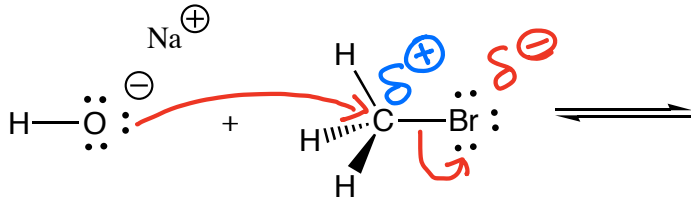


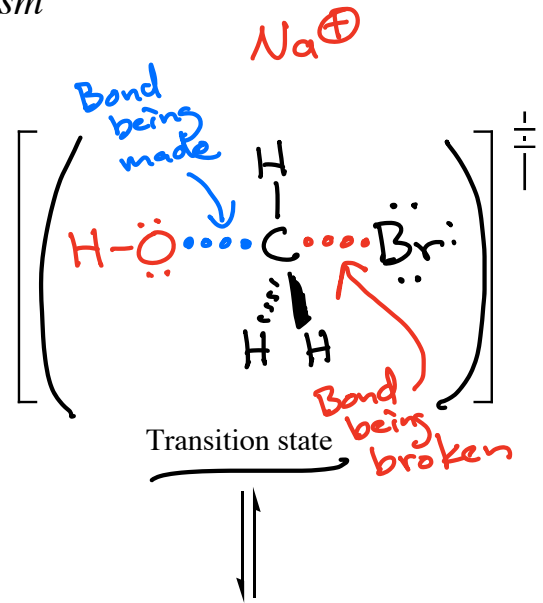




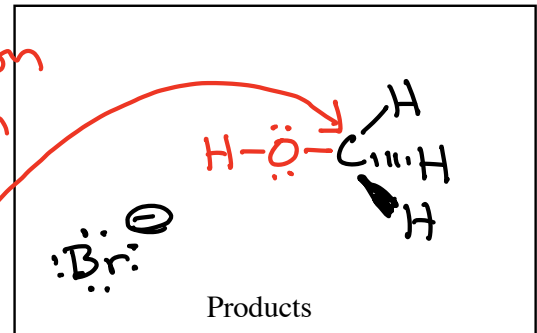
The S_N2 Mechanism



Nucleophile → must attack at the back of the C-Br bond. ⇒ This angle and direction of attack helps break the C-Br bond



The configuration at this carbon atom is inverted



Summary: The nucleophile attacks by making a new bond to C from the back of the C-X bond just as X leaves

Regiochemistry: N/A

Stereochemistry: **INVERSION** at the site of reaction

Example:

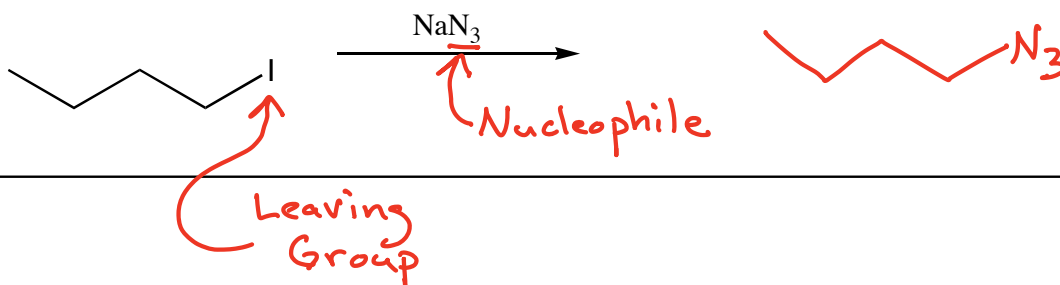


Table of Nucleophiles

Strong Nucleophiles

Br^- , I^- , R-S^- , H-S^- , $\text{N}\equiv\text{C}^-$, N_3^-

$\text{R-C}\equiv\text{C}^-$, R-O^- , H-O^- **Strong Bases**

Medium Nucleophiles

**R-CO_2^- , R-S-H , R_2S ,
 NH_3 , RNH_2 , R_2NH , NR_3**

Weak Nucleophiles

$\text{R-CO}_2\text{H}$, R-O-H , H_2O **Very Weak Bases**

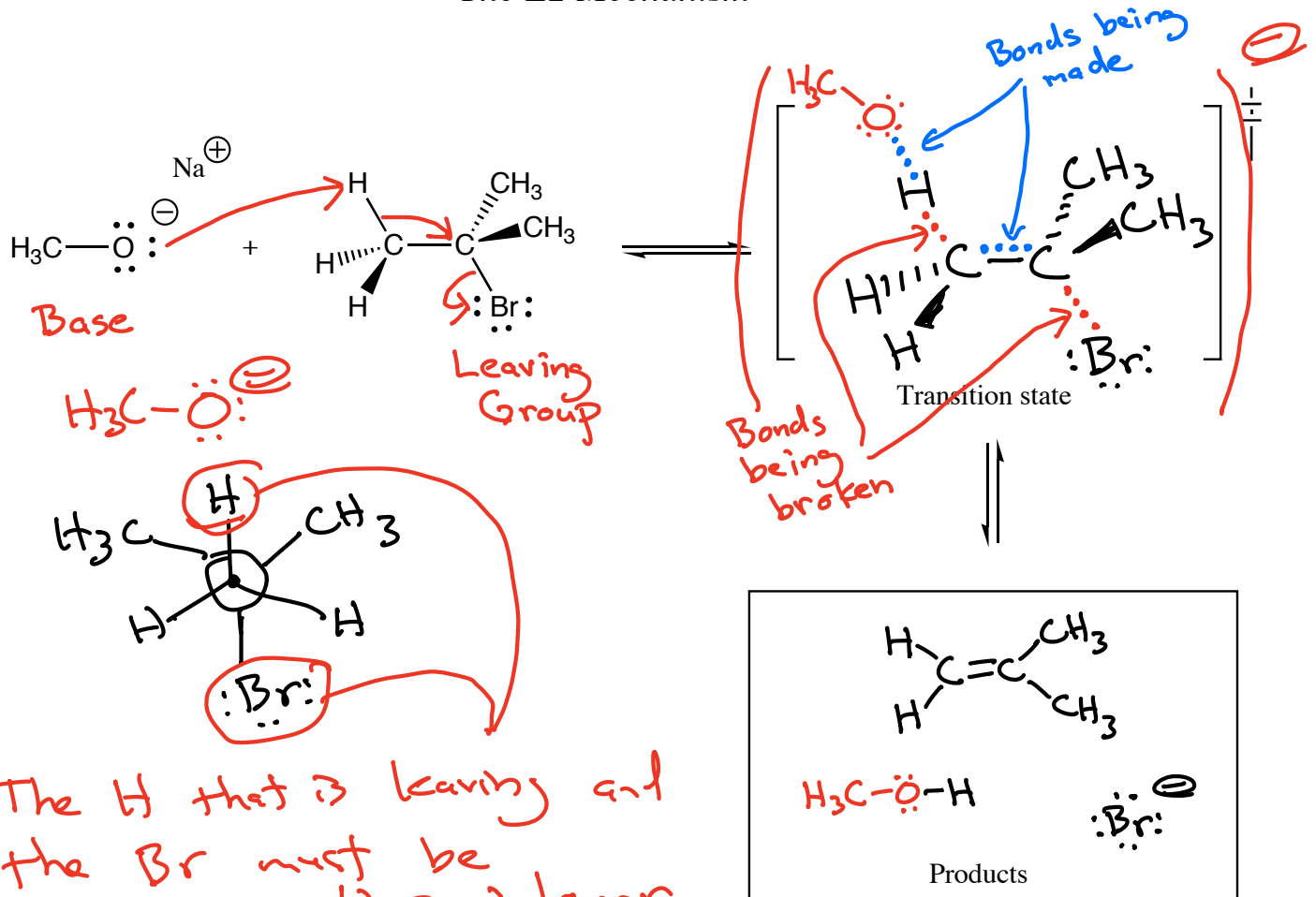
Special Case

Tert-Butoxide (tBuO^-) is a strong base, but is not a nucleophile due to steric hindrance.

2nd New Mechanism

Elimination → E2 ← Bimolecular → both the haloalkane and the base are involved in the rate-determining (slow) step of the reaction

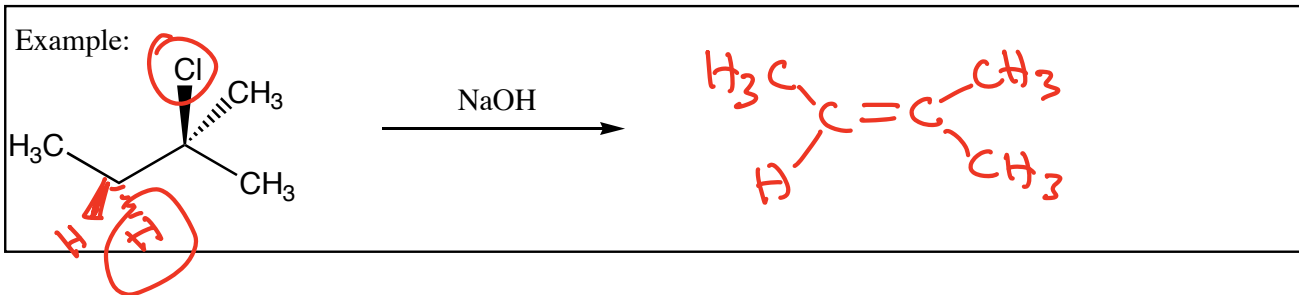
The E2 Mechanism



Summary: Base removes an H atom as a pi bond forms and the Br atom leaves
 → The H and Br must be anti-periplanar

Regiochemistry: Zaitsev's Rule → most stable alkene product

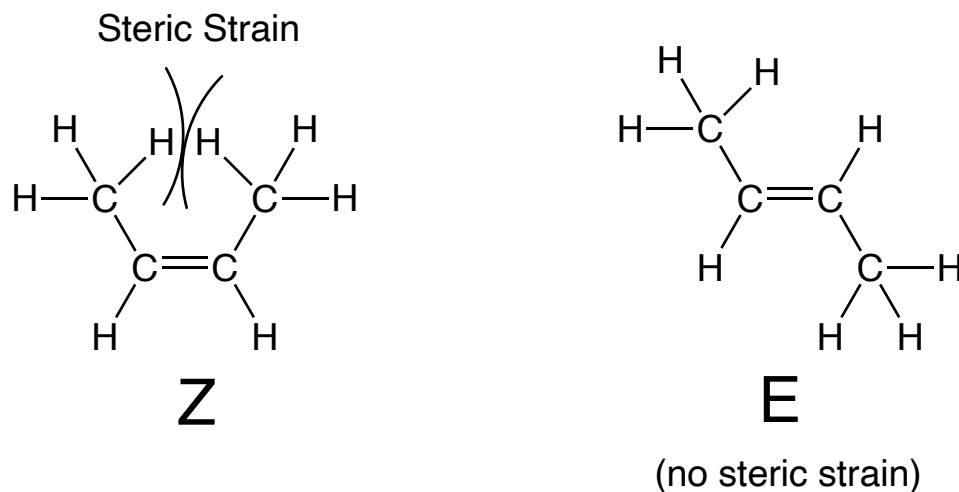
Stereochemistry: Determined by anti-periplanar transition state



Last seen October 7, 2024:

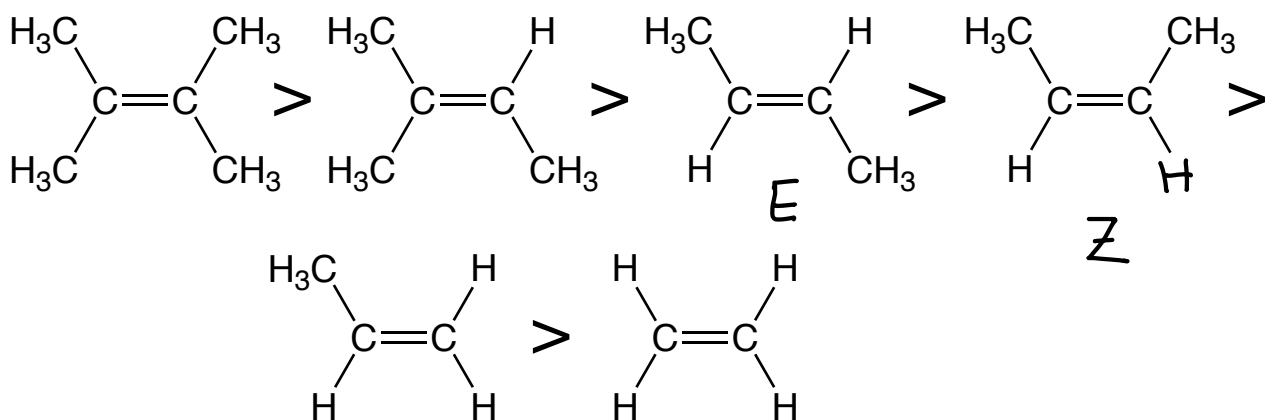
Special Alkene Bonus: Important material you will need to know!

Alkene stability part 1: Z (cis) groups larger than H atoms will crunch into each other causing steric strain.



Alkene stability part 2: For reasons we are not able to tell you, more substituted alkenes have more stable (stronger) pi bonds than alkenes with more H atoms on their sp^2 -hybridized C atoms (despite there being steric strain present in the most substituted alkenes).

Strongest Pi Bond



Weakest Pi Bond



***Time Capsule:
Zaitsev's rule follows
this trend!!***

Zaitsev's Rule \Rightarrow When there is a choice,

More alkyl groups (fewer H atoms on the sp^2 C atom of alkene) $\left\{ \begin{array}{l} \text{the more stable alkene} \\ \text{will be the predominant} \\ \text{product.} \end{array} \right.$

(trans over cis)

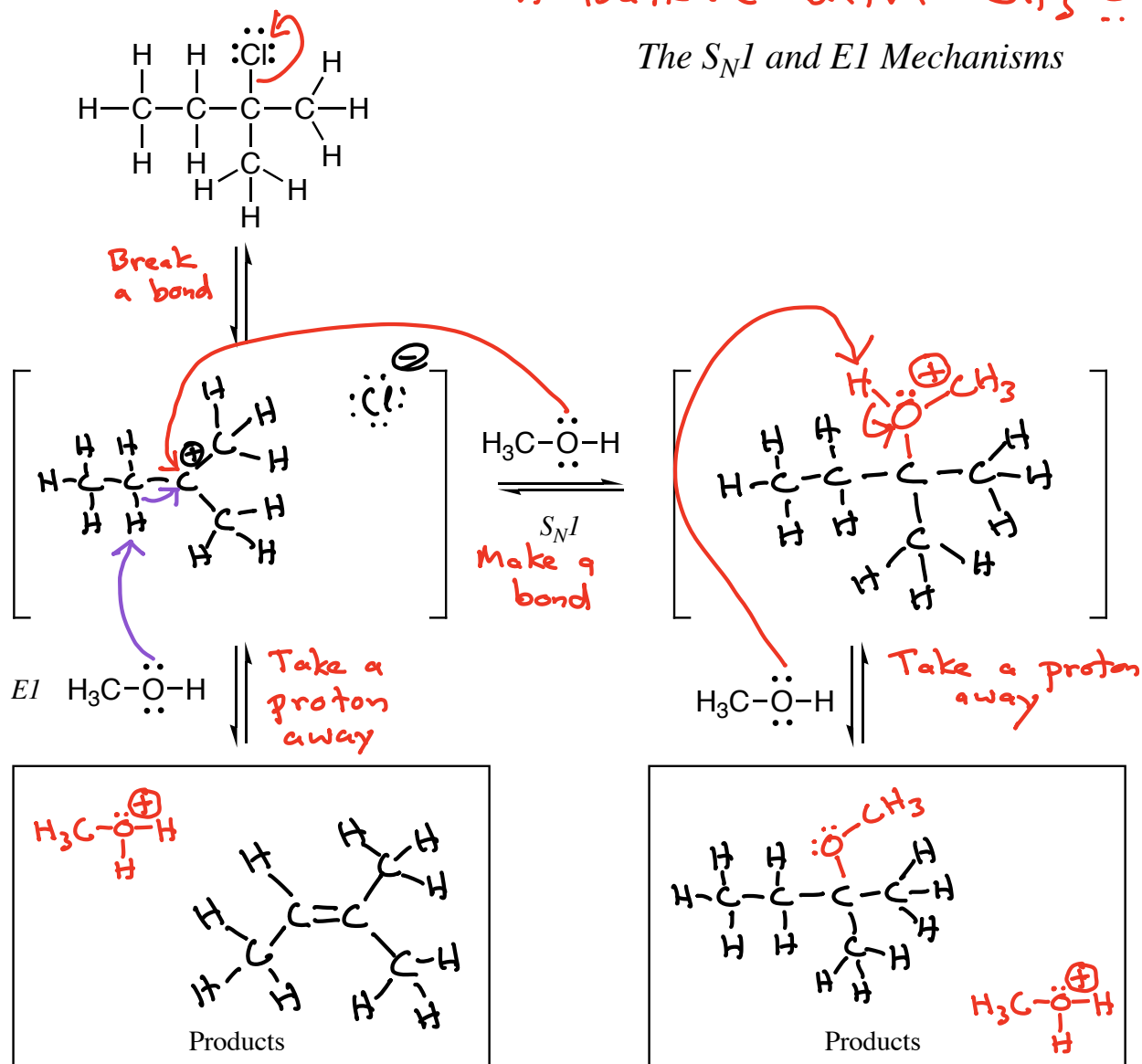
3rd and 4th Mechanisms \rightarrow these always occur together

S_N1 and $E1$

Unimolecular \rightarrow only the haloalkane is involved in the rate-limiting (slow) step of the reaction

Haloalkane with $\text{CH}_3\text{-}\ddot{\text{O}}\text{-H}$

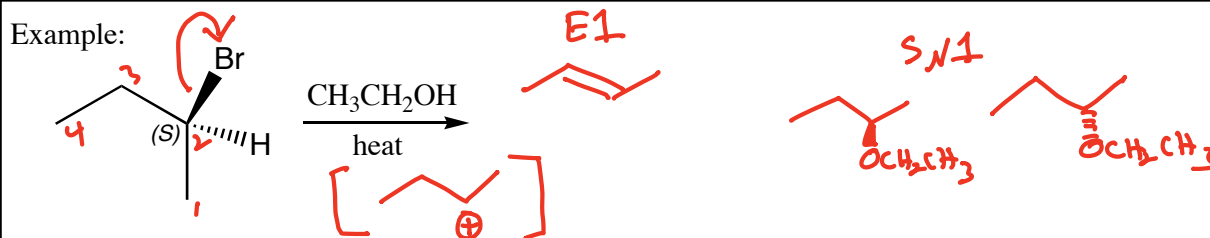
The $\text{S}_{\text{N}}1$ and $\text{E}1$ Mechanisms



Summary: For sterically hindered haloalkanes, the C-X bond breaks to give a carbocation intermediate that either reacts as an electrophile ($\text{S}_{\text{N}}1$) or has a proton taken away ($\text{E}1$)

Regiochemistry: $\text{E}1 \rightarrow$ Zaitsev's Rule

Stereochemistry: $\text{S}_{\text{N}}1 \rightarrow$ Scrambled \rightarrow not quite 1:1 exactly



These four mechanisms S_N2 , $E2$, S_N1 , $E1$ compete with each other

To understand which mechanism is appropriate, we analyze:

- 1) The nucleophile/base
- 2) The nature of the haloalkane

Nucleophiles are also bases



Electron rich molecule that can make a new bond



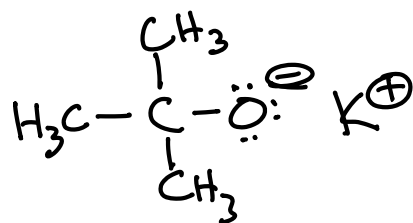
Electron rich molecule that can bond to a proton

Table of Nucleophiles

<p>Strong Nucleophiles</p> <p>Br^-, I^-, R-S^-, H-S^-, $\text{N}\equiv\text{C}^-$, N_3^-</p> <p>$\text{R-C}\equiv\text{C}^-$, R-O^-, H-O^- Strong Bases</p>
<p>Medium Nucleophiles</p> <p>R-CO_2^-, R-S-H, R_2S, NH_3, RNH_2, R_2NH, NR_3</p>
<p>Weak Nucleophiles</p> <p>$\text{R-CO}_2\text{H}$, R-O-H, H_2O Very Weak Bases</p>

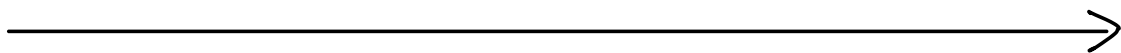
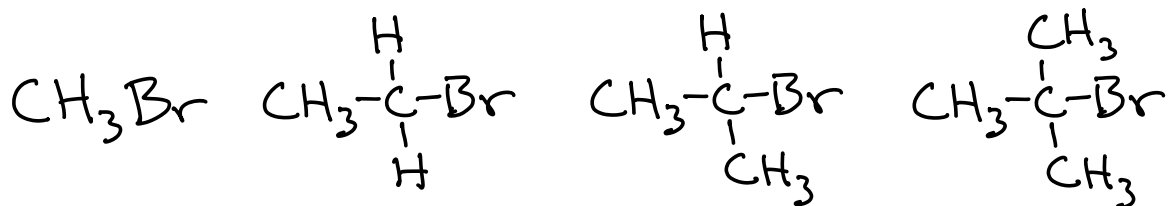
Special Case

Tert-Butoxide (tBuO^-) is a strong base, but is not a nucleophile due to steric hindrance.



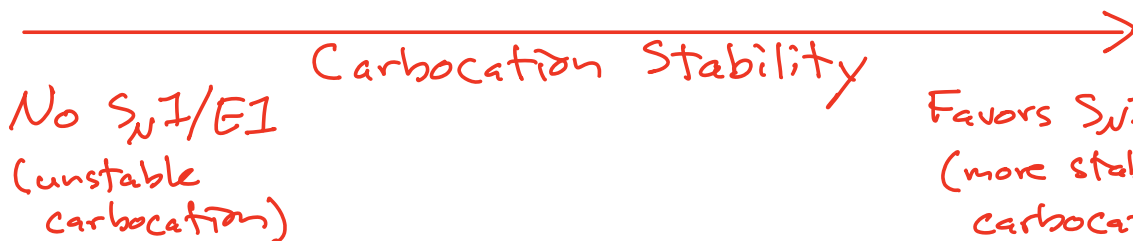
" KOtBu "
or
" tBuO^- "

Haloalkanes



$\text{S}_{\text{N}}2$
preferred

$\text{S}_{\text{N}}2$
prevented
(steric strain)



No $\text{S}_{\text{N}}1/\text{E}1$
(unstable carbocation)

Carbocation Stability

Favors $\text{S}_{\text{N}}1/\text{E}1$
(more stable carbocation)

Strong base prefers $\text{E}2$

Substitution/Elimination Decision Map

Methyl Halide \Rightarrow S_N2

Primary Haloalkane \Rightarrow $t\text{BuOK ?}$ \Rightarrow Yes \Rightarrow E2

No \Rightarrow S_N2

Secondary Haloalkane or Allylic/Benzylic Halides \Rightarrow Very Weak Base ? \Rightarrow Yes \Rightarrow $S_N1/E1$ *

Very Strong Base ? \Rightarrow Yes \Rightarrow E2 **

No \Rightarrow S_N2

Tertiary Haloalkane \Rightarrow Very Weak Base ? \Rightarrow Yes \Rightarrow $S_N1/E1$

No \Rightarrow E2

For S_N2 Remember Chiral Center INVERSION
 For E2 Remember anti-periplanar and Zaitsev
 For S_N1 Remember Chiral Center Scrambling
 For E1 Remember Zaitsev

* Note: With Very Weak Bases, S_N2 can compete here, but for the purposes of this class, assume $S_N1 / E1$ predominate

** Note: If $t\text{BuOK}$ is the very strong base, an appreciable amount of a non-Zaitsev product can be formed because the bulky $t\text{BuOK}$ will tend to react with the most accessible H atom.



Flashback
Oct. 20



Epic New Reaction



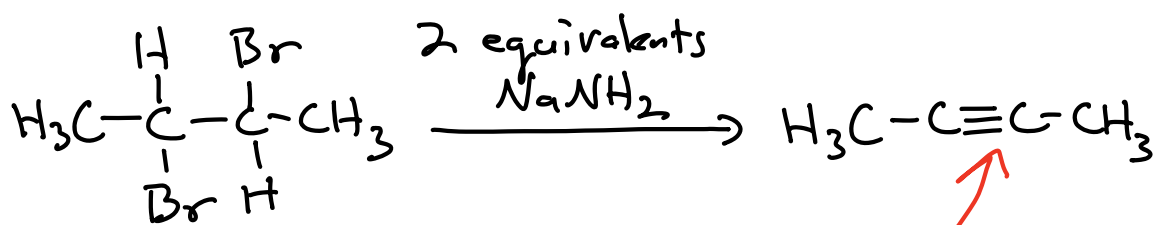
A primary
haloalkane



Time capsule: This is an $\text{S}_{\text{N}}2$ reaction. The haloalkane must be primary to avoid an $\text{E}2$ reaction.



c) Conversion of a vicinal dihalide into an alkyne



Vicinal dihalide

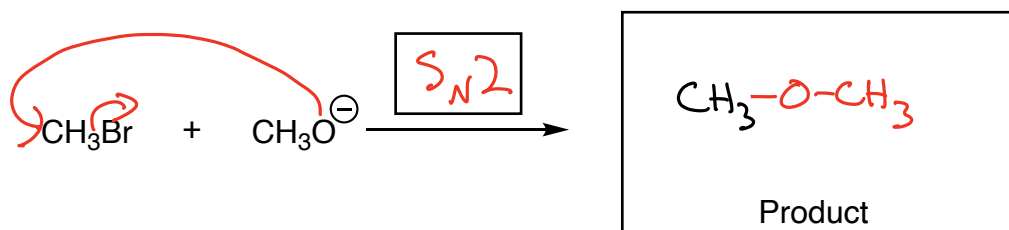
Note this alkyne is not terminal
(it is not on the end)



Time capsule → This is a double E2 reaction

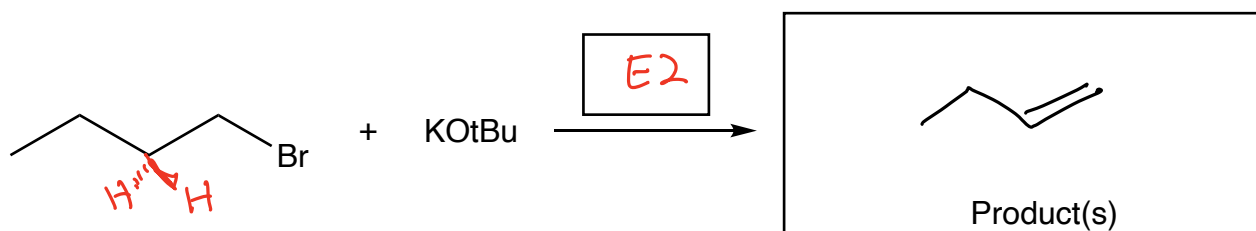
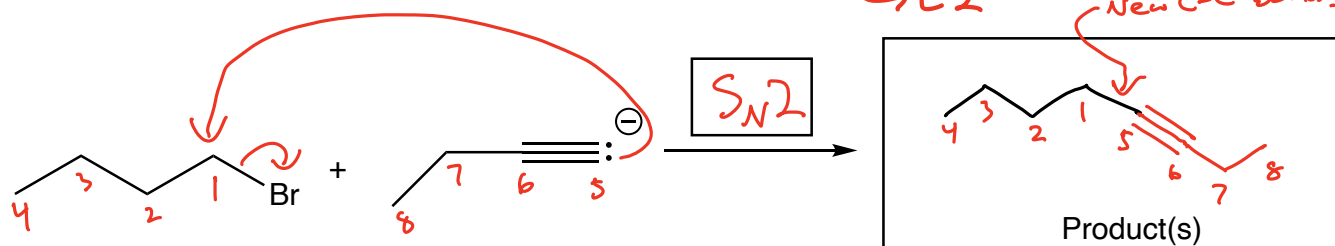
Substitution vs. Elimination Examples:

Methyl Haloalkanes (CH₃X) → Only S_N2 is possible



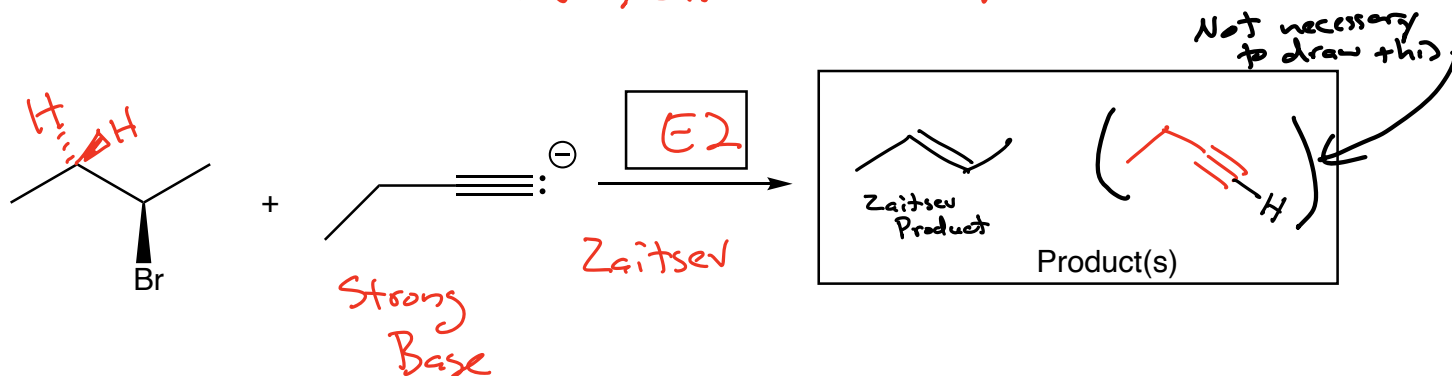
Primary (1°) Haloalkanes

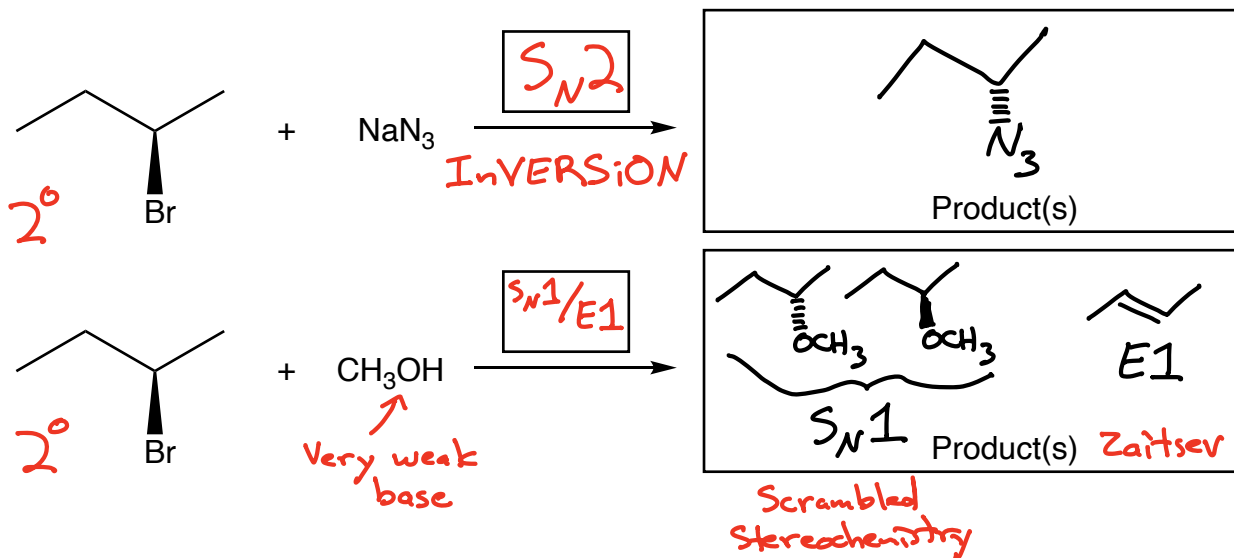
S_N2 with all but KOtBu (tBuO[⊖] K[⊕]) → E2



Secondary (2°) Haloalkanes

→ S_N2 with all but strong bases or very weak bases
→ E2 with strong bases
→ S_N1/E1 with very weak bases





Tertiary (3°) Haloalkanes

