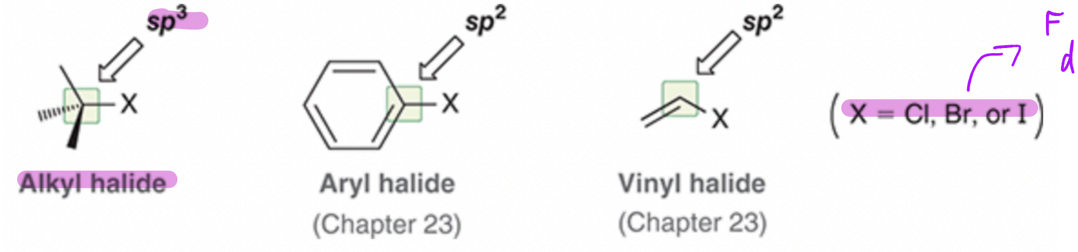
Session 10 Worksheet

Nucleophilic Reactions

Alkyl Halide: A compound with a halogen connected to an sp^3 - carbon



F not included due to reactivity

halogen — aromatic ring

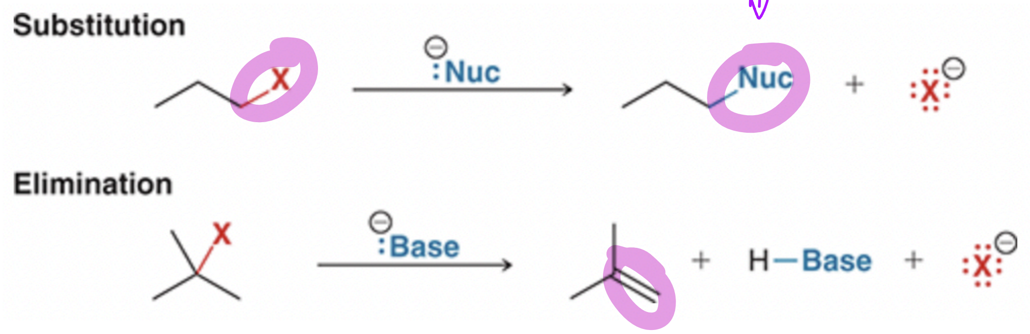
halogen = double bond

Alkyl halides undergo 2 types of reactions:

nucleophile replaces halogen

replaced the "X"

A π bond is formed



Nucleophile:

"nucleus-loving" attracted to a more + charge while being a − charged species

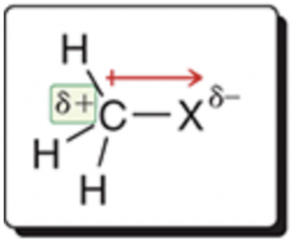
Electrophile:

"electron-loving" attracted to a − charge while being a + charged species

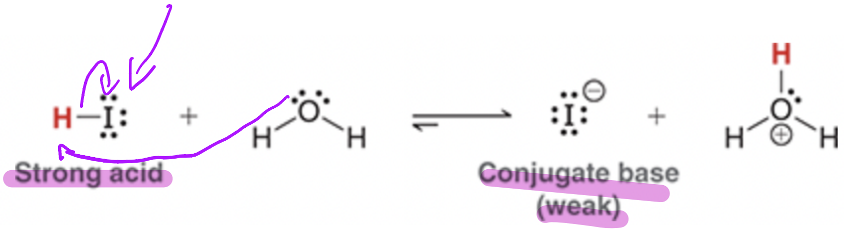
Leaving Group:

In an alkyl halide, the halogen serves to:

1. withdraw e^- density via induction



2. be a leaving group



Leaving Group:

A group capable of seperating from a compound

Good leaving groups:

Are the conj. base of an acid with a pKa less than 0!

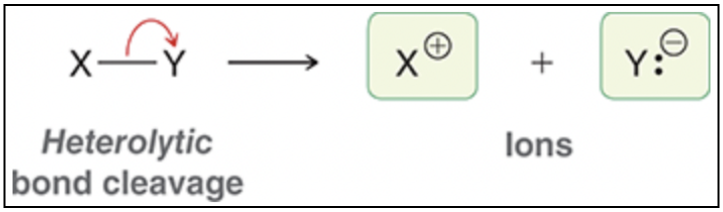
For halogens:

HF has a pKa of 3.2 so its a <u>bad</u> leaving group

I > Br > Cl > F

Additionally, C-F are very strong, requiring more energy to break

Heterolytic bond cleavage:



Types of mechanisms:

1. SN2 (concerted mechanism)
2. SN1 (stepwise mechanism)

Hammond Postulate

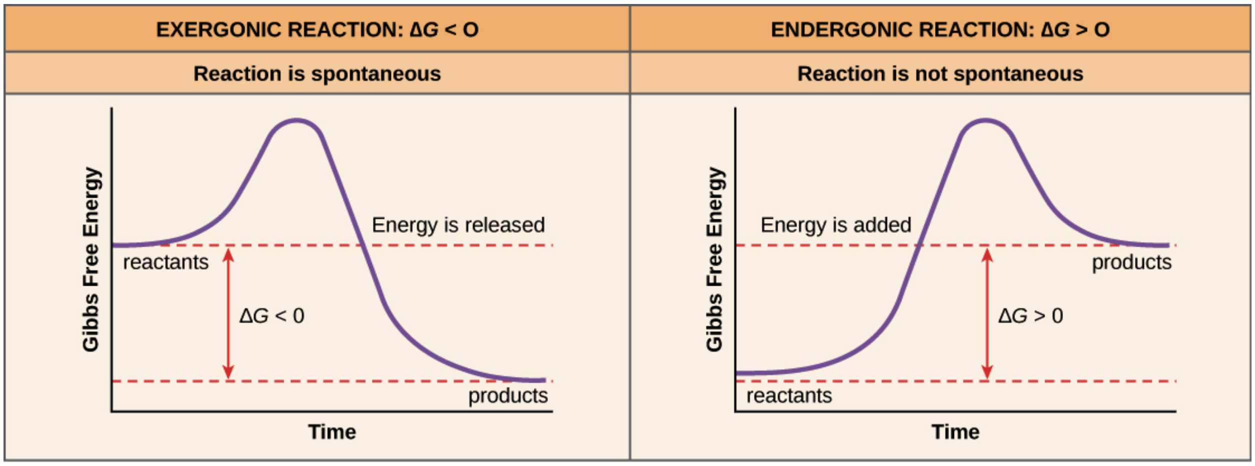
- A transition state will resemble the structure of the nearest stable species

Exergonic Reaction:

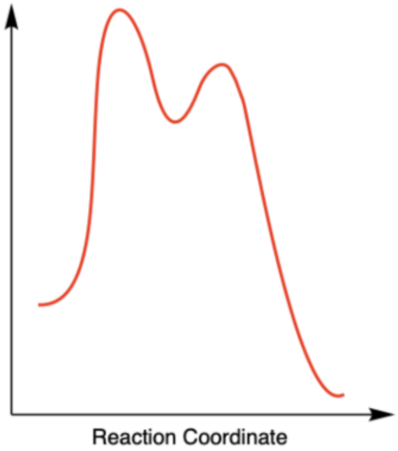
- Transition state looks more like the reactants
- releases energy (heat)

Endergonic Reaction:

- Transition state looks more like the products
- Takes energy from surroundings (gets cold)



Reaction Coordinate



Every peak represents a Transition state

Every valley represents an Intermediate

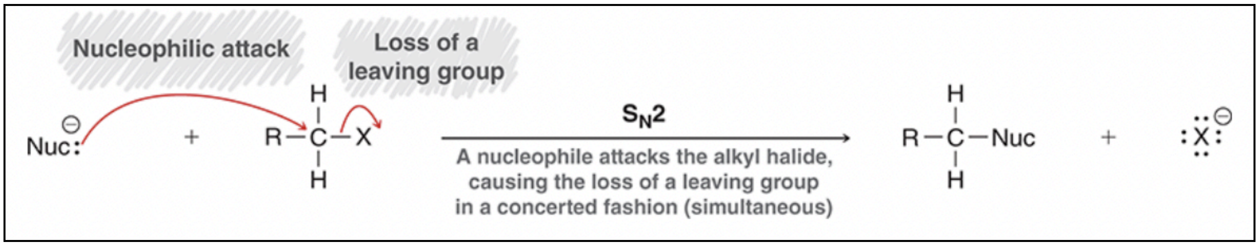
SN2 Reactions

nucleophilic

Substitution SN2 bimolecular

Concerted Mechanism:

Rxn happens ~~all steps~~ at the same time



A nucleophile attacks the alkyl halide, causing the loss of a leaving group in a concerted fashion (simultaneous)

Kinetics: 2nd order

Rate = k [alkyl halide] [nucleophile]

<u>Concept question</u>: What would happen if the concentration of the nucleophile were doubled?

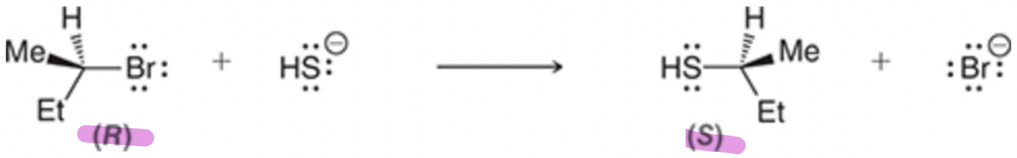
The reaction rate would double! (AKA reaction becomes 2x faster)

Sterospecificity of SN2:

Configuration inverts

R → S

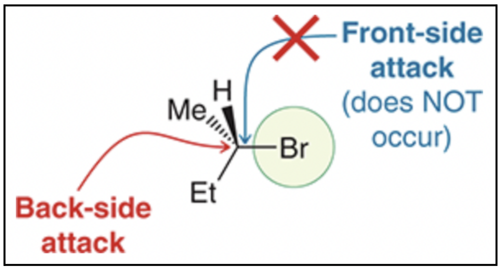
S → R



Nucleophiles attack: From the back (the side opposite of the leaving group)

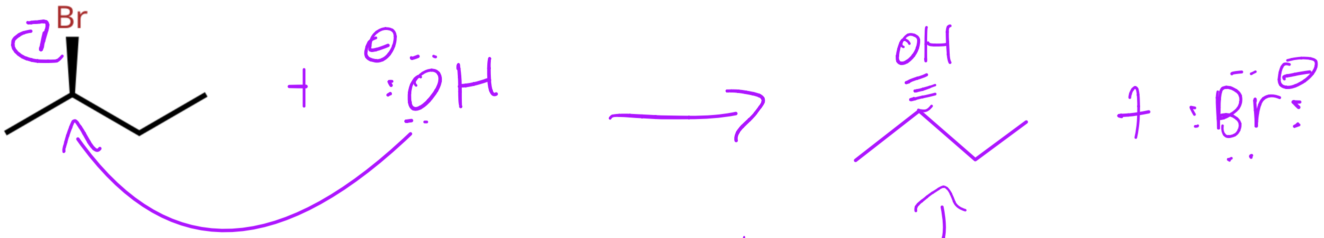
SN2 **WILL NOT** happen on a 3° alkyl halide because there is no room for a backside attack to occur

This is referred to a nucleophilic attack or backside attack



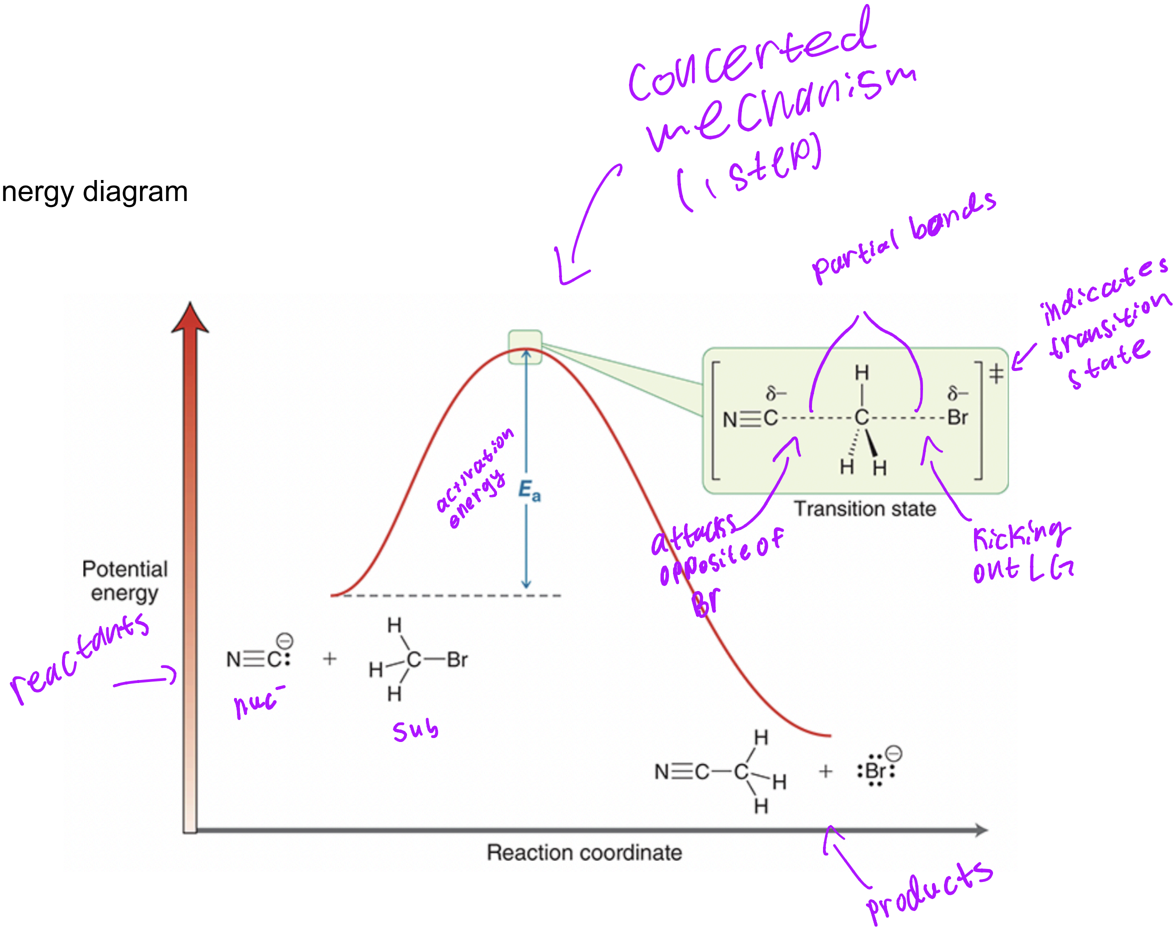
SN2 is stereospecific, meaning: configuration of the product is dependent on the configuration of the starting material

Example:



hydroxide hit molecule from the back, so we have an inversion of configuration

Free energy diagram



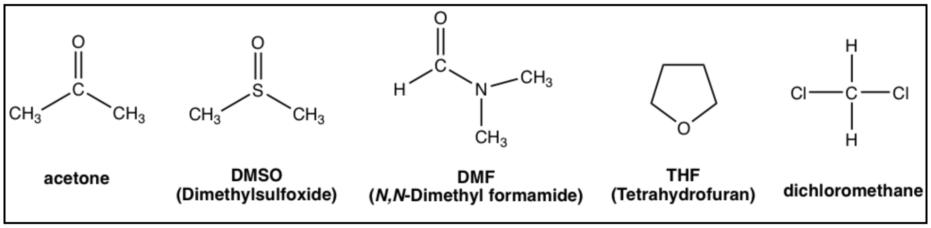
How many transition states does Sn2 have? How many intermediates?

1 T-state, 0 intermediates

SN2 requires a Primary and Secondary alkyl halide

Strong nucleophiles					
$:\ddot{I}:^{-}$	$:\ddot{Br}:^{-}$	$:\ddot{Cl}:^{-}$	$H\ddot{S}:^{-}$ $R\ddot{S}:^{-}$	$H\ddot{O}:^{-}$ $R\ddot{O}:^{-}$	$:N\equiv C:^{-}$

SN2 needs a polar aprotic solvent



acetone

DMSO (Dimethylsulfoxide)

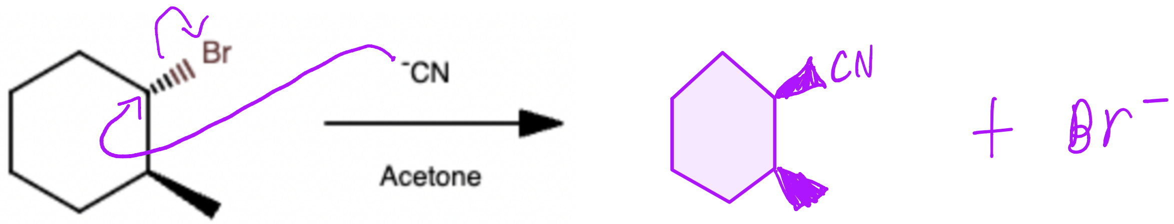
DMF (*N,N*-Dimethyl formamide)

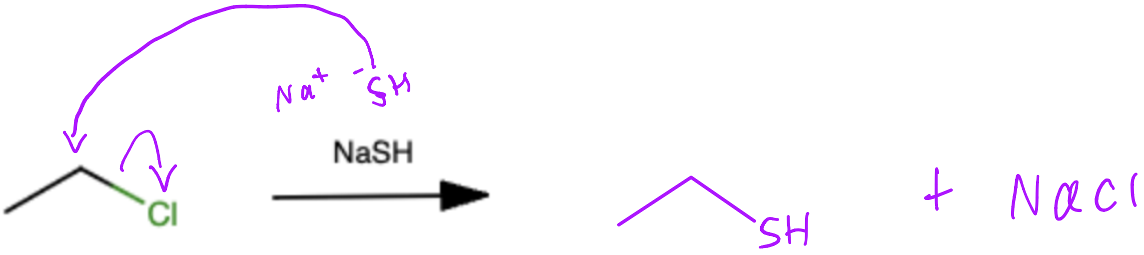
THF (Tetrahydrofuran)

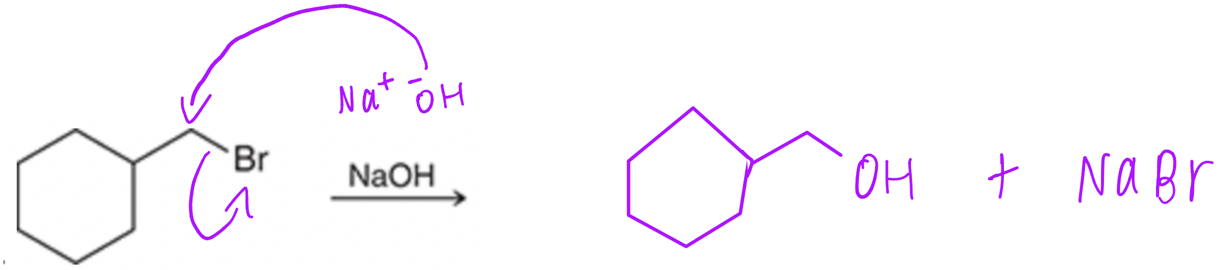
dichloromethane

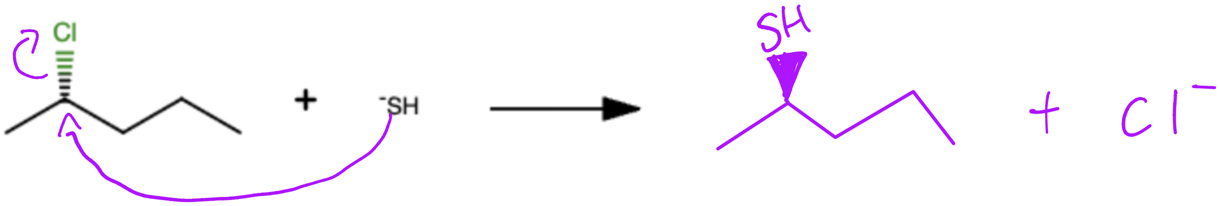
- aprotic means the compound has no acidic Hs
- Sn2 needs a polar aprotic solvent because they can dissolve the salt - nucleophile structure - but don't hinder the reactivity of the nucleophile
- Prevents Solvation effect

Practice: predict the products of the following SN2 reaction and draw the mechanism









Sn1 Reactions

nucleophilic

SN1

Substitution

unimolecular

Uses a Step-wise mechanism

Typically happens on a 3° alkyl halide

$3^\circ > 2^\circ$ (~~> 1° >~~ Me) doesn't happen

Kinetics:

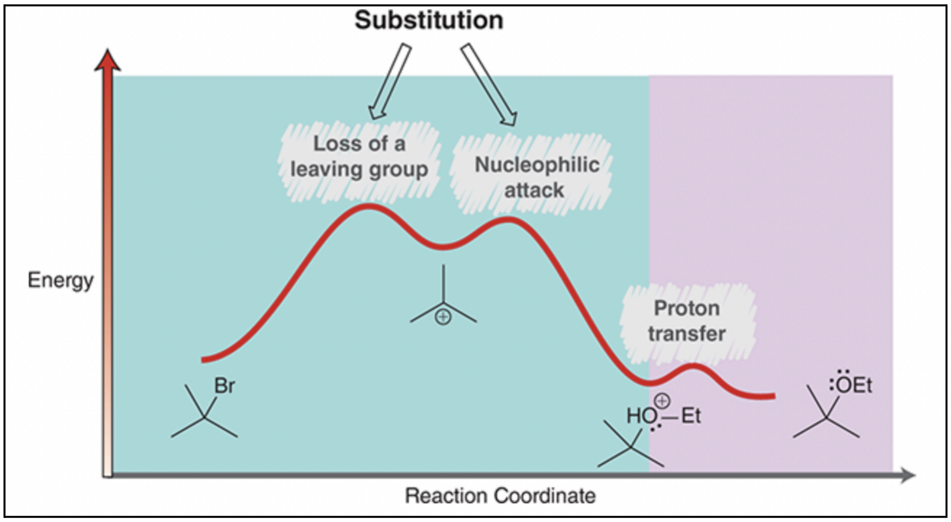
First order

Rate = K [Sub]

Rate-determining step (RDS):

Typically, k1 is the slowest RDS, and speeds up with K2 and K3 following after

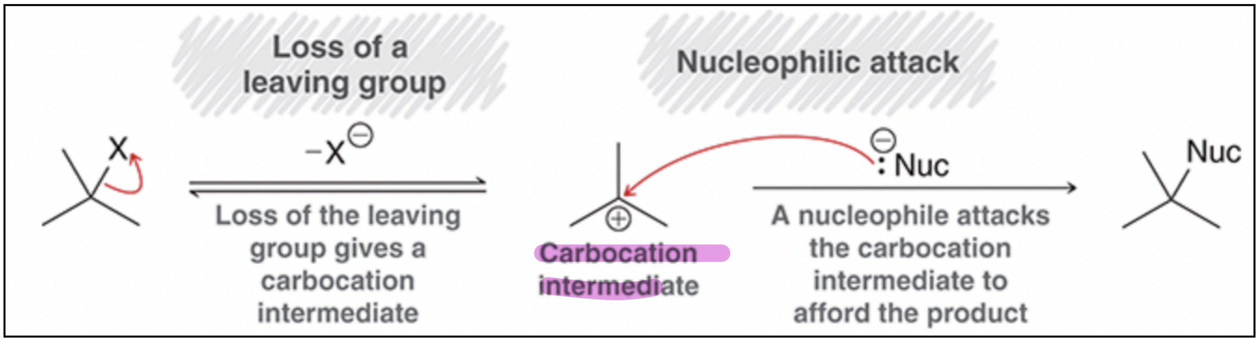
Free energy diagram:



How many transition states does Sn2 have? How many intermediates?

3 T-states, 2 intermediates

Mechanism of Sn1:



RDS

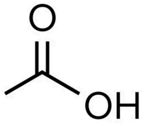
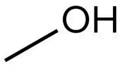
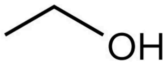
Sn1 Nucleophiles are usually weak

Common weak nucleophiles

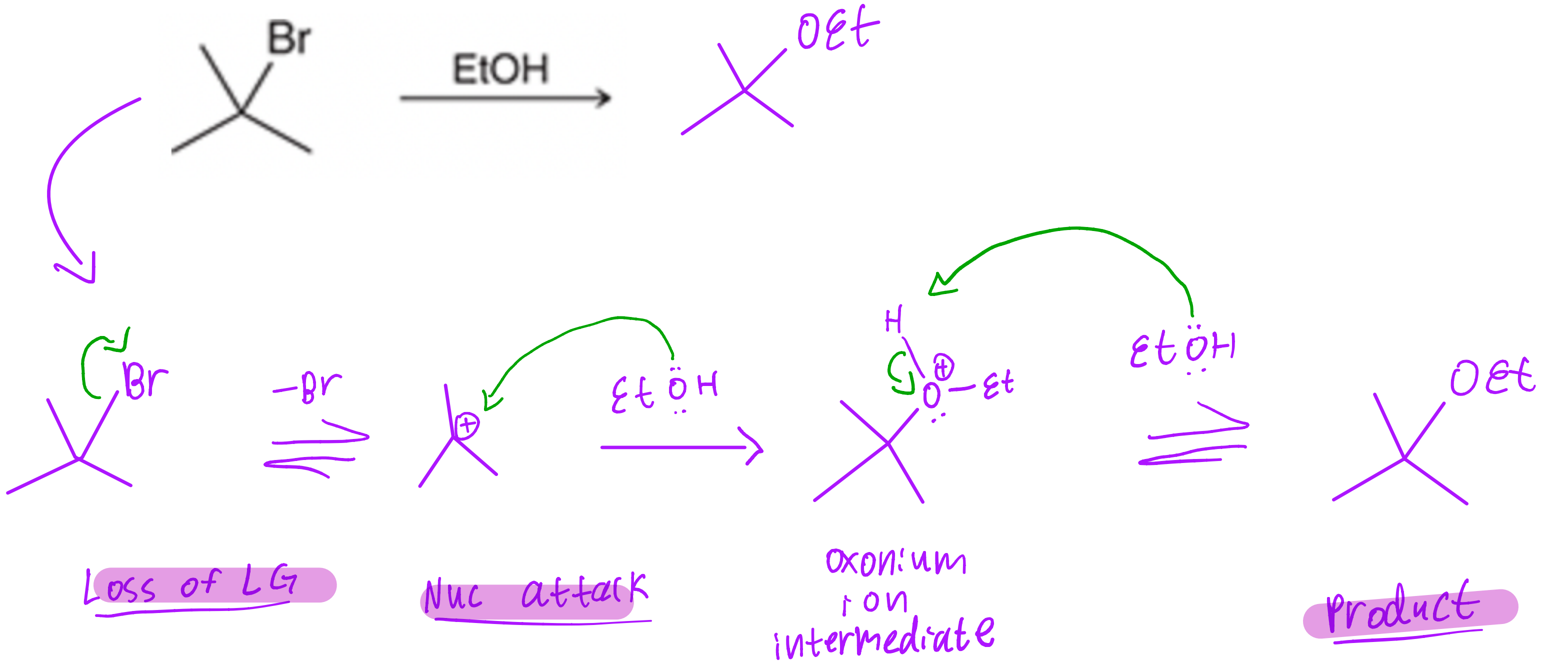
H_2O	ROH MeOH EtOH	ROOH

Sn1 needs a polar protic solvent

- contain acidic hydrogens and/or hydroxyl groups
- The solvent also acts like the nucleophile, a common occurence for Sn1
  - This is called solvolysis

Water	H_2O
Acetic acid	
Ammonia	NH_3
Methanol	
Ethanol	

Example:

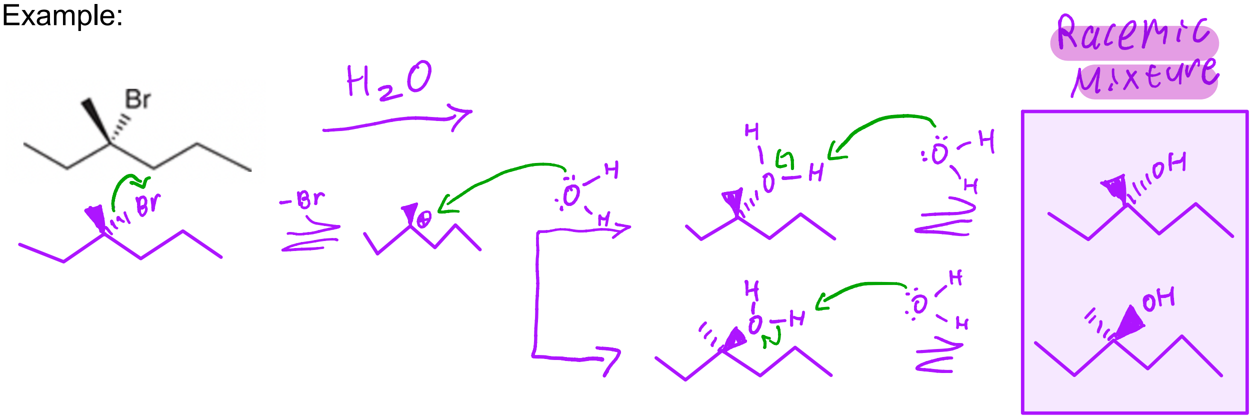


Stability of carbocations: 3° > 2° > 1° > Me

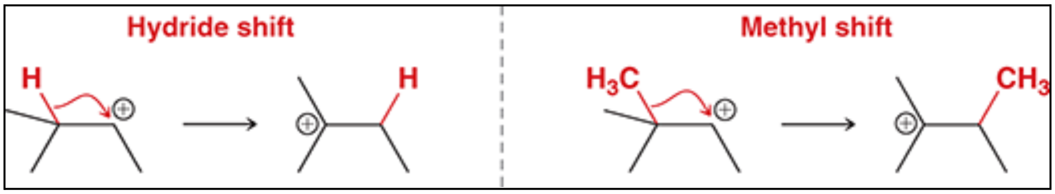
Carbocations have a trigonal planar structure, making the products of

Sn1 a Racemic mixture

Example:

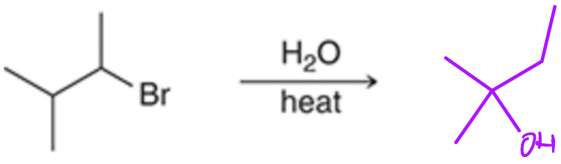


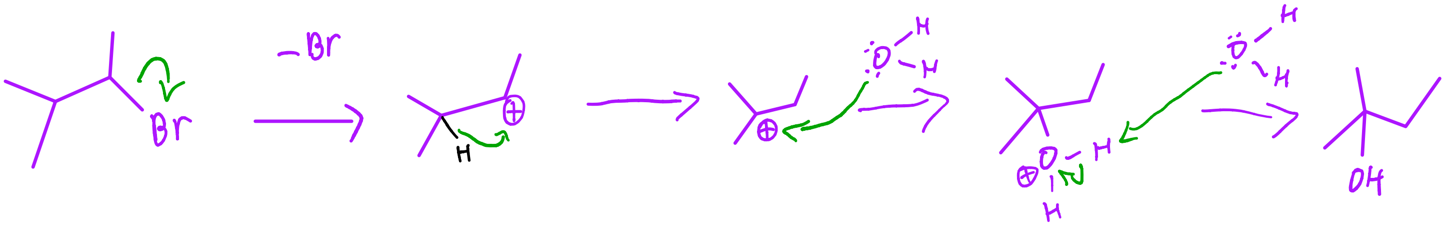
Carbocations can __rearrange__ to form the most stable product:



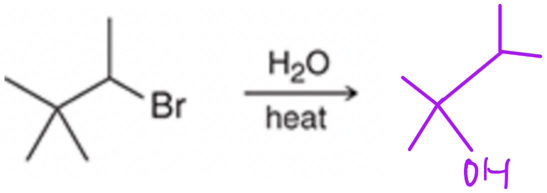
Example (hydride shift):

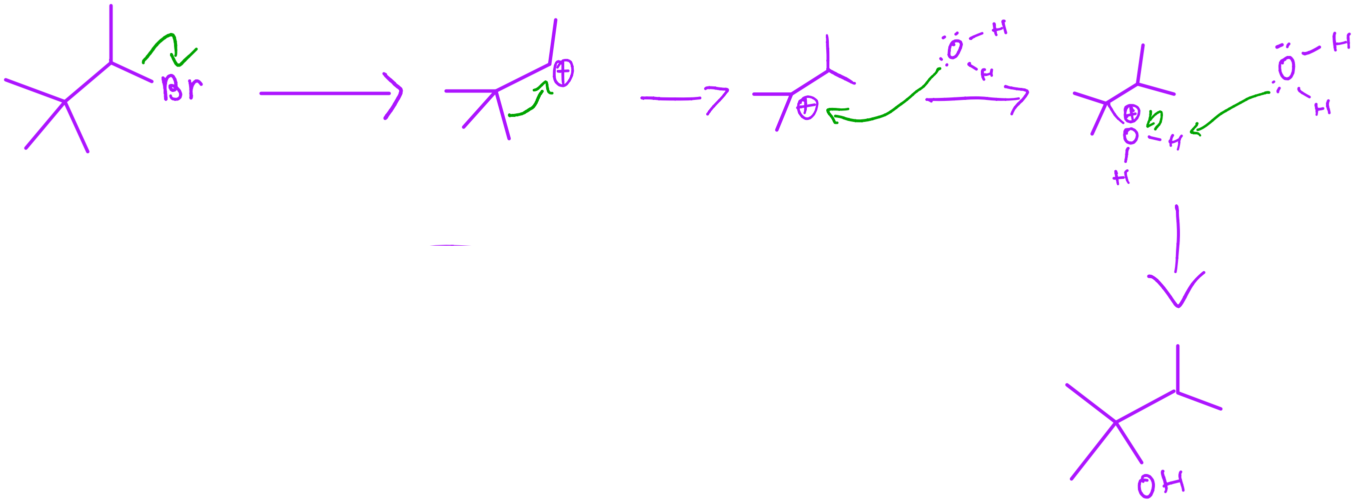
(hydride shift)



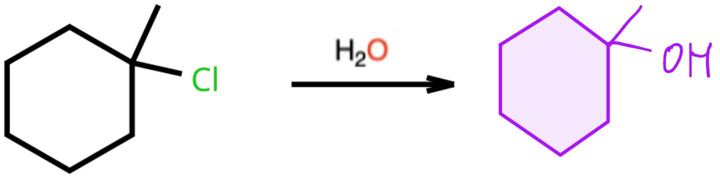


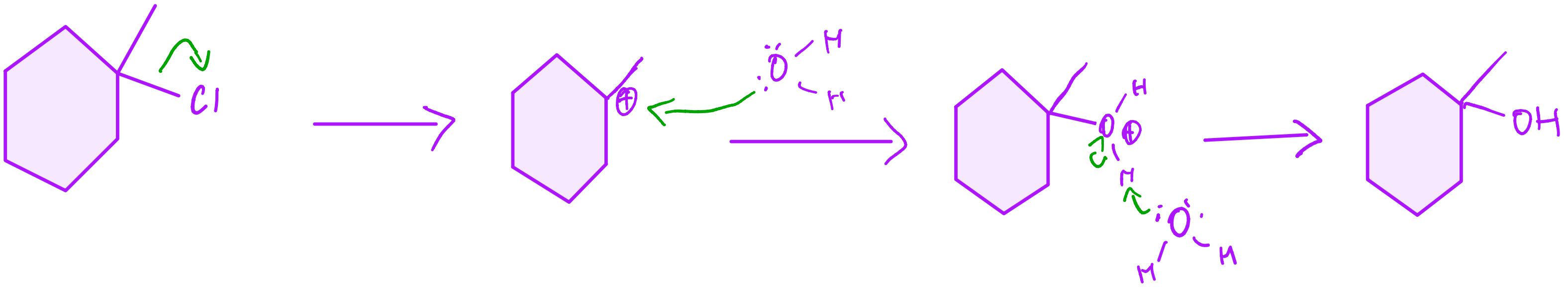
(methyl shift)

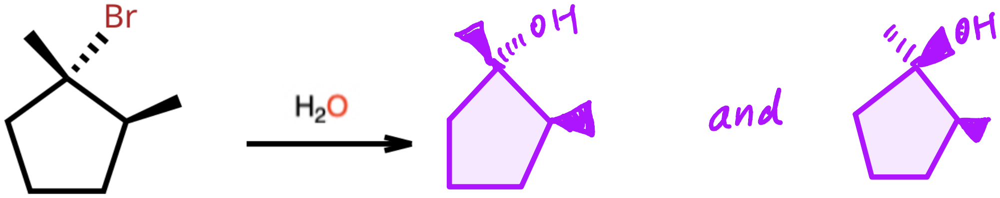


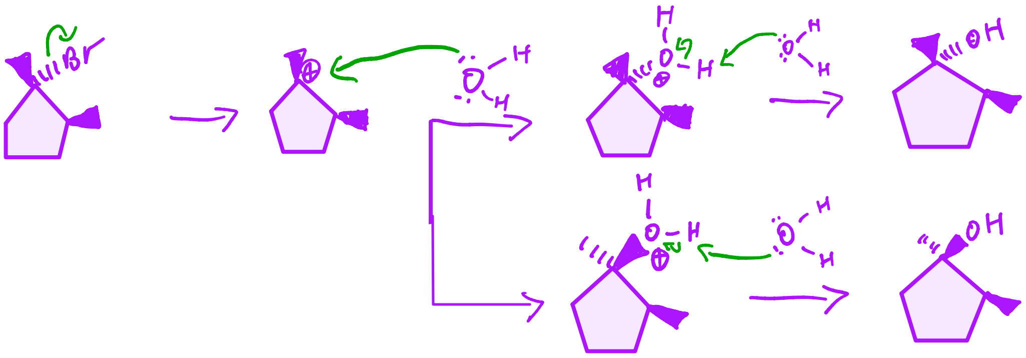


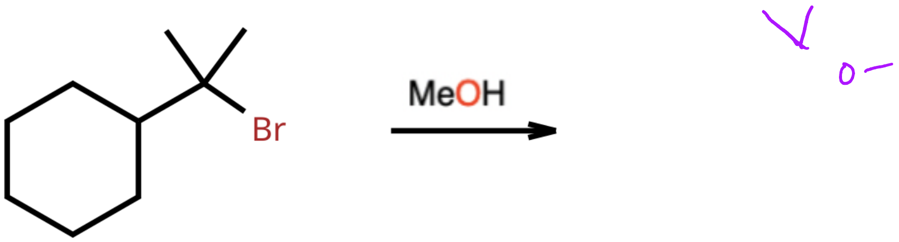
Practice

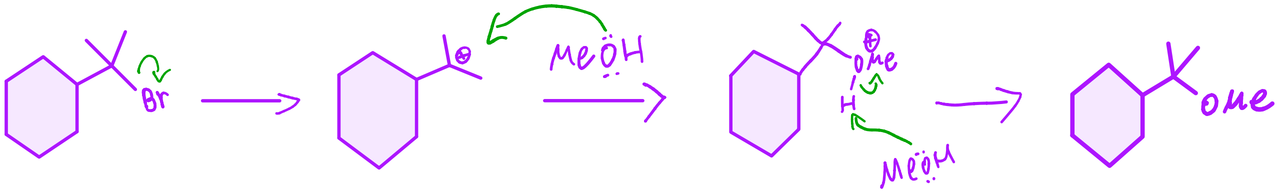

Cl
H$_2$O
OH

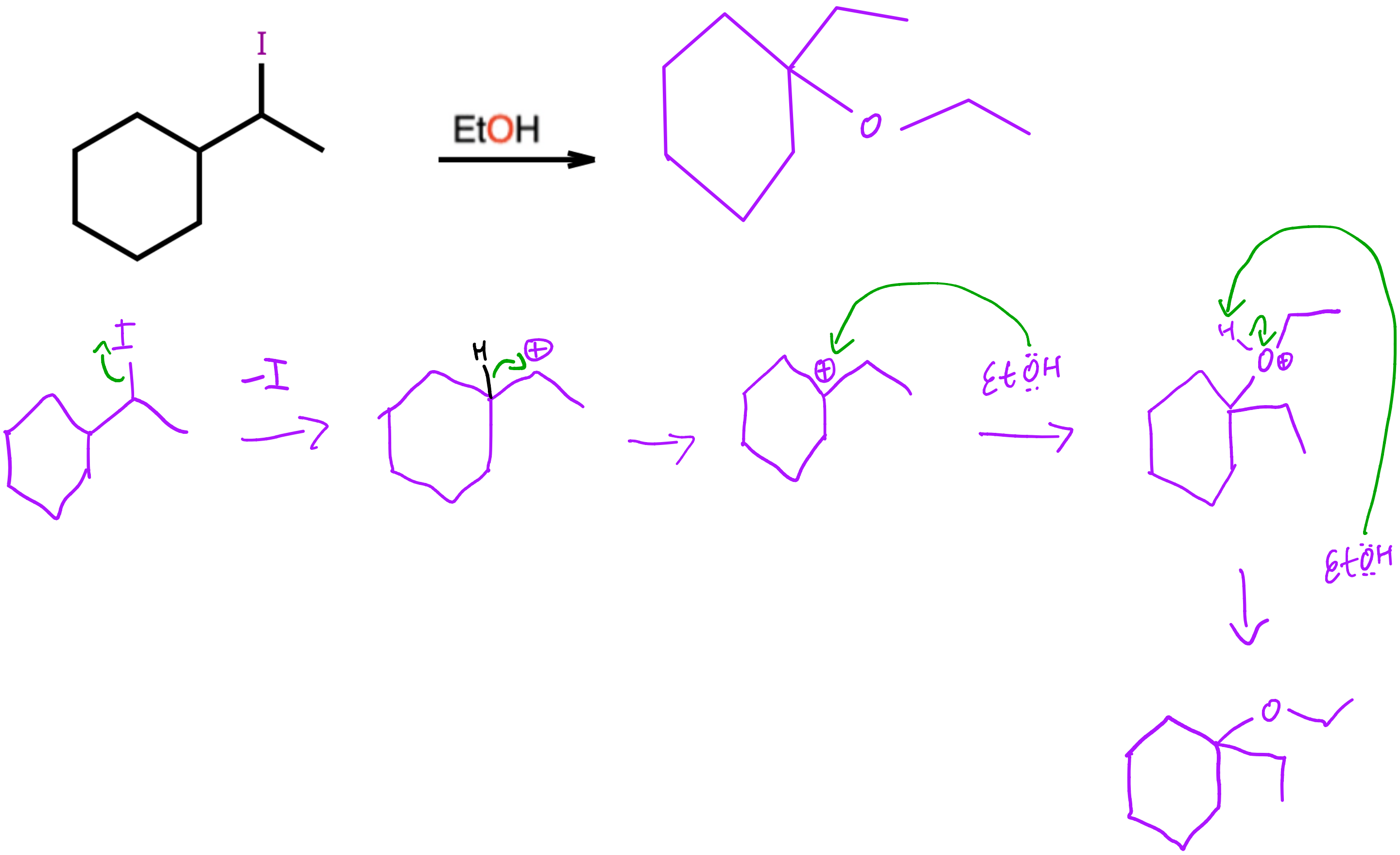

Cl
⊕
:Ö–H
H
O⊕
H
:Ö:
H
H
OH


Br
H$_2$O
OH
and
OH


Br
⊕
Ö–H
H
H
O⊕
H
Ö–H
H
OH
H
O–H
⊕
Ö–H
H
OH


Br
MeOH
O–


Br
⊕
MeÖH
⊕
OMe
H
MeÖH
OMe


I
EtOH
O
I
-I
H
⊕
⊕
EtÖH
H
O⊕
EtÖH
O