

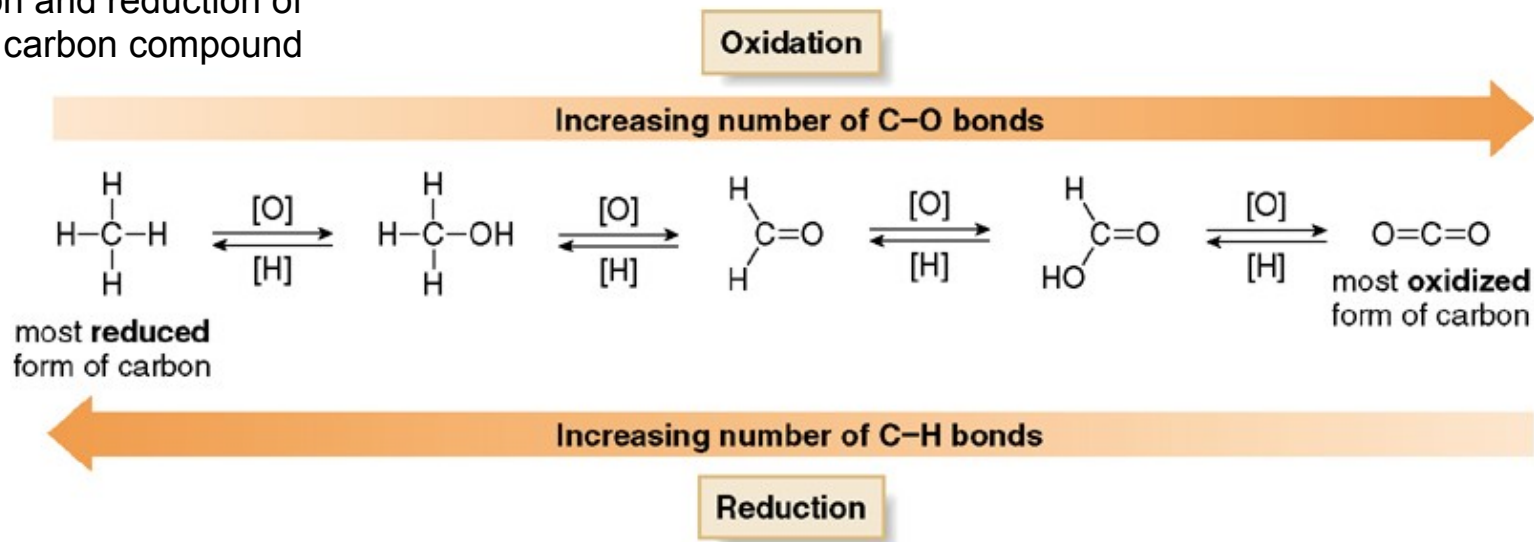
# Oxidation and Reduction

## Introduction

- Recall that oxidation results in an increase in the number of C—Z bonds (usually C—O bonds) or a decrease in the number of C—H bonds.
- Recall that reduction results in a decrease in the number of C—Z bonds (usually C—O bonds) or an increase in the number of C—H bonds.

Figure 12.1

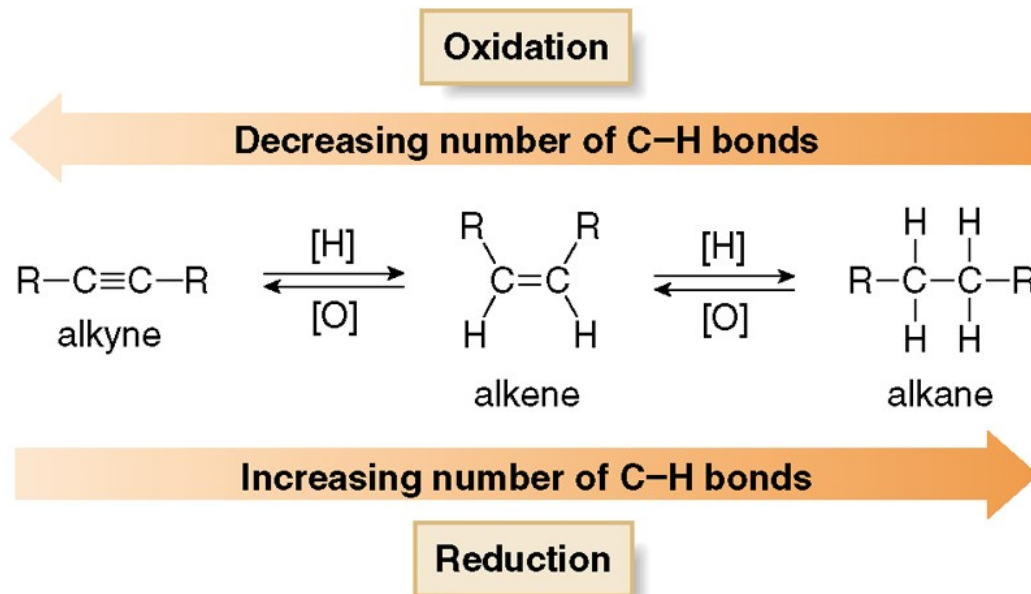
A general scheme for the oxidation and reduction of a carbon compound



- Sometimes two carbon atoms are involved in a single oxidation or reduction reaction, and the net change in the number of C—H or C—Z bonds at both atoms must be taken into account.
  - The conversion of an alkyne to an alkene, or an alkene to an alkane are examples of reduction because each process adds two new C—H bonds to the starting material.

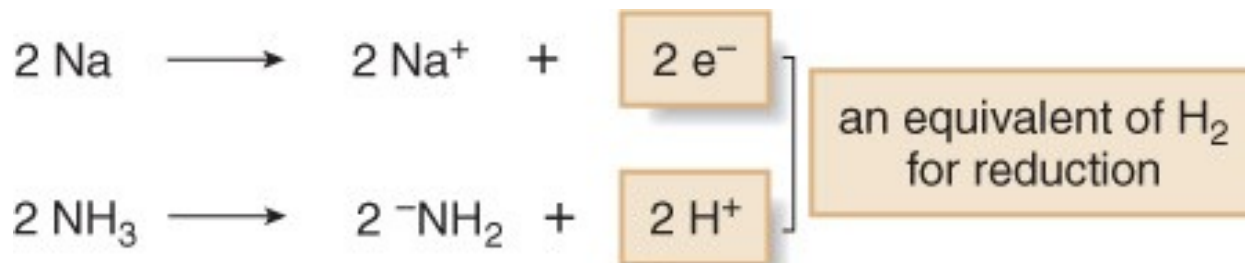
Figure 12.2

Oxidation and reduction of hydrocarbons

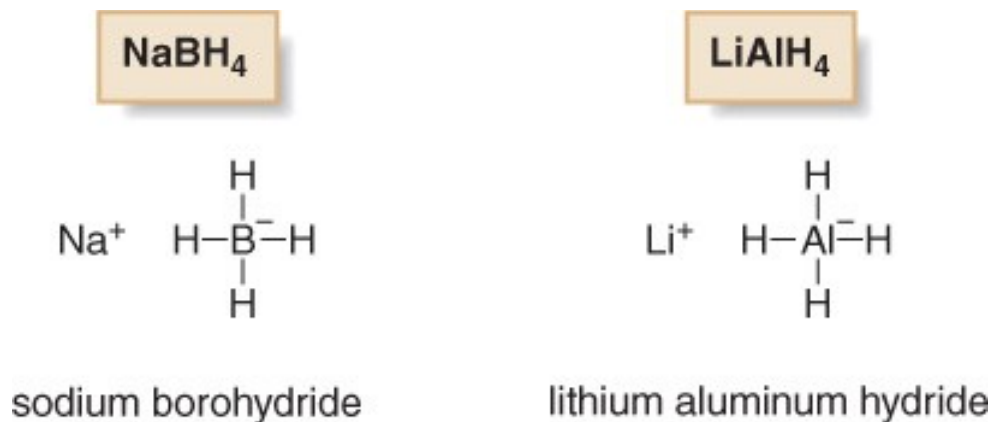


## Reducing Agents

- There are three types of reductions differing in how H<sub>2</sub> is added.
- The simplest reducing agent is H<sub>2</sub>. Reductions using H<sub>2</sub> are carried out with a metal catalyst.
- A second way is to add two protons and two electrons to a substrate—that is, H<sub>2</sub> = 2H<sup>+</sup> + 2e<sup>-</sup>.
  - Reductions of this sort use alkali metals as a source of electrons, and liquid ammonia as a source of protons.
  - These are called **dissolving metal reductions**.

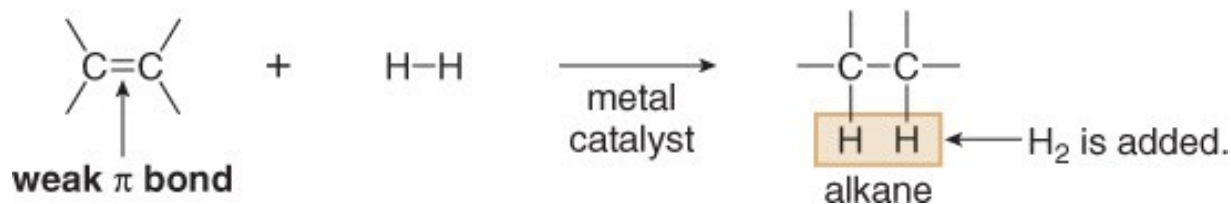


- The third way to add H<sub>2</sub> is to add **hydride (H<sup>-</sup>)** and a proton (H<sup>+</sup>).
- The most common hydride reducing agents contain a hydrogen atom bonded to boron or aluminum. Simple examples include **sodium borohydride (NaBH<sub>4</sub>)** and **lithium aluminum hydride (LiAlH<sub>4</sub>)**.
- NaBH<sub>4</sub> and LiAlH<sub>4</sub> deliver H<sup>-</sup> to the substrate, and then a proton is added from H<sub>2</sub>O or an alcohol.



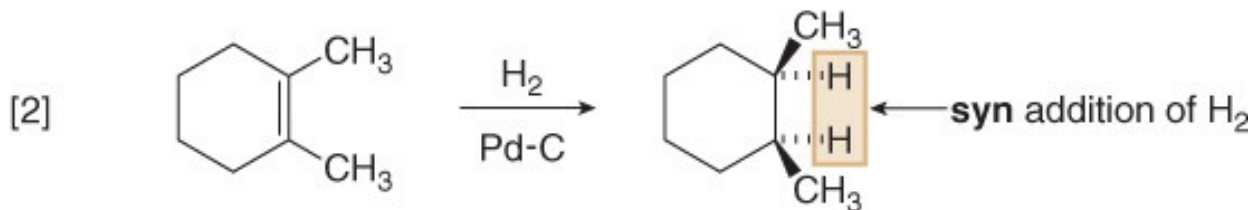
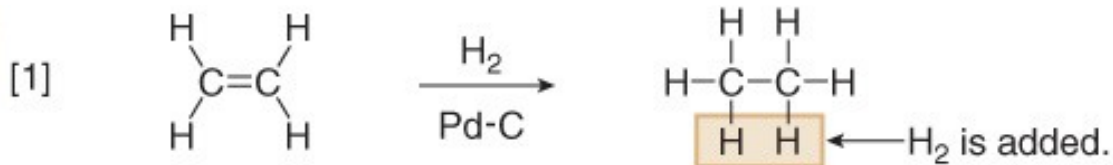
# Reduction of Alkenes—Catalytic Hydrogenation

## Hydrogenation—General reaction

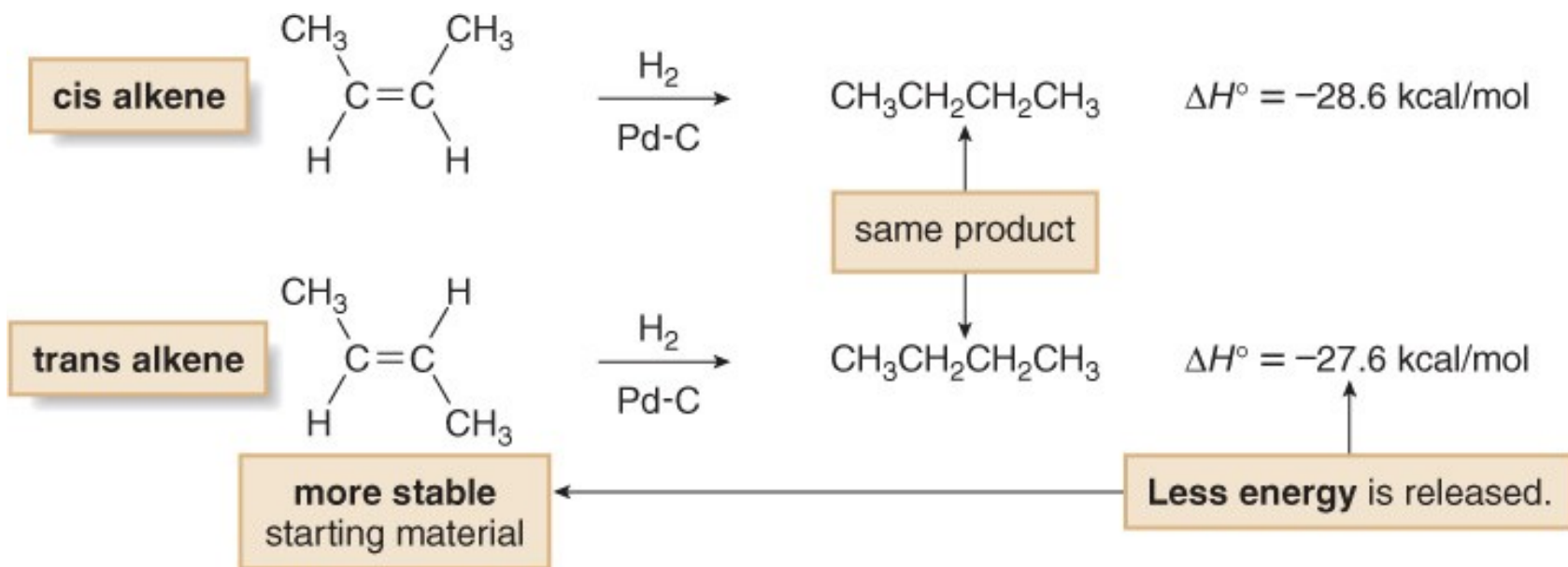


- The addition of H<sub>2</sub> occurs only in the presence of a metal catalyst, and thus it is called catalytic hydrogenation.
- The catalyst consists of a metal—usually Pd, Pt, or Ni, adsorbed onto a finely divided inert solid, such as charcoal.
- H<sub>2</sub> adds in a syn fashion.

## Examples



- The  $\Delta H^\circ$  of hydrogenation, also known as the heat of hydrogenation, can be used as a measure of the relative stability of two different alkenes that are hydrogenated to form the same alkane.



- When hydrogenation of two alkenes gives the same alkane, the more stable alkene has the smaller heat of hydrogenation.



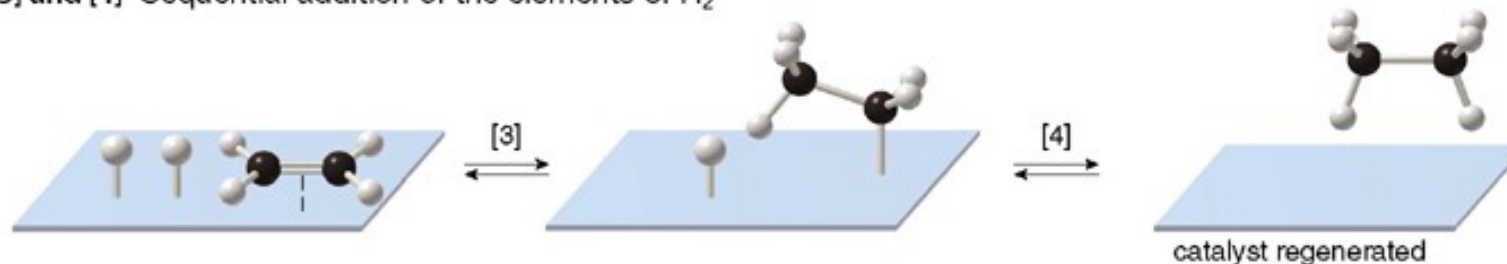
## Mechanism 12.1 Addition of H<sub>2</sub> to an Alkene—Hydrogenation

Steps [1] and [2] Complexation of H<sub>2</sub> and the alkene to the catalyst



- **H<sub>2</sub> adsorbs to the catalyst surface** with partial or complete cleavage of the H–H bond.
- The  $\pi$  bond of the alkene complexes with the metal.

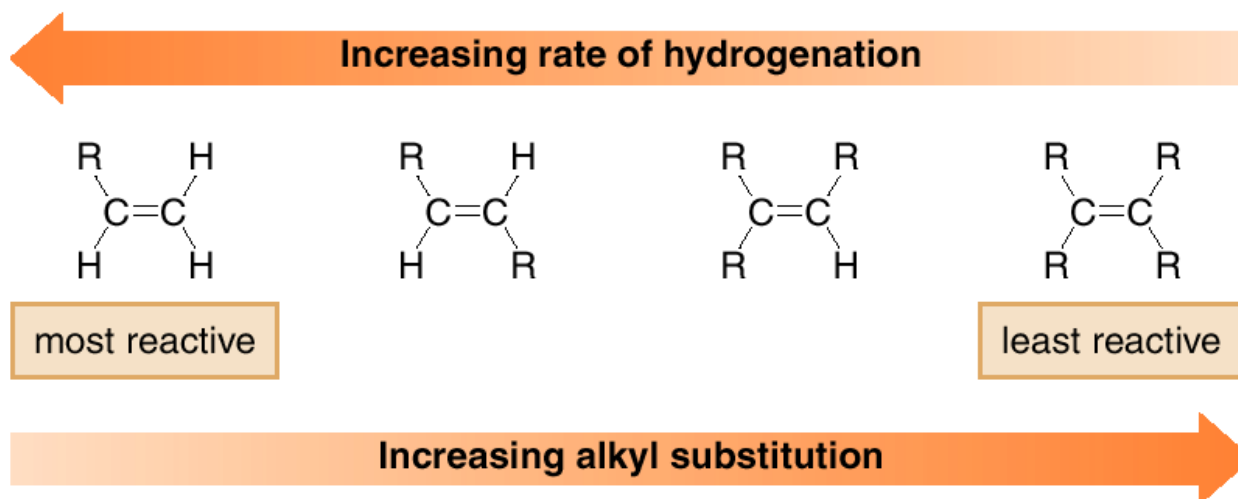
Steps [3] and [4] Sequential addition of the elements of H<sub>2</sub>



- **Two H atoms are transferred sequentially** to the  $\pi$  bond in Steps [3] and [4], forming the alkane.
- Because the product alkane no longer has a  $\pi$  bond with which to complex to the metal, it is released from the catalyst surface.

- **The mechanism explains two facts about hydrogenation:**

- Rapid, sequential addition of H<sub>2</sub> occurs from the side of the alkene complexed to the metal surface, resulting in syn addition.
- Less crowded double bonds complex more readily to the catalyst surface, resulting in faster reaction.

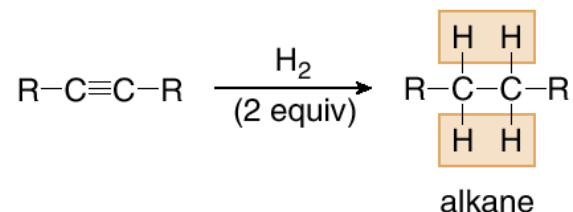




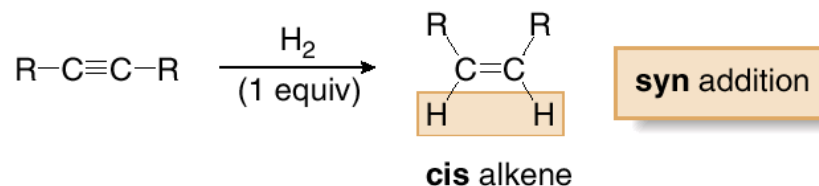
# Reduction of Alkynes

- There are three different ways in which H<sub>2</sub> can add to the triple bond:

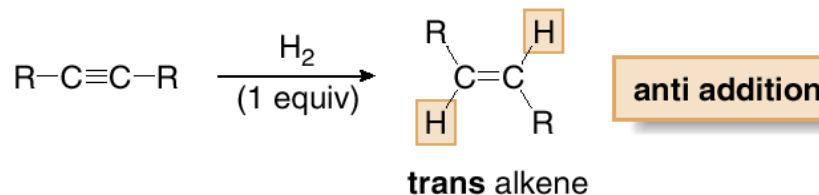
- Adding two equivalents of H<sub>2</sub> forms an alkane.



- Adding one equivalent of H<sub>2</sub> in a syn fashion forms a cis alkene.

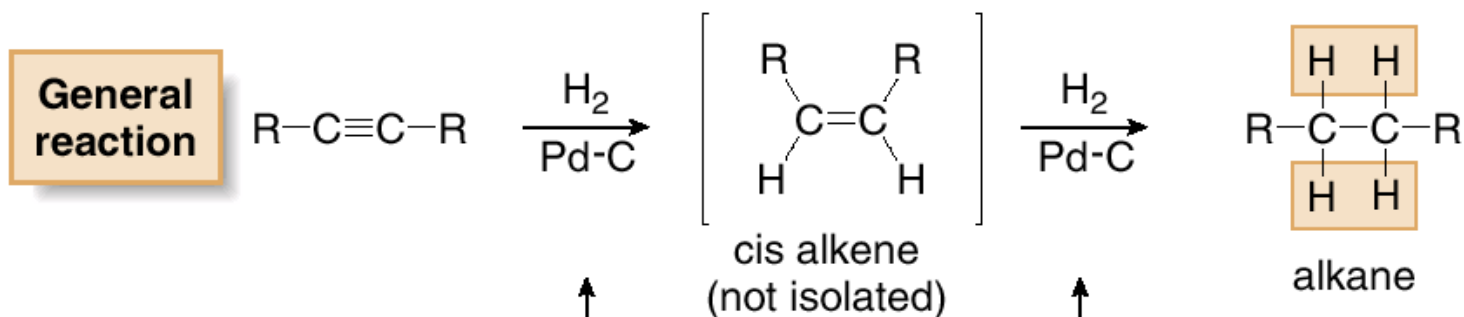


- Adding one equivalent of H<sub>2</sub> in an anti fashion forms a trans alkene.



# Reduction of an Alkyne to an Alkane

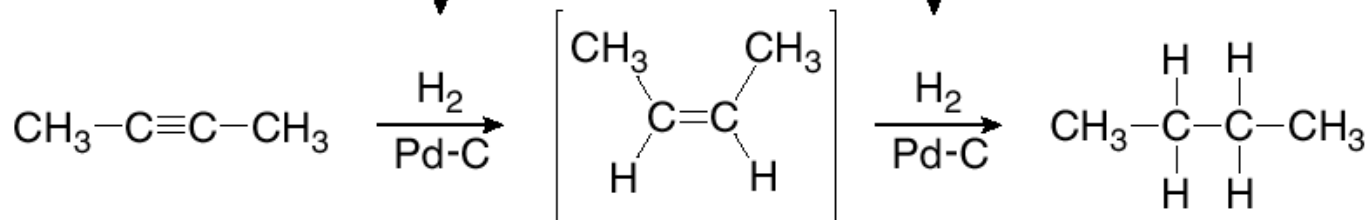
## Alkane formation:



first addition of H<sub>2</sub>

second addition of H<sub>2</sub>

**Example**

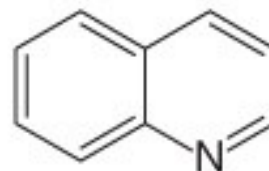


## Reduction of an Alkyne to a Cis Alkene

- Palladium metal is too reactive to allow hydrogenation of an alkyne to stop after one equivalent of H<sub>2</sub> adds.
- To stop at a cis alkene, a less active Pd catalyst is used—Pd adsorbed onto CaCO<sub>3</sub> with added lead(II) acetate and quinoline. This is called **Lindlar's catalyst**.
- Compared to Pd metal, the Lindlar catalyst is deactivated or “poisoned”.
- With the Lindlar catalyst, one equivalent of H<sub>2</sub> adds to an alkyne to form the cis product. The cis alkene product is unreactive to further reduction.

Pd on CaCO<sub>3</sub>  
+ Pb(OCOCH<sub>3</sub>)<sub>2</sub> + quinoline

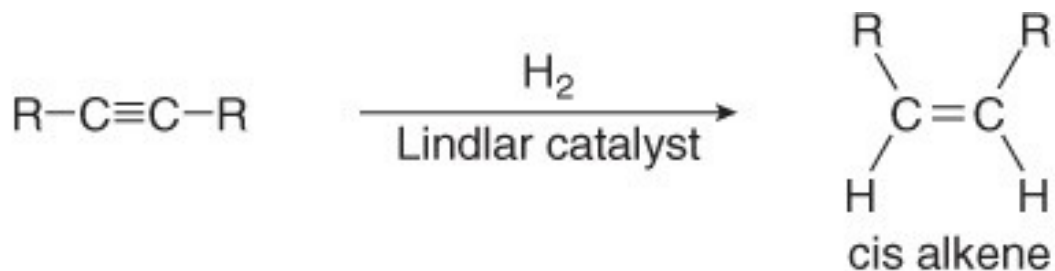
Lindlar catalyst



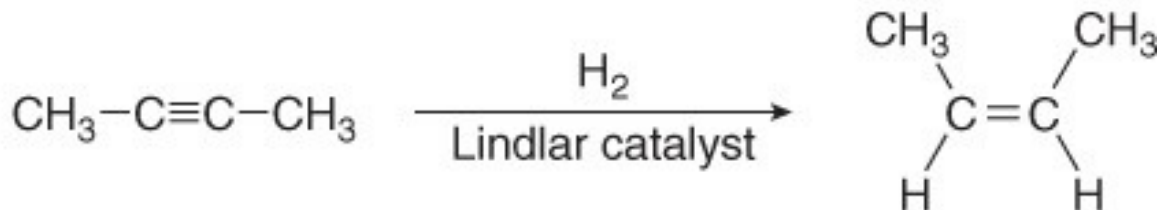
quinoline

- Reduction of an alkyne to a cis alkene is a stereoselective reaction, because only one stereoisomer is formed.

General reaction



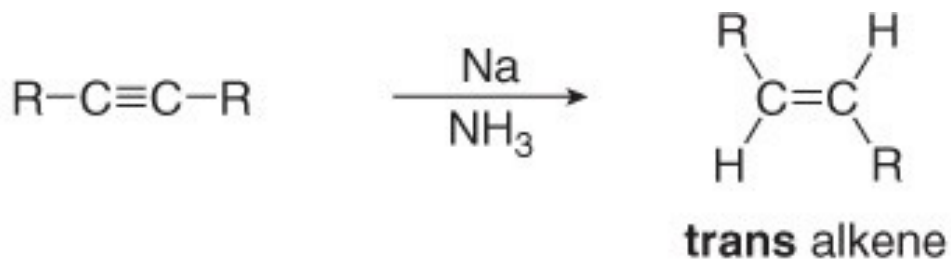
Example



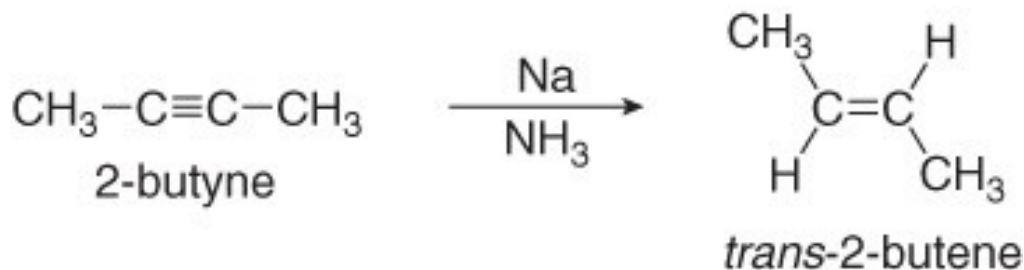
## Reduction of an Alkyne to a Trans Alkene

- In a **dissolving metal reduction** (such as Na in NH<sub>3</sub>), the elements of H<sub>2</sub> are added in an anti fashion to form a trans alkene.

General reaction



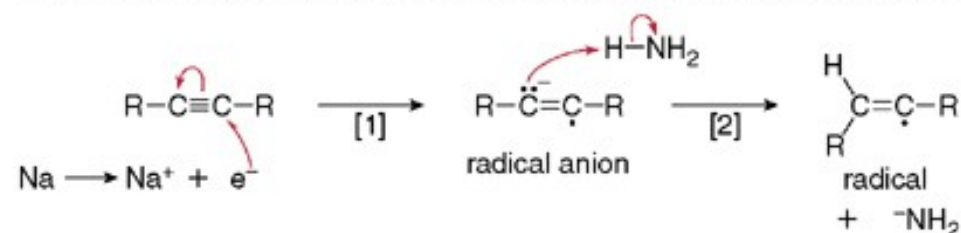
Example





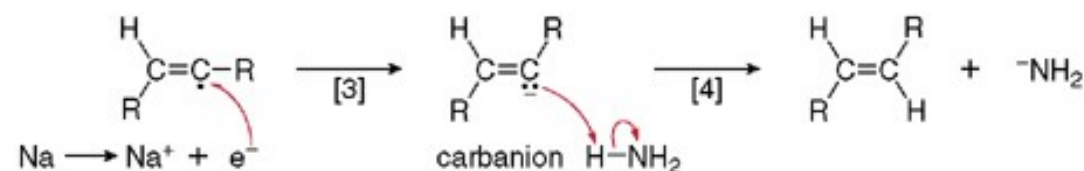
## Mechanism 12.2 Dissolving Metal Reduction of an Alkyne to a Trans Alkene

**Steps [1] and [2]** Addition of one electron and one proton to form a radical



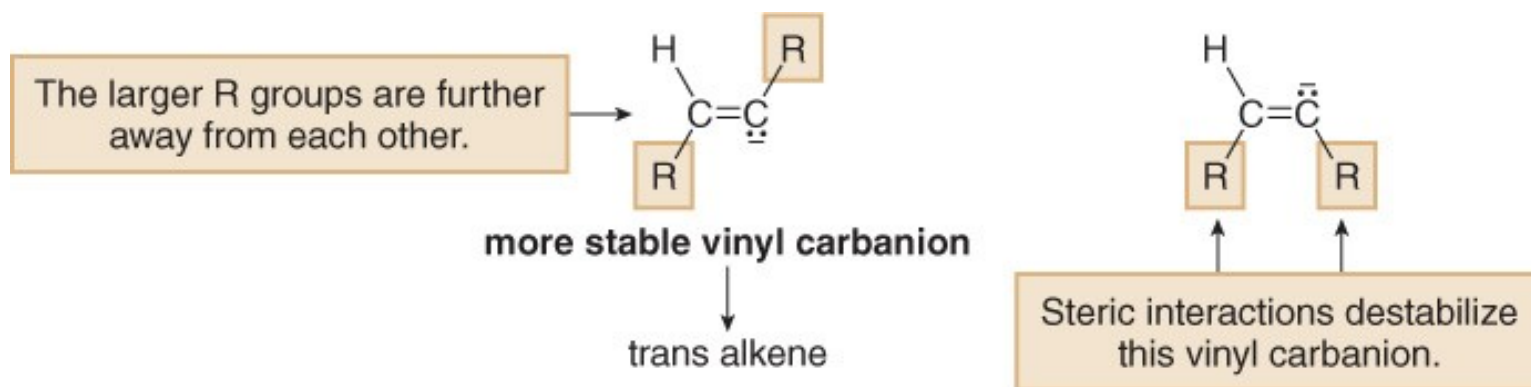
- Addition of an electron to the triple bond in Step [1] forms a **radical anion**, a species containing *both* a negative charge and an unpaired electron.
- Protonation of the anion with the solvent  $\text{NH}_3$  in Step [2] yields a **radical**. The net effect of Steps [1] and [2] is to add one hydrogen atom ( $\text{H}^\bullet$ ) to the triple bond.

**Steps [3] and [4]** Addition of one electron and one proton to form the trans alkene



- Addition of a second electron to the radical in Step [3] forms a **carbanion**.
- Protonation of the carbanion in Step [4] forms the trans alkene. These last two steps add the second hydrogen atom ( $\text{H}^\bullet$ ) to the triple bond.

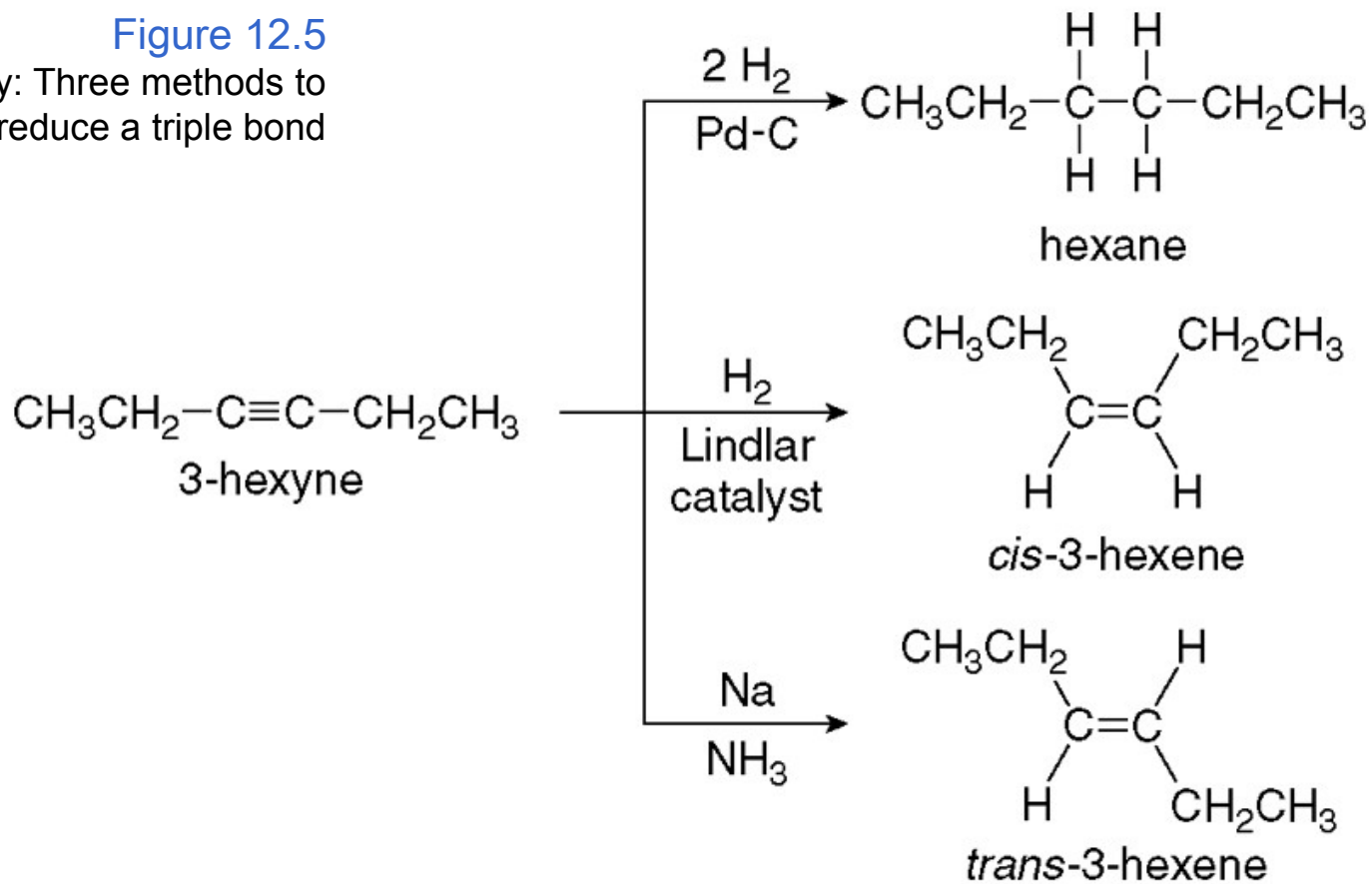
- Dissolving metal reduction of a triple bond with Na in NH<sub>3</sub> is a stereoselective reaction because it forms a trans product exclusively.
- Dissolving metal reductions always form the more stable trans product preferentially.
- The trans alkene is formed because the vinyl carbanion intermediate that is formed is more stable when the larger R groups are further away from each other to avoid steric interactions. Protonation of this anion leads to the more stable trans adduct.



# Summary of Alkyne Reductions

Figure 12.5

Summary: Three methods to reduce a triple bond





# Reduction of Polar C—X $\sigma$ Bonds

- Alkyl halides can be reduced to alkanes with  $\text{LiAlH}_4$ .
- Epoxide rings can be opened with  $\text{LiAlH}_4$  to form alcohols.

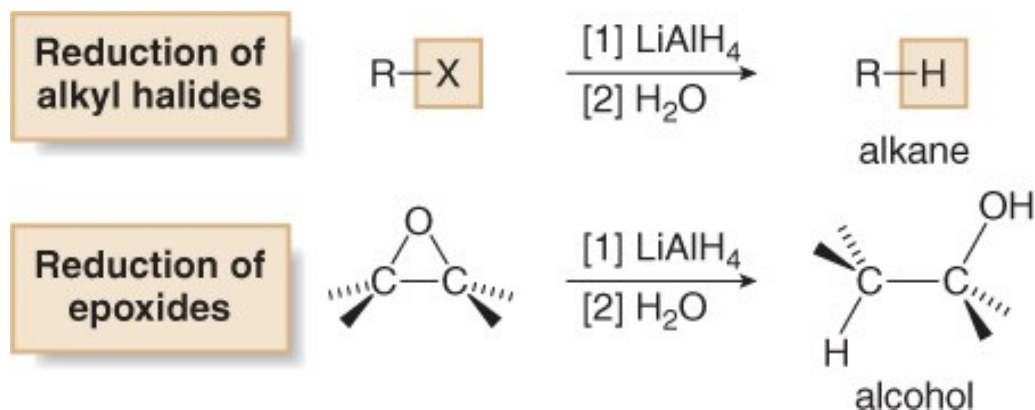
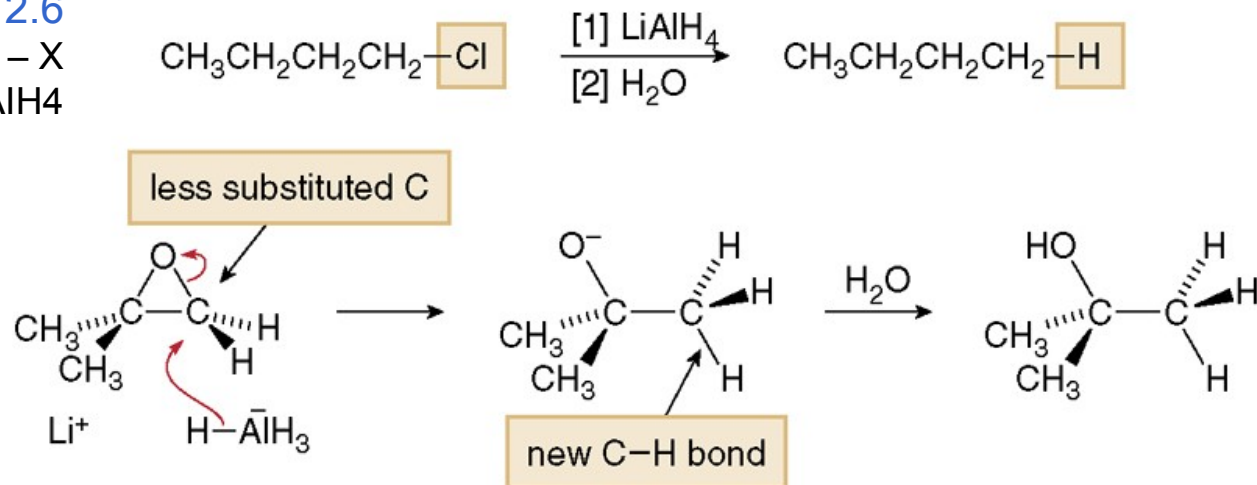


Figure 12.6

Examples of reduction of C—X  $\sigma$  bonds with  $\text{LiAlH}_4$





### Mechanism 12.3 Reduction of RX with LiAlH<sub>4</sub>

**One step** The nucleophile H<sup>-</sup> substitutes for X<sup>-</sup> in a single step.



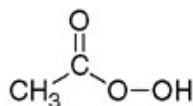
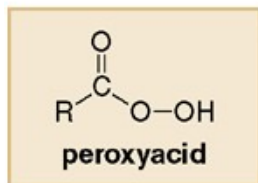
- This reaction follows an SN2 mechanism.
- Unhindered CH<sub>3</sub>X and 1° alkyl halides are more easily reduced than more substituted 2° and 3° halides.
- In unsymmetrical epoxides, nucleophilic attack of H<sup>-</sup> (from LiAlH<sub>4</sub>) occurs at the less substituted carbon atom.

# Oxidizing Agents

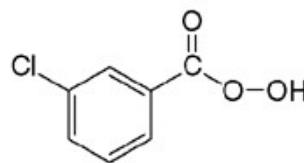
- There are two main categories of oxidizing agents:
  1. Reagents that contain an oxygen-oxygen bond
  2. Reagents that contain metal-oxygen bonds
- Oxidizing agents containing an O—O bond include O<sub>2</sub>, O<sub>3</sub> (ozone), H<sub>2</sub>O<sub>2</sub> (hydrogen peroxide), (CH<sub>3</sub>)<sub>2</sub>CHCOOH (*tert*-butyl hydroperoxide), and peroxyacids.
- **Peroxyacids (or peracids)** have the general formula RCO<sub>3</sub>H.

Figure 12.7

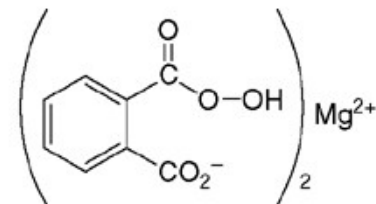
Common peroxyacids



peroxyacetic acid

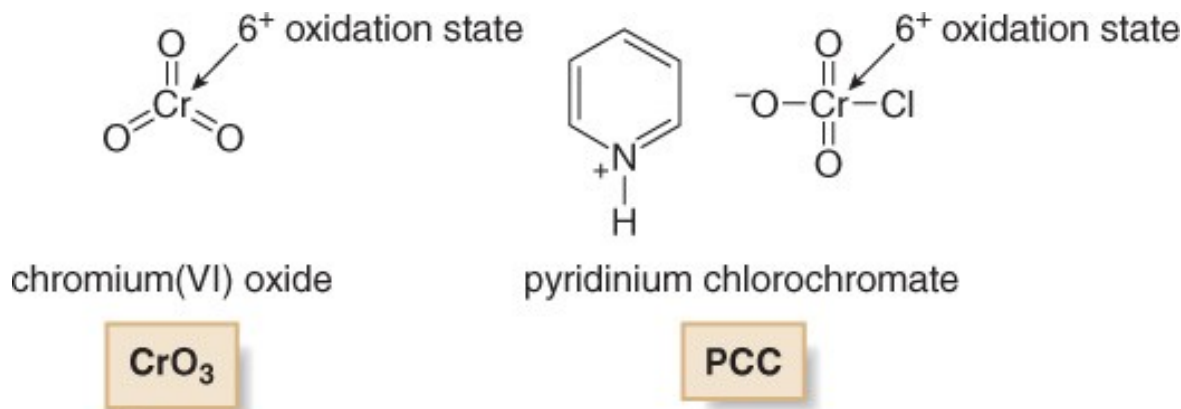


*meta*-chloroperoxybenzoic acid  
mCPBA



magnesium monoperoxyphthalate  
MMPP

- The most common oxidizing agents with metal-oxygen bonds contain either chromium +6 (six Cr—O bonds) or manganese +7 (seven Mn—O bonds).
- Common Cr<sup>6+</sup> reagents include CrO<sub>3</sub> and sodium or potassium dichromate (Na<sub>2</sub>Cr<sub>2</sub>O<sub>7</sub> and K<sub>2</sub>Cr<sub>2</sub>O<sub>7</sub>). Pyridinium chlorochromate (PCC) is a more selective Cr<sup>6+</sup> oxidant.

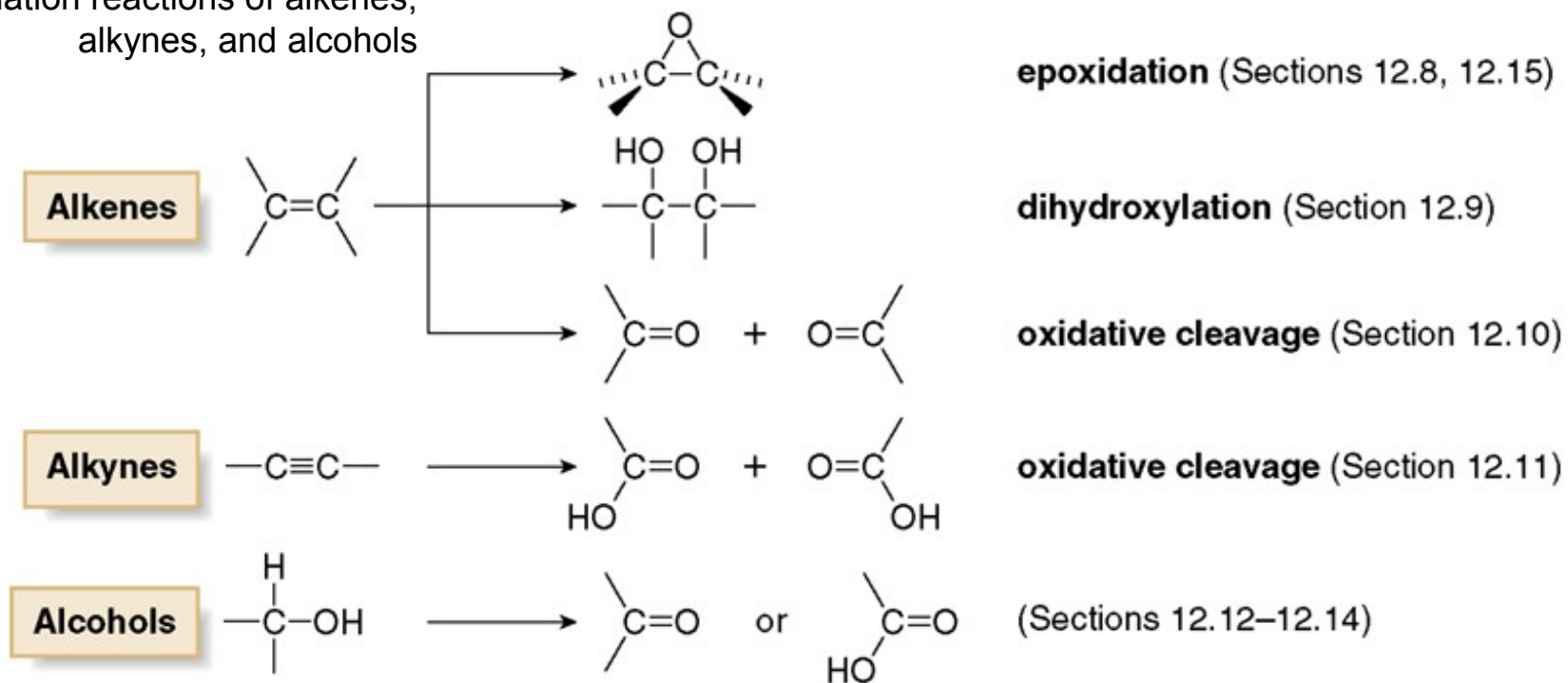


- The most common Mn<sup>7+</sup> reagent is KMnO<sub>4</sub> (potassium permanganate).
- Other oxidizing agents that contain metals include OsO<sub>4</sub> (osmium tetroxide) and Ag<sub>2</sub>O [silver(I) oxide].

# Oxidizing Reactions

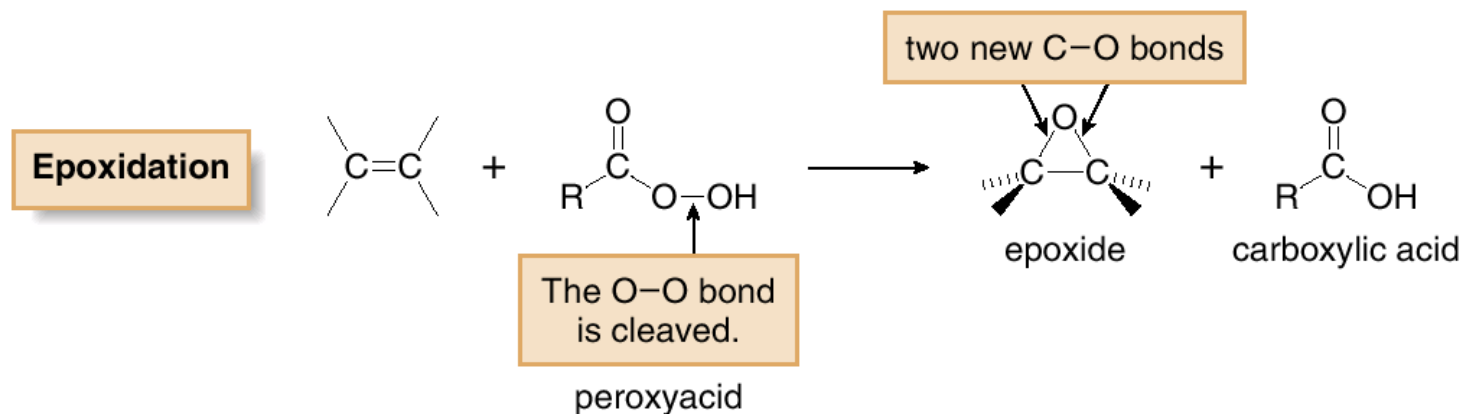
Figure 12.8

Oxidation reactions of alkenes, alkynes, and alcohols

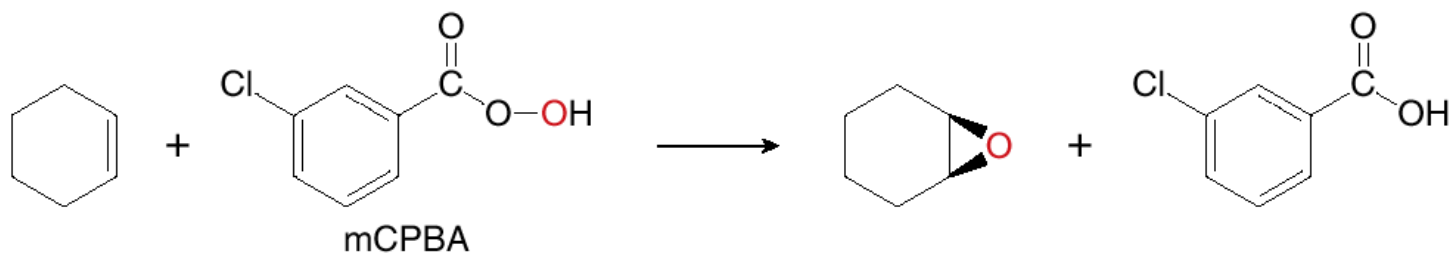
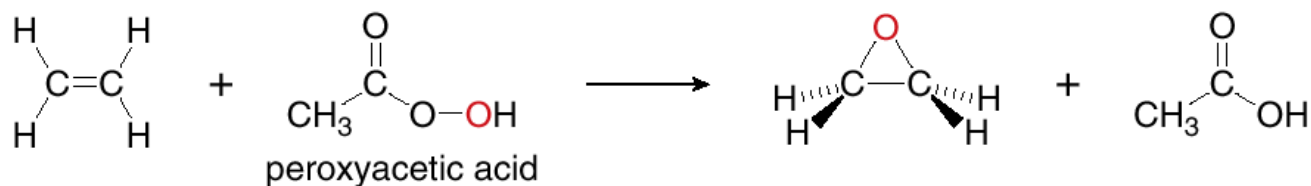


# Epoxidation

- **Epoxidation** is the addition of a single oxygen atom to an alkene to form an epoxide.
- Epoxidation is typically carried out with a peroxyacid.



## Examples



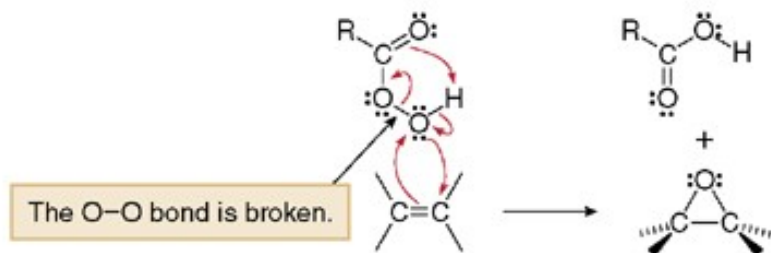
- **Epoxidation occurs via syn addition of an O atom to either side of a planar double bond. Thus, a cis alkene gives an epoxide with cis substituents. A trans alkene gives an epoxide with trans substituents.**

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### Mechanism 12.4 Epoxidation of an Alkene with a Peroxyacid

**One step** All bonds are broken or formed in a single step.



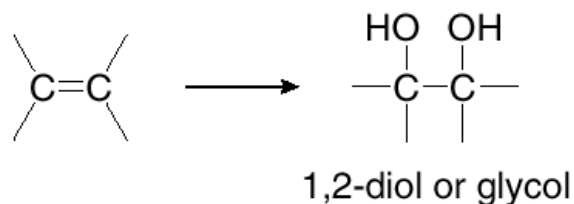
- Two C-O bonds are formed to one O atom with one electron pair from the peroxyacid and one from the  $\pi$  bond.
- The weak O-O bond is broken.

- **Epoxidation is stereospecific because cis and trans alkenes yield different stereoisomers as products.**

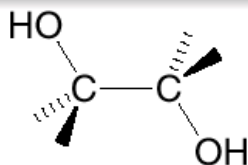
# Dihydroxylation

- **Dihydroxylation** is the addition of two hydroxy groups to a double bond, forming a 1,2-diol or glycol.
- Depending on the reagent, the two new OH groups can be added to the opposite sides (anti addition) or the same side (syn addition) of the double bond.

## Dihydroxylation—General reaction



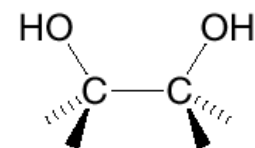
## Stereochemistry



## anti addition product

2 OH's added on **opposite** sides of the C=C

or

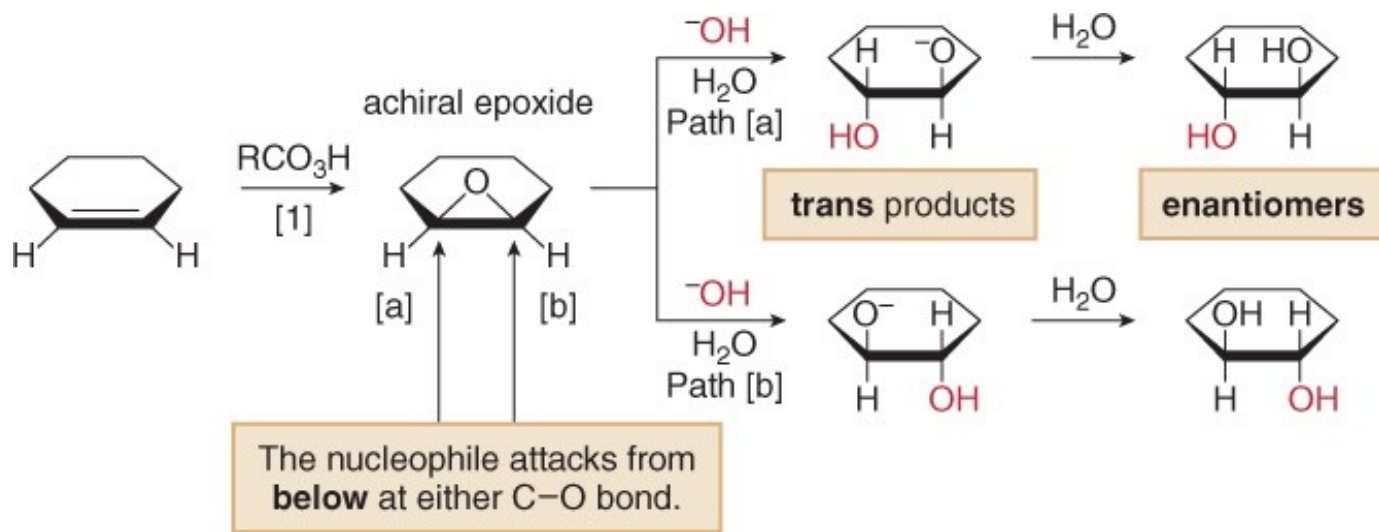
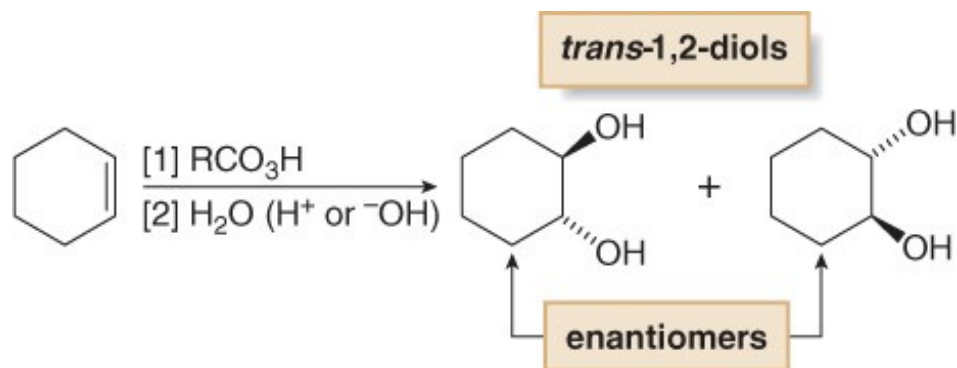


## syn addition product

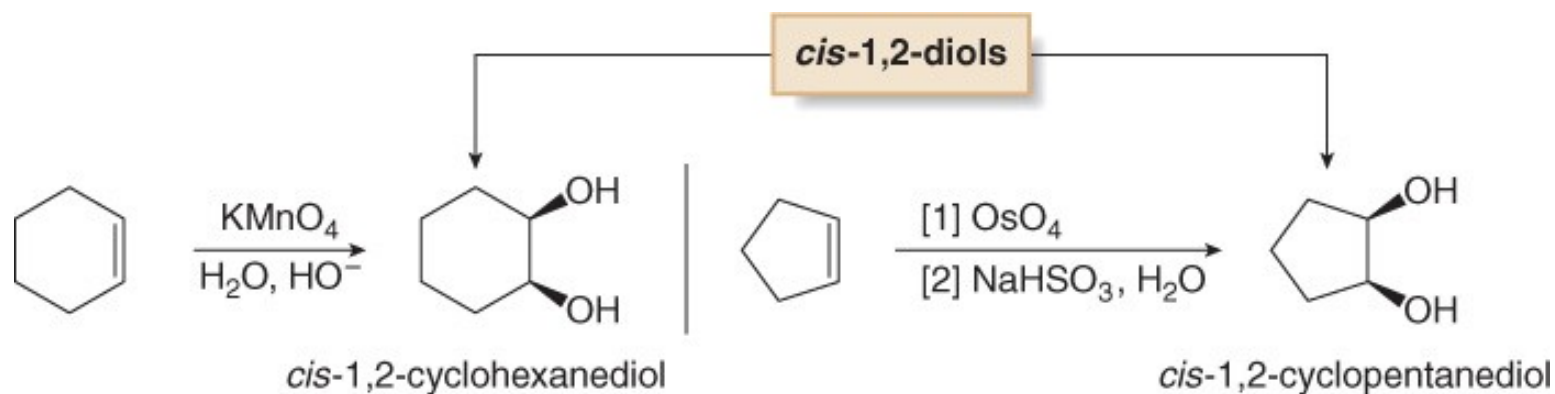
2 OH's added on the **same** side of the C=C



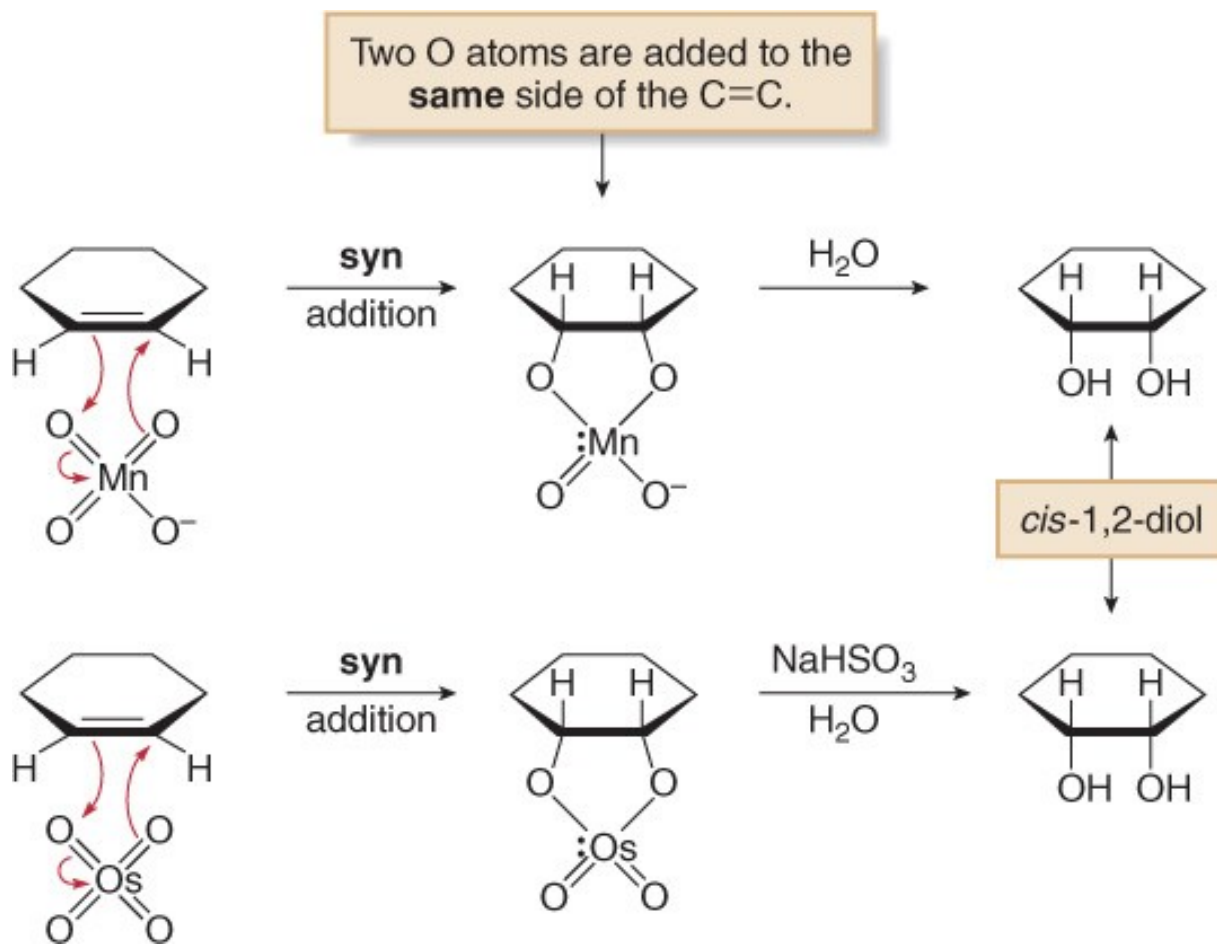
- **Anti dihydroxylation** is achieved in two steps—epoxidation, followed by ring opening with  $\text{OH}^-$  or  $\text{H}_3\text{O}^+$ .



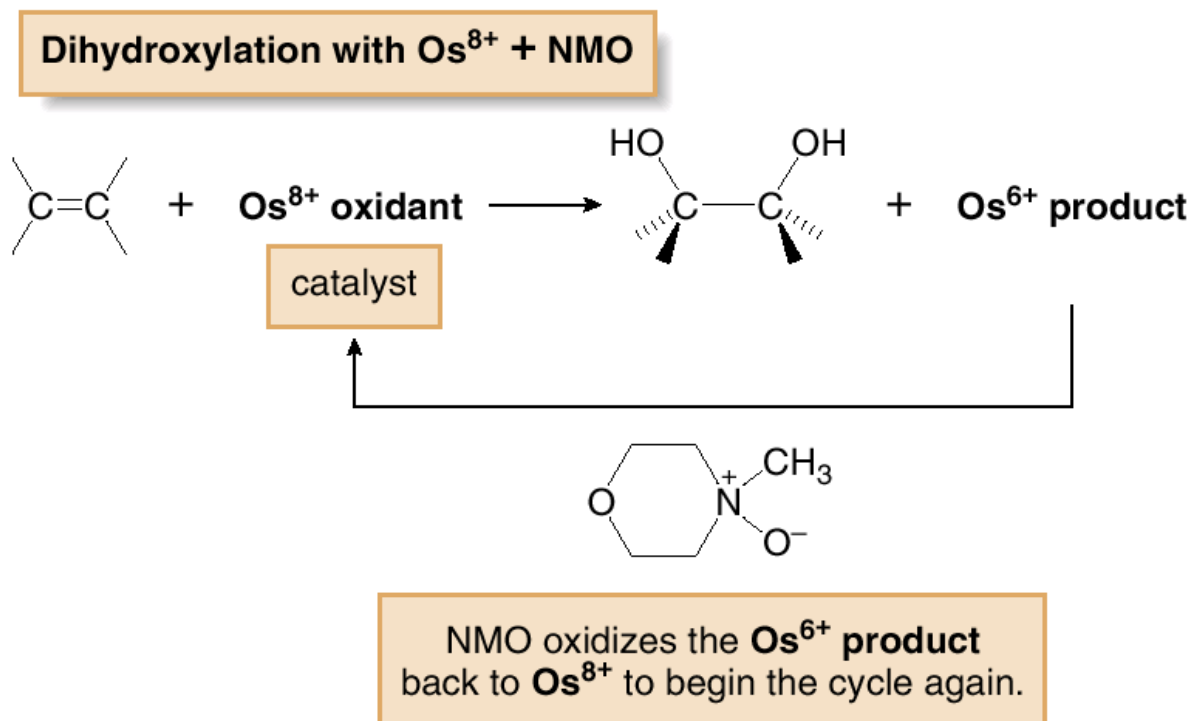
- **Syn hydroxylation** results when an alkene is treated with either  $\text{KMnO}_4$  or  $\text{OsO}_4$ .



- Each reagent adds two oxygen atoms in a **syn** fashion.
- Hydrolysis of the cyclic intermediate cleaves the metal oxygen bonds, forming a ***cis*-1,2-diol**.

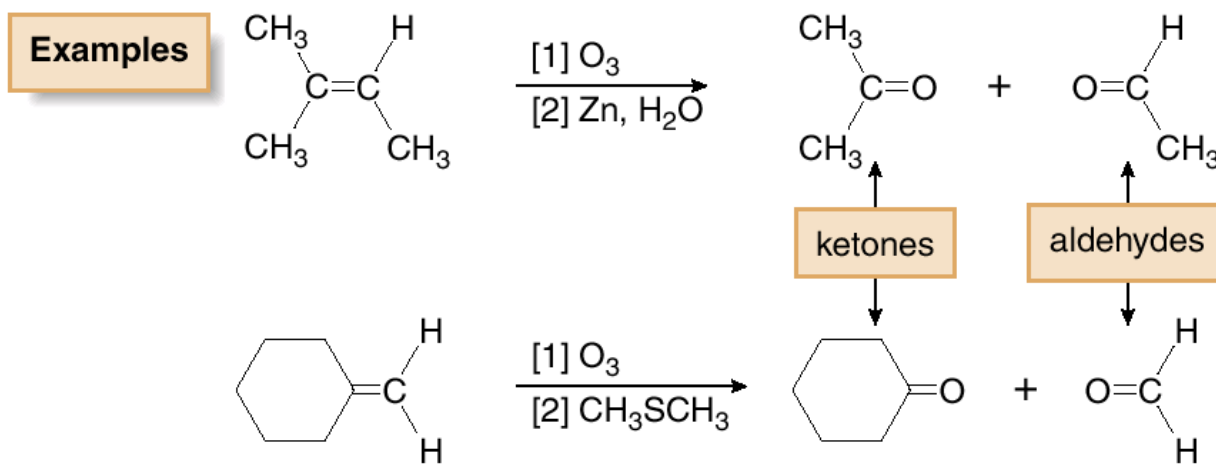
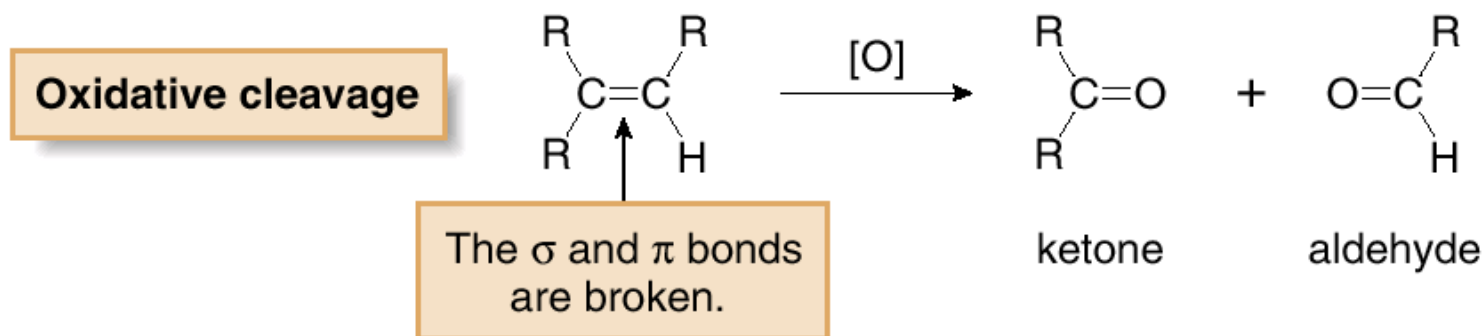


- Dihydroxylation can also be carried out by using a catalytic amount of  $\text{OsO}_4$ , if the oxidant *N*-methylmorpholine *N*-oxide (NMO) is also added.
- In the catalytic process, dihydroxylation of the double bond converts the  $\text{Os}^{8+}$  oxidant into an  $\text{Os}^{6+}$  product, which is then re-oxidized by NMO to  $\text{Os}^{8+}$ .



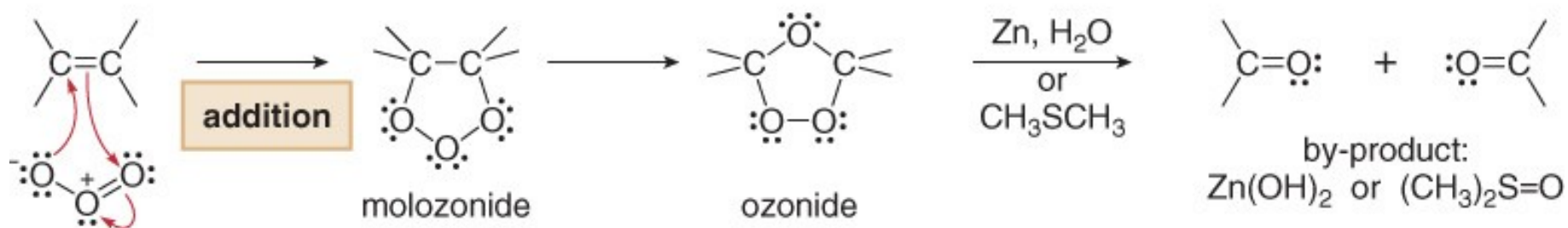
# Oxidative Cleavage of Alkenes

- Oxidative cleavage of an alkene breaks both the  $\sigma$  and  $\pi$  bonds of the double bond to form two carbonyl compounds. Cleavage with ozone ( $O_3$ ) is called **ozonolysis**.

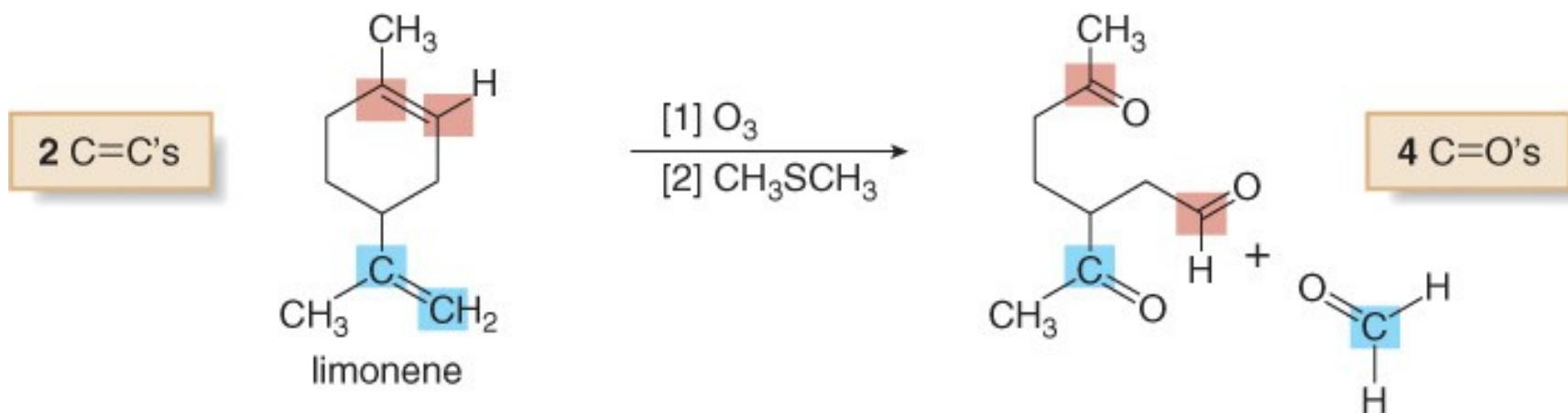


- Addition of O<sub>3</sub> to the π bond of an alkene forms an unstable intermediate called a **molozone**, which rearranges to an **ozonide** in a stepwise process.
- The unstable ozonide is reduced to afford carbonyl compounds. Zn (in H<sub>2</sub>O) or dimethylsulfide (CH<sub>3</sub>SCH<sub>3</sub>) are two common reagents used to convert the ozonide into carbonyl compounds.

The key intermediates in ozonolysis



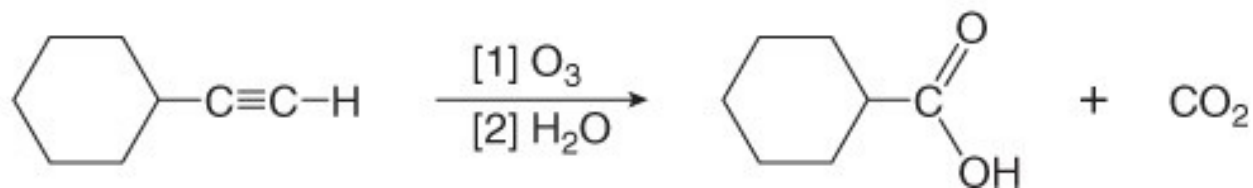
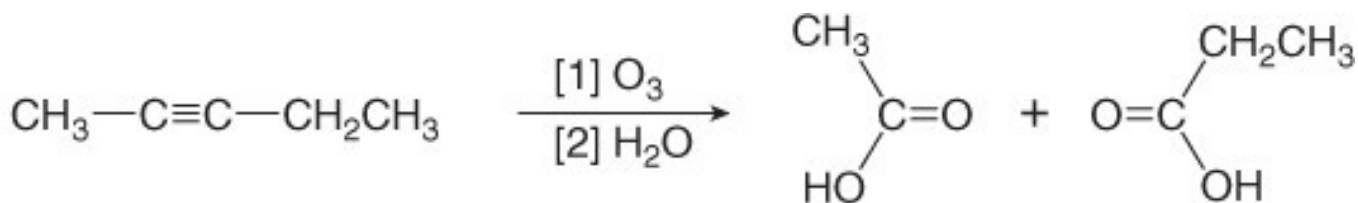
- Ozonolysis of dienes or other polyenes results in oxidative cleavage of all C=C bonds.
- It is important to note that when oxidative cleavage involves a double bond that is part of a ring, the ring opens up affording a single chain with two carbonyls at the carbons where the double bond was originally.



# Oxidative Cleavage of Alkynes

- Alkynes undergo oxidative cleavage of the  $\sigma$  and both  $\pi$  bonds.
- Internal alkynes are oxidized to carboxylic acids (RCOOH).
- Terminal alkynes afford a carboxylic acid and  $\text{CO}_2$  from the  $sp$  hybridized C—H bond.

Examples

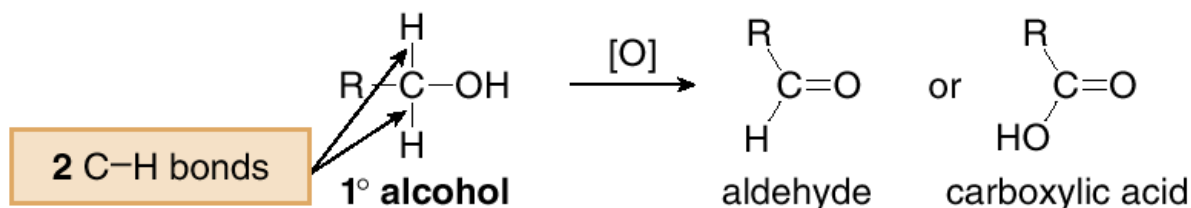




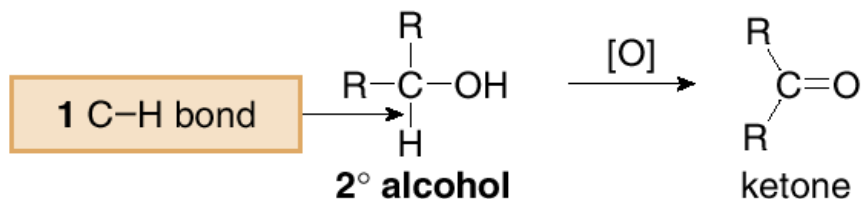
# Oxidation of Alcohols

- Alcohols are oxidized to a variety of carbonyl compounds.

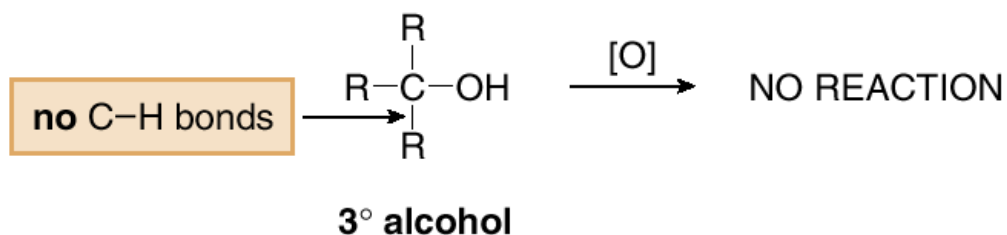
- 1° Alcohols** are oxidized to either **aldehydes** or **carboxylic acids** by replacing either one or two C–H bonds by C–O bonds.



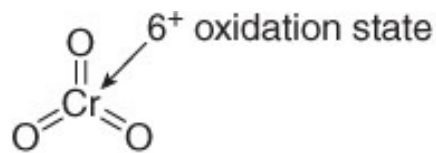
- 2° Alcohols** are oxidized to **ketones** by replacing the one C–H bond by a C–O bond.



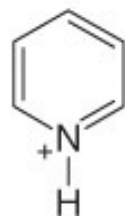
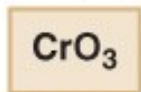
- 3° Alcohols** have **no H atoms on the carbon with the OH group**, so they are not easily oxidized.



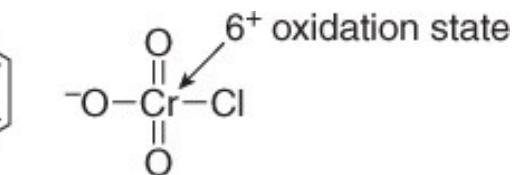
- Recall that the oxidation of alcohols to carbonyl compounds is typically carried out with  $\text{Cr}^{6+}$  oxidants, which are reduced to  $\text{Cr}^{3+}$  products.
- $\text{CrO}_3$ ,  $\text{Na}_2\text{Cr}_2\text{O}_7$ , and  $\text{K}_2\text{Cr}_2\text{O}_7$  are strong, nonselective oxidants used in aqueous acid ( $\text{H}_2\text{SO}_4 + \text{H}_2\text{O}$ ).
- PCC is soluble in  $\text{CH}_2\text{Cl}_2$  (dichloromethane) and can be used without strong acid present, making it a more selective, milder oxidant.



chromium(VI) oxide

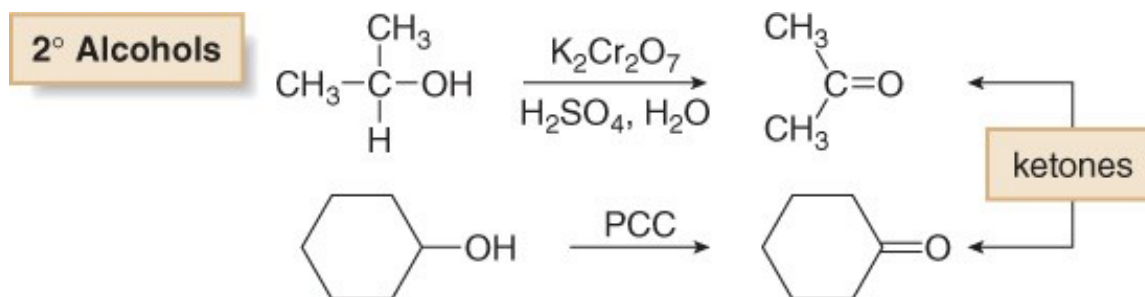


pyridinium chlorochromate



# Oxidation of 2° Alcohols

- Any of the Cr<sup>6+</sup> oxidants effectively oxidize 2° alcohols to ketones.

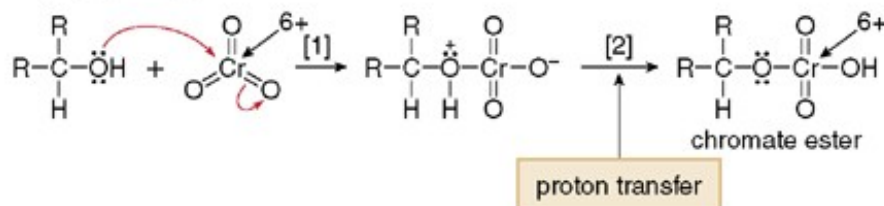


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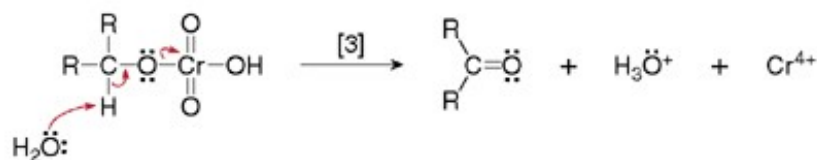
## Mechanism 12.5 Oxidation of an Alcohol with CrO<sub>3</sub>

Steps [1] and [2] Formation of the chromate ester



- Nucleophilic attack of the alcohol on the electrophilic metal followed by proton transfer forms a **chromate ester**. The C–H bond in the starting material (the 2° alcohol) is still present in the chromate ester, so there is no net oxidation in Steps [1] and [2].

Step [3] Removal of a proton to form the carbonyl group

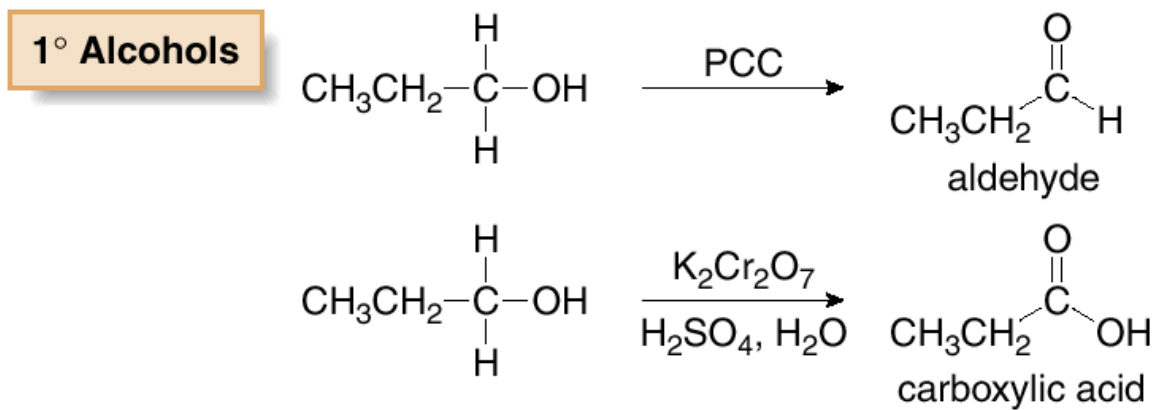


- In Step [3], a base ( $H_2O$  or a molecule of the starting alcohol) removes a proton, with the electron pair in the C–H bond forming the new  $\pi$  bond of the C=O. **Oxidation at carbon occurs in this step** because the number of C–H bonds decreases and the number of C–O bonds increases.

# Oxidation of 1° Alcohols

- 1° Alcohols are oxidized to either aldehydes or carboxylic acids, depending on the reagent.

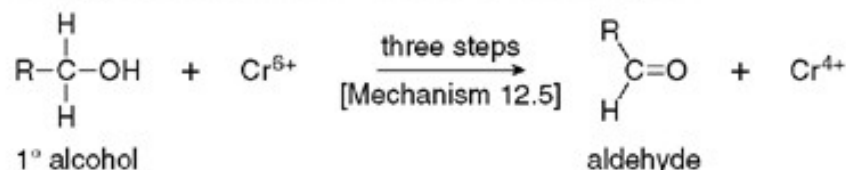
- 1° Alcohols are oxidized to aldehydes (RCHO) under mild reaction conditions—using PCC in CH<sub>2</sub>Cl<sub>2</sub>.
- 1° Alcohols are oxidized to carboxylic acids (RCOOH) under harsher reaction conditions: Na<sub>2</sub>Cr<sub>2</sub>O<sub>7</sub>, K<sub>2</sub>Cr<sub>2</sub>O<sub>7</sub>, or CrO<sub>3</sub> in the presence of H<sub>2</sub>O and H<sub>2</sub>SO<sub>4</sub>.





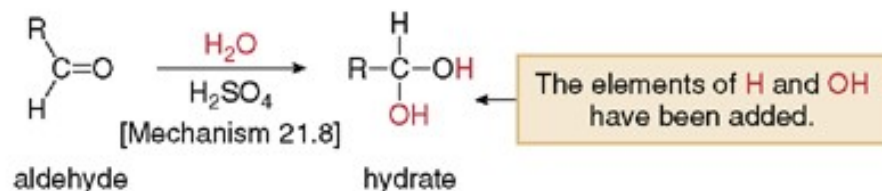
## Mechanism 12.6 Oxidation of a 1° Alcohol to a Carboxylic Acid

**Part [1]** Oxidation of a 1° alcohol to an aldehyde



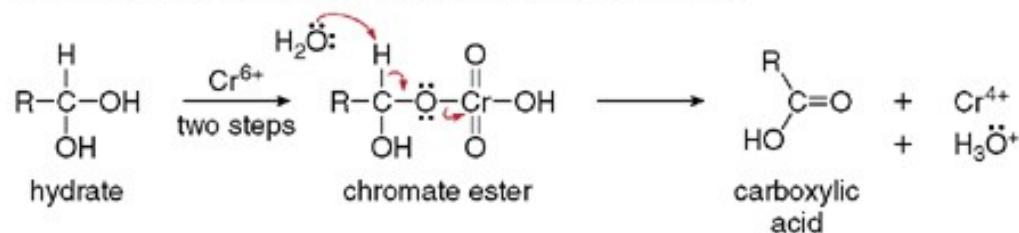
- Oxidation of a 1° alcohol to an aldehyde occurs by the three-step mechanism detailed in Mechanism 12.5.

**Part [2]** Addition of H<sub>2</sub>O to form a hydrate



- The aldehyde reacts with H<sub>2</sub>O to form a **hydrate**, a compound with two OH groups on the same carbon atom. Hydrates are discussed in greater detail in Section 21.13.

**Part [3]** Oxidation of the hydrate to a carboxylic acid



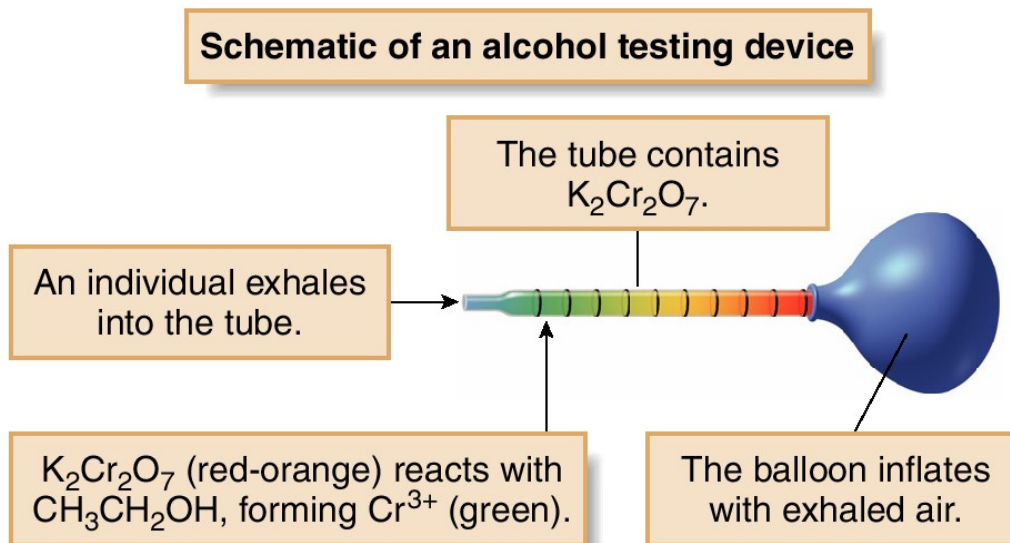
- The C–H bond of the hydrate is then oxidized with the Cr<sup>6+</sup> reagent, following Mechanism 12.5. Because the hydrate contains two OH groups, the product of oxidation is a carboxylic acid.

- **Cr<sup>6+</sup> oxidations are characterized by a color change, as the red-orange Cr<sup>6+</sup> reagent is reduced to green Cr<sup>3+</sup>.**
- **Some devices used to measure blood alcohol content make use of this color change—Oxidation of CH<sub>3</sub>CH<sub>2</sub>OH, the 1° alcohol in alcoholic beverages, with orange K<sub>2</sub>Cr<sub>2</sub>O<sub>7</sub> forms CH<sub>3</sub>COOH and green Cr<sup>3+</sup>.**
- **Blood alcohol level can be determined by having an individual blow into a tube containing K<sub>2</sub>Cr<sub>2</sub>O<sub>7</sub>, H<sub>2</sub>SO<sub>4</sub>, and an inert solid.**
- **The alcohol in the exhaled breath is oxidized by the Cr<sup>6+</sup> reagent, which turns green in the tube.**
- **The higher the concentration of CH<sub>3</sub>CH<sub>2</sub>OH in the breath, the more Cr<sup>6+</sup> is reduced, and the farther the green Cr<sup>3+</sup> color extends down the length of the sample tube.**
- **The extent of the green color is then correlated with blood alcohol levels.**

Figure 12.10

Blood alcohol screening

- The oxidation of  $\text{CH}_3\text{CH}_2\text{OH}$  with  $\text{K}_2\text{Cr}_2\text{O}_7$  to form  $\text{CH}_3\text{COOH}$  and  $\text{Cr}^{3+}$  was the first available method for the routine testing of alcohol concentration in exhaled air. Some consumer products for alcohol screening are still based on this technology.



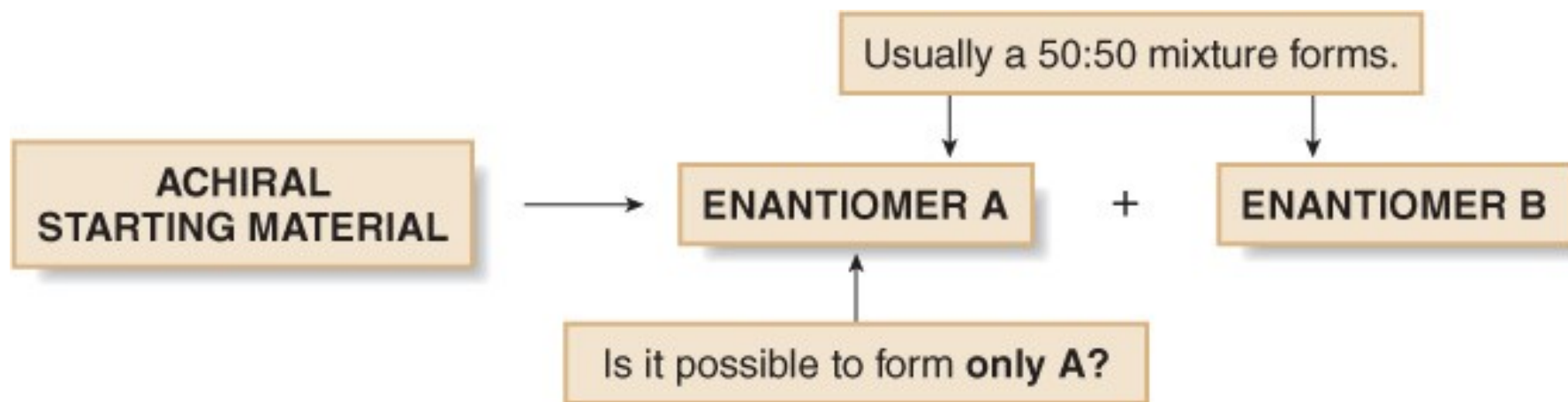
**Consumer product**



$\text{K}_2\text{Cr}_2\text{O}_7$

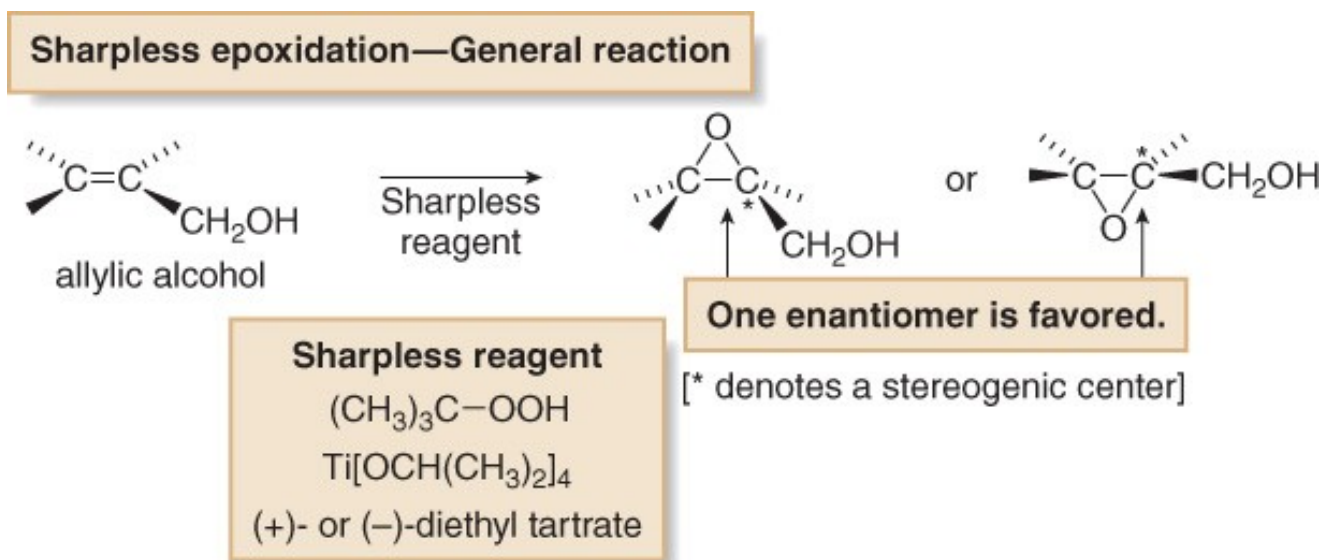
## The Sharpless Epoxidation

- Recall that in the reactions we have discussed thus far, an achiral starting material has reacted with an achiral reagent to give either an achiral product, or a racemic mixture of two enantiomers.

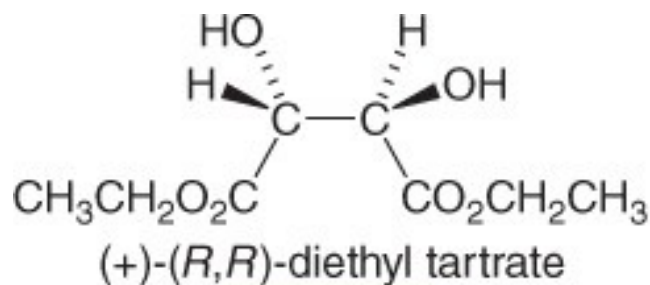




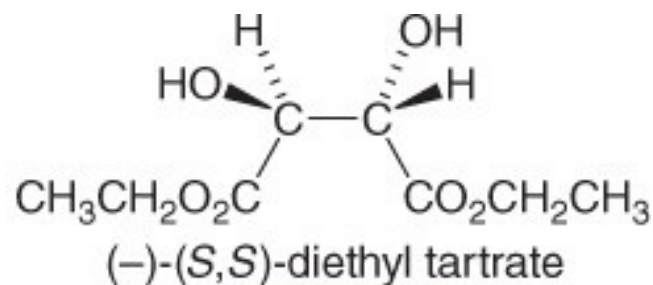
- In the **Sharpless epoxidation**, the double bonds of **allylic alcohols** are oxidized to epoxides.
- Since the formation of only one enantiomer is favored, the reaction is said to be **enantioselective**.
- An enantioselective reaction affords predominantly or exclusively one enantiomer.
- A reaction that converts an achiral starting material into predominantly one enantiomer is called an **asymmetric reaction**.



- The Sharpless reagent consists of three different components: *tert*-butylhydroperoxide (CH<sub>3</sub>)<sub>3</sub>COOH; a titanium catalyst—usually titanium(IV) isopropoxide, Ti[OCH(CH<sub>3</sub>)<sub>2</sub>]<sub>4</sub>; and diethyl tartrate (DET).
- There are two different chiral diethyl tartrate isomers, labeled as (+)-DET or (-)-DET to indicate the direction in which they rotate plane polarized light.
- The identity of the DET isomer determines which enantiomer is the major product obtained in the epoxidation.

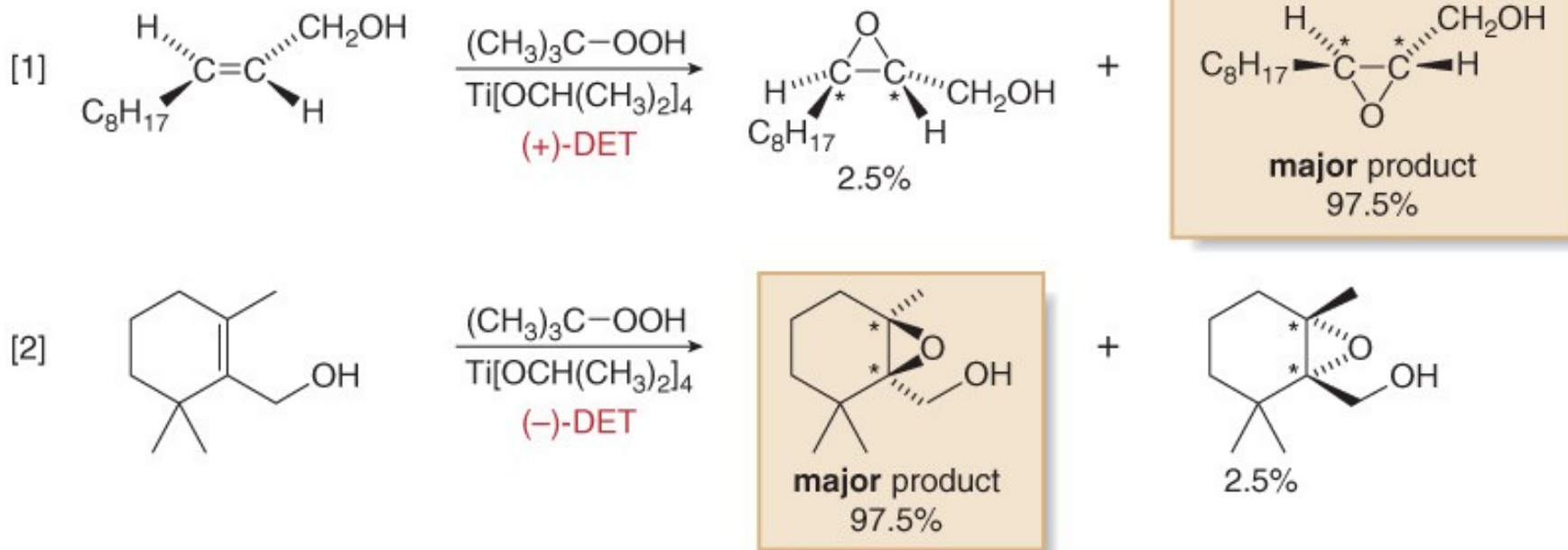


(+)-DET



(-)-DET

## Examples



[\* denotes a stereogenic center]

- Reactions [1] and [2] are highly enantioselective as each has an enantiomeric excess of 95% (i.e., 97.5% of the major enantiomer and 2.5% of the minor enantiomer).

- To determine which enantiomer is formed from a given isomer of DET, draw the allylic alcohol in a plane, with the OH group in the bottom right hand corner; then note that:

- Epoxidation with (-)-DET adds an oxygen atom from above the plane.
- Epoxidation with (+)-DET adds an oxygen atom from below the plane.

