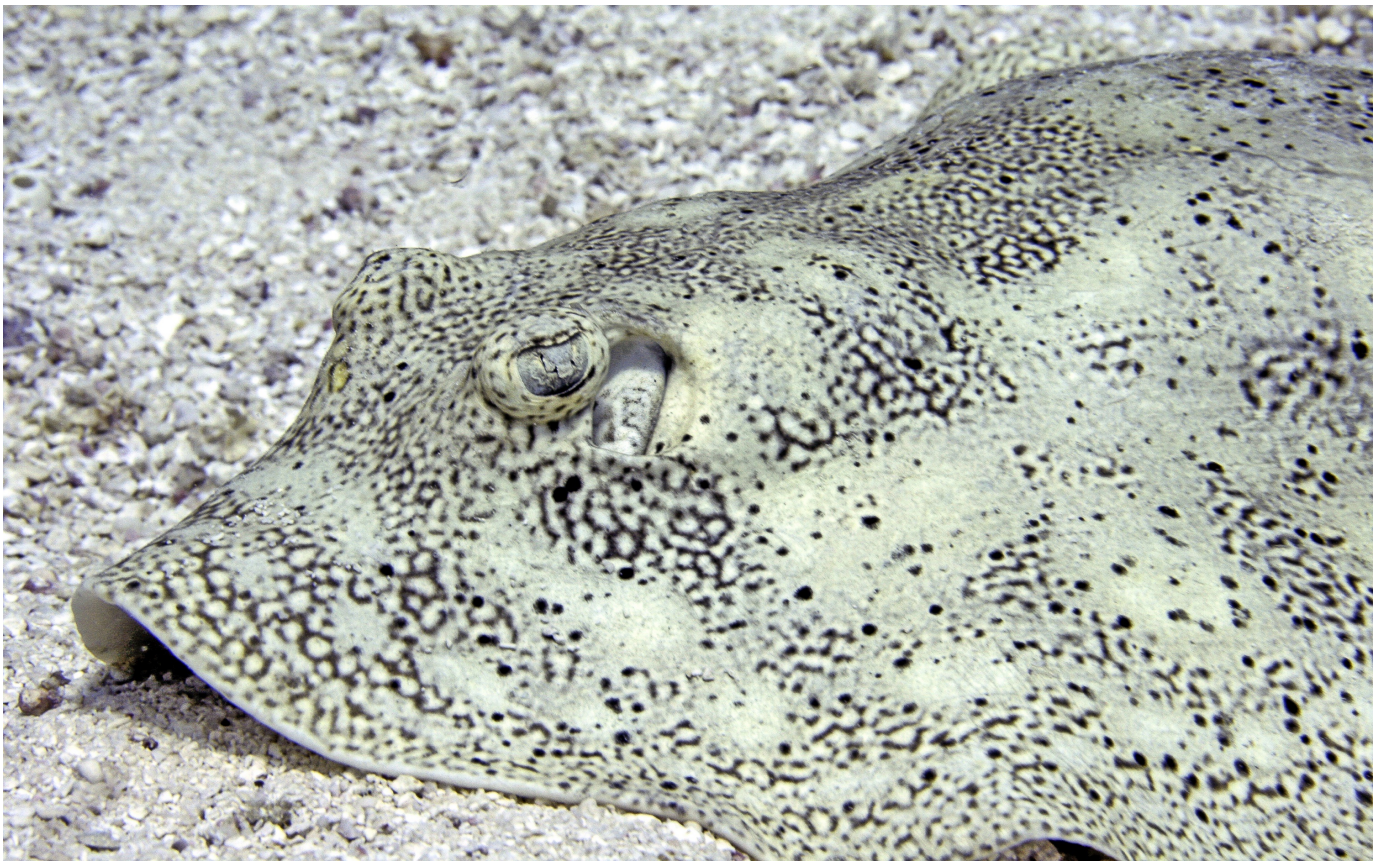
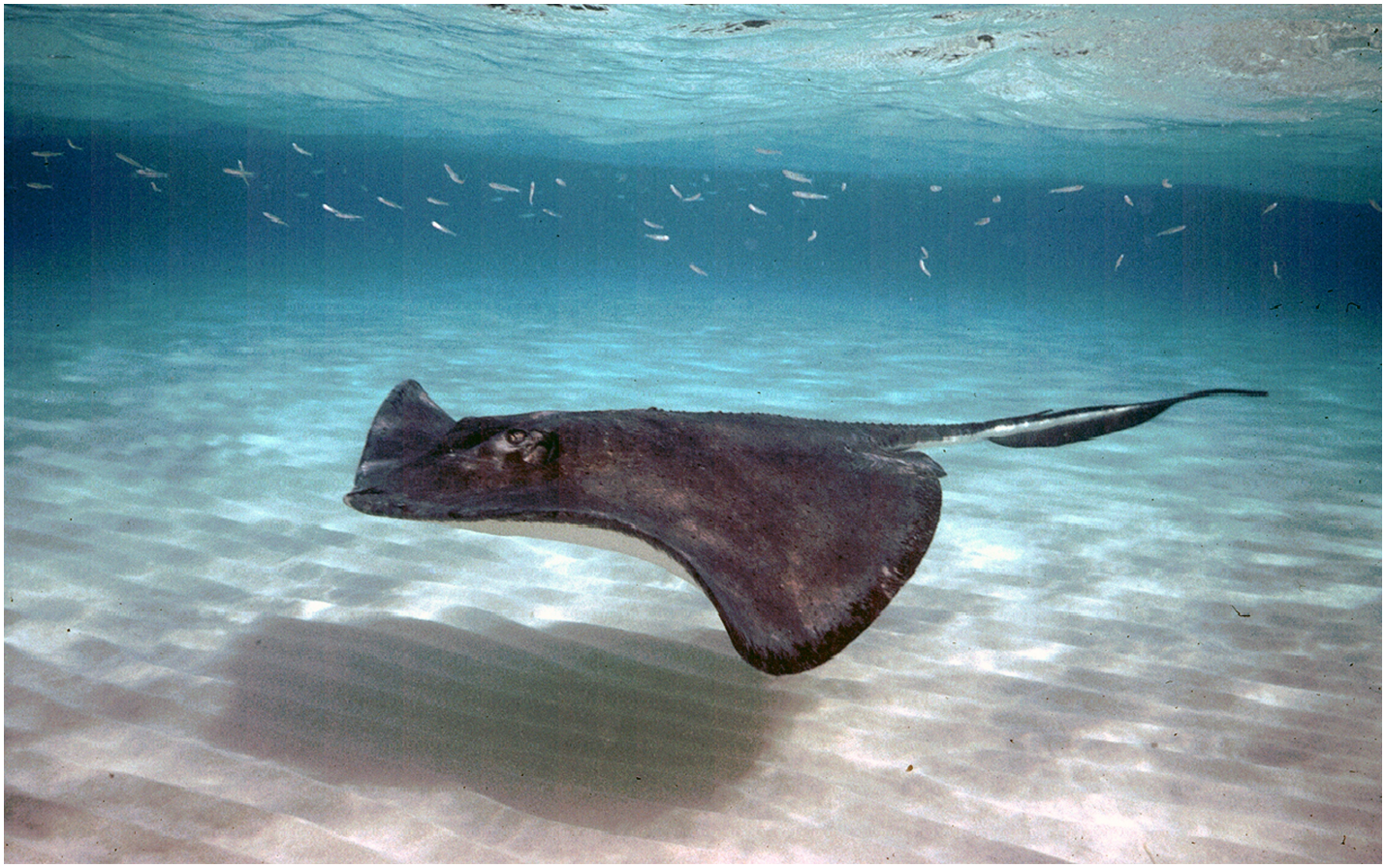
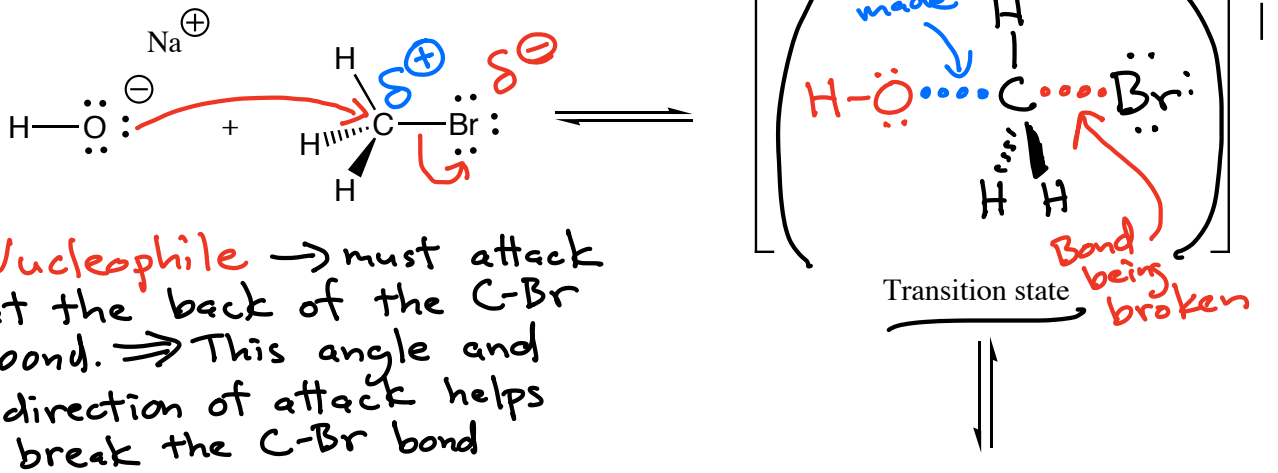
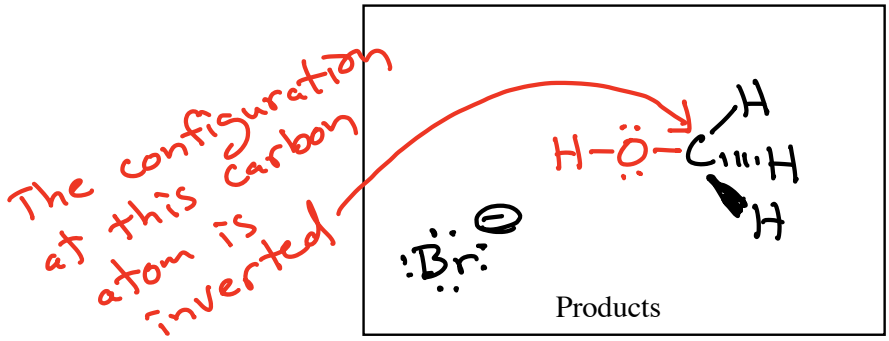




The S_N2 Mechanism



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

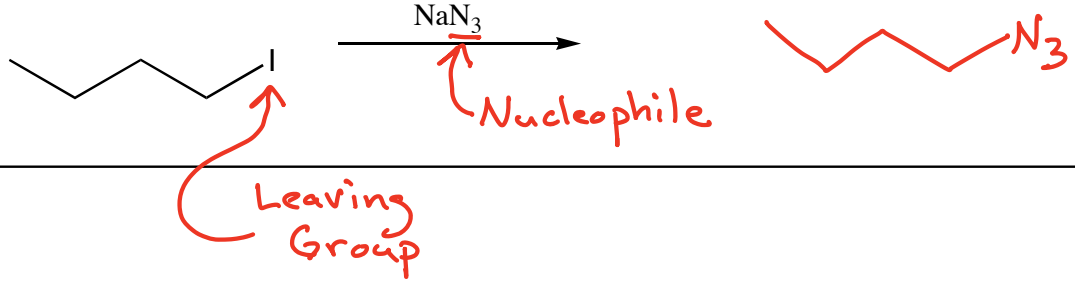


Summary: The nucleophile attacks by making a new bond to C from the back of the C-X bond just as X leaves

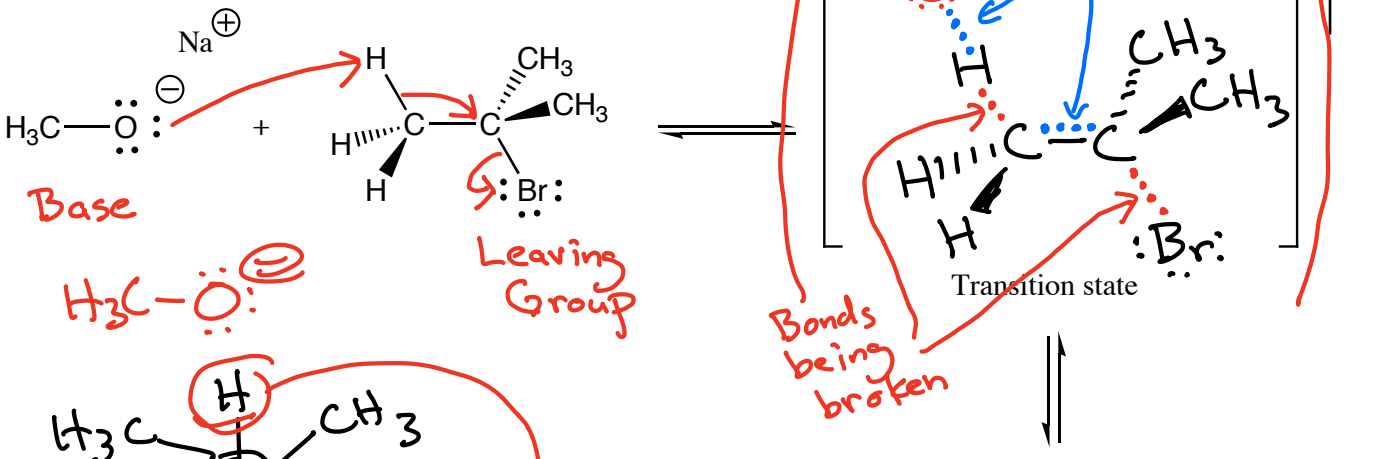
Regiochemistry: N/A

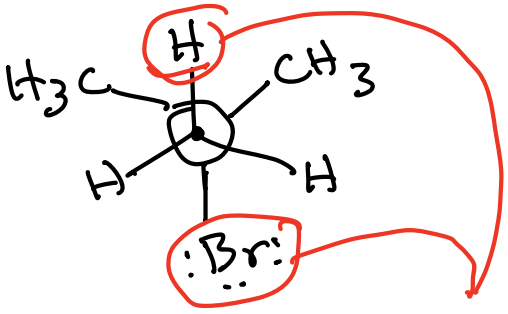
Stereochemistry: INVERSION at the site of reaction

Example:

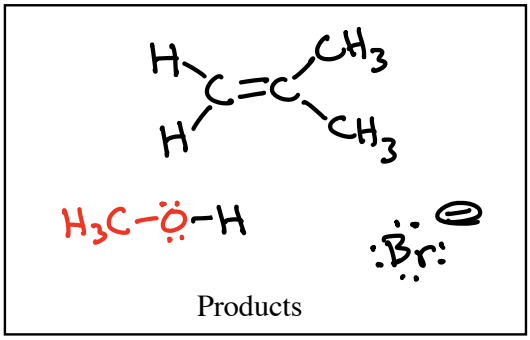


The E2 Mechanism





The H that is leaving and the Br must be anti-periplanar

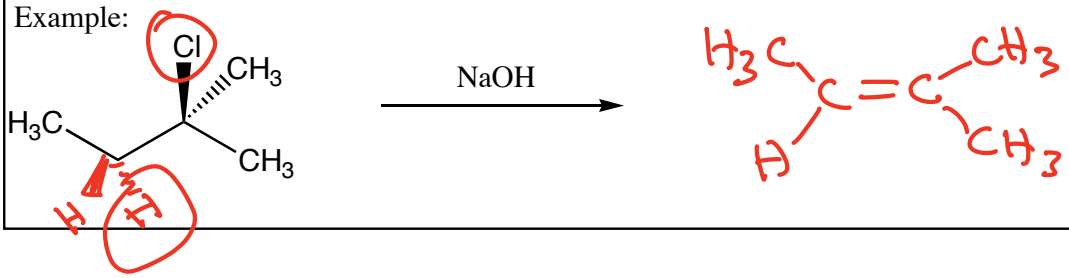


Summary: Base removes an H atom as a pi bond forms and the Br atom leaves → The H and Br must be anti-periplanar

Regiochemistry: Zaitsev's Rule → most stable alkene product

Stereochemistry: Determined by anti-periplanar transition state

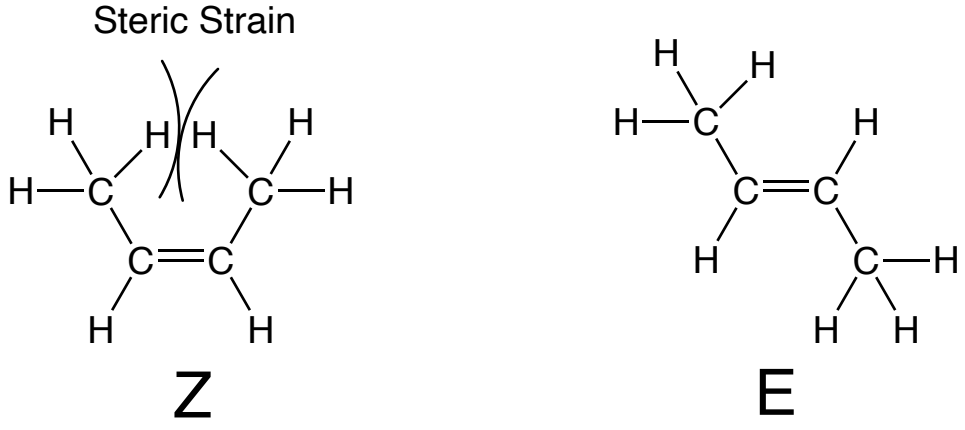
Example:



From Week 6

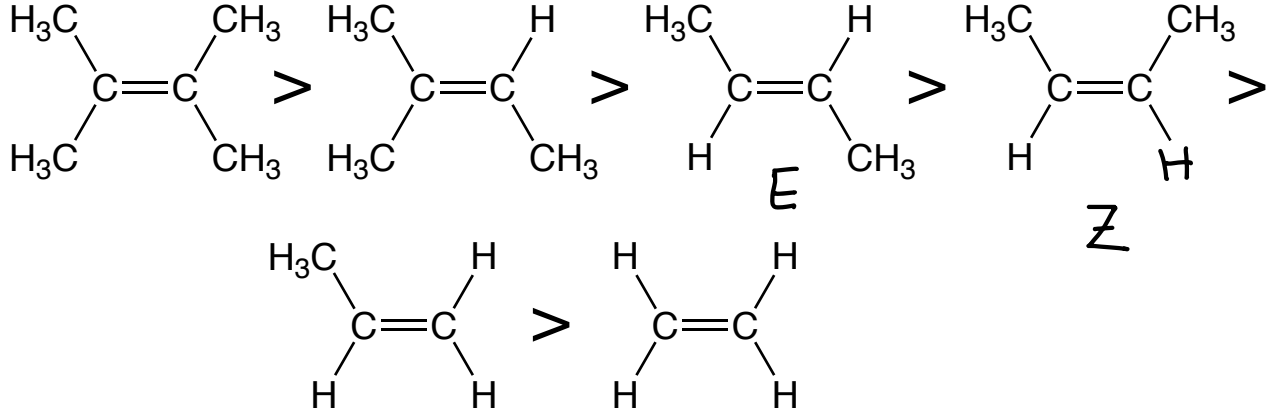
Special Alkene Bonus: Important material you will need to know!

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 ⇒ When there is a choice, the more stable alkene will be the predominant product.

More alkyl groups (fewer H atoms on the sp^2 C atom of alkene (trans over cis)

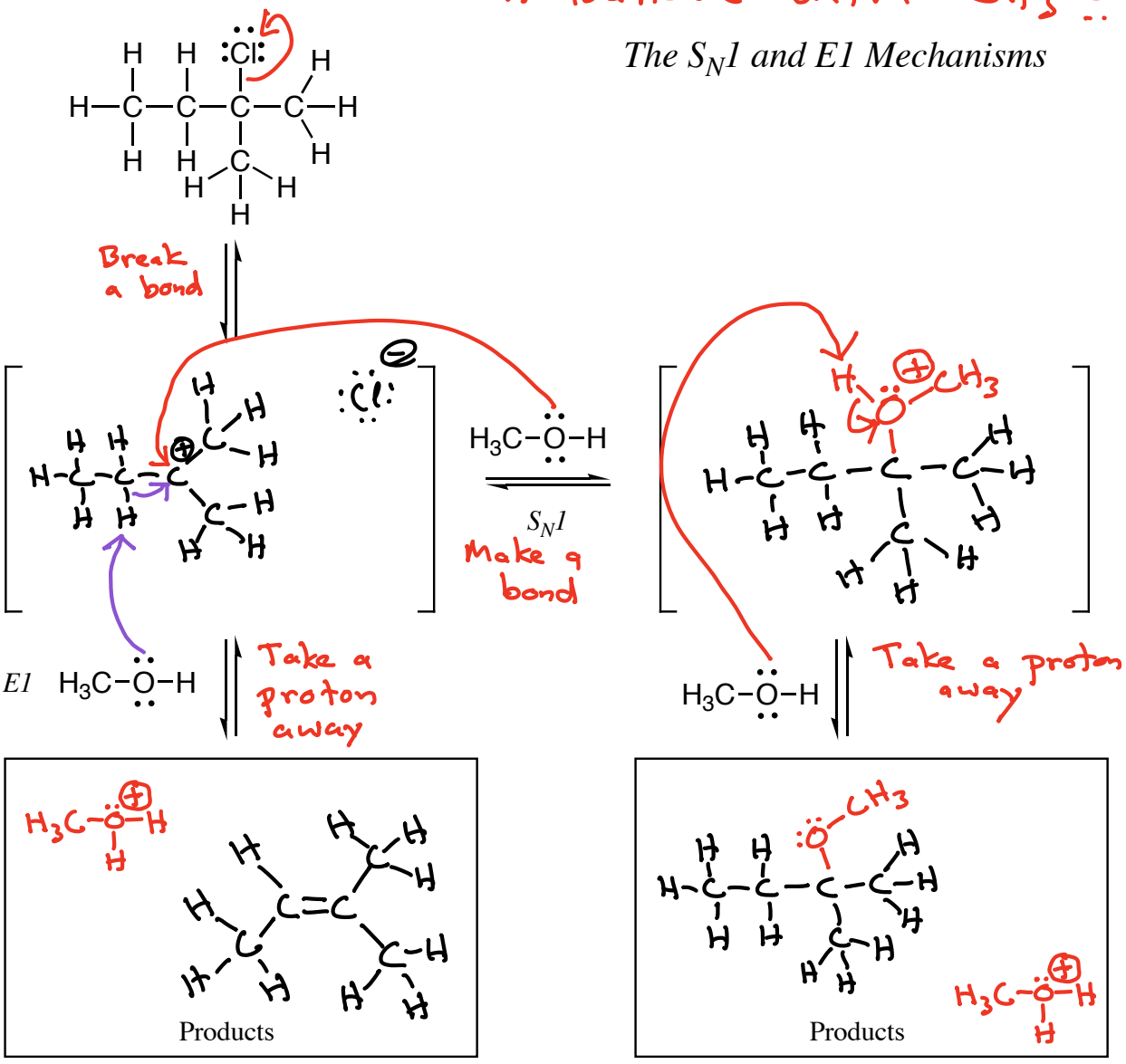
3rd and 4th Mechanisms → these always occur together

S_N1 and E1

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

Haloalkane with $CH_3\ddot{O}-H$

The S_N1 and E1 Mechanisms

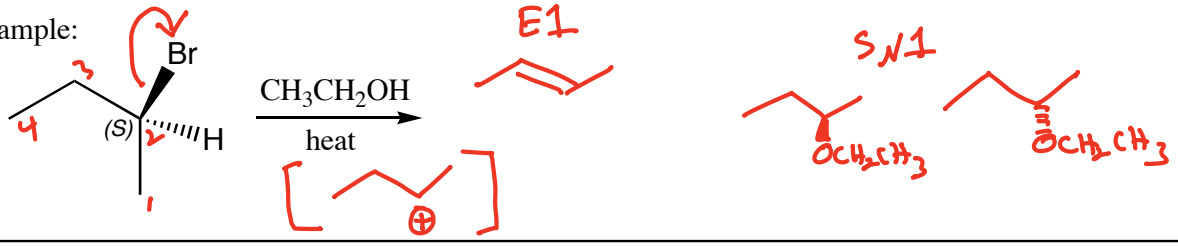


Summary: For sterically hindered haloalkanes, the C-X bond breaks to give a carbocation intermediate that either reacts as an electrophile (S_N1) or has a proton taken away (E1)

Regiochemistry: E1 → Zaitsev's Rule

Stereochemistry: S_N1 → Scrambled → not quite 1:1 exactly

Example:



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

Strong Nucleophiles

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

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

Medium Nucleophiles

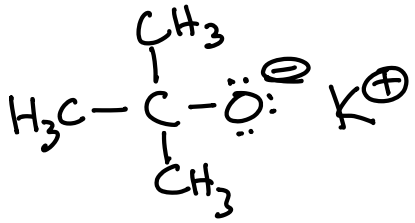
$R\text{-}CO_2^-$, R-S-H, R_2S,
NH_3, RNH_2, R_2NH, NR_3

Weak Nucleophiles

$R\text{-}CO_2H$, R-O-H, H_2O **Very Weak Bases**

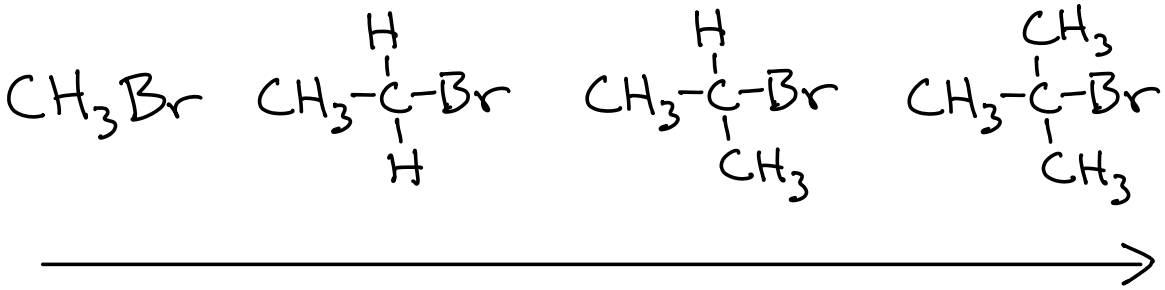
Special Case

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



"KOtBu"
or
"$tBuO^-$"

Haloalkanes



S_N2 preferred

S_N2 prevented (steric strain)

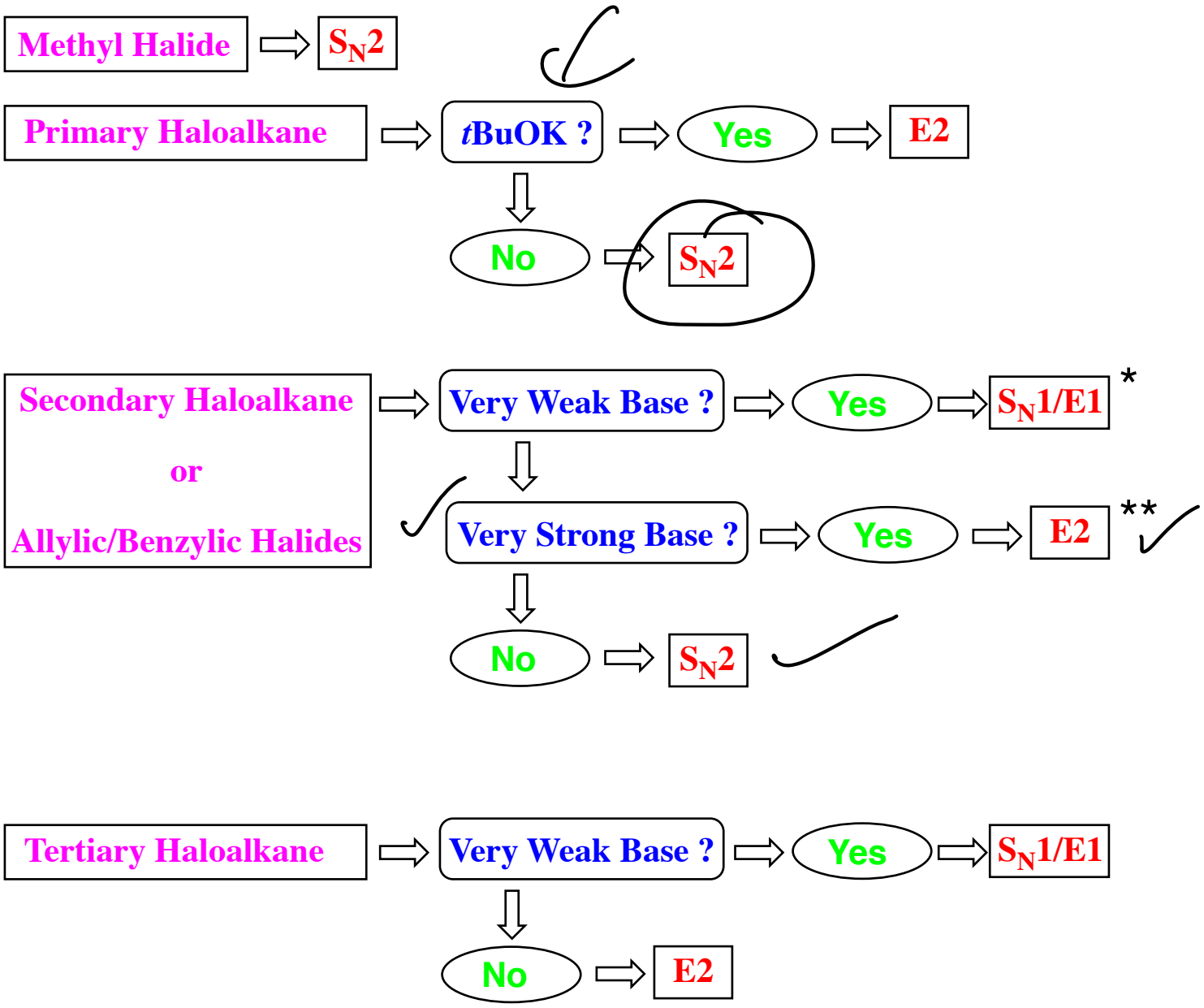
Carbocation Stability

No $S_N1/E1$ (unstable carbocation)

Favors $S_N1/E1$ (more stable carbocation)

Strong base prefers E2

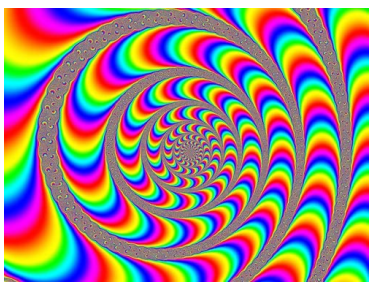
Substitution/Elimination Decision Map



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

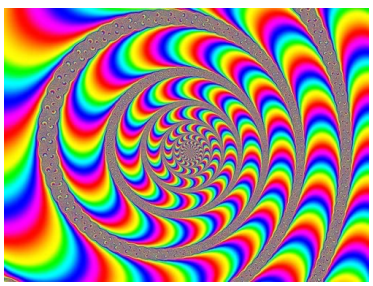
* Note: With Very Weak Bases, SN2 can compete here, but for the purposes of this class, assume SN1 / E1 predominate

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



Flashback

Oct. 20

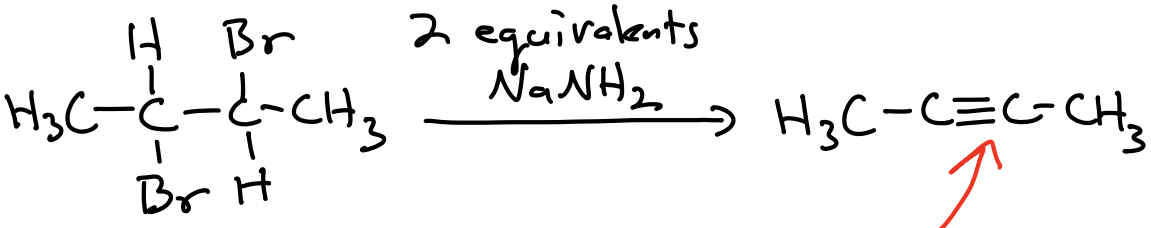


Epic New Reaction

A primary haloalkane

Time capsule: This is an S_N2 reaction. The haloalkane must be primary to avoid an E2 reaction.

c) Conversion of a vicinal dihalide into an alkyne



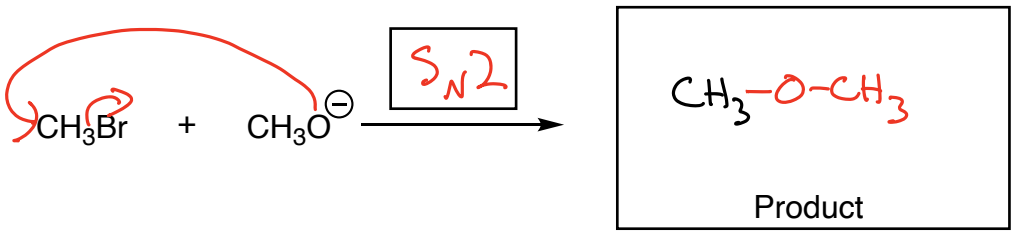
Vicinal dihalide

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

Time capsule → This is a double E2 reaction

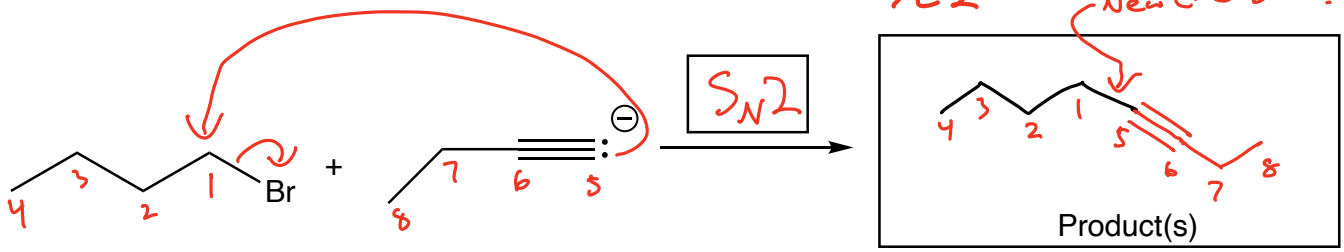
Substitution vs. Elimination Examples:

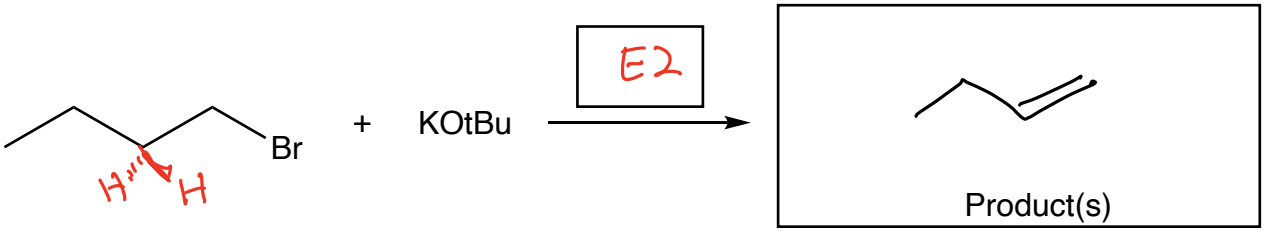
Methyl Haloalkanes (CH_3X) → Only S_N2 is possible



Primary (1°) Haloalkanes

S_N2 with all but KOtBu ($tBuO^{\ominus}K^{\oplus}$) → E2

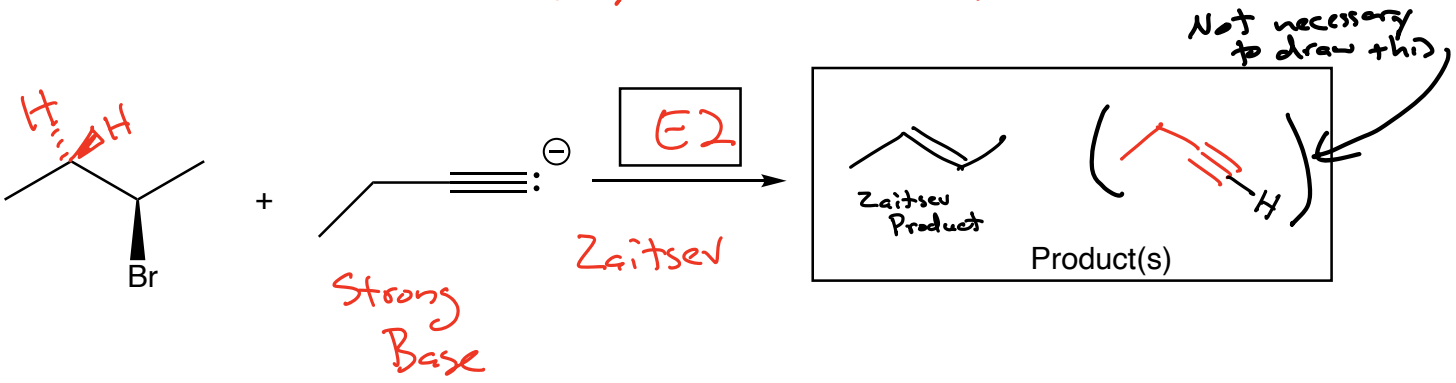


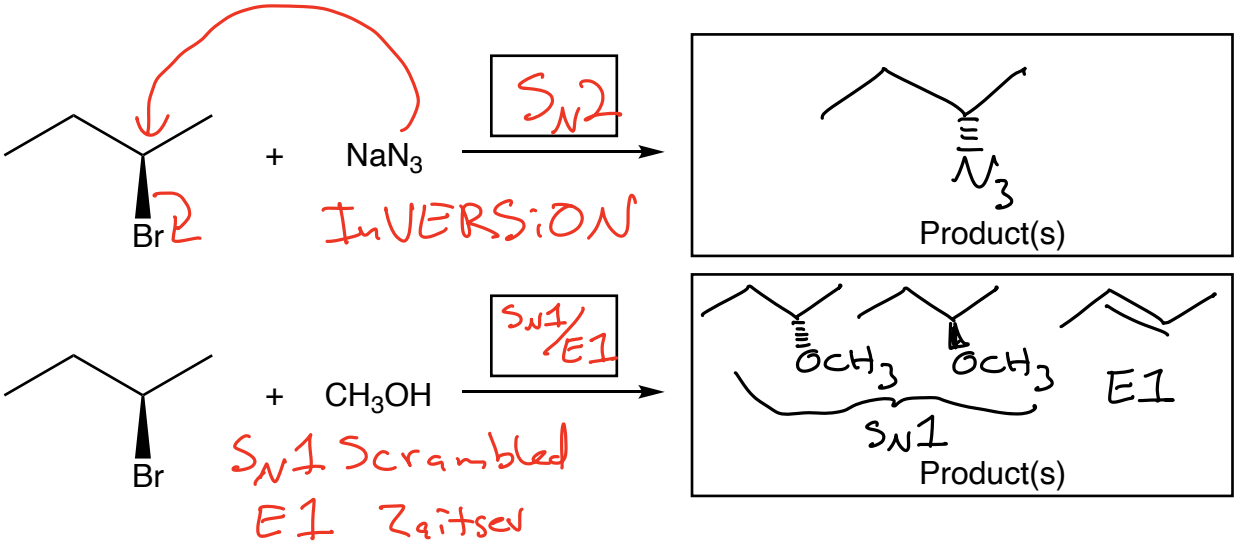


Secondary (2°) Haloalkanes → S_N2 with all but strong bases or very weak bases

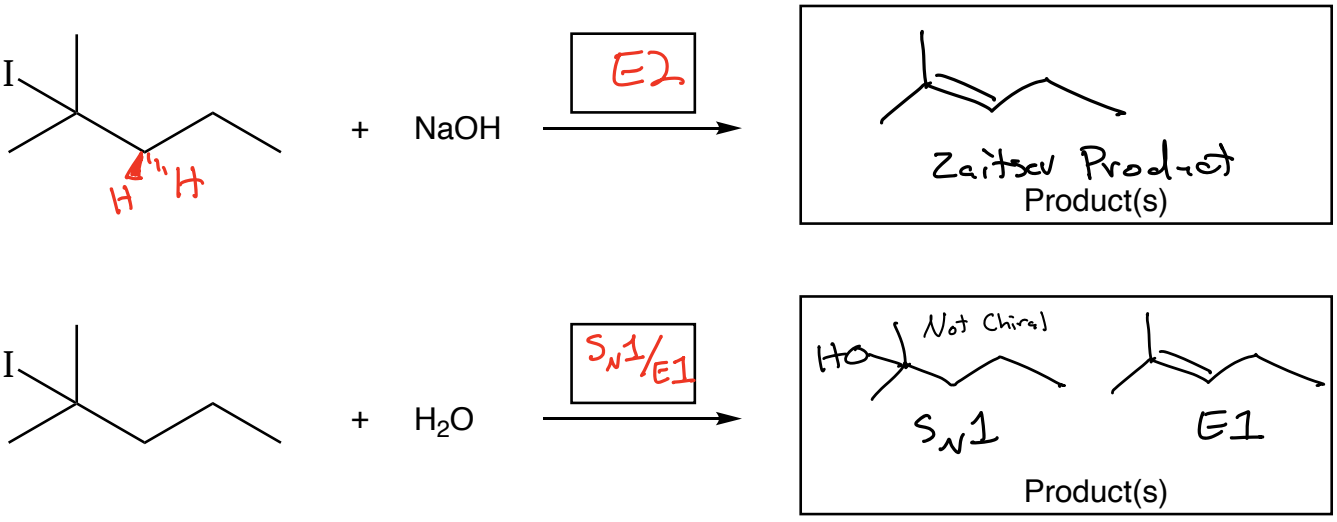
→ E2 with strong bases

→ S_N1/E1 with very weak bases

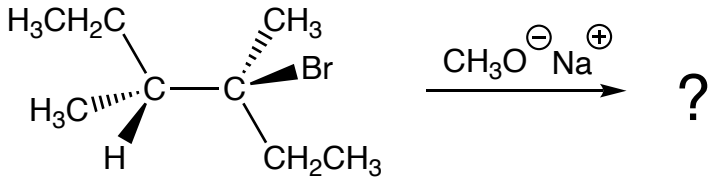




Tertiary (3°) Haloalkanes

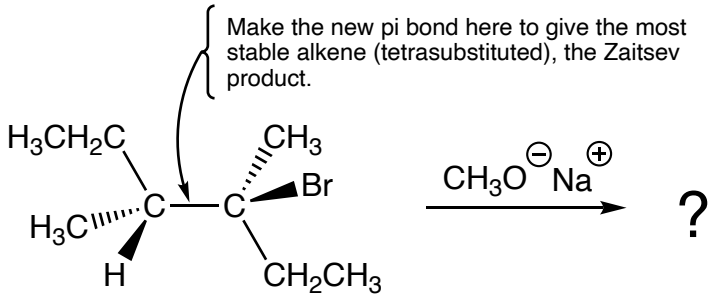


E2 Reaction Considerations:



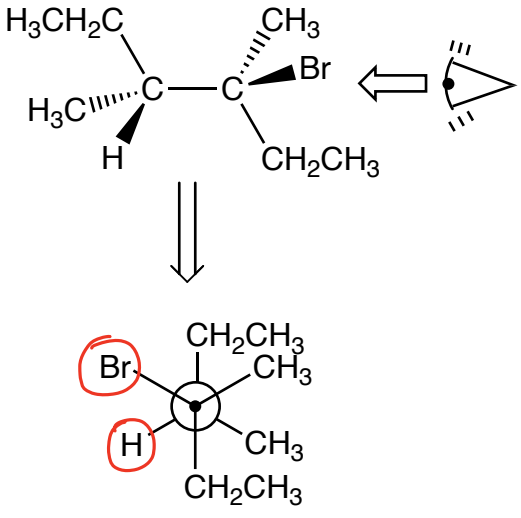
When analyzing highly substituted haloalkanes for a possible E2 reaction:

1. **You need to identify the most stable possible alkene (most highly substituted, *trans* over *cis*) that could be made (Zaitsev product).**



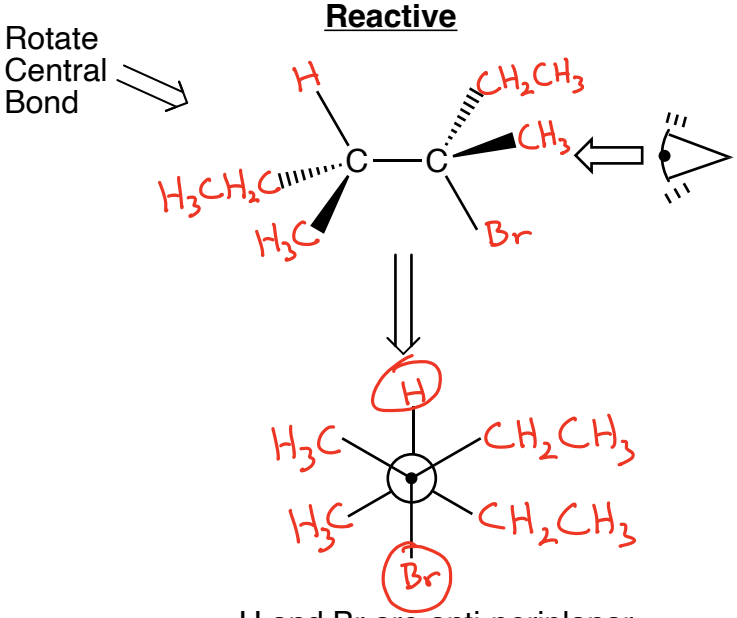
2. **Given the Zaitsev product you have identified, verify which anti-periplanar H atom(s) can be removed during the reaction to determine whether the product is E or Z.**
3. **You often need to rotate bonds to identify the particular H atom and configuration that reacts to give the alkene product.**

Not Reactive



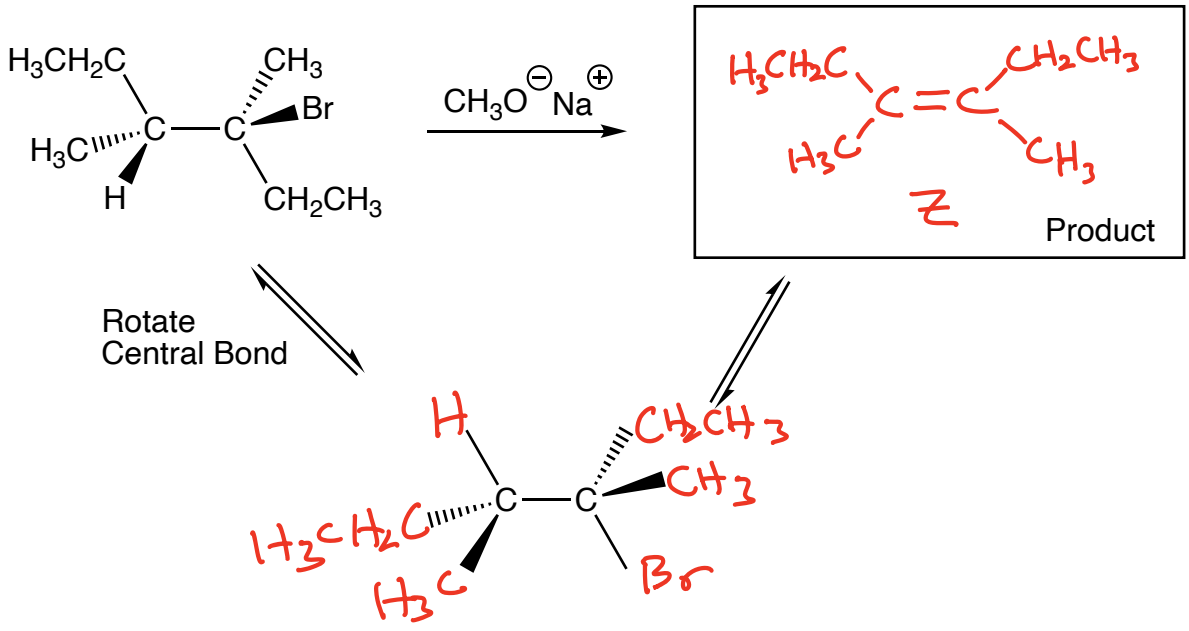
H and Br **not** anti-periplanar

Reactive

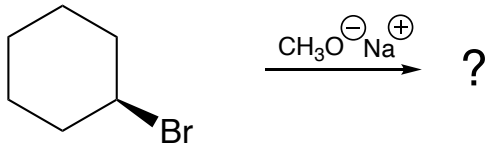


H and Br are anti-periplanar

Putting it all together:

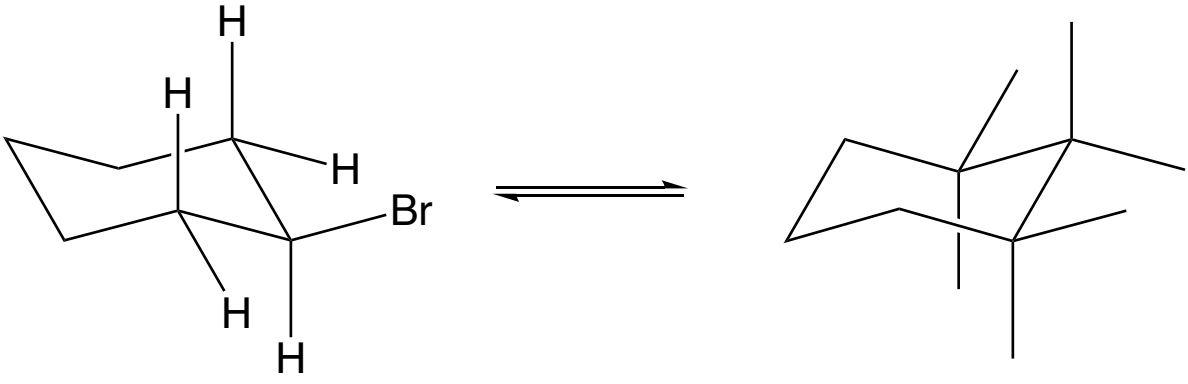


E2 Reaction of cyclohexane derivatives:



When analyzing highly substituted haloalkanes for a possible E2 reaction:

1. **You need to identify the most stable possible alkene (most highly substituted, *trans* over *cis*) that could be made (Zaitsev product).**
2. **Given the Zaitsev product you have identified, verify which anti-periplanar H atom(s) can be removed during the reaction to determine if that product can be made.**
3. **You often need to flip chairs in cyclohexane derivatives to identify the particular H atom and configuration that reacts to give the alkene product.**



Rule: