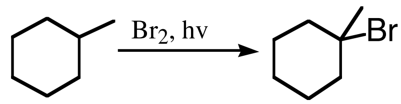
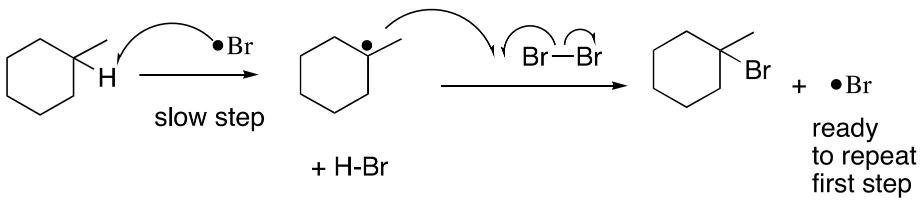
Chem 350 Jasperse Ch. 6 Summary of Reaction Types, Ch. 4-6, Test 2

1. Radical Halogenation (Ch. 4)

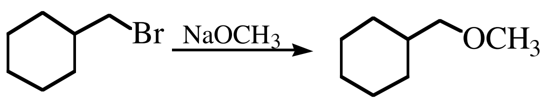


resonance stabilized>3°>2°>1°>alkenyl

Recognition: X_2, hv
Predicting product: Identify which carbon could give the most stable radical, and substitute a Br for an H on that carbon.
Stereochemistry: Leads to racemic, due to achiral radical intermediate.
Mech: Radical. Be able to draw propagation steps.

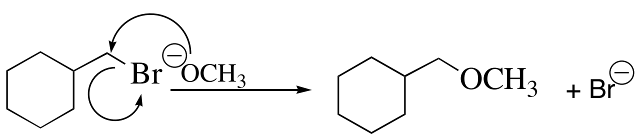


2. S_N2 Substitution



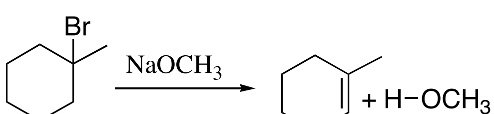
S_N2: 1°>2°>3°> alkenyl

Any of a large variety of nuclophiles or electrophiles can work.
Recognition: A. Anionic Nucleophile, and
B. 1° or 2° alkyl halide
(3° alkyl halides fail, will give E2 upon treatment with Anionic Nucleophile/Base. For 2° alkyl halides, S_N2 is often accompanied by variable amounts of E2.)
Predicting product: Replace the halide with the anion nucleophile
Stereochemistry: Leads to Inversion of Configuration
Mech: Be able to draw completely. Only one concerted step!



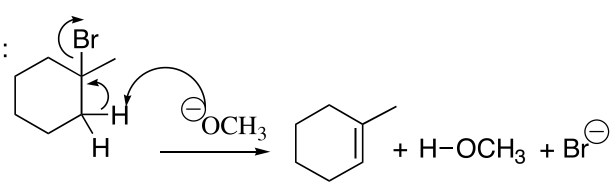
S_N2: 1°>2°>3°> alkenyl

3. E2 Reactions.



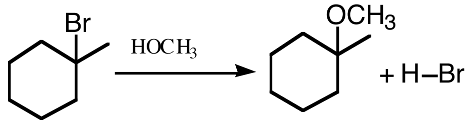
E2: 3°>2°>1°> alkenyl

Mech:



Recognition: A. Anionic Nucleophile/Base, and
B. 3° or 2° alkyl halide
(1° alkyl halides undergo S_N2 instead. For 2° alkyl halides, E2 is often accompanied by variable amounts of S_N2.)
Orientation: The most substituted alkene forms (unless a bulky base is used, ch. 7)
Predicting product: Remove halide and a hydrogen from the neighboring carbon that can give the most highly substituted alkene. The hydrogen on the neighboring carbon must be trans, however.
Stereochemistry: Anti elimination. The hydrogen on the neighbor carbon must be trans/anti.
Mech: Concerted. Uses anion. Be able to draw completely. Only one concerted step!

4. S_N1 Reactions.



S_N1: resonance >3°>2°>1°> alkenyl

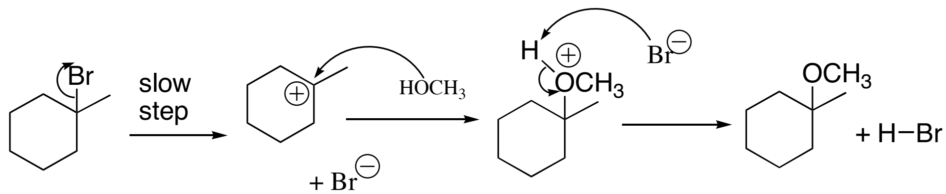
Recognition: A. Neutral, weak nucleophile. No anionic nucleophile/base, and
B. 3° or 2° alkyl halide. (Controlled by cation stability).

(1° alkyl halides undergo S_N2 instead. For 2° alkyl halides, S_N1 is often accompanied by variable amounts of E1.)

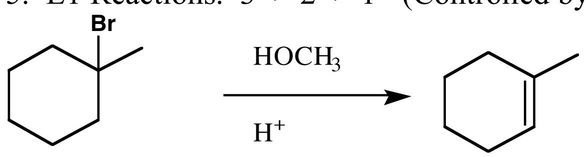
Predicting product: Remove halide and replace it with the nucleophile (minus an H atom!)

Stereochemistry: Racemization. The achiral cation intermediate forgets any stereochem.

Mech: Stepwise, 3 steps, via carbocation. Be able to draw completely.



5. E1 Reactions. 3° > 2° > 1° (Controlled by cation stability)



E1: 3°>2°>1

Recognition: A. Neutral, weak nucleophile. No anionic nucleophile/base, and
B. 3° or 2° alkyl halide. (Controlled by cation stability).

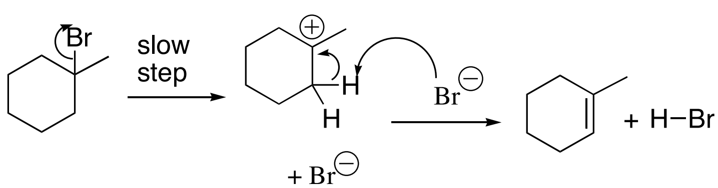
(For 2° alkyl halides, E1 is often accompanied by variable amounts of S_N1.)

Orientation: The most substituted alkene forms

Predicting the major product: Remove halide and a hydrogen from the neighboring carbon that can give the most highly substituted alkene. The hydrogen on the neighboring carbon can be cis or trans.

Stereochemistry: Not an issue. The eliminating hydrogen can be cis or trans. .

Mech: Stepwise, 2 steps, via carbocation. Be able to draw completely.



Sorting among S_N2, S_N1, E2, E1: How do I predict?

Step 1: **Check nucleophile/base**.

- If **neutral**, then **S_N1/E1** → mixture of both
- If **anionic**, then **S_N2/E2.**

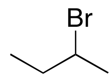
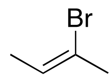
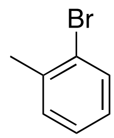
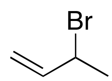
Step 2: If **anionic**, and in the **S_N2/E2**, then **Check the substrate**.

- 1° → **S_N2**
- 2° → **S_N2/E2 mixture.** Often more **S_N2**, but not reliable…
- 3° → **E2**

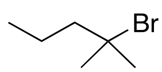
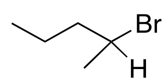
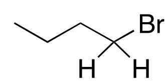
Ch. 5 Alkyl Halides: Nucleophilic Substitution and Elimination

6.1,2 Classification, Nomenclature

A. General Classification

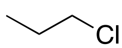
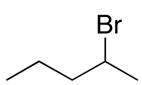
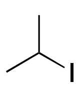
"alkyl halide"		Connected to an sp^3 carbon
"vinyl halide"		Connected to an sp^2 alkene carbon
"aryl halide"		Connected to an sp^2 aryl carbon
"allylic halide"		Connected to an sp^3 carbon that is connected to an sp^2 carbon

B. 1º, 2º, 3º Classification


3º

2º

1º

C. Systematic Naming: x-Haloalkane (test responsible) (Include number!)

D. Common Naming: "alkyl halide" (not tested)

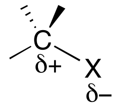
Structure	Formal Name	Common Name
	1-chloropropane	Propyl chloride
	2-bromopentane	
	2-iodopropane	Isopropyl iodide

Systematic Nomenclature: x-Haloalkane (test responsible)
Common: "alkyl halide" (not tested)

6.3 Uses:

- solvents
- anesthetics
- refrigerants
- pesticides
- **reactants**

6.4 Structure:

A. Polar 

B. Weak Bonds, Breakable

Stability	Bond	Bond Strength	Reactivity Toward Breakage
Most	C-Cl	81	Least
	C-Br	68	
least	C-I	53	Most

6.5 Physical Properties
- boiling point: controlled by molecular weight (London force)
- water solubility: low, no hydrogen-bonding
- density: greater than water, so they sink (unlike hydrocarbons, which float)

6.6 Preparation of Alkyl Halides
- Review: R-H + Br_2 → RBr + HBr (under photolysis, Ch. 4)
- We will learn other preparations in chapters 8 and 11

6.7 Basic Overview/Preview of Alkyl Halide Reactions: Substitution (S_N2 or S_N1) or Elimination (E2 or E1)

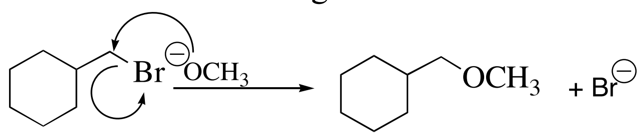
- Because R-X bonds are weak, halides are good leaving groups.

A. Substitution

R-X + NaZ or HZ → R-Z + NaX or HX
Anion or neutral

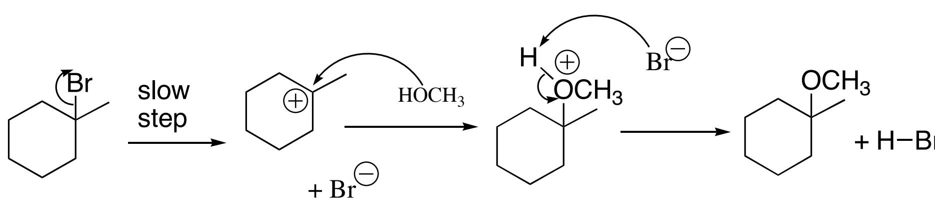
2 Variants

1. S_N2:
   - Anionic nucleophile
   - The R-X bond breaking is simultaneous with R-Z bond formation

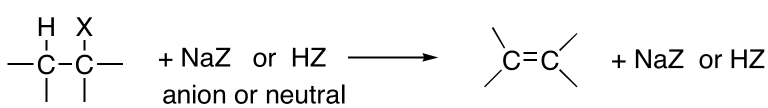


S_N2: 1°>2°>3°> alkenyl

2. S_N1:
   - Neutral nucleophile
   - The R-X bond breaks first to give a carbocation in the rate determining step; formation of the R-Z bond comes later

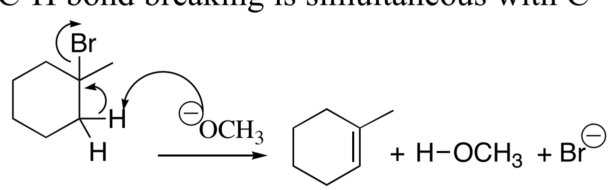


B. Elimination

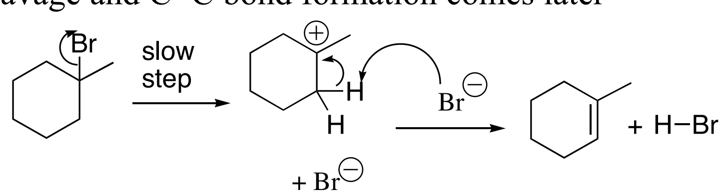


<u>2 Variants</u>

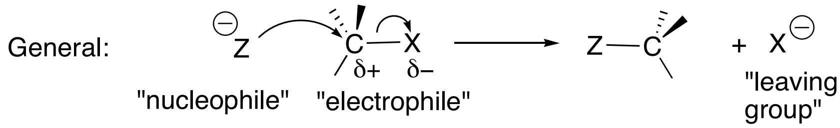
1. E2:
   - Anionic base
   - The R-X and C-H bond breaking is simultaneous with C=C bond formation



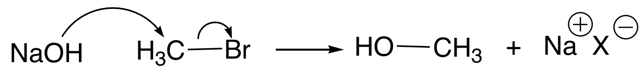
2. E1:
   - Neutral base
   - The R-X bond breaks first to give a carbocation in the rate determining step. C-H bond cleavage and C=C bond formation comes later



6.8 The S_N2 Reaction

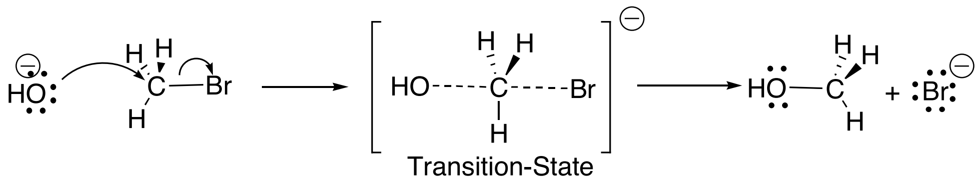


Example, with test-level mechanism:



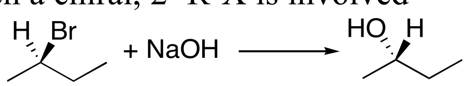
- double-barbed arrows (electron pairs move)
- Na^+ is a spectator

More Detailed Mechanism:



Notes:

- Simple, concerted one-step mechanism. No intermediates.
- The anion needs to be very reactive and thus not too stable. Normally **ANIONIC NUCLEOPHILE**.
- Both nucleophile and electrophile are involved in the rate determining step.
- Rate = $k[\text{anion}]^1[\text{R-X}]^1$
- 2^{nd} order rate law is why it's called S_N2: **S**ubstitution$_{\text{Nucleophilic}}$**2**nd order
- The nucleophile attacks opposite side from the leaving group.
- This "backside attack" (or opposite side attack) results in inversion of stereochemistry when a chiral, 2º R-X is involved

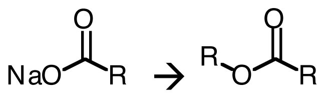


Inversion of Stereochemistry at Chiral Center

- The **transition state** involves a 5-bonded, trigonal bipyramidal carbon that **is more cluttered** than either the original tetrahedral reactant or the final tetrahedral product
- Steric crowding in the transition-state makes the reaction very, very, very sensitive to steric factors
    - For the electrophile R-X: CH_3-X > 1º R-X > 2º R-X > 3º R-X for steric reasons
    - For the nucleophile it also helps to be smaller rather than larger

6.9 Generality of S_N2 Reactions

-many kinds of nucleophiles, give many products

R-X + NaOH → R-OH	Alcohols
R-X + NaOR → R-O-R	Ethers
R-X + 	Esters
R-X + KI → R-I	Iodides
R-X + NaCN → R-CN	Nitriles
R-X + 	Alkynes

Etc.

<u>Notes</u>

- Most nucleophiles are **<u>ANIONS</u>**
- Various oxygen anions are good to make alcohols, ethers, or esters
- Halogen exchange useful route to iodides (more valuable and less accessible)
- There are a few neutral nucleophiles (not for test): nitrogen family

<u>Predicting Products for S_N2 Reactions</u>

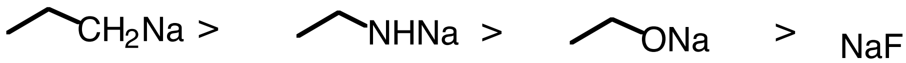
1. Don't change the structure for the carbon skeleton
2. **<u>Put the nucleophile in exactly the spot where the halide began…</u>**
3. Unless the halide was attached to a **<u>chiral</u>** center; in that case invert the configuration for the product
   - If the halide was "wedged", the nucleophile should be "hashed"
   - If the halide was "hashed", the nucleophile should be "wedged"
4. Don't mess with any "spectator" portions: whatever was attached to the nucleophilic anion at the beginning should still be attached at the end

6.10, 6.11 Structural Factors that Impact S_N2

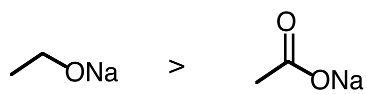
1. Nucleophile
   a. Anion versus Neutral: Should be **ANIONIC**

   b. Anion Stability: Less Stable should be More Reactive (Reactant Stability-Reactivity Principle)

      1) -anion nucleophilicity decreases across a **horizontal row** (electronegativity factor)



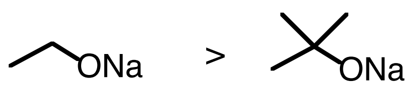
      2) -anion nucleophilicity decreases when an anion is stabilized by **resonance**



      3) -anion nucleophilicity increases down a **vertical column**

NaSeH > NaSH > NaOH

   c. Size: all else equal, smaller is better than bigger

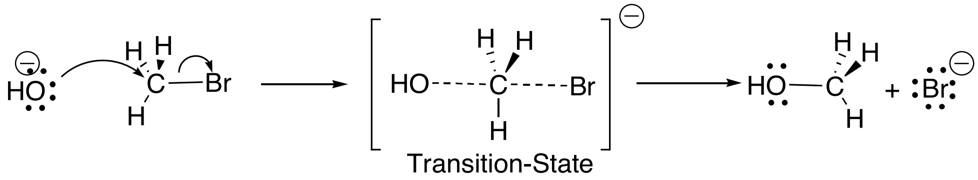


2. Electrophile
   - **Substrate: Allylic > 1º > 2º > >> 3º, alkenyl, aryl**
     - **3º and alkenyl, aryl never do S_N2**
     - transition-state stability-reactivity principle
     - Steric clutter in the transition state explains the 1º > 2º > >> 3º pattern
     - Allylic benefits from a complex orbital resonance effect in the T-state
     - Alkenyl/aryl halides are bad for some molecular orbital reasons (backside attack doesn't work, particularly for aryl halides)

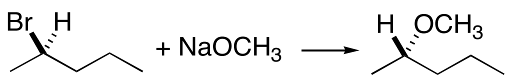
   - **Leaving Group: R-I > R-Br > R-Cl**
     - reactant stability-reactivity principle
     - weaker bonds break faster

6.12 Inversion of Stereochem in S_N2

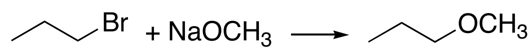
In the mechanism, the nucleophile attacks from the "backside" or opposite side from the leaving group → inverts configuration



- Inversion occurs mechanistically in **every** S_N2 reaction
- But inversion is chemically relevant **only** when a chiral carbon is involved

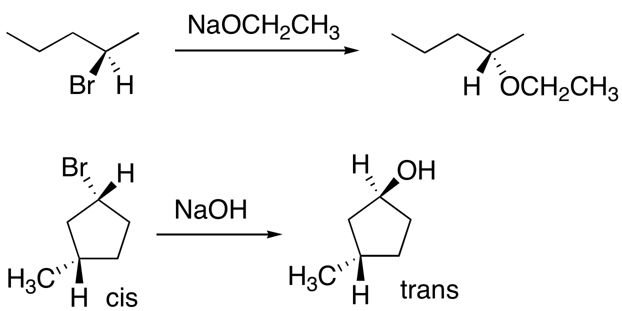


Inversion matters, since product is chiral



Inversion doesn't matter, for achiral product

Predicting products when chiral carbons undergo inversion:
- Keep the carbon skeleton fixed
- If leaving group is "hashed", the nucleophile will end up "wedged" in the product
- If leaving group is "wedged", the nucleophile will end up "hashed" in the product



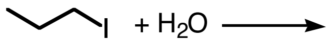
Two Standard Proofs for S_N2 mechanism:
- Inversion of configuration on a chiral carbon
- 2nd order rate law

Predicting Products for S_N2 Reactions

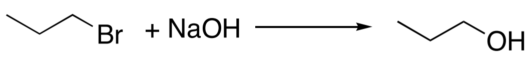
1. Don't change the structure for the carbon skeleton
2. **Put the nucleophile in exactly the spot where the halide began…**
3. Unless the halide was attached to a **chiral** center; in that case invert the configuration for the product
   - If the halide was "wedged", the nucleophile should be "hashed"
   - If the halide was "hashed", the nucleophile should be "wedged"
4. Don't mess with any "spectator" portions: whatever was attached to the nucleophilic anion at the beginning should still be attached at the end

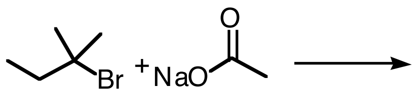
S_N2 Problems: For each of the following

a. Identify whether or not an S_N2 reaction would take place?
b. If not, why not?
c. For those that could undergo S_N2 substitution, draw in the product.

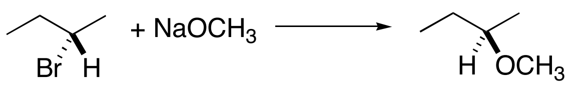
1. 

Not, neutral

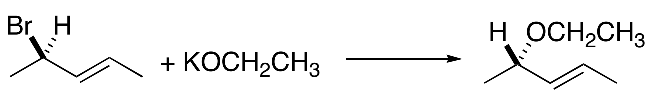
2. 

3. 

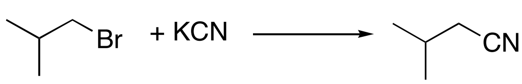
Not, 3°

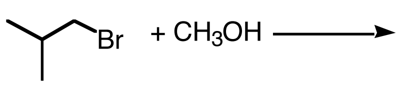
4. 

Inversion

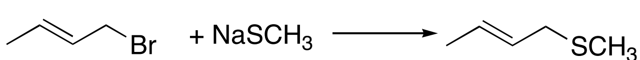
5. 

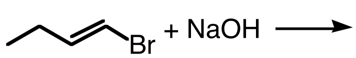
Inversion

6. 

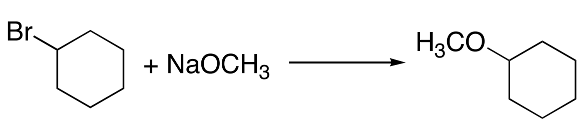
7. 

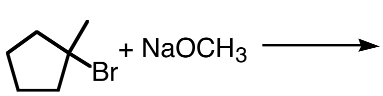
Not, neutral

8. 

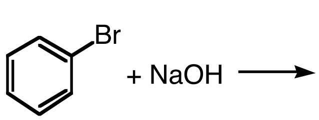
9. 

Not, vinyl

10. 

11. 

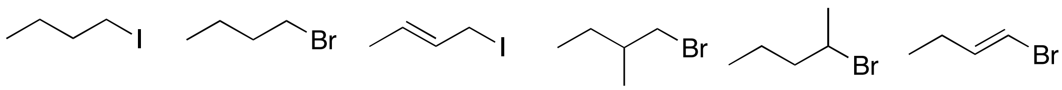
Not, 3°

12. 

Not, aryl

More S_N2 Problems

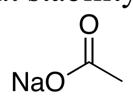
1. Rank the reactivity toward $NaOCH_3$ (For any problem like this, try to recognize what kind of a reaction it is, so that you know what stability/reactivity issues apply).



2 3 1 4 5 6

Issues: S_N2 with anion. Iodide > bromide. Allyl > 1º > 2º > vinyl. #4 is sterically more cluttered than #3

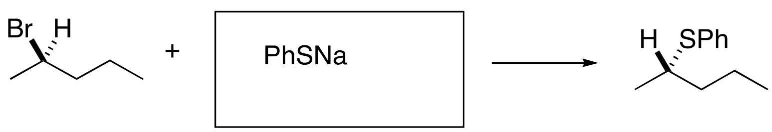
2. Rank Reactivity toward  (For any problem like this, try to recognize what kind of a reaction it is, so that you know what stability/reactivity issues apply).

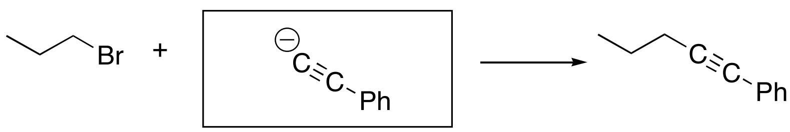
$NaNH_2$ $NaOCH_3$  CH_3OH

1 2 3 4

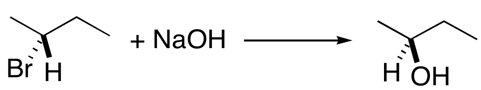
Issues: Stability/reactivity principles. 1. Anion vs neutral. (Why methanol is way last) 2. Electronegativity. (N vs O anions) 3. Resonance (#2 vs #3)

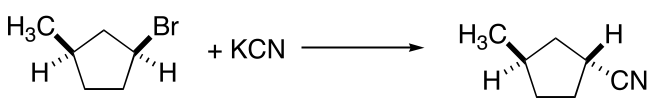
3. What nucleophile should you use to accomplish the following transformations?





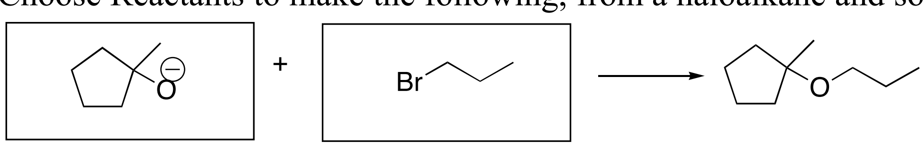
4. Draw the Products, Including Stereochemistry. (Stereochemistry will matter for S_N2 and S_N1 reactions anytime the haloalkane is 2º)





Issue: Inversion. Notice that ring goes from cis to trans.

5. Choose Reactants to make the following, from a haloalkane and some nucleophile.



Issues: Electrophile needs to be 1º or 2º, but can't be 3º

6.13 S_N1 = **S**ubstitution$_{\text{Nucleophilic}}$**1**st Order = "Solvolysis"

Dramatic difference in mechanism, rates, structure dependence, and stereochemical outcome (compared to S_N2)

General: R-X + Z-H → R-X + HX
neutral

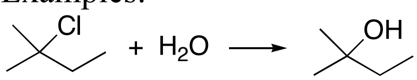
Neutral, non-anionic nucleophiles do the substitution

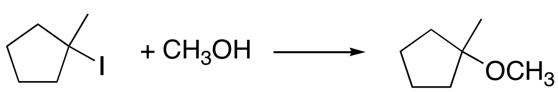
- Often this is just the solvent (H_2O, ROH, RCO_2H are common)
  - For this reasons, these reactions are often called "solvolysis" reactions
- Heat is often required
- Acid is sometimes used to accelerate S_N1 reactions

Predicting Products for S_N1 Reactions

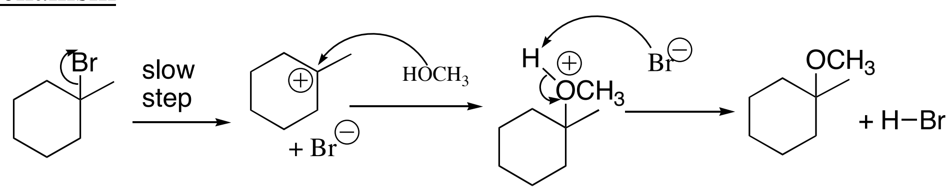
1. Don't change the structure for the carbon skeleton
2. Connect "R" and "Z", while taking the halide off of the electrophile and H off of the nucleophile
3. Unless the halide was attached to a **chiral** center, a **racemic mixture** will result
4. Maintain the integrity of the spectator attachments

Examples:





3-Step Mechanism



- Step 1: Carbocation Formation. THIS IS THE SLOW STEP
  - Therefore the rate is controlled by cation stability!
- Step 2: Carbocation capture by neutral molecule (usually a solvent molecule)
  - When cation and neutral combine, a cation is produced!
- Step 3: Deprotonation to get neutral

Notes:

1. Carbocation formation is key
2. Rate = k[R-X] → First order
3. Rate does not depend on concentration of nucleophile
4. See cations, not anions. Acidic, not basic conditions. Neutral, not anionic nucleophile.
5. Charge and atoms must balance in step 2. Thus, the oxygen retains the hydrogen.
6. Oxygen eventually loses the H, but only in step 3.
7. Rate can be enhanced by $AgNO_3$. The Ag+ cation helps strip the halide off in step 1.

<u>Structural</u> Factors that Impact S_N1 Rates

<u>Nucleophile</u>: Should be **<u>NEUTRAL</u>**, but otherwise non-factor

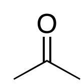
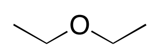
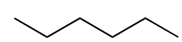
<u>Electrophile</u>

1. Substrate: Allylic > 3º > 2º > > 1º > alkenyl, aryl
   - Resonance is huge
   - alkenyl, aryl never do S_N2, 1º only with $AgNO_3$
   - product stability-reactivity principle: in the rate-determining step, the more stable the product **<u>cation</u>**, the faster it will form
   - In terms of 1º, 2º, 3º, S_N1 and S_N2 have exactly opposite patterns

2. Leaving Group: R-I > R-Br > R-Cl
   - reactant stability-reactivity principle: in the rate determining step, the weaker the C-X bond, the faster it will break
   - This pattern is the same as for S_N2

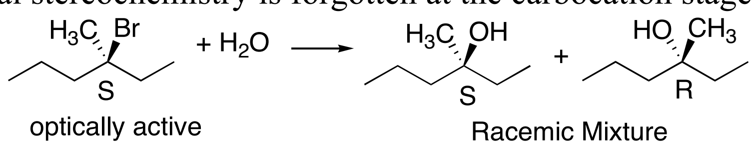
3. $AgNO_3$ Helps
   - Ag+ helps strip the halide off in step one

4. Polar Solvent Helps
   - A polar solvent helps to stabilize the ions that form in the rate-determining step

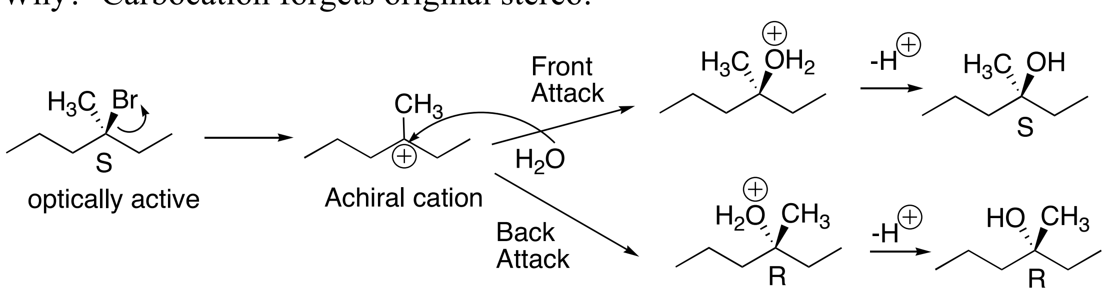
Solvent Polarity:	Most				Least
Solvent	H_2O	CH_3OH			
Relative Rate	8000	1000	1	0.001	0.0001

6.14 S_N1 Stereo: Racemization

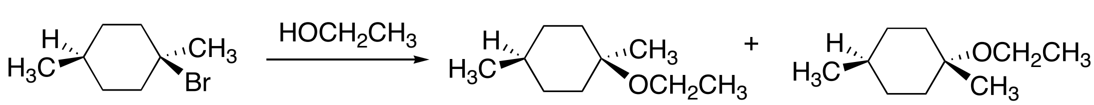
Original stereochemistry is forgotten at the carbocation stage, get racemic R/S mixture



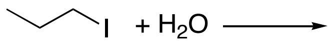
Why? Carbocation forgets original stereo:



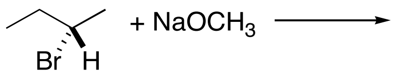
Ex.



S_N1 Problems: For the following, which are and aren't S_N1 candidates? If not, why not? What would be the product if they are S_N1 candidates?

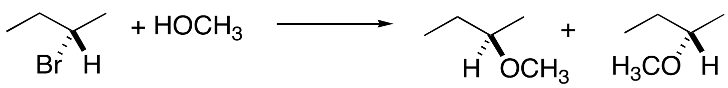
1. 

Not, 1°

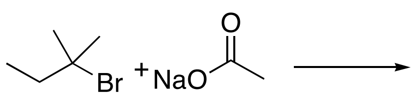
2. 

Not, S_N2, anionic

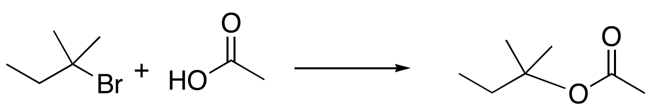
3.

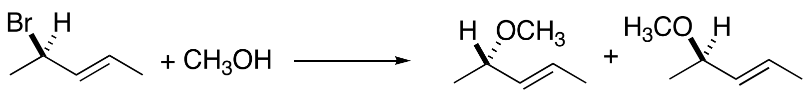
4. 

Racemic

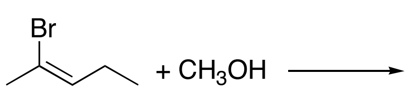
5. 

Not, S_N2, anionic

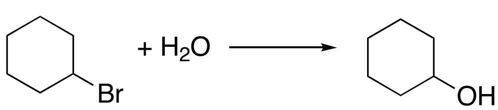
6. 

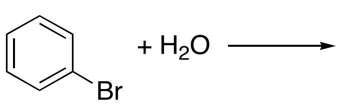
7. 

Racemic

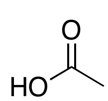
8. 

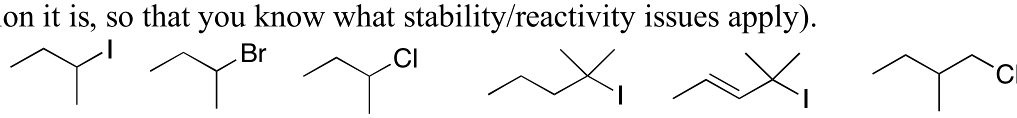
Not, vinyl

9. 

10. 

Not, Aryl

11. Rank Reactivity towards  (For any problem like this, try to recognize what kind of a reaction it is, so that you know what stability/reactivity issues apply).



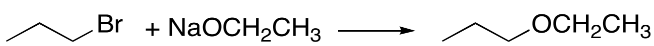
3 4 5 2 1 6

Issues: Allylic > 3° > 2° > 1° I > Br > Cl

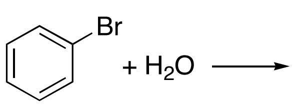
6.16 Comparing S_N2 vs S_N1

		S_N1	S_N2
1	**Nucleophile**	**Neutral, weak**	**Anionic, strong**
2	**Substrate**	**3º R-X > 2º R-X**	**1º R-X > 2º R-X**
	Allylic effect…	Allylic Helps	Allylic helps
3	Leaving Group	I > Br > Cl	I > Br > Cl
4	Solvent	Polar needed	Non-factor
5	Rate Law	K[RX]	k[RX][Anion]
6	Stereochemistry (on chiral, normally 2º R-X)	Racemization	Inversion
7	Ions	Cationic	Anionic
8	Rearrangements	Problem at times	Never

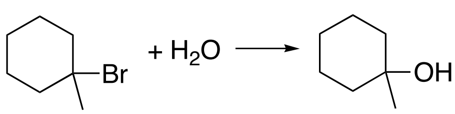
1. Identify as S_N1 or S_N2 or No Reaction. Draw the Product(s), if a reaction occurs.

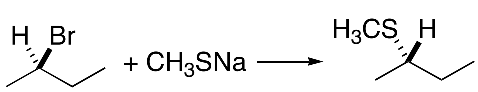
a. 

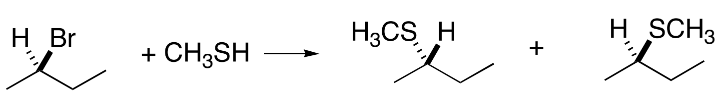
S_N2, anion, 1º

b. 

No reaction, aryl

c. 

d. 

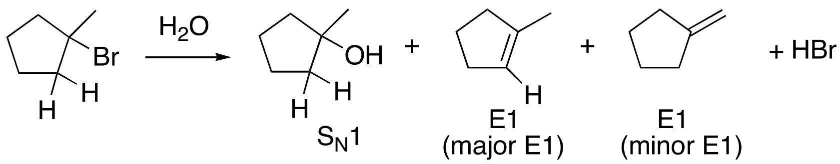
e. 

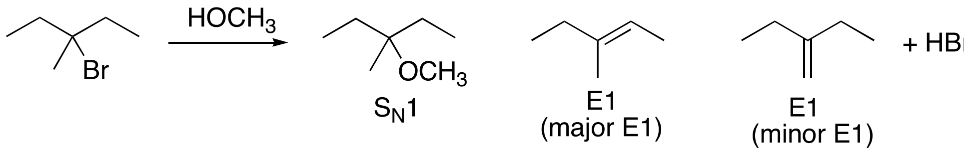
Racemic

2. Which fit S_N1, which fit S_N2?
   a. Faster in presence of silver nitrate? S_N1
   b. Faster in water than in hexane? S_N1
   c. When the moles of reactant is kept the same, but the volume of solvent is cut in half, the reaction rate increases by 2-fold? S_N1
   d. By 4-fold? S_N2
   e. 2-bromobutane reacts faster than 1-bromobutane? S_N1
   f. 2-bromobutane reacts slower than 1-bromobutane? S_N2

6-17 E1 Elimination Reactions

Examples:

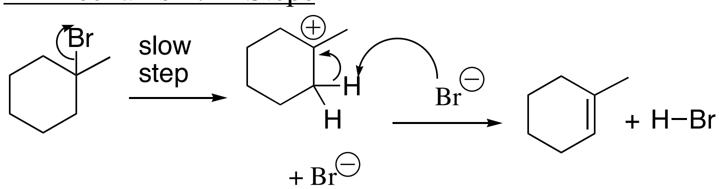




Notes

- Under S_N1 conditions, some elimination product(s) form as well
- E1 and S_N1 normally compete, resulting in mixtures
  - This is not good from a synthetic perspective.
- **Structurally Isomeric Alkenes can form**
  - **The double bond must involve the original halogenated carbon and any neighbor carbon (that had a hydrogen to begin with that can be eliminated)**
  - **Normally the alkene with fewer alkene H's is formed more extensively over alkenes with more alkene H's. (More C-substituted alkene is major).**
- Neutral/acidic (the formula starts neutral, but acid is produced)
- 1^{st} order rate law $\quad r = k[RX]^1$

E1 Mechanism: 2 Steps



- Step 1: Carbocation Formation. THIS IS THE SLOW STEP
  - Therefore the rate is controlled by cation stability! Just like S_N1!
  - Benefits from exactly the same factors that speed up S_N1 (3° > 2°, RI > RBr, polar solvent, etc..)
- Step 2: Deprotonation from a carbon that neighbors the cation (and the original halogenated carbon)
  - Draw bromide as base for simplicity
  - But often it's actually water or alcohol solvent that picks up the proton

E1 Summary

Recognition: A. Neutral, weak nucleophile. No anionic nucleophile/base, and
B. 3° or 2° alkyl halide. (Controlled by cation stability).

(For 2° alkyl halides, E1 is often accompanied by variable amounts of S_N1.)

Orientation: The most substituted alkene forms

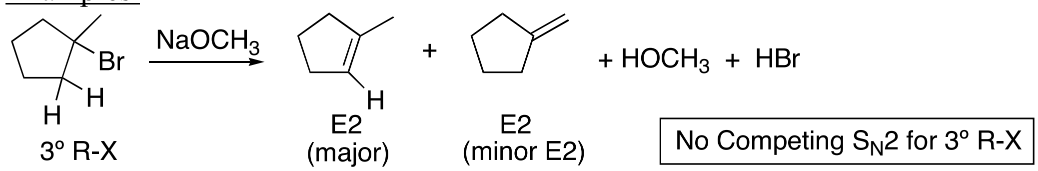
Predicting the major product: Remove halide and a hydrogen from the neighboring carbon that can give the most highly substituted alkene. The hydrogen on the neighboring carbon can be cis or trans.

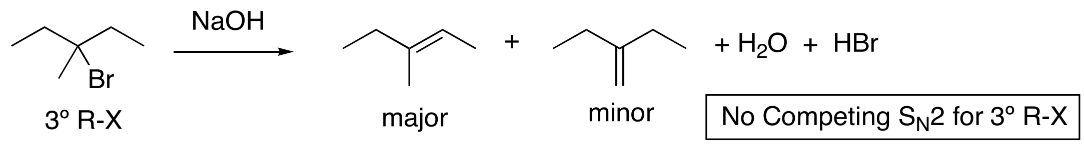
Stereochemistry: Not an issue. The eliminating hydrogen can be cis or trans. .

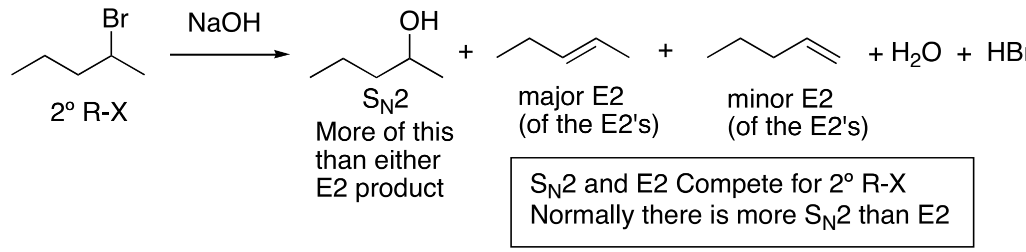
Mech: Stepwise, 2 steps, via carbocation. Be able to draw completely.

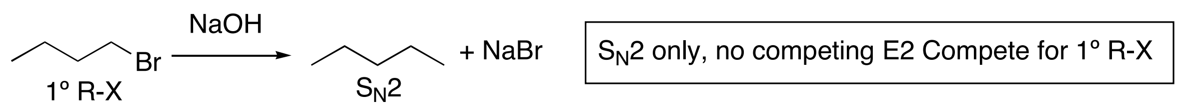
6-19 E2 Reaction (2nd Order, Under Anionic/Basic S_N2 type Conditions)

Examples





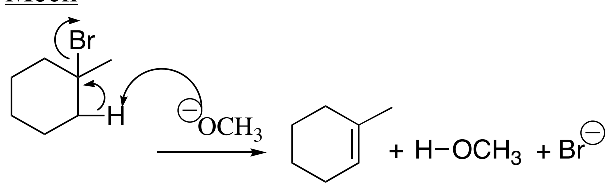




Notes

- E2 happens with **anionic nucleophiles/bases**, when S_N2 is hindered
- Reactivity: 3° R-X > 2° R-X.
  - o 1° R-X and vinyl or aryl halides do not undergo E2.
- Structurally Isomeric Alkenes can form
  - o The double bond must involve the original halogenated carbon and any neighbor carbon (that had a hydrogen to begin with that can be eliminated)
  - o Normally the alkene with fewer alkene H's is formed more extensively over alkenes with more alkene H's. (More C-substituted alkene is major).

Mech



- anionic. Anion base gets things started.
- 2nd order rate law. Rate = $k[R\text{-}X]^1[\text{anion base}]^1$
- It all happens in one concerted step, but there are three arrow to show all the bond making and breaking

Bonds Made	Bonds Broken
Base to hydrogen	C-X bond
C=C pi bond	C-H bond

E2 Summary

Recognition: A. Anionic Nucleophile/Base, and
B. 3º or 2º alkyl halide

(1º alkyl halides undergo S_N2 instead. For 2º alkyl halides, E2 is often accompanied by variable amounts of S_N2.)

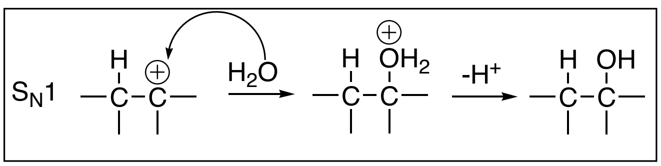
Orientation: The most substituted alkene forms (unless a bulky base is used, ch. 7)

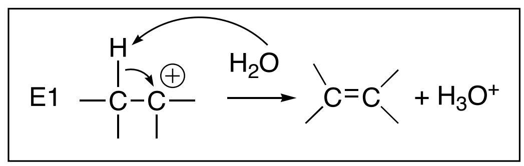
Predicting product: Remove halide and a hydrogen from the neighboring carbon that can give the most highly substituted alkene. The hydrogen on the neighboring carbon must be trans, however.

Stereochemistry: Anti elimination. The hydrogen on the neighbor carbon must be trans/anti.

Mech: Concerted. Uses anion. Be able to draw completely. Only one concerted step!

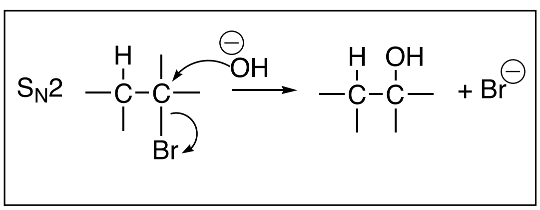
S_N1 vs E1

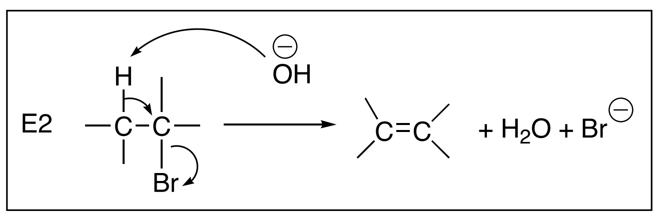




- Both satisfy the carbocation. They just meet it's bonding need with different electrons.

S_N2 vs E2

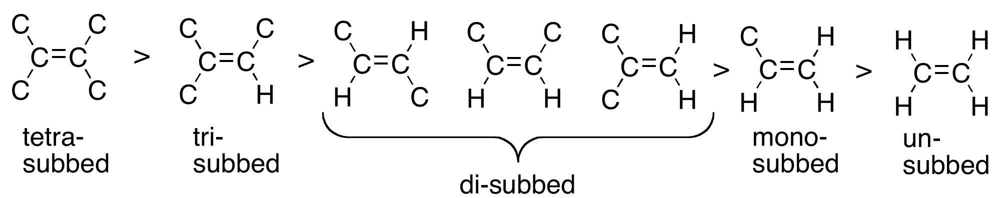


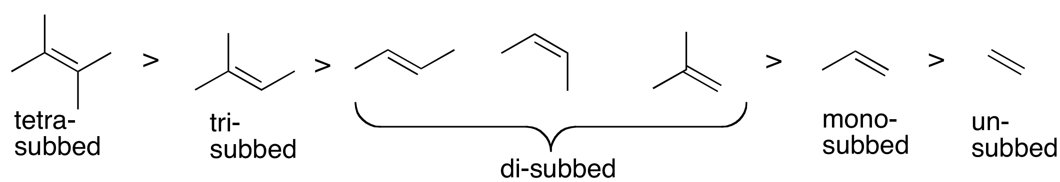


- Both provide an electron pair to displace the C-Br bond pair. They just use different electrons.
- Both involve the anion. It's called the nucleophile in the S_N2, the base in the E2.
- The S_N2 involves a crowded transition state, and thus is strongly impacted by steric factors. The E2 does not have any steric problems (and in fact alleviates them).
- The difference in steric profile explains why for S_N2, 1º > 2º > 3º, but that for E2, the reactivity of 3º is just fine.

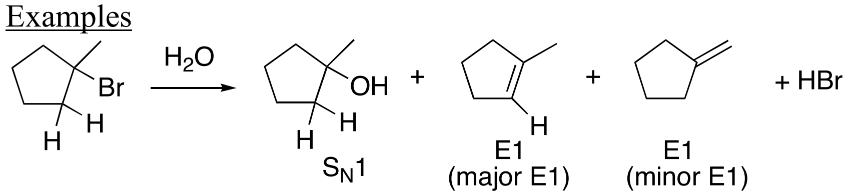
6-18 Zaitsev's Rule: When E1 or E2 elimination can give more than 1 structurally isomeric alkene, **<u>the more highly Carbon-substituted alkene form will predominate over a less highly carbon-substituted alkene</u>**.

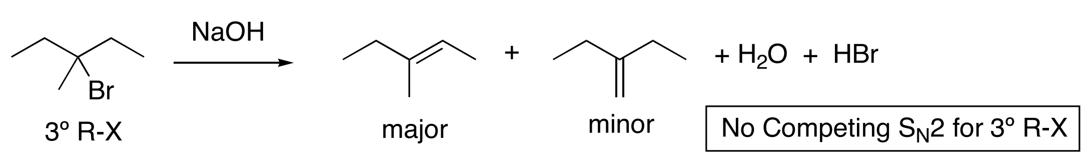
- **<u>The fewer H's on the product alkene the better.</u>**
  - o Every Alkene has four attachments. The fewer of these that are H's, the better.
  - o When pictures are drawn in which the H's are not shown, the more highly substituted alkenes turn out to be the best.
- Why? Product Stability-Reactivity Rule. Alkenes with more C's and fewer H's attached are more stable.
- Alkene Stability is shown below: tetra- > tri- > di- > mono- > unsubstituted
  - o Why?
    - ▪ Alkene carbons are somewhat electron poor due to the inferior overlap of pi bonds. (One carbon doesn't really "get" as much of the other carbon's electron as is the case in a nice sigma bond).
    - ▪ Since alkyl groups are electron donors, they stabilize electron-deficient alkene carbons.
    - ▪ Analogous to why electron-donating alkyls give the 3° > 2° > 1° stability pattern for cations and radicals

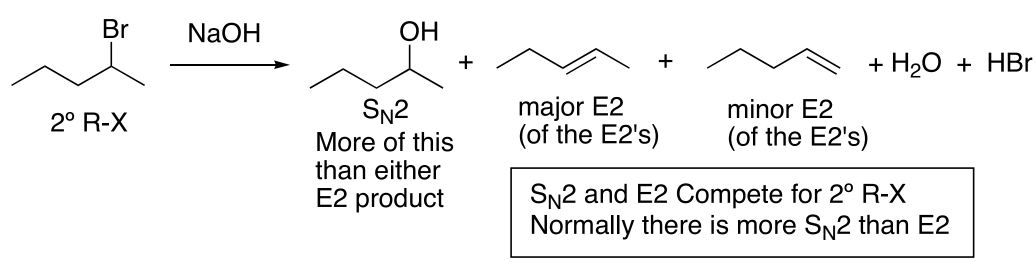




<u>Examples</u>

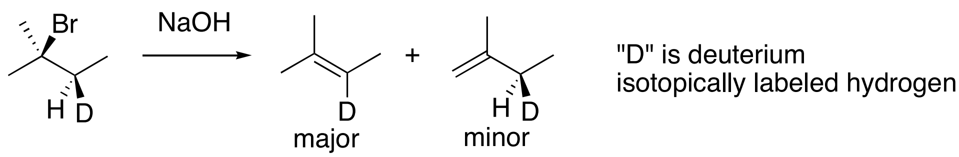




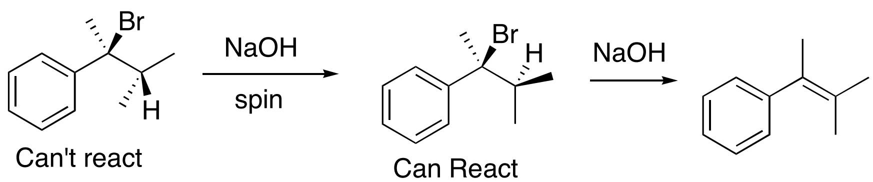


6-20 Stereochemistry of E2 Eliminations

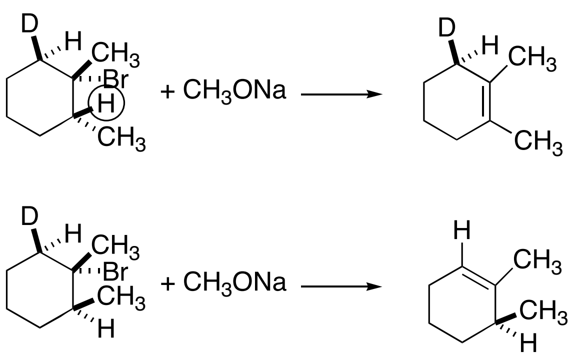
- For E2 (not for E1) C-H and C-X bonds must be in the same plane (**<u>coplanar</u>**)
- The halogen and the hydrogen being removed must be **<u>trans</u>** to each
- Why?
  - o Due to orbital overlap requirements.
  - o In the concerted E2 mechanism, the electrons from the hydrogen must essentially come in backside to the leaving halide
    - ▪ just as in backside-attack S_N2 mechanism



- Sometimes, a molecule will need to single-bond spin into an eclipsed conformation to enable it to do a trans-elimination.



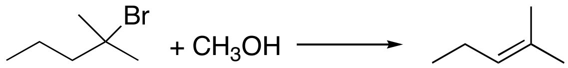
- Eliminations in **<u>Cyclic Compounds</u>** are Often impacted by the Trans Requirement



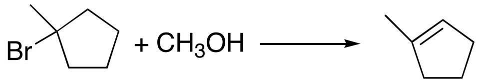
<u>6.21 Comparing E2 vs E1</u>

		<u>E1</u>	**<u>E2</u>**
1	**Nucleophile/Base**	**Neutral, weak, acidic**	**Anionic, strong, basic**
2	Substrate	3º R-X > 2º R-X	3º RX > 2º RX > 1º RX
	Allylic effect…	Allylic Helps	Non-factor
3	Leaving Group	I > Br > Cl	I > Br > Cl
4	Solvent	Polar needed	Non-factor
5	Rate Law	K[RX]	k[RX][Anion]
6	Stereochemistry	Non-selective	Trans requirement
7	Ions	Cationic	Anionic
8	Rearrangements	Problem at times	Never
9	Orientation	Zaitsev's Rule: Prefer more substituted alkene	Zaitsev's Rule: Prefer more Substituted alkene (assuming trans requirement permits)

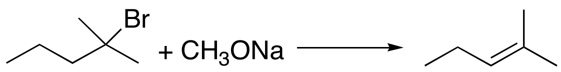
Elimination Problems: Draw the major Elimination Product for the following Reactions. Classify as E1 or E2. (There may be accompanying S_N2 or S_N1 material, but to whatever degree elimination occurs, draw the major product.)

1. 

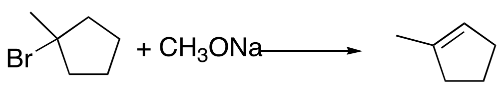
E1

2. 

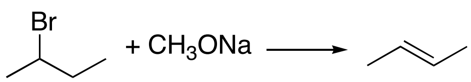
E1

3. 

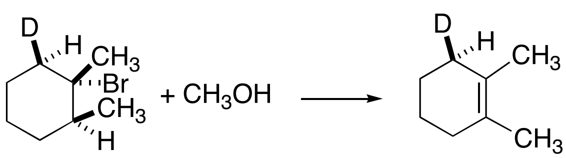
E2

4. 

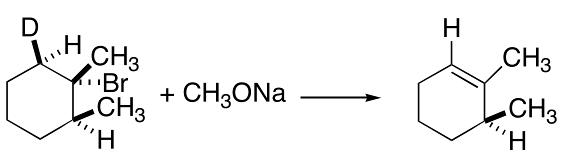
E2

5. 

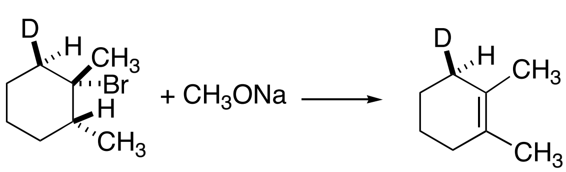
E2

6. 

E1

7. 

E2

8. 

E2

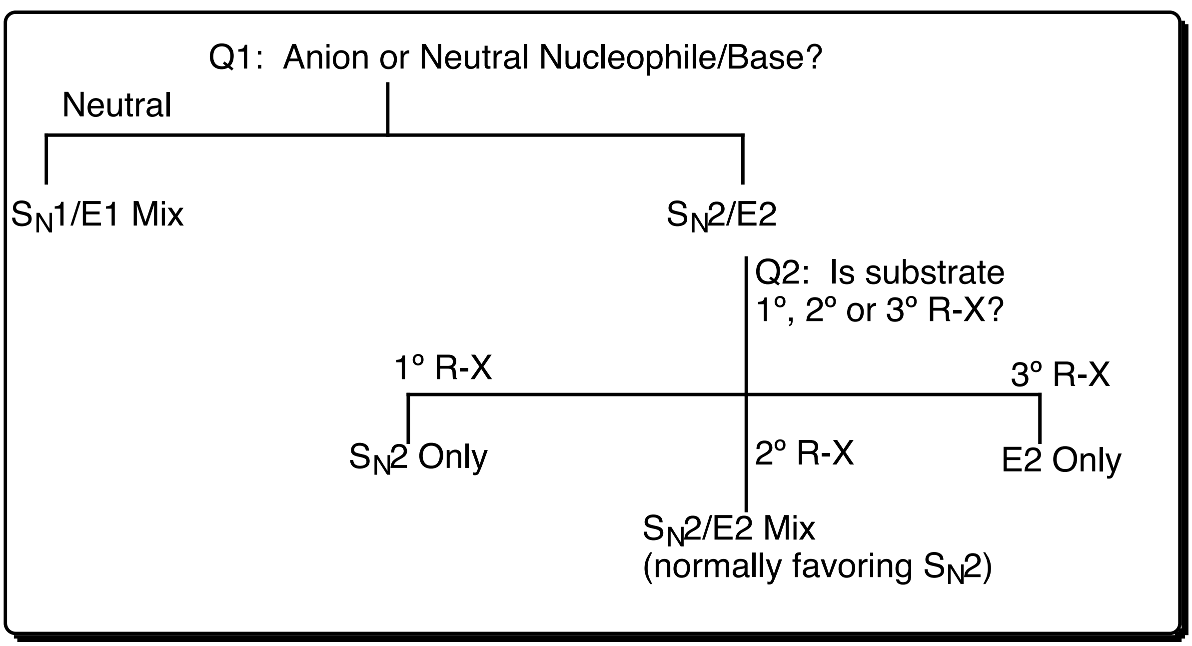
<u>Comparing S_N2 vs S_N1 vs E2 vs E1: How Do I Predict Which Happens When?</u>

Step 1: **<u>Check nucleophile/base</u>**.
- If **<u>neutral</u>**, then **<u>S_N1/E1</u>** → mixture of both
- If **<u>anionic</u>**, then **<u>S_N2/E2.</u>**

Step 2: If **<u>anionic</u>**, and in the **<u>S_N2/E2</u>** pool, then **<u>Check the substrate</u>**.
  - 1º → **<u>S_N2</u>**
  - 2º → **<u>S_N2/E2 mixture.</u>** Often more **<u>S_N2</u>**, but not reliable…
  - 3º → **<u>E2</u>**

Notes:

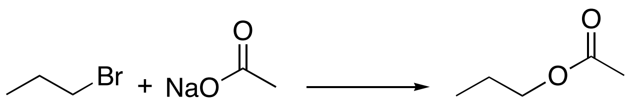
1º R-X	S_N2 only	No E2 or S_N1/E1 (cation too lousy for S_N1/E1; S_N2 too fast for E2 to compete)
3º R-X	E2 (anionic) or S_N1/E1 (neutral/acidic)	No S_N2 (sterics too lousy)
2º R-X	mixtures common	



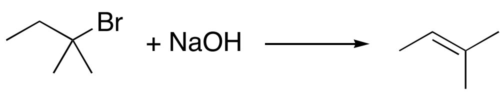
- Note: Aryl and Vinyl Halides will not undergo **<u>any</u>** of these types of reactions.
- If you see Br_2/hv type recipe, then you're back in the chapter 4 world of radical halogenation

For each mixture,

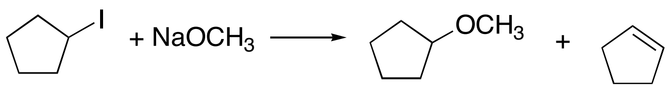
- Classify the Type of Reaction (or “no reaction”)
- Draw the <u>major</u> product. (Or both a substitution and elim product..)

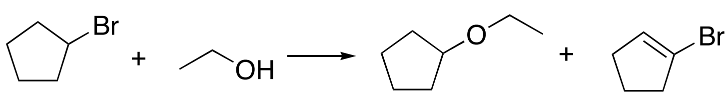
1. 

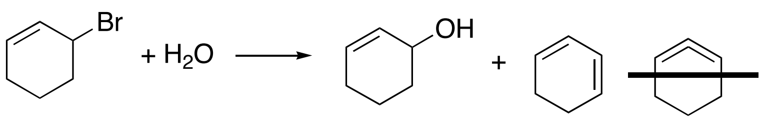
SN2, anionic, 1°

2. 

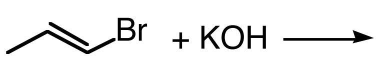
E2 Anionic, 3°

3. 

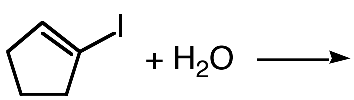
4. 

5. 

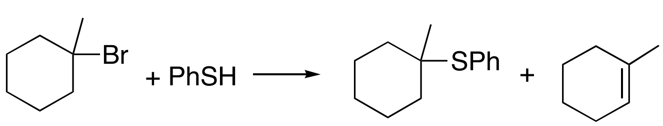
Can't make an sp center in a ring, bond angle reasons

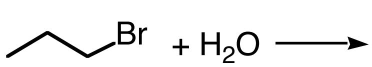
6. 

No reaction, vinyl

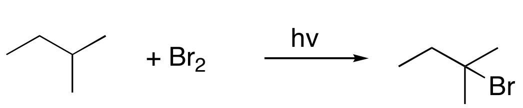
7. 

No reaction, vinyl

8. 

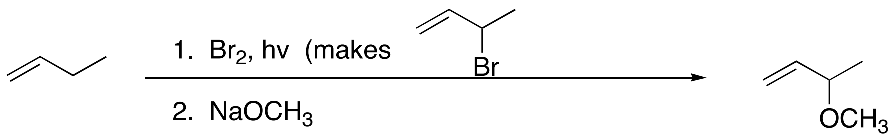
9. 

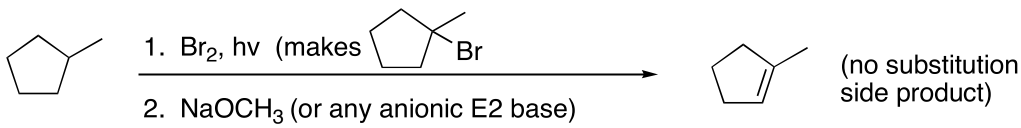
No reaction, neutral, 1°

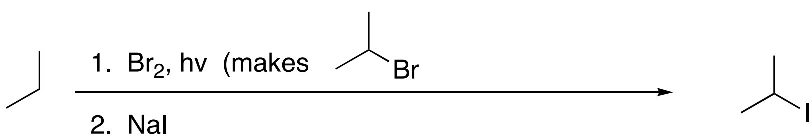
10. 

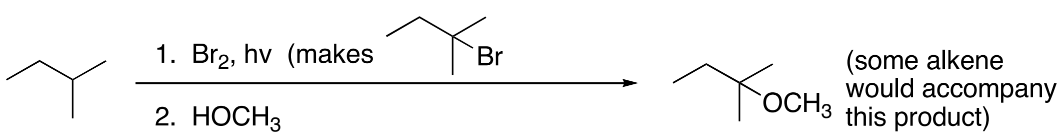
<u>Design Synthetic Plans for converting the starting materials into the target molecules.</u>

- In each case, **<u>more than one chemical operation will be required</u>**.
- Strategy: R-H → R-Br (via bromination) → Substitution product (via S_N2) or alkene (via E2)

1. 

2. 

3. 

4. 

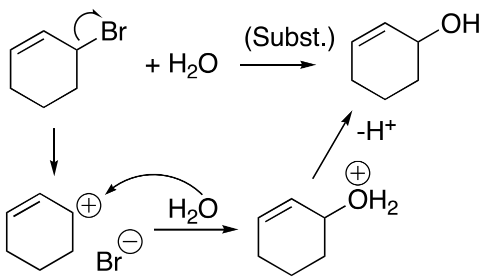
<u>Keys:</u>

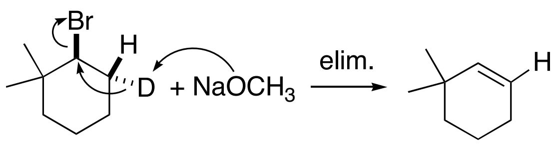
- These can't be done directly, in a single operation
- Each sequence ends up increasing the number of functional groups in the ultimate product.

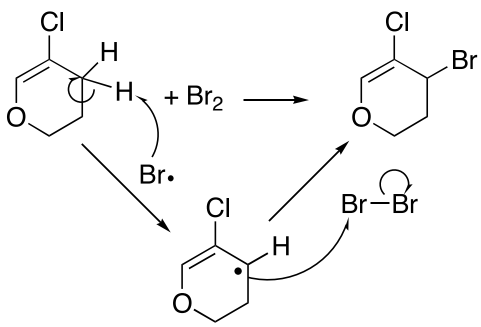
- **The key reaction for increasing the functionality**: R-H → R-Br

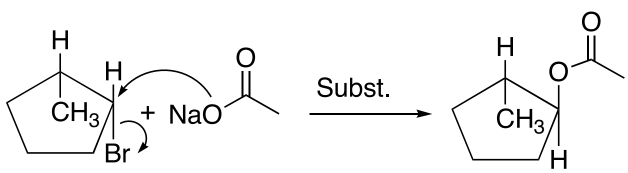
- Once you're converted the starting material to an R-Br you can interconvert that functional group into something else by substitution, or into an alkene by elimination

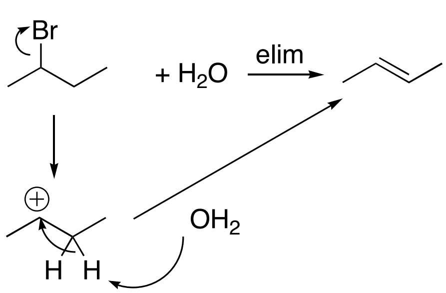
Draw the **mechanism** for formation of the major product in each of the following reactions. In some cases where both elimination and substitution might compete, the problem specifies whether to draw the substitution or elimination mechanism.

1. 

2. 

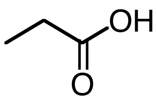
3. 

4. 

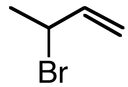
5. 

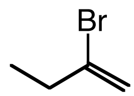
Rank the Reactivity of the chemicals shown toward the thing in the box. Keys:

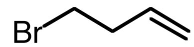
- Identify the type of reaction that would be involved
- Think about the rate-determining step and how reactant or product or transition-state stability would influence the rate.

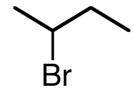


1.
Neutral, $S_N1/E1$

 1

 4

 3

 2

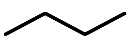
Br_2, hv

2.
Radical Halogenation
Radical Stability

$H_3C{-}CH_3$ 3

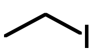
 2

 1



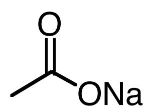
3.
Radical Halogenation
Reactant Stability/Reactivity

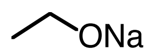
Cl•	Br•	I•
1	2	3

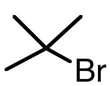


4.
Primary, S_N2

CH_3OH 3 Neutral

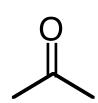
 2 resonance

 1

 (S_N1)

5.

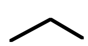
Solvent: Pentane 3

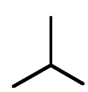
 2

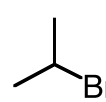
H_2O 1

NaOH

6.
Anionic, S_N2

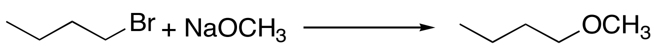
 1

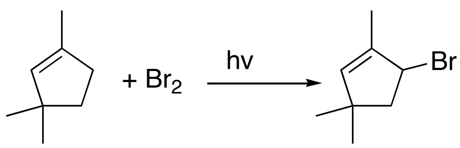
 2

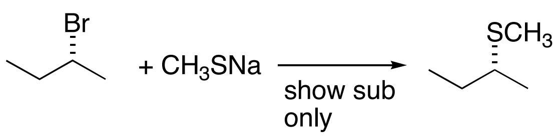
 3

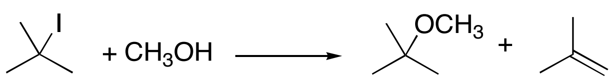
Give the Major Product(s) for each of the following. If it's likely to give a mixture of both substitution and elimination, just draw the substitution product. Designate stereochemical outcomes when stereochemistry is relevant (2º substrates).

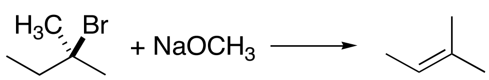
Key: Try to recognize what type of reaction will happen first.

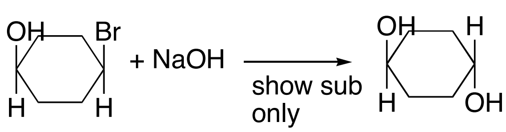


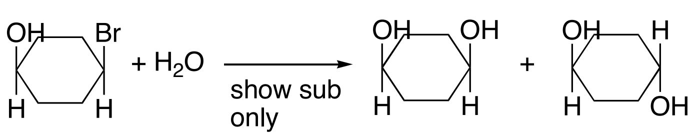




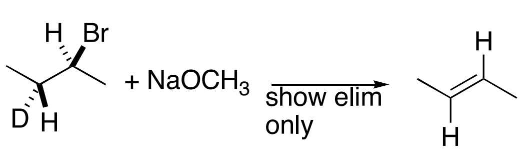






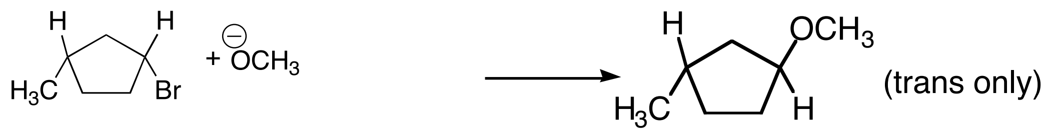


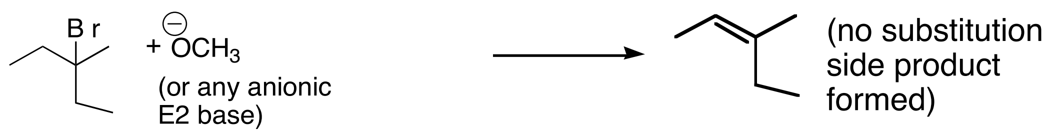
cis/trans mixture due to racemization type process

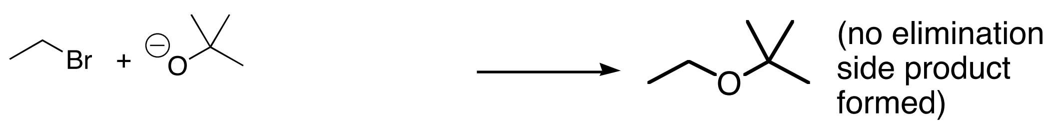


Provide Reactants for the Following (One of the Starting Chemicals must be an R-Br)

1 

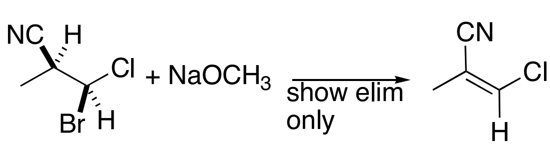
2 

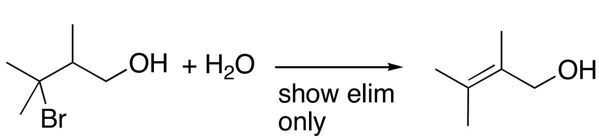
3 

4 

5 

Draw the Major Alkene Isomer, Following Elimination

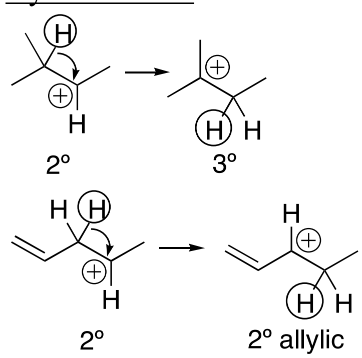
6. 

7. 

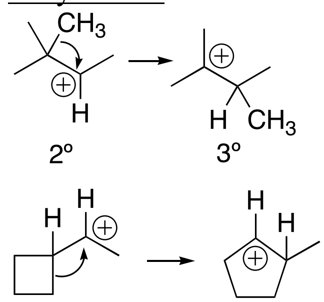
6-15 Cation Rearrangements (and their impact in S_N1 and E1 reactions)

1. Carbocations are very unstable, and sometimes rearrange to other carbocations that are more stable.
2. A rearrangement requires that a superior cation will result. Four cases:
   - 2° → 3°
   - non-allylic → allylic
   - strained ring → unstrained or less strained ring
   - 1° cation → 2° or 3° cation (rare, since 1° cations are hard to make and pretty rare)

Hydride Shifts

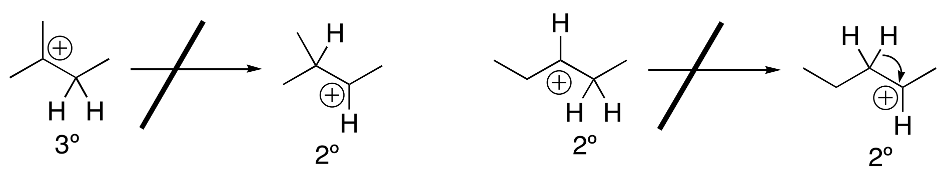


Alkyl Shifts

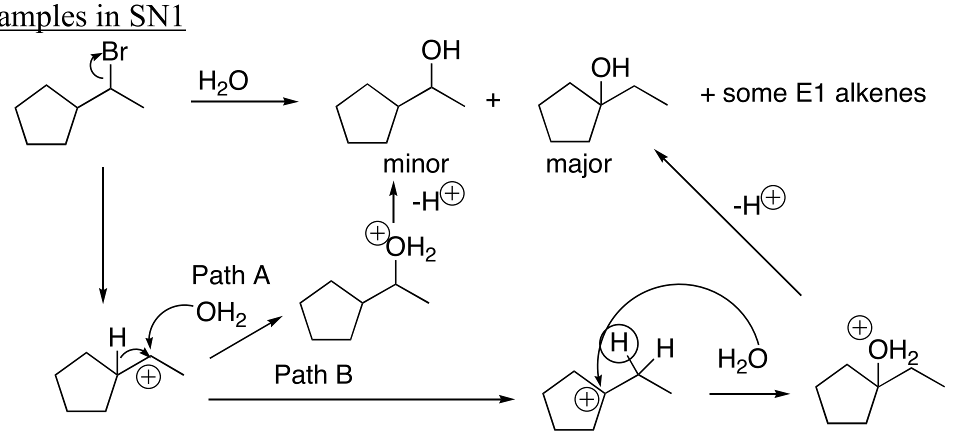


3. Two processes for cation rearrangement:
   - Hydride shift (an H jumps over)
   - Alkyl shift (a carbon jumps over)
4. The resulting rearranged cation must always be on a carbon directly adjacent to the original
5. Cation rearrangement does not occur if you start with a pretty good cation in the first place.
   - Thus, most cation mechanisms that start with 2° or 3° cations don't undergo rearrangement because rearrangement does not lead to improved cation stability

Why Bother?
No Stability Gain,
No Motive,
Won't Happen



Examples in SN1



- Product mixture results from competition between Path A and Path B.