. Now we will consider the logic of organic synthesis and the important process of retrosynthetic analysis. Then we will apply nucleophilic substitution (in the specific case of alkylation of alkynide anions) and **hydrogenation** reactions to the synthesis of some simple target molecules.

7.15A Why Do Organic Synthesis?

Organic synthesis is the process of building organic molecules from simpler precursors. Syntheses of organic compounds are carried out for many reasons. Chemists who develop new drugs carry out organic syntheses in order to discover molecules with structural attributes that enhance certain medicinal effects or reduce undesired side effects. Crixivan, whose structure is shown below, was designed by small-scale synthesis in a research laboratory and then quickly moved to large-scale synthesis after its approval as a drug. In other situations, organic synthesis may be needed to test a hypothesis about a reaction mechanism or about how a certain organism metabolizes a compound. In cases like these we often will need to synthesize a particular compound "labeled" at a certain position (e.g., with deuterium, tritium, or an isotope of carbon).

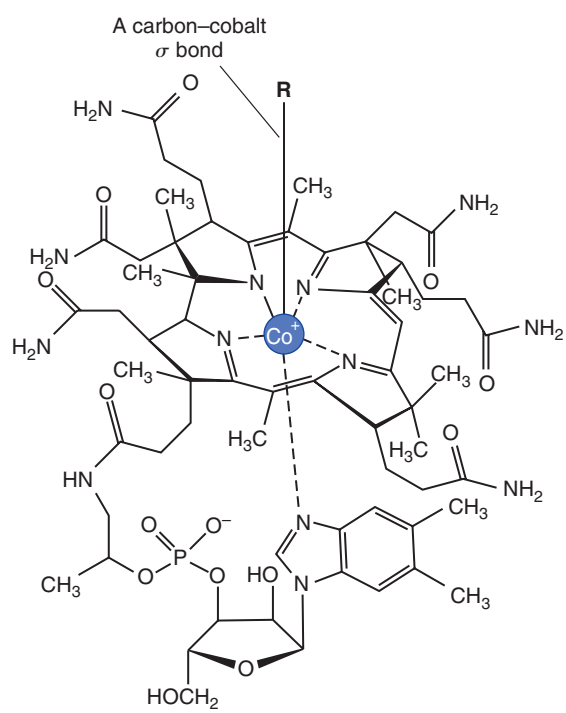


Crixivan (an HIV protease inhibitor)

A very simple organic synthesis may involve only one chemical reaction. Others may require from several to 20 or more steps. A landmark example of organic synthesis is that of vitamin B_{12}, announced in 1972 by R. B. Woodward (Harvard) and A. Eschenmoser (Swiss Federal Institute of Technology). Their synthesis of vitamin B_{12} took 11 years, required more than 90 steps, and involved the work of nearly 100 people. We will work with much simpler examples, however.

An organic synthesis typically involves two types of transformations:

1. reactions that convert functional groups from one to another
2. reactions that create new carbon–carbon bonds.

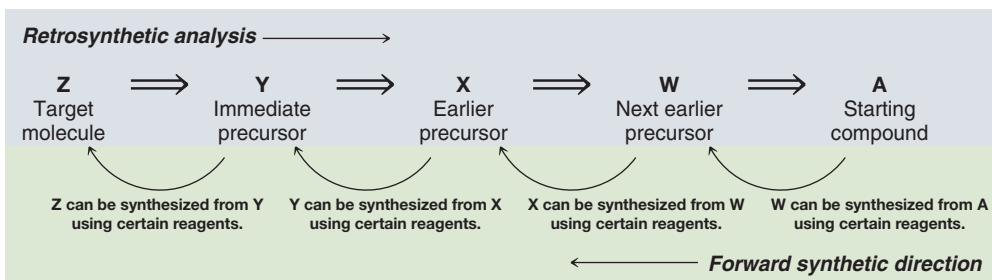


Vitamin B_{12}

You have studied examples of both types of reactions already. For example, hydrogenation transforms the carbon–carbon double- or triple-bond functional groups in alkenes and alkynes to single bonds (actually removing a functional group in this case), and alkylation of alkynide anions forms carbon–carbon bonds. Ultimately, at the heart of organic synthesis is the orchestration of functional group interconversions and carbon–carbon bond-forming steps. Many methods are available to accomplish both of these things.

7.15B Retrosynthetic Analysis—Planning an Organic Synthesis

Sometimes it is possible to visualize from the start all the steps necessary to synthesize a desired (target) molecule from obvious precursors. Often, however, the sequence of transformations that would lead to the desired compound is too complex for us to "see" a path from the beginning to the end. In this case, since we know where we want to finish (the target molecule) but not where to start, we envision the sequence of steps that is required in a backward fashion, one step at a time. We begin by identifying immediate precursors that could react to make the target molecule. Once these have been chosen, they in turn become new intermediate target molecules, and we identify the next set of precursors that could react to form them, and so on, and so on. This process is repeated until we have worked backward to compounds that are sufficiently simple that they are readily available in a typical laboratory:



- The process we have just described is called **retrosynthetic analysis**.
- The open arrow is called a **retrosynthesis arrow,** and means that a molecule can be synthesized from its most immediate precursor by some chemical reaction.

Although some of the earliest organic syntheses likely required some type of analytical planning, it was E. J. Corey who first formalized a set of global principles for chemical synthesis, a process which he termed retrosynthetic analysis, that enabled anyone to plan a complex molecule synthesis. Once retrosynthetic analysis has been completed, to actually carry out the synthesis we conduct the sequence of reactions from the beginning, starting with the simplest precursors and working step by step until the target molecule is achieved.

- When doing retrosynthetic analysis it is necessary to generate as many possible precursors, and hence different synthetic routes, as possible (Fig. 7.11).

We evaluate all the possible advantages and disadvantages of each path and in so doing determine the most efficient route for synthesis. The prediction of which route is most feasible is usually based on specific restrictions or limitations of reactions in the sequence, the

Corey was awarded the Nobel Prize in Chemistry in 1990 for finding new ways of synthesizing organic compounds, which, in the words of the Nobel committee, "have contributed to the high standards of living and health enjoyed … in the Western world."

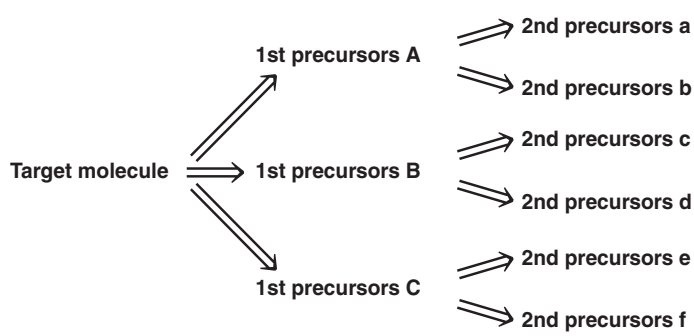


FIGURE 7.11 Retrosynthetic analysis often discloses several routes from the target molecule back to varied precursors.

availability of materials, or other factors. We shall see an example of this in Section 7.16C. In actuality more than one route may work well. In other cases it may be necessary to try several approaches in the laboratory in order to find the most efficient or successful route.

7.15C Identifying Precursors

In the case of functional groups we need to have a toolbox of reactions from which to choose those we know can convert one given functional group into another. You will develop such a toolbox of reactions as you proceed through your study of organic chemistry. Similarly, with regard to making carbon–carbon bonds in synthesis, you will develop a repertoire of reactions for that purpose. In order to choose the appropriate reaction for either purpose, you will inevitably consider basic principles of structure and reactivity.

As we stated in Sections 3.3A and 7.12:

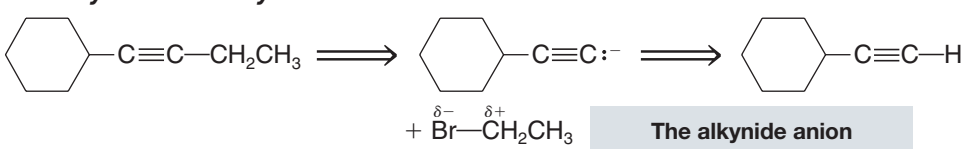
- Many organic reactions depend on the interaction of molecules that have complementary full or partial charges.

One very important aspect of retrosynthetic analysis is being able to identify those atoms in a target molecule that could have had complementary (opposite) charges in synthetic precursors. Consider, for example, the synthesis of 1-cyclohexyl-1-butyne. On the basis of reactions learned in this chapter, you might envision an alkynide anion and an alkyl halide as precursors having complementary polarities that when allowed to react together would lead to this molecule:

Helpful Hint

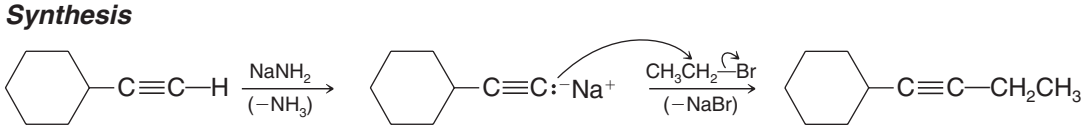
Over time you will add to your toolbox reactions for two major categories of synthetic operations: carbon–carbon bond formation and functional group interconversion.

Retrosynthetic Analysis



The alkynide anion and alkyl halide have complementary polarities.

Synthesis



Sometimes, however, it will not at first be obvious where the retrosynthetic bond disconnections are in a target molecule that would lead to oppositely charged or complementary precursors. The synthesis of an alkane would be such an example. An alkane does not contain carbon atoms that could directly have had opposite charges in precursor molecules. However, if one supposes that certain carbon–carbon single bonds in the alkane could have arisen by hydrogenation of a corresponding alkyne (a functional group interconversion), then, in turn, two atoms of the alkyne could have been joined from precursor molecules that had complementary charges (i.e., an alkynide anion and an alkyl halide).

THE CHEMISTRY OF... From the Inorganic to the Organic

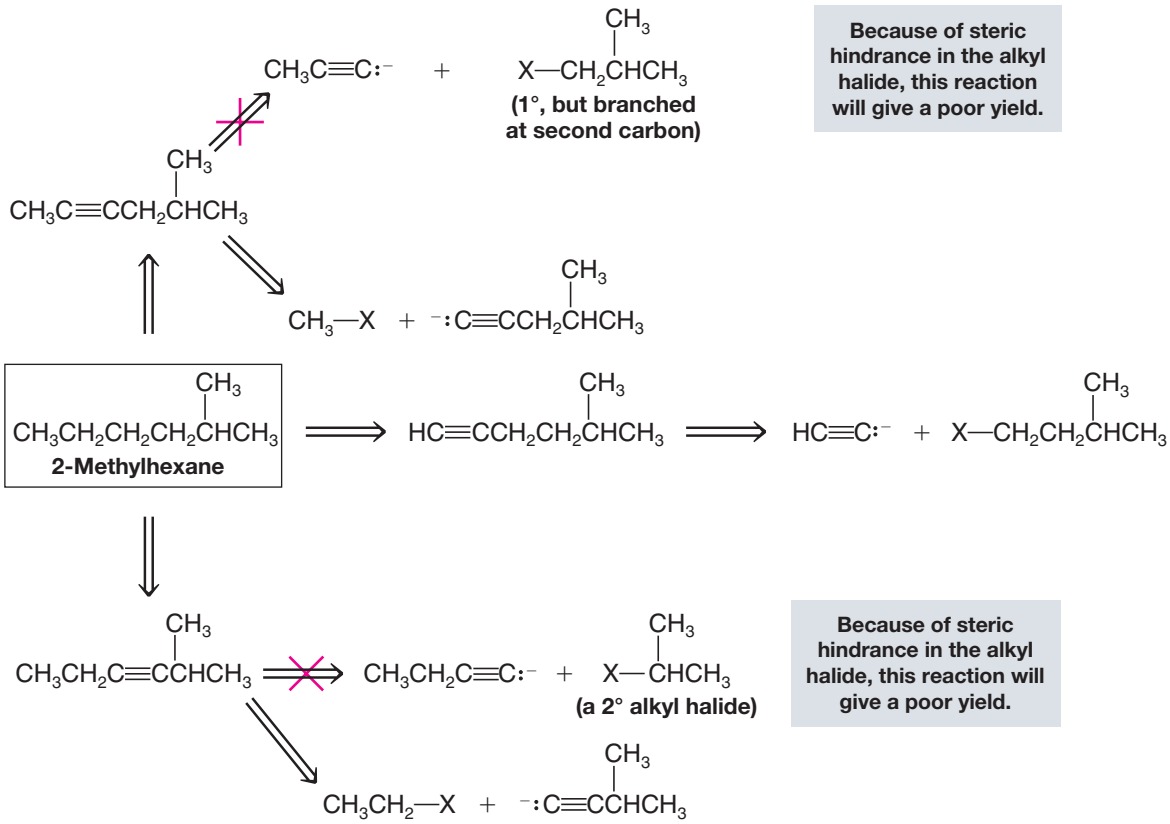
In 1862, Friedrich Wöhler discovered calcium carbide (CaC_2) by heating carbon with an alloy of zinc and calcium. He then synthesized acetylene by allowing the calcium carbide to react with water:

$$C \xrightarrow{\text{zinc-calcium alloy, heat}} CaC_2 \xrightarrow{2H_2O} HC{\equiv}CH + Ca(OH)_2$$

Acetylene produced this way burned in lamps of some lighthouses and in old-time miners' headlamps. From the standpoint of organic synthesis, it is theoretically possible to synthesize anything using reactions of alkynes to form carbon–carbon bonds and to prepare other functional groups. Thus, while Wöhler's 1828 conversion of ammonium cyanate to urea was the first synthesis of an organic compound from an inorganic precursor (Section 1.1A), his discovery of calcium carbide and its reaction with water to form acetylene gives us a formal link from inorganic materials to the entire realm of organic synthesis.

Consider the following retrosynthetic analysis for **2-methylhexane:**

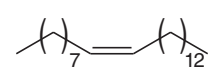
Retrosynthetic Analysis



As indicated in the retrosynthetic analysis above, we must bear in mind the limitations that exist for the reactions that would be applied in the synthetic (forward) direction. In the example above, two of the pathways have to be discarded because they involve the use of a 2° alkyl halide or a primary halide branched at the second (beta) carbon (Sections 6.13A, 7.11).

SOLVED PROBLEM 7.9

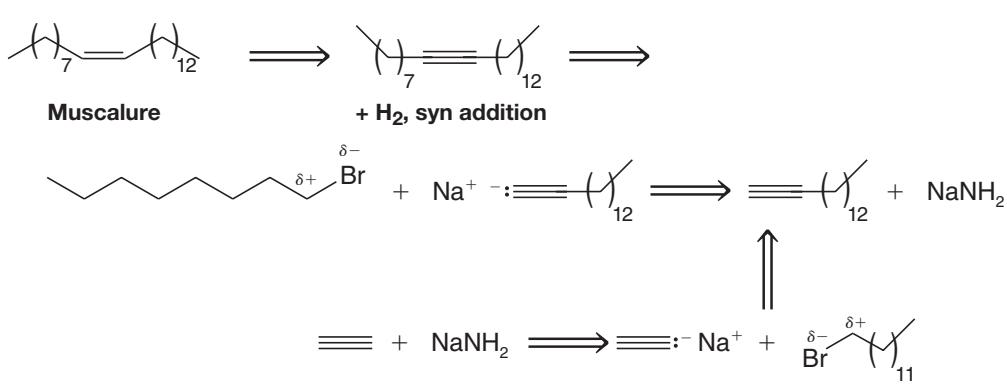
Outline a retrosynthetic pathway that leads from 'muscalure', the sex attractant pheromone of the common housefly back to the simplest alkyne, ethyne (acetylene). Then show the synthesis. You may use any inorganic compounds, or solvents, you need and alkyl halides of any length necessary.



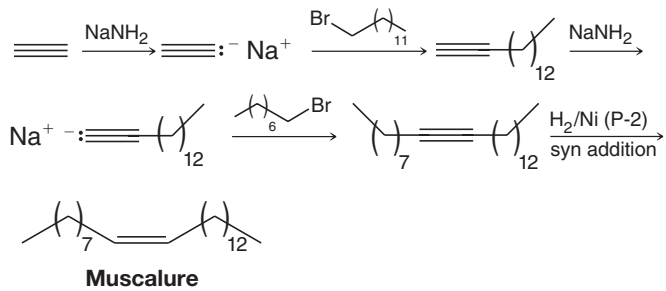
Muscalure

STRATEGY AND ANSWER: We make use of two reactions that we have just studied in this chapter: syn addition of hydrogen to an alkyne, and alkylation of alkynide ions.

Retrosynthetic Analysis



Synthesis



Muscalure

PRACTICE PROBLEM 7.23

Referring to the retrosynthetic analysis for 2-methylhexane in this section, write reactions for those synthesis routes that are feasible.

PRACTICE PROBLEM 7.24

(a) Devise retrosynthetic schemes for all conceivable alkynide anion alkylation syntheses of the insect pheromones undecane and 2-methylheptadecane (see "The Chemistry of… Pheromones" box in Chapter 4). **(b)** Write reactions for two feasible syntheses of each pheromone.

7.15D Raison d'Etre

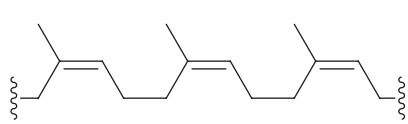
Solving synthetic puzzles by application of retrosynthetic analysis is one of the joys of learning organic chemistry. As you might imagine, there is skill and some artistry involved. Over the years many chemists have set their minds to organic synthesis, and because of this we have all prospered from the fruits of their endeavors.

[WHY Do These Topics Matter?

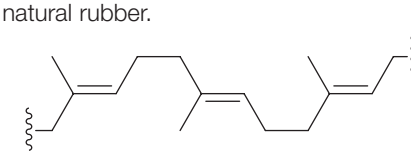
ALKENE GEOMETRY, RUBBER, AND THE CHEMISTRY OF VISION

The (*E*) or (*Z*) configurations of substituted double bonds is not just a matter for exercise sets and exams. In the real world, they define the properties of many compounds. For example, natural rubber, which can be obtained from the sap of certain trees, has all (*Z*) configurations about its trisubstituted double bonds. Some other trees make the all (*E*) version, a compound known as gutta percha. While gutta percha is also a latex-like material, the change in stereochemistry actually makes it inelastic so that it does not have the same useful properties as natural rubber.

Bjorn Svensson/Photo Researchers, Inc.



Natural rubber (*Z* configuration)



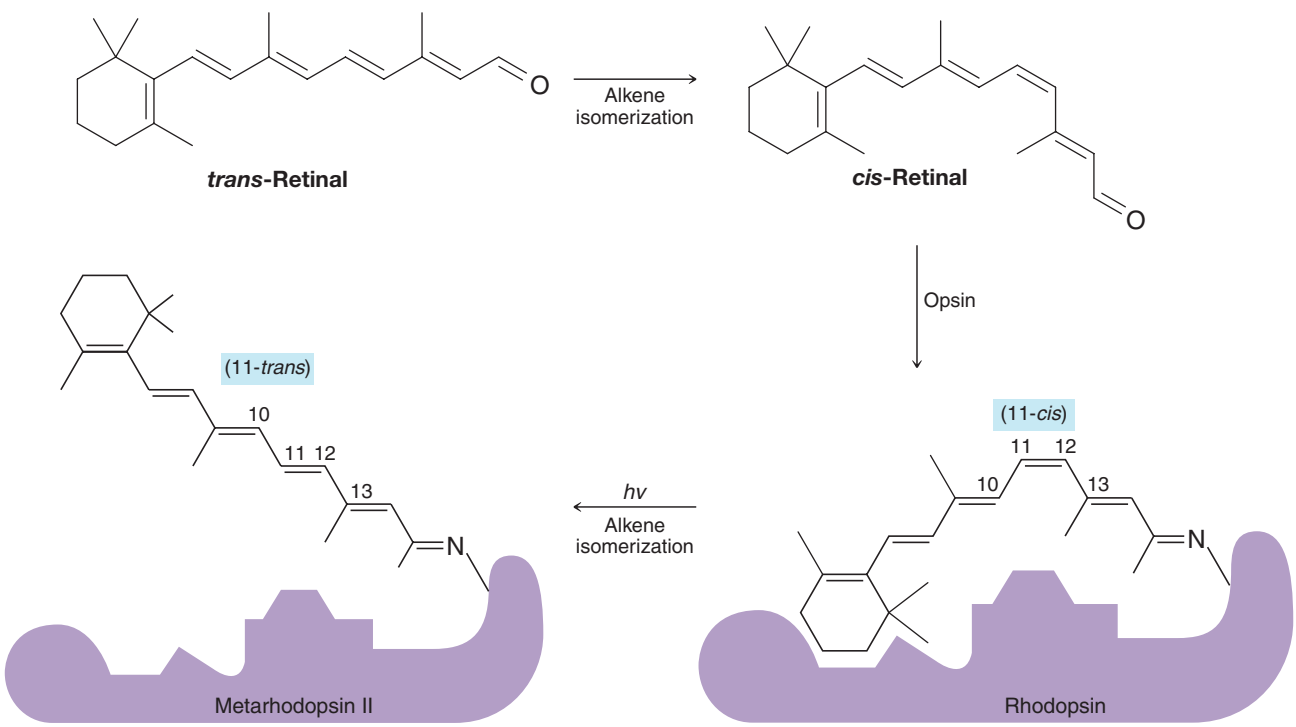
Gutta percha (*E* configuration)

Alkene stereochemistry is also critical to our ability to see. In our eyes, the key molecule is a compound called *trans*-retinal, a material that can be synthesized in our bodies and that comes from our diets through foods like carrots.

(continues on next page)

Image Source

In order for retinal to participate in the vision process, one particular double bond within it must first be isomerized from trans to cis through a process that breaks the π-bond, rotates about a single bond, and reforms the π-bond. This new stereochemical orientation places several carbon atoms in a different orientation than they were in the trans configuration. The value of that change, however, is that the new spatial orientation of *cis*-retinal allows it to fit into a receptor in a protein known as opsin in our retinas and merge with it through a general reaction process we will learn more about in Chapter 16; this step generates a new complex known as rhodopsin. The key thing to understand for now, however, is that when rhodopsin is exposed to light of a certain wavelength (of which we will learn more in Chapter 13), the cis double bond isomerizes back to the more stable all trans configuration through a series of steps to become metarhodopsin II as shown below. It is believed that the repositioning of the cyclohexene ring within the retinal portion of metarhodopsin II following this isomerization induces some further conformational changes within the protein. These changes ultimately lead to a nerve impulse that is interpreted by our brains as vision. The picture shown here is but a small part in the overall process, but these initial, critical steps are based solely on alkene stereochemistry. As such, it really does matter whether a double bond is cis or trans, (*E*) or (*Z*)!



SUMMARY AND REVIEW TOOLS

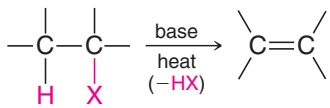
In this chapter we described methods for the synthesis of alkenes using dehydrohalogenation, dehydration of alcohols, and reduction of alkynes. We also introduced the alkylation of alkynide anions as a method for forming new carbon–carbon bonds, and we introduced retrosynthetic analysis as a means of logically planning an organic synthesis.

The study aids for this chapter include the list of methods below that we have mentioned for synthesizing alkenes, as well as key terms and concepts (which are hyperlinked to the Glossary from the bold, blue terms in the *WileyPLUS* version of the book at wileyplus.com). Following the end of chapter problems you will find graphical overviews of the mechanisms for E2 and E1 reactions, a Synthetic Connections scheme for alkynes, alkenes, alkyl halides, and alcohols, and a Concept Map regarding organic synthesis involving alkenes.

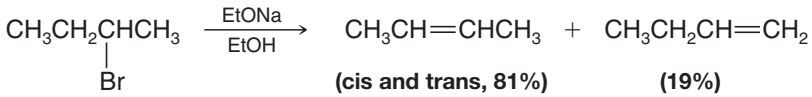
SUMMARY OF METHODS FOR THE PREPARATION OF ALKENES AND ALKYNES

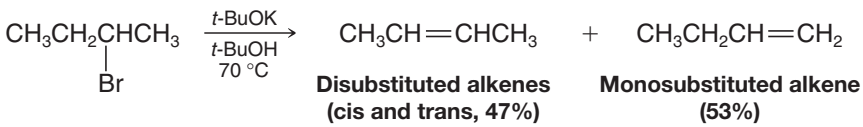
1. Dehydrohalogenation of alkyl halides (Section 7.6):

General Reaction



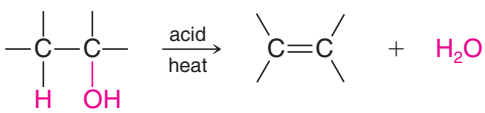
Specific Examples



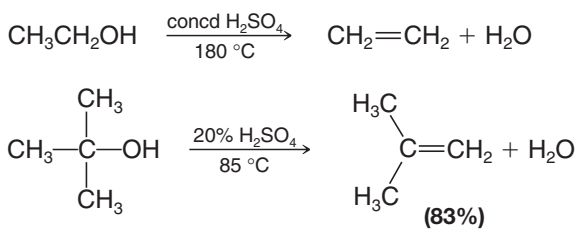


2. Dehydration of alcohols (Sections 7.7 and 7.8):

General Reaction

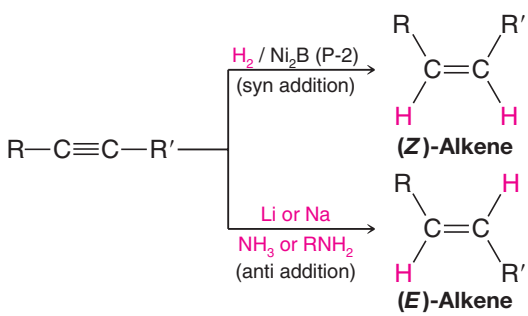


Specific Examples



3. Hydrogenation of alkynes (Section 7.15):

General Reaction



In subsequent chapters we shall see a number of other methods for alkene synthesis.

PROBLEMS

Note to Instructors: Many of the homework problems are available for assignment via *WileyPLUS*, an online teaching and learning solution.

STRUCTURE AND NOMENCLATURE

7.25 Each of the following names is incorrect. Give the correct name and explain your reasoning.

(a) *trans*-3-Pentene
(b) 1,1-Dimethylethene
(c) 2-Methylcyclohexene
(d) 4-Methylcyclobutene
(e) (*Z*)-3-Chloro-2-butene
(f) 5,6-Dichlorocyclohexene

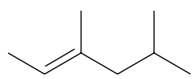
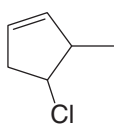
7.26 Write a structural formula for each of the following:

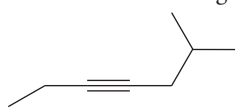
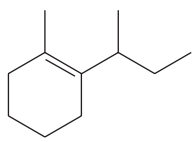
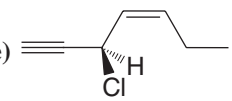
(a) 3-Methylcyclobutene
(b) 1-Methylcyclopentene
(c) 2,3-Dimethyl-2-pentene
(d) (*Z*)-3-Hexene
(e) (*E*)-2-Pentene
(f) 3,3,3-Tribromopropene
(g) (*Z*,4*R*)-4-Methyl-2-hexene
(h) (*E*,4*S*)-4-Chloro-2-pentene
(i) (*Z*)-1-Cyclopropyl-1-pentene
(j) 5-Cyclobutyl-1-pentene
(k) (*R*)-4-Chloro-2-pentyne
(l) (*E*)-4-Methylhex-4-en-1-yne

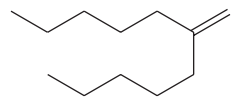
7.27 Write three-dimensional formulas for and give names using (*R*)–(*S*) and (*E*)–(*Z*) designations for the isomers of:

(a) 4-Bromo-2-hexene
(b) 3-Chloro-1,4-hexadiene
(c) 2,4-Dichloro-2-pentene
(d) 2-Bromo-4-chlorohex-2-en-5-yne

7.28 Give the IUPAC names for each of the following:

(a) 
(b) 

(c) 
(d) 
(e) 

(f) 

7.29 Without consulting tables, arrange the following compounds in order of decreasing acidity:

Pentane 1-Pentene 1-Pentyne 1-Pentanol

SYNTHESIS

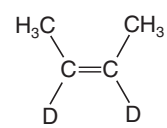
7.30 Outline a synthesis of propene from each of the following:

(a) Propyl chloride
(b) Isopropyl chloride
(c) Propyl alcohol
(d) Isopropyl alcohol
(e) 1,2-Dibromopropane
(f) Propyne

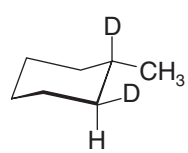
7.31 Outline a synthesis of cyclopentene from each of the following:

(a) Bromocyclopentane
(b) Cyclopentanol

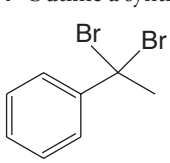
7.32 Starting with ethyne, outline syntheses of each of the following. You may use any other needed reagents, and you need not show the synthesis of compounds prepared in earlier parts of this problem.

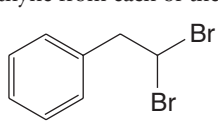
(a) Propyne
(b) 1-Butyne
(c) 2-Butyne
(d) *cis*-2-Butene
(e) *trans*-2-Butene
(f) 1-Pentyne
(g) 2-Hexyne
(h) (*Z*)-2-Hexene
(i) (*E*)-2-Hexene
(j) 3-Hexyne
(k) $CH_3CH_2C{\equiv}CD$
(l) 

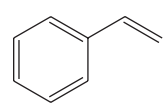
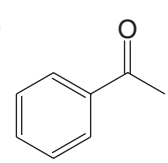
7.33 Starting with 1-methylcyclohexene and using any other needed reagents, outline a synthesis of the following deuterium-labeled compound:



7.34 Outline a synthesis of phenylethyne from each of the following:

(a) 

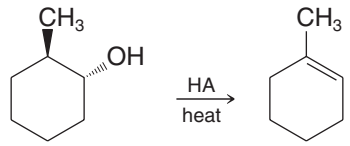
(b) 

(c) 
(d) 

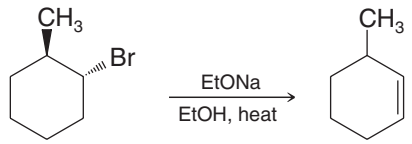
DEHYDROHALOGENATION AND DEHYDRATION

7.35 Write a three-dimensional representation for the transition state structure leading to formation of 2-methyl-2-butene from reaction of 2-bromo-2-methylbutane with sodium ethoxide.

7.36 When *trans*-2-methylcyclohexanol (see the following reaction) is subjected to acid-catalyzed dehydration, the major product is 1-methylcyclohexene:

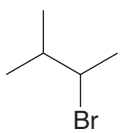


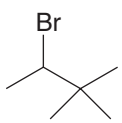
However, when *trans*-1-bromo-2-methylcyclohexane is subjected to dehydrohalogenation, the major product is 3-methylcyclohexene:

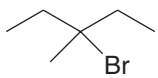


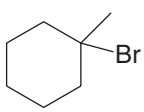
Account for the different products of these two reactions.

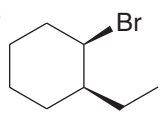
7.37 Write structural formulas for all the products that would be obtained when each of the following alkyl halides is heated with sodium ethoxide in ethanol. When more than one product results, you should indicate which would be the major product and which would be the minor product(s). You may neglect cis–trans isomerism of the products when answering this question.

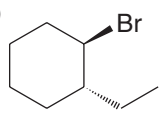
(a) 

(b) 

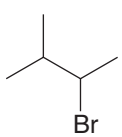
(c) 

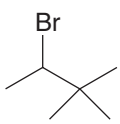
(d) 

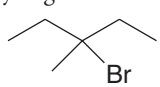
(e) 

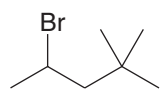
(f) 

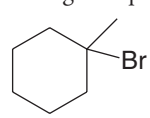
7.38 Write structural formulas for all the products that would be obtained when each of the following alkyl halides is heated with potassium *tert*-butoxide in *tert*-butyl alcohol. When more than one product results, you should indicate which would be the major product and which would be the minor product(s). You may neglect cis–trans isomerism of the products when answering this question.

(a) 

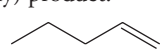
(b) 

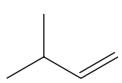
(c) 

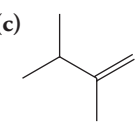
(d) 

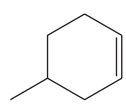
(e) 

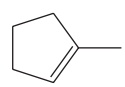
7.39 Starting with an appropriate alkyl halide and base, outline syntheses that would yield each of the following alkenes as the major (or only) product:

(a) 

(b) 

(c) 

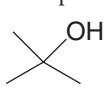
(d) 

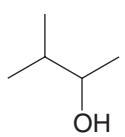
(e) 

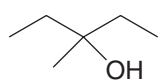
7.40 Arrange the following alcohols in order of their reactivity toward acid-catalyzed dehydration (with the most reactive first):

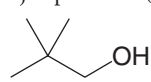
1-Pentanol 2-Methyl-2-butanol 3-Methyl-2-butanol

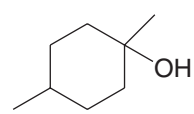
7.41 Give the products that would be formed when each of the following alcohols is subjected to acid-catalyzed dehydration. If more than one product would be formed, designate the alkene that would be the major product. (Neglect cis–trans isomerism.)

(a) 

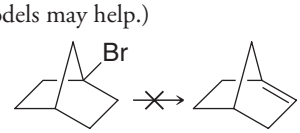
(b) 

(c) 

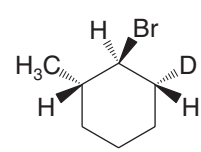
(d) 

(e) 

7.42 1-Bromobicyclo[2.2.1]heptane does not undergo elimination (below) when heated with a base. Explain this failure to react. (Construction of molecular models may help.)

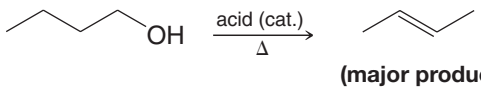


7.43 When the deuterium-labeled compound shown at right is subjected to dehydrohalogenation using sodium ethoxide in ethanol, the only alkene product is 3-methylcyclohexene. (The product contains no deuterium.) Provide an explanation for this result.



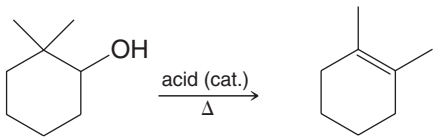
7.44 Provide a mechanistic explanation for each of the following reactions:

(a)



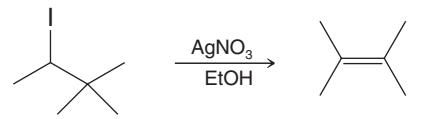
(major product)

(b)



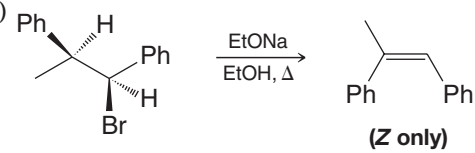
(major product)

(c)



(major product)

(d)

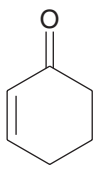


(*Z* only)

INDEX OF HYDROGEN DEFICIENCY

7.45 What is the index of hydrogen deficiency (IHD) (degree of unsaturation) for each of the following compounds?

(a)



(b) $C_6H_8Br_4$

7.46 Caryophyllene, a compound found in oil of cloves, has the molecular formula $C_{15}H_{24}$ and has no triple bonds. Reaction of caryophyllene with an excess of hydrogen in the presence of a platinum catalyst produces a compound with the formula $C_{15}H_{28}$. How many **(a)** double bonds and **(b)** rings does a molecule of caryophyllene have?

7.47 Squalene, an important intermediate in the biosynthesis of steroids, has the molecular formula $C_{30}H_{50}$ and has no triple bonds.

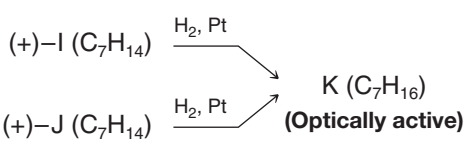
(a) What is the index of hydrogen deficiency of squalene?

(b) Squalene undergoes catalytic hydrogenation to yield a compound with the molecular formula $C_{30}H_{62}$. How many double bonds does a molecule of squalene have?

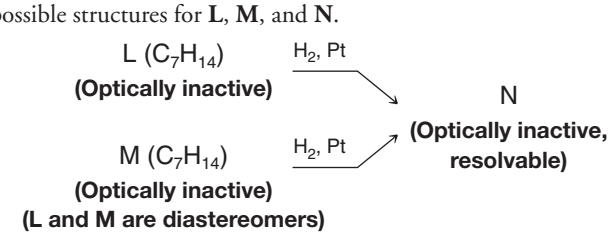
(c) How many rings?

STRUCTURE ELUCIDATION

7.48 Compounds **I** and **J** both have the molecular formula C_7H_{14}. Compounds **I** and **J** are both optically active and both rotate plane-polarized light in the same direction. On catalytic hydrogenation **I** and **J** yield the same compound **K** (C_7H_{16}). Compound **K** is optically active. Propose possible structures for **I**, **J**, and **K**.



7.49 Compounds **L** and **M** have the molecular formula C_7H_{14}. Compounds **L** and **M** are optically inactive, are nonresolvable, and are diastereomers of each other. Catalytic hydrogenation of either **L** or **M** yields **N**. Compound **N** is optically inactive but can be resolved into separate enantiomers. Propose possible structures for **L**, **M**, and **N**.



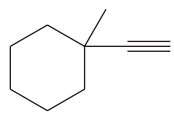
CHALLENGE PROBLEMS

7.50 Propose structures for compounds **E–H**. Compound **E** has the molecular formula C_5H_8 and is optically active. On catalytic hydrogenation **E** yields **F**. Compound **F** has the molecular formula C_5H_{10}, is optically inactive, and cannot be resolved into separate enantiomers. Compound **G** has the molecular formula C_6H_{10} and is optically active. Compound **G** contains no triple bonds. On catalytic hydrogenation **G** yields **H**. Compound **H** has the molecular formula C_6H_{14}, is optically inactive, and cannot be resolved into separate enantiomers.

7.51 Consider the interconversion of *cis*-2-butene and *trans*-2-butene.
(a) What is the value of $\Delta H°$ for the reaction *cis*-2-butene → *trans*-2-butene (see Section 7.3A)?
(b) Assume $\Delta H° \cong \Delta G°$. What minimum value of $\Delta G^{‡}$ would you expect for this reaction (see Section 1.13A)?
(c) Sketch a free-energy diagram for the reaction and label $\Delta G°$ and $\Delta G^{‡}$.

7.52 **(a)** Partial dehydrohalogenation of either (1*R*,2*R*)-1,2-dibromo-1,2-diphenylethane or (1*S*,2*S*)-1,2-dibromo-1,2-diphenylethane enantiomers (or a racemate of the two) produces (*Z*)-1-bromo-1,2-diphenylethene as the product, whereas **(b)** partial dehydrohalogenation of (1*R*,2*S*)-1,2-dibromo-1,2-diphenylethane (the meso compound) gives only (*E*)-1-bromo-1,2-diphenylethene. **(c)** Treating (1*R*,2*S*)-1,2-dibromo-1,2-diphenylethane with sodium iodide in acetone produces only (*E*)-1,2-diphenylethene. Explain these results.

7.53 **(a)** Using reactions studied in this chapter, show steps by which this alkyne could be converted to the seven-membered ring homolog of the product obtained in Problem 7.44(b).



(b) Could the homologous products obtained in these two cases be relied upon to show infrared absorption in the 1620–1680-cm^{-1} region?

7.54 Predict the structures of compounds **A**, **B**, and **C**:

A is an unbranched C_6 alkyne that is also a primary alcohol.

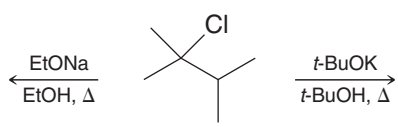
B is obtained from **A** by use of hydrogen and nickel boride catalyst or dissolving metal reduction.

C is formed from **B** on treatment with aqueous acid at room temperature. Compound **C** has no infrared absorption in either the 1620–1680-cm^{-1} or the 3590–3650-cm^{-1} region. It has an index of hydrogen deficiency of 1 and has one chirality center but forms as the racemate.

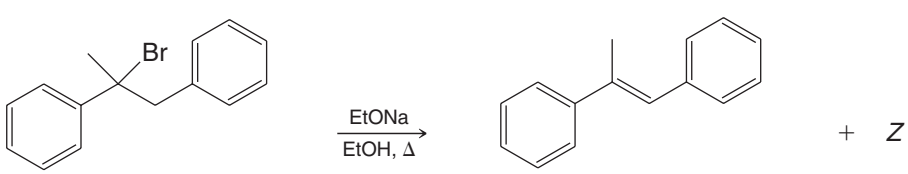
7.55 What is the index of hydrogen deficiency for **(a)** $C_7H_{10}O_2$ and **(b)** $C_5H_4N_4$?

LEARNING GROUP PROBLEMS

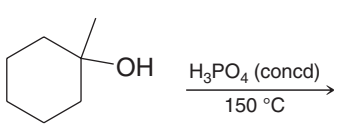
1. Write the structure(s) of the major product(s) obtained when 2-chloro-2,3-dimethylbutane (either enantiomer) reacts with **(a)** sodium ethoxide (EtONa) in ethanol (EtOH) at 80 °C or (in a separate reaction) with **(b)** potassium *tert*-butoxide (*t*-BuOK) in *tert*-butyl alcohol (*t*-BuOH) at 80 °C. If more than one product is formed, indicate which one would be expected to be the major product. **(c)** Provide a detailed mechanism for formation of the major product from each reaction, including a drawing of the transition state structures.



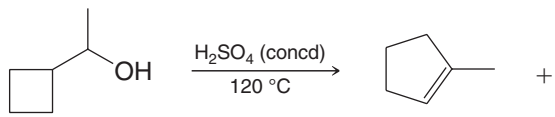
2. Explain using mechanistic arguments involving Newman projections or other three-dimensional formulas why the reaction of 2-bromo-1,2-diphenylpropane (either enantiomer) with sodium ethoxide (EtONa) in ethanol (EtOH) at 80 °C produces mainly (*E*)-1,2-diphenylpropene [little of the (*Z*) diastereomer is formed].



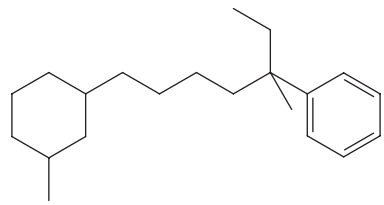
3. **(a)** Write the structure of the product(s) formed when 1-methylcyclohexanol reacts with 85% (coned) H_3PO_4 at 150 °C. **(b)** Write a detailed mechanism for the reaction.



4. Consider the reaction of 1-cyclobutylethanol (1-hydroxyethylcyclobutane) with concentrated H_2SO_4 at 120 °C. Write structures of all reasonable organic products. Assuming that methylcyclopentene is one product, write a mechanism that accounts for its formation. Write mechanisms that account for formation of all other products as well.



5. Consider the following compound:



(a) Develop all reasonable retrosynthetic analyses for this compound (any diastereomer) that, at some point, involve carbon–carbon bond formation by alkylation of an alkynide ion.

(b) Write reactions, including reagents and conditions, for syntheses of this compound that correspond to the retrosynthetic analyses you developed above.

(c) Infrared spectroscopy could be used to show the presence of certain impurities in your final product that would result from leftover intermediates in your syntheses. Which of your synthetic intermediates would show IR absorptions that are distinct from those in the final product, and in what regions of the IR spectrum would the absorptions occur?

(d) Draw a three-dimensional structure for either the cis or trans form of the target molecule. Use dashed and solid wedges where appropriate in the alkyl side chain and use a chair conformational structure for the ring. (*Hint:* Draw the structure so that the carbon chain of the most complicated substituent on the cyclohexane ring and the ring carbon where it is attached are all in the plane of the paper. In general, for three-dimensional structures choose an orientation that allows as many carbon atoms as possible to be in the plane of the paper.)

Reaction Summary of E2 and E1 elimination

E2 via small base

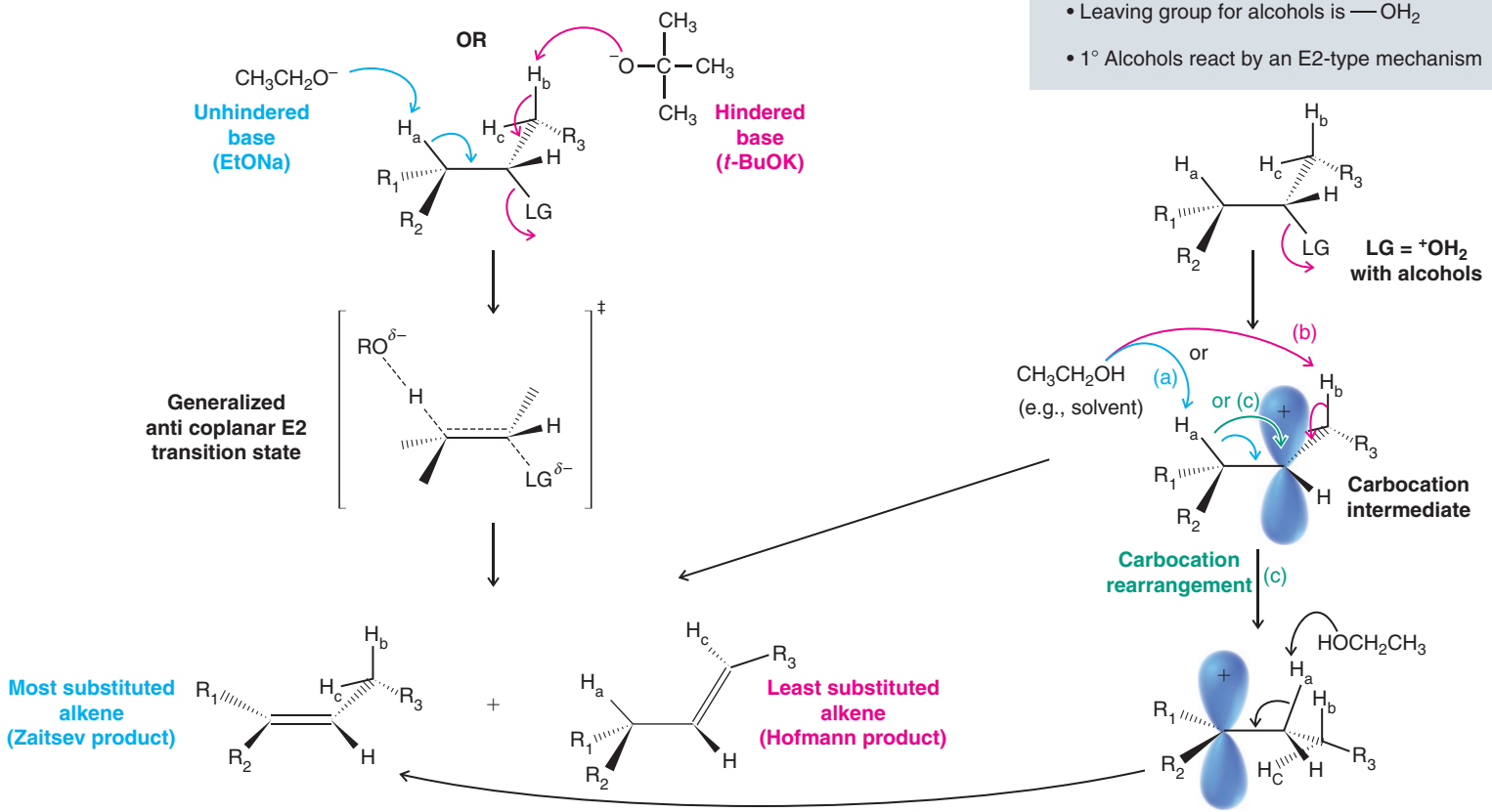
- Strong **unhindered base**, e.g., CH_3CH_2ONa (EtONa), HO^-
- Predominant formation of **most substituted alkene** (Zaitsev product)
- Anti coplanar transition state
- Bimolecular in rate-determining step

E2 via bulky base

- Strong **hindered base**, e.g. $(CH_3)_3COK$ (*t*-BuOK)
- Predominant formation of **least substituted alkene** (Hofmann product)
- Anti coplanar transition state
- Bimolecular in rate-determining step

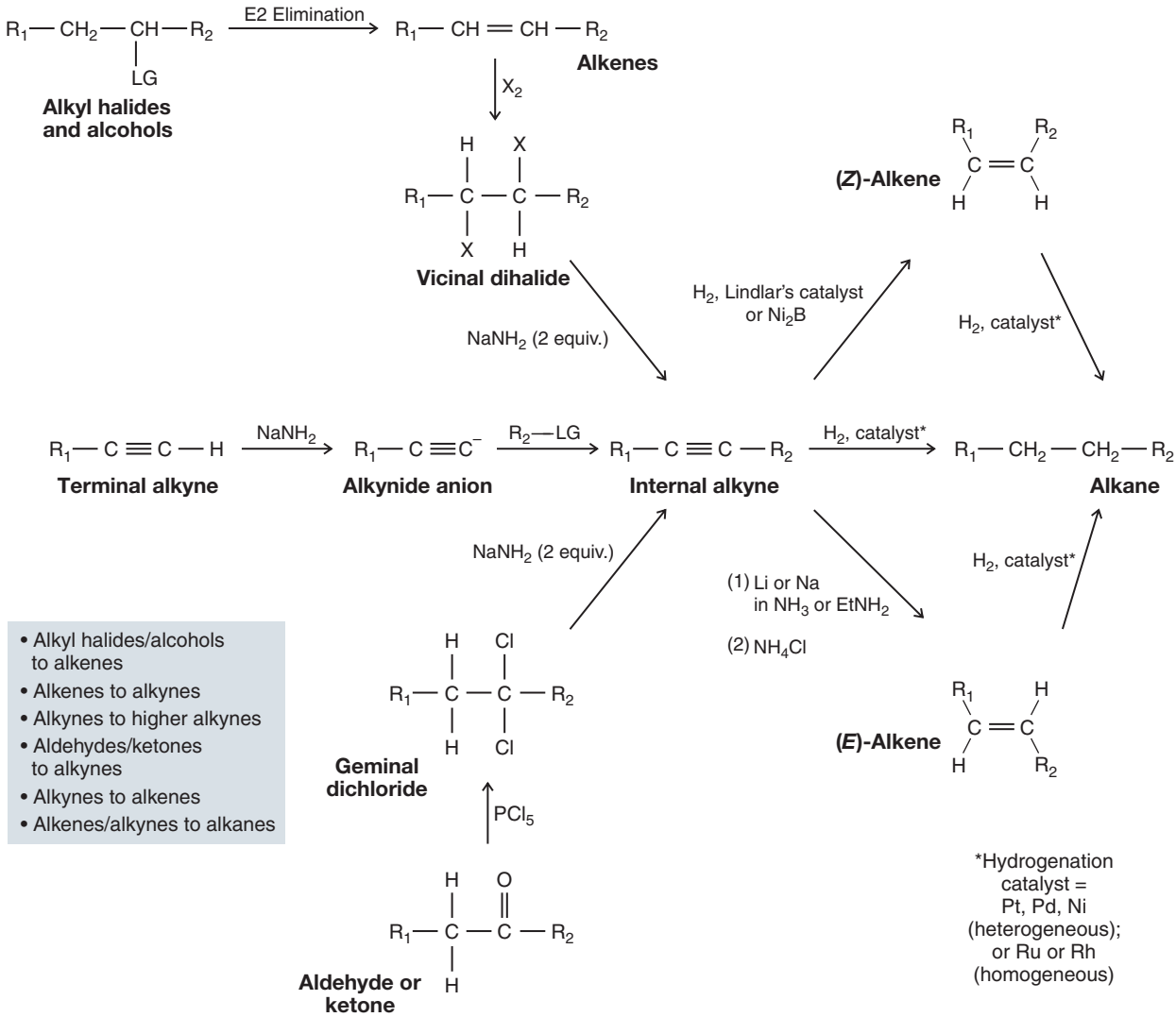
E1 (including Alcohol Dehydration)

- Absence of strong base (solvent is often the base)
- Alcohols require **strong acid catalyst**
- Carbocation formation is unimolecular rate-determining step
- Carbocation **may rearrange**
- Predominant formation of most substituted alkene (Zaitsev product)
- Leaving group for alcohols is $-\overset{+}{O}H_2$
- 1° Alcohols react by an E2-type mechanism



SUMMARY AND REVIEW TOOLS

Synthetic Connections of Alkynes, Alkenes, Alkyl Halides, and Alcohols



CONCEPT MAP