Objective 11

Apply Reactivity Principles to Substitution and Elimination Reactions:
compare size and strength of nucleophile to predict major product

Given Reactants ----> Predict Products

How to figure out how reactants react.

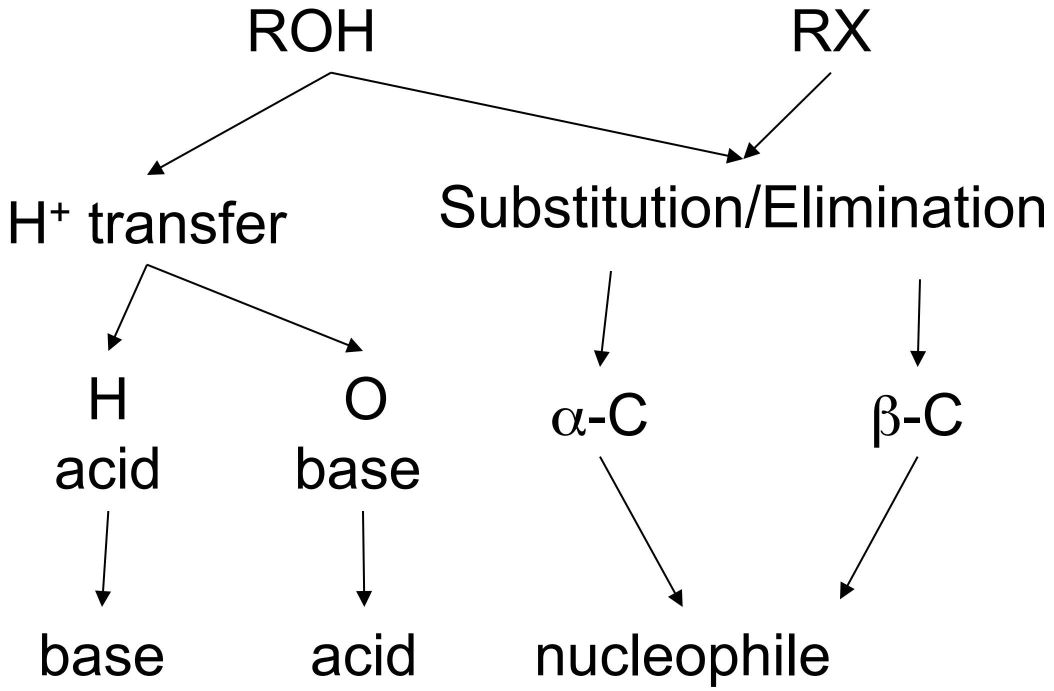
Problem Solving Strategy / Protocol / Sequence of Steps:

Identify functional group.

What reaction type occurs with this functional group?

At what atom does this reaction type occur?

What reagent is needed for this reaction type to occur?



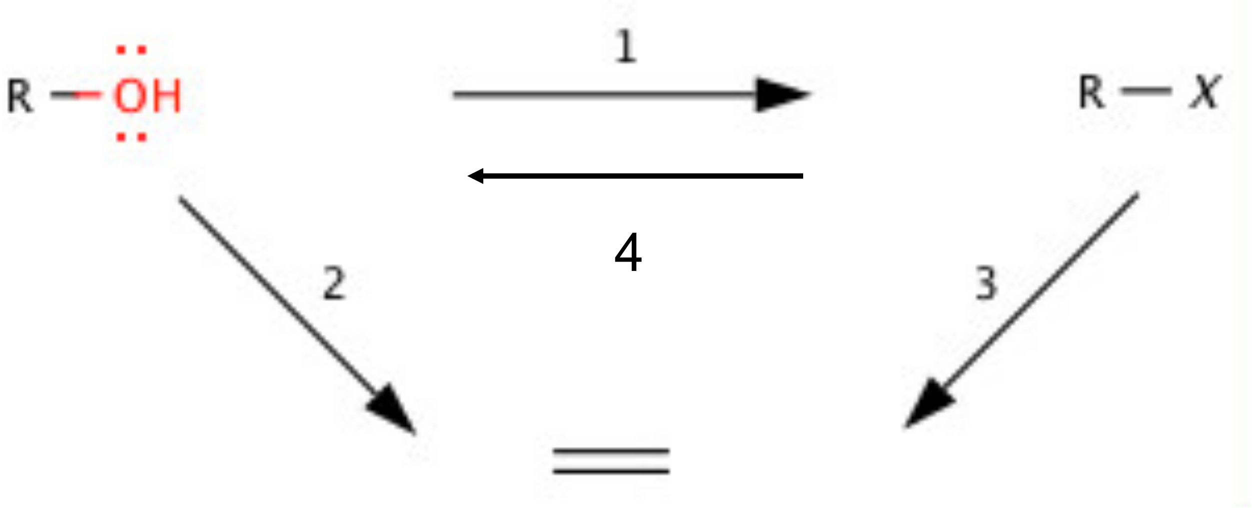
ROH RX

H^+ transfer Substitution/Elimination

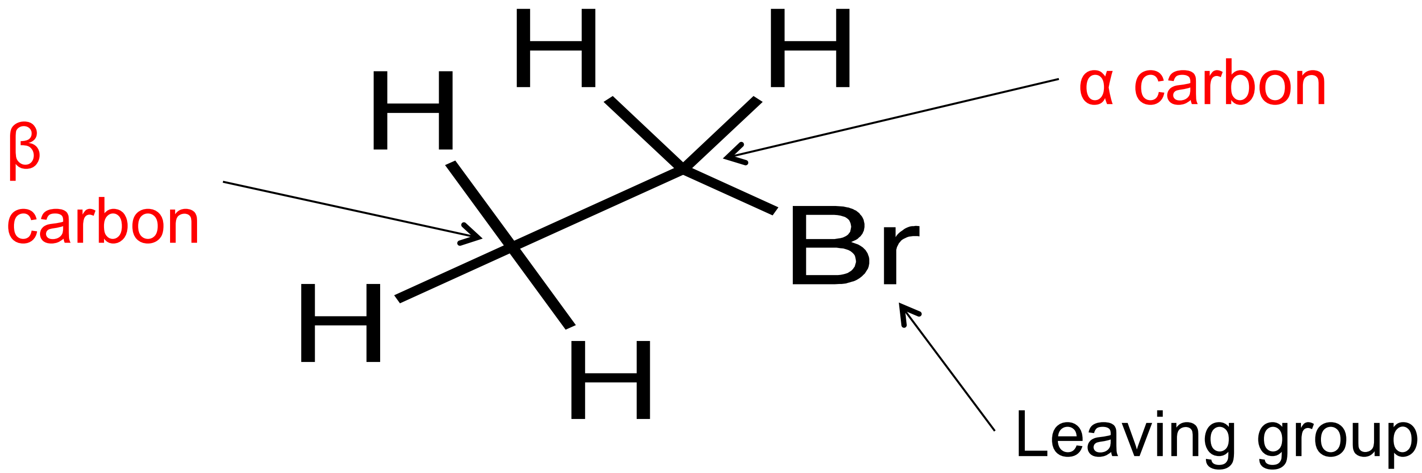
H acid O base α-C β-C

base acid nucleophile

Summary of Functional Group Reactions: (so far)

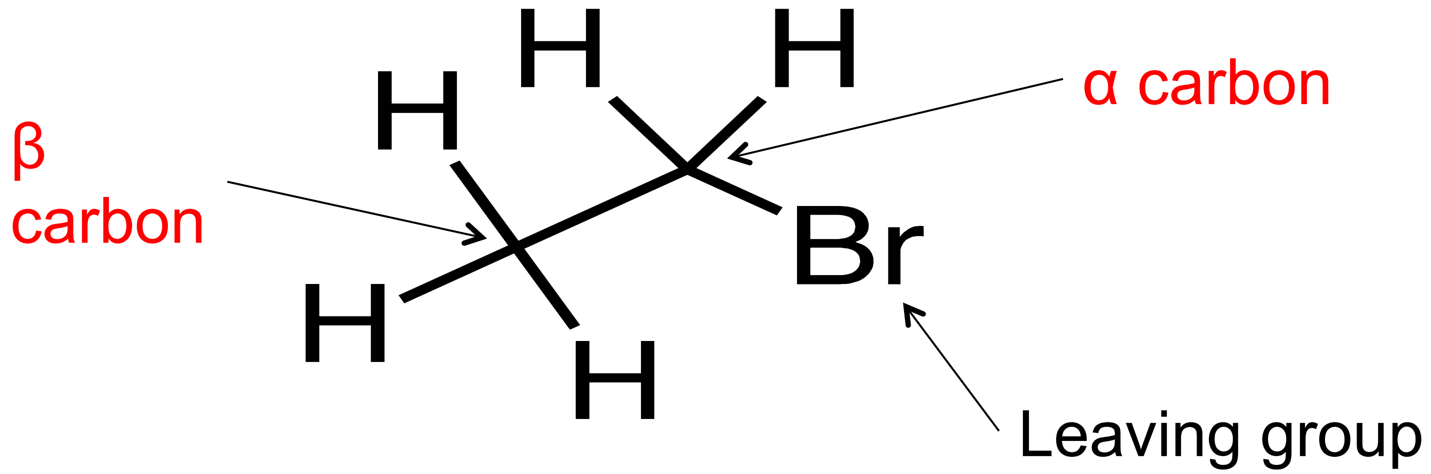


Reaction	Reaction Type (Substitution/Elimination)	Reaction Conditions
1		
2		
3		
4		



<u>Intro to Reactivity</u>: A nucleophile (Nu:$^-$) can react with the:

a. α carbon	TRUE	FALSE
b. β carbon	TRUE	FALSE
c. Br	TRUE	FALSE
d. H bonded to α carbon	TRUE	FALSE
e. H bonded to β carbon	TRUE	FALSE



Intro to Reactivity: A nucleophile (Nu:$^-$) can react with the:

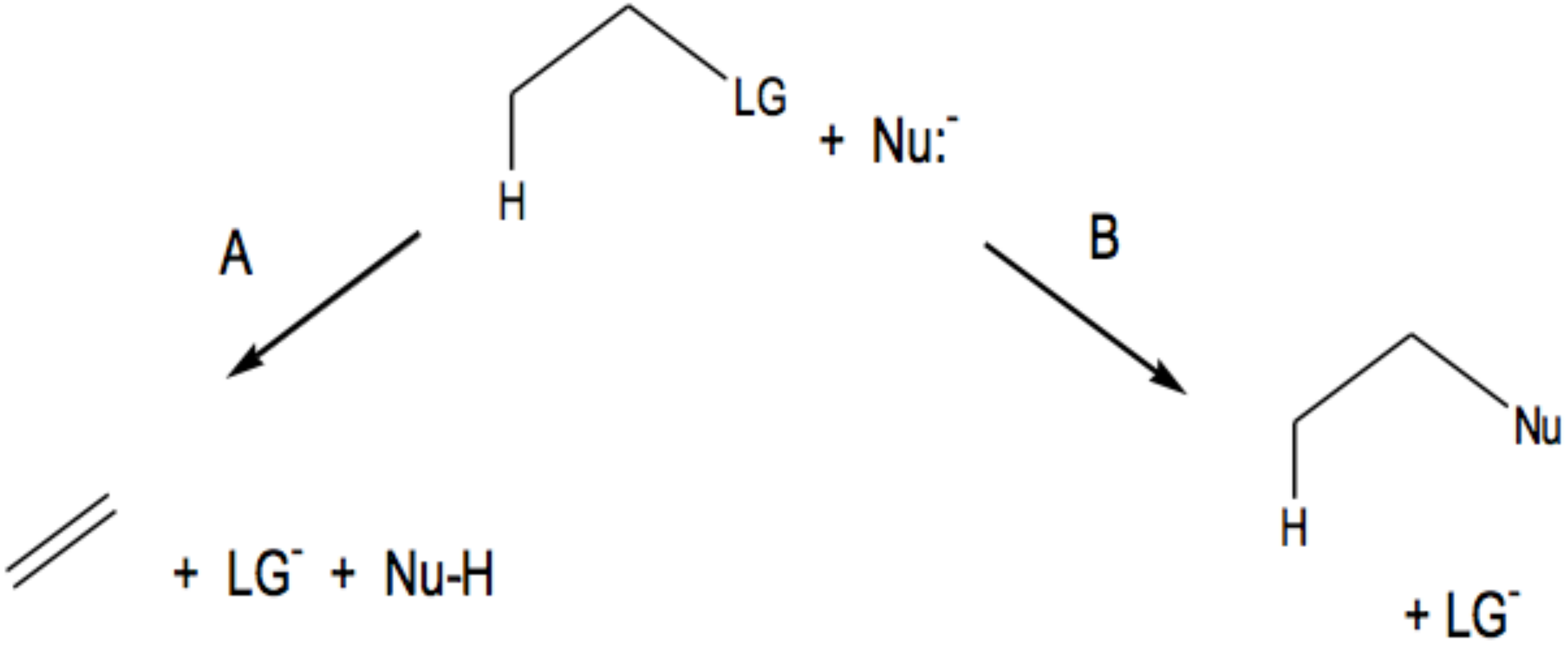
1. α carbon (carbon bonded to the Br) = Substitution Reaction

2. H bonded to β carbon (H bonded to the carbon adjacent to the α carbon = Elimination Reaction

Substitution and Elimination Reactions:

Similar: *Involve a Nucleophile and Leaving Group*

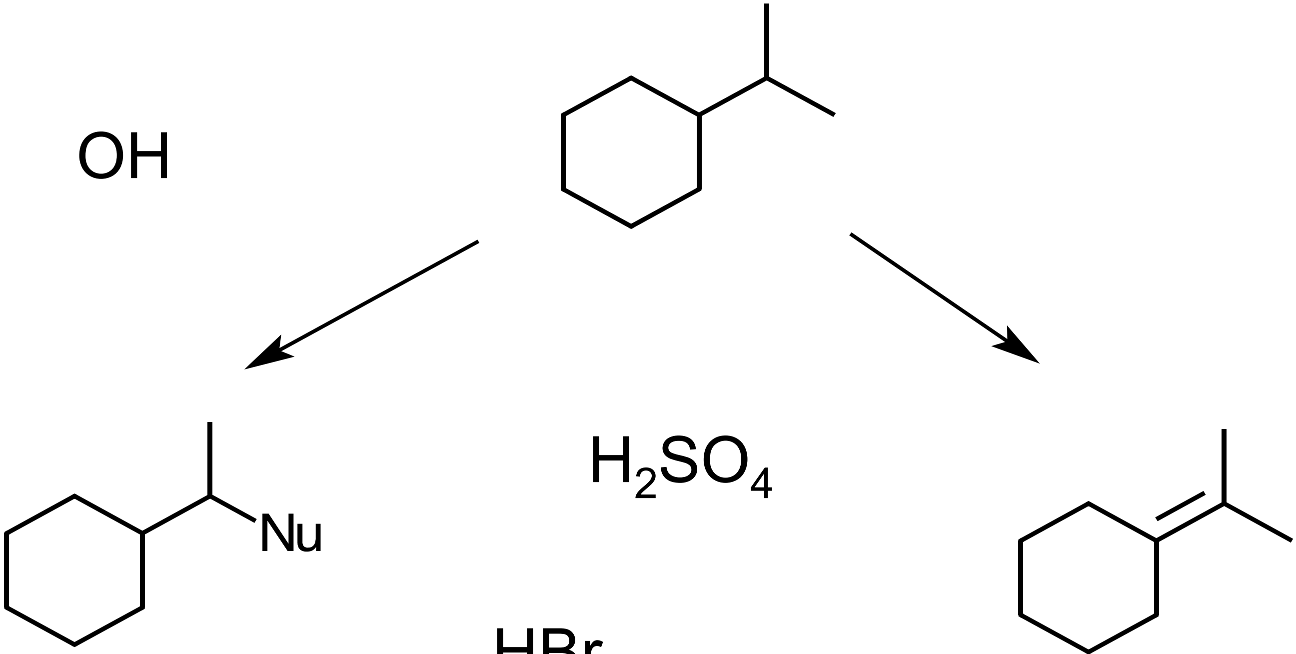
Different: *$Nu:^-$ Reacts at Different Atom*



where LG = leaving group and $Nu:^-$ = nucleophile

1. Circle the atoms at which a reaction occurs in the reactant (substrate).
2. a. What type of reaction is A? Use curved arrows to show reaction.
b. What type of reaction is B? Use curved arrows to show reaction.

What "Ingredients" are Needed for a Substitution or Elimination Reaction?



OH

Br

NaBr

H_2SO_4

HBr

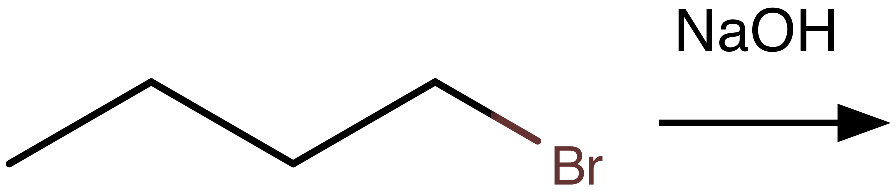
LG

$Nu:^-$ = NH_3, CH_3OH

Place each "ingredient" in the "right" place.
Draw the structure of each reactant and product.

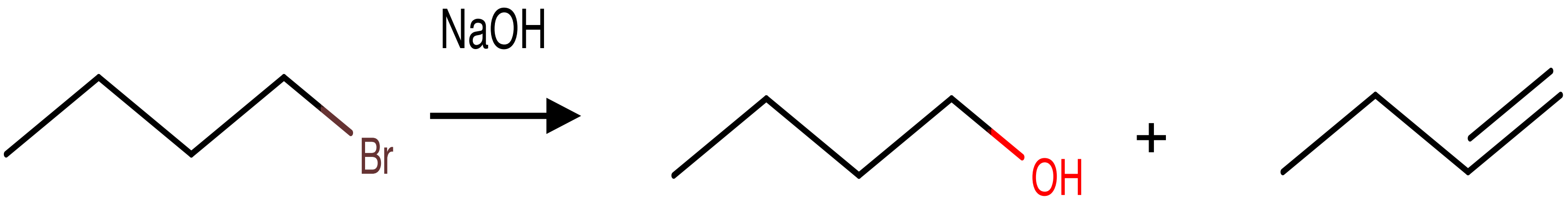
Objective:

1. Identify the β carbon in reactant.
2. Predict the Substitution and Elimination products of this reaction:



Objective:

Which product, substitution or elimination, is the major product? Why?

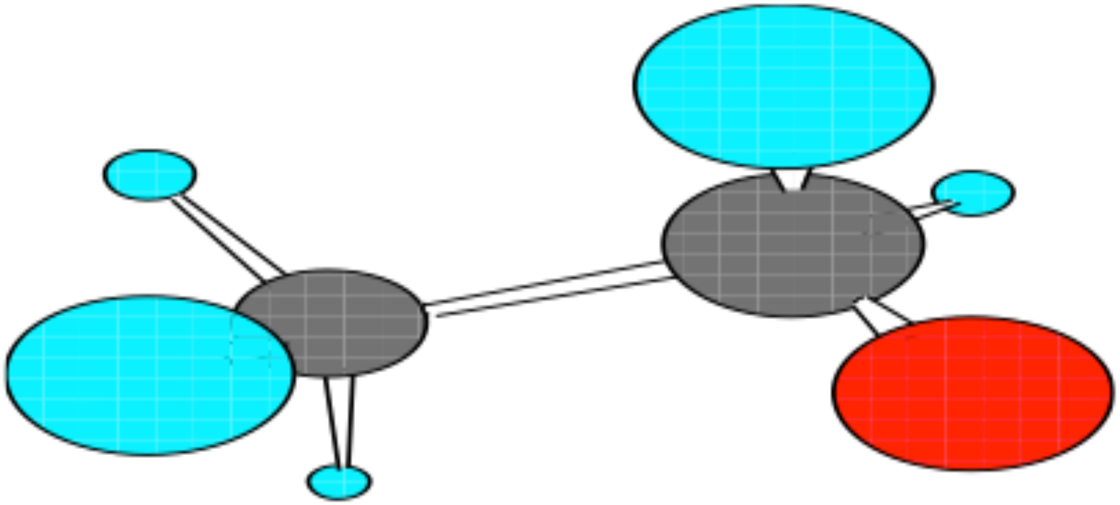


Substitution

Elimination

Substitution and Elimination Reactions Compete for Nu:⁻

Substrate: H-C-C-LG   Leaving Group in red



Substitution: Nu:⁻ reacts at α -C.

Elimination: Nu:⁻ reacts at H bonded to β -C.

Factors: Type of C (1°, 2°, 3°) bonded to LG
Reactivity of α -C vs. H bonded to β -C
Access to α -C by Nu:⁻
Access to H bonded to β -C by Nu:⁻
Nu:⁻: Size and Strength
Good or poor LG

W
H
O

W
I
N
S
?

Elimination is Usually Favored Over Substitution

"Characteristic reactions of alkyl halides with Lewis bases is ***elimination***." (Carey, 8th ed., p. 344)

2^o and 3^o R-X + strong base favor elimination.

1^o R-X + small, strong bases (e.g., NaOEt) ***favor substitution.***

1^o R-X + large, strong bases (e.g., NaO-t-Bu) ***favor elimination.***

"As crowding at the carbon that bears the leaving group decreases, the rate of nucleophilic substitution becomes faster than the rate of elimination." (Carey, 8th ed., p. 344)

1^o and 2^o R-X + weak base favor substitution.

Weak Base is a base weaker than OH^-.

"A second factor that can tip the balance in favor of substitution is weak basicity of the nucleophile." (Carey, 8th ed., p. 345)

3^o R-X without anionic base favor substitution.

Use solvent as $Nu:^-$.

"Usually substitution predominates over elimination in 3^o R-X only when anionic Lewis bases are absent." (Carey, 8th ed., p. 345)

Nucleophile Strength, Carey, “Organic Chemistry”, 8th ed., p. 333, Table 8.4

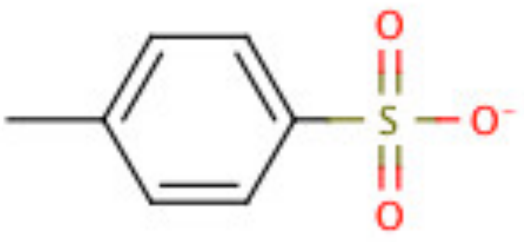
Reactivity Class	Nucleophile	Reactivity
Very Good	I^-, HS^-, RS^-	$> 10^5$
Good	Br^-, OH^-, RO^-, CN^-, N_3^-	10^4
Fair	NH_3, Cl^-, F^-, RCO_2^-	10^3
Weak	H_2O, ROH	1
Very Weak	RCO_2H	10^{-2}

Nu:$^-$ strength matches Base strength *<u>except</u>* for I^-, Br^-, Cl^-, F^-.

a. Which Nu:$^-$ are big? Which Nu:$^-$ are small? (Hint: See R group)
b. Which Nu:$^-$ favors substitution?
c. Which Nu:$^-$ favors elimination?

Leaving Groups, Carey, “Organic Chemistry”, 8th ed., p. 348, Table 8.9

Excellent	TsO^-, NH_3
Very Good	I^-, H_2O
Good	Br^-
Fair	Cl^-
Poor	F^-
Very Poor	OH^-, NH_2^-, RO^-



Tosylate = TsO^-

Best LG are weak bases.

How does a LG affect reaction rate?

Another way to make -OH into a better LG:

Tosyl chloride

1. If a $Nu:^-$ has equal access to a α-C or H bonded to a β-C, it will react at the:
a. α-C
b. H bonded to a β-C

2. The α-C is ______ electrophilic than a H bonded to a β-C.
a. More
b. Less
c. Same

3. A weak $Nu:^-$ reacts at the:
a. α-C
b. H bonded to a β-C

4. A large $Nu:^-$ reacts at the:
a. α-C
b. H bonded to a β-C

1. If a $Nu:^-$ has equal access to a α-C or H bonded to a β-C, it will react at the:

a. [✓ α-C] ***See Question 2***
b. H bonded to a β-C

2. The α-C is ______ electrophilic than a H bonded to a β-C.

a. [✓ More]
b. Less
c. Same

3. A weak $Nu:^-$ reacts at the:

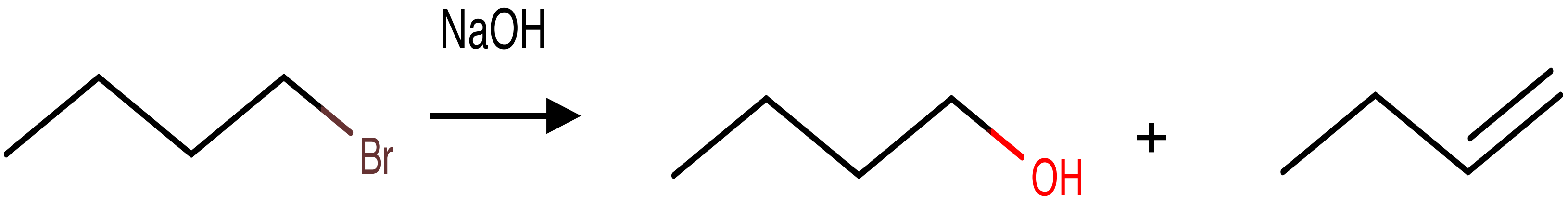
a. [✓ α-C] ***See Question 2***
b. H bonded to a β-C

4. A large $Nu:^-$ reacts at the:

a. α-C
b. [✓ H bonded to a β-C] ***Easier access***

Objective:

Which product, substitution or elimination, is the major product? Why?



Substitution

major
product

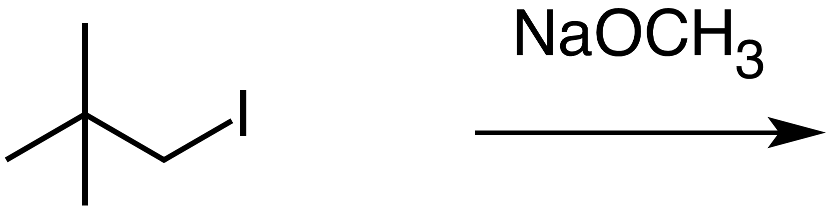
Elimination

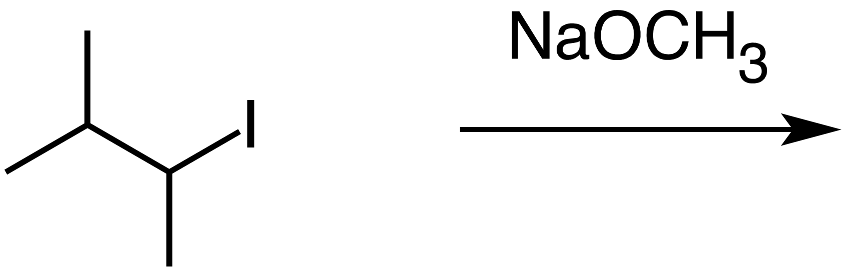
minor
product

1-bromobutane = 1^{o} RX

OH^{-} = strong base (Nu:$^{-}$)

Objective: Predict the Substitution and Elimination products of each reaction:





Predict the product distribution in each reaction.
In other words, does more substitution product form or more elimination product or the ***same*** amount of each.

Determine R-X type.
ID the nucleophile as big or small, strong or weak.
Predict the substitution product and elimination product.
Which product is the major product? Why?