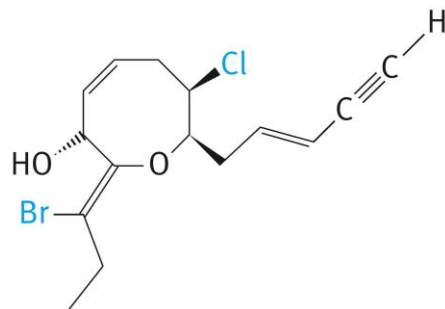
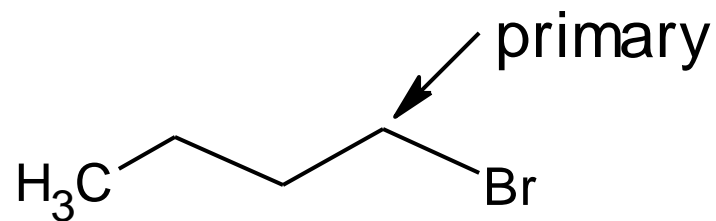


Chapter 6: Organic Halogen Compounds; Substitution and Elimination Reactions

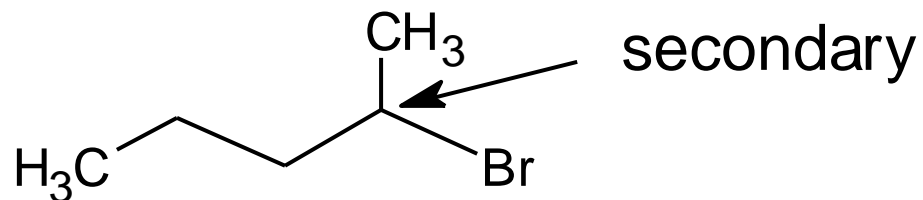
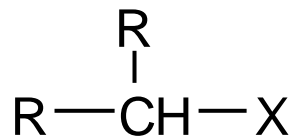


Types of Alkyl halides:

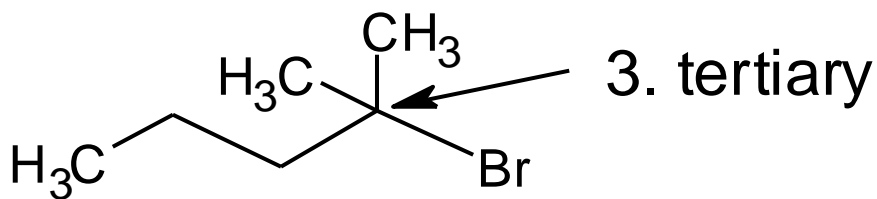
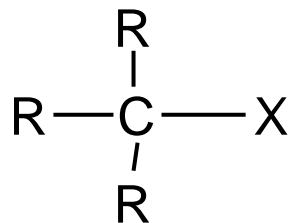
1. primary



2. secondary



3. tertiary



Reactions of Alkylhalides

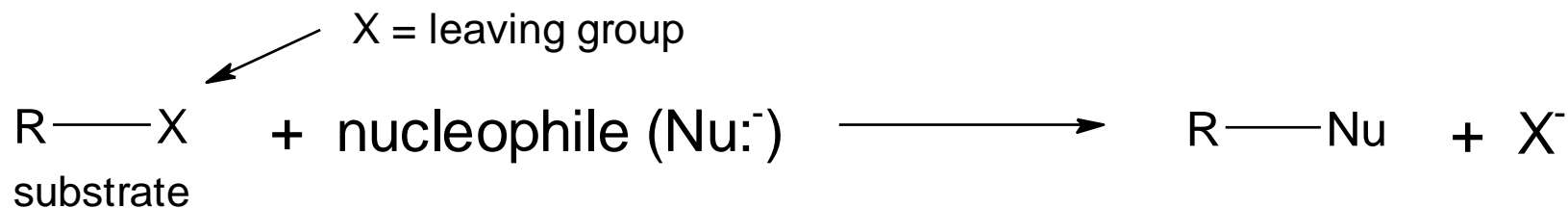
1- Nucleophilic Substitution

Elements of nucleophilic substitution reactions

A- Nucleophile

B- Substrate

C- Leaving group



Name	Formula	Name	Comments
oxophiles			
hydroxide	$\text{R}-\ddot{\text{O}}\text{H}$	alcohol	
alkoxide	$\text{R}-\ddot{\text{O}}\text{R}$	ether	
water	$\text{R}-\overset{+}{\text{O}}\begin{matrix} \text{H} \\ \diagup \\ \text{H} \end{matrix}$	alkyloxonium ion	These ions lose a proton and the products are alcohols and ethers. $\xrightarrow{-\text{H}^+} \begin{matrix} \ddot{\text{O}}\text{H} \\ \text{R} \end{matrix}$ (alcohol) $\xrightarrow{-\text{H}^+} \begin{matrix} \ddot{\text{O}} \\ \text{R} \end{matrix}$ (ether)
alcohol	$\text{R}-\overset{+}{\text{O}}\begin{matrix} \text{R} \\ \diagup \\ \text{H} \end{matrix}$	dialkyloxonium ion	
carboxylate	$\text{R}-\overset{\text{O}}{\parallel}{\ddot{\text{O}}}\text{C}-\text{R}$	ester	
nitrogenophiles			
ammonia	$\text{R}-\overset{+}{\text{N}}\text{H}_3$	alkylammonium ion	With a base, these ions readily lose a proton to give amines. $\xrightarrow{-\text{H}^+} \begin{matrix} \ddot{\text{N}}\text{H}_2 \\ \text{R} \end{matrix}$ $\xrightarrow{-\text{H}^+} \begin{matrix} \ddot{\text{N}}\text{H} \\ \text{R}_2 \end{matrix}$ $\xrightarrow{-\text{H}^+} \text{R}_3\text{N}:$
primary amine	$\text{R}-\overset{+}{\text{N}}\text{H}_2\text{R}$	dialkylammonium ion	
secondary amine	$\text{R}-\overset{+}{\text{N}}\text{HR}_2$	trialkylammonium ion	
tertiary amine	$\text{R}-\overset{+}{\text{N}}\text{R}_3$	tetraalkylammonium ion	

Sulfur nucleophiles

10. HS^- hydrosulfide $\text{R}-\ddot{\text{S}}\text{H}$ thiol
11. RS^- mercaptide $\text{R}-\ddot{\text{S}}\text{R}$ thioether (sulfide)
12. R_2S^+ thioether $\text{R}-\overset{+}{\text{S}}\text{R}_2$ trialkylsulfonium ion

Halogen nucleophiles

13. $:\text{I}^-$ iodide $\text{R}-\ddot{\text{I}}$ alkyl iodide

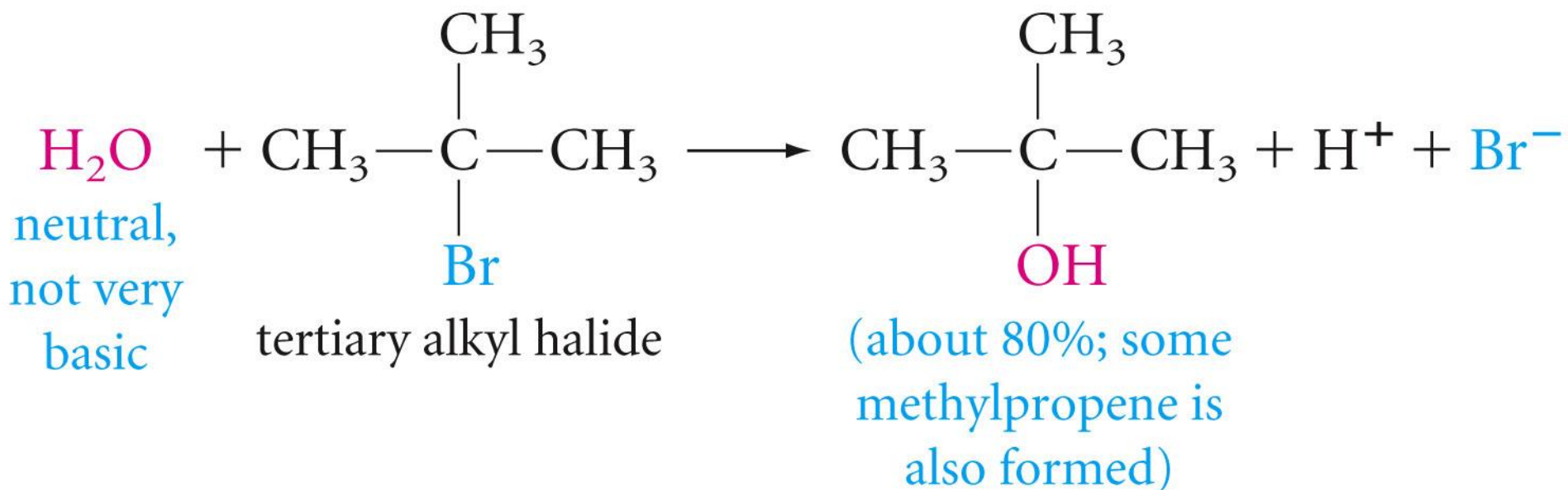
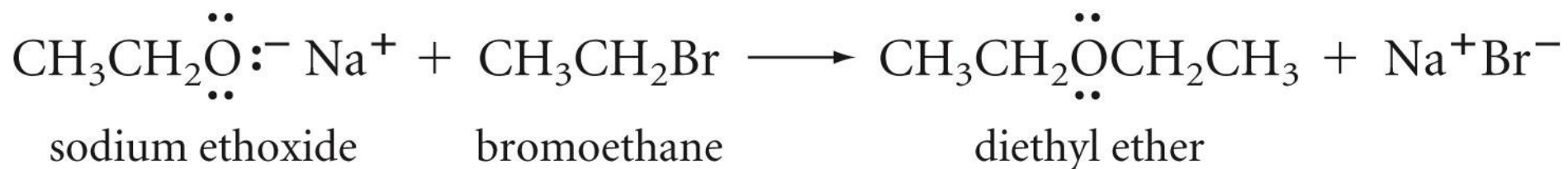
The usual solvent is acetone. Sodium iodide is soluble in acetone, but sodium bromide and sodium chloride are not.

Carbon nucleophiles

14. $^-:\text{C}\equiv\text{N}:$ cyanide $\text{R}-\text{C}\equiv\text{N}:$ alkyl cyanide (nitrile)
15. $^-:\text{C}\equiv\text{CR}$ acetylide $\text{R}-\text{C}\equiv\text{CR}$ alkyne

Sometimes the isonitrile, $\text{R}-\overset{+}{\text{N}}\equiv\overset{-}{\text{C}}:$, is formed.

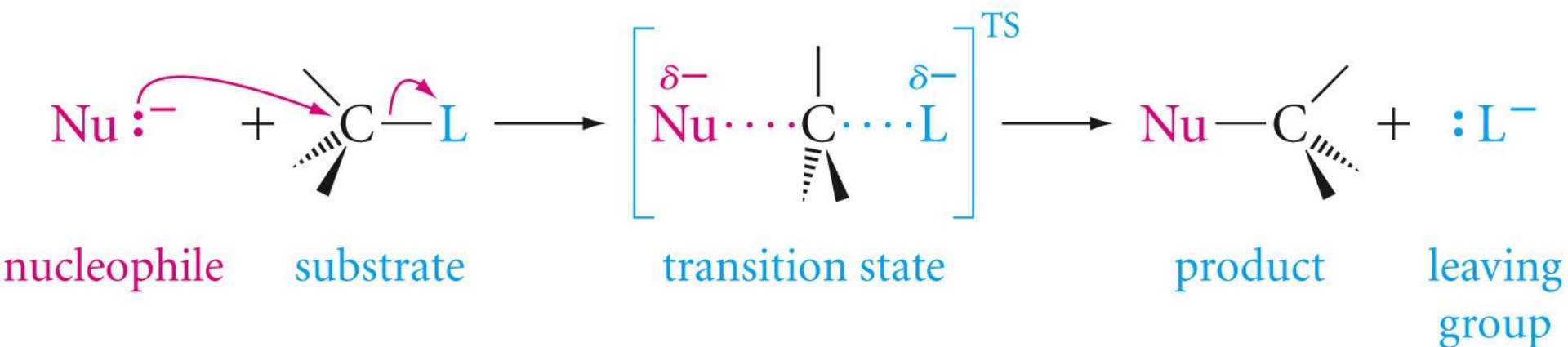
Examples



Nucleophilic Substitution Mechanism

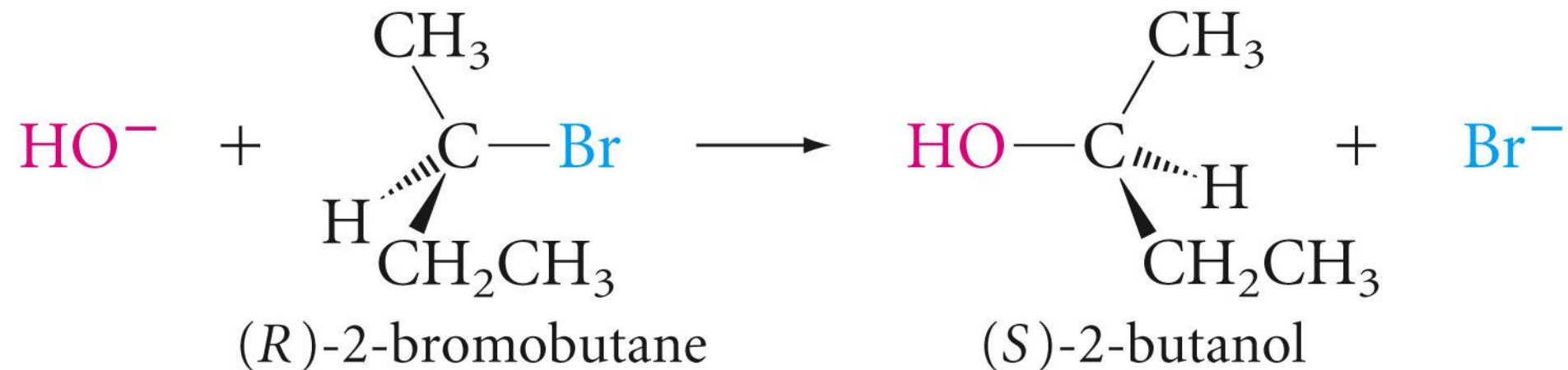
molecular nucleophilic substitution mechanism

S_N2 Mechanism



Characteristic of S_N2 mechanism

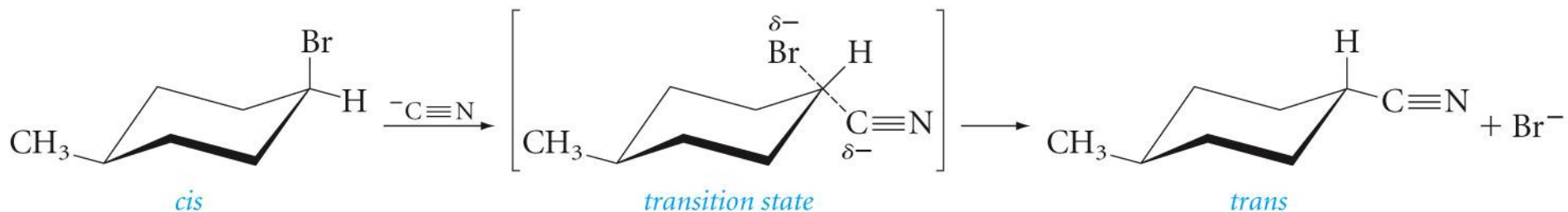
1. Rate of reaction = constant $[\text{alkylhalide}][\text{Nucleophile}]$
2. Inversion in stereochemistry of the product compared to the reactant
3. primary halide $>$ secondary $>$ tertiary



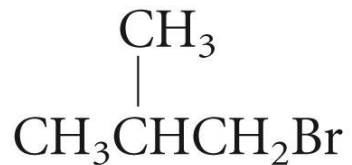
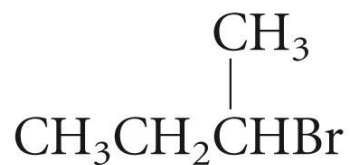
S_N2 displacement reactions occur with inversion of configuration. For example, if we treat *(R)*-2-bromobutane with sodium hydroxide, we obtain *(S)*-2-butanol

Example;

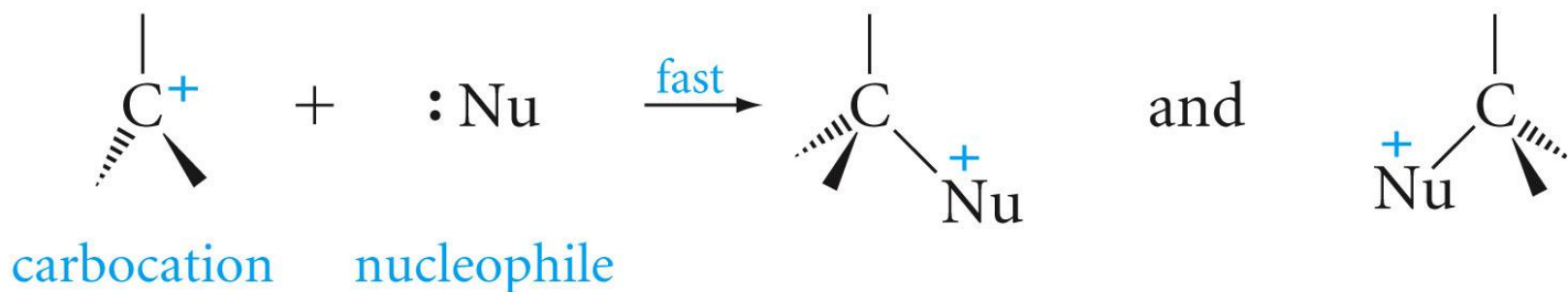
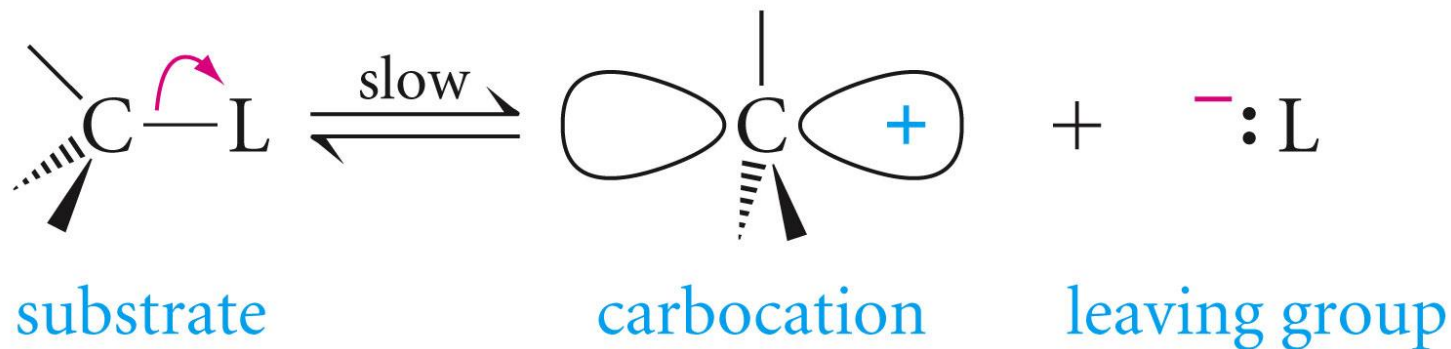
Predict the product of the S_N2 reaction of *cis*-4-methylcyclohexyl bromide with cyanide ion



Arrange the following compounds in order of decreasing S_N2 reactivity toward sodium ethoxide

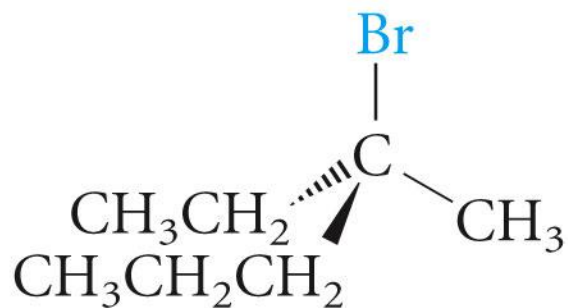


The S_N1 Mechanism

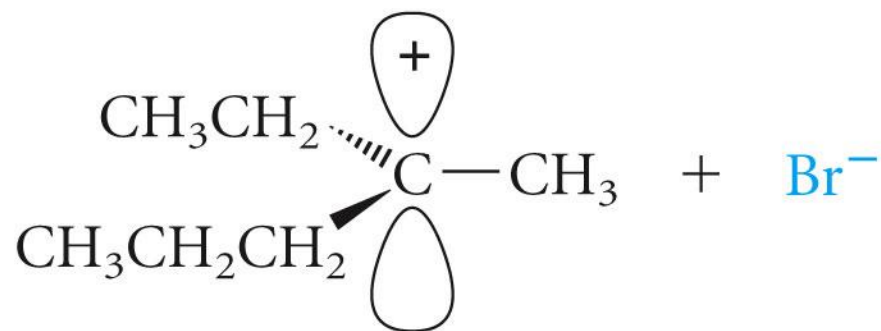


Characteristic of S_N1 mechanism

1. Rate of reaction = constant [alkylhalide]
2. Inversion and retention in stereochemistry of the product compared to the reactant. Forming racemic mixture.
3. tertiary halide > secondary > primary halide

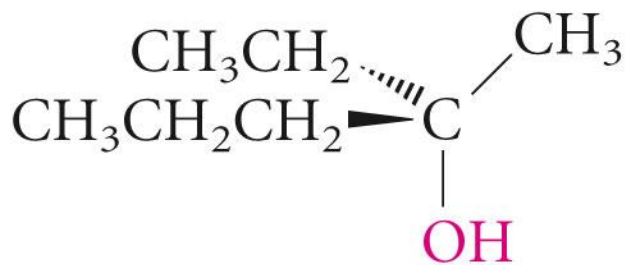


(R)-3-bromo-3-methylhexane



carbocation intermediate

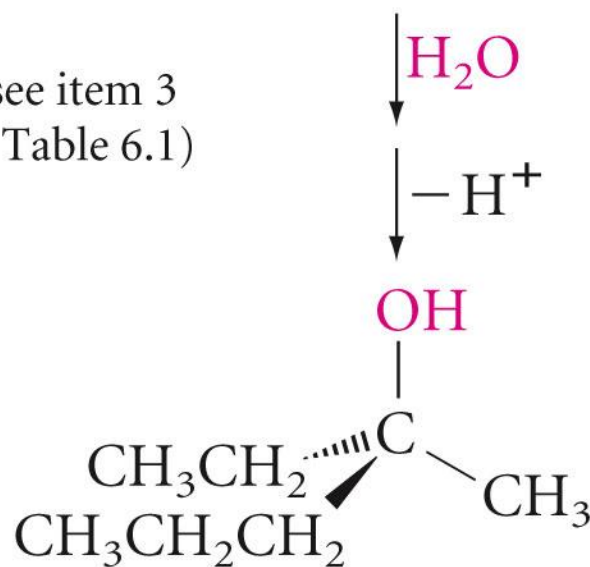
(see item 3
in Table 6.1)



50% *S*

(product from attack on the
bottom face of the carbocation)

+



50% *R*

(product from attack on the
top face of the carbocation)

Table 6.2 Comparison of S_N2 and S_N1 Substitutions

Variables	S_N2	S_N1
Halide structure		
Primary or CH_3	Common	Rarely*
Secondary	Sometimes	Sometimes
Tertiary	Rarely	Common
Stereochemistry	Inversion	Racemization
Solvent	Rate is retarded by polar protic solvents and increased by polar aprotic solvents	Because the intermediates are ions, the rate is increased by polar solvents
Nucleophile	Rate depends on nucleophile concentration; mechanism is favored when the nucleophile is an anion	Rate is independent of nucleophile concentration; mechanism is more likely with neutral nucleophiles

*Allyl and benzyl substrates are the common exceptions (see Problem 6.7b).

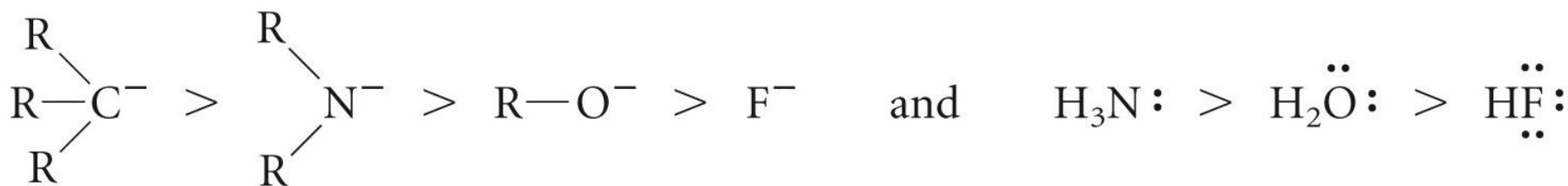
1. Negative ions are more nucleophilic, or better suppliers, than the corresponding neutral molecules.



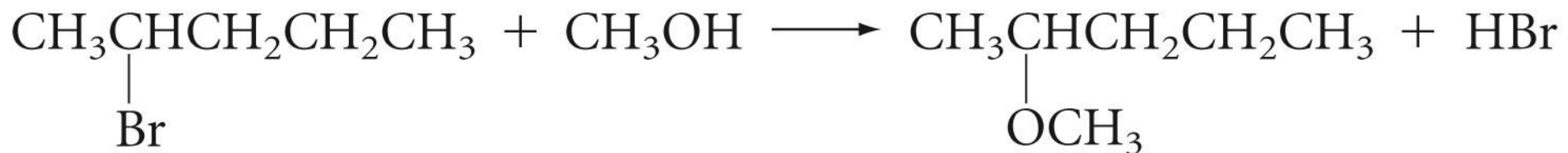
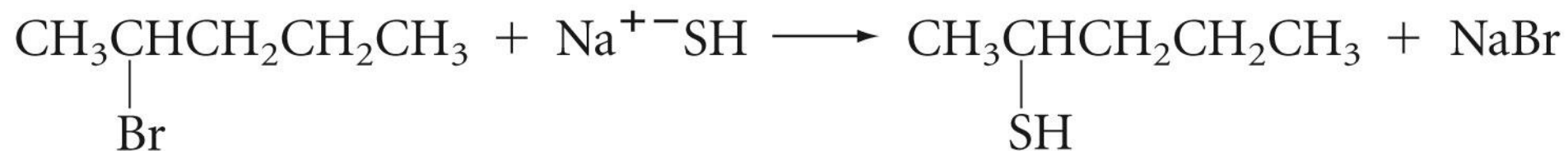
2. Elements low in the periodic table tend to be more nucleophilic than elements above them in the same column



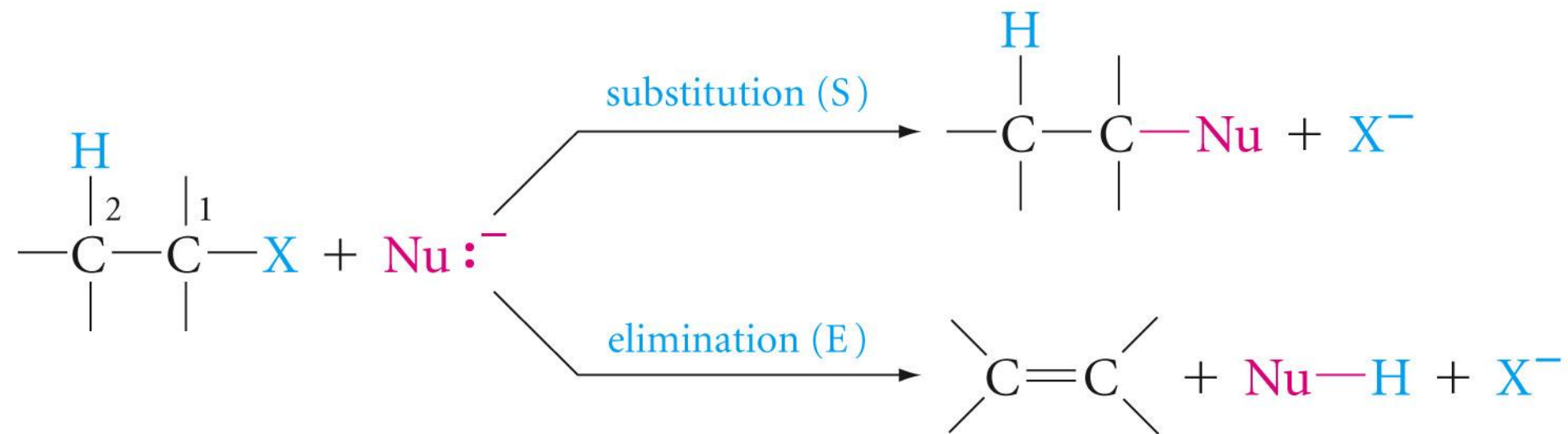
3. Across a row in the periodic table, more electronegative elements (the more tightly an element holds electron to itself) tend to be less nucleophilic.

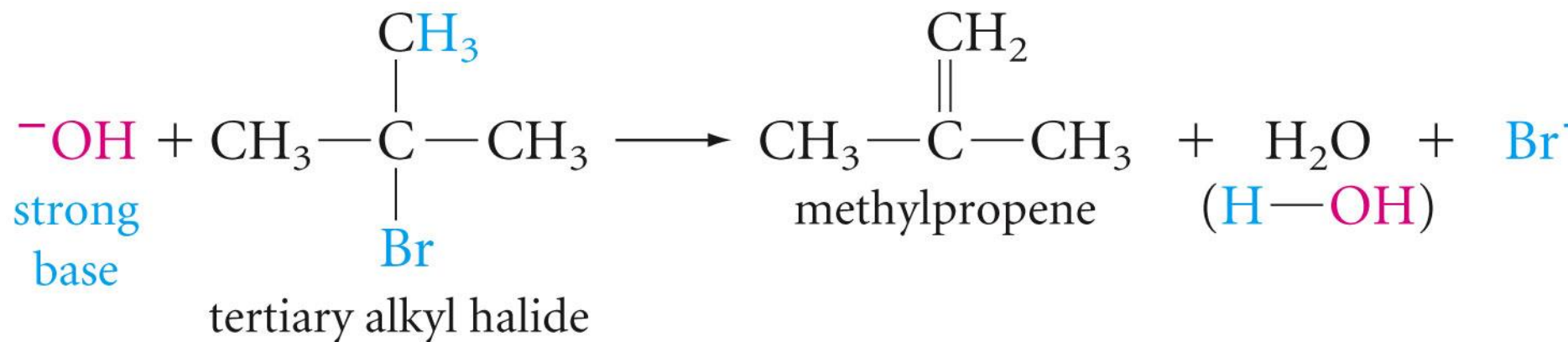
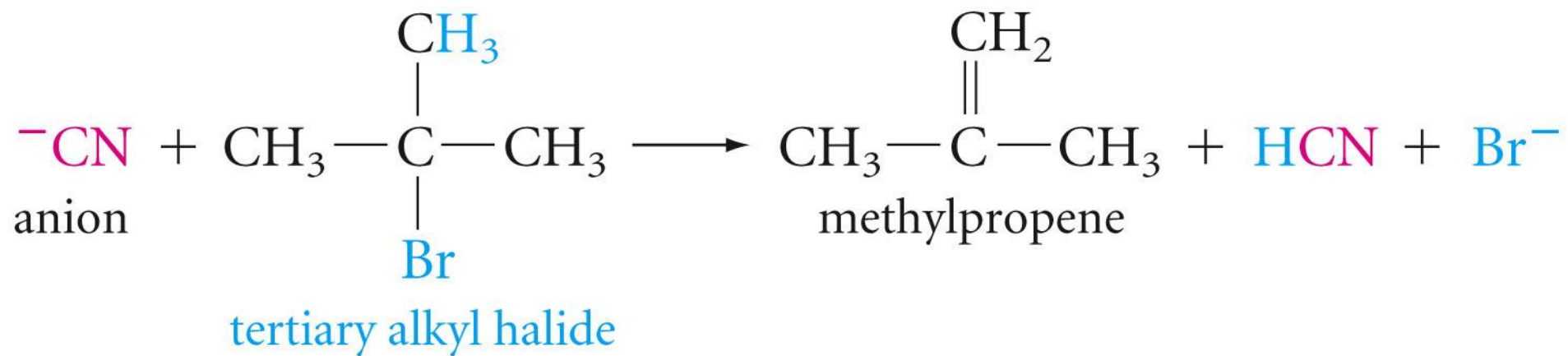


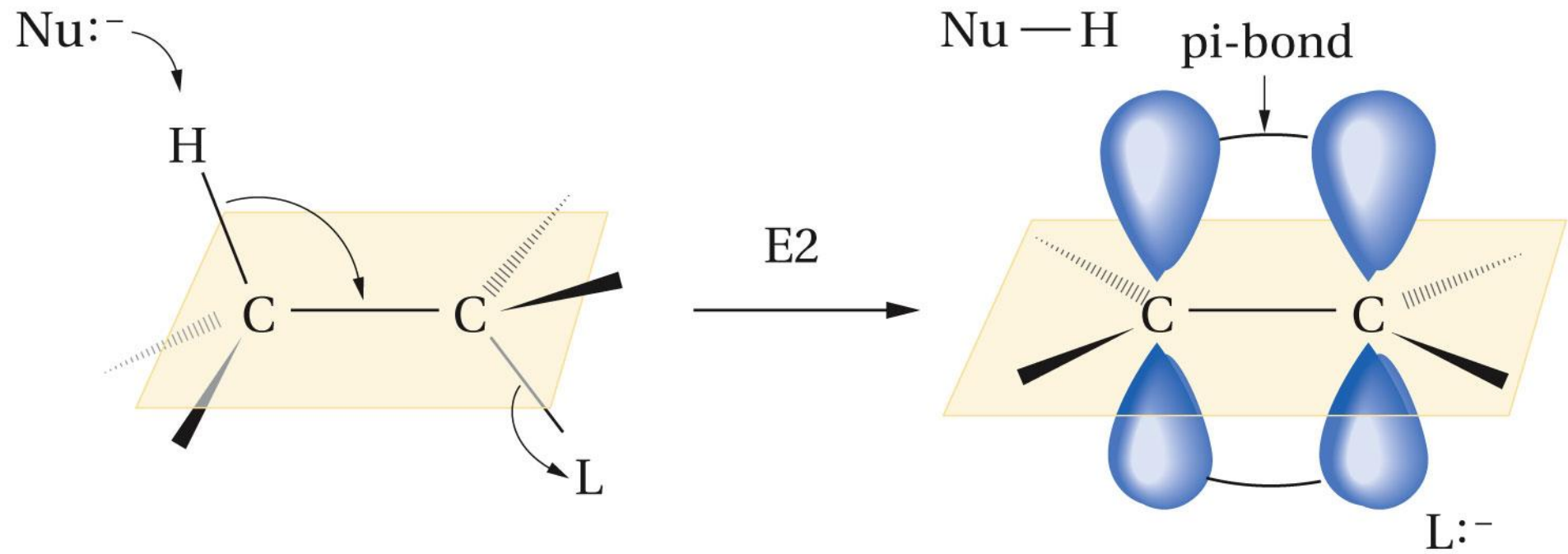
Which mechanism, S_N1 or S_N2, would you predict for each of the following reactions?



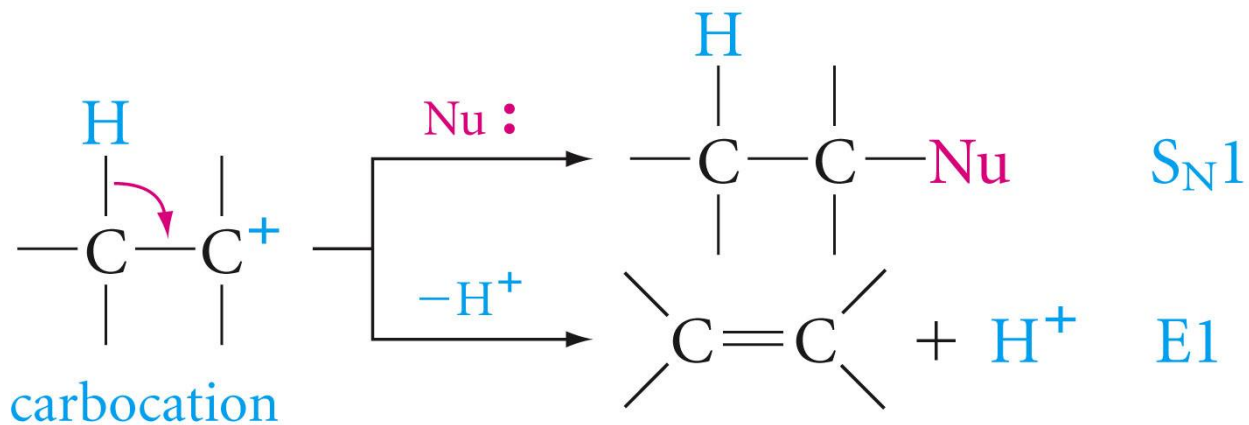
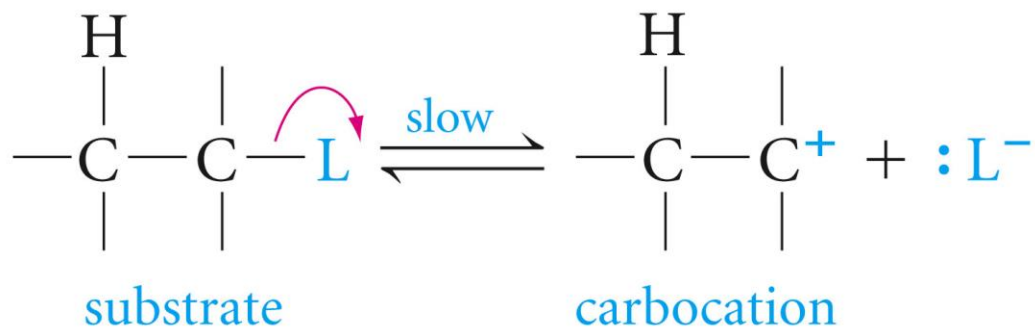
2- Dehydrohalogenation, and Elimination Reaction; The E2 and E1 Mechanisms





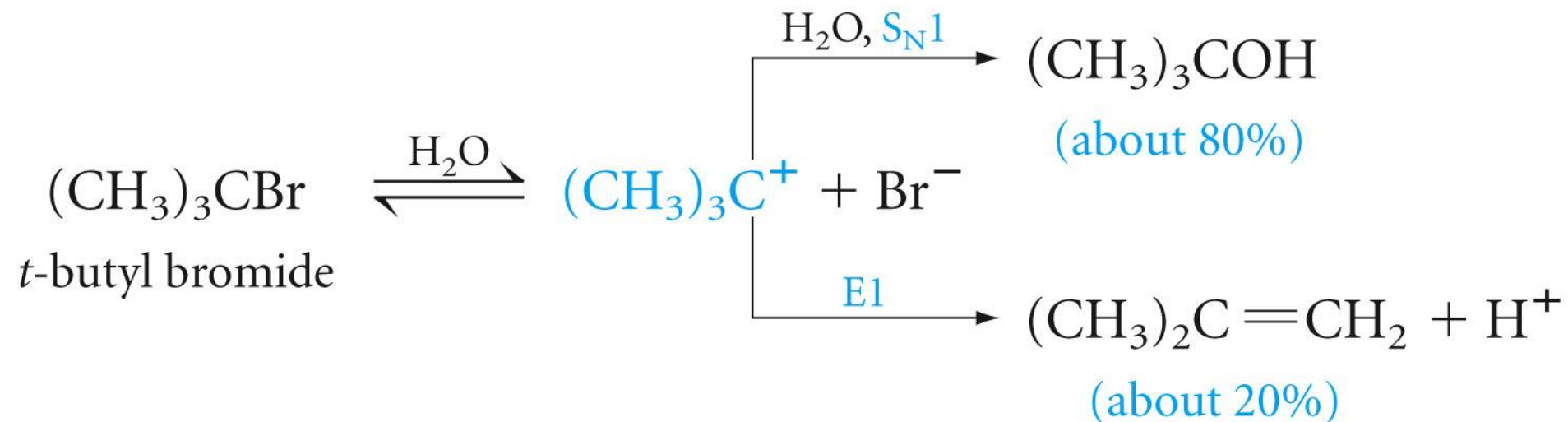


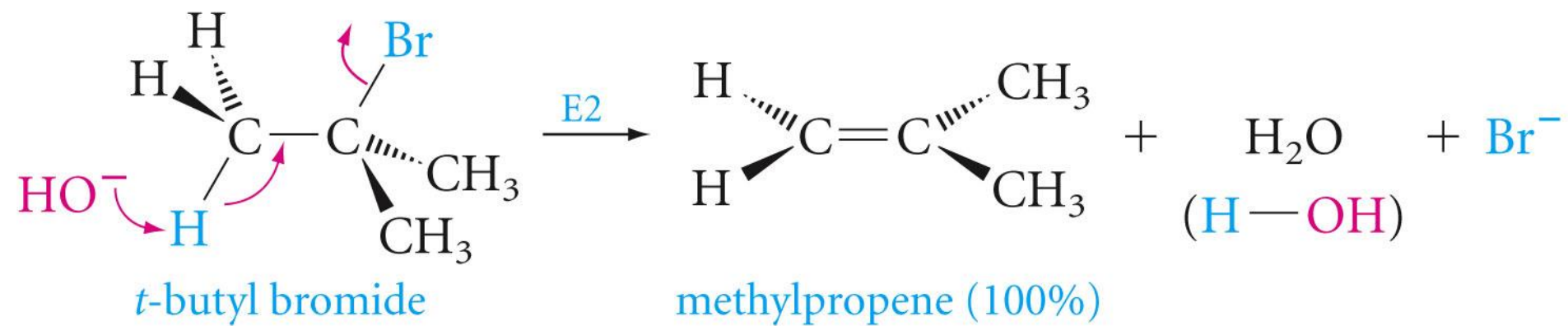
E1 mechanism



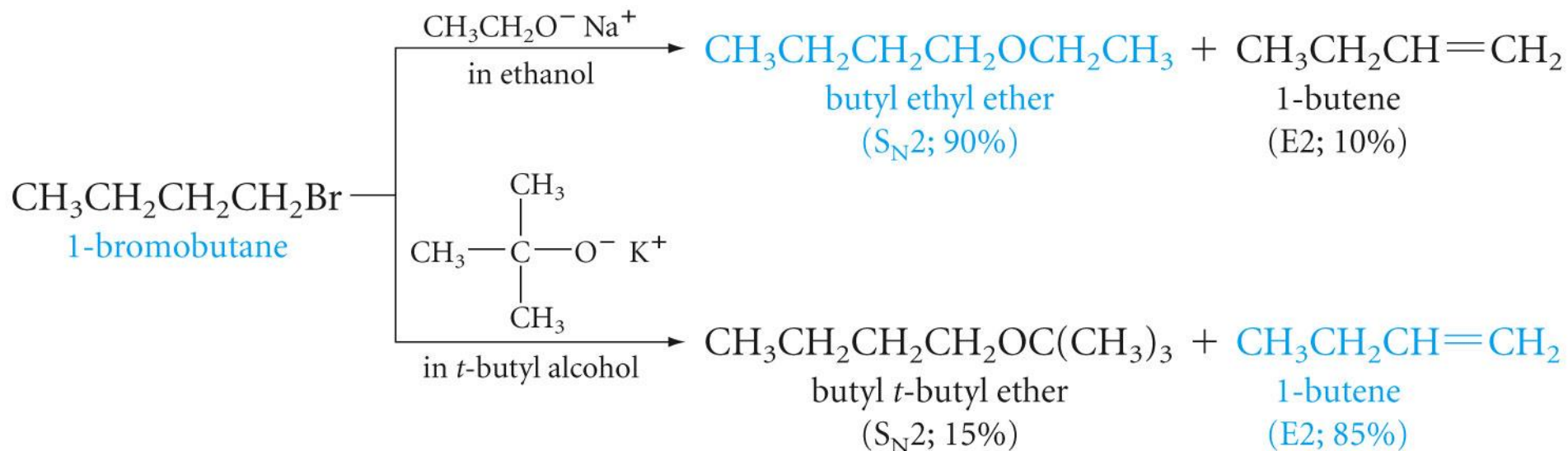
Substitution and Elimination in Competition

Tertiary Halides





Primary Halides



Secondary Halides

