

Quiz 2

March 23, Friday

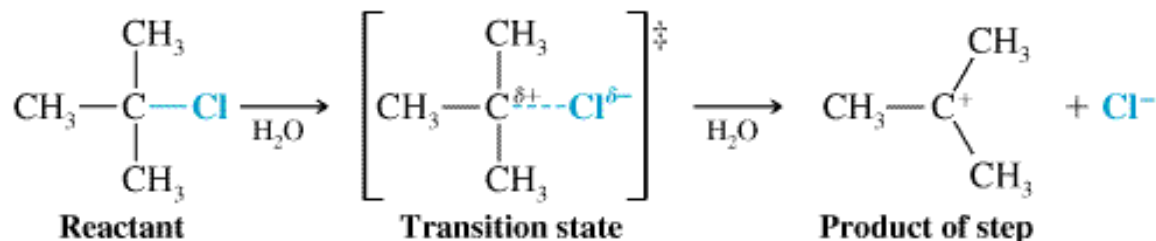
Chapter 5–6

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

Solvent Effect on S_N1: Ionizing Ability of the Solvent

The **stability of carbocations** is the primary factor for the rate in S_N1.

Ionization of the Leaving Group

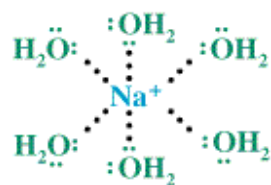
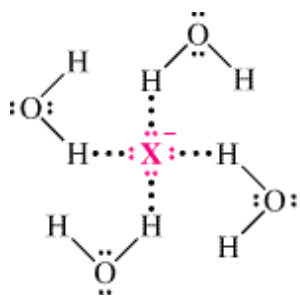


→ How the environment (solvent) would affect the stability of the transition state and the products (carbocation) of the step?

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

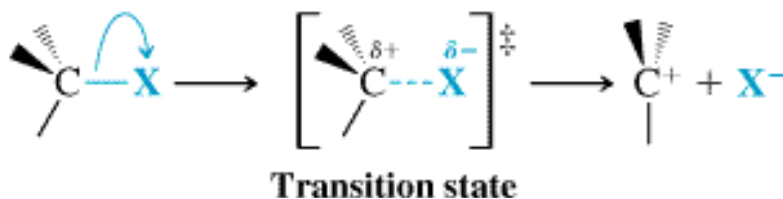
Solvent	Formula	Dielectric Constant
Water	H ₂ O	80
Formic acid	HCO ₂ H	59
Dimethyl sulfoxide (DMSO)	CH ₃ SOCH ₃	49
<i>N,N</i> -Dimethylformamide (DMF)	HCON(CH ₃) ₂	37
Acetonitrile	CH ₃ C≡N	36
Methanol	CH ₃ OH	33
Hexamethylphosphoramide (HMPA)	[(CH ₃) ₂ N] ₃ P=O	30
Ethanol	CH ₃ CH ₂ OH	24
Acetone	CH ₃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



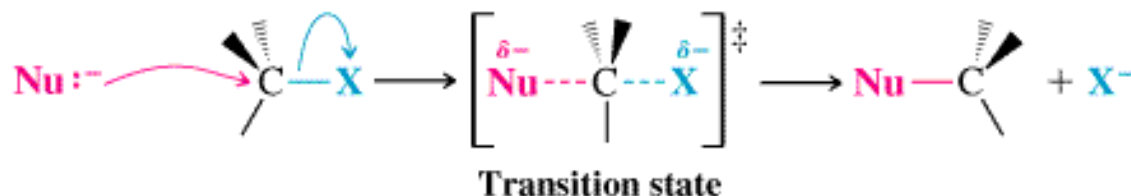
↑
Increasing
solvent
polarity
↓

Nature of the Leaving Group

S_N1 Reaction (rate-limiting step)



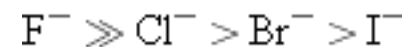
S_N2 Reaction



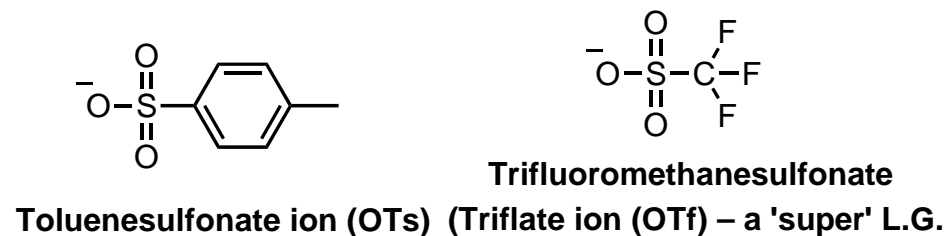
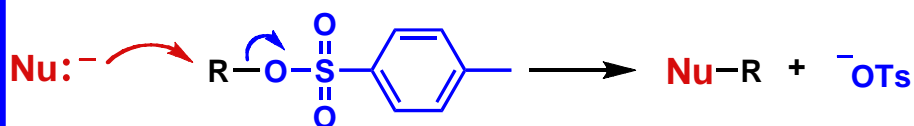
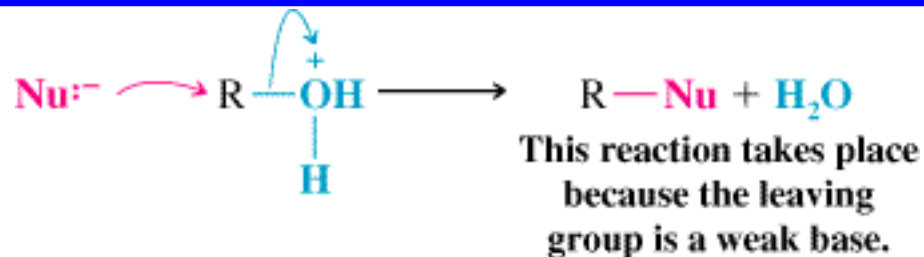
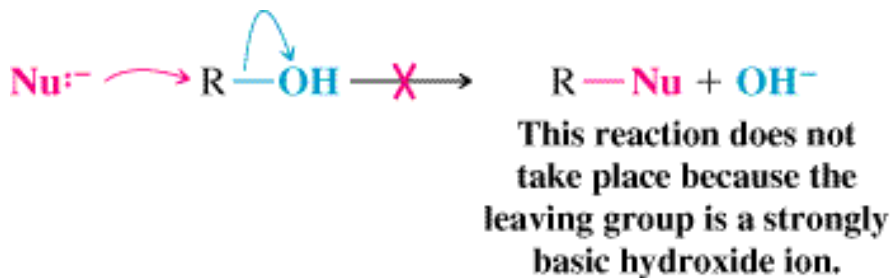
Leaving group capacity



Basicity

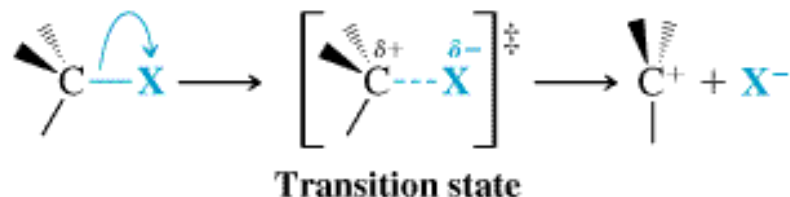


Stabilization of the developing negative charge at the leaving group will stabilize the transition state, which will lower the free energy of activation. Thus, strongly basic ions rarely acts as leaving groups.

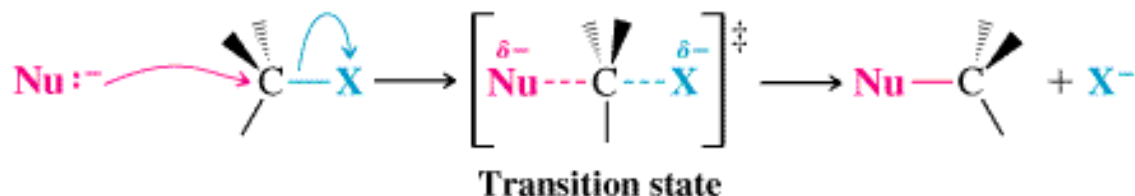


Summary: S_N1 vs. S_N2

S_N1 Reaction (rate-limiting step)



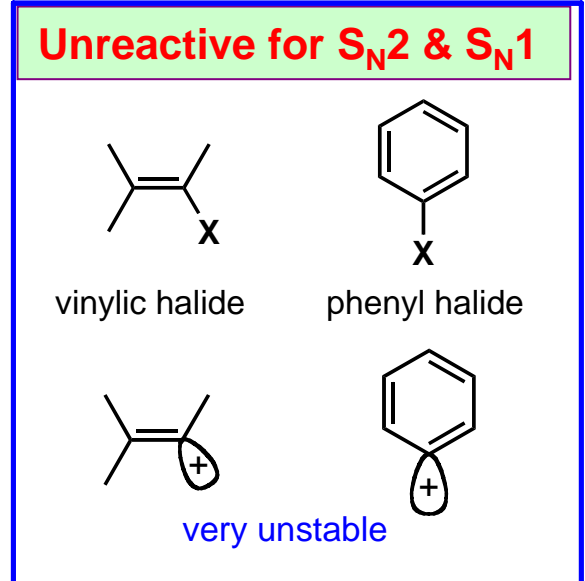
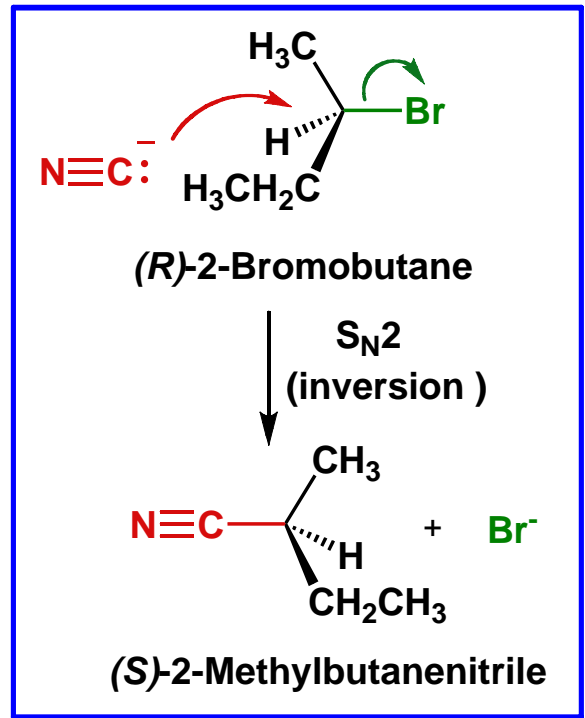
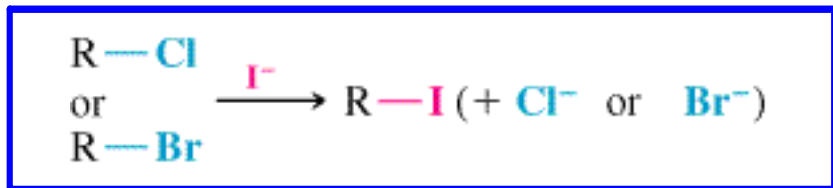
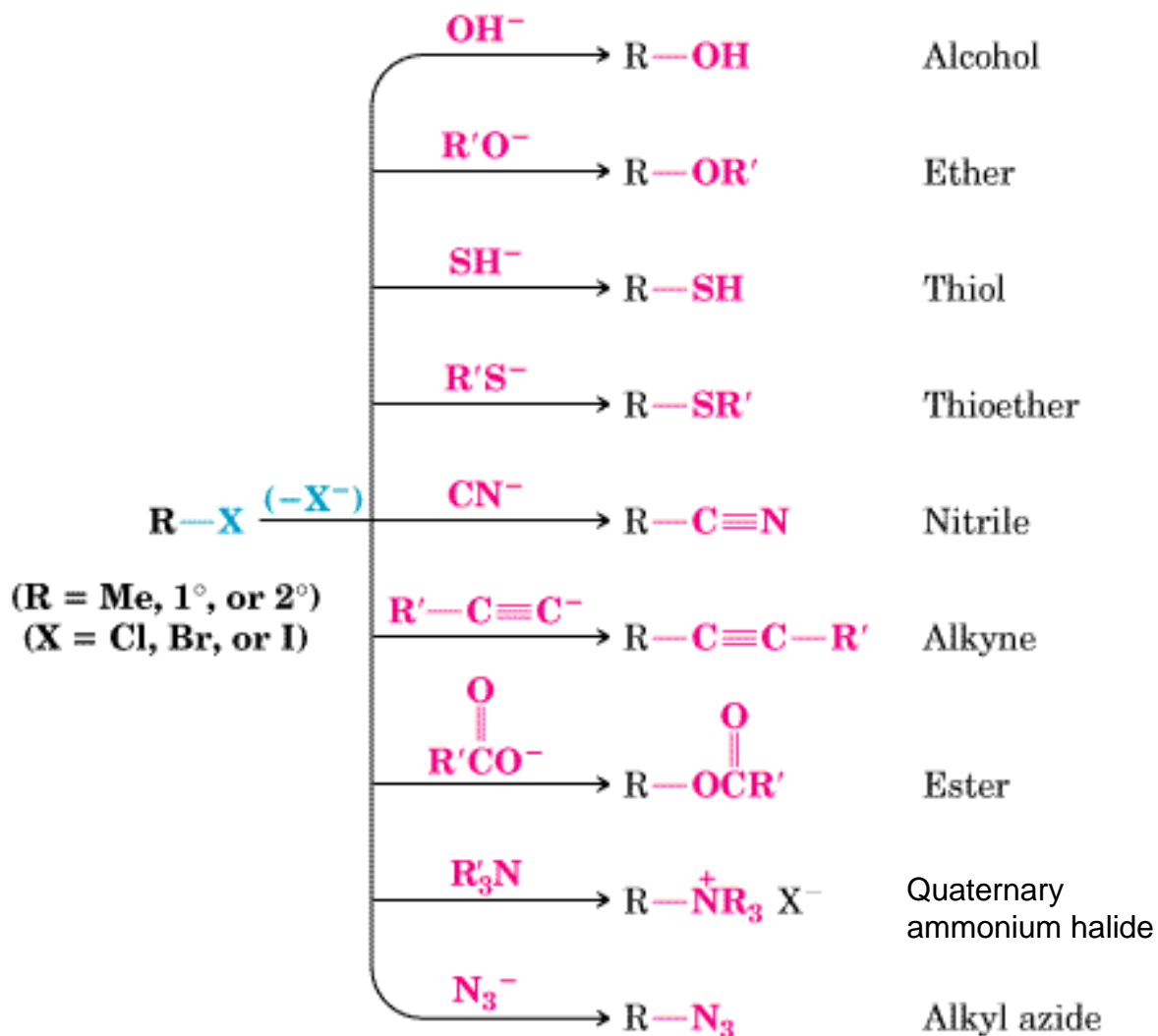
S_N2 Reaction



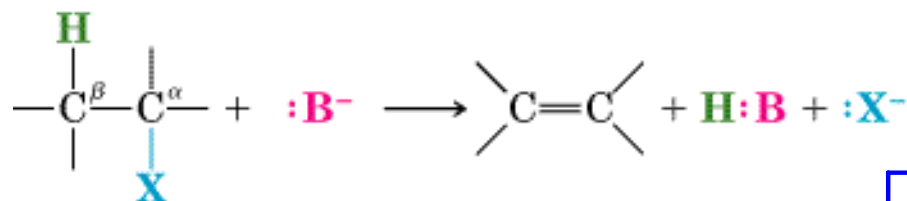
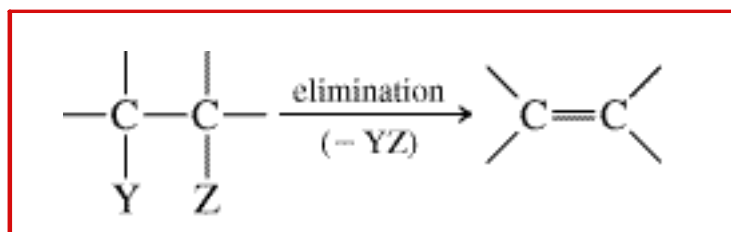
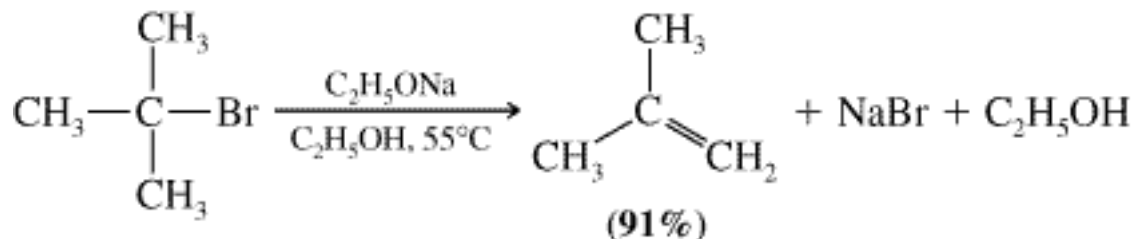
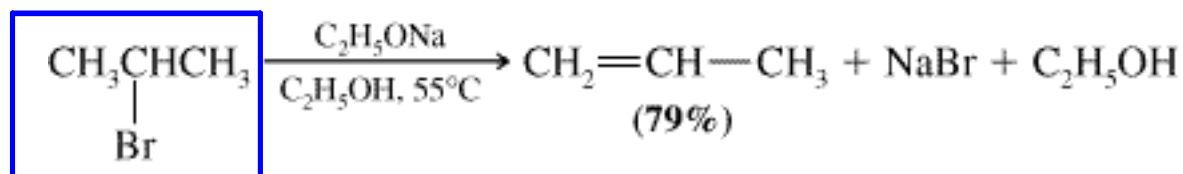
Factors Favoring S_N1 versus S_N2 Reactions

Factor	S _N 1	S _N 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 _N 1 and S _N 2 (the weaker the base after the group departs, the better the leaving group)	

Functional Group Transformations via S_N2 Reaction



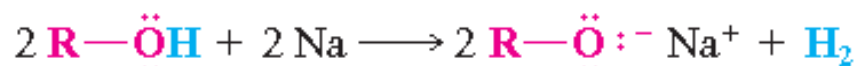
Elimination Reactions of Alkyl Halides: Dehydrohalogenation



1,2-elimination or β -elimination

A base

Dehydrohalogenation



Alcohol

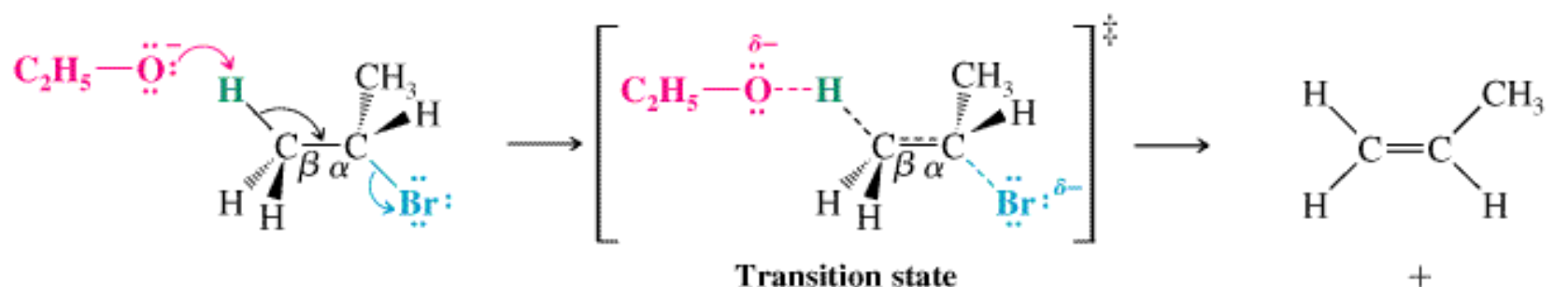
Sodium
alkoxide

The E2 Reaction (Dehydrohalogenation): Mechanism



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

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

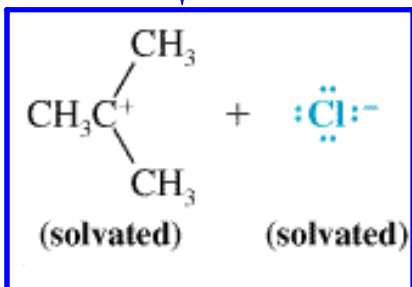
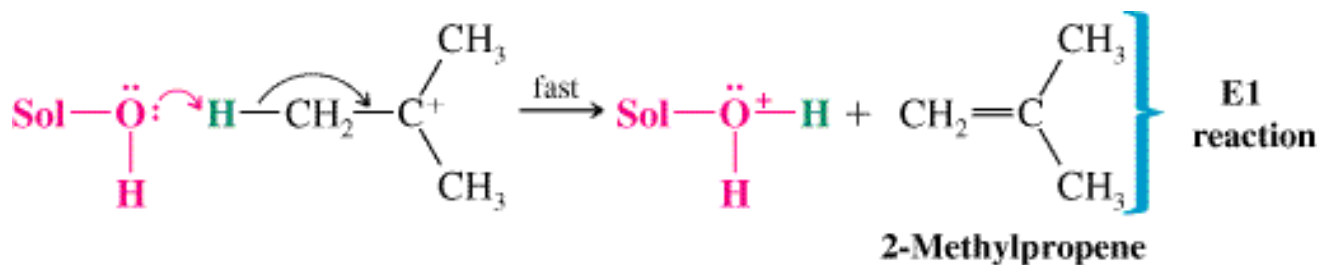
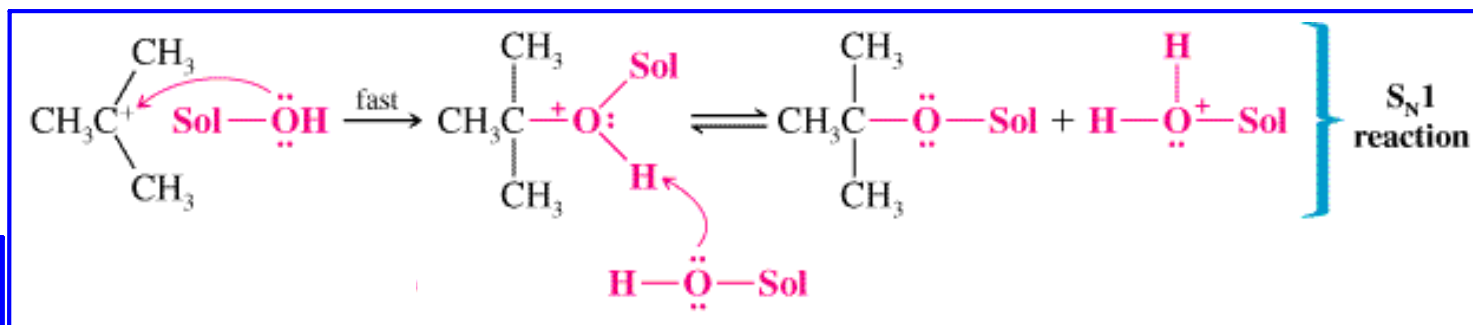
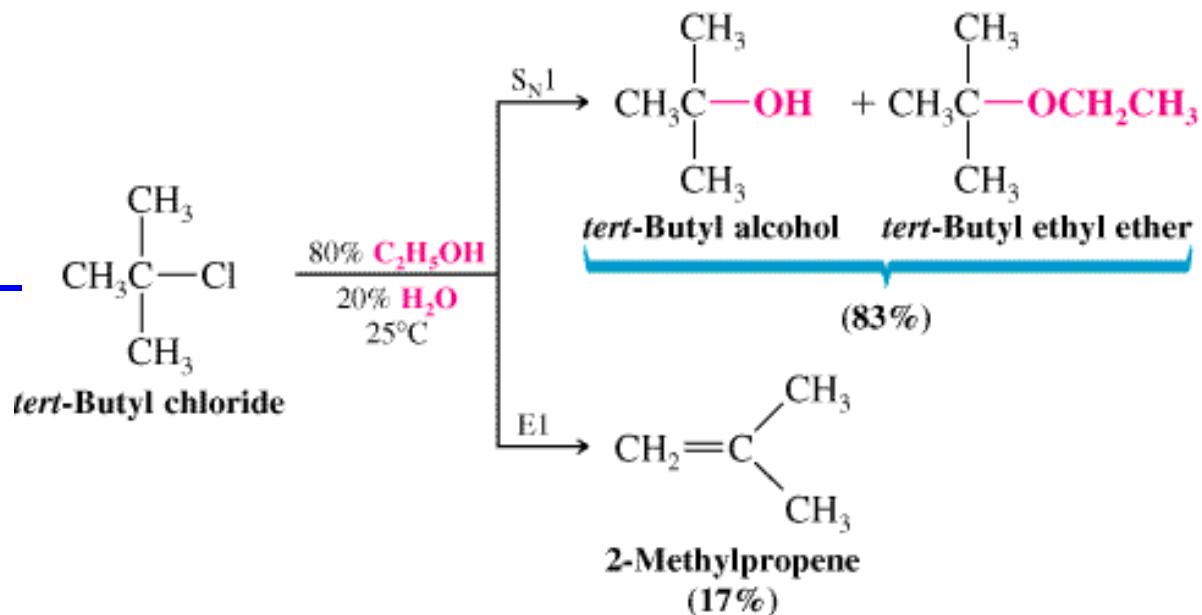


The basic ethoxide ion begins to remove a proton from the β carbon using its electron pair to form a bond to it. At the same time, the electron pair of the β C—H bond begins to move in to become the π bond of a double bond, and the bromine begins to depart with the electrons that bonded it to the α carbon

Partial bonds in the transition state extend from the oxygen atom that is removing the β 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 π 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.

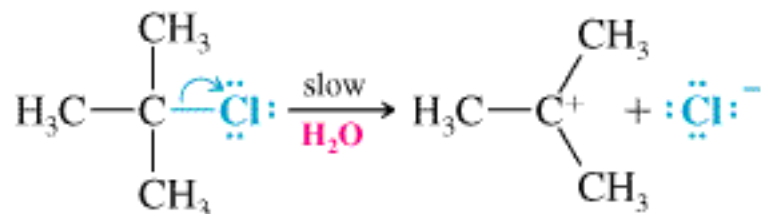
The E1 Reaction



The E1 Reaction: Mechanism



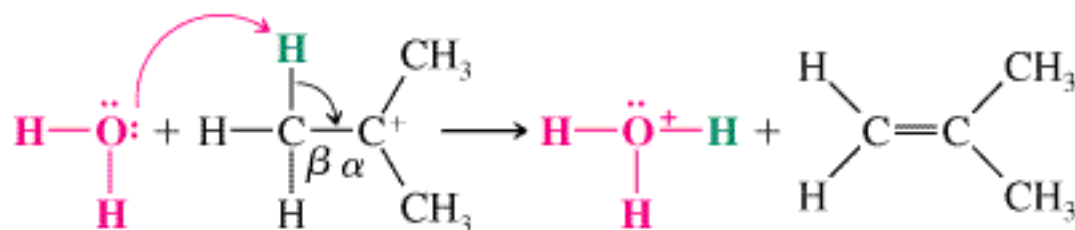
Step 1



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

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

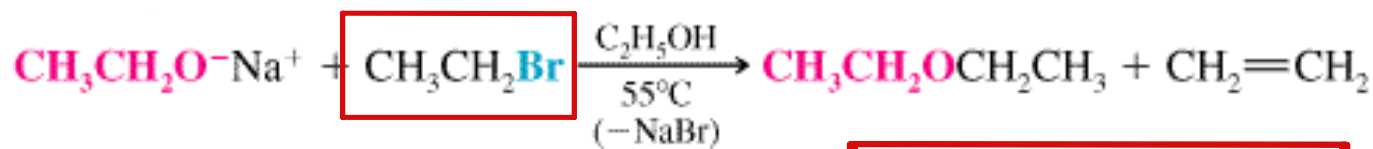
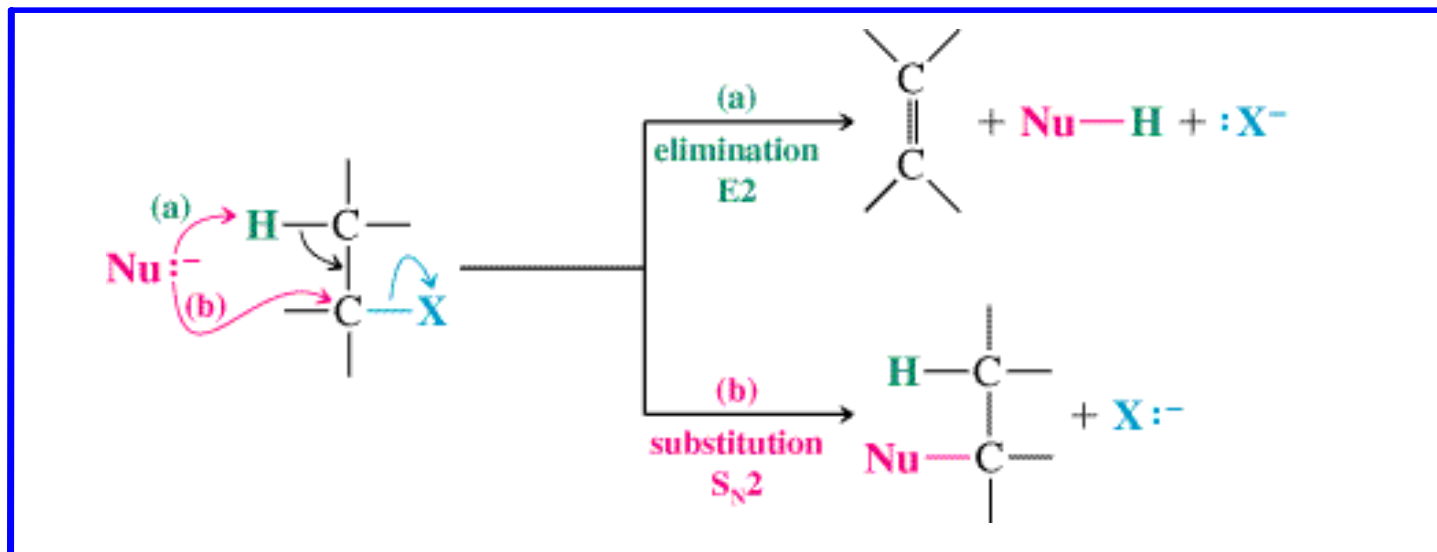
Step 2



A molecule of water removes one of the hydrogens from the β carbon

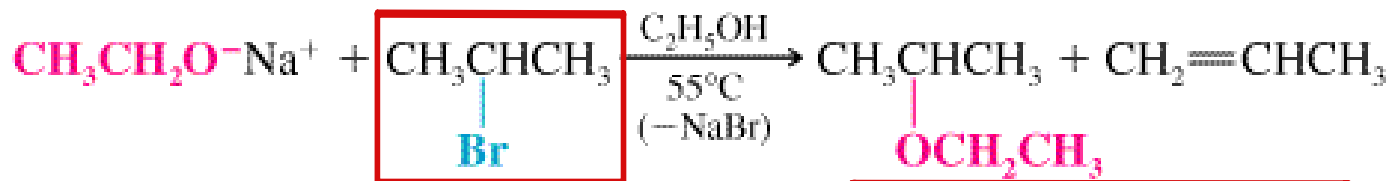
This step produces the alkene and a hydronium ion.

S_N2 vs. E2 – Substrate Structure



Primary substrate

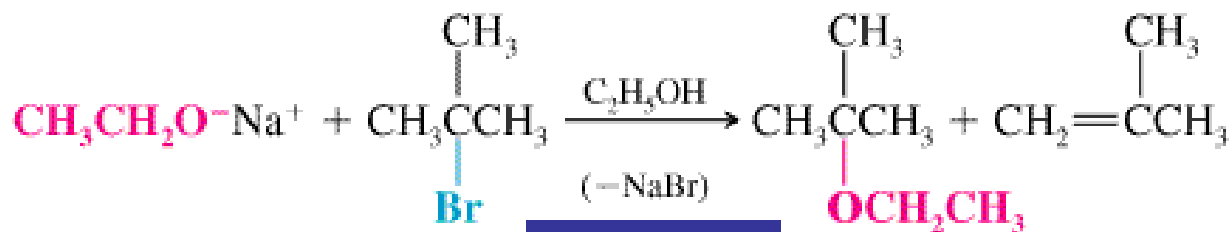
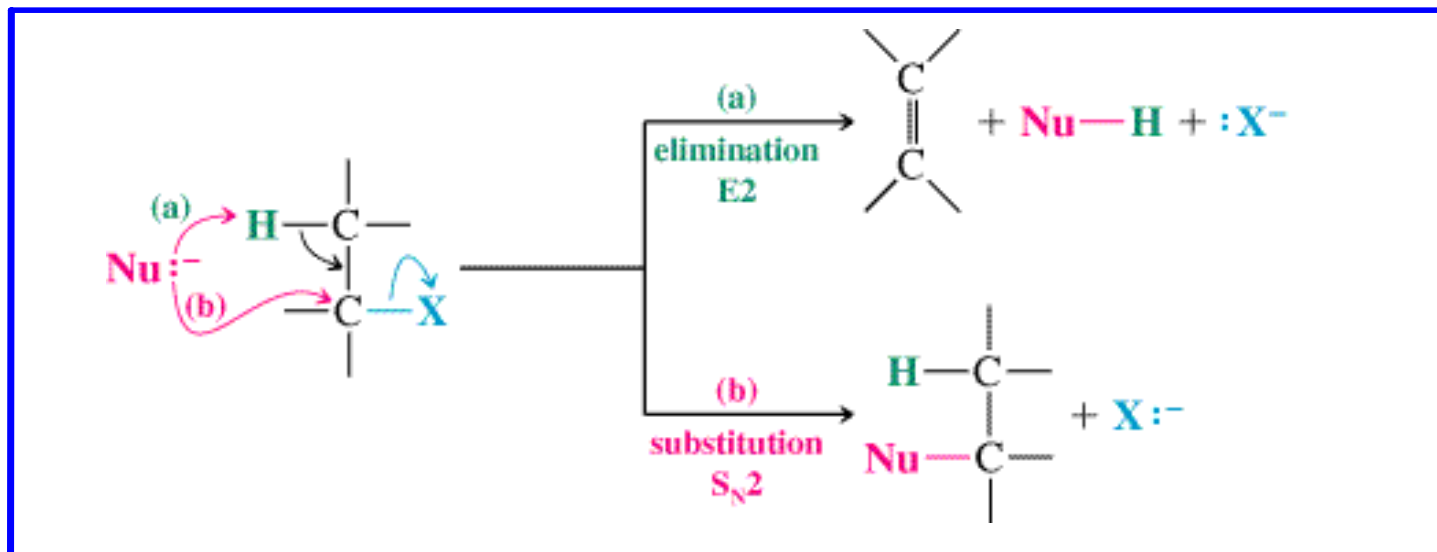
S _N 2 (90%)	E2 (10%)
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Secondary substrate

S _N 2 (21%)	E2 (79%)
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S_N1 vs. E1/E2 – Temperature

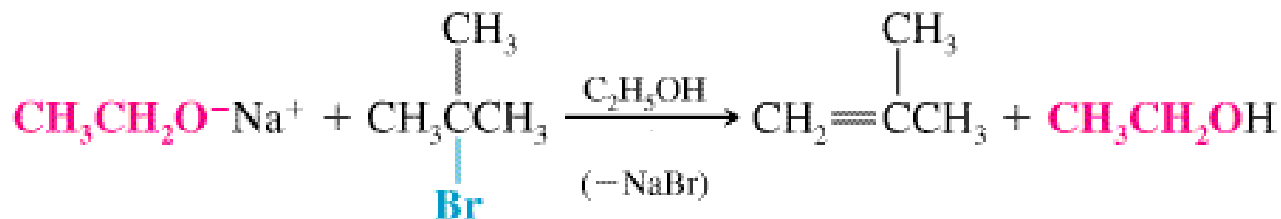


Tertiary substrate

at 25 ° C

S_N1
(9%)

Mainly E2
(91%)



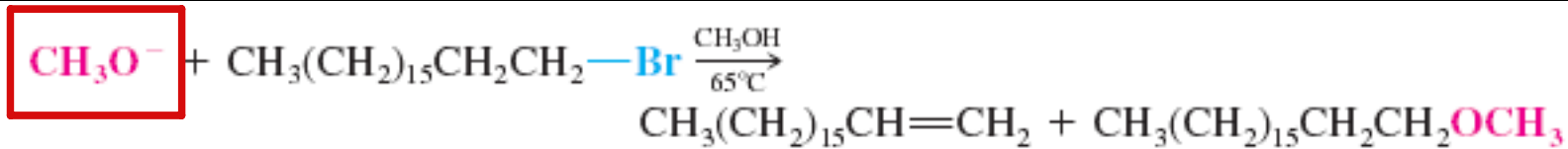
at 55 ° C

E2 + E1
(100%)

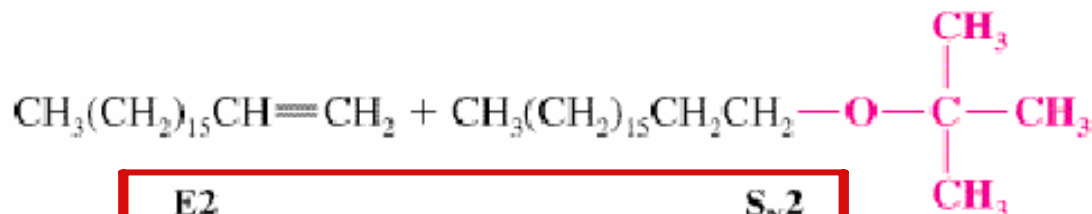
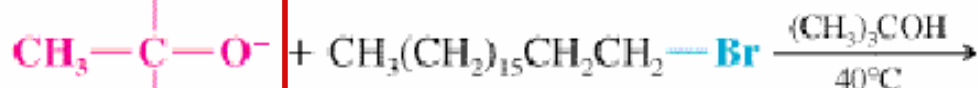
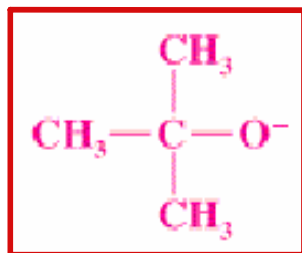
$$\Delta G^\circ = \Delta H^\circ -$$

$$T\Delta S^\circ$$

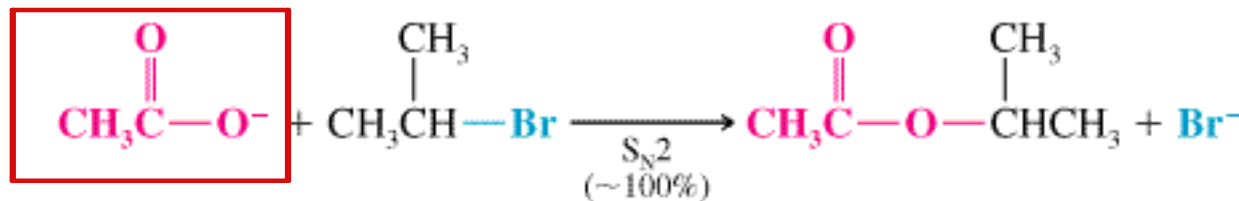
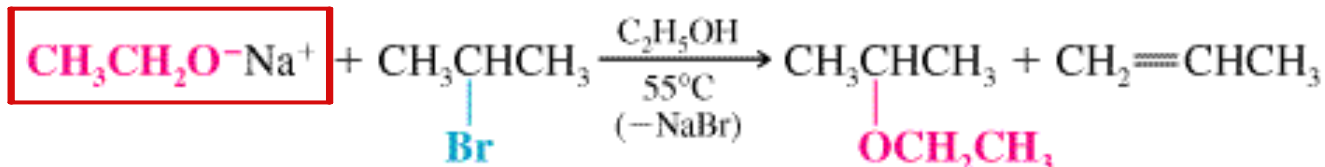
S_N2 vs. E2 – Base / Nucleophile



Size of base/nucleophile



Basicity and Polarizability



Substitution (S_N2, S_N1) vs. Elimination (E2, E1)



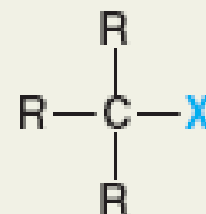
Methyl



1°



2°



3°

Bimolecular Reactions Only

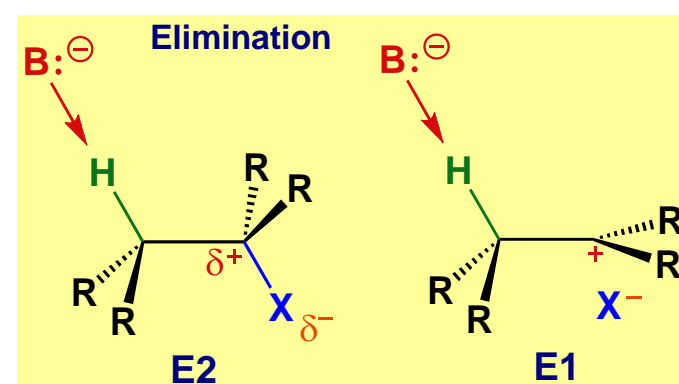
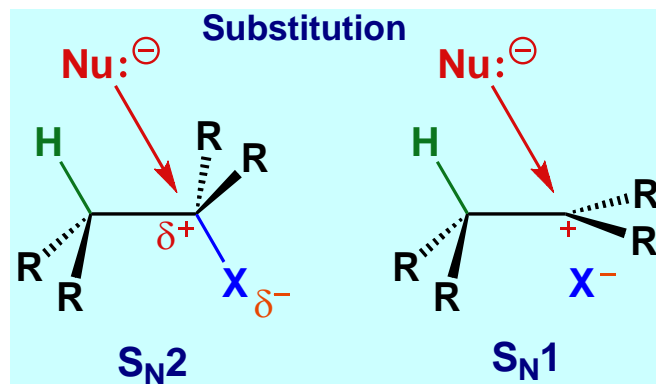
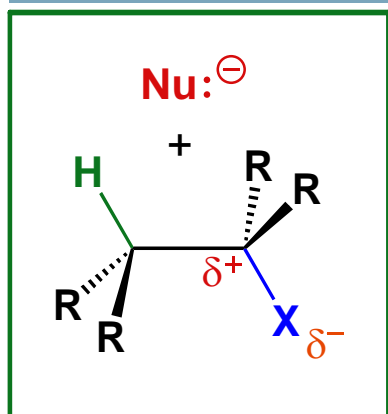
Gives S_N2 reactions

Gives mainly S_N2 except with a hindered strong base [e.g., (CH₃)₃CO⁻] and then gives mainly E2

Gives mainly S_N2 with weak bases (e.g., I⁻, CN⁻, RCO₂⁻) and mainly E2 with strong bases (e.g., RO⁻)

S_N1/E1 or E2

No S_N2 reaction. In solvolysis gives S_N1/E1, and at lower temperatures S_N1 is favored. When a strong base (e.g., RO⁻) is used, E2 predominates.

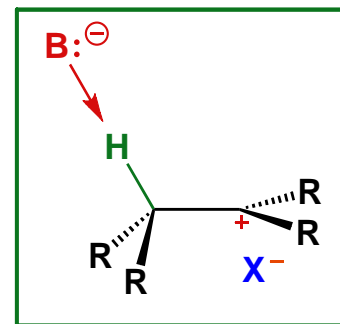
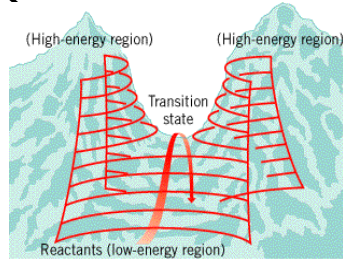
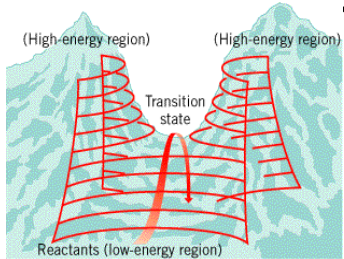
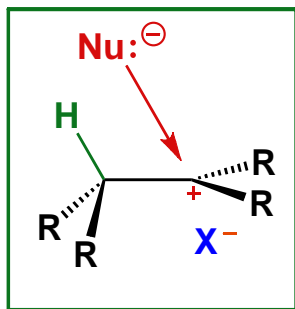
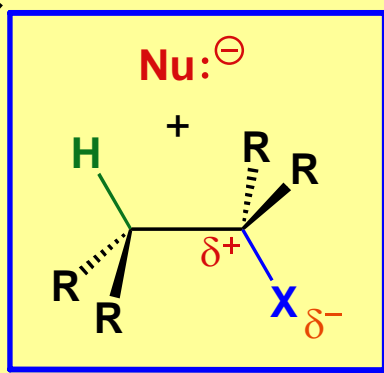
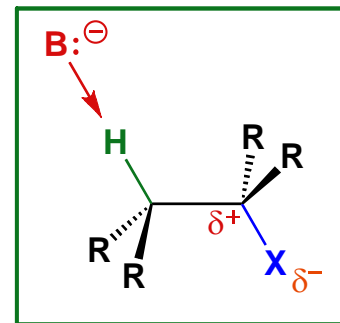
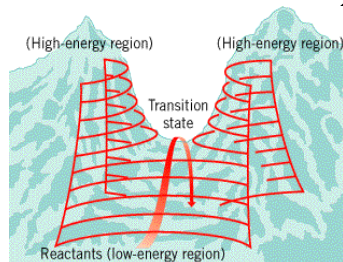
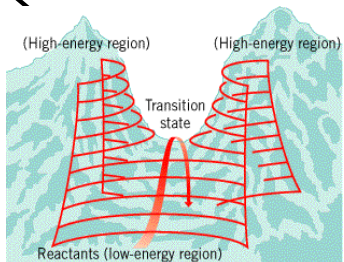
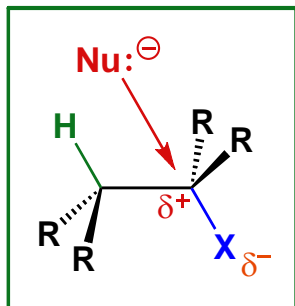


Substitution (S_N2, S_N1) vs. Elimination (E2, E1)

S_N2

E2

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



S_N1

Product

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

E1

