

# Quiz 2

**March 23, Friday**

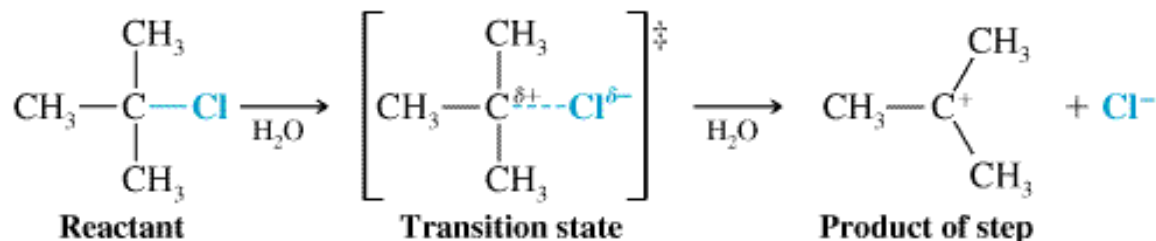
**Chapter 5–6**

**Practice Quiz** available at  
<http://www.chem.wisc.edu/courses/343/lee/>

# Solvent Effect on S<sub>N</sub>1: Ionizing Ability of the Solvent

The **stability of carbocations** is the primary factor for the rate in S<sub>N</sub>1.

*Ionization of the Leaving Group*



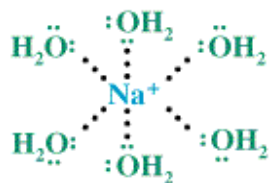
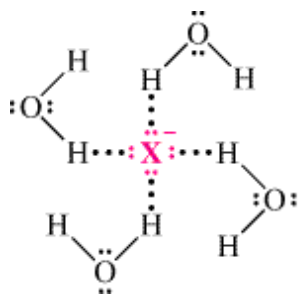
→ How the environment (solvent) would affect the stability of the transition state and the products (carbocation) of the step?

**Polar protic solvent:** greatly increases the rate of ionization due to its effective solvation of cations and anions. The rough measure of solvent polarity = **Dielectric Constant**

**Dielectric Constants of Common Solvents**

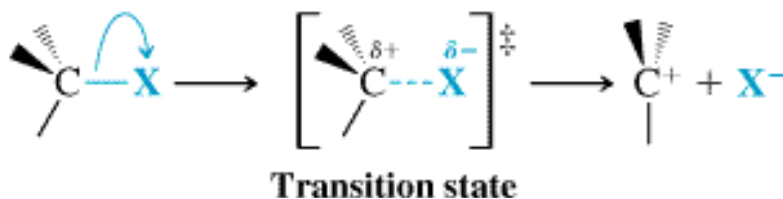
Solvent	Formula	Dielectric Constant
Water	H <sub>2</sub> O	80
Formic acid	HCO <sub>2</sub> H	59
Dimethyl sulfoxide (DMSO)	CH <sub>3</sub> SOCH <sub>3</sub>	49
<i>N,N</i> -Dimethylformamide (DMF)	HCON(CH <sub>3</sub> ) <sub>2</sub>	37
Acetonitrile	CH <sub>3</sub> C≡N	36
Methanol	CH <sub>3</sub> OH	33
Hexamethylphosphoramide (HMPA)	[(CH <sub>3</sub> ) <sub>2</sub> N] <sub>3</sub> P=O	30
Ethanol	CH <sub>3</sub> CH <sub>2</sub> OH	24
Acetone	CH <sub>3</sub> COCH <sub>3</sub>	21
Acetic acid	CH <sub>3</sub> CO <sub>2</sub> H	6

↑  
Increasing solvent polarity

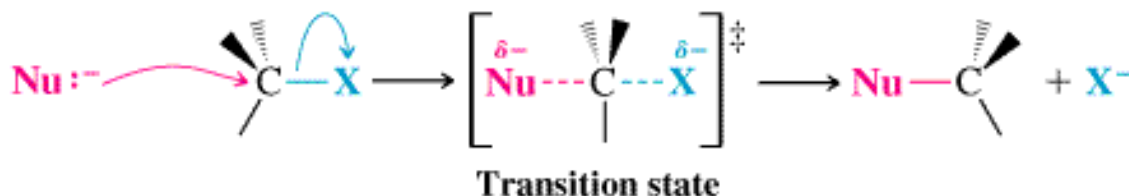


# Nature of the Leaving Group

$S_N1$  Reaction (rate-limiting step)



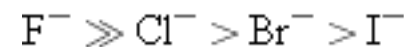
$S_N2$  Reaction



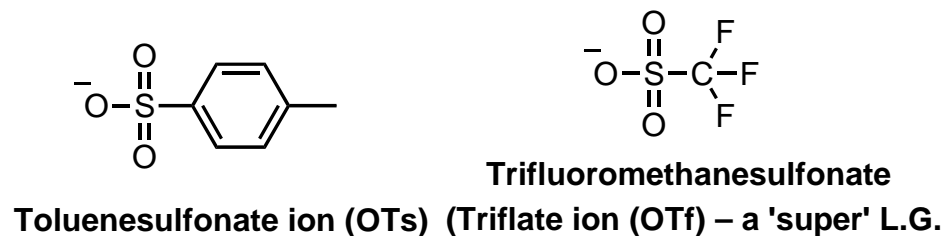
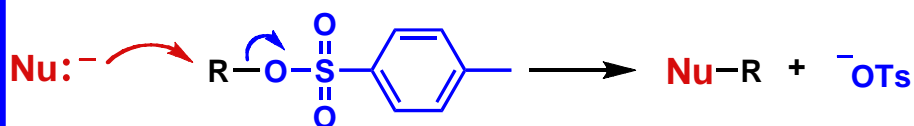
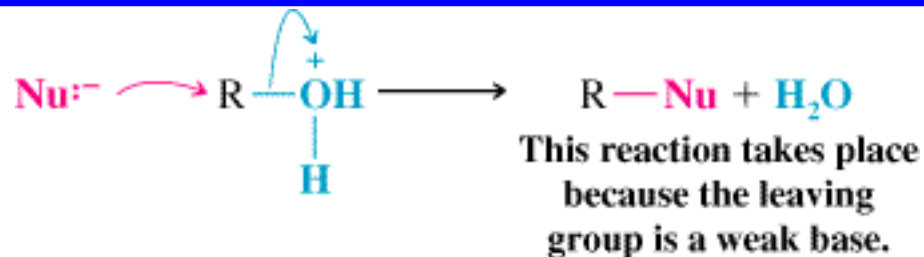
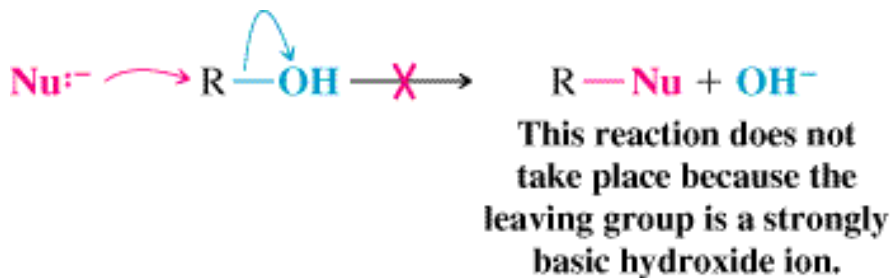
Leaving group capacity



Basicity

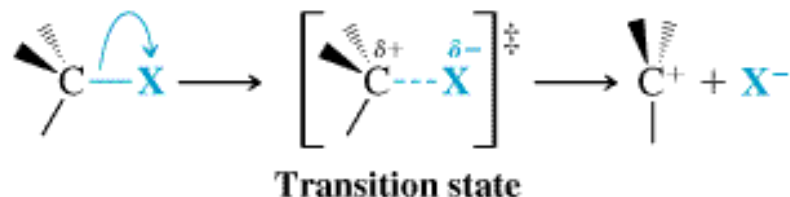


Stabilization of the developing negative charge at the leaving group will stabilize the transition state, which will lower the free energy of activation. Thus, strongly basic ions rarely acts as leaving groups.

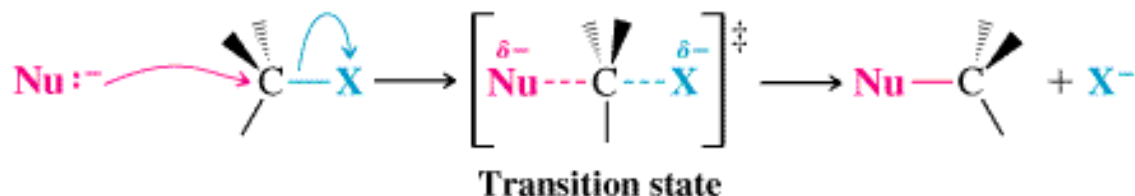


# Summary: S<sub>N</sub>1 vs. S<sub>N</sub>2

*S<sub>N</sub>1 Reaction (rate-limiting step)*



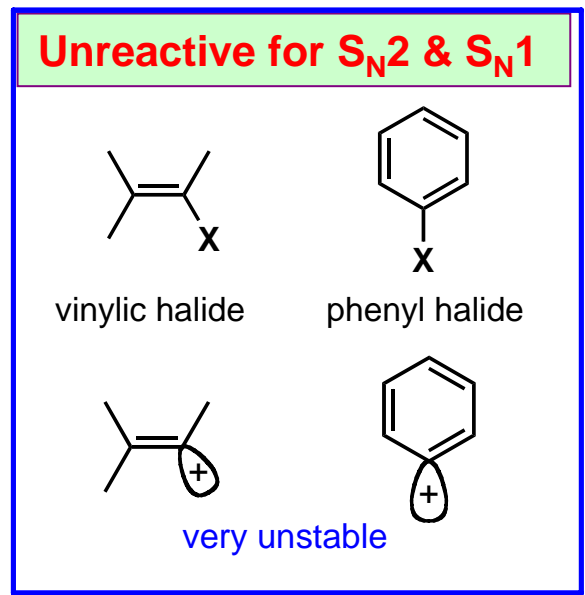
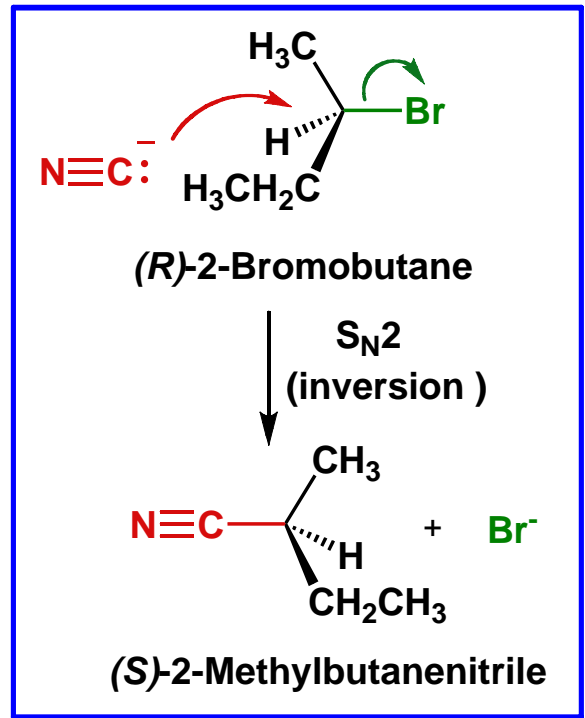
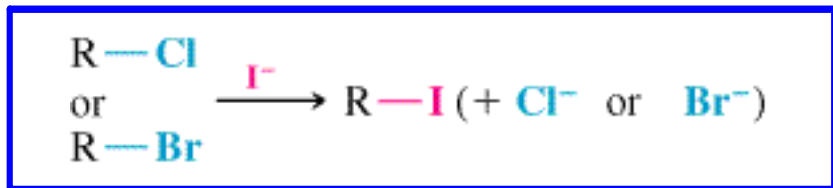
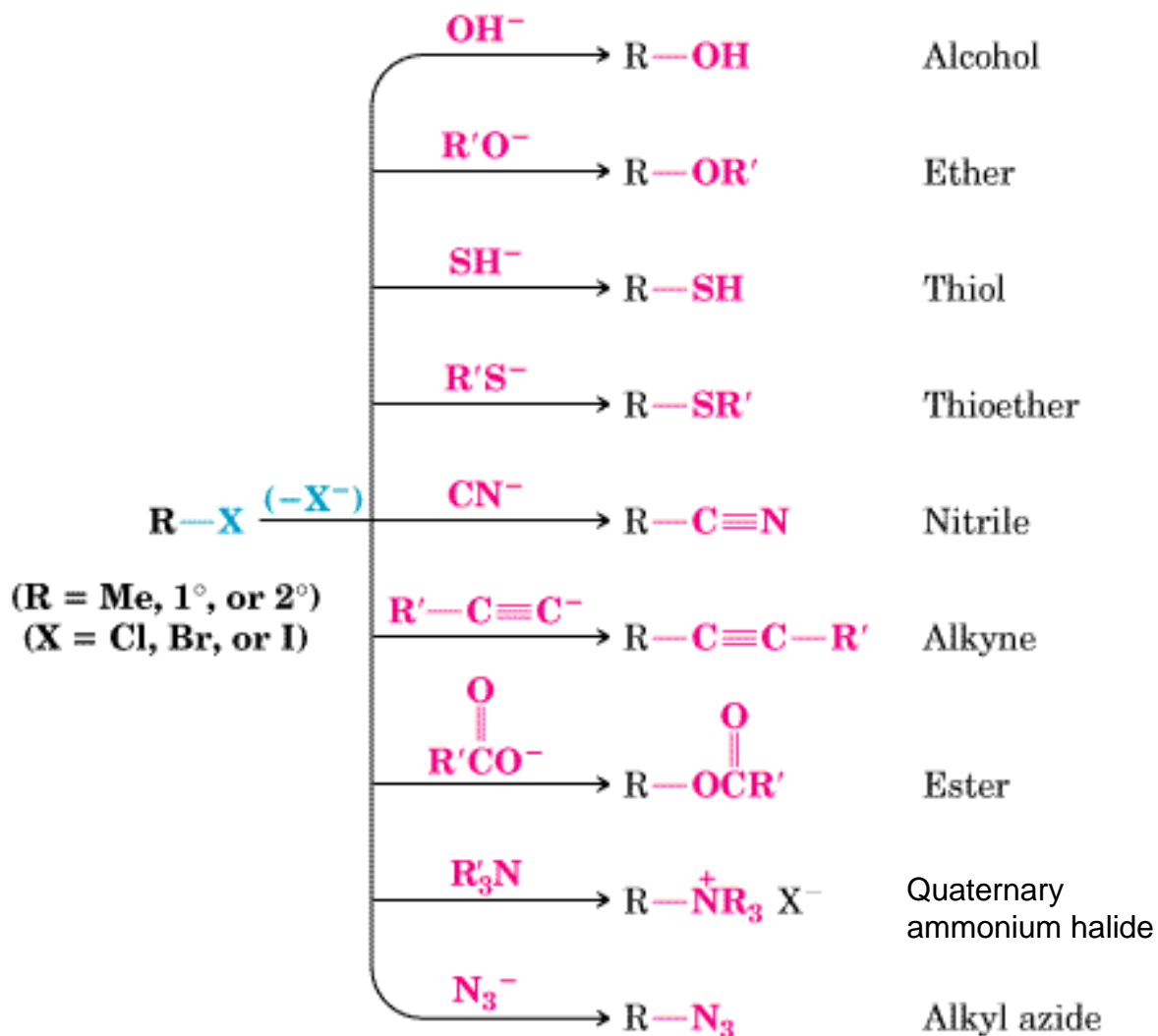
*S<sub>N</sub>2 Reaction*



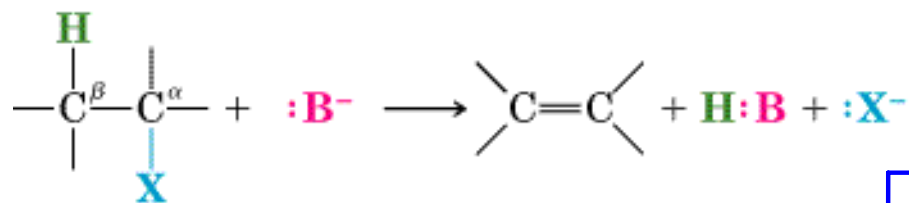
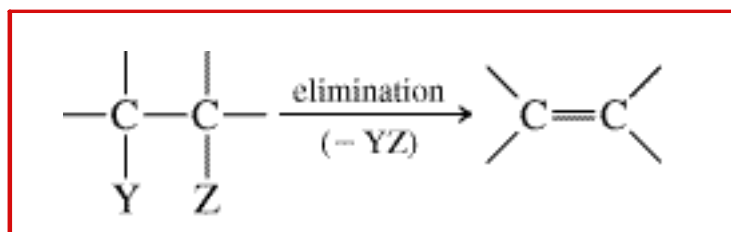
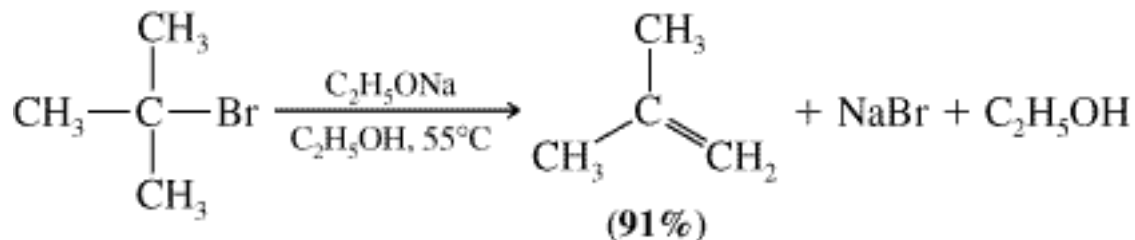
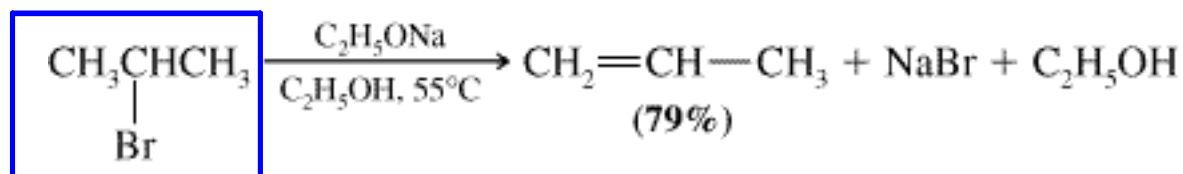
## Factors Favoring S<sub>N</sub>1 versus S<sub>N</sub>2 Reactions

Factor	S <sub>N</sub> 1	S <sub>N</sub> 2
Substrate	3° (requires formation of a relatively stable carbocation)	Methyl > 1° > 2° (requires unhindered substrate)
Nucleophile	Weak Lewis base, neutral molecule, nucleophile may be the solvent (solvolysis)	Strong Lewis base, rate favored by high concentration of nucleophile
Solvent	Polar protic (e.g., alcohols, water)	Polar aprotic (e.g., DMF, DMSO)
Leaving group	I > Br > Cl > F for both S <sub>N</sub> 1 and S <sub>N</sub> 2 (the weaker the base after the group departs, the better the leaving group)	

# Functional Group Transformations via S<sub>N</sub>2 Reaction



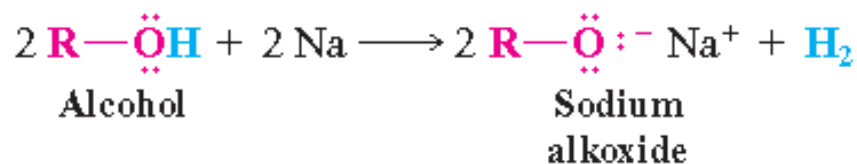
# Elimination Reactions of Alkyl Halides: Dehydrohalogenation



1,2-elimination or  $\beta$ -elimination

A base

Dehydrohalogenation

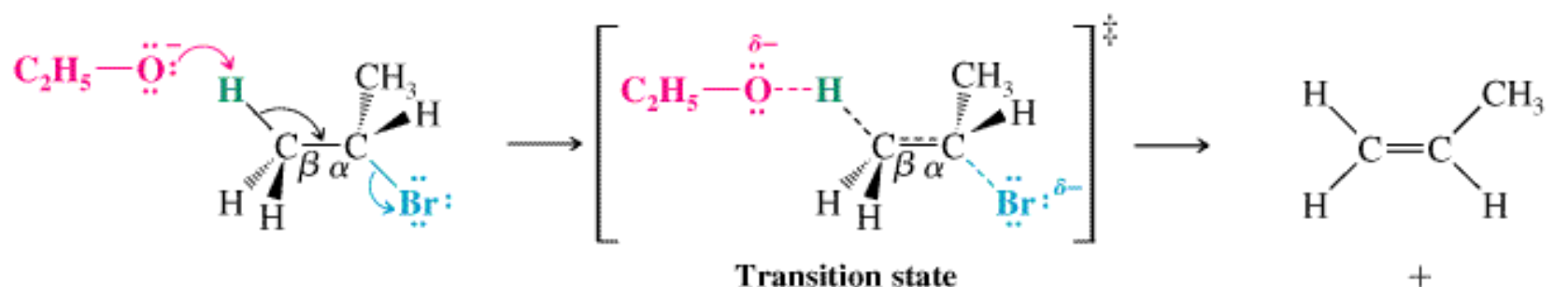


# The E2 Reaction (Dehydrohalogenation): Mechanism



$$\text{Rate} \propto [\text{CH}_3\text{CHBrCH}_3] [\text{C}_2\text{H}_5\text{O}^-]$$

$$\text{Rate} = k [\text{CH}_3\text{CHBrCH}_3] [\text{C}_2\text{H}_5\text{O}^-]$$

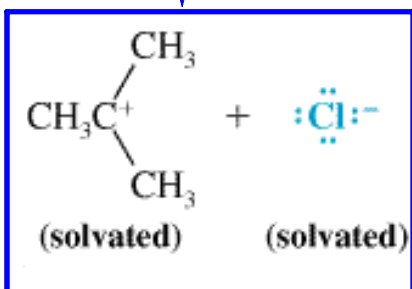
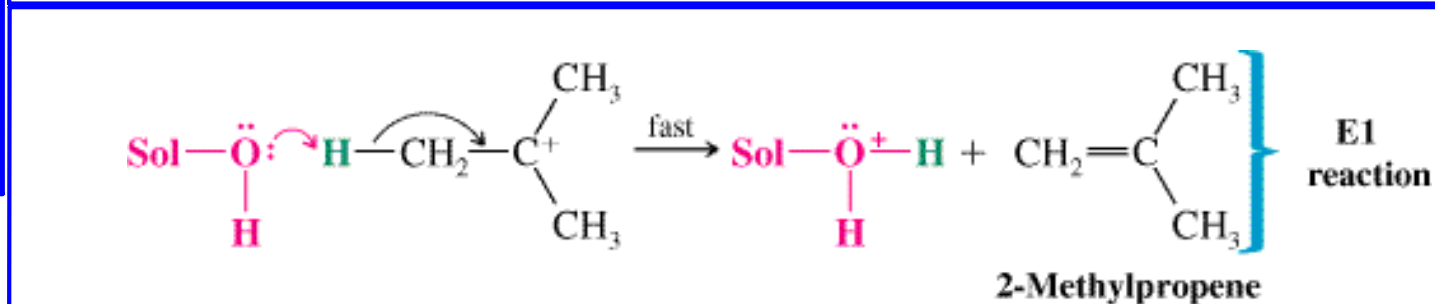
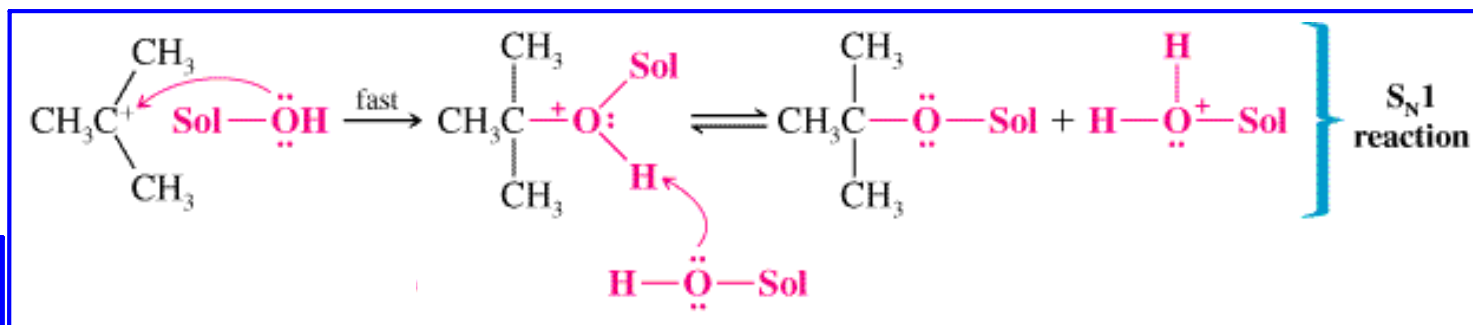
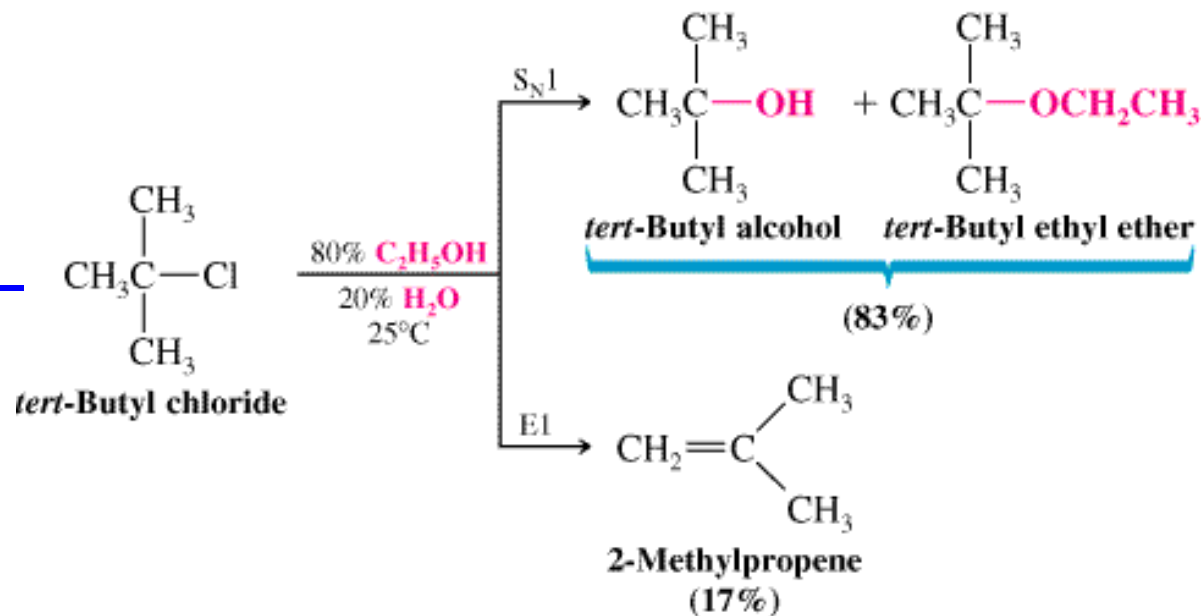


The basic ethoxide ion begins to remove a proton from the  $\beta$  carbon using its electron pair to form a bond to it. At the same time, the electron pair of the  $\beta$  C—H bond begins to move in to become the  $\pi$  bond of a double bond, and the bromine begins to depart with the electrons that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

Partial bonds in the transition state extend from the oxygen atom that is removing the  $\beta$  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.

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.

# The E1 Reaction

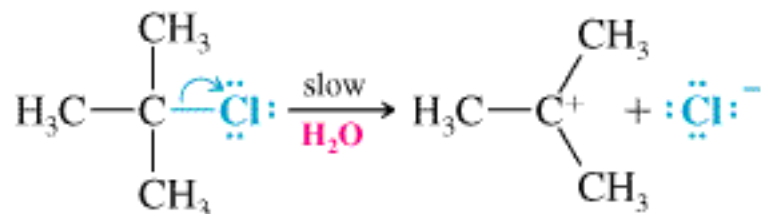




# The E1 Reaction: Mechanism



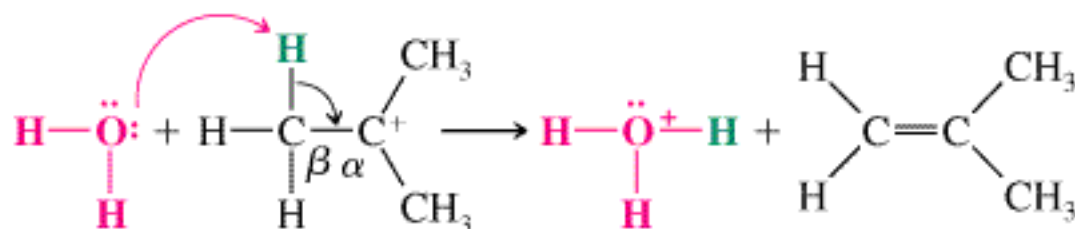
## Step 1



Aided by the polar solvent, a chlorine departs with the electron

This slow step produces the relatively stable 3° carbocation + chloride ion.

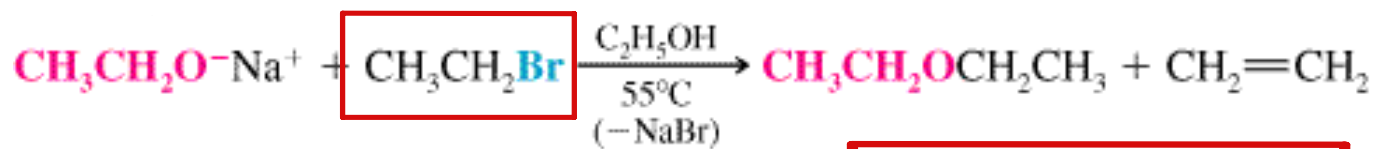
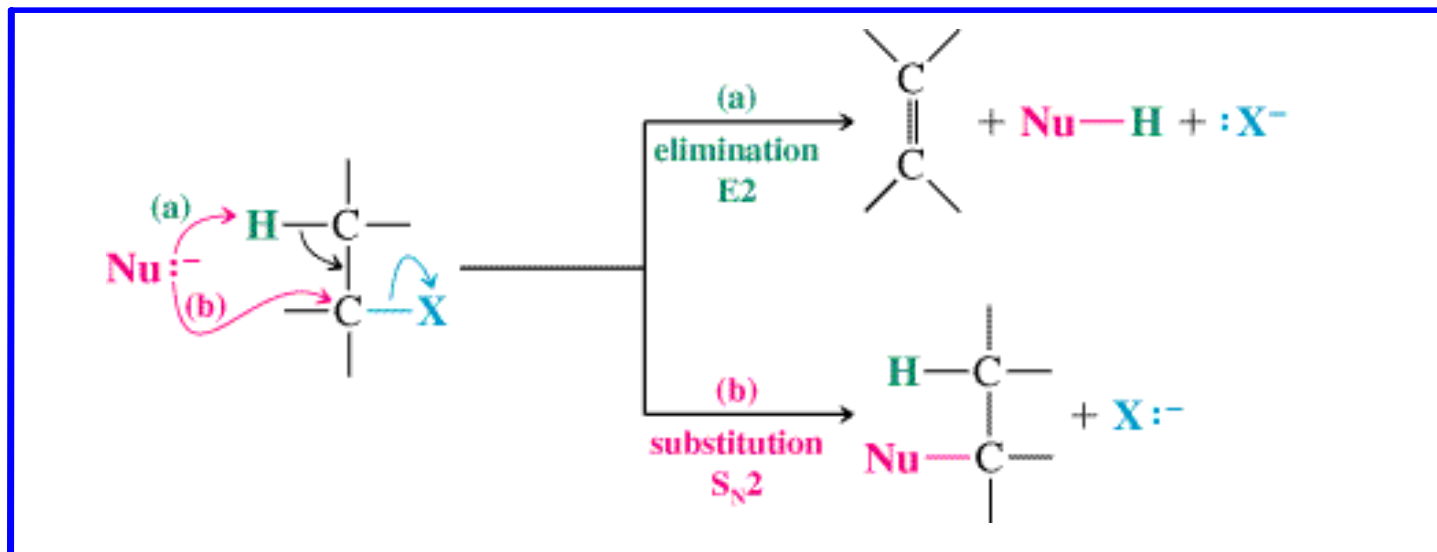
## Step 2



A molecule of water removes one of the hydrogens from the  $\beta$  carbon

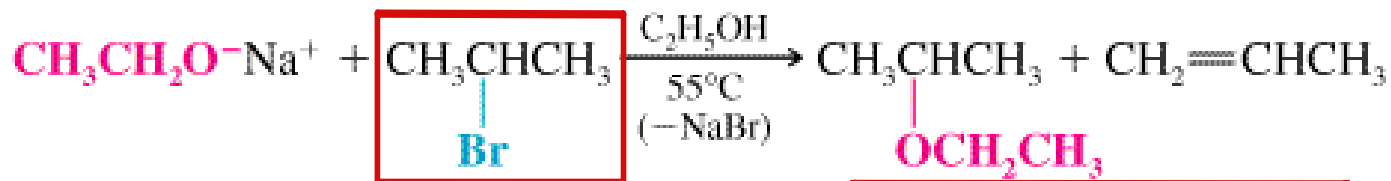
This step produces the alkene and a hydronium ion.

# S<sub>N</sub>2 vs. E2 – Substrate Structure



Primary substrate

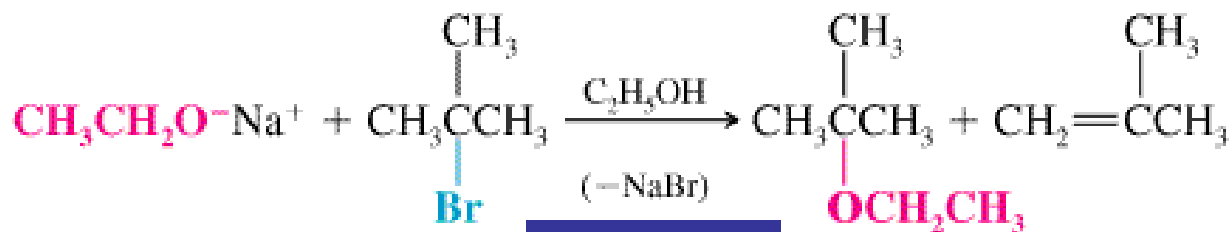
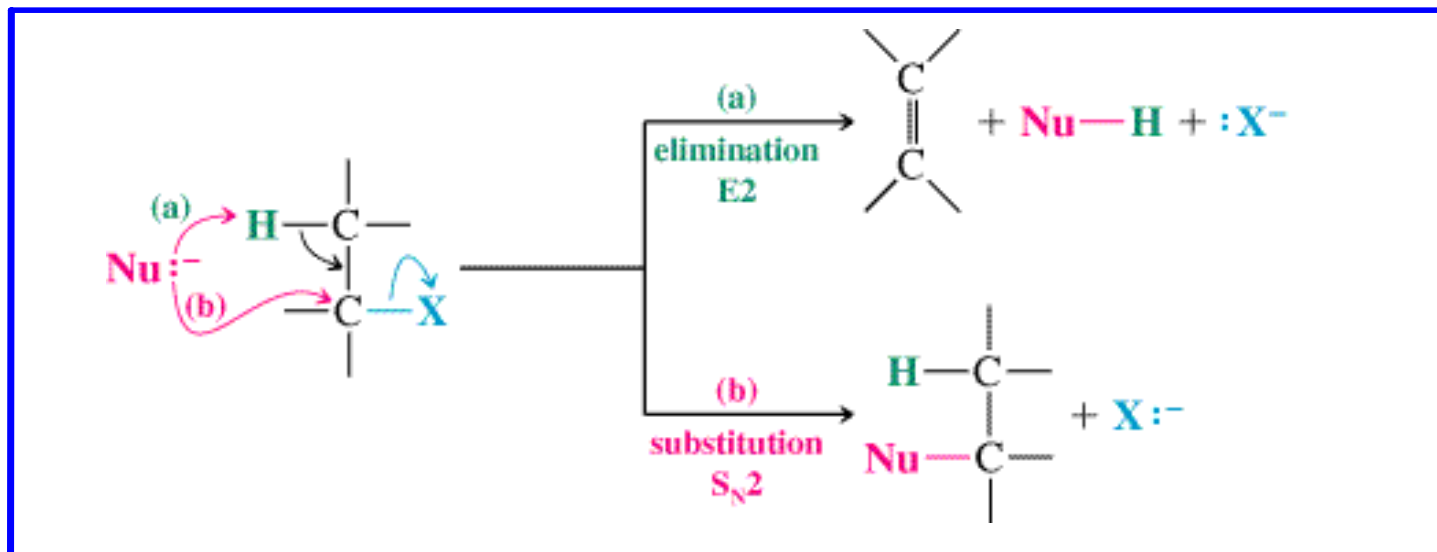
S <sub>N</sub> 2 (90%)	E2 (10%)
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Secondary substrate

S <sub>N</sub> 2 (21%)	E2 (79%)
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# S<sub>N</sub>1 vs. E1/E2 – Temperature

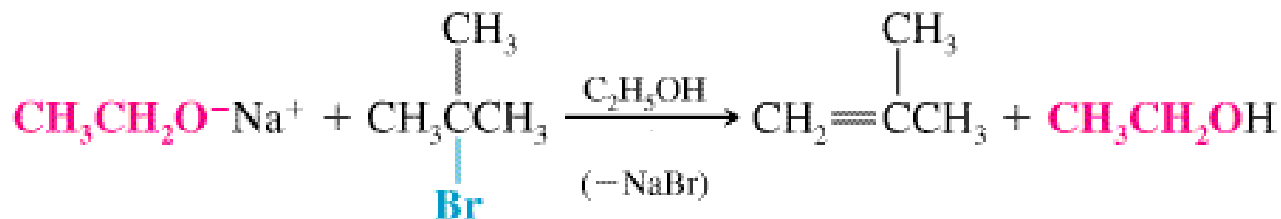


Tertiary substrate

at 25 ° C

S<sub>N</sub>1  
(9%)

Mainly E2  
(91%)



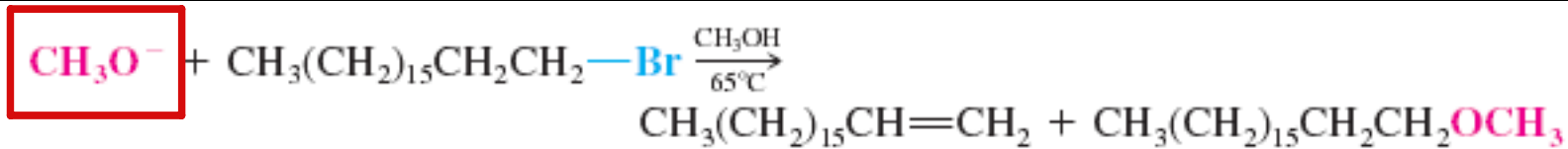
at 55 ° C

E2 + E1  
(100%)

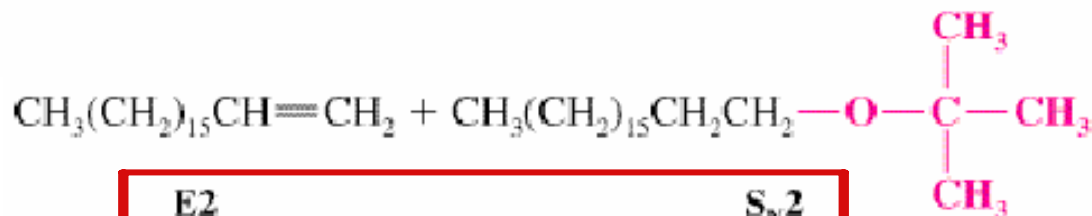
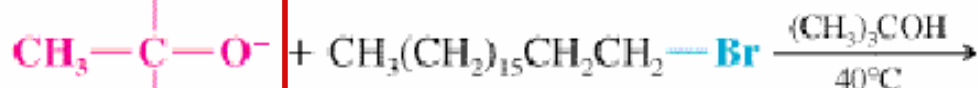
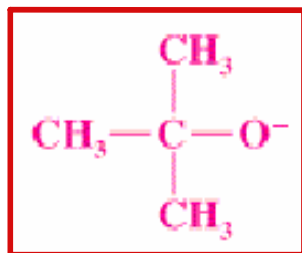
$$\Delta G^\circ = \Delta H^\circ -$$

$$T\Delta S^\circ$$

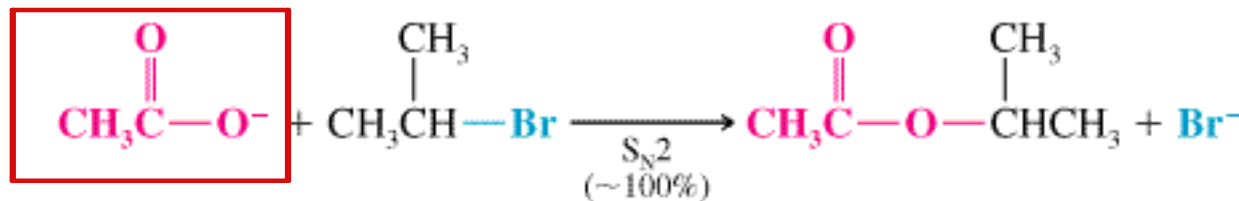
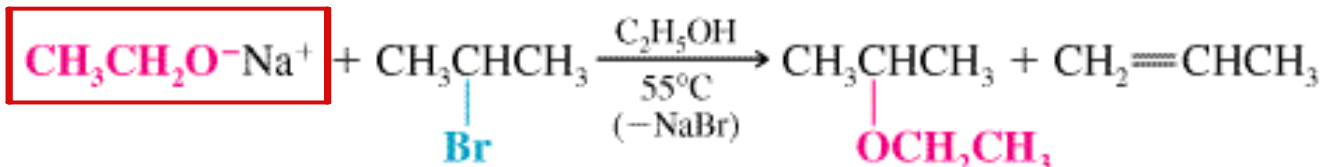
# S<sub>N</sub>2 vs. E2 – Base / Nucleophile



Size of base/nucleophile



Basicity and Polarizability



# Substitution (S<sub>N</sub>2, S<sub>N</sub>1) vs. Elimination (E2, E1)



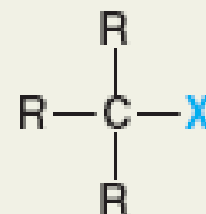
Methyl



1°



2°



3°

## Bimolecular Reactions Only

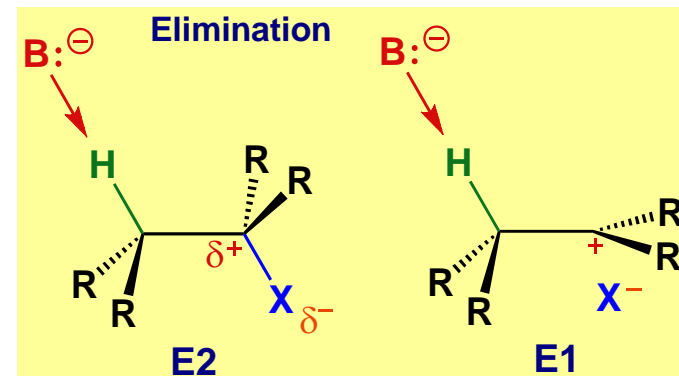
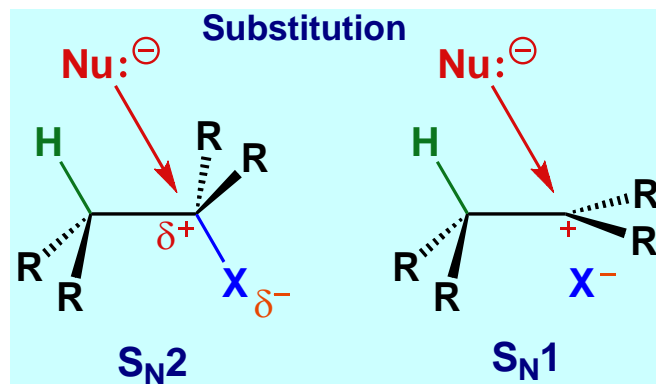
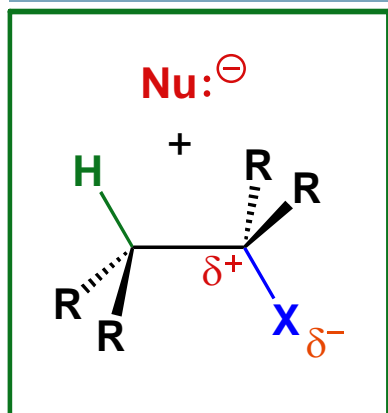
Gives S<sub>N</sub>2 reactions

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>)

## S<sub>N</sub>1/E1 or E2

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.

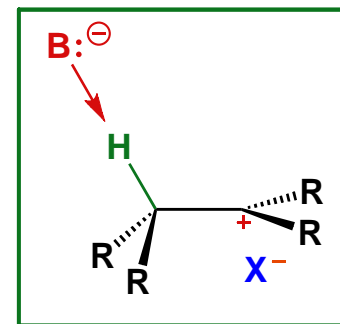
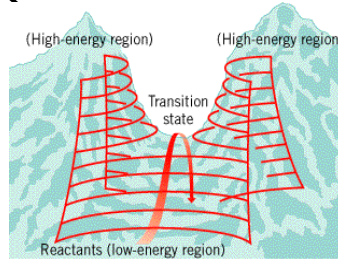
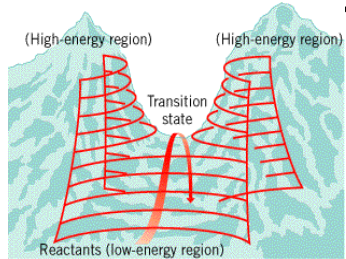
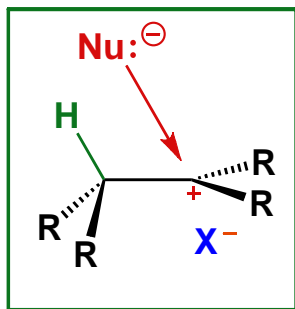
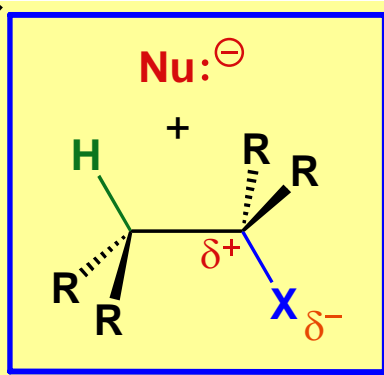
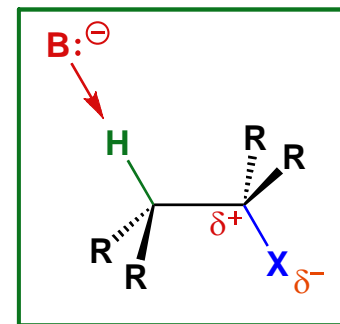
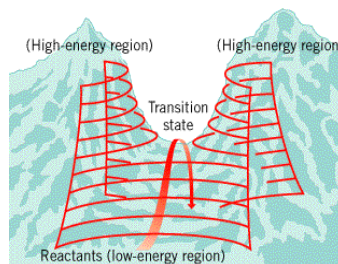
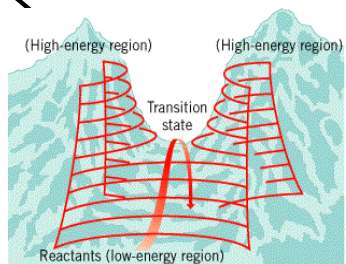
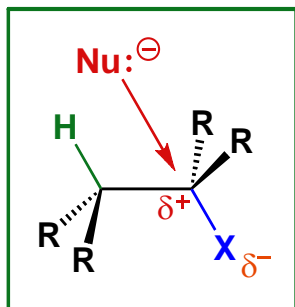


# Substitution (S<sub>N</sub>2, S<sub>N</sub>1) vs. Elimination (E2, E1)

**S<sub>N</sub>2**

**E2**

$$\Delta G^\ddagger = \Delta H^\ddagger - T\Delta S^\ddagger$$



**S<sub>N</sub>1**

Product

$$\Delta G^\circ = \Delta H^\circ - T\Delta S^\circ$$

**E1**

