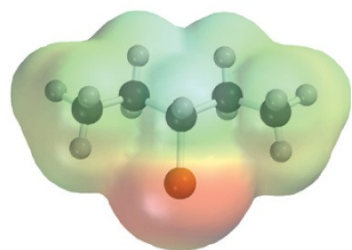


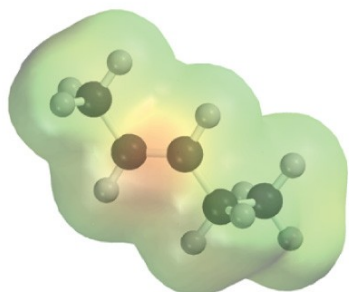
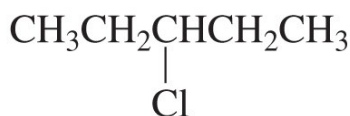
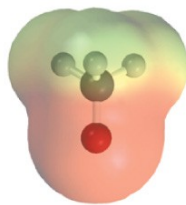
Organic Chemistry

6th Edition

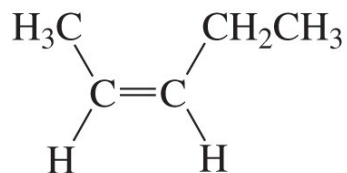
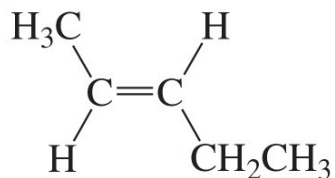
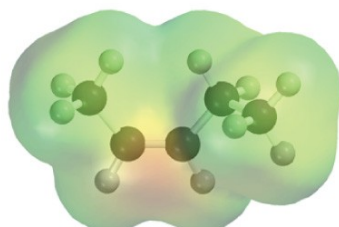
Paula Yurkanis Bruice



+



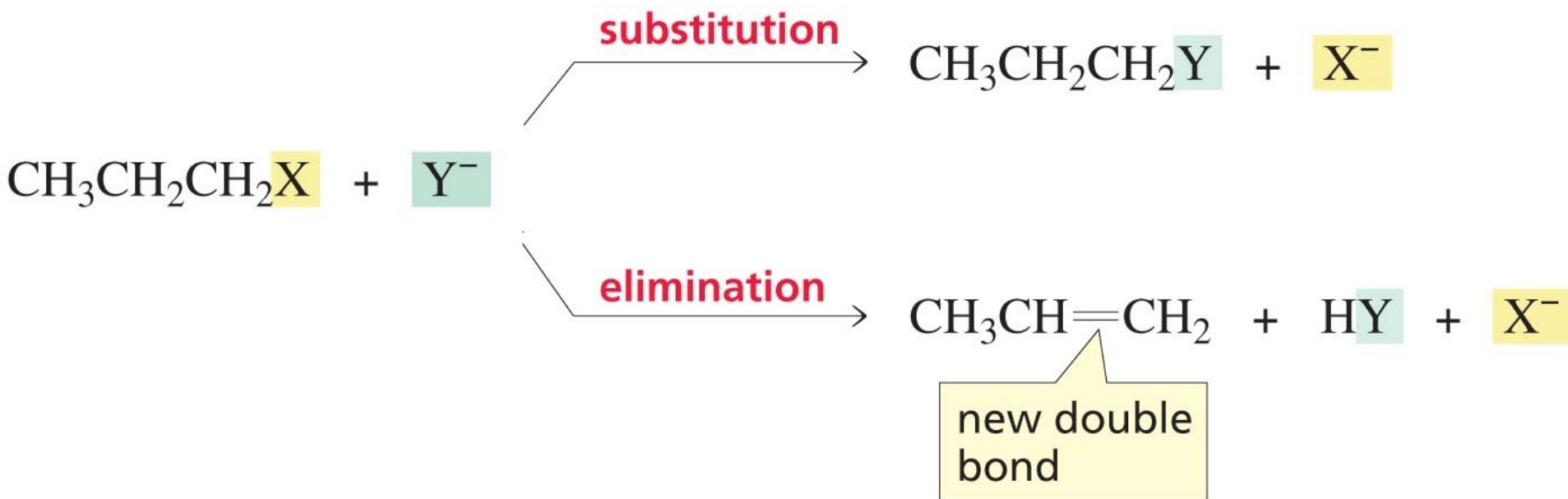
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Chapter 9

Elimination Reactions of Alkyl Halides Competition Between Substitution and Elimination

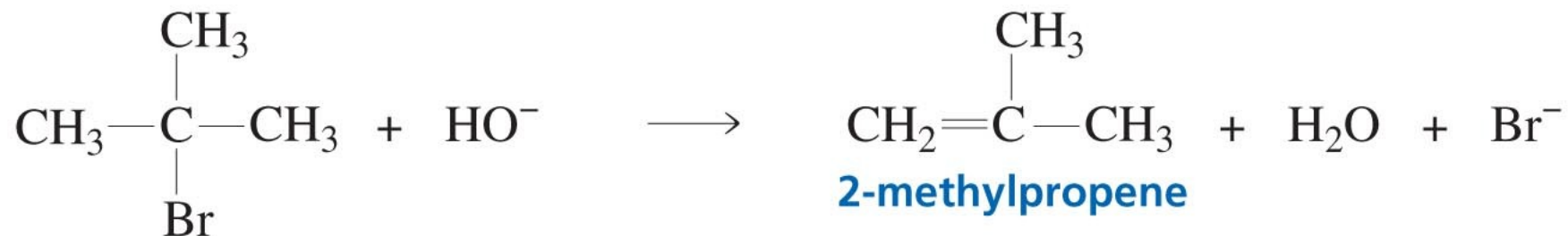
In addition to substitution, an alkyl halide can undergo an elimination reaction



The E2 Reaction

- reaction and mechanism
- kinetics
- Stereochemistry
- regioselectivity
- substrate structure
- Base
- leaving groups
- solvents

The E2 Reaction

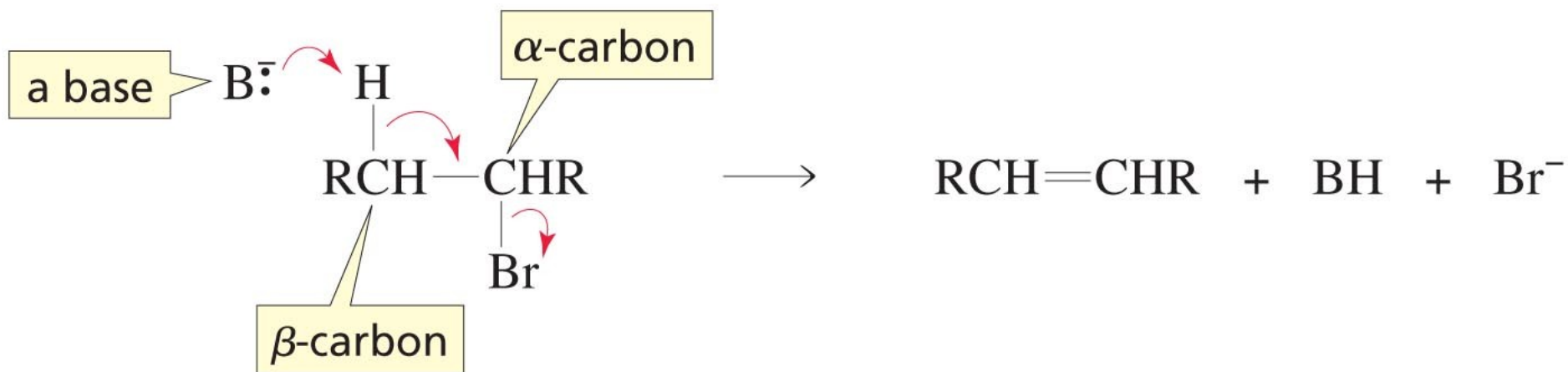


2-bromo-2-methylpropane

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Hydroxide cannot act as a nucleophile in this reaction because of the bulky tertiary halide. Rather, hydroxide acts as a base and abstracts a proton.

An E2 reaction is also called a β -elimination or a 1,2-elimination reaction:



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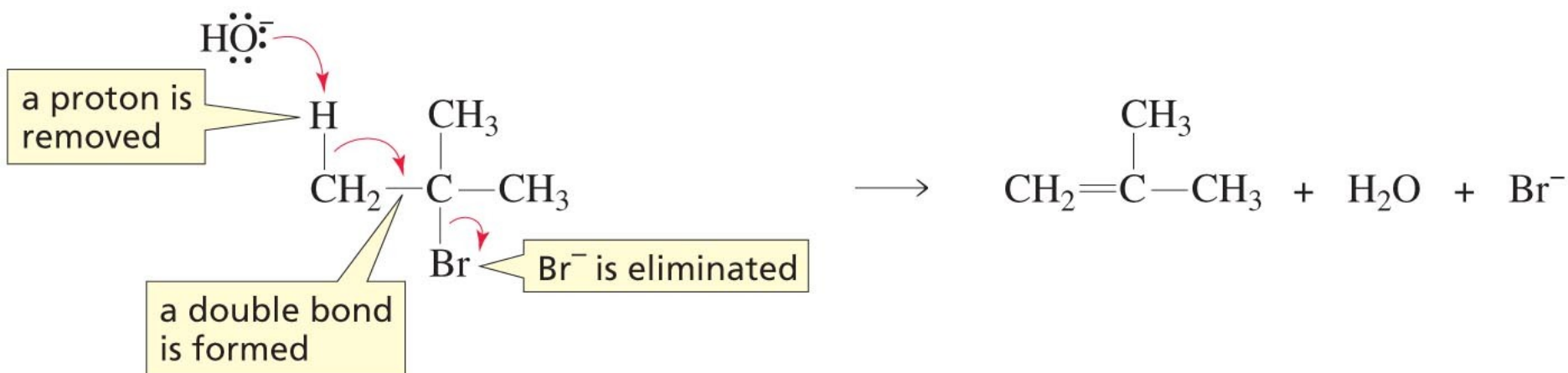
The weaker the base, the better it is as a leaving group

relative reactivities of alkyl halides in an E2 reaction



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The removal of a proton and a halide ion is called dehydrohalogenation:



kinetics

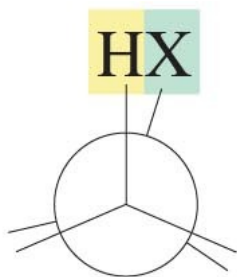
$$\text{rate} = k[\text{alkyl halide}][\text{base}]$$

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stereochemistry

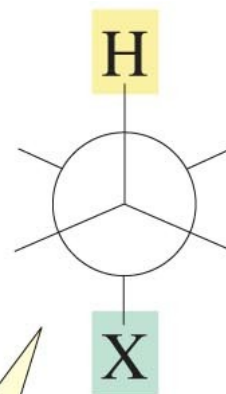
Stereochemistry of the E2 Reaction

The bonds to the eliminated groups (H and X) must be in the same plane



substituents are syn-periplanar

an eclipsed conformation

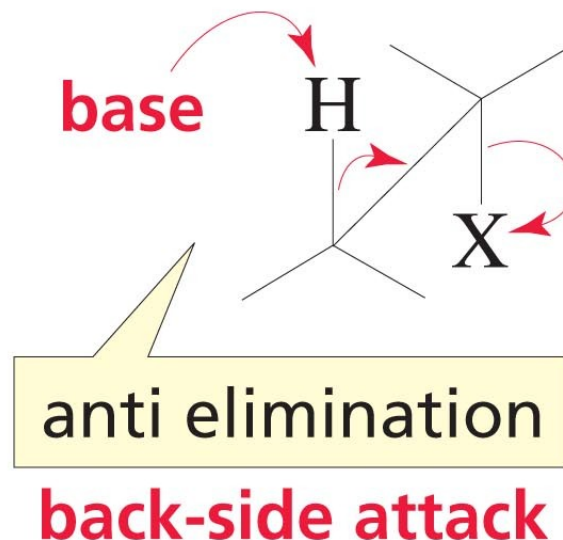
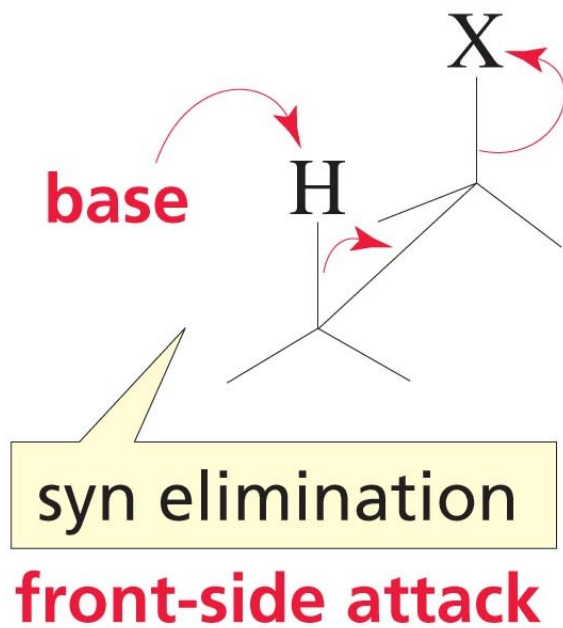


substituents are anti-periplanar

a staggered conformation

The anti elimination is favored over the syn elimination

Another view of the E2 reaction mechanism

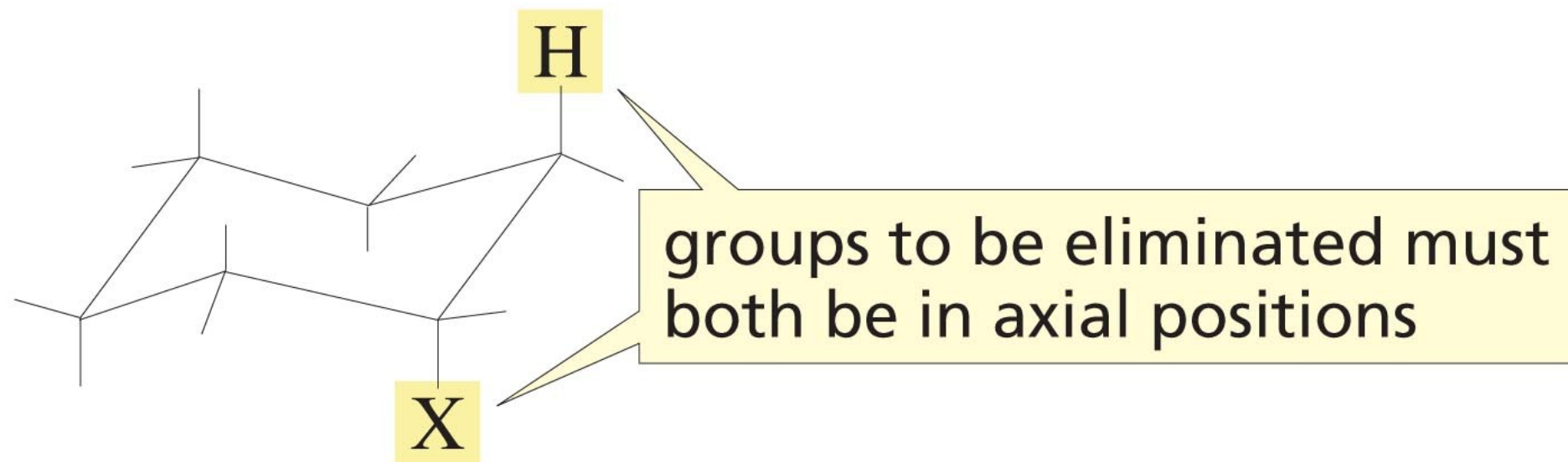


The best overlap of the interacting orbitals is achieved through back-side attack

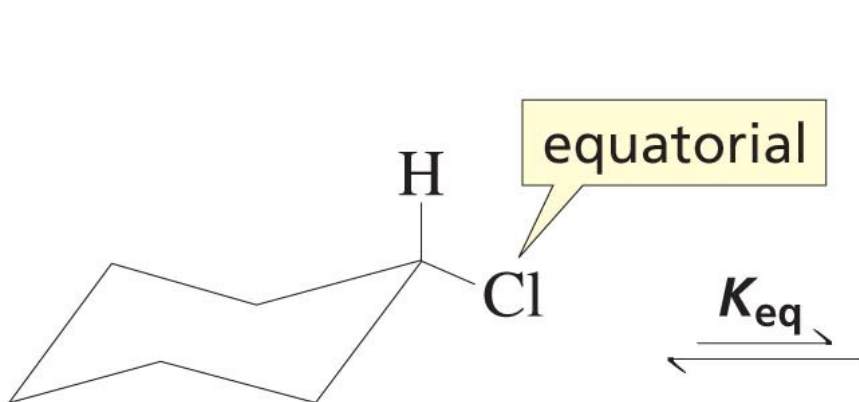
Anti elimination avoids repulsion of the electron-rich base

Elimination from Cyclic Compounds

In an E2 reaction, groups to be eliminated must be in axial positions



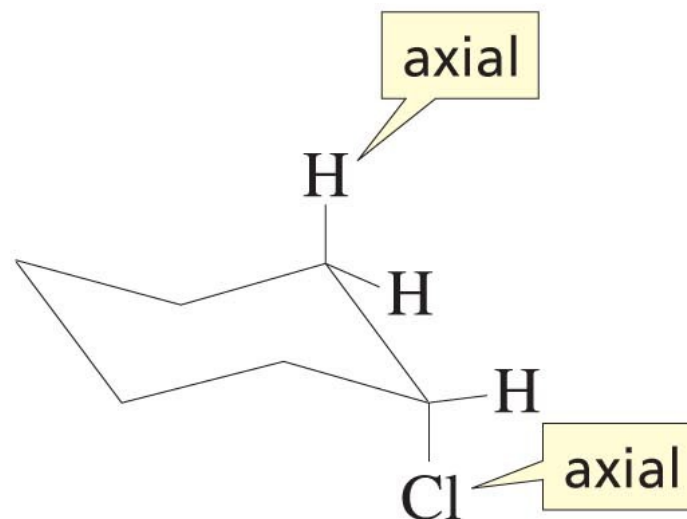
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more stable

$\downarrow$ HO^-
E2 conditions

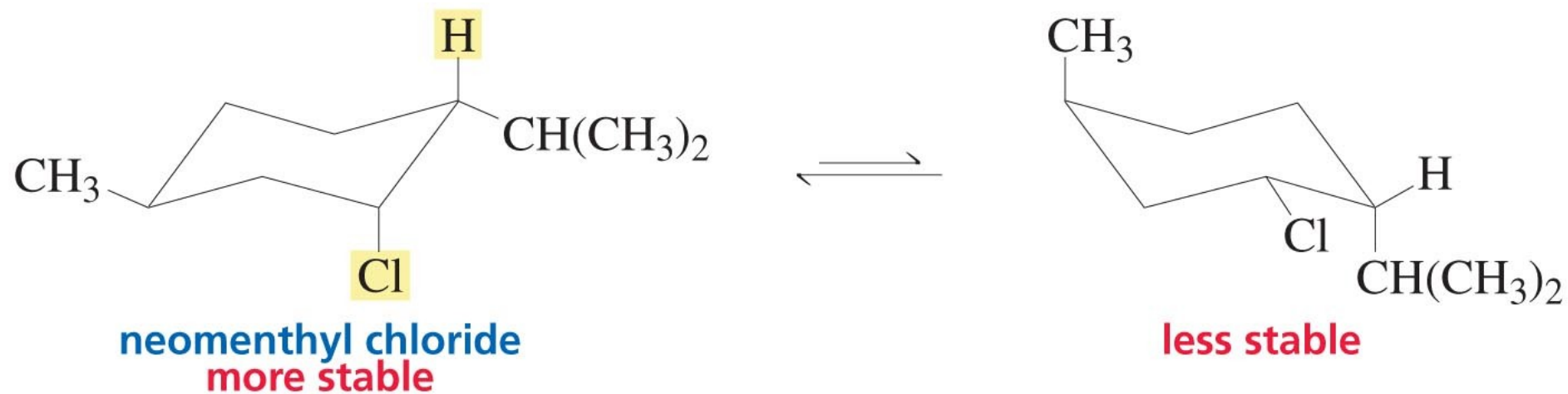
no reaction



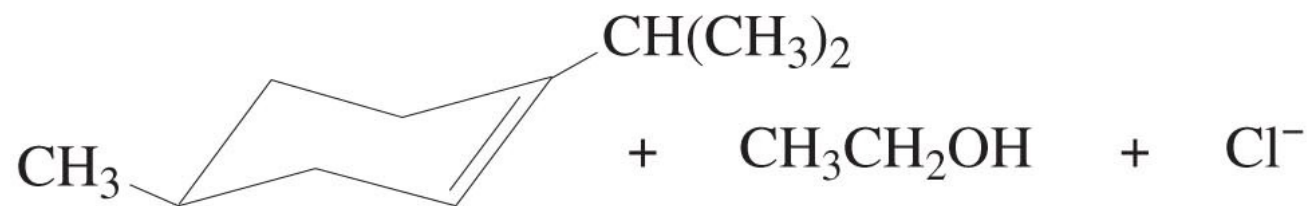
less stable

$k' \downarrow$ HO^-
E2 conditions

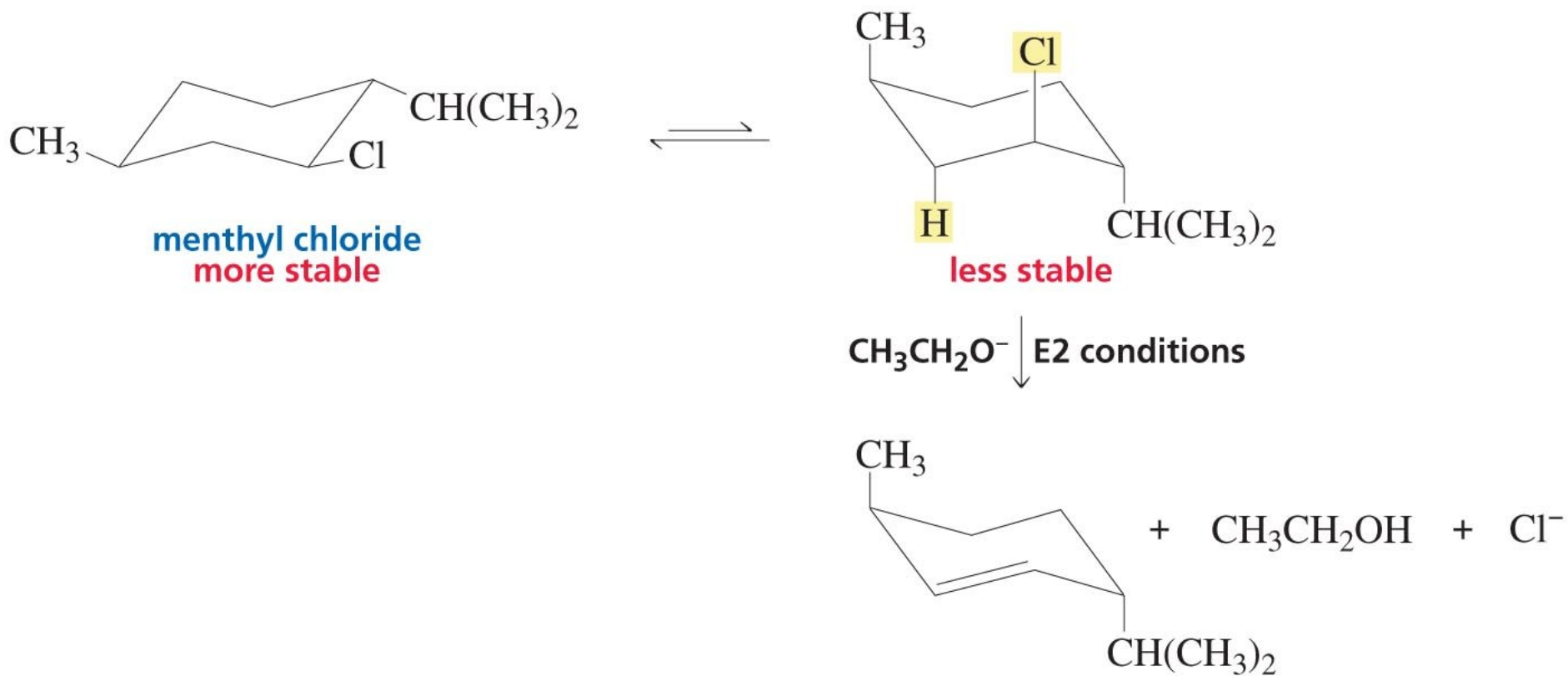




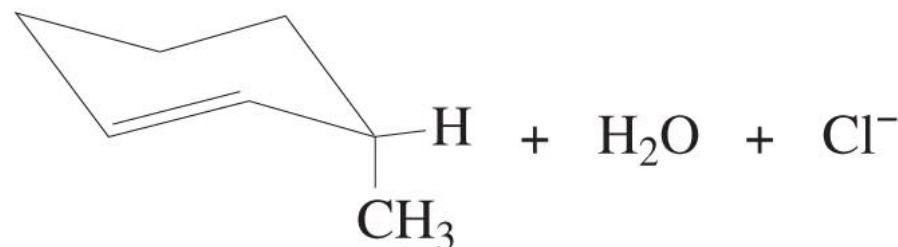
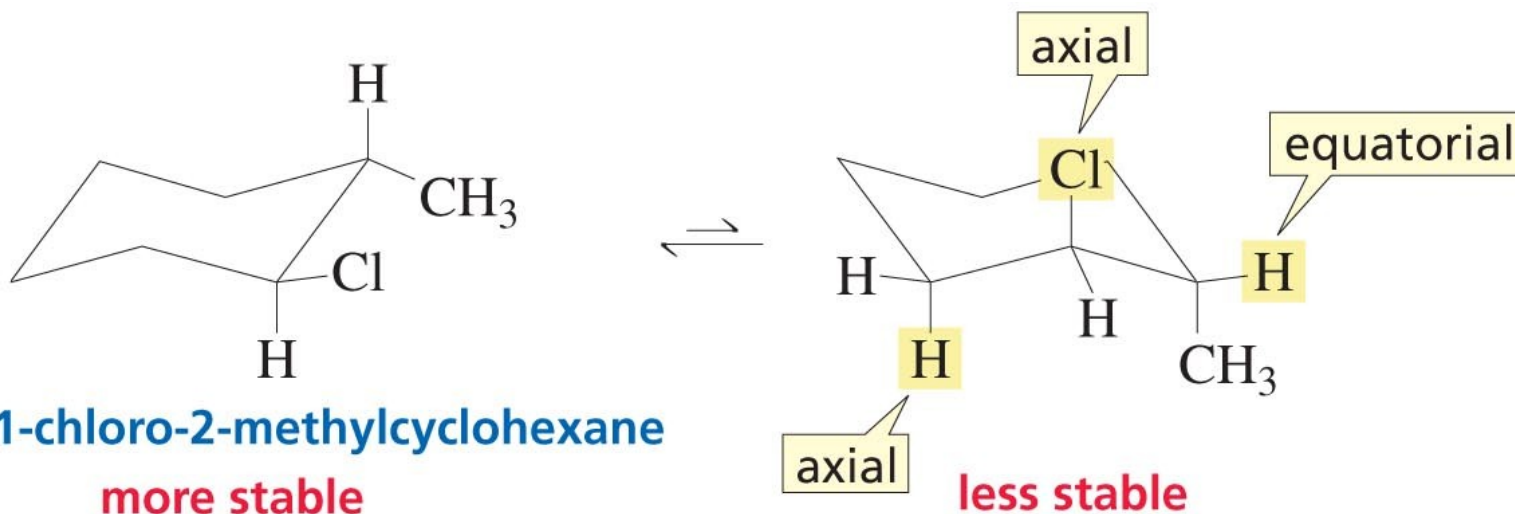
$\text{CH}_3\text{CH}_2\text{O}^-$
 $\downarrow$
 E2 conditions



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The hydrogen that is removed and the leaving group both have to be in the axial position, therefore...



$$K_{eq} = \frac{\text{[more stable conformer]}}{\text{[less stable conformer]}}$$

large number

small number

for a reaction that takes place
through the more stable conformer

$$K_{eq} = \frac{\text{[less stable conformer]}}{\text{[more stable conformer]}}$$

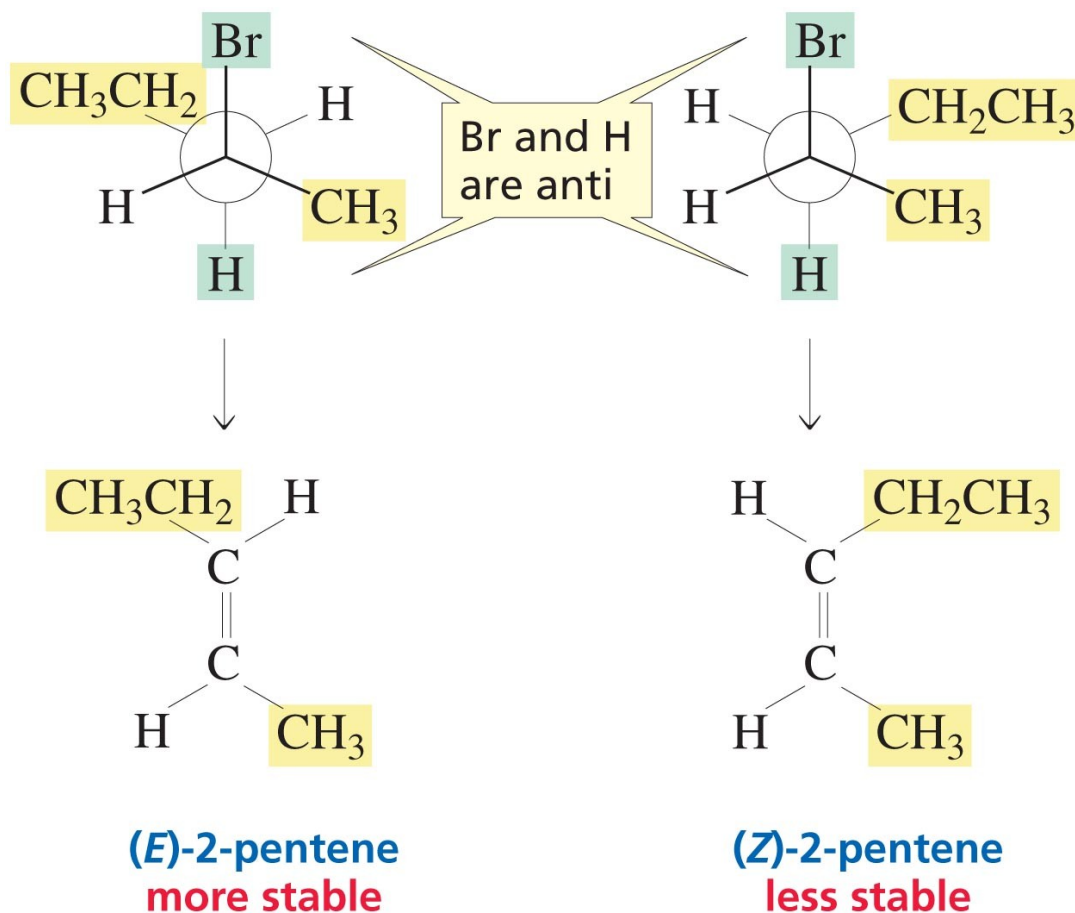
small number

large number

for a reaction that takes place
through the less stable conformer

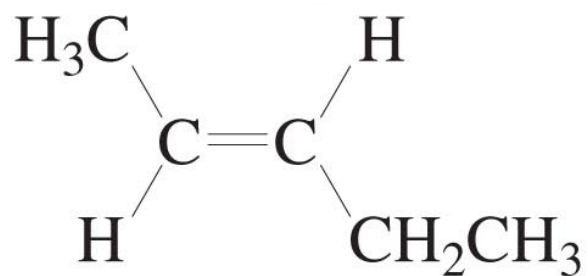
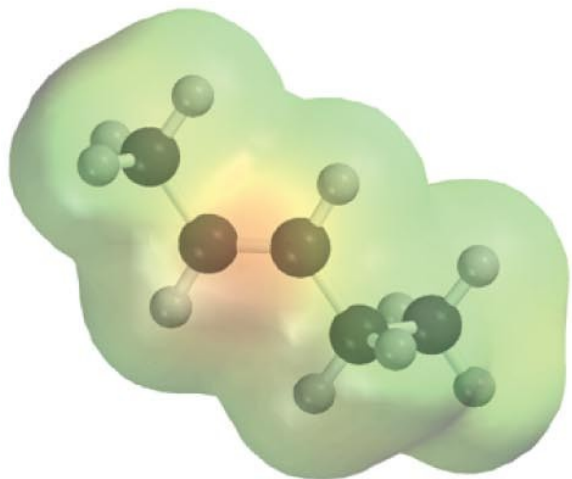
Elimination of 2-bromopentane

Consider the stereoselectivity of the E2 reaction



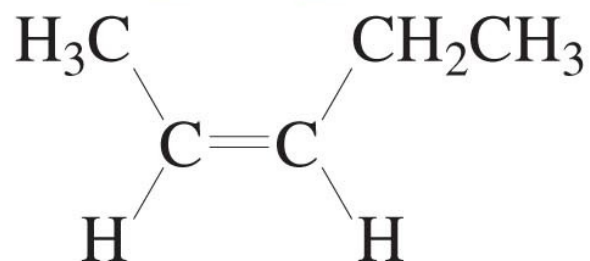
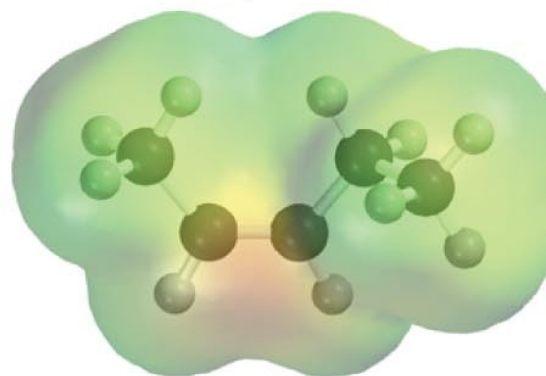
The alkene with the bulkiest groups on opposite sides of the double bond will be formed in greater yield, because it is the more stable alkene

interacting electron
clouds cause steric strain



(E)-2-pentene

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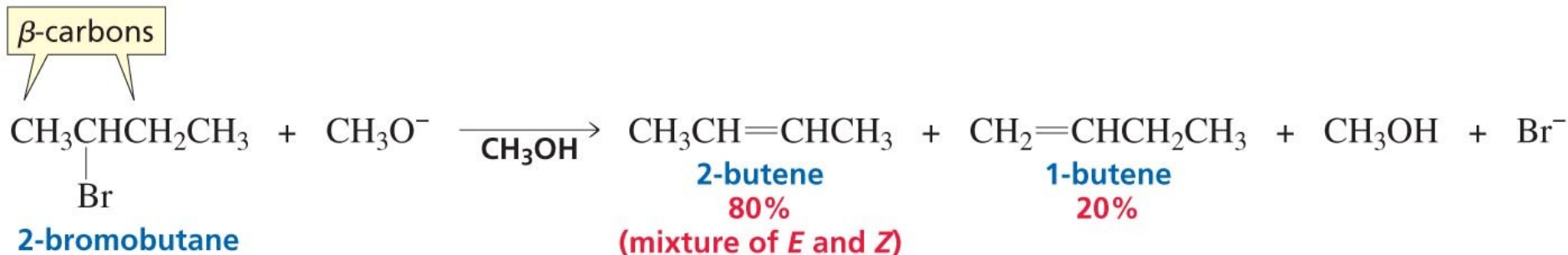


(Z)-2-pentene

Regioselectivity of the E2 Reaction

The Regioselectivity of the E2 Reaction

The major product of an E2 reaction is the most stable alkene:



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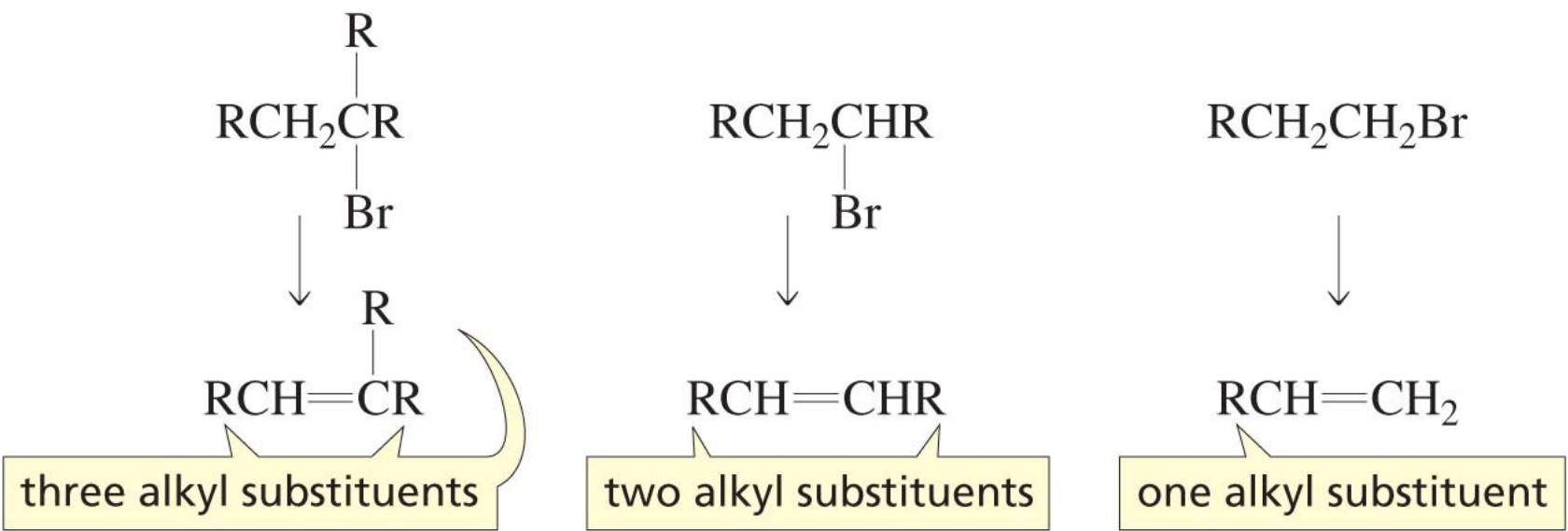
The Zaitsev Rule

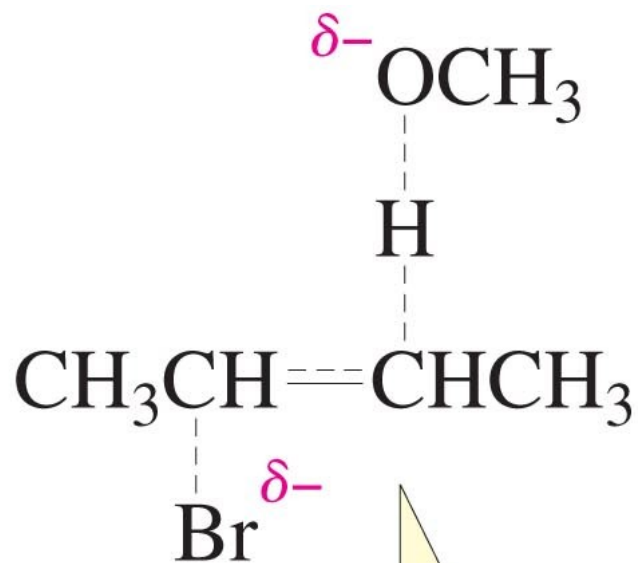
The more substituted alkene product is obtained when a proton is removed from the β -carbon that is bonded to the fewest hydrogens

The most stable alkene is generally (but not always) the most substituted alkene

relative reactivities of alkyl halides in an E2 reaction

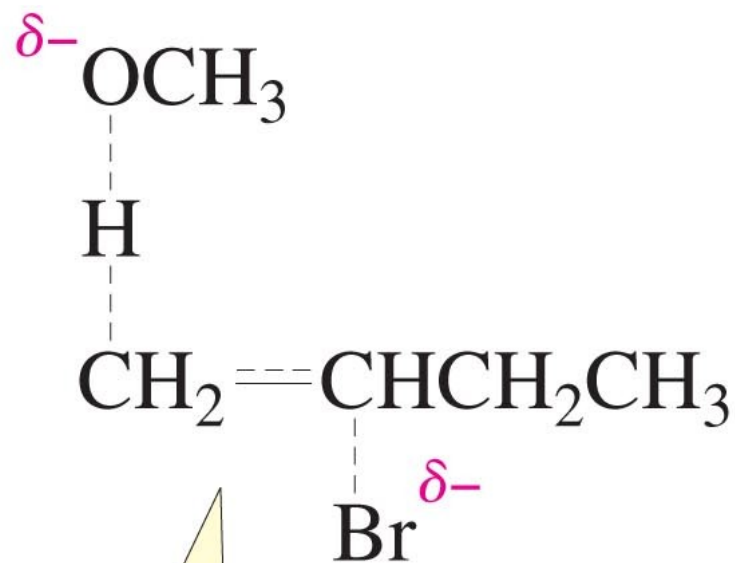
tertiary alkyl halide > secondary alkyl halide > primary alkyl halide





transition state leading
to 2-butene

more stable



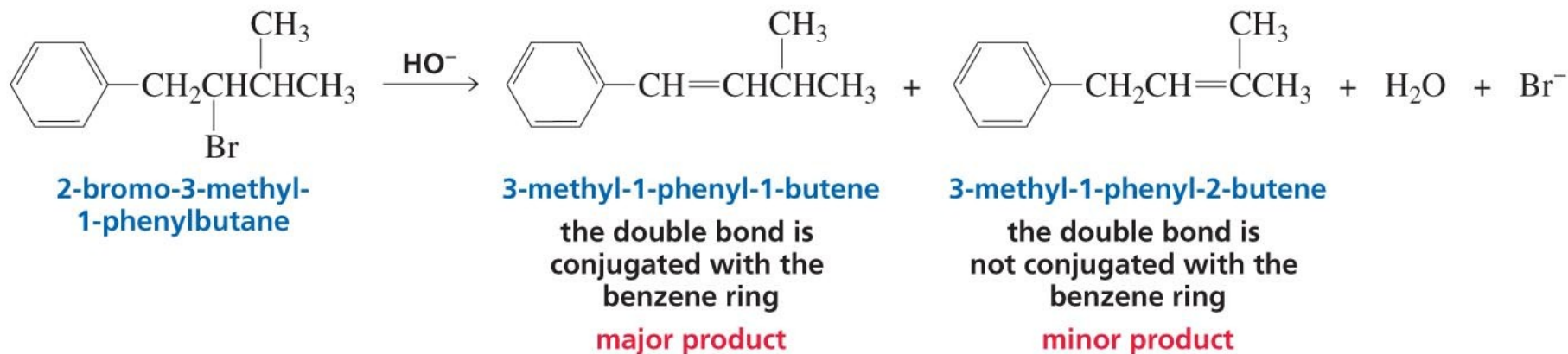
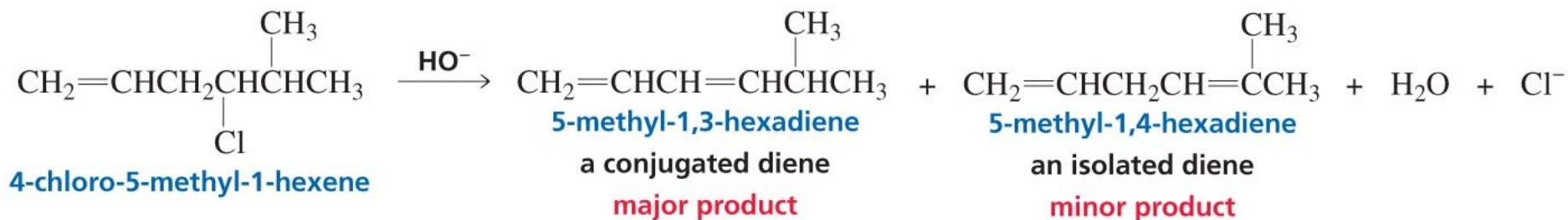
transition state leading
to 1-butene

less stable

Exception to Zaitsev's rule

Based on Substrate

Conjugated alkene products are preferred over the more substituted alkene product:

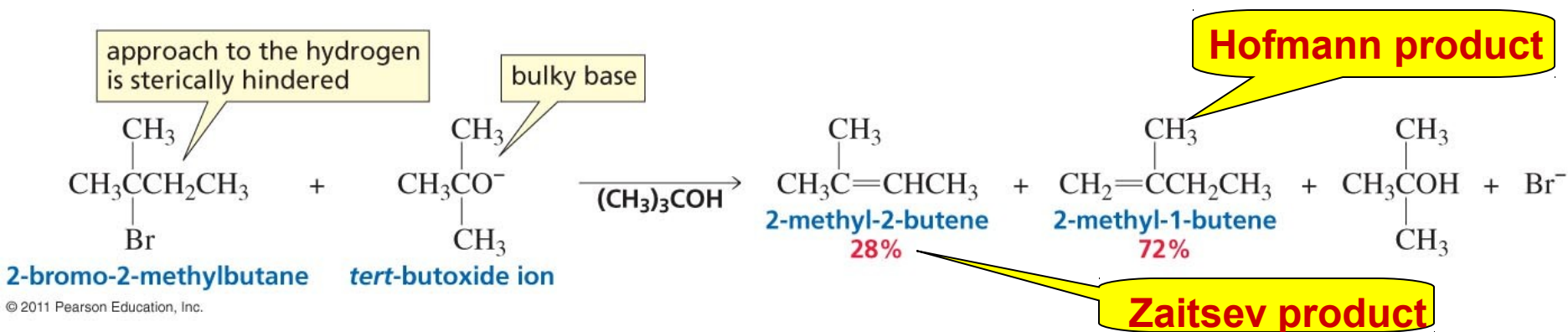


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Do not use Zaitsev's rule to predict the major product in these cases

Based on Base

Bulky bases affect the product distribution resulting in the Hofmann product, the least substituted alkene:



However, it takes a lot of steric hindrance for the less stable product to be the major product:

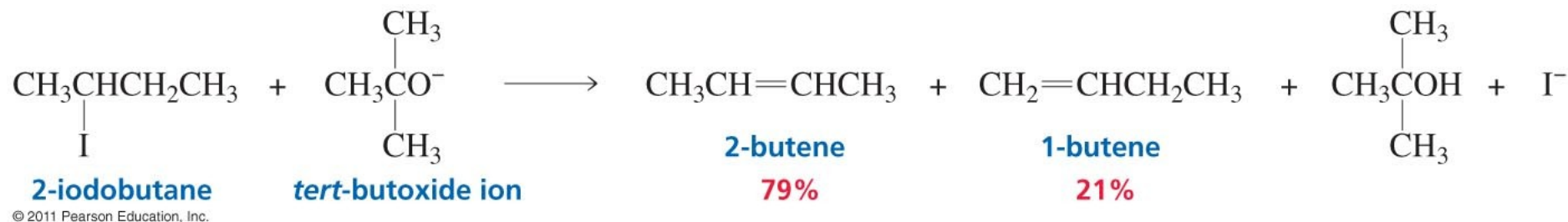
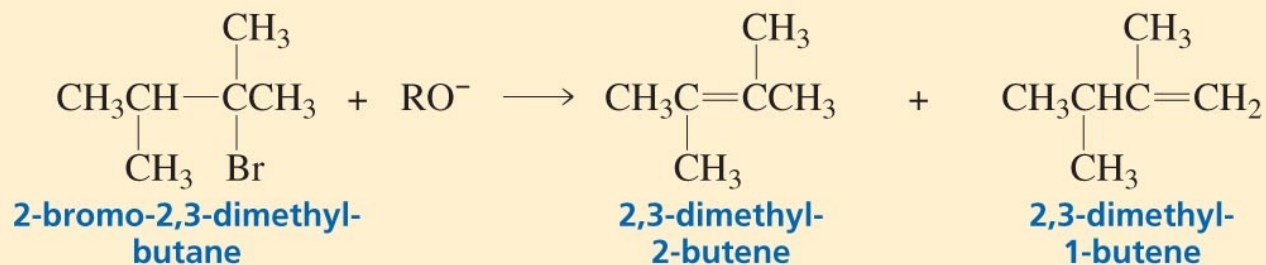


Table 9.1 Effect of the Steric Properties of the Base on the Distribution of Products in an E2 Reaction

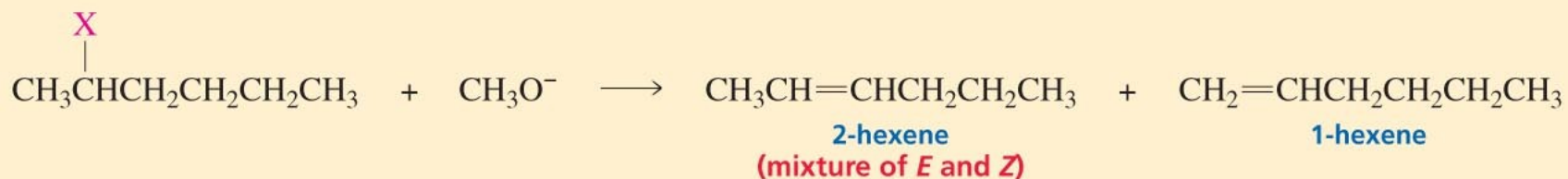


Base	More substituted alkene	Less substituted alkene
$\text{CH}_3\text{CH}_2\text{O}^-$	79%	21%
$\begin{array}{c} \text{CH}_3 \\ \\ \text{CH}_3\text{CO}^- \\ \\ \text{CH}_3 \end{array}$	27%	73%
$\begin{array}{c} \text{CH}_3 \\ \\ \text{CH}_3\text{CO}^- \\ \\ \text{CH}_2\text{CH}_3 \end{array}$	19%	81%
$\begin{array}{c} \text{CH}_2\text{CH}_3 \\ \\ \text{CH}_3\text{CH}_2\text{CO}^- \\ \\ \text{CH}_2\text{CH}_3 \end{array}$	8%	92%

Based on leaving group

Another exception to Zaitsev's rule

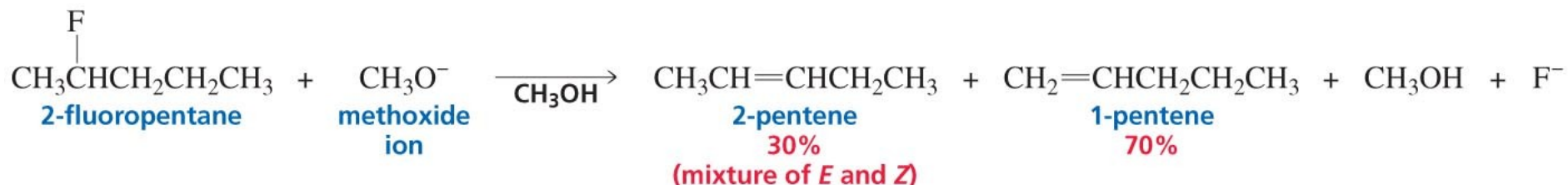
Table 9.2 Products Obtained from the E2 Reaction of CH_3O^- and 2-Halohehexanes



Leaving group	Conjugate acid	$\text{p}K_{\text{a}}$	More substituted product	Less substituted product
$\text{X} = \text{I}$	HI	-10	81%	19%
$\text{X} = \text{Br}$	HBr	-9	72%	28%
$\text{X} = \text{Cl}$	HCl	-7	67%	33%
$\text{X} = \text{F}$	HF	3.2	30%	70%

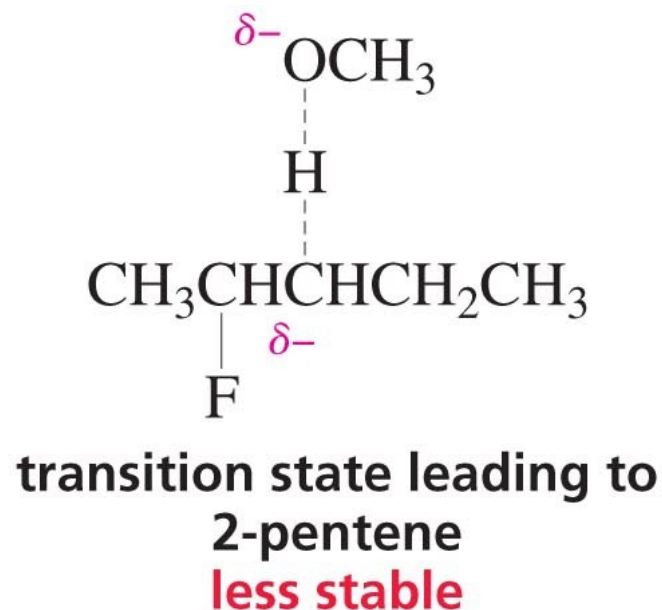
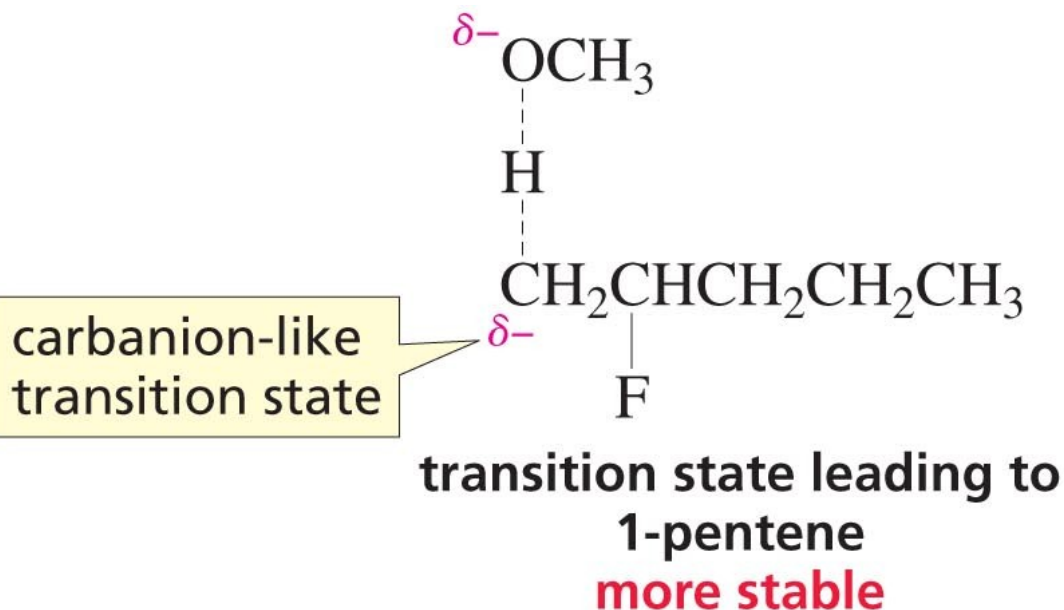
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Consider the elimination of 2-fluoropentane...



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A carbanion-like transition state



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E2 Reactions

- Substrate : primary halides
- Base: high concentration of strong base
- Solvent : aprotic polar solvent

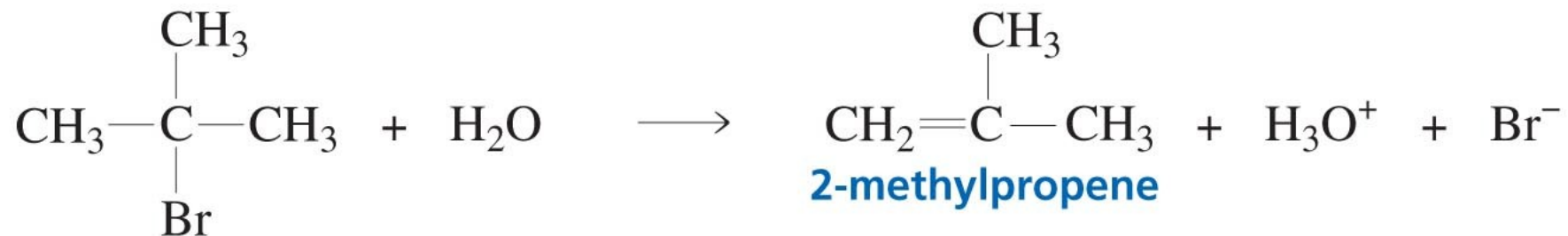
E1 Reactions

The E1 Reaction

- reaction and mechanism
- kinetics
- Stereochemistry
- Regioselectivity
- Carbocation rearrangement

Reaction and mechanism

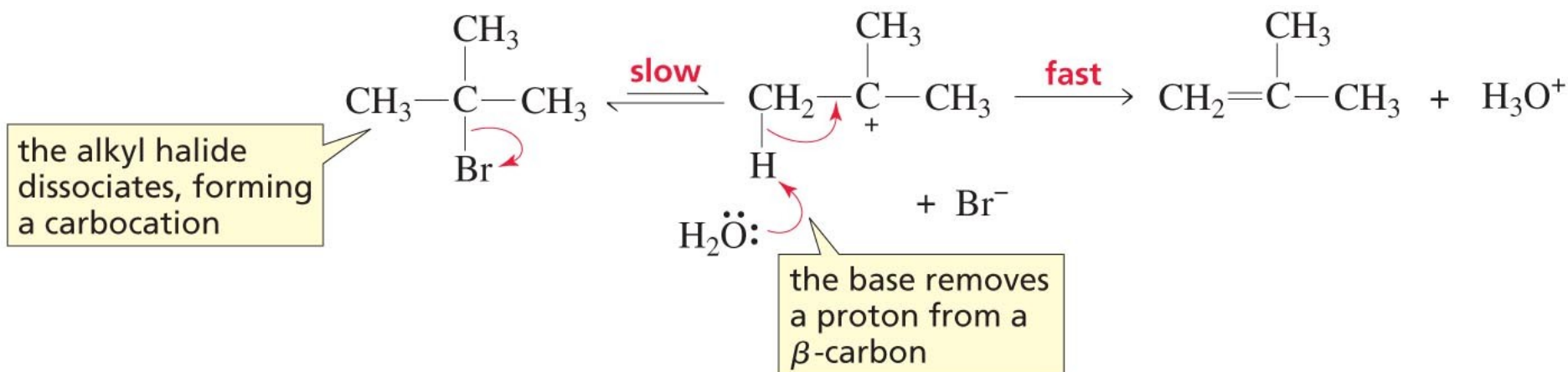
The E1 Reaction



2-bromo-2-methylpropane

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The E1 reaction, like the S_N1 reaction, involves a carbocation intermediate:



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kinetics

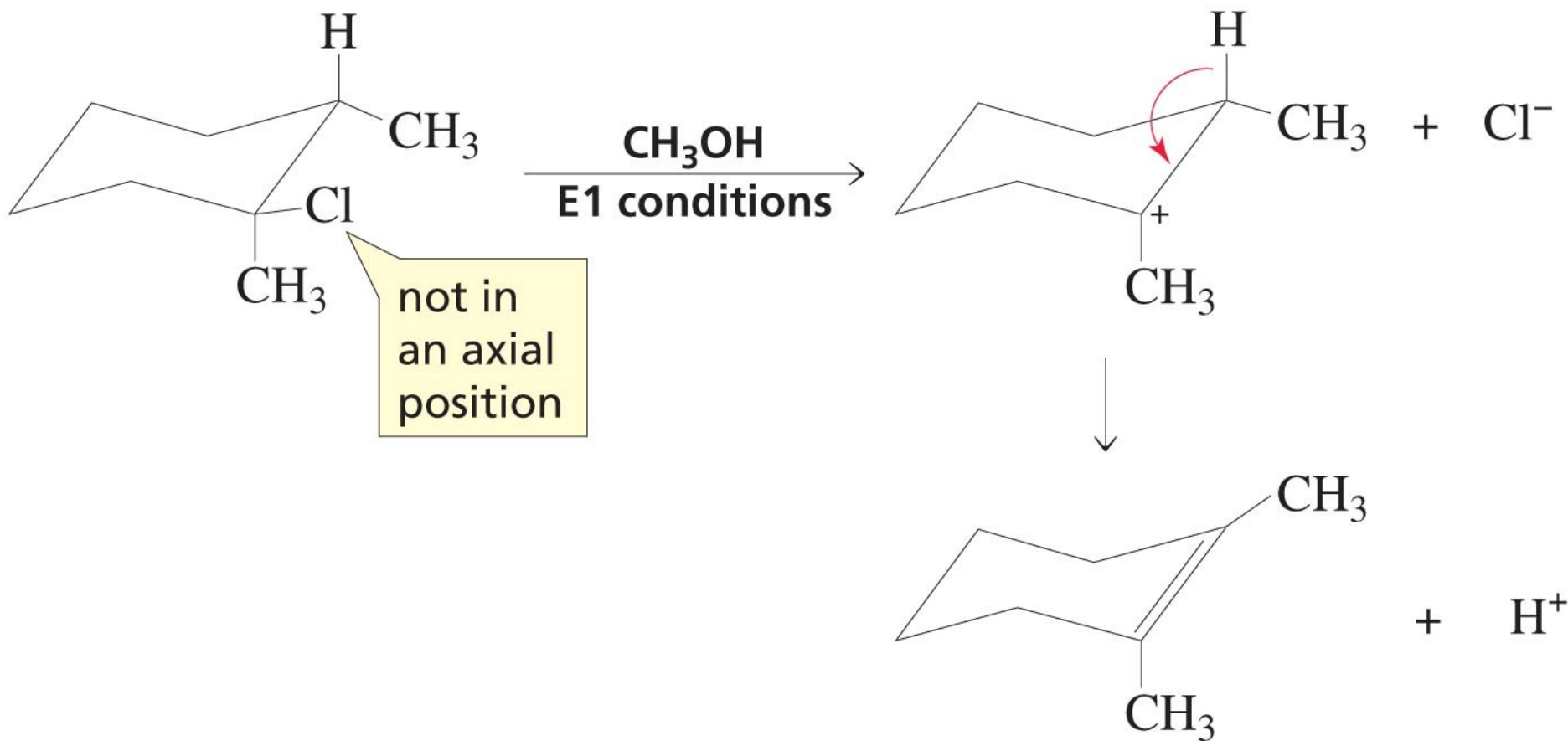
$$\text{rate} = k[\text{alkyl halide}]$$

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A unimolecular reaction:

stereochemistry

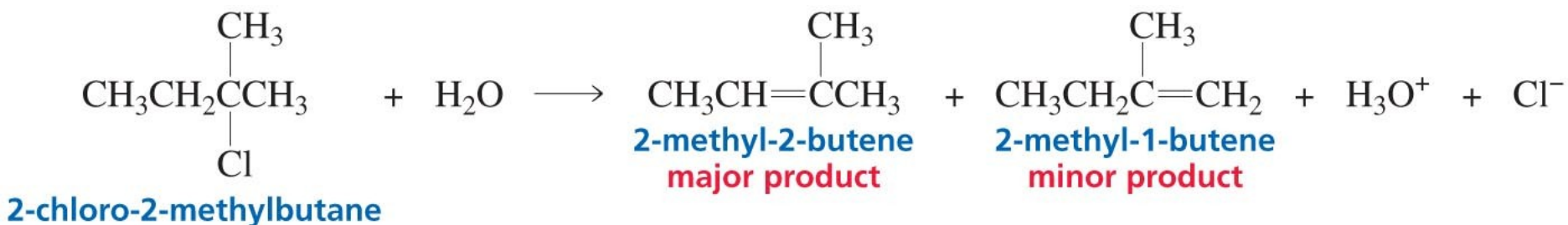
E1 Elimination from Cyclic Compounds



No axial orientation required for the E1 reaction.

Regioselectivity of the E1 Reaction

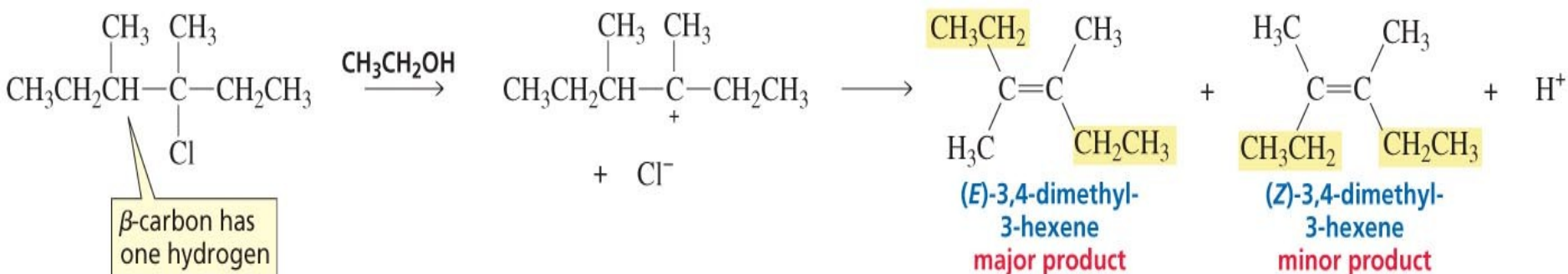
The major product in an E1 reaction is generally the more substituted alkene



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Stereochemistry of the E1 Reaction

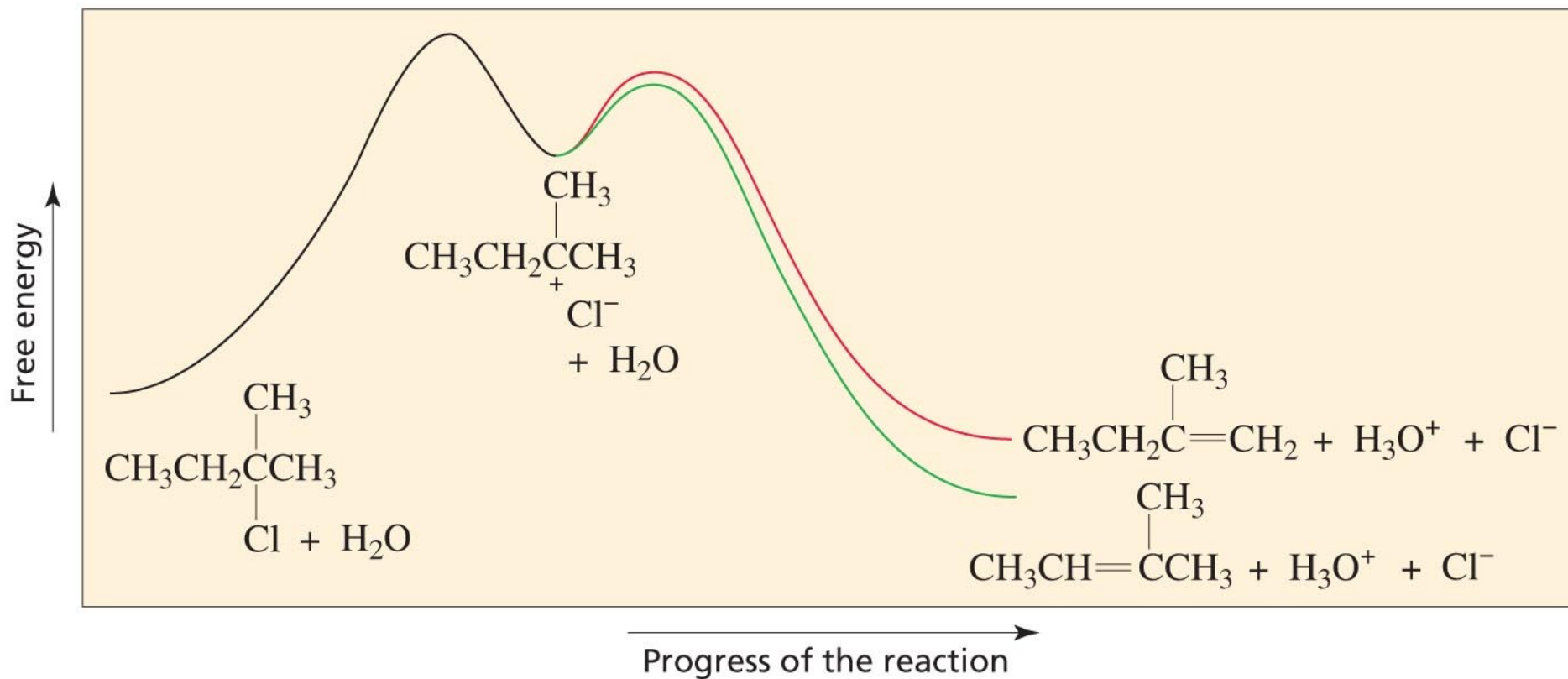
Both syn and anti elimination can occur in an E1 reaction



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The major stereoisomer obtained from an E1 reaction is the alkene in which the bulkiest substituents are on opposite sides of the double bond

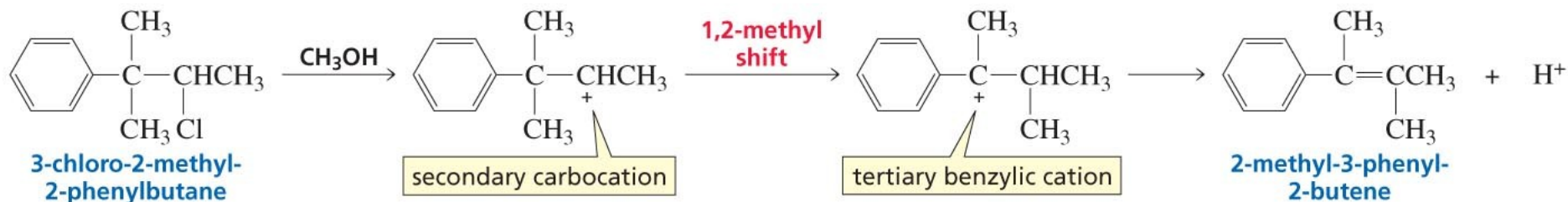
Reaction coordinate diagram for the E1 reaction of 2-chloro-2-methylbutane



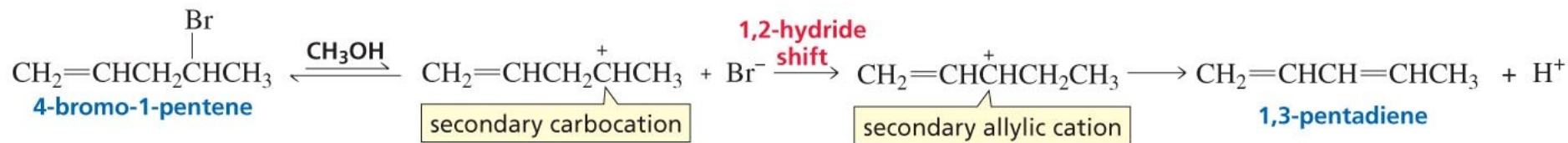
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Carbocation rearrangement

Because the E1 reaction forms a carbocation intermediate, we need to consider carbocation rearrangement

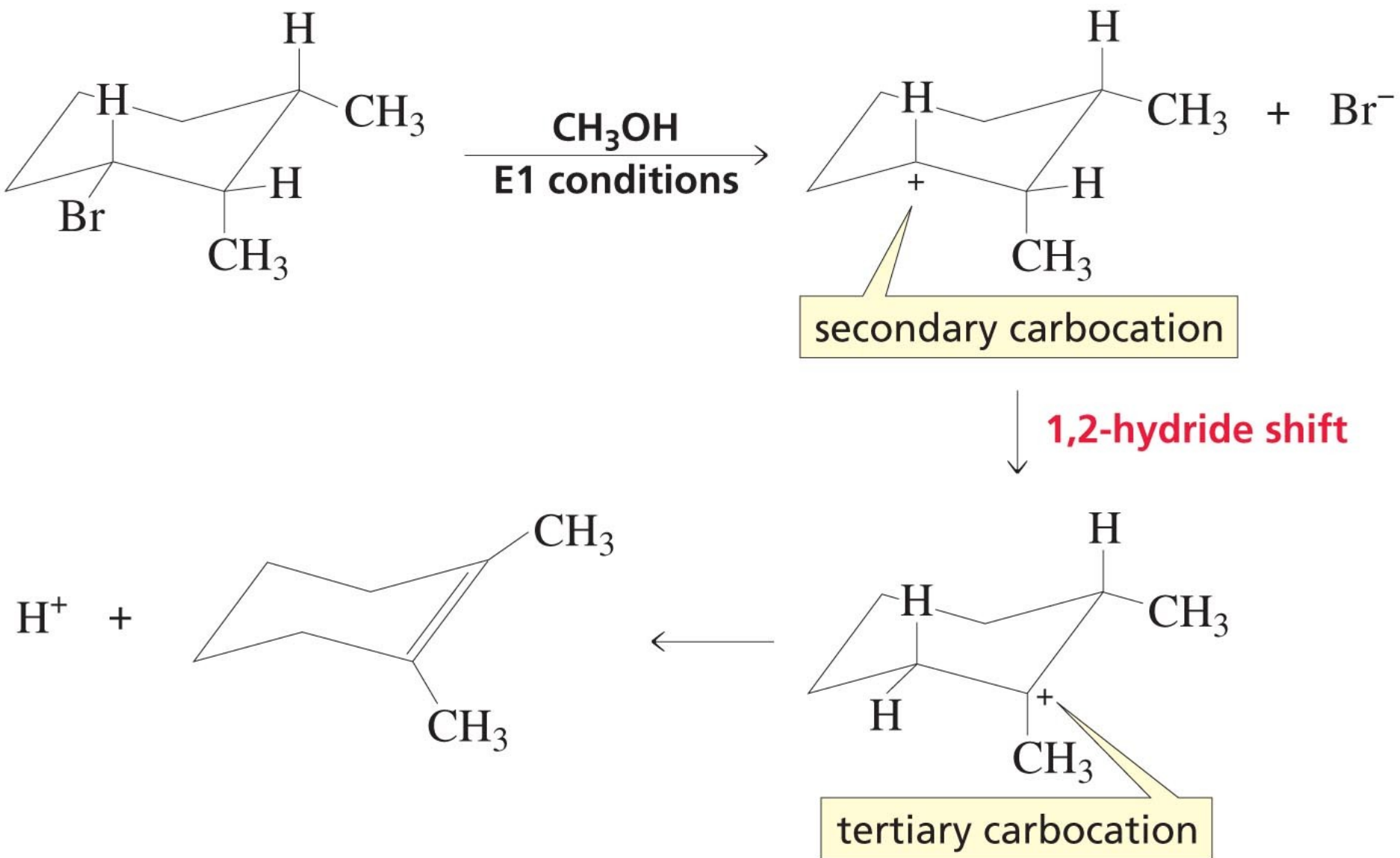


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- 1-bromo 2,3 dimethyl cyclohexane



Because the first step is the rate-determining step, the rate of an E1 reaction depends both on the ease with which the carbocation is formed and how readily the leaving group leaves

relative reactivities of alkyl halides in an E1 reaction = relative stabilities of carbocations



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relative reactivities of alkyl halides in an E1 reaction



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Competition Between E2 and E1 Reactions

Table 9.3 Summary of the Reactivity of Alkyl Halides in Elimination Reactions

Primary alkyl halide	E2 only
Secondary alkyl halide	E1 and E2
Tertiary alkyl halide	E1 and E2

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An E2 is favored by a high concentration of strong base and an aprotic polar solvent

An E1 is favored by a weak base and a protic polar solvent

Competition Between Substitution and Elimination

Alkyl halides can undergo S_N2 , S_N1 , E2, and E1

1) decide whether the reaction conditions favor S_N2 /E2 or S_N1 /E1

- S_N2 /E2 reactions are favored by a high concentration of a good nucleophile/strong base

- S_N1 /E1 reactions are favored by a poor nucleophile/weak base

2) decide how much of the product will be the substitution product and how much of the product will be the elimination product

Table 9.6 Summary of the Products Expected in Substitution and Elimination Reactions

Class of alkyl halide	S _N 2 versus E2	S _N 1 versus E1
Primary alkyl halide	Primarily substitution, unless there is steric hindrance in the alkyl halide or nucleophile, in which case elimination is favored	Cannot undergo S _N 1/E1 reactions
Secondary alkyl halide	Both substitution and elimination; the stronger and bulkier the base and the higher the temperature, the greater the percentage of elimination	Both substitution and elimination
Tertiary alkyl halide	Only elimination	Both substitution and elimination

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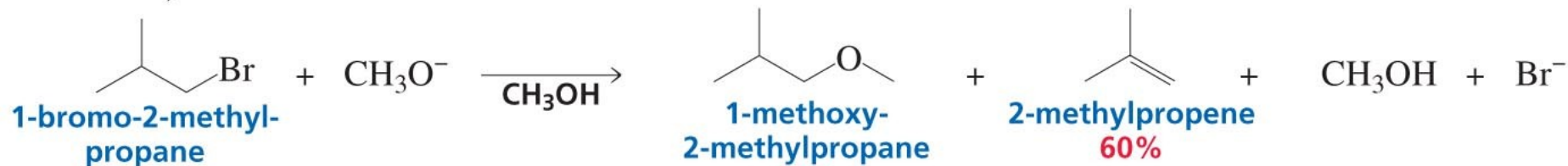
Table 9.4 Stereochemistry of Substitution and Elimination Reactions

Reaction	Products
S_N1	Both stereoisomers (<i>R</i> and <i>S</i>) are formed (more inverted than retained).
E1	Both <i>E</i> and <i>Z</i> stereoisomers are formed (more of the stereoisomer with the bulkiest groups on opposite sides of the double bond).
S_N2	Only the inverted product is formed.
E2	Both <i>E</i> and <i>Z</i> stereoisomers are formed (more of the stereoisomer with the bulkiest groups on opposite sides of the double bond) unless the β -carbon of the reactant is bonded to only one hydrogen, in which case only one stereoisomer is formed; its configuration depends on the configuration of the reactant.

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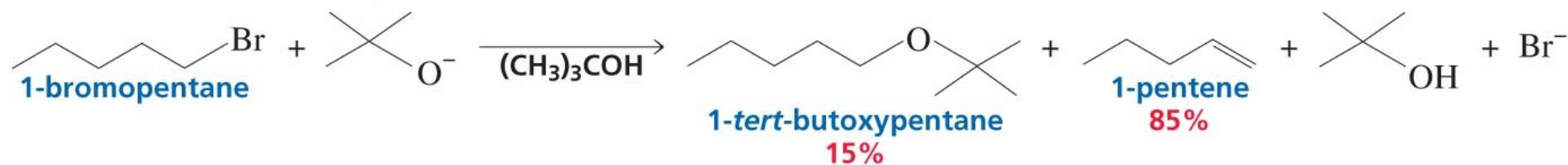
A bulky alkyl halide or a sterically hindered nucleophile encourages elimination over substitution

the primary alkyl halide is sterically hindered



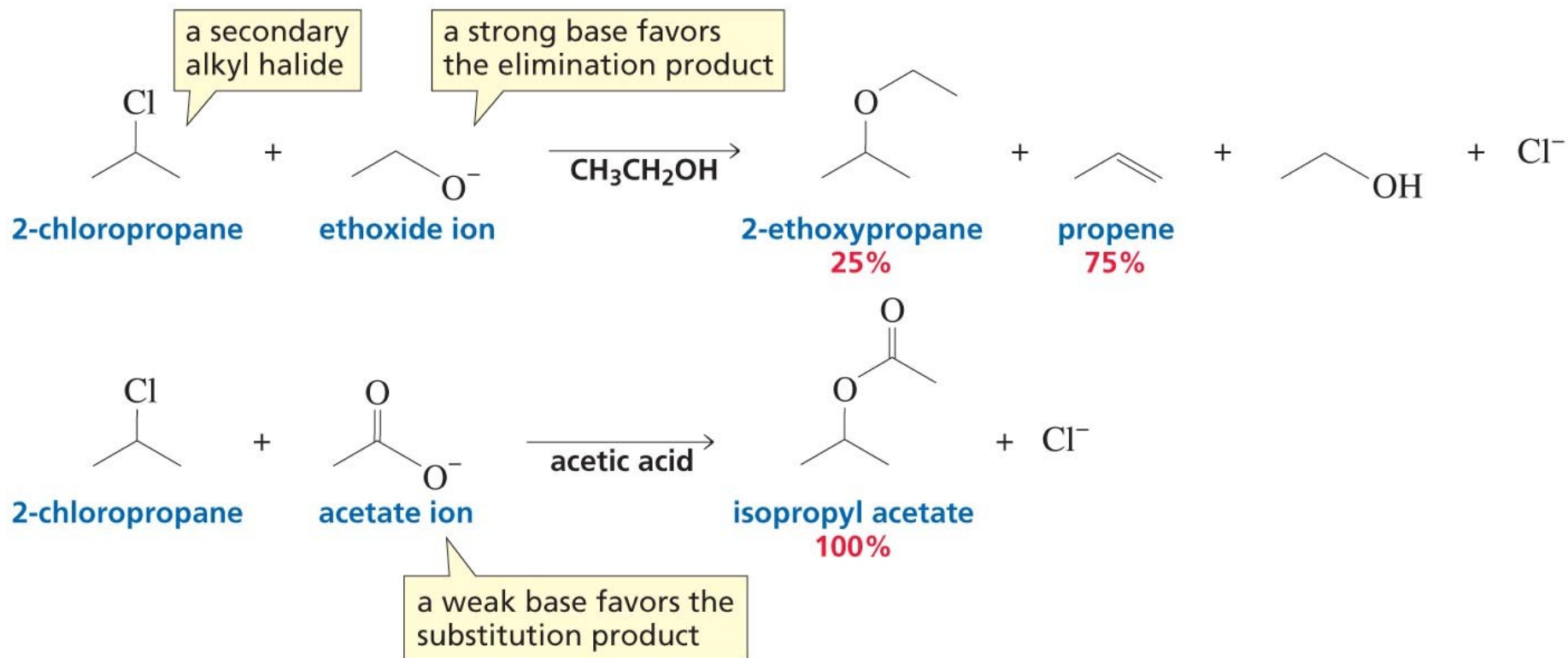
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the nucleophile is sterically hindered



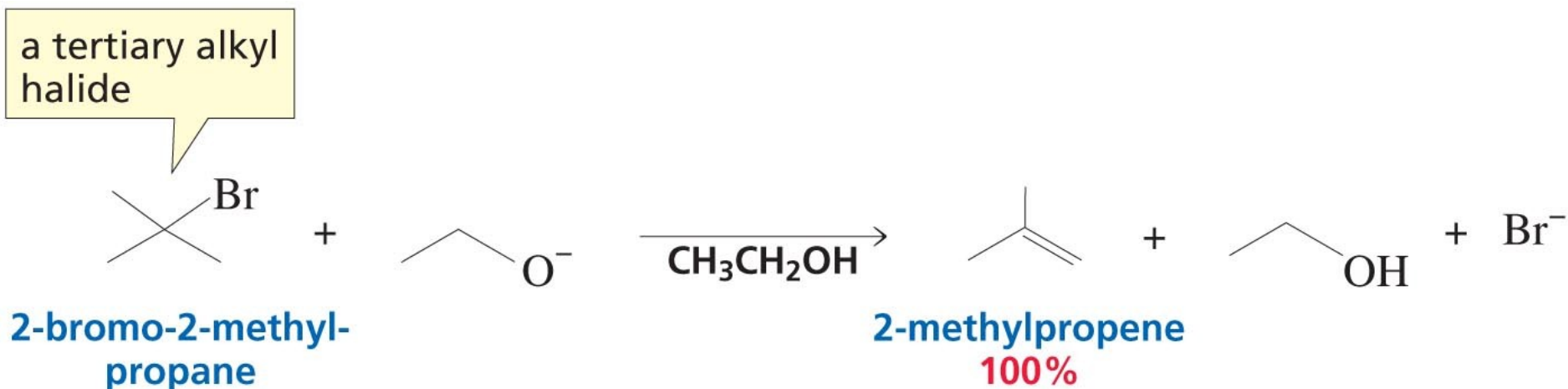
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A strong or a bulky base encourages elimination over substitution



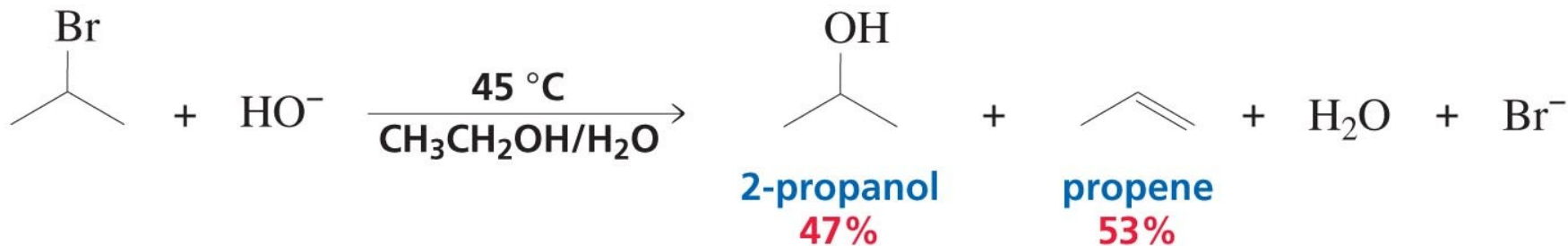
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Tertiary alkyl halides undergo only elimination under $S_N2/E2$ conditions:

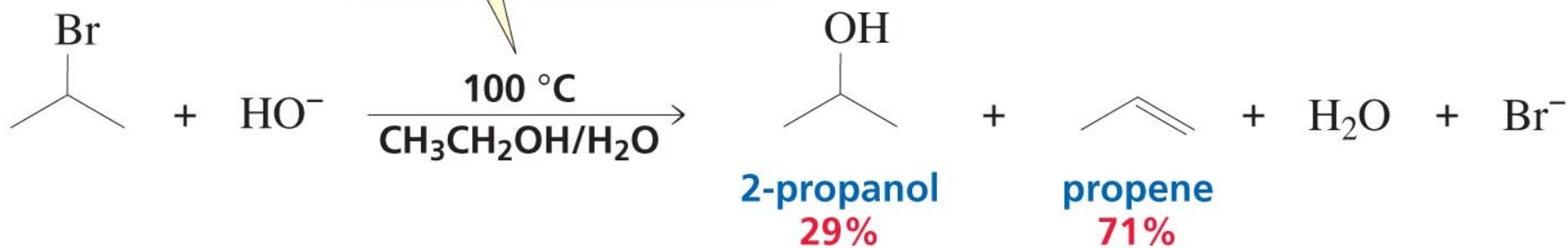


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High temperature favors elimination over substitution:



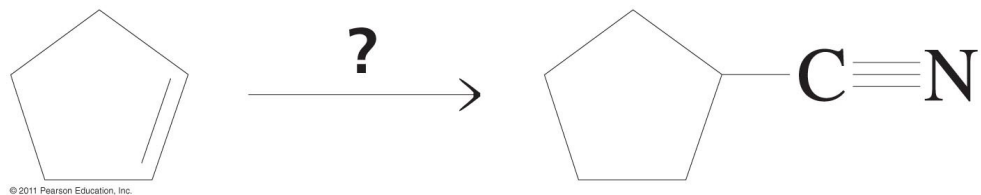
a higher temperature
favors elimination



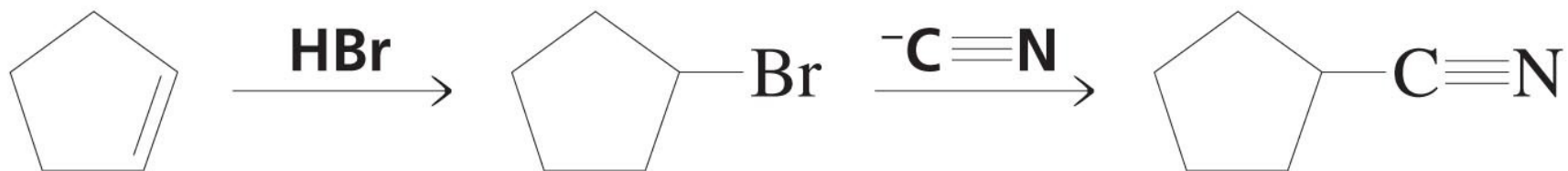
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Why? Because elimination is entropically favorable.

Synthesis Example



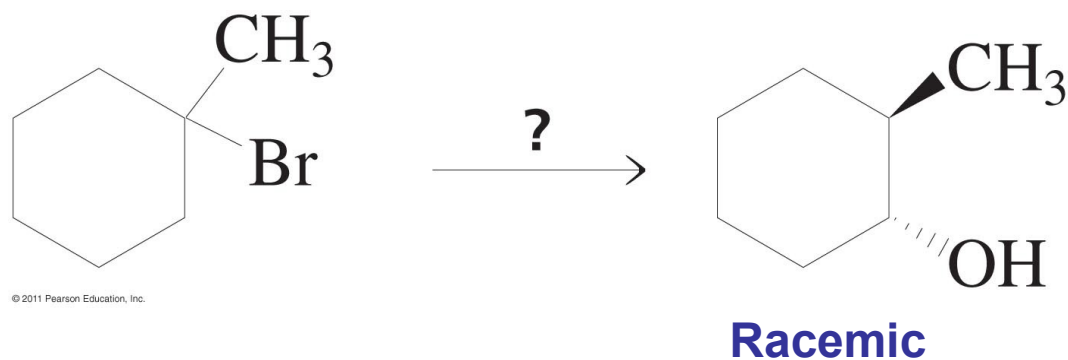
synthesis



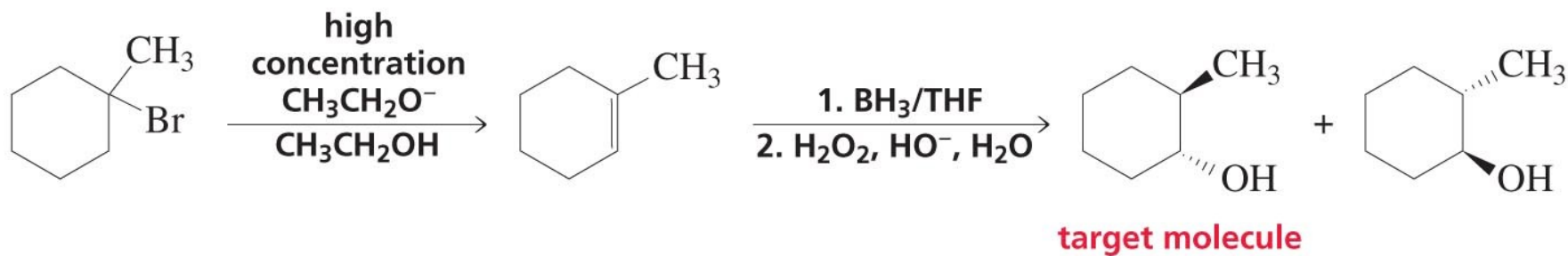
target molecule

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Synthesis Example



synthesis

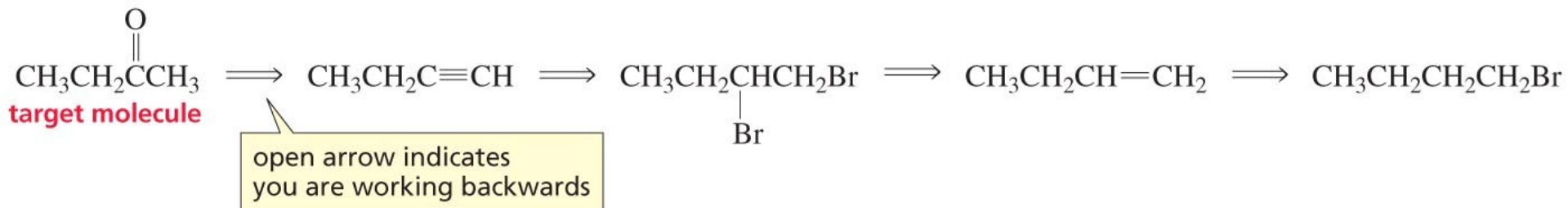


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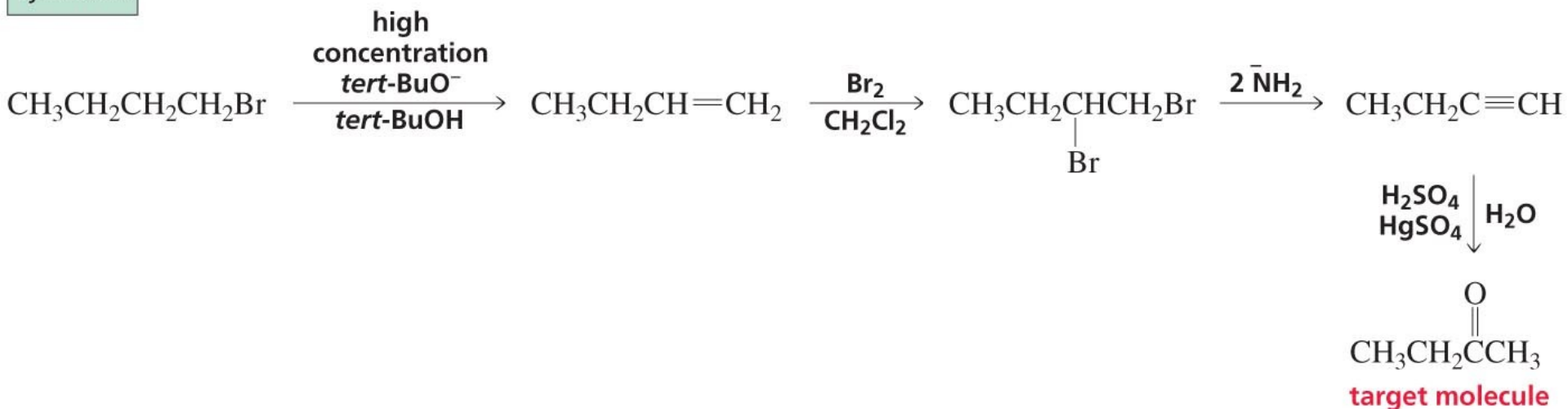
Synthesis Example



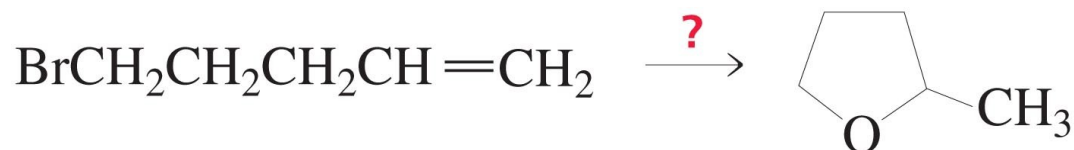
retrosynthetic analysis



synthesis

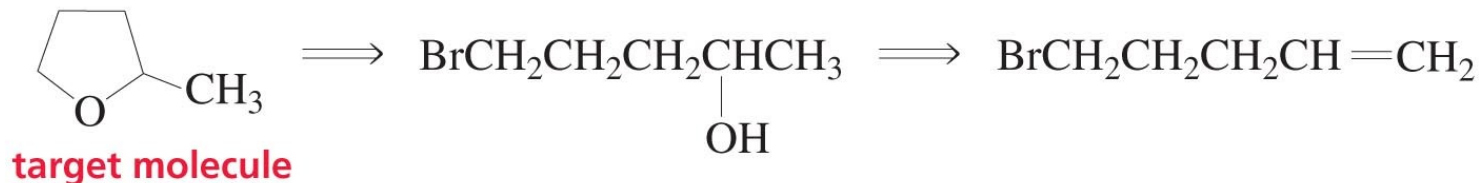


Synthesis Example



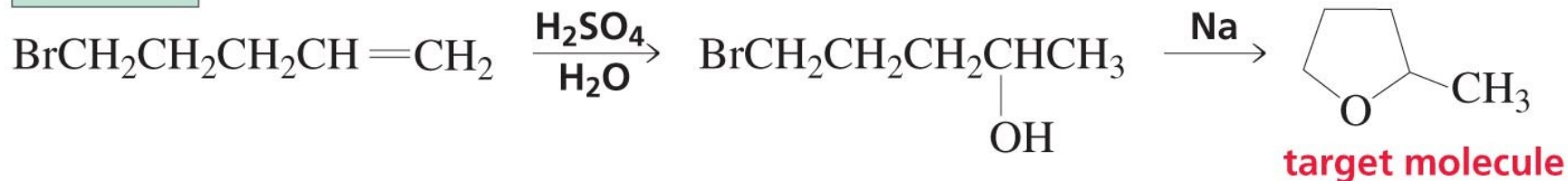
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retrosynthetic analysis



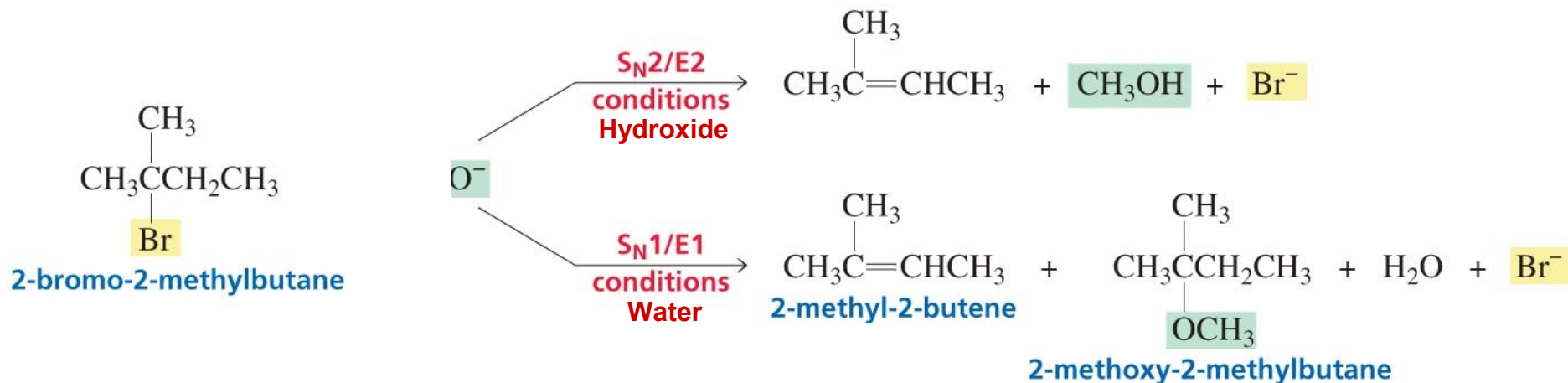
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synthesis



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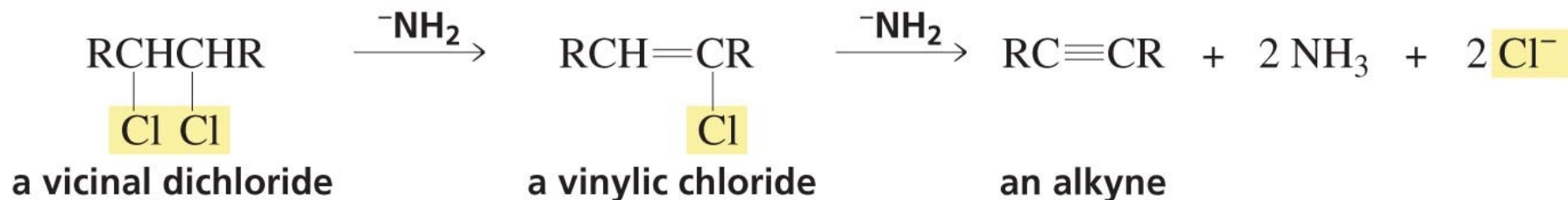
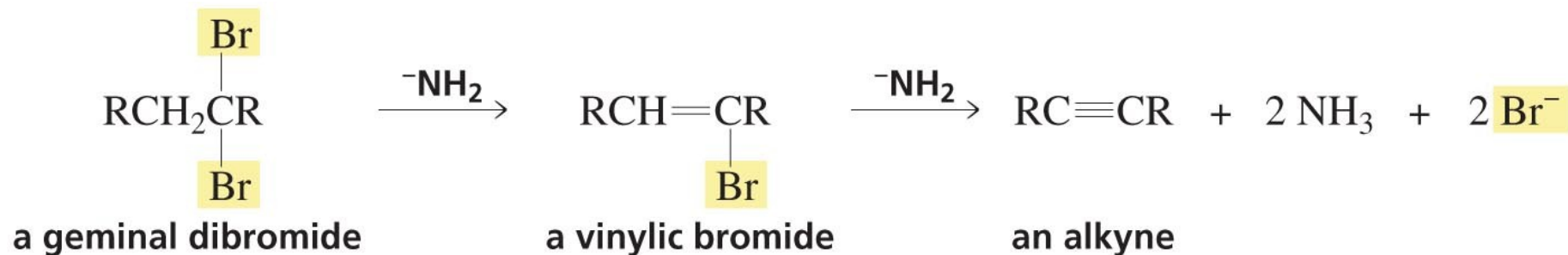
The E2 reaction should be used if you want to synthesize an alkene:



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Consecutive E2 Elimination Reactions

Requires a strong base NaNH_2 . Reaction carried out in liquid ammonia.



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