

# Learning Guide for Chapter 10 - Alkyl Halides II

## I. Elimination Reactions of Alkyl Halides

Introduction

Mechanisms

Beta hydrogens, constitutional isomers, and stereoisomers

E2 vs E1

Strong and Weak Bases

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Rearrangements

Stereochemistry

Solvents

Eliminations of Aryl and Vinyl Halides

## II. Substitution vs Elimination

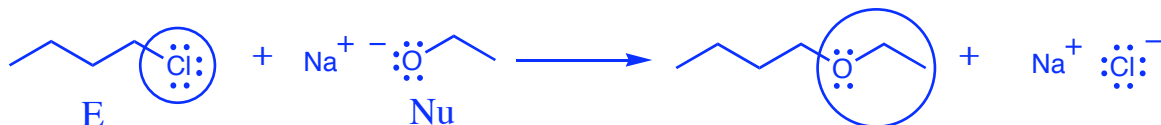
## III. Using Elimination for Synthesis

### I. Elimination Reactions of Alkyl Halides

#### Introduction

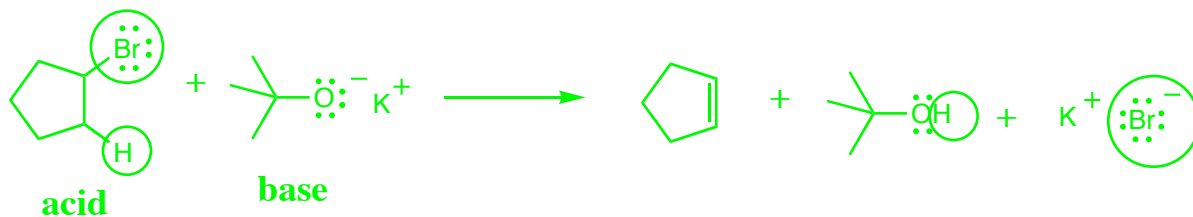
Describe the result of a substitution reaction. Give an example.

halide is replaced by a Nu



How is an elimination reaction different? Give an example.

halide and H are removed, C=C remains



What does it mean to say that substitution and elimination reactions are competing reactions?

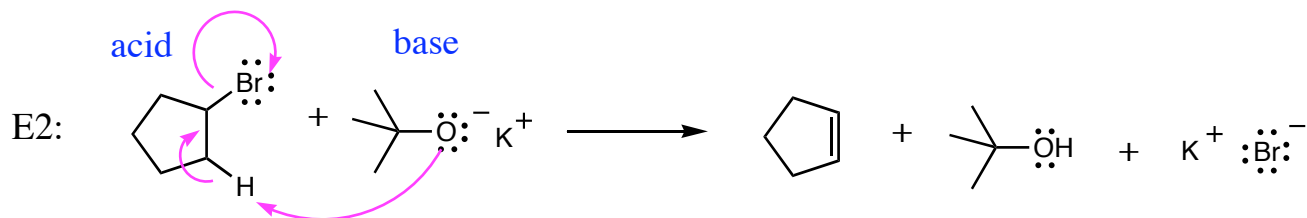
they occur under similar conditions

one or the other may be favored, or both may occur

Mechanisms

What are the two mechanisms by which elimination may occur? **E2 and E1**

Consider the following mechanisms:



Draw in the arrows to show how this reaction occurred.

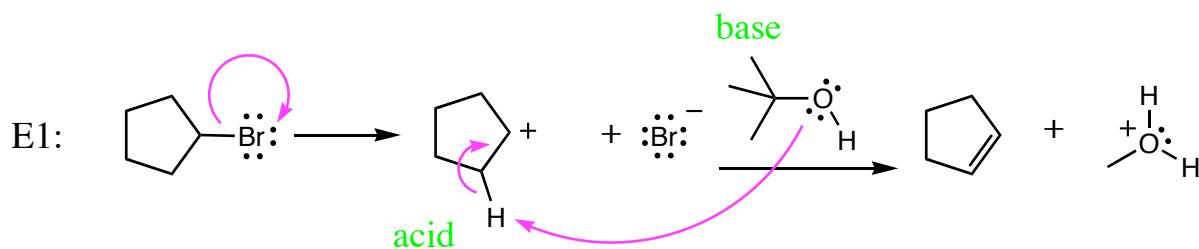
What type of Lewis acid/base reaction is this? **displacement**

How could this mechanism be described? **deprotonate-push off**

Identify the acid and the base.

Why can the alkyl halide behave as an acid? **halogen can leave, so e- can come in**

Why is the alkoxide a good base? **negative charge, lone pair of e-, hindered, so it won't act as a Nu**



Draw in the arrows to show how this reaction occurred.

What types of Lewis acid/base reactions occur? **dissociation, displacement**

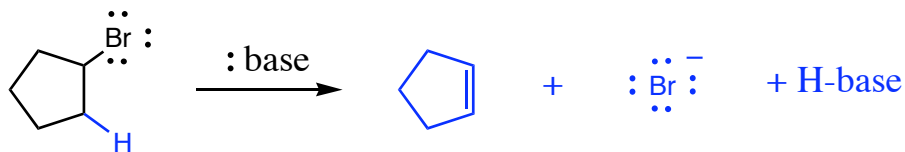
How could this mechanism be described? **fall off deprotonate-fall in**

Identify the acid and the base.

Why can the carbocation behave as an acid? **there is an empty orbital, so e- can come in**

# Beta hydrogens, constitutional isomers, and stereoisomers

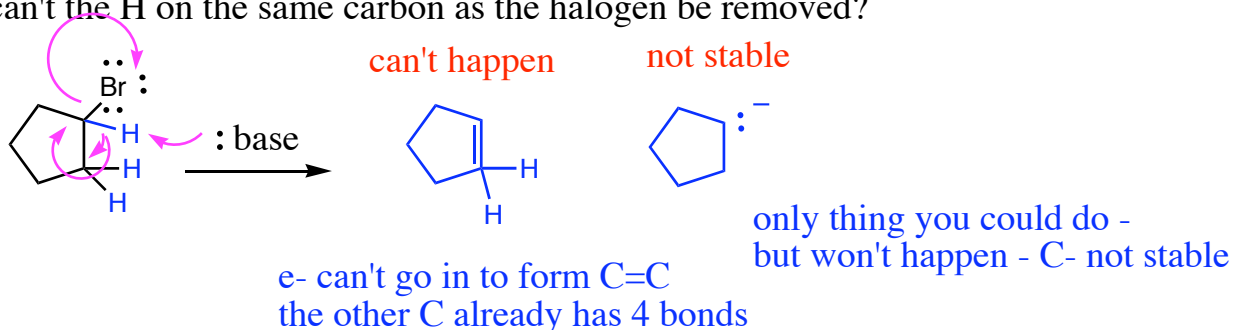
What is the relationship between the halogen and the H that is removed? Why?



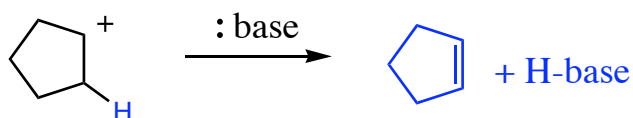
on two C's that are next to each other (neighbors)

C=C can only be formed between 2 C's next to each other

Why can't the H on the same carbon as the halogen be removed?



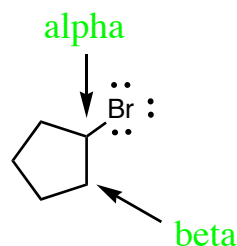
What is the relationship between the carbocation and the H that is removed?



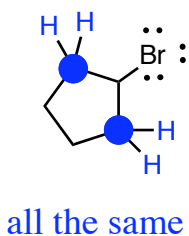
on neighboring C same reason!

What is this relationship called?

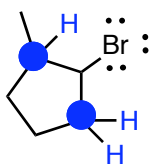
carbons are labeled alpha, beta, etc  
these are the beta hydrogens



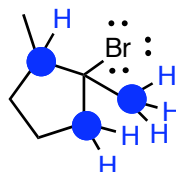
Is it possible for there to be more than one set of beta hydrogens? **yes!**



all the same

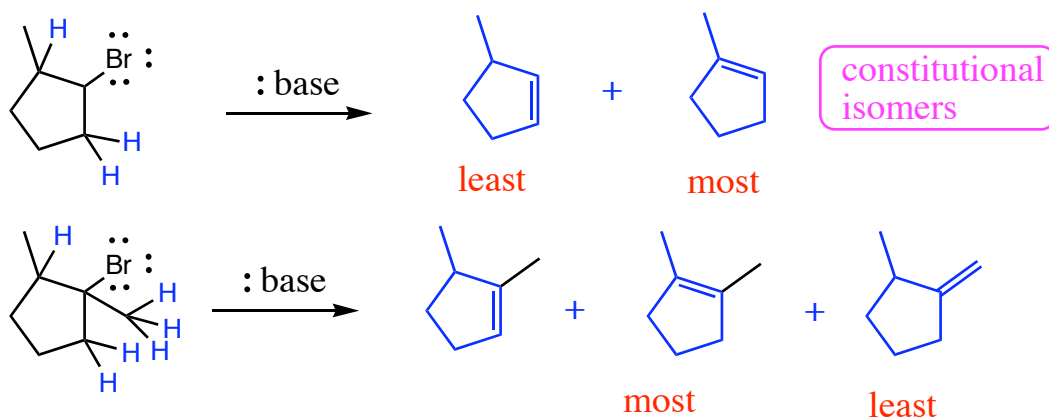


two different sets



three different sets

What two elimination products could be formed from the following compounds?  
What is their relationship?

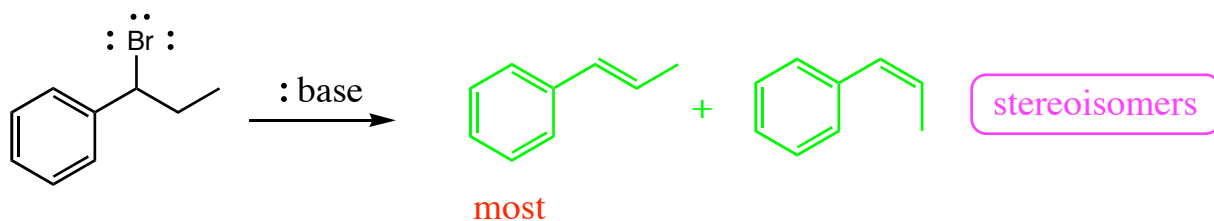


Not all isomers will be formed in equal amounts. Which are favored?

the most substituted    the ones with the most C attached to C=C

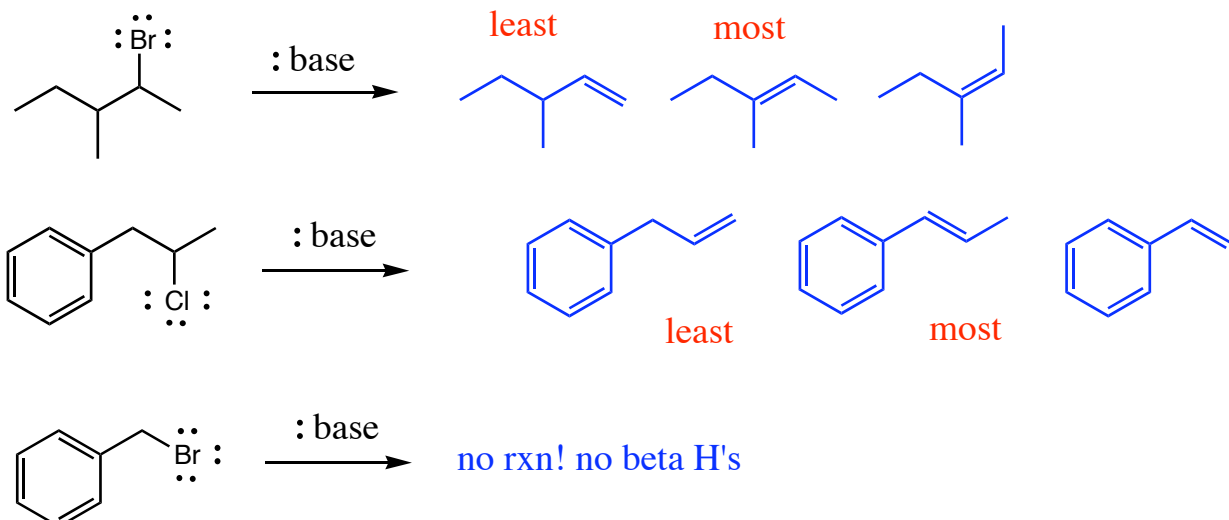
Zaitsev's rule

What two elimination products could be formed from the following compounds?  
What is their relationship?



Which isomer will be favored?    E or trans > Z or cis

Give all products of the following reactions. Indicate which is favored.



E2 vs. E1

How are the E2 and E1 reactions the same? both need a leaving group and a base  
both lose an X and an H, both give a C=C

What are the two bases used in the examples? Which do you think is stronger, and why?

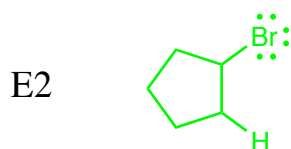


stronger base - negatively charged



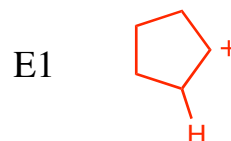
weaker base - neutral

What are the two acids used in the examples? Which do you think is stronger, and why?



weaker acid  
stable compound

pK<sub>a</sub> unknown



stronger acid  
incomplete octet  
very unstable

pK<sub>a</sub> -2

How do the strengths of the acid and base go together?

E2 - stronger base, weaker acid

E1 - weaker base, stronger acid

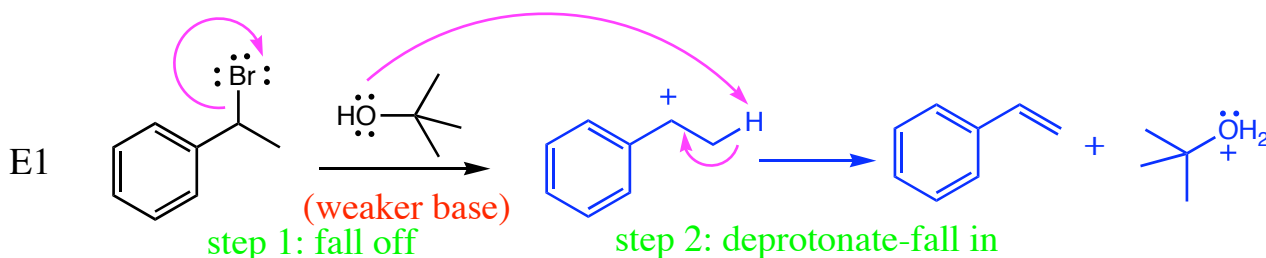
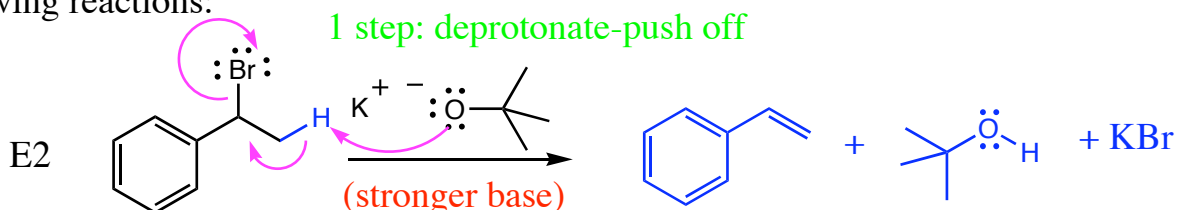
Scenario A: strong base added to alkyl halide

base attacks! - E2

Scenario B: weak base added to alkyl halide

base can't attack, sits around waiting until alkyl halide dissociates, then  
attacks carbocation - E1

Following the pattern of the reactions given previously, draw the mechanisms for the following reactions:



Strong and Weak Bases

What do nucleophiles and bases have in common? a pair of electrons that can attack

What is the difference between how the base attacks and how the nucleophile attacks?

base attacks H's  
Nu attacks C's

Could one molecule act as both a nucleophile and a base? yes!

What do  $S_N2$  and E2 have in common? 1 step, strong Nu or base

What do  $S_N1$  and E1 have in common? more than one step, weak Nu or base  
carbocation formation

What factors make a nucleophile stronger?

NaOH vs  $H_2O$  negative charge

$HC\equiv CNa$  vs NaOH less EN atom

NaSH vs NaOH bigger atom

$CH_3CH_2ONa$  vs  $(CH_3)_3COK$  less steric hindrance

How do these same factors affect the strength of bases?

NaOH vs  $H_2O$  negative charge - stronger base same

$HC\equiv CNa$  vs NaOH less EN atom - stronger base same

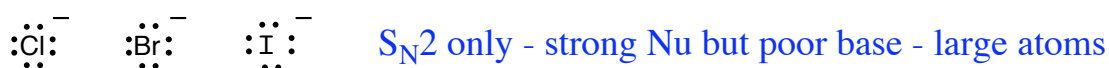
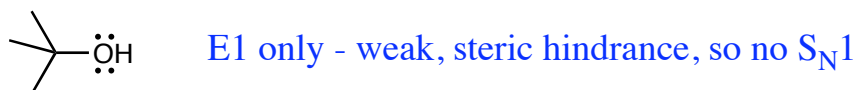
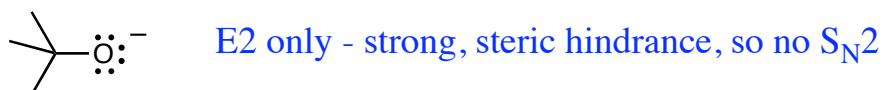
NaSH vs NaOH bigger atom - weaker base opposite

$CH_3CH_2ONa$  vs  $(CH_3)_3COK$  less steric hindrance - no effect

Which reactions will the following molecules participate in?

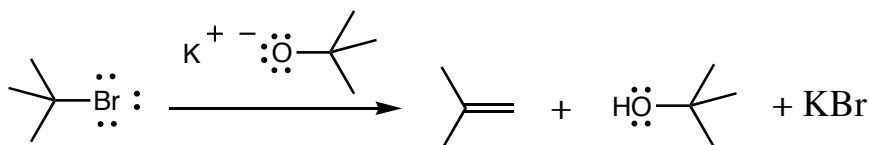
NaOH strong Nu or base - E2 and  $S_N2$

$H_2O$  weak Nu or base - E1 and  $S_N1$



### Rate laws

Consider the following E2 reaction.

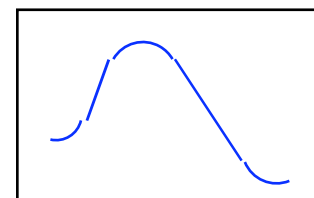
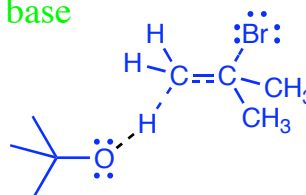


Draw the energy diagram for this reaction.

What is the rate-limiting step? What reagents are involved?

the only step; both alkyl halide and base

Draw the structure of the transition state.



What would happen to the rate of the reaction if you

doubled the concentration of the alkyl halide? rate would double

doubled the concentration of the base? rate would double

What is the order of the alkyl halide? the base? the reaction? 1st order in both

Write the rate law:  $\text{rate} = k[\text{RX}][\text{base}]$

2nd order overall

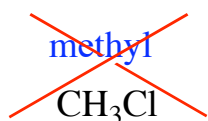
What does E2 stand for? elimination 2nd order

How does the halogen affect the reaction rate?

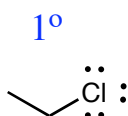
larger atoms have longer bonds which are easier to break, so they react faster



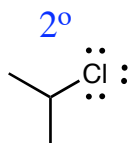
How does the structure of the alkyl halide affect the rate?



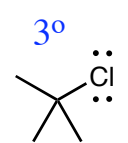
no beta H's



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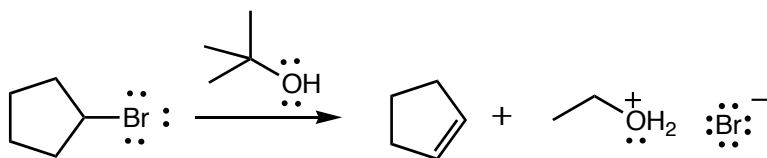


opposite of  $\text{S}_{\text{N}}2$

steric hindrance doesn't affect the ability to take a H

more substituted alkyl halides form more stable alkenes

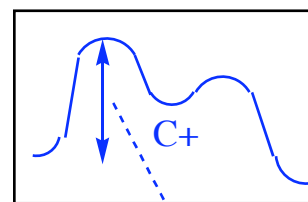
Consider the following E1 reaction.



Draw the energy diagram for this reaction.

Which is the rate limiting step?

fall off - creating a  $\text{C}^+$

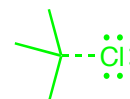


$E_a$  of rate limiting step

Which reagents are involved in the rate limiting step?

only the alkyl halide

Draw the structure of the transition state for this step.



What would happen to the reaction rate if you

doubled the concentration of the alkyl halide? rate would double

doubled the concentration of the nucleophile or base? nothing!

What order is the alkyl halide? the base? the reaction? alkyl halide 1st order

base 0th order

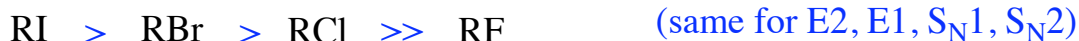
Write the rate law:  $\text{rate} = k[\text{RX}]$

1st order overall

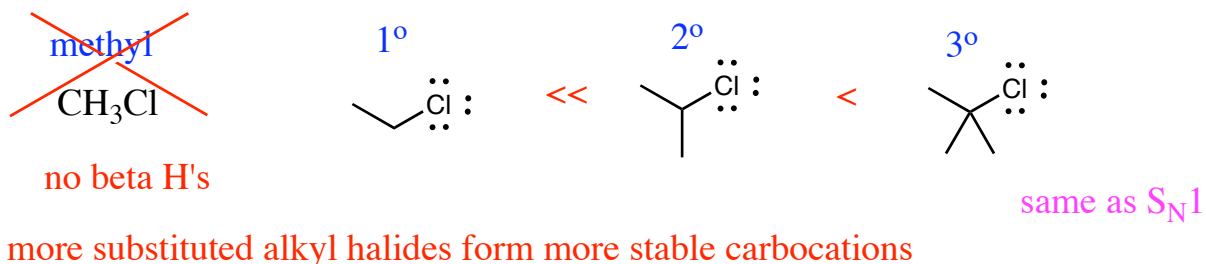
What does E1 stand for? Elimination 1st order



How does the halogen affect the reaction rate? longer bond is easier to break



How does the structure of the alkyl halide affect the rate?



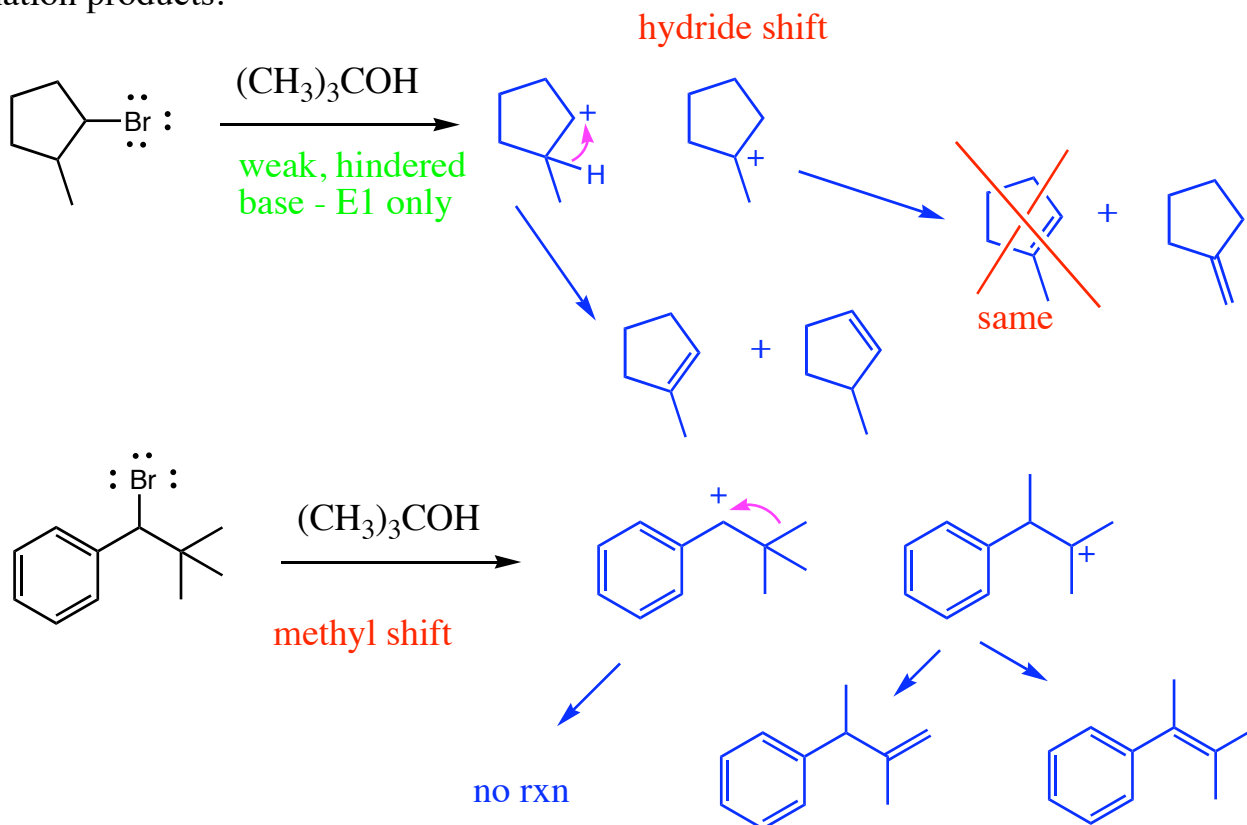
## Rearrangements

Which elimination reaction has the possibility of rearrangements? E1

Which alkyl halides are most likely to rearrange? 2° 3° - already as stable as it can get; 1° - don't usually form

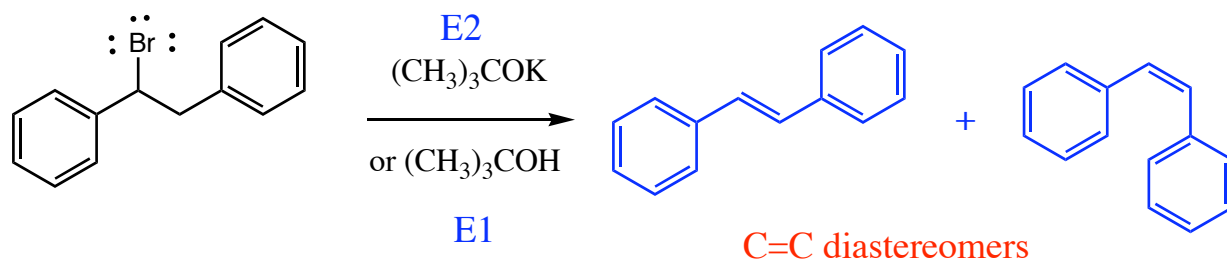
What kinds of rearrangements can occur? alkyl shifts (usually methyl), hydride shifts

What rearrangement will occur in the following reactions? Draw the carbocation and the elimination products.



## Stereochemistry

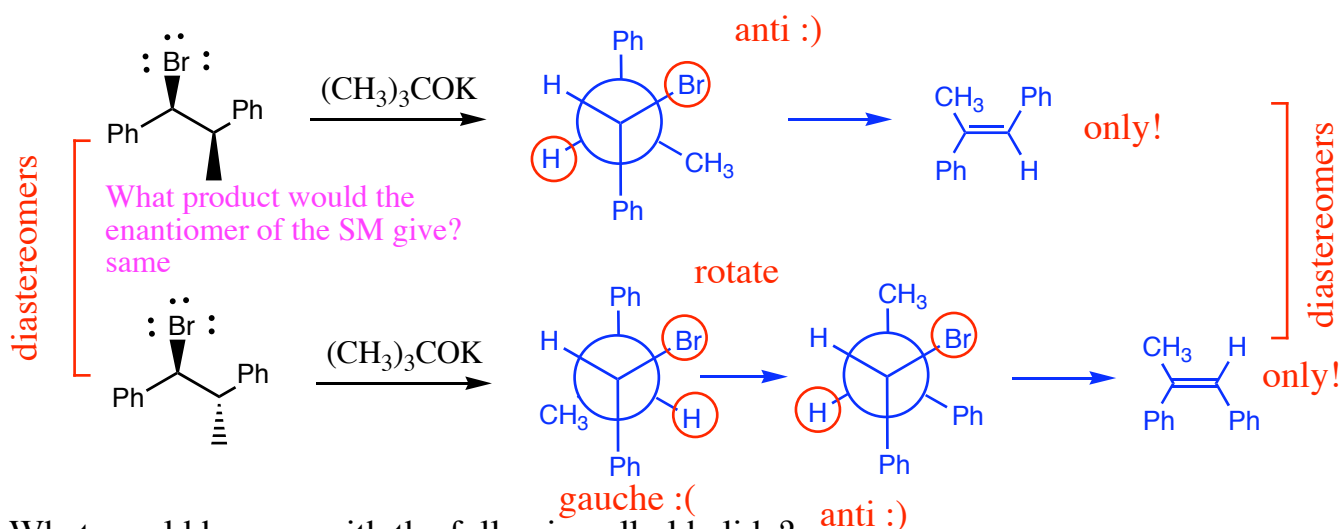
What types of stereoisomers can be formed in an elimination reaction?



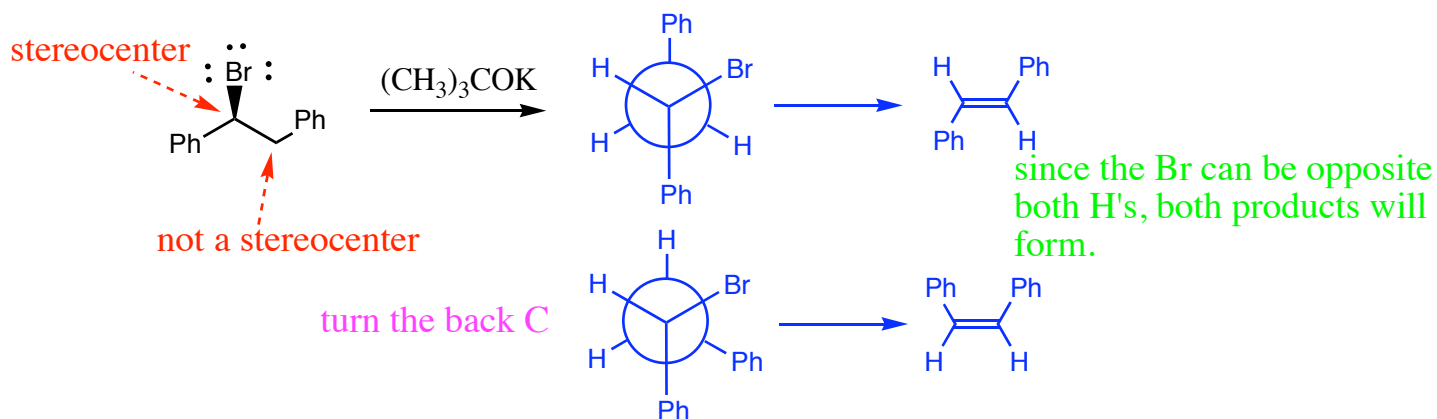
What orientation is required in order for an E2 reaction to occur?

halide, H must be anti to each other

Which stereoisomer will be formed from the following alkyl halides?

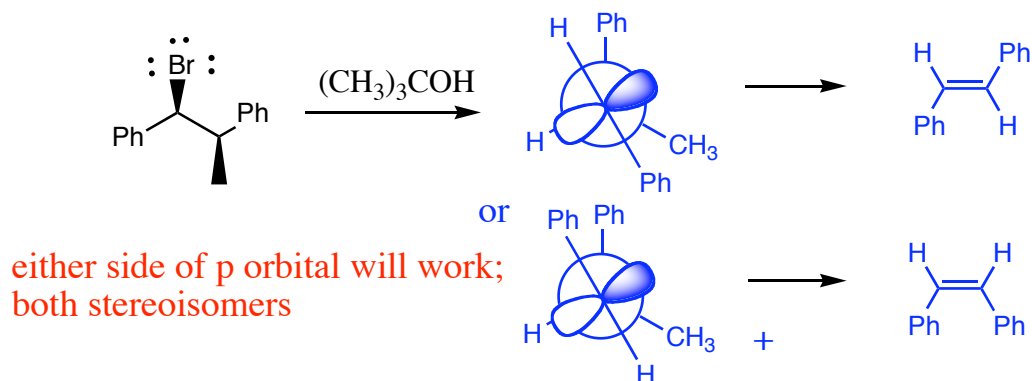


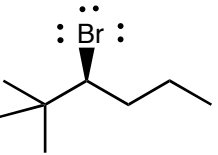
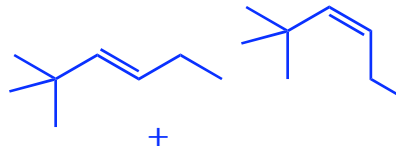
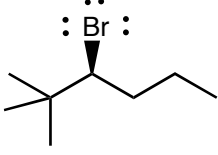
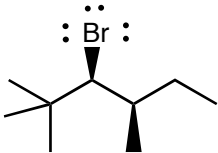
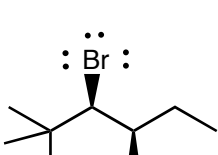
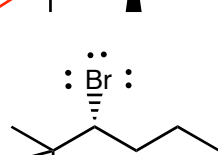
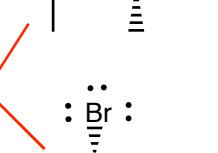
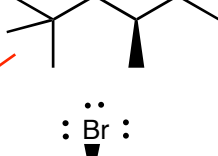
What would happen with the following alkyl halide?



Under what conditions will an E2 reaction give only one stereoisomer?

if both C's are chiral, only one position in which H is anti to X



	$\xrightarrow[(E2)]{(CH_3)_3COK}$	two diastereomers	
	$\xrightarrow[(E1)]{(CH_3)_3COH}$	two diastereomers (plus rearrangements)	"
	$\xrightarrow[(E1)]{(CH_3)_3COH}$	two diastereomers (plus rearrangements)	"
	$\xrightarrow[(E2)]{(CH_3)_3COK}$	only one	which? - use models!
	$\xrightarrow[(E2)]{(CH_3)_3COK}$	only one	same as above
	$\xrightarrow[(E2)]{(CH_3)_3COK}$	only one	opposite one
	$\xrightarrow[(E2)]{(CH_3)_3COK}$	only one	opposite one

Solvents

What kinds of solvents were best for  $S_N2$  reactions? **polar, aprotic**

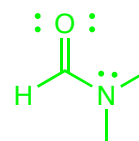
Why? **solvent needs to dissolve ionic reactants, H-bonding with Nu slows it down**

What kinds of solvents were best for  $S_N1$  reactions? **polar, protic**

Why? **H-bonding can help stabilize  $C^+$**

Which of these is E2 most like? What kind of solvents would be best?

**$S_N2$  - polar aprotic: acetone, acetonitrile, dimethylformamide (DMF)**

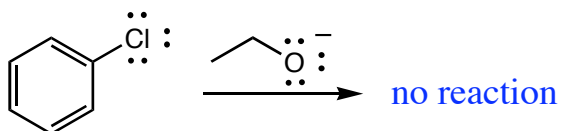
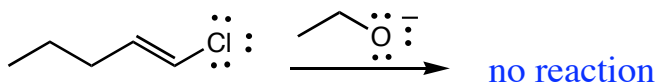


Which of these is E1 most like? What kind of solvents would be best?

**$S_N1$  - polar protic: water, alcohols**

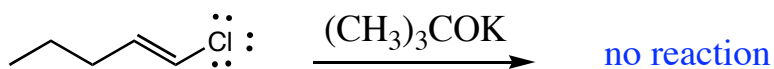
Eliminations of aryl and vinyl halides

Can aryl and vinyl halides undergo  $S_N2$  or  $S_N1$  reactions? **nope!**

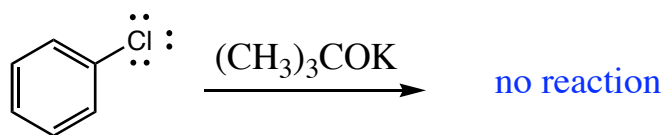


**Nu can't get in behind;  
 $sp^2$  C's don't form  $C^+$**

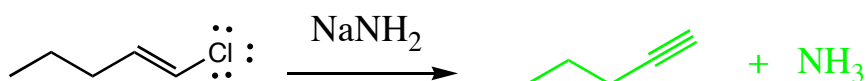
Can aryl and vinyl halides undergo elimination? **yes - but only with a much stronger base**



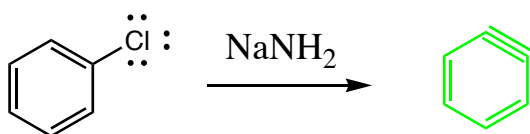
**$(CH_3)_3COH$  pKa 18**



**$NH_3$  pKa 36**



**Ch 13 - alkynes**



**Ch 18 - aromatic rings**

**unstable!**

## Summary of Elimination Reactions

### E2 reactions:

result: halide and H removed  
alkene formed

mechanism: 1 step  
deprotonate-push off

reagent: strong base

stereochemistry: anti elimination

rate law:  $\text{rate} = k[\text{RX}][\text{base}]$

alkyl halides:  $3^\circ > 2^\circ \gg 1^\circ > \text{methyl}$   
 $\text{RI} > \text{RBr} > \text{RCl} \gg \text{RF}$

rearrangements? no

solvent: polar, aprotic

### E1 reactions:

result: halide and H removed  
alkene formed

mechanism: 2 steps  
fall off  
deprotonate-fall in

reagent: weak base (often the solvent)

stereochemistry: none

rate law:  $\text{rate} = k[\text{RX}]$

alkyl halides:  $3^\circ > 2^\circ \gg 1^\circ > \text{methyl}$   
 $\text{RI} > \text{RBr} > \text{RCl} \gg \text{RF}$

rearrangements? yes

solvent: polar, protic (usually base)

## II. Elimination vs Substitution

What does it mean to say that elimination and substitution are competing reactions?

they can both happen under the same conditions

you have to figure out which is fastest, or if there will be a mixture

What reagents does substitution require? alkyl halide, Nu

What reagents does elimination require? alkyl halide, base

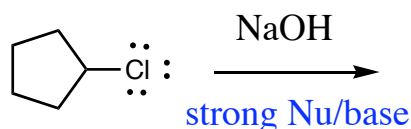
Can some molecules act as nucleophiles or bases? yes

The following criteria can help us decide:

1) How can we choose between 1st and 2nd order reactions?

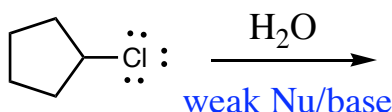
strong Nu or base -  $S_N2$  or E2

weak Nu or base -  $S_N1$  or E1



$S_N2$  or E2

both substitution and elimination may occur;  
but one may be faster than the other



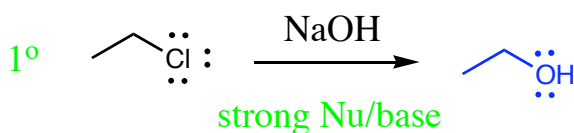
$S_N1$  or E1

2) How can we choose between substitution and elimination reactions?

A) use reaction rates

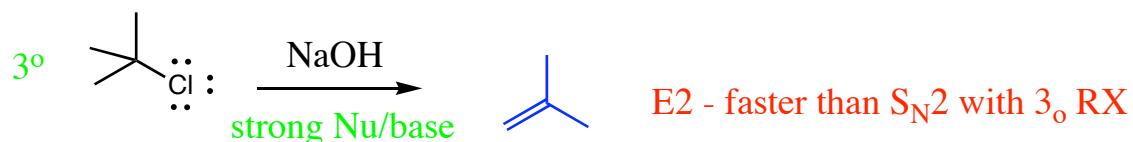
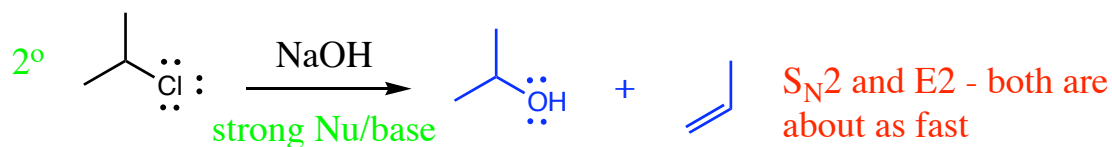
$S_N2$ :  $1^\circ > 2^\circ \gg 3^\circ$  less steric hindrance reacts faster

E2:  $3^\circ > 2^\circ > 1^\circ$  more substituted alkene is formed faster



$S_N2$  only - faster than E2 with  $1^\circ$  RX

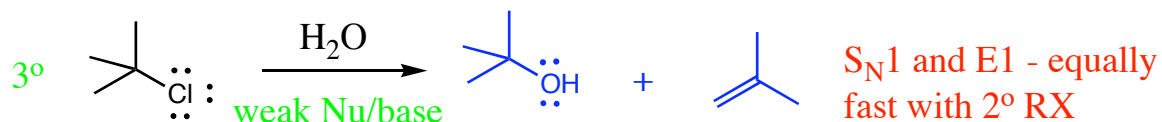
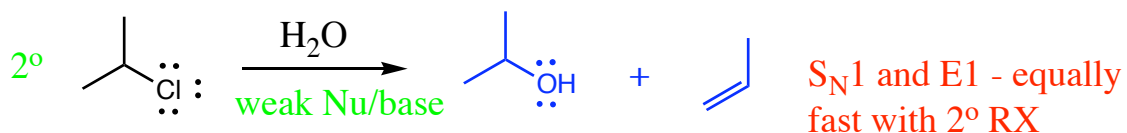
STRONG



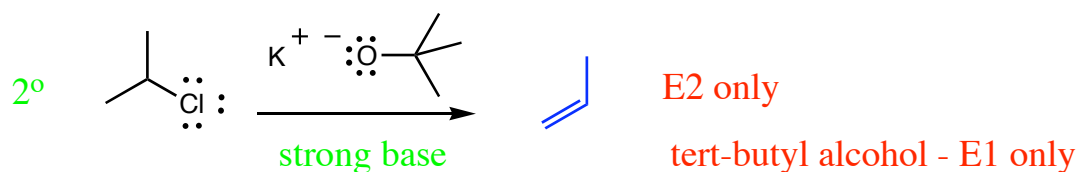
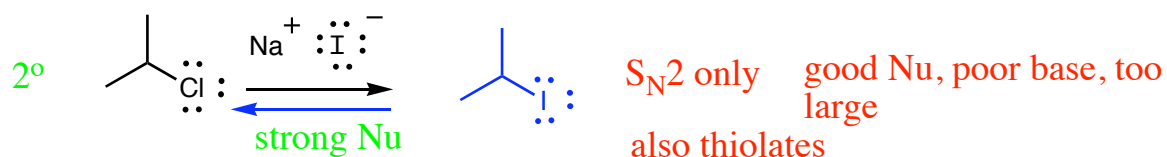
WEAK

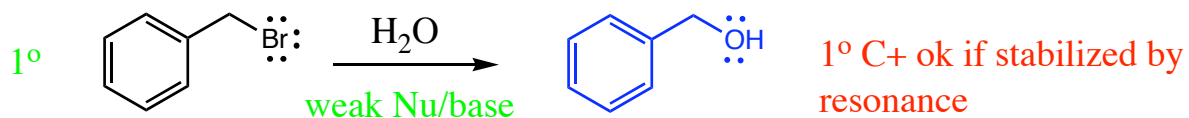
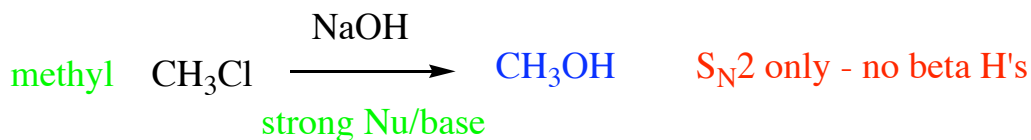
$S_N1$ :  $3^\circ > 2^\circ \gg 1^\circ$  more stable  $C^+$  is faster

E1:  $3^\circ > 2^\circ \gg 1^\circ$  more stable  $C^+$  is faster

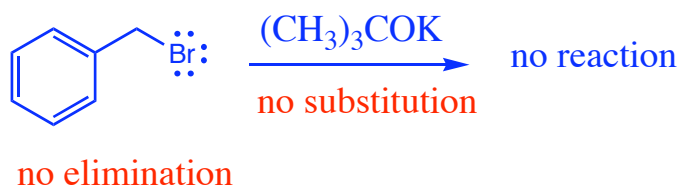


B) Watch out for special cases





Would it be possible to have a reaction in which no product was formed?



Summary:

	strong Nu	weak Nu
$1^\circ \text{RX}$	$\text{S}_{\text{N}}2$	no rxn
$2^\circ \text{RX}$	$\text{S}_{\text{N}}2$ and E2	$\text{S}_{\text{N}}1$ and E1
$3^\circ \text{RX}$	E2	$\text{S}_{\text{N}}1$ and E1

exceptions:  $\text{tert-butoxide}$  or  $\text{tert-butyl alcohol}$  - elimination only  
 halides and thiolates - substitution only  
 no beta H's - substitution only  
 benzylic RX -  $1^\circ \text{C}^+$  ok



### III. Synthesis Using Elimination

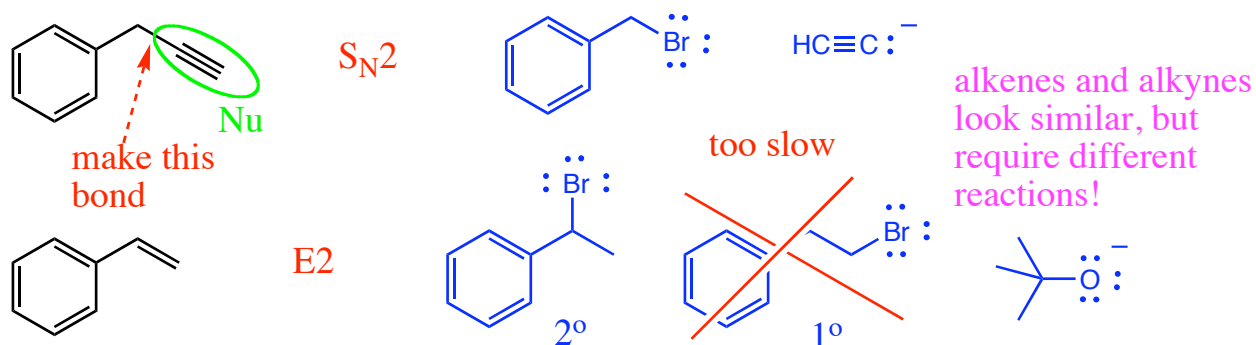
What kinds of functional groups can be made using substitution reactions?

nitriles, alkynes, alcohols, ethers, thiolates, other alkyl halides

What kinds of functional groups can be made using elimination reactions?

alkenes

What starting materials and reagents could be used to make the following compounds?

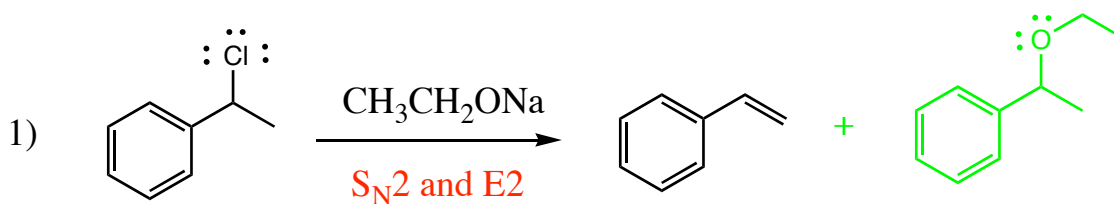


In order to have a good synthesis, what must be true?

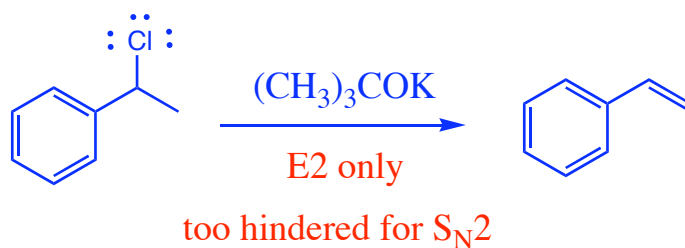
reaction should be fast

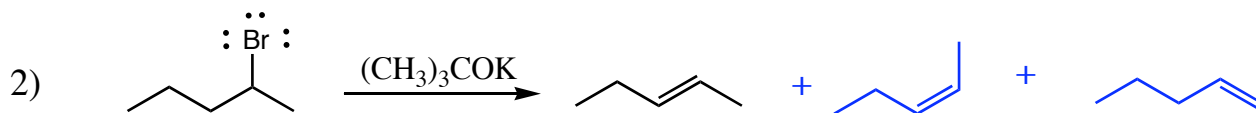
no other major products formed

What will go wrong in the following examples? What can be done about it? Rewrite the reaction so that it will work (if possible).

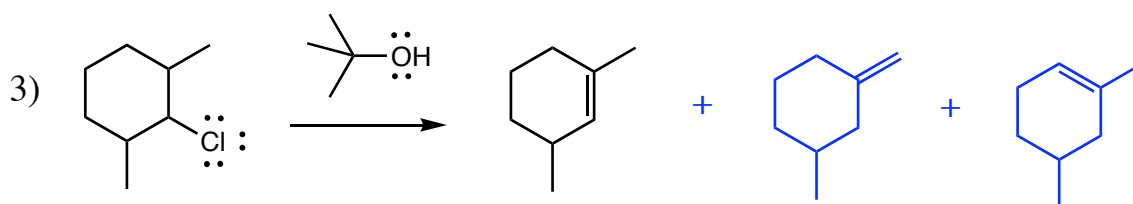
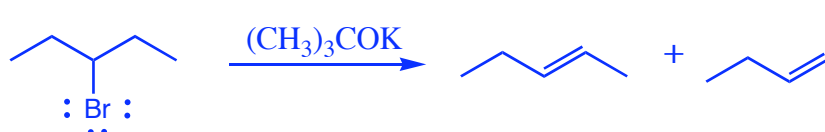


interference from substitution - use hindered reagents

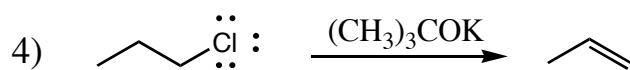




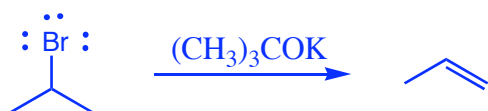
constitutional isomers - choose alkyl halide carefully  
stereoisomers - nothing (yet)



rearrangements - avoid E1 mechanism by using a strong base



slow - 1° alkyl halide - choose a different one



Write a good synthesis for the following compounds, or explain why you can't.

