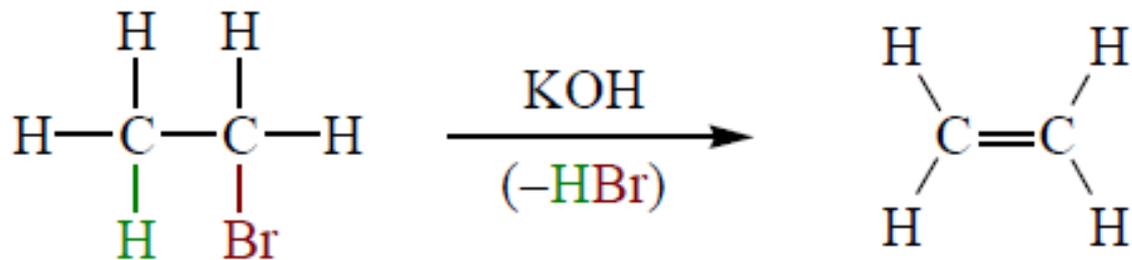


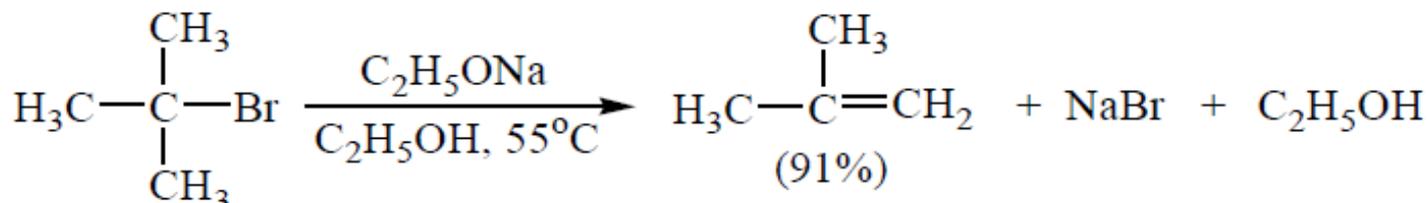
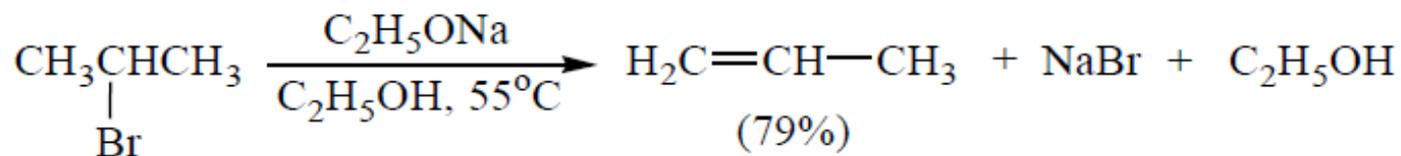
# Elimination Reactions

Heating an alkyl halide with a strong base causes elimination of a molecule of HX

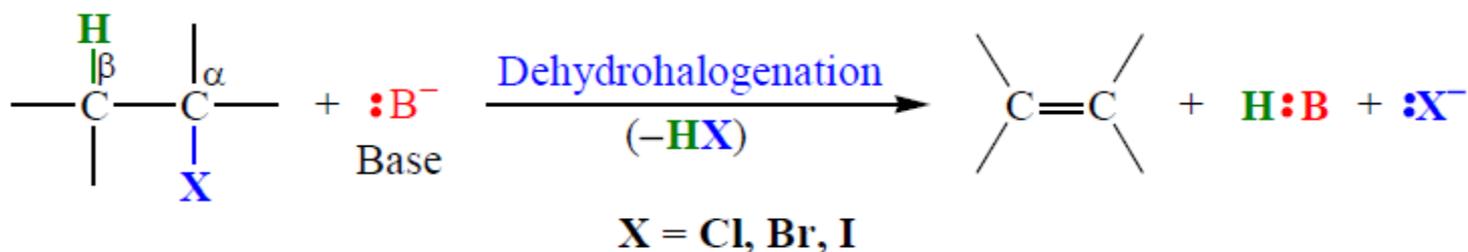
## Elimination Reactions:



An elimination reaction (**Dehydrohalogenation**)



### Dehydrohalogenation:



alpha ( $\alpha$ ) carbon atom:

beta ( $\beta$ ) hydrogen atom:

$\beta$ -elimination (1,2-elimination):

Potassium hydroxide dissolved in ethanol and the sodium salts of alcohols (such as sodium ethoxide) are often used as the base for dehydrohalogenation. The sodium salt of an alcohol (a sodium alkoxide) can be prepared by treating an alcohol with sodium metal

- **MECHANISMS OF DEHYDROHALOGENATIONS**

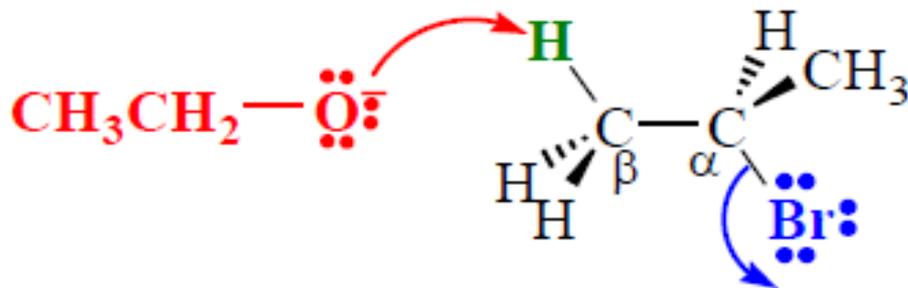
1. **E2 reaction.** Rate equation



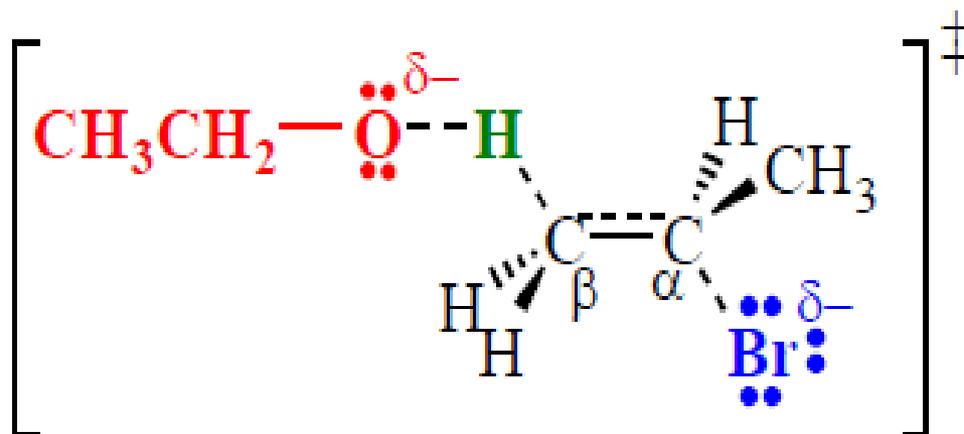
2. **E1 reaction**

# E2 Mechanism

The basic ethoxide ion begins to remove a proton from the  $\beta$ -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 bromide begins to depart with the electrons that bonded it to the  $\alpha$  carbon

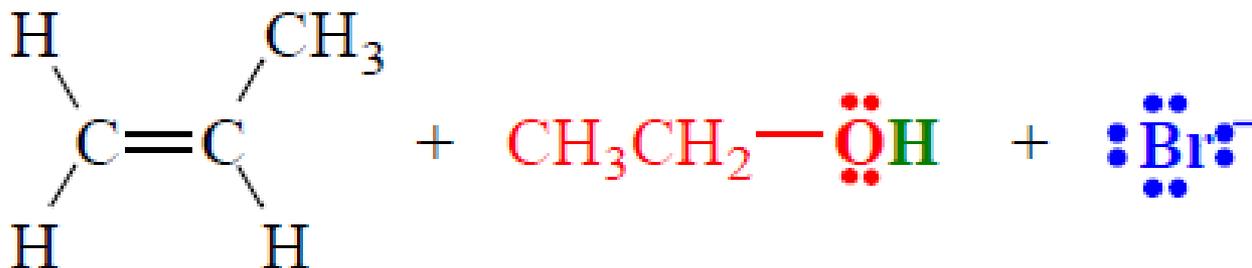


- Partial bonds now exist between the oxygen and the  $\beta$  hydrogen and between the  $\alpha$  carbon and the bromine. The carbon-carbon bond is developing double bond character.



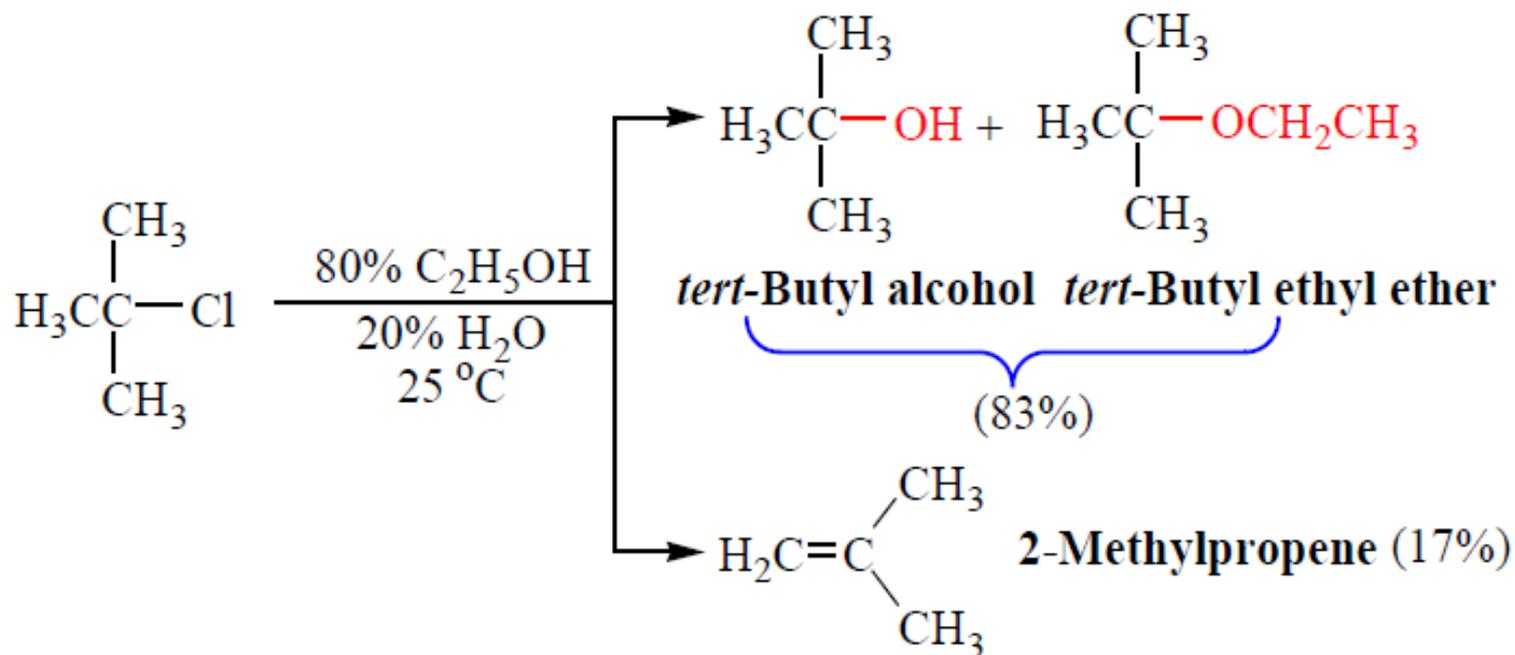
Transition state

- Now the double bond of the alkene 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.

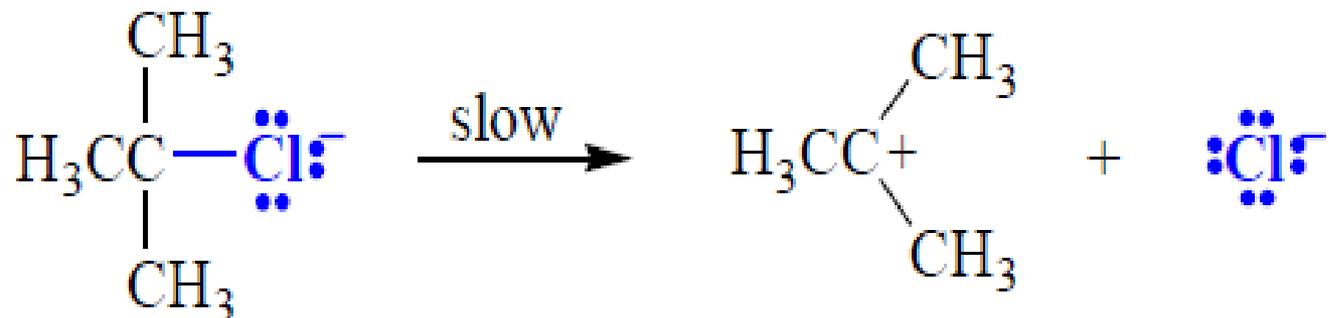


# E1 Mechanism

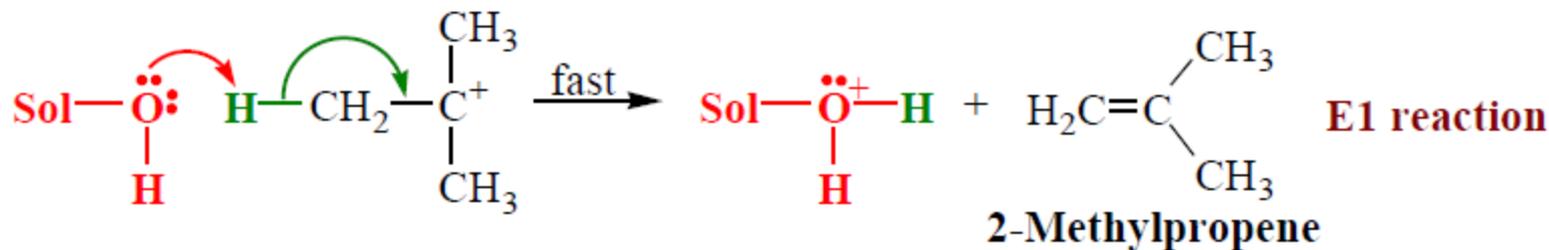
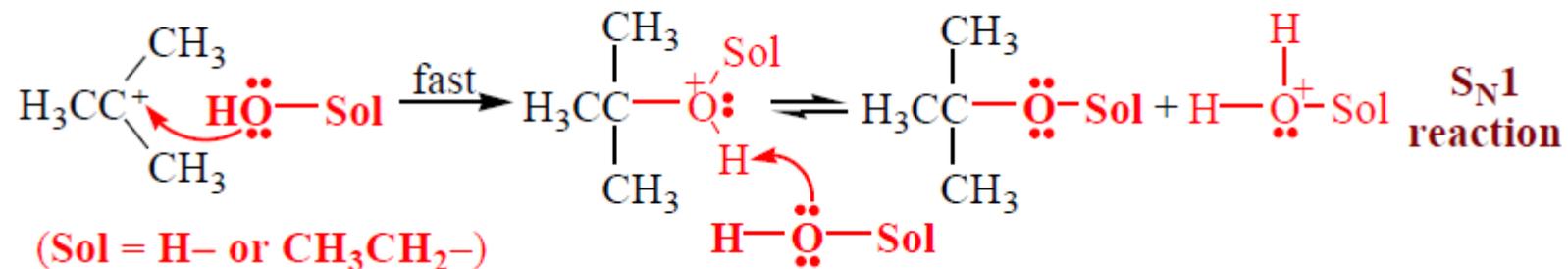
- Treating *tert*-butyl chloride with 80% aqueous ethanol at 25°C gives ***substitution products*** in 83% yield and an ***elimination product*** in 17% yield.



The initial step for reactions is the formation of a *tert*-butyl cation.

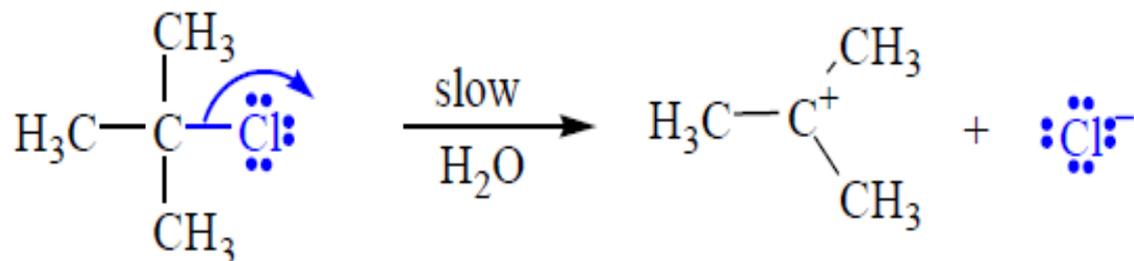


Whether substitution or elimination takes place depends on the next step (the fast step)

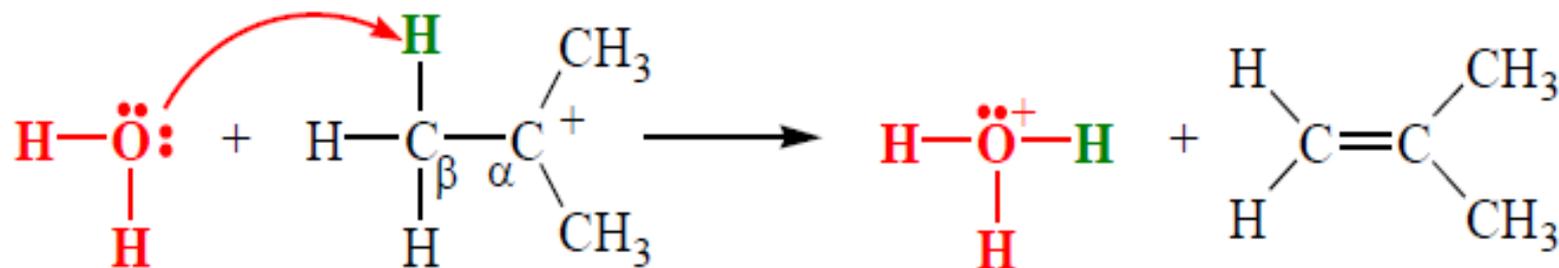


**The E1 reaction almost always accompany SN1 reactions.**

**Step-1 : Aided by the polar solvent a chlorine departs with the electron pair that bonded it to the carbon.**



**Step-2 : A molecule of water removes one of the hydrogens from the  $\beta$  carbon of the carbocation. An electron pair moves in to form a double bond between the  $\alpha$  and  $\beta$  carbon atoms**



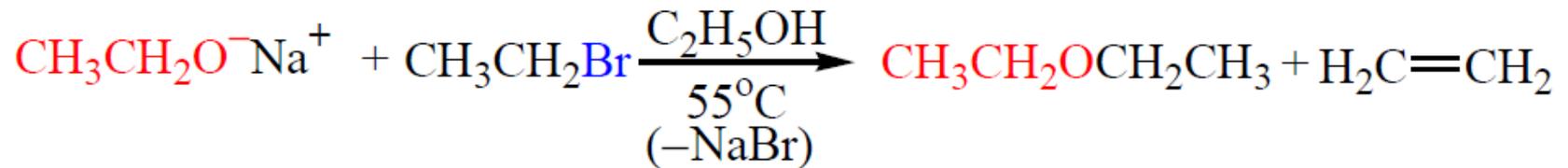
# SUBSTITUTION VERSUS ELIMINATION

1. Because the reactive part of a nucleophile or a base is an unshared electron pair, all nucleophiles are potential bases and all bases are potential nucleophiles.
2. Nucleophileic substitution reactions and elimination reactions often compete with each other.

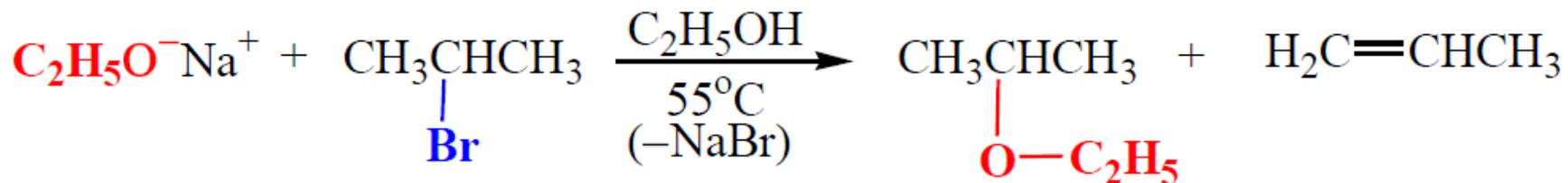
## $S_N2$ vs $E2$

Since eliminations occur best by an  $E2$  path when carried out with a high concentration of a strong base (and thus a high concentration of a strong nucleophile), substitution reactions by an  $S_N2$  path often compete with the elimination reaction. When the nucleophile (base) attacks a  $\beta$  carbon atom, elimination occurs. When the nucleophile (base) attacks the carbon atom bearing the leaving group, substitution results.

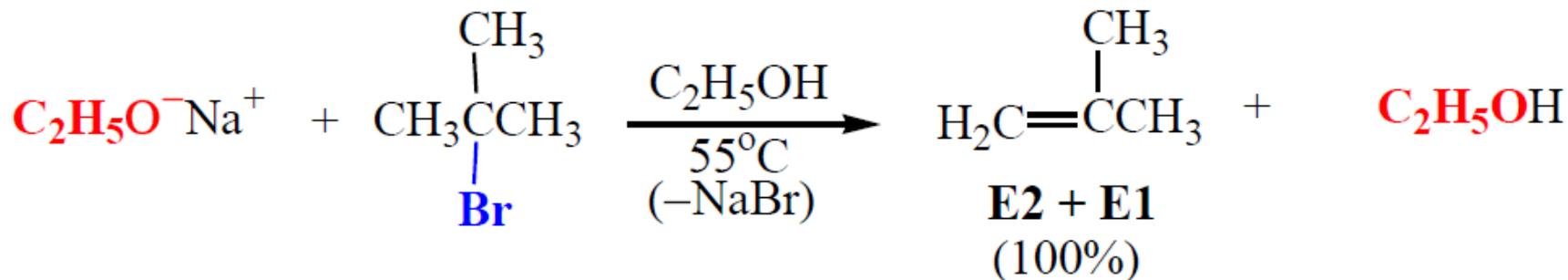
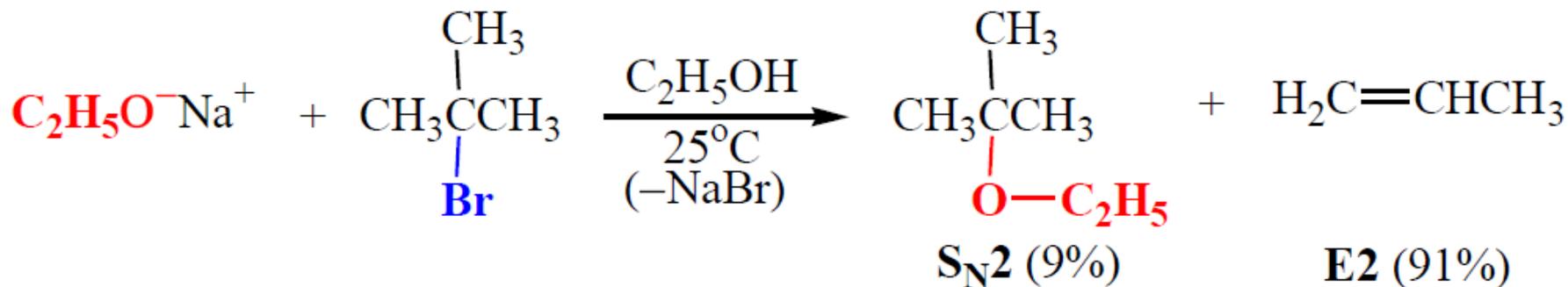
***Primary halides and ethoxide: substitution is favored***



## Secondary halides: elimination is favored



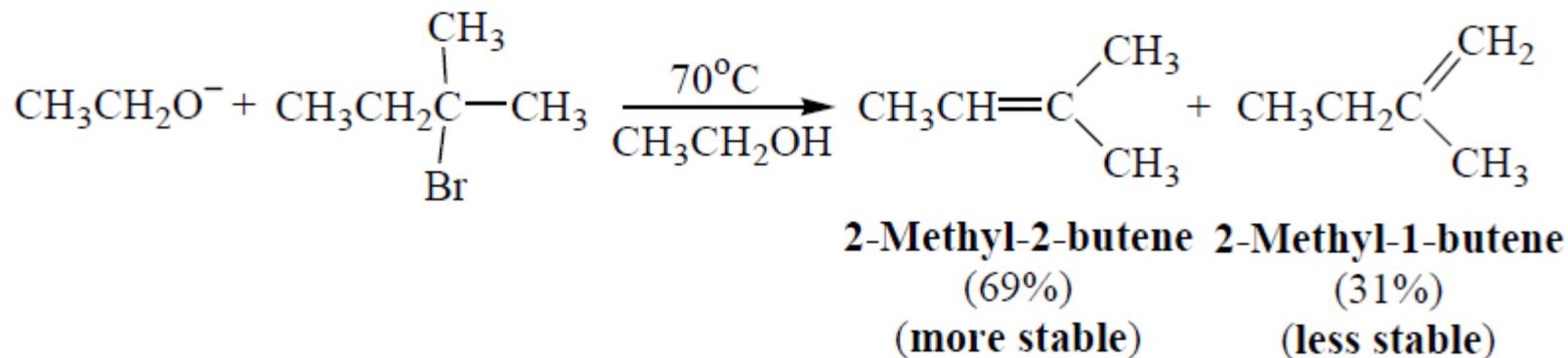
*Tertiary* halides: **no S<sub>N</sub>2 reaction, elimination reaction is highly favored**



# In Tertiary Halides

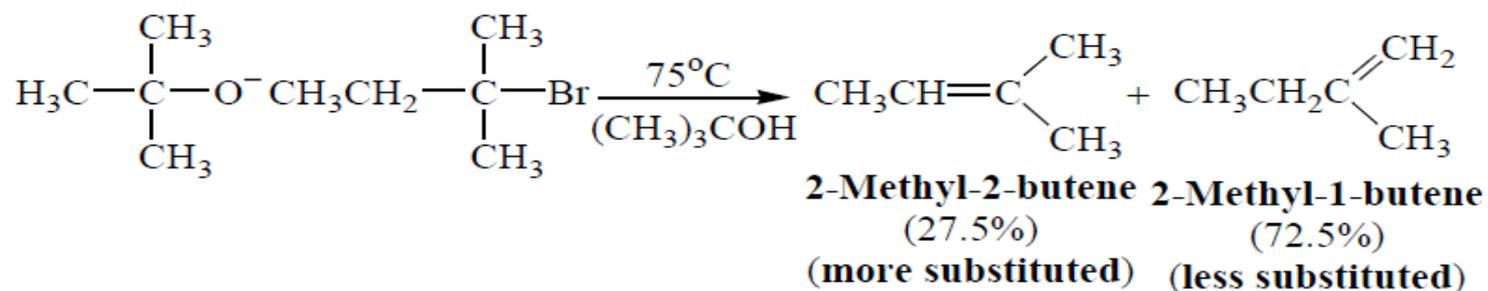
- Elimination is favored when the reaction is carried out at higher temperature.
- Eliminations have higher free energies of activation than substitutions because eliminations have a greater change in bonding (more bonds are broken and formed).
- Eliminations have higher entropies than substitutions because eliminations have a greater number of products formed than that of starting compounds).
- Any substitution that occurs must take place through an SN1 mechanism

**Zaitsev rule:** an elimination occurs to give the most stable, more highly substituted alkene



## AN EXCEPTION TO ZAITSEV'S RULE

A bulky base such as potassium *tert*-butoxide in *tert*-butyl alcohol favors the formation of **the less substituted alkene** in dehydrohalogenation reactions



The reason for leading to **Hofmann's** product:

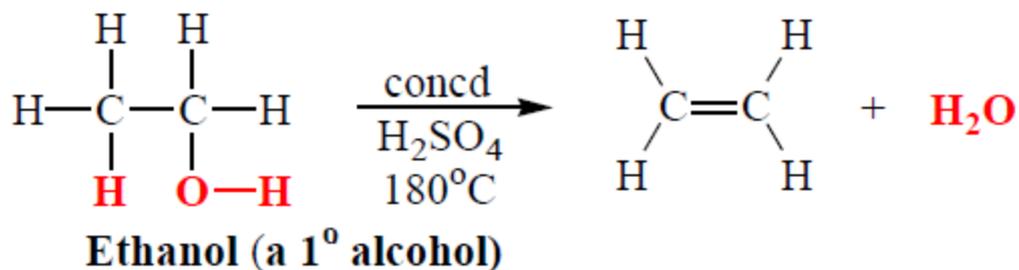
- i) The steric bulk of the base.
- ii) The association of the base with the solvent molecules make it even larger.
- iii) *tert*-Butoxide removes one of the more exposed ( $1^\circ$ ) hydrogen atoms instead of the internal ( $2^\circ$ ) hydrogen atoms due to its greater crowding in the transition state.

## Dehydration of alcohols:

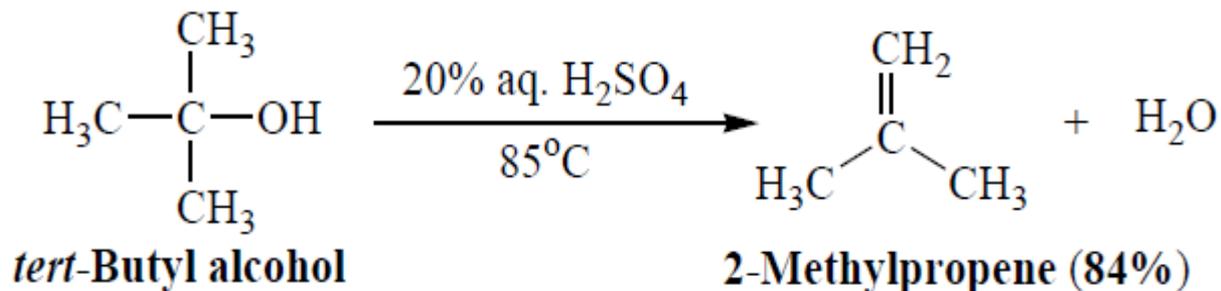
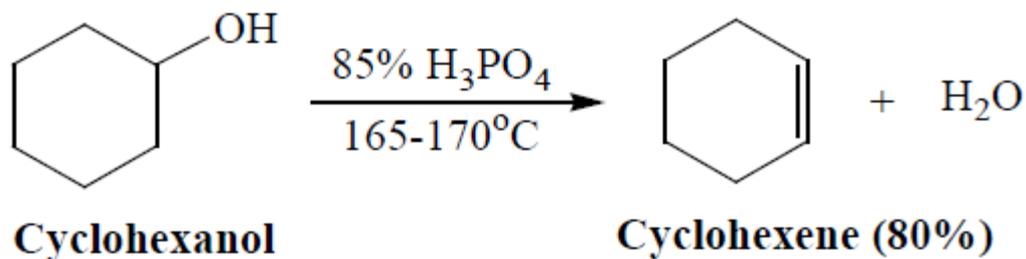
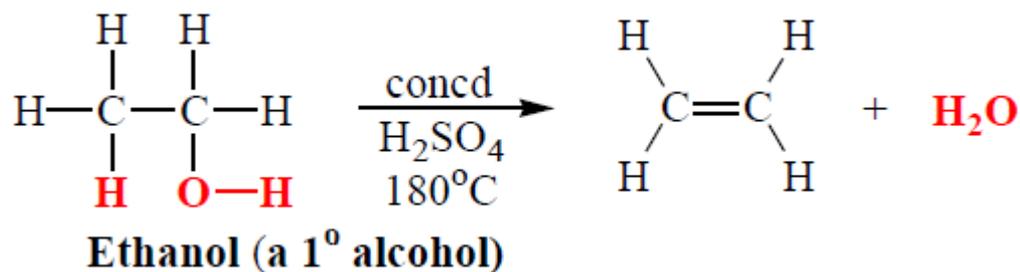
Heating most alcohols with a strong acid causes them to lose a molecule of water and form an alkene

The reaction is an **elimination** and is favored at higher temperatures. 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 ( $\text{Al}_2\text{O}_3$ ) are often used in industrial, fast phase dehydrations.

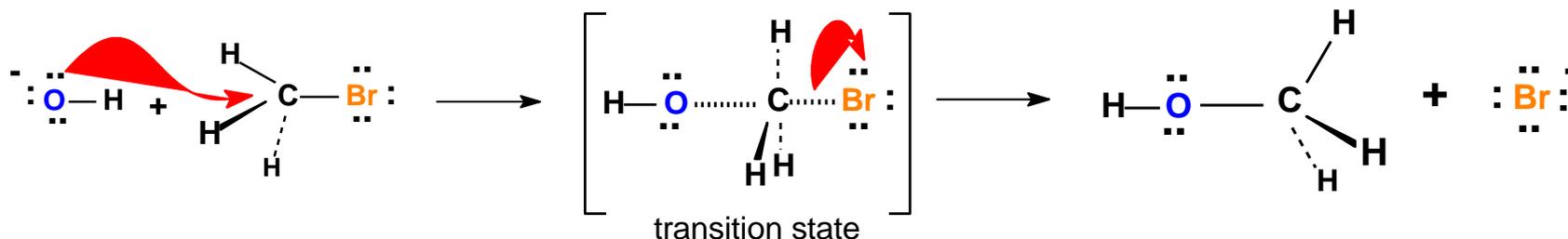


Primary alcohols are the most difficult to dehydrate,  
Secondary alcohols usually dehydrate under milder conditions,  
Tertiary alcohols are usually dehydrated under extremely mild conditions.

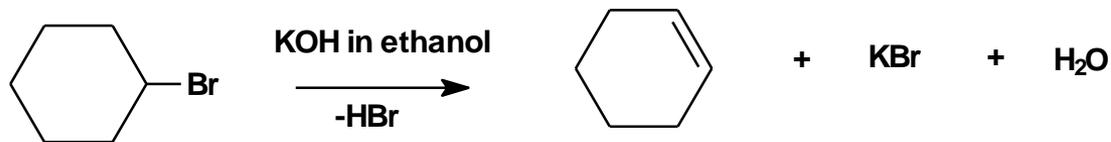


## Elimination Reactions, E1 and E2:

• We have seen that alkyl halides may react with basic nucleophiles such as NaOH via substitution reactions.



• Also recall our study of the preparation of alkenes. When a 2° or 3° alkyl halide is treated with a strong base such as NaOH, dehydrohalogenation occurs producing an alkene – an elimination (E2) reaction.

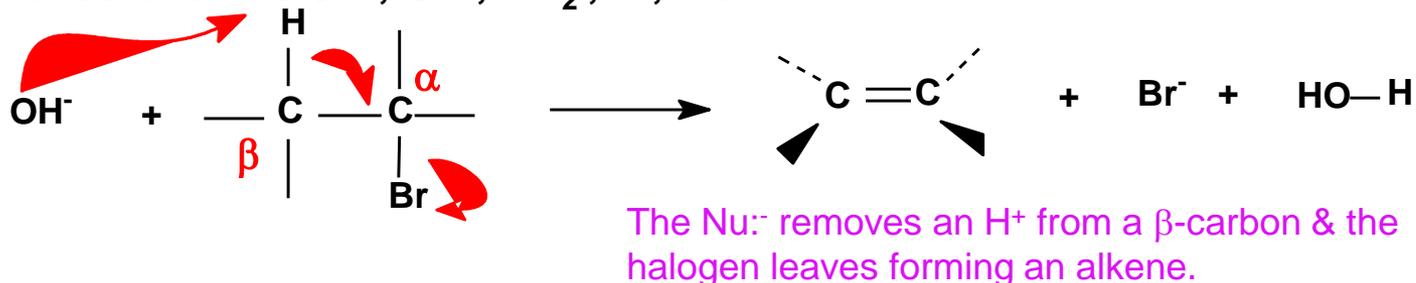


• bromocyclohexane + KOH → cyclohexene (80 % yield)

• Substitution and elimination reactions are often in competition. We shall consider the determining factors after studying the mechanisms of elimination.

## E2 Reaction Mechanism

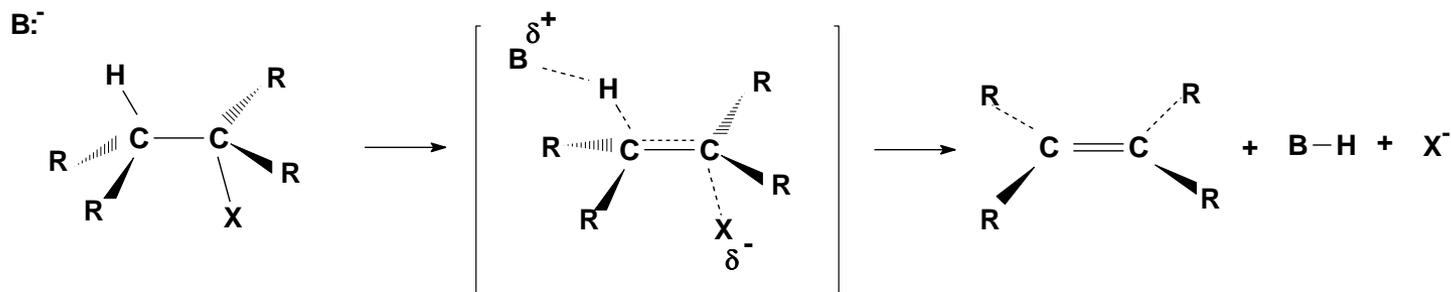
- There are 2 kinds of elimination reactions, E1 and E2.
- E2 = Elimination, Bimolecular (2nd order). Rate =  $k [RX] [Nu:^-]$
- E2 reactions occur when a 2° or 3° alkyl halide is treated with a strong base such as  $OH^-$ ,  $OR^-$ ,  $NH_2^-$ ,  $H^-$ , etc.



- All strong bases, like  $OH^-$ , are good nucleophiles. In 2° and 3° alkyl halides the α-carbon in the alkyl halide is hindered. In such cases, a strong base will 'abstract' (remove) a hydrogen ion ( $H^+$ ) from a β-carbon, before it hits the α-carbon. Thus strong bases cause elimination (E2) in 2° and 3° alkyl halides and cause substitution ( $S_N2$ ) in unhindered methyl° and 1° alkyl halides.

## E2 Reaction Mechanism

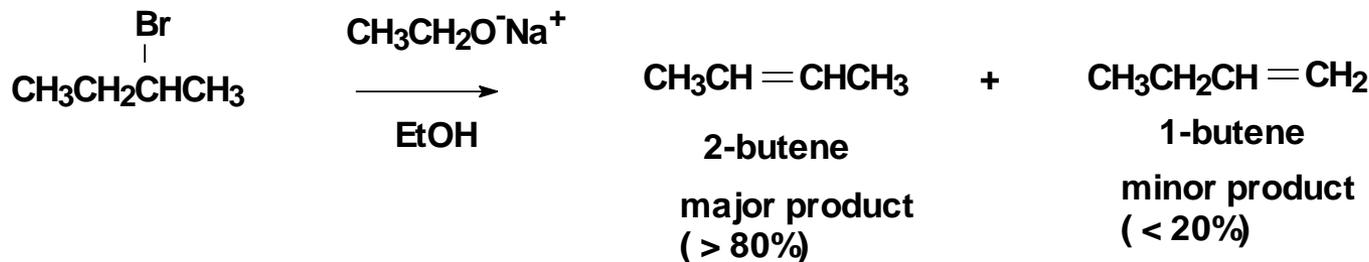
•In E2 reactions, the Base to H  $\sigma$  bond formation, the C to H  $\sigma$  bond breaking, the C to C  $\pi$  bond formation, and the C to Br  $\sigma$  bond breaking all occur simultaneously. No carbocation intermediate forms.



•Reactions in which several steps occur simultaneously are called '*concerted reactions*'.

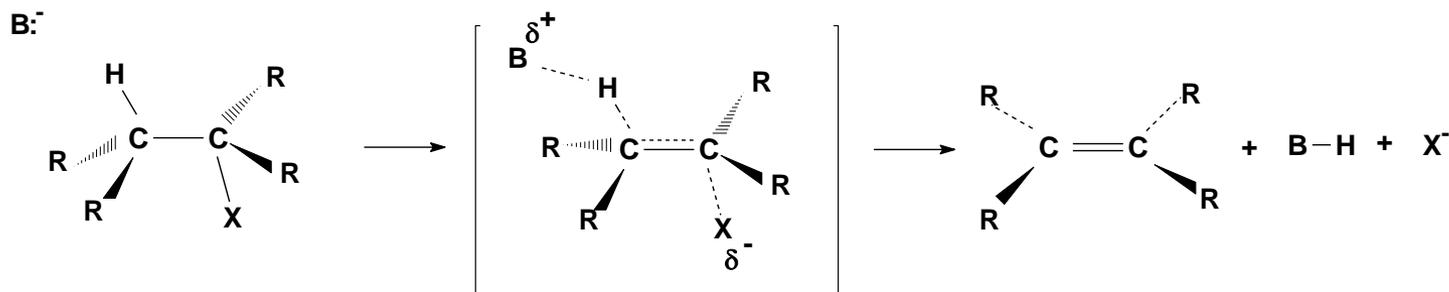
### Zaitsev's Rule:

•Recall that in elimination of HX from alkenes, the more highly substituted (more stable) alkene product predominates.



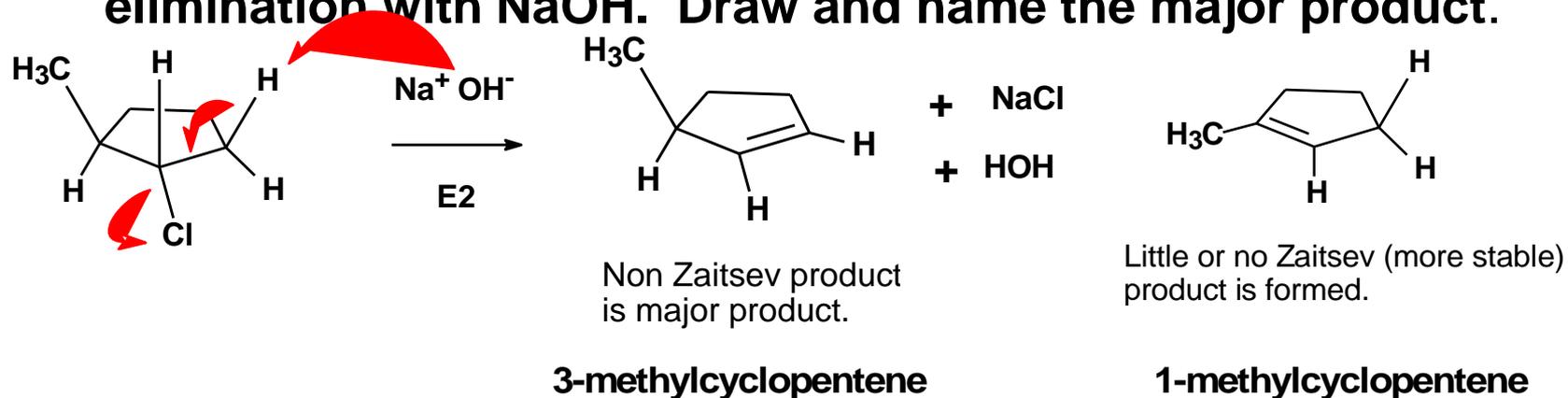
## E2 Reactions are 'antiperiplanar'

- ❑ E2 reactions, do not always follow Zaitsev's rule.
- ❑ E2 eliminations occur with anti-periplanar geometry, i.e., periplanar means that all 4 reacting atoms - H, C, C, & X - all lie in the same plane. Anti means that H and X (the eliminated atoms) are on opposite sides of the molecules.
- ❑ Look at the mechanism again and note the opposite side & same plane orientation of the mechanism:



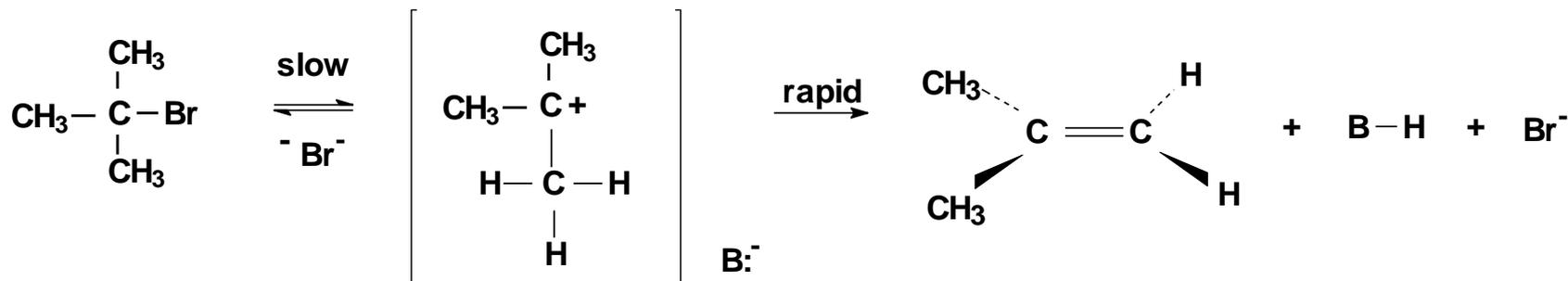
## Antiperiplanar E2 Reactions in Cyclic Alkyl Halides

- When E2 reactions occur in open chain alkyl halides, the Zaitsev product is usually the major product. Single bonds can rotate to the proper alignment to allow the antiperiplanar elimination.
- In cyclic structures, however, single bonds cannot rotate. We need to be mindful of the stereochemistry in cyclic alkyl halides undergoing E2 reactions.
- See the following example.
- **Trans -1-chloro-2-methylcyclopentane undergoes E2 elimination with NaOH. Draw and name the major product.**



## E1 Reactions

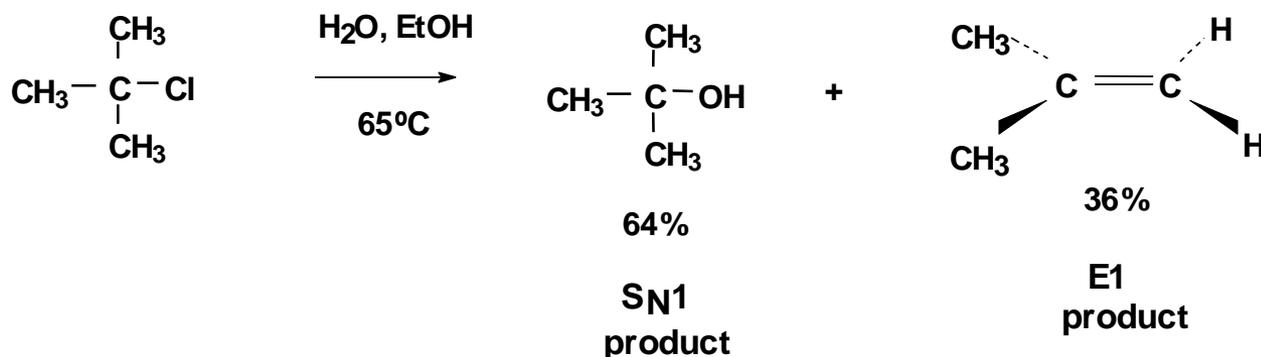
- Just as  $S_N2$  reactions are analogous to  $E_2$  reactions, so  $S_N1$  reactions have an analog, E1 reaction.
- E1 = Elimination, unimolecular (1st order); Rate =  $k \times [RX]$



- E1 eliminations, like  $S_N1$  substitutions, begin with unimolecular dissociation, but the dissociation is followed by loss of a proton from the  $\beta$ -carbon (attached to the  $\text{C}^+$ ) rather than by substitution.
- E1 &  $S_N1$  normally occur in competition, whenever an alkyl halide is treated in a protic solvent with a nonbasic, poor nucleophile.
- Note: The best E1 substrates are also the best  $S_N1$  substrates, and mixtures of products are usually obtained.

## E1 Reactions

- As with E2 reactions, E1 reactions also produce the more highly substituted alkene (Zaitsev's rule). However, unlike E2 reactions where no  $C^+$  is produced,  $C^+$  rearrangements can occur in E1 reactions.
- e.g., t-butyl chloride +  $H_2O$  (in EtOH) at  $65\text{ }^\circ\text{C}$   $\rightarrow$  t-butanol + 2-methylpropene



- In most unimolecular reactions,  $S_N1$  is favored over E1, especially at low temperature. Such reactions with mixed products are not often used in synthetic chemistry.
- If the E1 product is desired, it is better to use a strong base and force the E2 reaction.
- Note that increasing the strength of the nucleophile favors  $S_N1$  over E1. Can you postulate an explanation?

## Predicting Reaction Mechanisms

1. Non basic, good nucleophiles, like  $\text{Br}^-$  and  $\text{I}^-$  will cause substitution not elimination. In  $3^\circ$  substrates, only  $\text{S}_{\text{N}}1$  is possible. In  $\text{Me}^\circ$  and  $1^\circ$  substrates,  $\text{S}_{\text{N}}2$  is faster. For  $2^\circ$  substrates, the mechanism of substitution depends upon the solvent.
2. Strong bases, like  $\text{OH}^-$  and  $\text{OR}^-$ , are also good nucleophiles. Substitution and elimination compete. In  $3^\circ$  and  $2^\circ$  alkyl halides, E2 is faster. In  $1^\circ$  and  $\text{Me}^\circ$  alkyl halides,  $\text{S}_{\text{N}}2$  occurs.
3. Weakly basic, weak nucleophiles, like  $\text{H}_2\text{O}$ ,  $\text{EtOH}$ ,  $\text{CH}_3\text{COOH}$ , etc., cannot react unless a  $\text{C}^+$  forms. This only occurs with  $2^\circ$  or  $3^\circ$  substrates. Once the  $\text{C}^+$  forms, both  $\text{S}_{\text{N}}1$  and E1 occur in competition. The substitution product is usually predominant.
4. High temperatures increase the yield of elimination product over substitution product. ( $\text{DG} = \text{DH} - \text{TDS}$ ) Elimination produces more products than substitution, hence creates greater entropy (disorder).
5. Polar solvents, both protic and aprotic, like  $\text{H}_2\text{O}$  and  $\text{CH}_3\text{CN}$ , respectively, favor unimolecular reactions ( $\text{S}_{\text{N}}1$  and E1) by stabilizing the  $\text{C}^+$  intermediate. Polar aprotic solvents enhance bimolecular reactions ( $\text{S}_{\text{N}}2$  and E2) by activating the nucleophile.

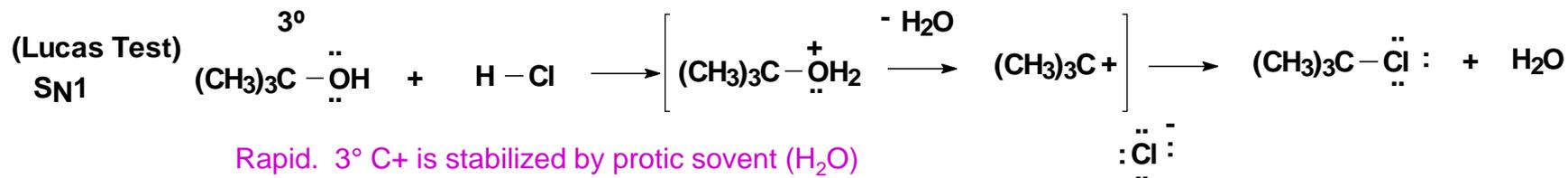
## Predicting Reaction Mechanisms

| alkyl halide (substrate) | good Nu <sup>-</sup><br>nonbasic<br>e.g., bromide<br><b>Br<sup>-</sup></b> | good Nu <sup>-</sup><br>strong base<br>e.g., ethoxide<br><b>C<sub>2</sub>H<sub>5</sub>O<sup>-</sup></b> | good Nu <sup>-</sup><br>strong bulky base<br>e.g., t-butoxide<br><b>(CH<sub>3</sub>)<sub>3</sub>CO<sup>-</sup></b> | very poor Nu <sup>-</sup><br>nonbasic<br>e.g., acetic acid<br><b>CH<sub>3</sub>COOH</b> |
|--------------------------|--|---|--|---|
| Me                       | S <sub>N</sub> 2   | S <sub>N</sub> 2  | S <sub>N</sub> 2   | no reaction   |
| 1°                       | S <sub>N</sub> 2   | S <sub>N</sub> 2  | E2 (S <sub>N</sub> 2)  | no reaction   |
| 2°                       | S <sub>N</sub> 2   | E2  | E2   | S <sub>N</sub> 1, E1  |
| 3°                       | S <sub>N</sub> 1   | E2  | E2   | S <sub>N</sub> 1, E1  |

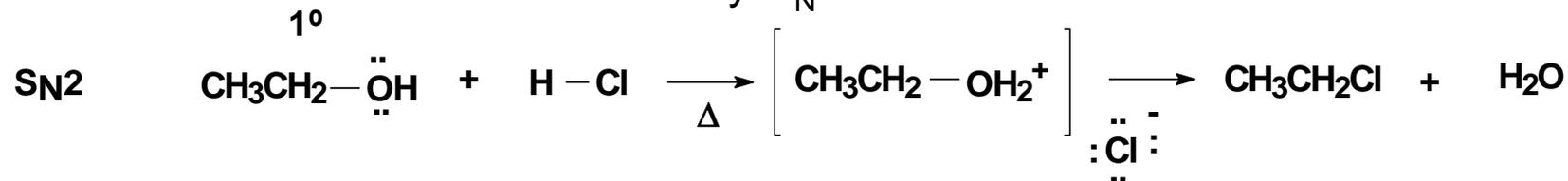
Strong bulky bases like t-butoxide are hindered. They have difficulty hitting the  $\alpha$ -carbon in a 1° alkyl halide. As a result, they favor E2 over S<sub>N</sub>2 products.

## Preparation of Alkyl Halides from Alcohols

- Alkyl halides can be prepared from alcohols by reaction with HX, i.e., the substitution of a halide on a protonated alcohol.



- OH<sup>-</sup> is a poor leaving group, i.e., is not displaced directly by nucleophiles. Reaction in acid media protonates the OH group producing a better leaving group (H<sub>2</sub>O). 2° and 3° alcohols react by S<sub>N</sub>1 but Me<sup>o</sup> and 1° alcohols react by S<sub>N</sub>2.

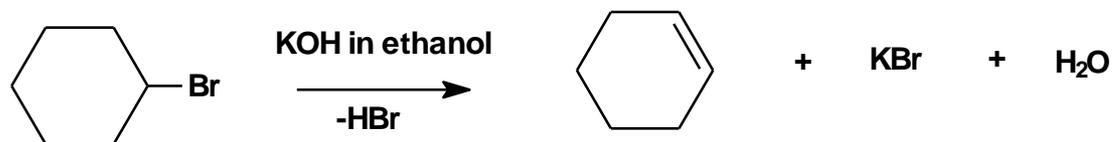


Very slow. Protic solvent inhibits the nucleophile.

- Draw the mechanism of the reaction of isopropyl alcohol with HBr.
- What products form if concentrated H<sub>2</sub>SO<sub>4</sub> is used in place of aq. HCl?

## Preparation of Alkenes from Alkyl Halides

•On Slide 22 we noted that 2° and 3° alkyl halides can be dehydrohalogenated with a strong base such as OH<sup>-</sup> producing an alkene.



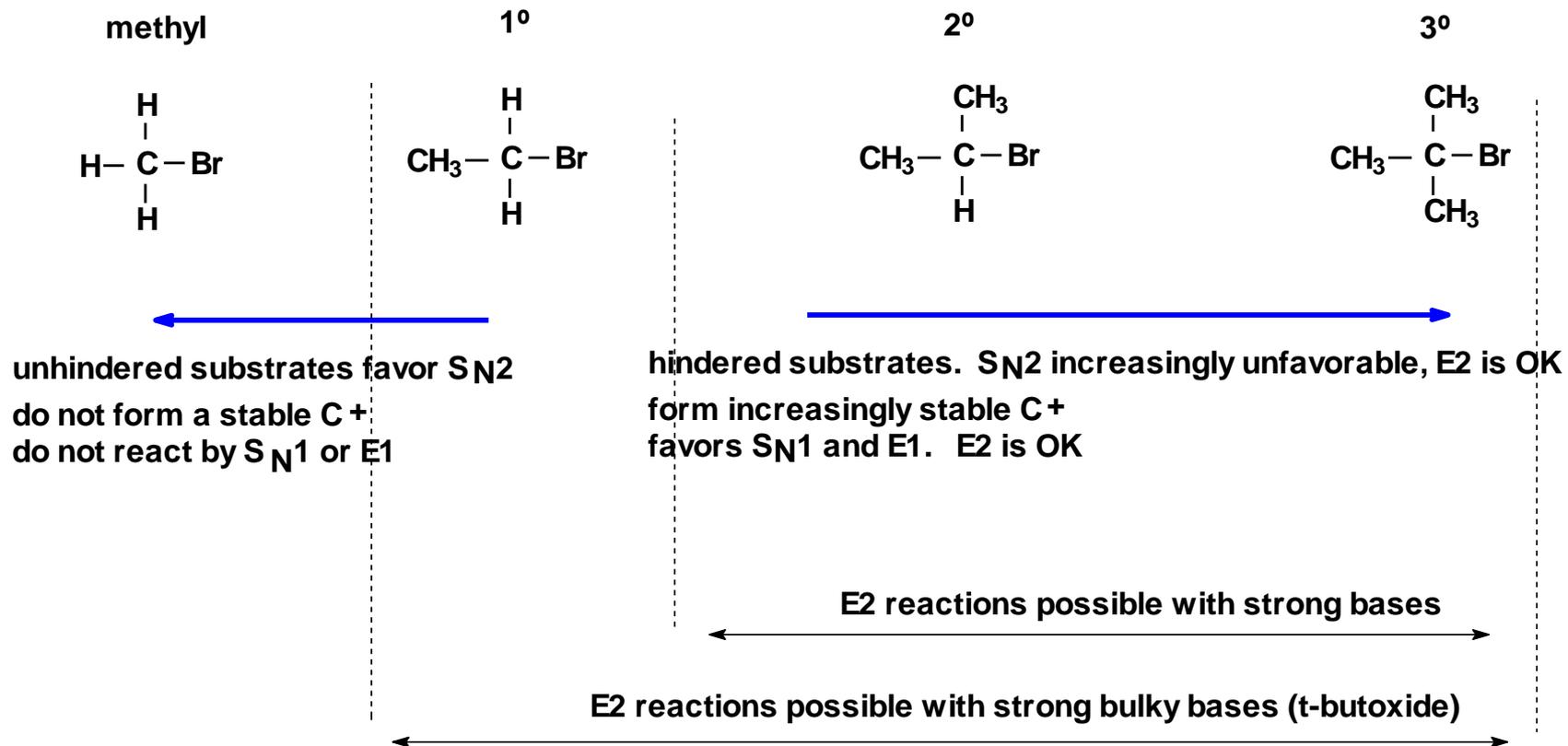
•bromocyclohexane + KOH → cyclohexene (80 % yield)

•Clearly, this is an E2 reaction.

- Predict the mechanism that occurs with a Me<sup>o</sup> or 1° alkyl halide.
- Predict the products and mechanism that occur with isopentyl chloride and KOH

## Summary of S<sub>N</sub>/Elimination Reactions

### • Alkyl Halide Substrate Reactivity:



## Summary of S<sub>N</sub>/Elimination Reactions

### • Reactivity of Nucleophiles:

|   |                       |                       |                                    |   |                       |                                   |                       |
|---|-----------------------|-----------------------|------------------------------------|---|-----------------------|-----------------------------------|-----------------------|
| <b>HS<sup>-</sup></b>   | <b>CN<sup>-</sup></b> | <b>I<sup>-</sup></b>  | <b>CH<sub>3</sub>O<sup>-</sup></b> | <b>HO<sup>-</sup></b>   | <b>NH<sub>3</sub></b> | <b>Cl<sup>-</sup></b>             | <b>H<sub>2</sub>O</b> |
| 125,000   | 125,000               | 100,000               | 25,000                             | 16,000  | 1000                  | 700                               | 1                     |
| ←————→  |                       |                       |                                    | ←————→  |                       |                                   |                       |
| good nucleophiles which are weak bases favor S <sub>N</sub> reactions |                       |                       |                                    | good nucleophiles which are also strong bases favor elimination |                       |                                   |                       |
| pK <sub>b</sub> = 23  | pK <sub>b</sub> = 22  | pK <sub>b</sub> = 21  | pK <sub>b</sub> = 11               | pK <sub>b</sub> = -1.7  | pK <sub>b</sub> = -2  | pK <sub>b</sub> = -21             |                       |
| <b>I<sup>-</sup></b>  | <b>Br<sup>-</sup></b> | <b>Cl<sup>-</sup></b> | <b>F<sup>-</sup></b>               | <b>HO<sup>-</sup></b>   | <b>RO<sup>-</sup></b> | <b>H<sub>2</sub>N<sup>-</sup></b> |                       |
| 30,000  | 10,000                | 200                   | 1                                  | 0   | 0                     | 0                                 |                       |

• Note that poor nucleophiles that are also weak bases (H<sub>2</sub>O, ROH, CH<sub>3</sub>COOH, etc.) do not undergo any reaction unless a C<sup>+</sup> is formed first. If a C<sup>+</sup> can form (as with a 2<sup>o</sup>, 3<sup>o</sup>, any benzylic, or any allylic halides), then E1 and S<sub>N</sub>1

generally occur together. ■

### • Leaving Group Activity:

good leaving groups favor both substitution and elimination reactions

poor leaving groups make both substitution and elimination reactions unfavorable

# Reactivity of alkyl halides toward substitution and elimination

| <i>Halide type</i>      | <i>S<sub>N</sub>1</i>                                     | <i>S<sub>N</sub>2</i>   | <i>E1</i>   | <i>E2</i>                                   |
|-------------------------|---|---|---|---|
| <b>Primary halide</b>   | Does not occur  | <b>Highly favored</b>   | Does not occur  | Occurs when strong, hindered bases are used |
| <b>Secondary halide</b> | Can occur under solvolysis conditions in polar solvents   | <b>Favored by good nucleophiles in polar aprotic solvents</b> | Can occur under solvolysis conditions in polar solvents | <b>Favored when strong bases are used</b>   |
| <b>Tertiary halide</b>  | <b>Favored by nonbasic nucleophiles in polar solvents</b> | Does not occur  | Occurs under solvolysis conditions                      | <b>Highly favored when bases are used</b>   |

# Effects of reaction variables on substitution and elimination reactions

| <i>Reaction</i>       | <i>Solvent</i>   | <i>Nucleophile/base</i>  | <i>Leaving group</i>   | <i>Substrate structure</i>   |
|-----------------------|--|--|--|--|
| <b>S<sub>N</sub>1</b> | <b>Very strong effect;</b> reaction favored by polar solvents    | <b>Weak effect;</b> reaction favored by good nucleophile/weak base     | <b>Strong effect;</b> reaction favored by good leaving group | <b>Strong effect;</b> reaction favored by 3°, allylic, and benzylic substrates |
| <b>S<sub>N</sub>2</b> | <b>Strong effect;</b> reaction favored by polar aprotic solvents | <b>Strong effect;</b> reaction favored by good nucleophile/weak base   | <b>Strong effect;</b> reaction favored by good leaving group | <b>Strong effect;</b> reaction favored by 1°, allylic, and benzylic substrates |
| <b>E1</b>             | <b>Very strong effect;</b> reaction favored by polar solvents    | <b>Weak effect;</b> reaction favored by weak base                      | <b>Strong effect;</b> reaction favored by good leaving group | <b>Strong effect;</b> reaction favored by 3°, allylic, and benzylic substrates |
| <b>E2</b>             | <b>Strong effect;</b> reaction favored by polar aprotic solvents | <b>Strong effect;</b> reaction favored by poor nucleophile/strong base | <b>Strong effect;</b> reaction favored by good leaving group | <b>Strong effect;</b> reaction favored by 3° substrates                        |

## Overall Summary of S<sub>N</sub>1, S<sub>N</sub>2, E1 and E2 Reactions

| CH <sub>3</sub> X<br>Methyl      | RCH <sub>2</sub> X<br>1°   | RR'CHX<br>2°   | RR'R''CX<br>3°  |
|----------------------------------|--|--|---|
|                                  | <b>Bimolecular reactions only</b>  |  | <b>S<sub>N</sub>1/E1 or E2</b>  |
| Gives S <sub>N</sub> 2 reactions | Gives mainly S <sub>N</sub> 2 except with a hindered strong base [e.g., (CH <sub>3</sub> ) <sub>3</sub> CO <sup>-</sup> ] and then gives mainly E2 | Gives mainly S <sub>N</sub> 2 with weak bases (e.g., I <sup>-</sup> , CN <sup>-</sup> , RCO <sub>2</sub> <sup>-</sup> ) and mainly E2 with strong bases (e.g., RO <sup>-</sup> ) | No S <sub>N</sub> 2 reaction. In solvolysis gives S <sub>N</sub> 1/E1, and at lower temperatures S <sub>N</sub> 1 is favored. When a strong base (e.g., RO <sup>-</sup> ) is used E2 predominates |