## Elimination Reactions

Course Name: General Chemistry

Course Code: CHEM F111

Lecture Instructor Name: Prof. Subhasish Roy

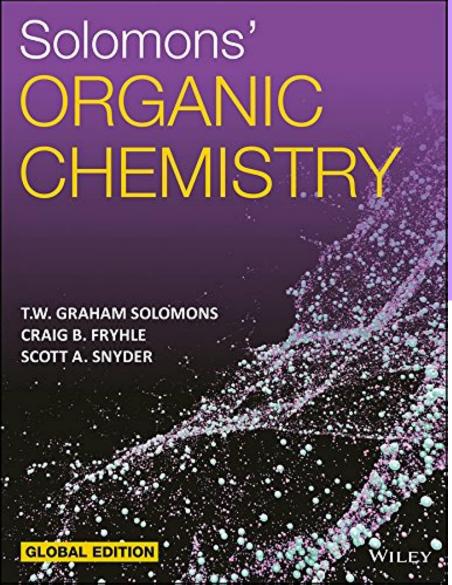
**Department**: Chemistry

Email: subhasishr@goa.bits-pilani.ac.in

Chamber No: C 223

Chamber Consultation Hours: Thursday 4:00 PM to 4:50 PM

# Text and Reference Books



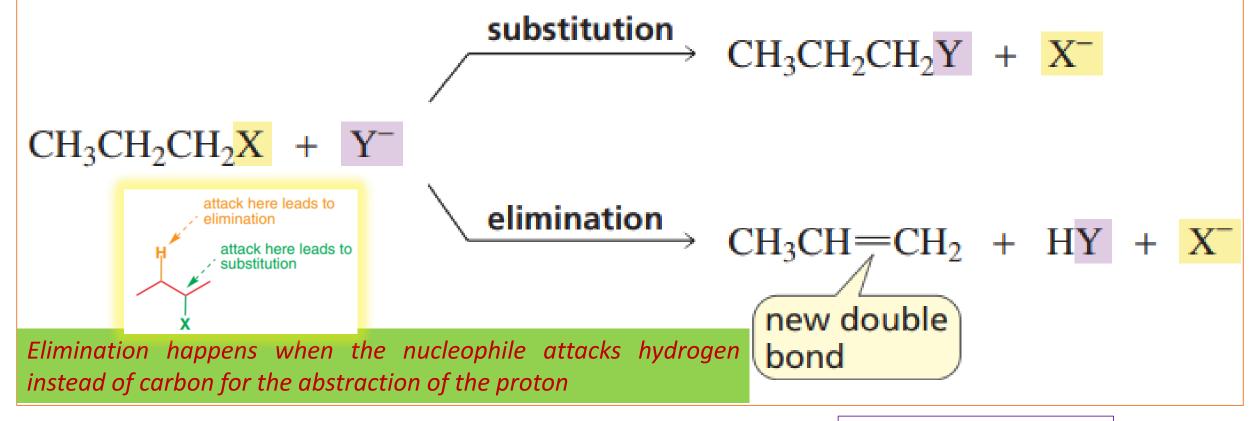
Most of the Lecture Slides are made from the text book. I am gratefully acknowledging Solomon's Organic Chemistry Book and many other Organic Chemistry Books.

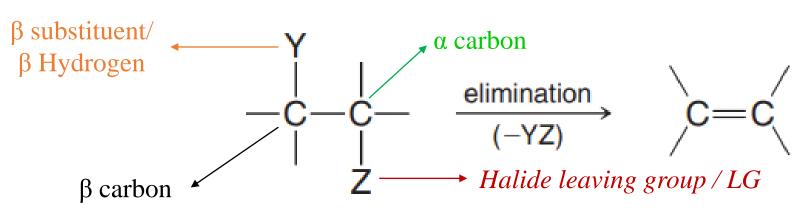
# Elimination Reactions

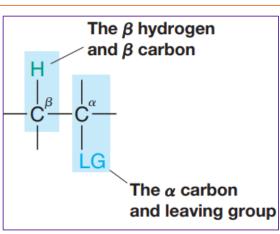
### Contents

- 7.5 Synthesis of Alkenes via Elimination Reactions
- **7.6** Dehydrohalogenation of Alkyl Halides
- 7.7 Acid-Catalyzed Dehydration of Alcohols
- 7.8 Carbocation Stability and the Occurrence of Molecular Rearrangements
- 7.9 The Acidity of Terminal Alkynes
- 7.10 Synthesis of Alkynes by Elimination Reactions
- 7.11 Terminal Alkynes Can Be Converted to Nucleophiles for Carbon–Carbon Bond Formation
- **7.12** Hydrogenation of Alkenes
- **20.12** Eliminations Involving Ammonium Compounds

### 7.5 Synthesis of Alkenes via Elimination Reactions







### NUCLEOPHILE

#### **AFFECTS**

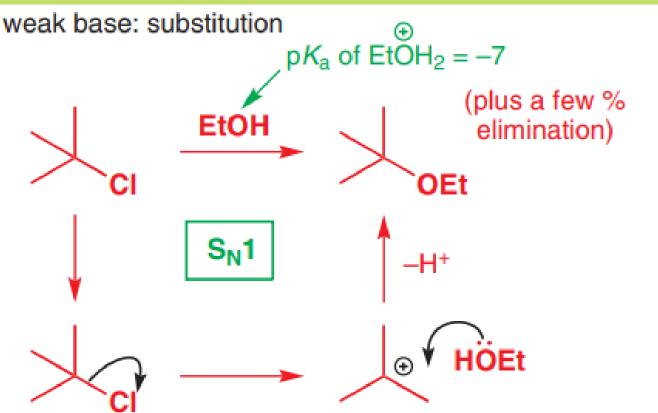
### **ELIMINATION**

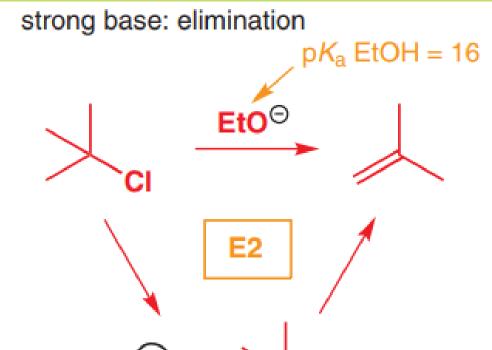
#### **VERSUS**

### **SUBSTITUTION?**

THE

**HOW** 

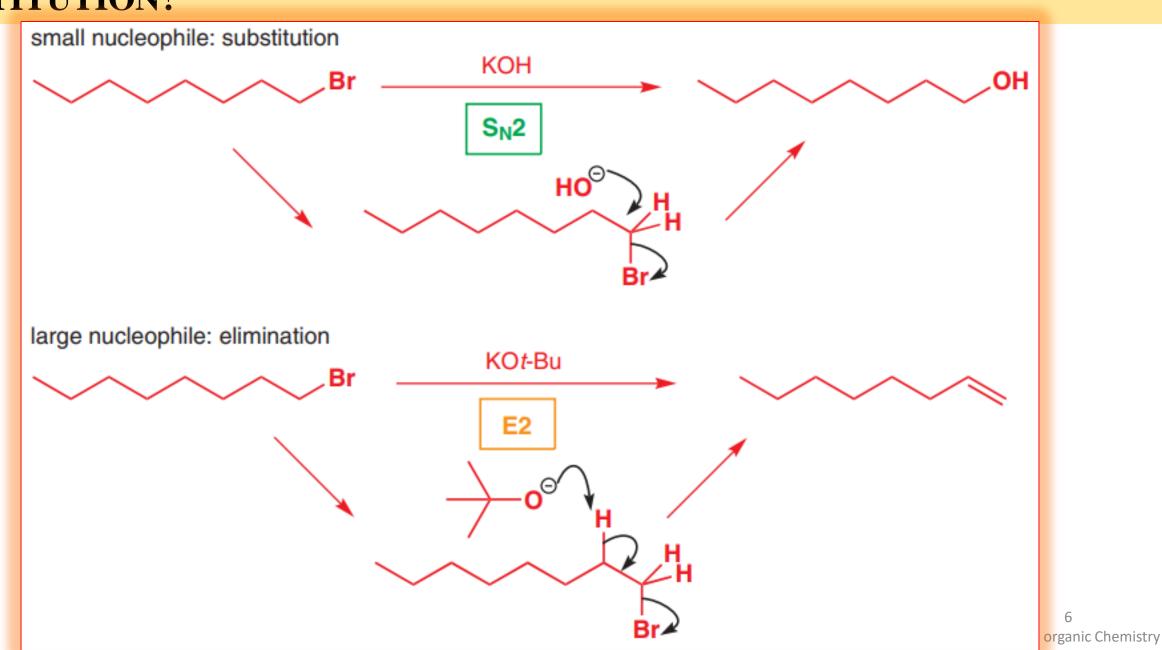




#### Elimination versus substitution

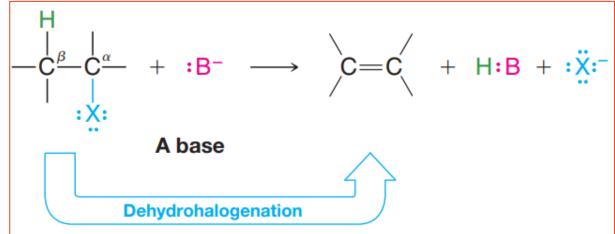
- Nucleophiles that are strong bases favour elimination over substitution.
- Nucleophiles (or bases) that are bulky favour elimination over substitution.
- · High temperatures favour elimination over substitution.

# HOW THE NUCLEOPHILE AFFECTS ELIMINATION VERSUS SUBSTITUTION?



### 6.15A Dehydrohalogenation

A widely used method for synthesizing alkenes is the elimination of HX from adjacent atoms of an alkyl halide. Heating the alkyl halide with a strong base causes the reaction to take place.



### 6.15B Bases Used in Dehydrohalogenation

Various strong bases have been used for dehydrohalogenations. Potassium hydroxide dissolved in ethanol (KOH/EtOH) is a reagent sometimes used, but the conjugate bases of alcohols, such as sodium ethoxide (EtONa), often offer distinct advantages. The conjugate base of an alcohol (an alkoxide) can be prepared by treating an alcohol with an alkali metal.

$$2 R - \ddot{O}H + 2 Na \longrightarrow 2 R - \ddot{O}: Na^{+} + H_{2}$$

Alcohol

Sodium

alkoxide

This reaction is an oxidation–reduction reaction. Metallic sodium reacts with hydrogen atoms that are bonded to oxygen atoms to generate hydrogen gas, sodium cations, and the alkoxide anion. The reaction with water is vigorous and at times explosive.

Sodium alkoxides can also be prepared by allowing an *alcohol to react with*  $2 \, H\ddot{O}H + 2 \, Na \longrightarrow 2 \, H\ddot{O}: \, Na^+ + H_2$ **sodium hydride** (NaH). The hydride ion (H:-) is a very strong base. (The pKa of  $H_{2}$  is 35).

$$R-\ddot{O}_{\longrightarrow}H$$
 +  $Na^+:H^ \longrightarrow$   $R-\ddot{O}:^ Na^+$  +  $H-H$ 

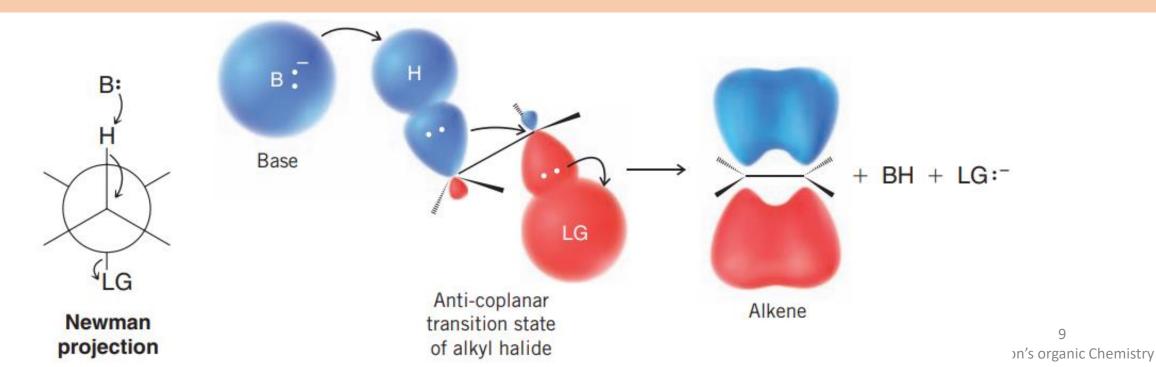
Potassium tert-butoxide (t-BuOK) is another highly effective dehydrohalogenating reagent. It can be made by the reaction below, or purchased as a solid.

Sodium (and potassium) alkoxides are usually prepared by using an excess of the alcohol, and the excess alcohol becomes the solvent for the reaction. Sodium ethoxide is frequently prepared in this way using excess ethanol.

### 6.15C Mechanisms of Dehydrohalogenations

Elimination reactions occur by a variety of mechanisms. With alkyl halides, two mechanisms are especially important because they are closely related to the  $S_N2$  and  $S_N1$  reactions that we have just studied. One mechanism, called the E2 reaction, is bimolecular in the rate-determining step; the other mechanism is the E1 reaction, which is unimolecular in the rate-determining step.

# 6.15C Mechanisms of Dehydrohalogenations: E2 reaction mechanism In E2 eliminations the loss of the leaving group and removal of the proton are concerted.

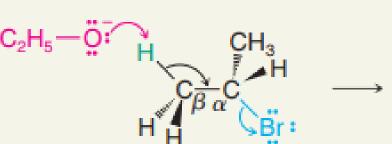


### 6.15C Mechanisms of Dehydrohalogenations: E2

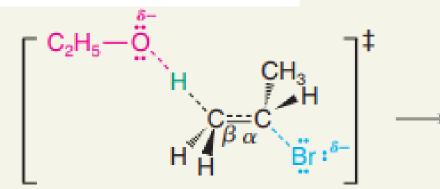
$$C_2H_5O^- + CH_3CHBrCH_3 \longrightarrow CH_2 = CHCH_3 + C_2H_5OH + Br^-$$

Mechanism

Rate = 
$$k[CH_3CHBrCH_3][C_2H_5O^-]$$

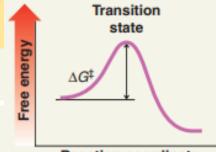


The basic ethoxide ion begins to remove a proton from the B carbon using its electron pair to form a bond to it. At the same time, the electron pair of the  $\beta$  C—H bond begins to move in to become the  $\pi$  bond of a double bond, and the bromine begins to depart with the electrons that bonded it to the α carbon.



Transition state

Partial bonds in the transition state extend from the oxygen atom that is removing the B hydrogen, through the carbon skeleton of the developing double bond, to the departing leaving group. The flow of electron density is from the base toward the leaving group as an electron pair fills the  $\pi$ bonding orbital of the alkene.



Reaction coordinate An E2 reaction has one transition state

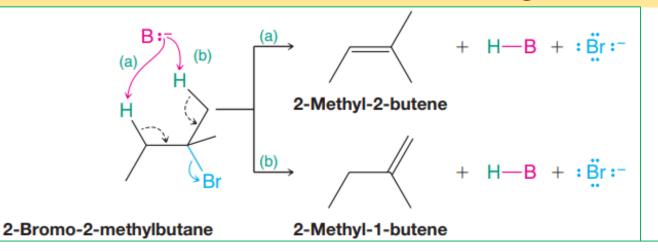
At completion of the reaction, the double bond is fully formed and the alkene has a trigonal planar geometry at each carbon atom. The other products are a molecule of ethanol and a bromide ion.

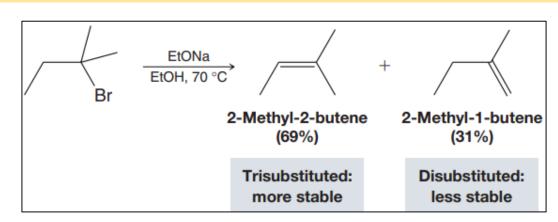
### 7.6A How To Favor an E2 Mechanism

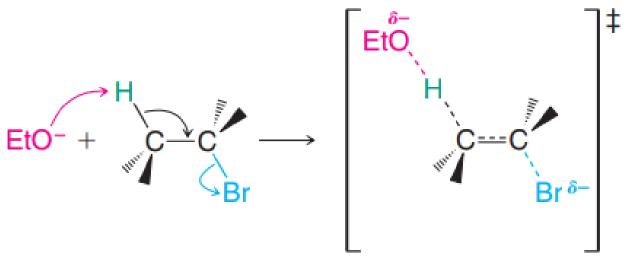
- ☐ Use a secondary or tertiary alkyl halide if possible. Why?
- Because steric hindrance in the substrate will inhibit substitution.
- ☐ When a synthesis must begin with a primary alkyl halide, use a bulky base. Why?
- Because the steric bulk of the base will inhibit substitution.
- ☐ Use a high concentration 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.
- □ 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 above criterion. 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.)
- ☐ 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  $\Delta S^{\circ}$  in the Gibbs free-energy equation,  $\Delta G^{\circ} = \Delta H^{\circ} T \Delta S^{\circ}$  is significant, and  $\Delta S^{\circ}$  will be increased by higher temperature since T is a coefficient, leading to a more negative (favorable)  $\Delta G^{\circ}$ .

Solomon's organic Chemistry

### 7.6B Zaitsev's [Russian chemist A. N. Zaitsev (1841–1910) who formulated it. (Zaitsev's name is also transliterated as Zaitzev, Saytzeff, Saytseff, or Saytzev.)] Rule: Formation of the More Substituted Alkene Is Favored with a Small Base: Regioselectivity of E2 Reactions







Transition state for an E2 reaction

The  $\beta$  hydrogen and leaving group are anti coplanar.

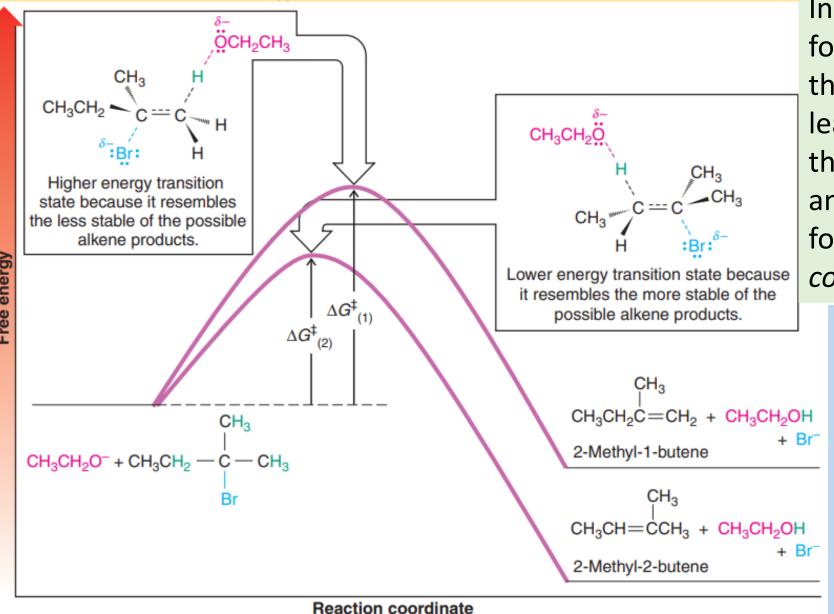
$$\longrightarrow$$
 EtOH + C=C + Br

The carbon-carbon bond has the developing character of a double bond.

substituted alkene as major product

### 7.6B Zaitsev's Rule: Formation of the More Substituted Alkene Is

**Favored with a Small Base** 

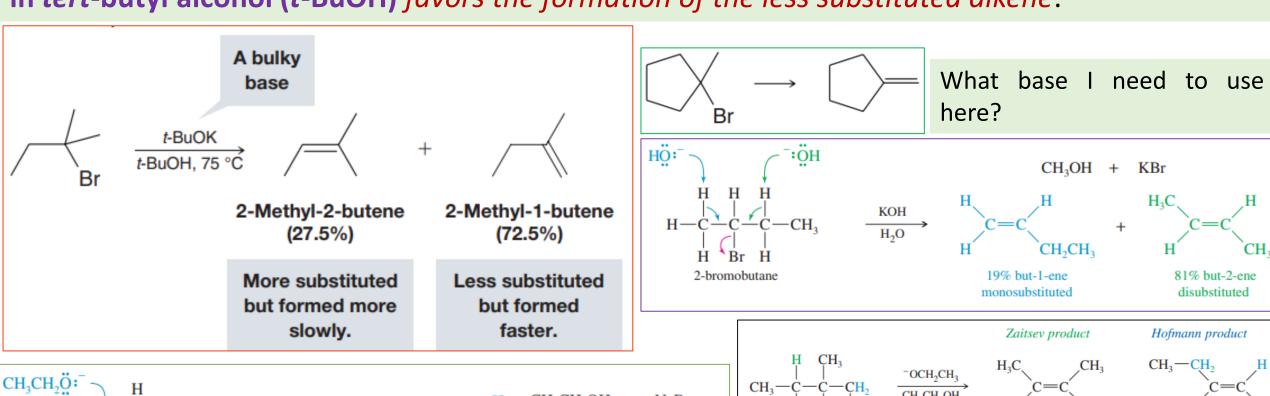


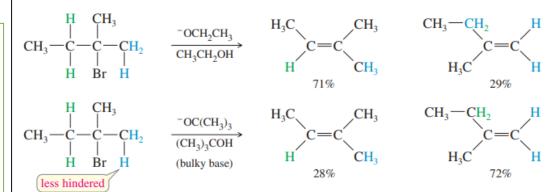
In general, the preferential formation of one product because the free energy of activation leading to its formation is lower than that for another product, and therefore the rate of its formation faster, is called *kinetic control of product formation*.

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.

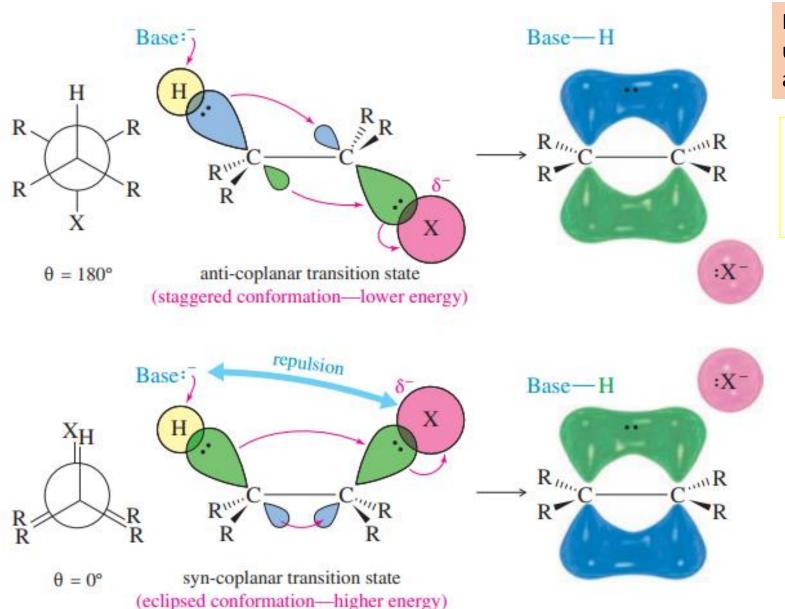
# 7.6C Formation of the Less Substituted Alkene (Hofmann rule) Using a Bulky Base

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:

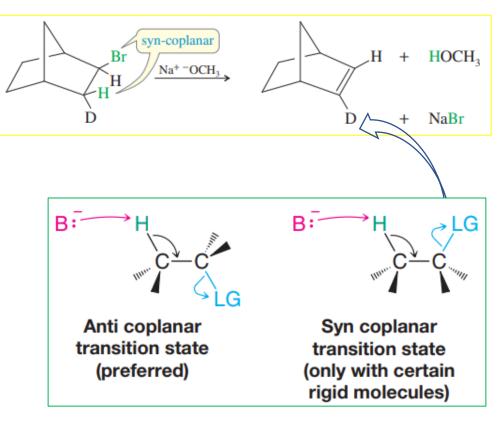




# 7.6D The Stereochemistry of E2 Reactions: The Orientation of Groups in the Transition State



Remember that syn-coplanar eliminations are unusual, however, and anti-coplanar eliminations are more common.



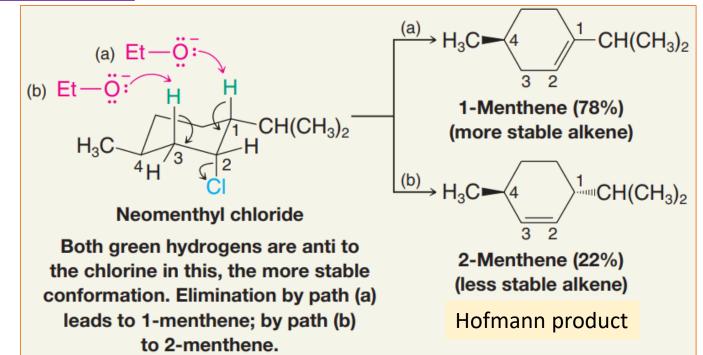
# 7.6D The Stereochemistry of E2 Reactions: The Orientation of Groups in the Transition State

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.

What products we can expect from these two different reactant after E2 reactions separately?

$$\begin{array}{c} Ph \\ Br \downarrow S \\ H \downarrow CH_3 \end{array} = \begin{array}{c} H_3C \downarrow C \\ Ph \end{array} \begin{array}{c} Br \\ (rotate) \end{array} \begin{array}{c} H_3C \downarrow C \\ H_3C \downarrow C \end{array} \begin{array}{c} H_3C \downarrow C \\ H_3C \downarrow C \end{array} \begin{array}{c} H_3C \downarrow C \\ H_3C \downarrow C \end{array} \begin{array}{c} H_3C \downarrow C \\ H_3C \downarrow C \end{array} \begin{array}{c} H_3C \downarrow C \\ H_3C \downarrow C \end{array} \begin{array}{c} H_3C \downarrow C \\ H_3C \downarrow C \end{array} \begin{array}{c} H_3C \downarrow C \\ H_3C \downarrow C \end{array} \begin{array}{c} H_3C \downarrow C \\ H_3C \downarrow C \end{array} \begin{array}{c} H_3C \downarrow C \\ H_3C \downarrow C \end{array} \begin{array}{c} H_3C \downarrow C \\ H_3C \downarrow C \end{array} \begin{array}{c} H_3C \downarrow C \\ H_3C \downarrow C \end{array} \begin{array}{c} H_3C \downarrow C \\ H_3C \downarrow C \end{array} \begin{array}{c} H_3C \downarrow C \\ H_3C \downarrow C \end{array} \begin{array}{c} H_3C \downarrow C \\ H_3C \downarrow C \end{array} \begin{array}{c} H_3C \downarrow C \\ H_3C \downarrow C \end{array} \begin{array}{c} H_3C \downarrow C \\ H_3C \downarrow C \end{array} \begin{array}{c} H_3C \downarrow C \\ H_3C \downarrow C \end{array} \begin{array}{c} H_3C \downarrow C \\ H_3C \downarrow C \end{array} \begin{array}{c} H_3C \downarrow C \\ H_3C \downarrow C \end{array} \begin{array}{c} H_3C \downarrow C \\ H_3C \downarrow C \end{array} \begin{array}{c} H_3C \downarrow C \\ H_3C \downarrow C \end{array} \begin{array}{c} H_3C \downarrow C \\ H_3C \downarrow C \end{array} \begin{array}{c} H_3C \downarrow C \\ H_3C \downarrow C \end{array} \begin{array}{c} H_3C \downarrow C \\ H_3C \downarrow C \end{array} \begin{array}{c} H_3C \downarrow C \\ H_3C \downarrow C \end{array} \begin{array}{c} H_3C \downarrow C \\ H_3C \downarrow C \end{array} \begin{array}{c} H_3C \downarrow C \\ H_3C \downarrow C \end{array} \begin{array}{c} H_3C \downarrow C \\ H_3C \downarrow C \end{array} \begin{array}{c} H_3C \downarrow C \\ H_3C \downarrow C \end{array} \begin{array}{c} H_3C \downarrow C \\ H_3C \downarrow C \end{array} \begin{array}{c} H_3C \downarrow C \\ H_3C \downarrow C \end{array} \begin{array}{c} H_3C \downarrow C \\ H_3C \downarrow C \end{array} \begin{array}{c} H_3C \downarrow C \\ H_3C \downarrow C \end{array} \begin{array}{c} H_3C \downarrow C \\ H_3C \downarrow C \end{array} \begin{array}{c} H_3C \downarrow C \\ H_3C \downarrow C \end{array} \begin{array}{c} H_3C \downarrow C \\ H_3C \downarrow C \end{array} \begin{array}{c} H_3C \downarrow C \\ H_3C \downarrow C \\ H_3C \downarrow C \end{array} \begin{array}{c} H_3C \downarrow C \\ H_3C \downarrow C \\ H_3C \downarrow C \\ H_3C \downarrow C \end{array} \begin{array}{c} H_3C \downarrow C \\ H_3C$$



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

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.

2-Menthene (100%)

The transition state for the E2 elimination is anti coplanar.

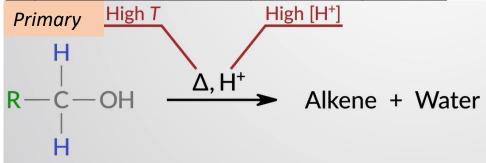
#### 7.7 Acid-Catalyzed Dehydration of Alcohols

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

### Dehydration of alcohols depends on the following factors:

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

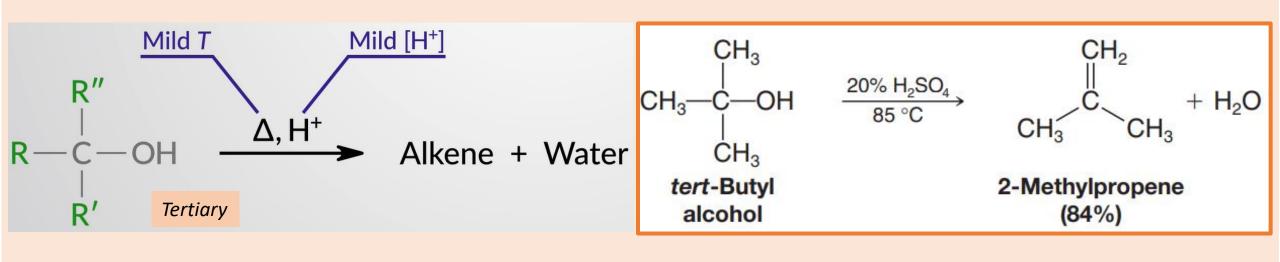


B. <u>Secondary alcohols usually dehydrate under milder conditions. Cyclohexanol, for example, dehydrates in 85%</u> phosphoric acid at 165–170 8C:

$$\begin{array}{c|c} & \underline{\mathsf{Moderate}\,T} & \underline{\mathsf{Moderate}\,[\mathsf{H}^+]} \\ & \mathsf{H} \\ & \mathsf{R} - \mathsf{C} - \mathsf{OH} & & \\ & & \\ & \mathsf{Alkene} + \mathsf{Water} \\ & & \\ & \mathsf{R'} & \underline{\mathsf{Secondary}} \\ \end{array}$$

OH 
$$\frac{85\% \text{ H}_3\text{PO}_4}{165-170 \text{ °C}} + \text{H}_2\text{O}$$
 Cyclohexanol Cyclohexane (80%)

### A. <u>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:</u>



• The relative ease with which alcohols undergo dehydration is  $3^{\circ} > 2^{\circ} > 1^{\circ}$ .

2. Some primary and secondary alcohols also undergo rearrangements of their carbon skeletons during dehydration. Such a rearrangement occurs in the

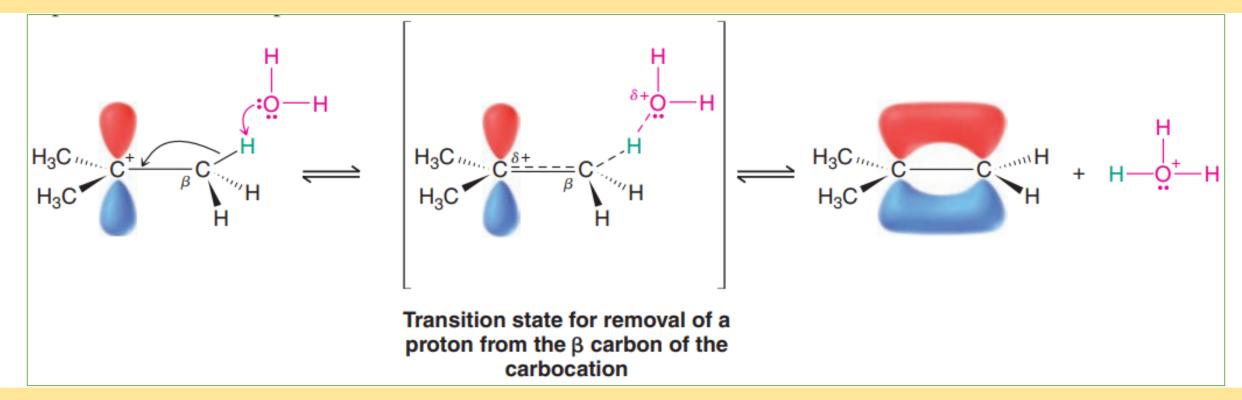
dehydration of 3,3-dimethyl-2-butanol:

Notice that the carbon skeleton of the reactant is

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

β hydrogen

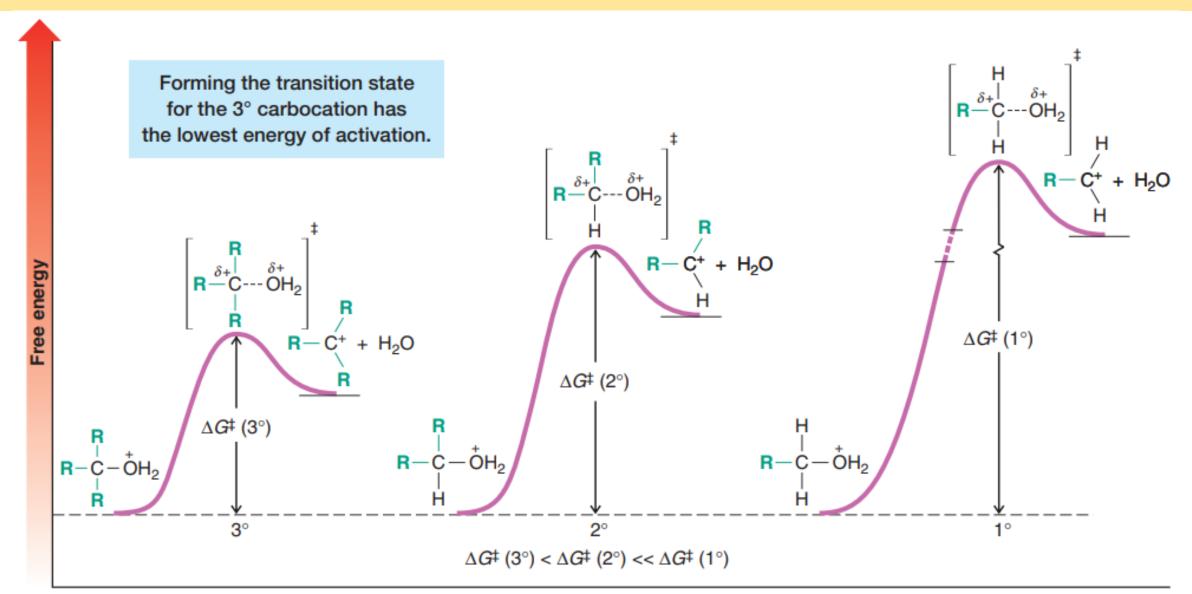
#### 7.7A An E1 Reaction: Transition State



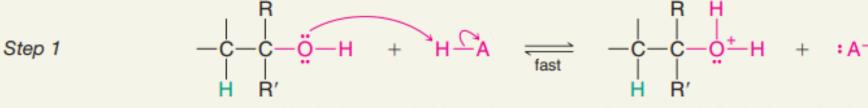
#### 7.7B Carbocation Stability and the Transition State

Solomon's organic Chemistry

# Forming the transition state for the 3° carbocation has the lowest energy of activation



#### Acid-Catalyzed Dehydration of Secondary or Tertiary Alcohols: An E1 Reaction



2° or 3° Alcohol (R' may be H)

Step 2

Step 3

Acid catalyst (typically sulfuric or phosphoric acid) Protonated alcohol

Conjugate base

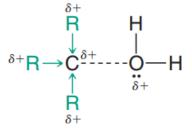
The alcohol accepts a proton from the acid in a fast step.

$$-\overset{\mathsf{R}}{\mathsf{C}} - \overset{\mathsf{H}}{\mathsf{C}} \overset{\mathsf{H}}{\overset{\mathsf{C}}{\mathsf{C}}} \overset{\mathsf{H}}{\overset{\mathsf{H}}{\mathsf{C}}} + \overset{\mathsf{H}}{\overset{\mathsf{C}}{\mathsf{C}}} \overset{\mathsf{H}}{\overset{\mathsf{H}}{\mathsf{C}}} + \overset{\mathsf{H}}{\overset{\mathsf{C}}{\mathsf{C}}} \overset{\mathsf{H}}{\overset{\mathsf{H}}{\mathsf{C}}} + \overset{\mathsf{H}}{\overset{\mathsf{C}}{\mathsf{C}}} \overset{\mathsf{H}}{\overset{\mathsf{H}}{\mathsf{C}}} \overset{\mathsf{H}}{\overset{\mathsf{H}}{\mathsf{C}}} \overset{\mathsf{H}}{\overset{\mathsf{H}}{\mathsf{C}}} + \overset{\mathsf{H}}{\overset{\mathsf{C}}{\mathsf{C}}} \overset{\mathsf{H}}{\overset{\mathsf{H}}{\mathsf{C}}} \overset{\mathsf{H}}{\overset{\mathsf{H}}} \overset{\mathsf{H}}{\overset{\mathsf{H}}{\mathsf{C}}} \overset{\mathsf{H}}{\overset{\mathsf{H}}} \overset{\mathsf{H}}{\overset{\mathsf{H}}} \overset{\mathsf{H}}{\overset{\mathsf{H}}{\mathsf{C}}} \overset{\mathsf{H}}{\overset{\mathsf{H}}} \overset{\mathsf{H}}} \overset{\mathsf{H}}{\overset{\mathsf{H}}} \overset{\mathsf{H}}{\overset{\mathsf{H}}} \overset{\mathsf{H}}{\overset{\mathsf{H}}} \overset{\mathsf{H}}{\overset{\mathsf{H}}} \overset{\mathsf{H}}} \overset{\mathsf{H}}{\overset{\mathsf{H}}} \overset{\mathsf{H}}{\overset{\mathsf{H}}} \overset{\mathsf{H}}} \overset{\mathsf{H}}{\overset{\mathsf{H}}} \overset{\mathsf{H}}} \overset{\mathsf{H}}{\overset{\mathsf{H}}} \overset{\mathsf{H}}{\overset{\mathsf{H}}} \overset{\mathsf{H}}} \overset{\mathsf{H}}{\overset{\mathsf{H}}} \overset{\mathsf{H}}} \overset{\mathsf{H}}{\overset{\mathsf{H}}} \overset{\mathsf{H}}} \overset{\mathsf{H}}{\overset{\mathsf{H}}} \overset{\mathsf{H}}} \overset{\mathsf{H}} \overset{\mathsf{H}}} \overset{\mathsf{H}}{\overset{\mathsf{H}}} \overset{\mathsf{H}}} \overset{\mathsf{H}} \overset{\mathsf{H}}} \overset{\mathsf{H}} \overset{\mathsf{H}}} \overset{\mathsf{H}}} \overset{\mathsf{H}} \overset{\mathsf{H}}} \overset{\mathsf{H}} \overset{\mathsf{H}}} \overset{\mathsf{H}}} \overset{\mathsf{H}} \overset{\mathsf{H}}} \overset{\mathsf{H}}} \overset{\mathsf{H}} \overset{\mathsf{H}}} \overset{\mathsf$$

The protonated alcohol loses a molecule of water to become a carbocation.

This step is slow and rate determining.

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).



Transition state leading to 3° carbocation (most stable)

$$\begin{matrix} \overset{\delta^{+}}{\mathsf{R}} & \mathsf{H} \\ \overset{\delta^{+}}{\mathsf{R}} & \overset{\downarrow}{\mathsf{C}} \\ \overset{\delta^{+}}{\mathsf{C}} & \overset{\bullet}{\mathsf{C}} \\ & \overset{\vdots}{\delta^{+}} & \mathsf{H} \\ \mathsf{H} \end{matrix}$$

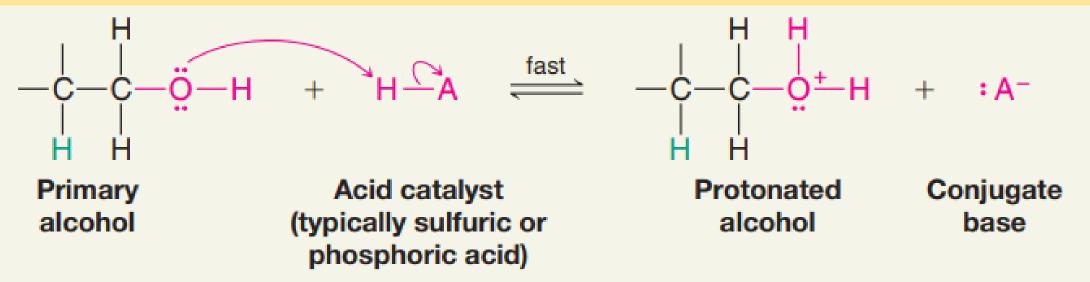
Transition state leading to 2° carbocation

$$\begin{matrix} \mathsf{A} & \mathsf{H} & \mathsf{H} \\ \mathsf{A} & \mathsf{C} & \mathsf{A} \\ \mathsf{A} & \mathsf{C} & \mathsf{A} \\ \mathsf{A} & \mathsf{A} \end{matrix}$$

Transition state leading to 1° carbocation (least stable)

23
Solomon's organic Chemistry

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



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

A base removes a hydrogen from the  $\beta$  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.

#### E1 vs E2 Reaction Mechanism

 E1 describes an elimination reaction (E) in which the rate-determining step is unimolecular (1) and does not involve the base. The leaving group leaves in this step, and the proton is removed in a separate second step.

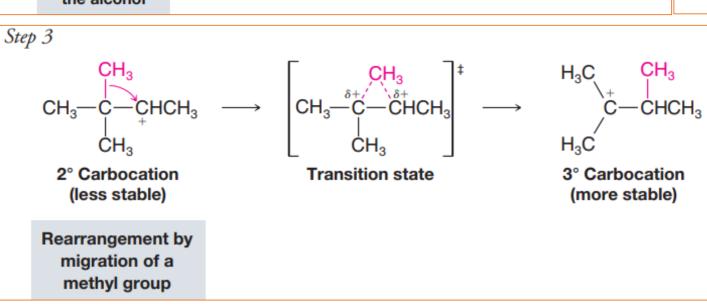
general mechanism for E1 elimination

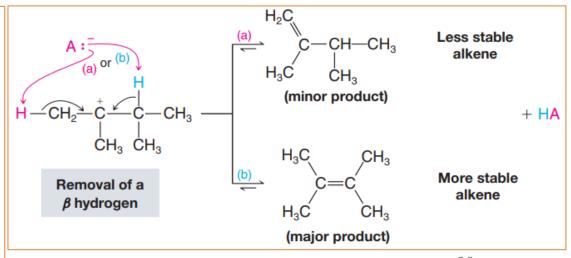
E2 describes an elimination (E) that has a bimolecular (2) rate-determining step that
must involve the base. Loss of the leaving group is simultaneous with removal of the
proton by the base.

general mechanism for E2 elimination

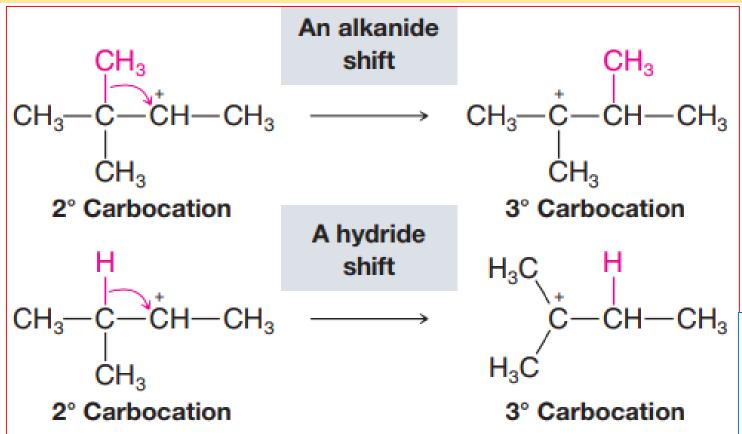
### 7.8A Rearrangements During Dehydration of Secondary Alcohols

The less stable, secondary carbocation rearranges to a more stable tertiary carbocation:





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



carbocation.

They occur almost invariably when an alkanide shift

or hydride shift can lead to a more stable

CH<sub>3</sub> CHCH<sub>3</sub> 

3° Carbocation

change in ring size, as the following example show.

Rearrangements of carbocations can also lead to a

### 7.8B Rearrangement After Dehydration of a Primary Alcohol

The  $\pi$  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.\*

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<sub>N</sub>1 process.)

### 7.9 The Acidity of Terminal Alkynes

A terminal alkyne is ~10<sup>20</sup> times more acidic than an alkene or alkane.

### Relative Acidity

#### Most acidic

Least acidic

$$H - \ddot{O}H > H - \ddot{O}R > H - C \equiv CR > H - \ddot{N}H_2 > H - CH = CH_2 > H - CH_2CH_3$$
  
p $K_a$  15.7 16-17 25 38 44 50

### Relative Basicity

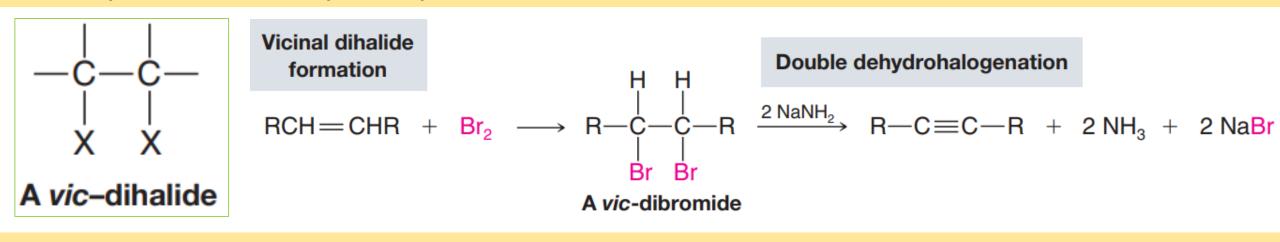
**Least basic** 

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.

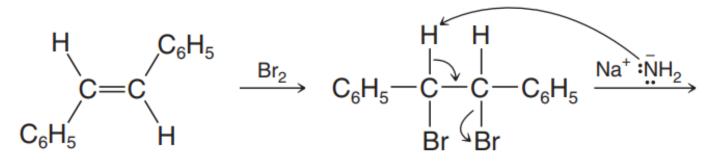
Most basic

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

### 7.10 Synthesis of Alkynes by Elimination Reactions



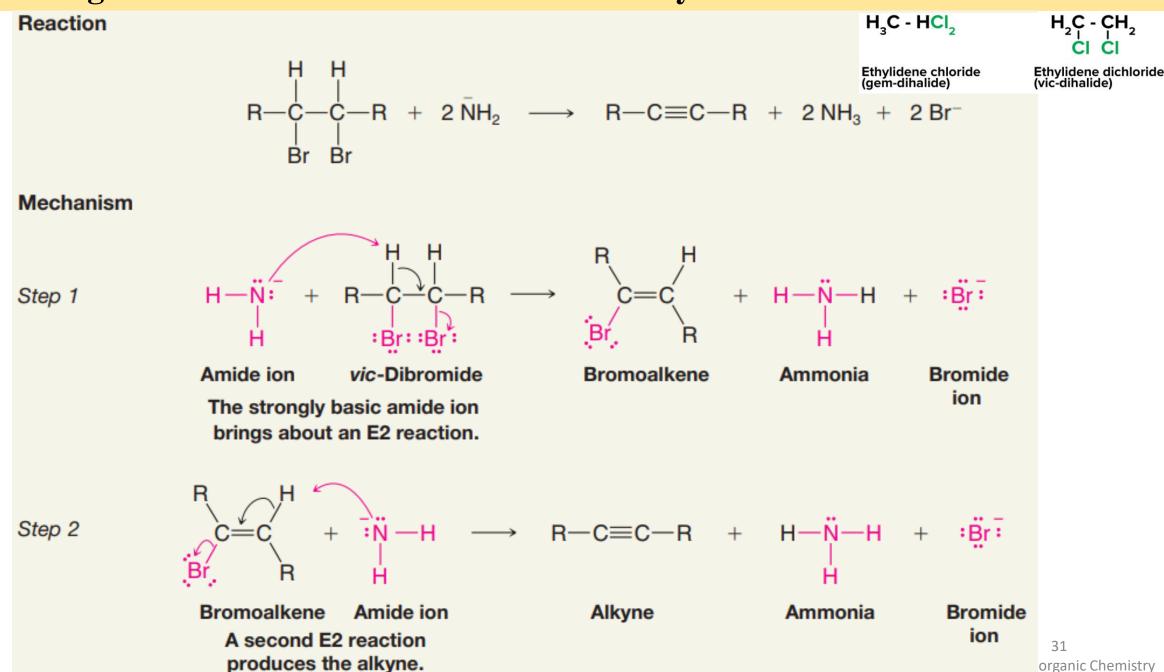
#### 7.10A Laboratory Application of This Alkyne Synthesis



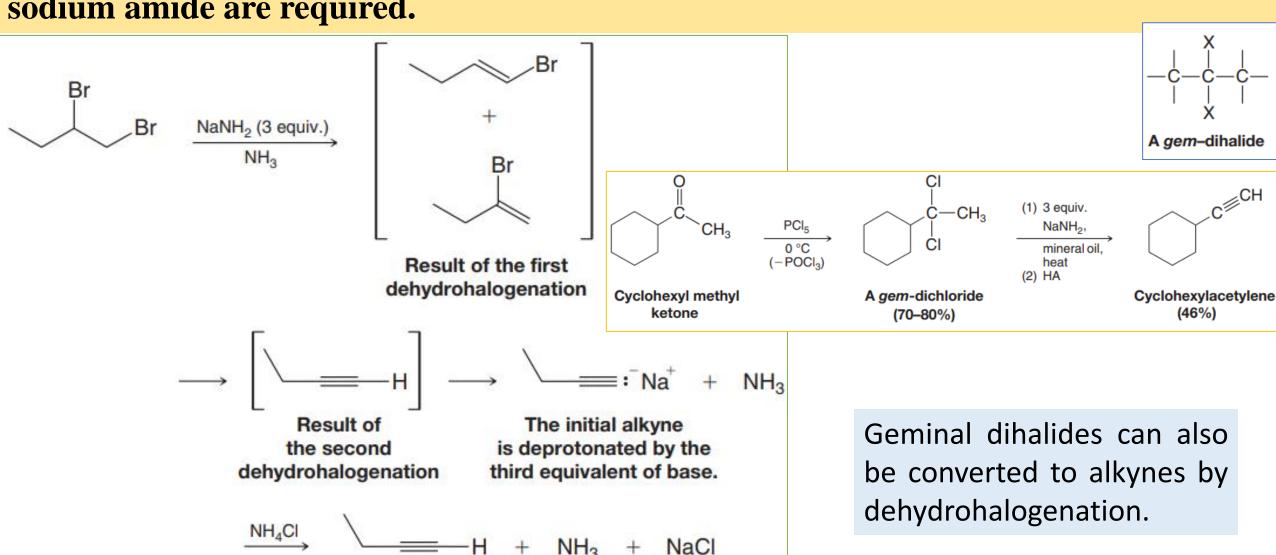
1,2-Diphenylethene

$$C_6H_5$$
 $C = C$ 
 $C_6H_5$ 
 $C_6H_5$ 
 $C_6H_5$ 
 $C_6H_5$ 
 $C_6H_5$ 
 $C_6H_5$ 
 $C_6H_5$ 
 $C_6H_5$ 
 $C_6H_5$ 
 $C_6H_5$ 

### Dehydrohalogenation of vic-Dibromides to Form Alkynes



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.



1-Butyne

### 7.11 terminal alkynes can be converted to nucleophiles for carbon–carbon bond

formation

General Example

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

Specific Example

halide

alkynide

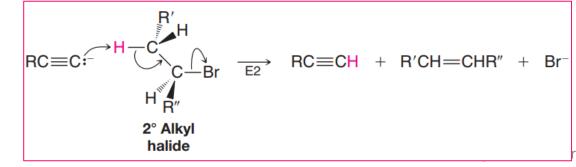
(R or R' or both may be hydrogen.)

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

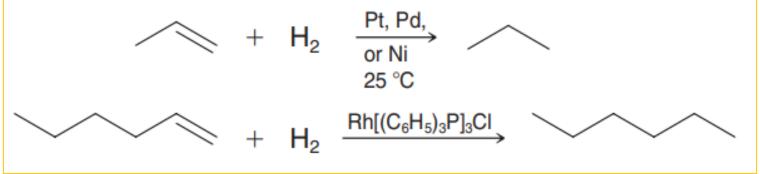
$$CH_3CH_2C \equiv C : Na^+ + CH_3CH_2 \xrightarrow{\text{CH}_2} Br \xrightarrow{\text{liq. NH}_3} CH_3CH_2C \equiv CCH_2CH_3 + NaBr$$

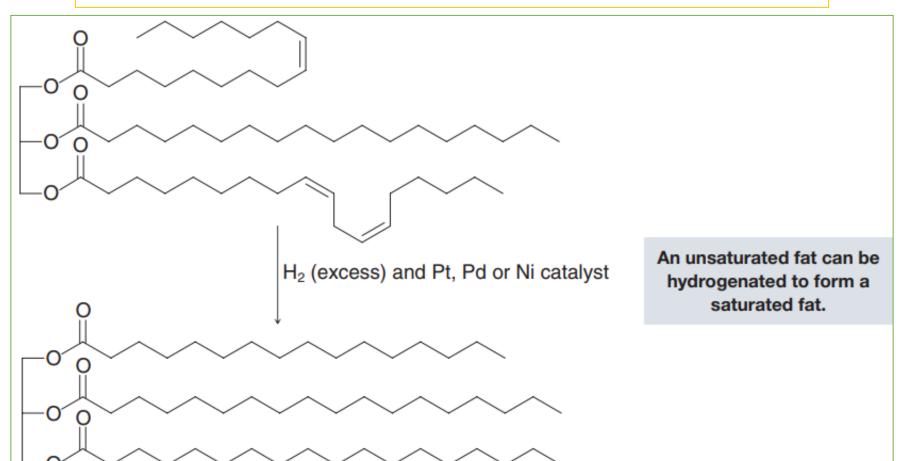
$$3-\text{Hexvne}$$

Sodium 1° Alkvl 3-Hexyne (75%)



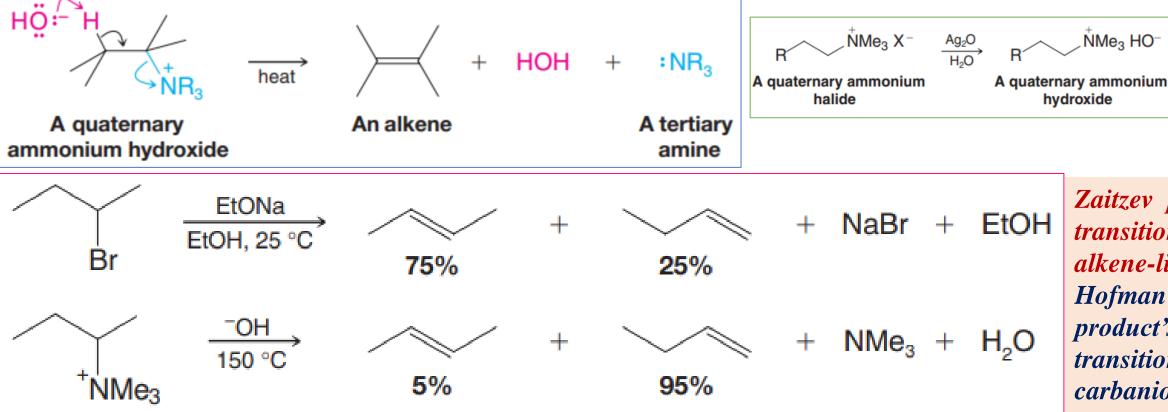
### 7.12 Hydrogenation of Alkenes





34

### 20.12A The Hofmann Elimination



Zaitzev product's transition state is alkene-like and Hofman product's transition state is carbanion-like.

NMe<sub>3</sub> HO

2AgX ↓

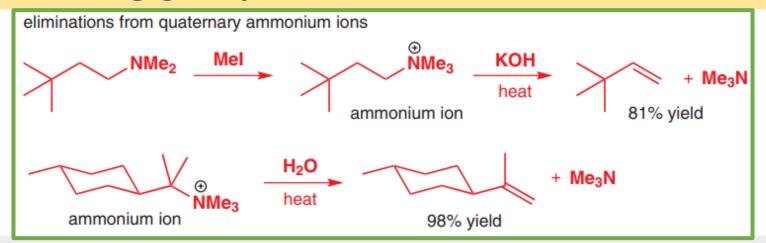
In between primary and secondary carbanions, primary carbanion is more stable than secondary carbanion and thus less substituted alkene is major product for Hofmann elimination. Nevertheless, the negative charge generating on carbon is driven by the presence of positively

charged ammonium ion.

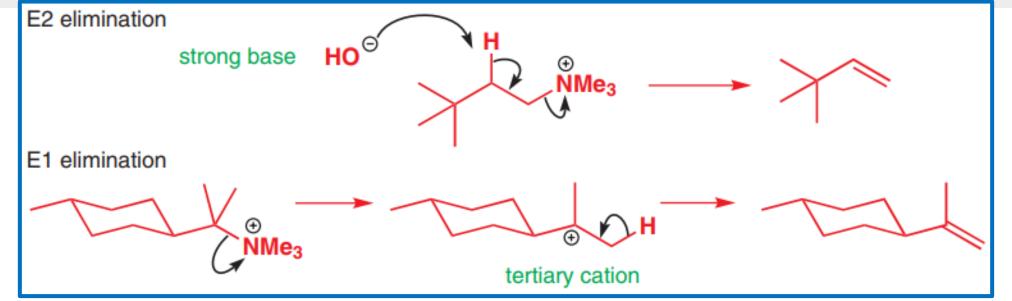
### 20.12B The Cope Elimination

Tertiary amine oxides undergo the elimination of a dialkylhydroxylamine when they are heated. The reaction is called the Cope elimination, it is a syn elimination and proceeds through a cyclic transition state.

## The role of the leaving group: How to Conclude E1 or E2

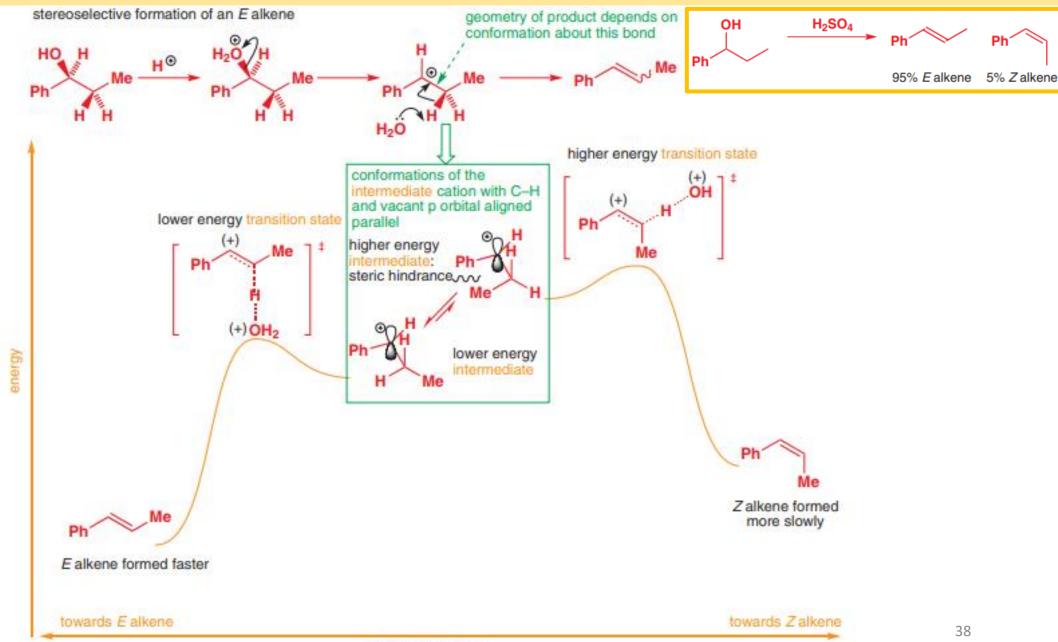


Both E1 and E2 are possible, and from what you have read so far you should be able to spot that there is one of each here: in the first example, a stabilized cation cannot be formed (so E1 is impossible), but a strong base is used, allowing E2. In the second, a stabilized tertiary cation could be formed (so either E1 or E2 might occur), but no strong base is present, so the mechanism must be E1.

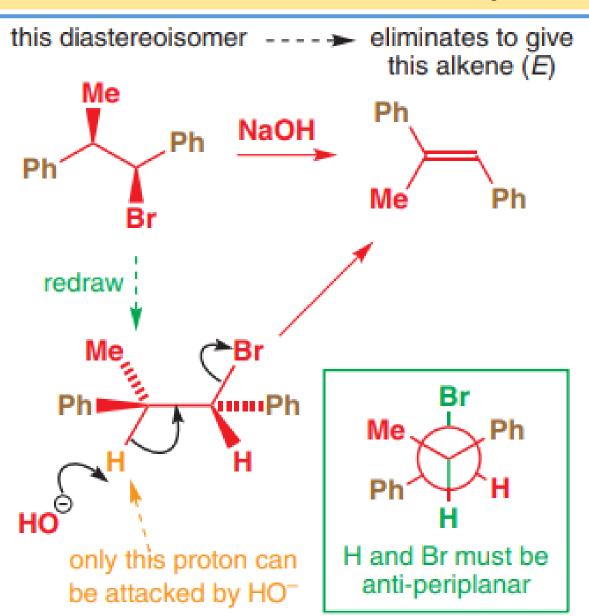


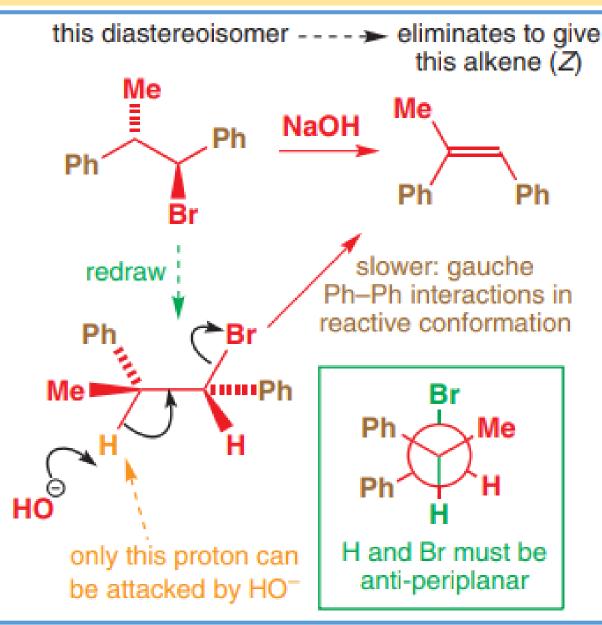
#### E1 reactions can be stereoselective

Mechanism and Transition states:



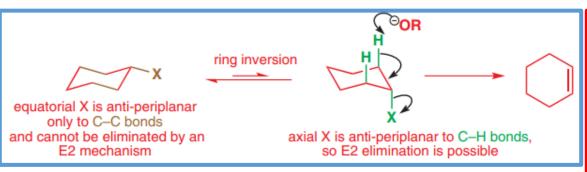
## E2 reactions can be stereospecific

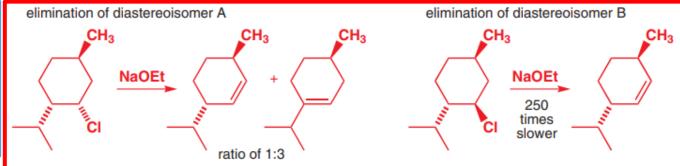




# For E2 elimination in cyclohexanes, both C-H and C-X must be axial and anti-periplanar to each other:

Explain the following chemical reactions. This is also given in slide no 16 and 17.

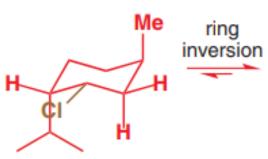




#### **Explanation**

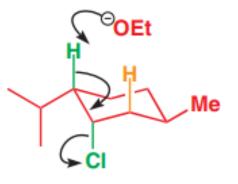
#### conformation of diastereoisomer A

No C-H bonds antiperiplanar to the C-Cl bond: no elimination



disfavoured; axial i-Pr

two anti-periplanar C–H bonds: either can eliminate to give different products



favoured; equatorial i-Pr

#### conformation of diastereoisomer B

No C-H bonds antiperiplanar to the C-Cl bond: no elimination

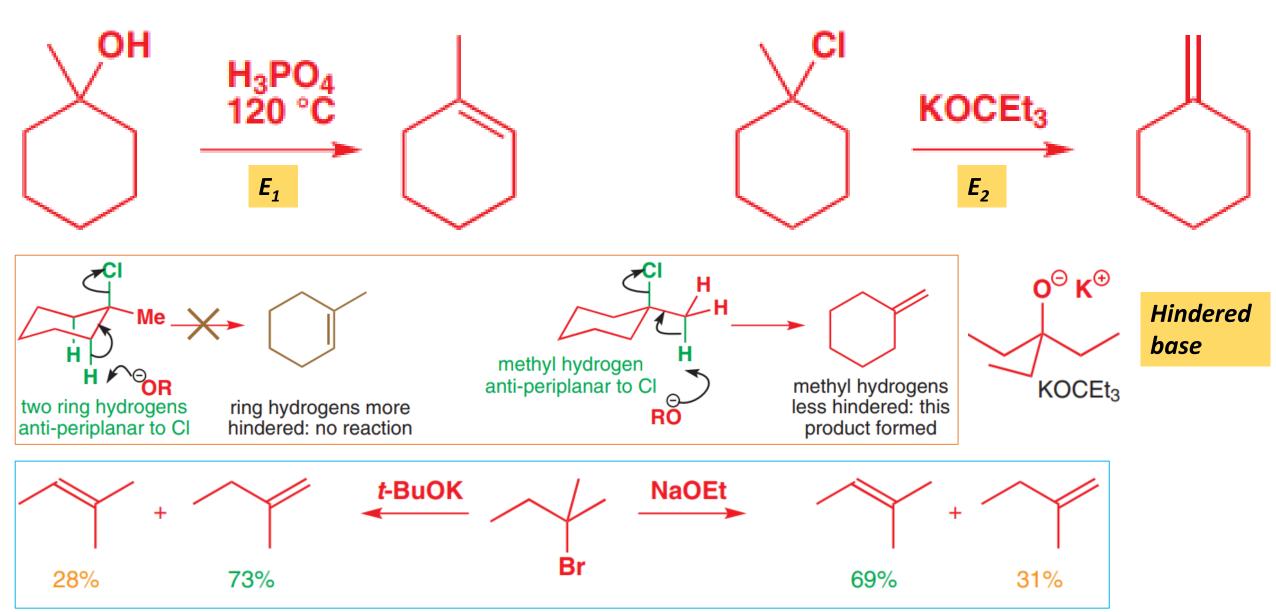
One anti-periplanar C-H bond: single alkene formed

Me

ring inversion

disfavoured: axial i-Pr

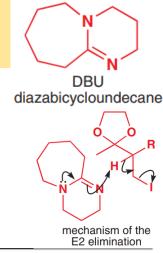
## The regioselectivity of E<sub>2</sub> eliminations



## **Summary**

#### Elimination regioselectivity

- E1 reactions give the more substituted alkene.
- E2 reactions may give the more substituted alkene, but become more regioselective for the less substituted alkene with more hindered bases.

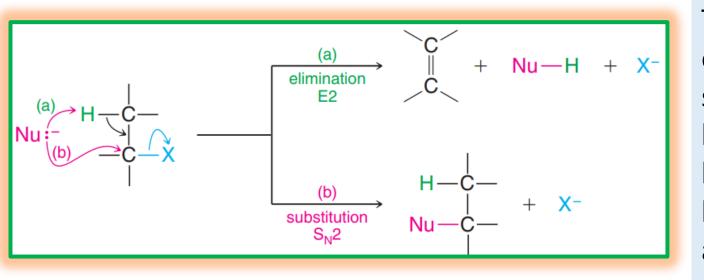


		Poor nucleophile (e.g. H <sub>2</sub> O, ROH)	Weakly basic nucleophile (e.g. I <sup>-</sup> , RS <sup>-</sup> )	Strongly basic, unhindered nucleophile (e.g. RO)	Strongly basic, hindered nucleophile (e.g. DBU, <i>t</i> -BuO <sup>-</sup> )
methyl	H <sub>3</sub> C-X	no reaction	S <sub>N</sub> 2	S <sub>N</sub> 2	S <sub>N</sub> 2
primary (unhindered)	<b>∕</b> x	no reaction	S <sub>N</sub> 2	S <sub>N</sub> 2	E2
primary (hindered)	X	no reaction	S <sub>N</sub> 2	E2	E2
secondary	$\downarrow_{\mathbf{x}}$	S <sub>N</sub> 1, E1 (slow)	S <sub>N</sub> 2	E2	E2
tertiary	$\searrow_{\mathbf{x}}$	E1 or S <sub>N</sub> 1	S <sub>N</sub> 1, E1	E2	E2

## Summary

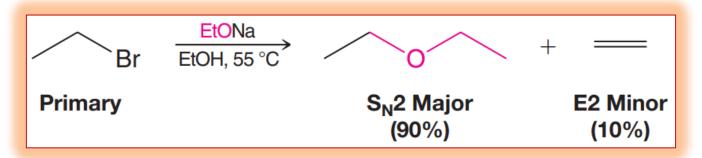
	Strong base Weak nucleophile	Strong base Strong nucleophile			Weak base Strong nucleophile	Weak base Weak nucleophile	
<b>1</b> °	E2	<b>E2</b>	S <sub>N</sub> 2		S <sub>N</sub> 2		
<b>2</b> °	E2		E2	S <sub>N</sub> 2	S <sub>N</sub> 2	$\bigwedge$	
<b>3</b> °	E2	E2			S <sub>N</sub> 1	S <sub>N</sub> 1	E1

## $6.18A S_N 2$ versus E2



The following examples illustrate the effects of several parameters on substitution and elimination: relative steric hindrance in the substrate (class of alkyl halide), temperature, size of the base/nucleophile (EtONa versus *t*-BuOK), and the effects of basicity and polarizability.

**Primary Substrate** When the substrate is a primary halide and the **base is strong and** unhindered, like ethoxide ion, substitution is highly favored because the base can easily approach the carbon bearing the leaving group:



## $6.18A S_N 2$ versus E2

Secondary Substrate With secondary halides, however, a strong base favors elimination because steric hindrance in the substrate makes substitution more difficult:

Tertiary Substrate With tertiary halides, steric hindrance in the substrate is severe and an  $S_N$ 2 reaction cannot take place. Elimination is highly favored, especially when the reaction is carried out at higher temperatures. Any substitution that occurs must take place through an

 $S_N$ 1 mechanism:

45
Solomon's organic Chemistry

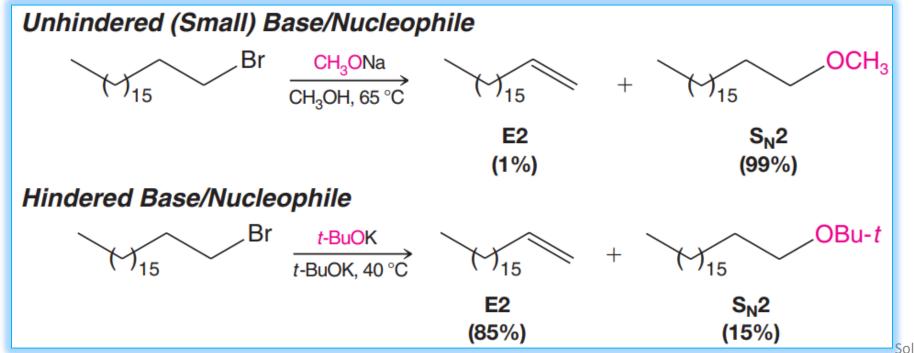
## **Temperature**

further enhances the entropy effect.

Increasing the reaction temperature favors elimination (E1 and E2) over substitution. Elimination reactions have greater free energies of activation than substitution reactions because more bonding changes occur during elimination. When higher temperature is used, the proportion of molecules able to surmount the energy of activation barrier for elimination increases more than the proportion of molecules able to undergo substitution, although the rate of both substitution and elimination will be increased. Furthermore, elimination reactions are entropically favored over substitution because the products of an elimination reaction are greater in number than the reactants. Additionally, because temperature is the coefficient of the entropy term in the Gibbs free-energy equation  $\Delta G = \Delta H - T\Delta S$ , an increase in temperature

## Size of the Base/Nucleophile

Increasing the reaction temperature is one way of favorably influencing an elimination reaction of an alkyl halide. Another way is to use a strong sterically hindered base such as the tert-butoxide ion. The bulky methyl groups of the tert-butoxide ion inhibit its reaction by substitution, allowing elimination reactions to take precedence. We can see an example of this effect in the following two reactions. The relatively unhindered methoxide ion reacts with octadecyl bromide primarily by substitution, whereas the bulky tert-butoxide ion gives mainly elimination.



47

## **Basicity and Polarizability**

Another factor that affects the relative rates of  $E_2$  and  $S_N2$  reactions is the relative basicity and polarizability of the base/nucleophile. Use of a strong, slightly polarizable base such as hydroxide ion, amide ion ( ${}^{-}NH_2$ ), or alkoxide ion (especially a hindered one) tends to increase the likelihood of elimination ( $E_2$ ). Use of a weakly basic ion such as a chloride ion ( $CI^{-}$ ) or an acetate ion ( $CH_3CO_2^{-}$ ) or a weakly basic and highly polarizable one such as Br,  $I^{-}$ , or  $RS^{-}$  increases the likelihood of substitution ( $S_N2$ ). Acetate ion, for example, reacts with isopropyl bromide almost exclusively by the  $S_N2$  path:

## 6.18B Tertiary Halides: S<sub>N</sub>1 versus E1

- $\square$  In most unimolecular reactions the  $S_N1$  reaction is favored over the  $E_1$  reaction, especially at lower temperatures.
- ☐ In general, however, substitution reactions of tertiary halides do not find wide use as synthetic methods. Such halides undergo eliminations much too easily.
- $\square$  Increasing the temperature of the reaction favors reaction by the E1 mechanism at the expense of the  $S_N1$  mechanism.
- $\square$  If an elimination product is desired from a tertiary substrate, it is advisable to use a strong base so as to encourage an  $E_2$  mechanism over the competing  $E_1$  and  $S_N$ 1 mechanisms.

## **Summary**

	REGIOCHEMICAL OUTCOME	STEREOCHEMICAL OUTCOME				
S <sub>N</sub> 2	The nucleophile attacks the $lpha$ position, where the leaving group is connected.	The nucleophile replaces the leaving group with inversion of configuration.				
E2	The Zaitsev product is generally favored over the Hofmann product, unless a sterically hindered base is used, in which case the Hofmann product will be favored.	This process is stereoselective, because when applicable, a <i>trans</i> disubstituted alkene will be favored over a <i>cis</i> disubstituted alkene. This process is also stereospecific. Specifically, when the $\beta$ position of the substrate has only one proton, the stereoisomeric alkene resulting from <i>anti</i> -periplanar elimination will be obtained (exclusively, in most cases).				
S <sub>N</sub> 1	The nucleophile attacks the carbocation, which is generally where the leaving group was originally connected, unless a carbocation rearrangement took place.	The nucleophile replaces the leaving group to give a nearly racemic mixture. In practice, there is generally a slight preference for inversion over retention of configuration, as a result of the effect of ion pairs.				
E1	The Zaitsev product is always favored over the Hofmann product.	The process is stereoselective. When applicable, a <i>trans</i> disubstituted alkene will be favored over a <i>cis</i> disubstituted alkene.				