

# TOPIC 7. ELIMINATION REACTIONS

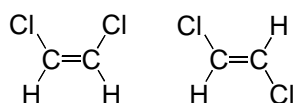
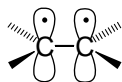
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## OBJECTIVES

1. Describe mechanisms for elimination of a leaving group and adjacent proton to form a pi-bond.
2. Discuss the effect of starting material ("substrate"), leaving group, and reaction conditions on the course and outcome of a reaction.
3. Describe syntheses of alkenes and alkynes.
4. Use combinations of elimination and substitution reactions in developing two-step syntheses of value-added compounds.

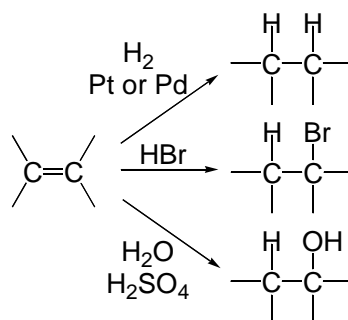
# ALKENES: STRUCTURE, NOMENCLATURE, AND STABILITY

## Structure



## Preview of Reactivity

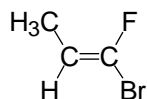
Additions (Topic 8)



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## Systematic Nomenclature

e.g.,

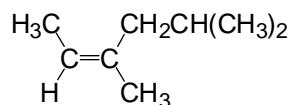


Assign Cahn-Ingold-Prelog priority to substituents on each  $sp^2$  carbon  
Highest priority on

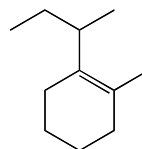
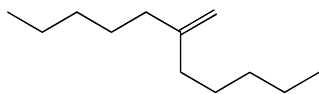
same side: *Z* (zusammen=same)

opposite sides: *E* (entgegen=opposite)

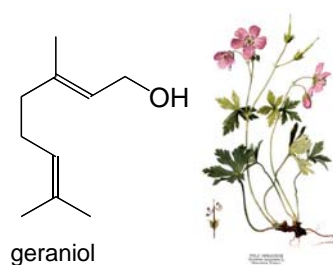
*Problem:* Name the following compound



*Problem:* Provide IUPAC names for the following alkenes

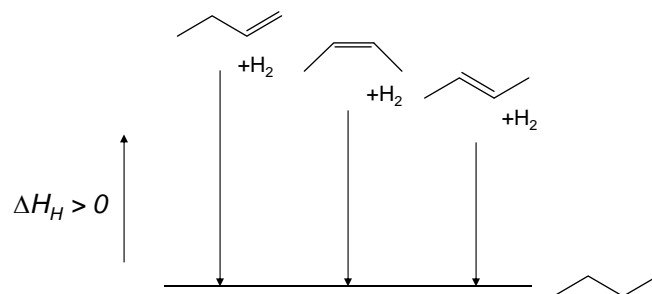
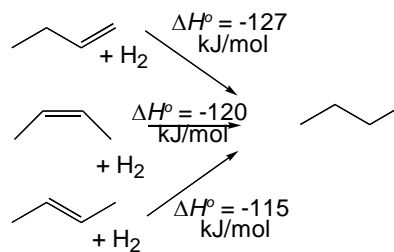
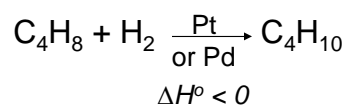


*Problem:* Determine the *E/Z* configurations of the double bonds in each of the following alkenes

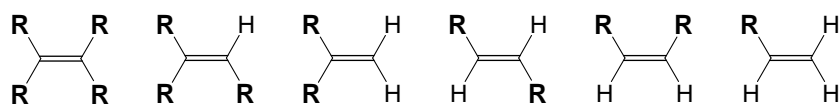


## Relative Stability

*Heats of Hydrogenation*



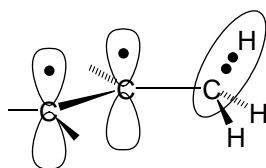
Overall Stability



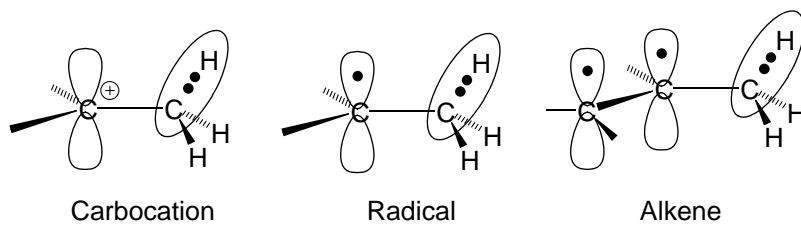
number of substituents

Number of substituents  $\uparrow \Rightarrow$

Remember hyperconjugation?



Hyperconjugation accounts for the enhanced stability of cations, radicals and alkenes with higher degrees of substitution.



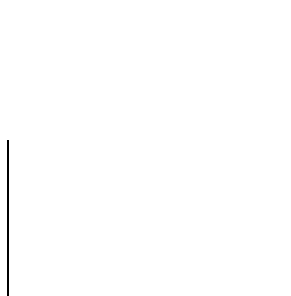
Carbocation

Radical

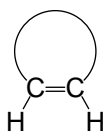
Alkene

relative stability

stability explains



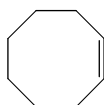
## Cycloalkenes



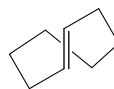
cyclopropene  
cyclobutene  
cyclopentene

cyclohexene  
cycloheptene

cyclooctene



*cis* cyclooctene

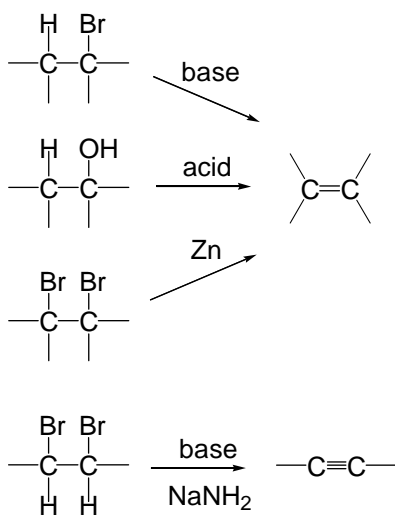


*trans* cyclooctene

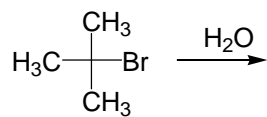
strain energies: 15 kcal/mol 27 kcal/mol

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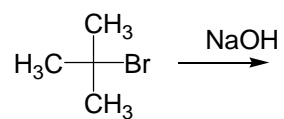
## PREVIEW OF FORMATION OF ALKENES & ALKYNES BY ELIMINATION REACTIONS



## BASE-PROMOTED DEHYDROHALOGENATION OF ALKYL HALIDES



but:

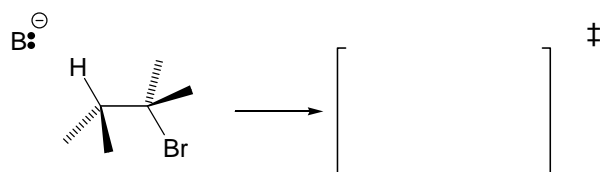


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## ELIMINATION MECHANISMS

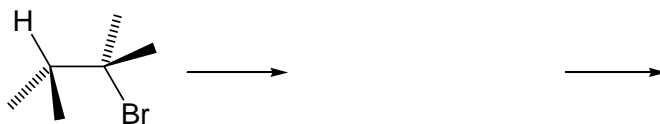
### Bimolecular Elimination (E2) Reaction

$$\text{Rate} = k[\text{R-L}][\text{base}]$$



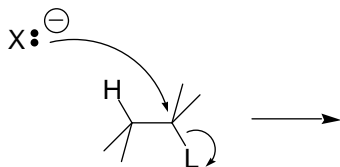
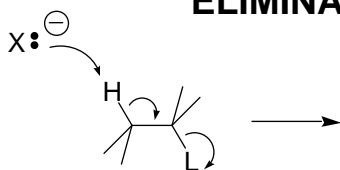
## Unimolecular Elimination (E1) Reaction

Rate =  $k[\text{R-L}]$ , independent of [base]



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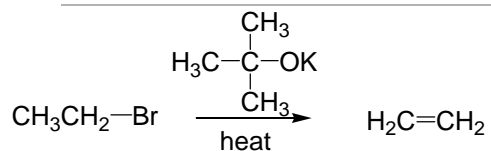
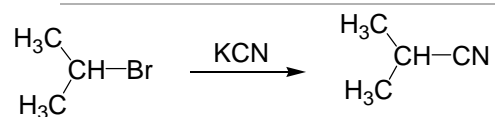
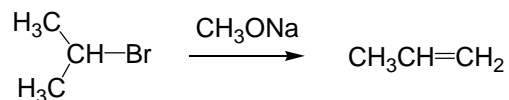
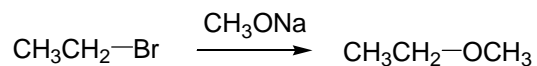
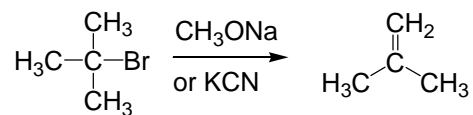
## $\text{S}_{\text{N}}2$ SUBSTITUTION VERSUS $\text{E}2$ ELIMINATION



Substitution and elimination mechanisms might be competitive pathways in a reaction mixture. The outcome of a reaction depends on:

- the *structure* of the substrate (steric hindrance to nucleophilic attack)
- the *basicity* of the nucleophile

## Observations and Explanations



## Summary

3° substrates only undergo substitution with weakly basic nucleophiles (ROH, H<sub>2</sub>O, RCO<sub>2</sub>H). Stronger bases promote elimination. 1° substrates generally undergo substitution unless the base itself is sterically crowded (e.g., *t*-BuO<sup>-</sup>).

Substrate	Nucleophile/Base	Mechanism
3°	<i>weak bases:</i> ROH, H <sub>2</sub> O, RCO <sub>2</sub> H give solvolysis	S <sub>N</sub> 1 (some E1 on heating)
	<i>strong bases:</i> anionic bases (HO <sup>-</sup> , RO <sup>-</sup> , NH <sub>2</sub> <sup>-</sup> ), NH <sub>3</sub>	E2
No S <sub>N</sub> 2 with 3° substrates		



## Summary

3° substrates only undergo substitution with weakly basic nucleophiles (ROH, H<sub>2</sub>O, RCO<sub>2</sub>H). Stronger bases promote elimination. 1° substrates generally undergo substitution unless the base itself is sterically crowded (e.g., *t*-BuO<sup>-</sup>).

<i>Substrate</i>	<i>Nucleophile/Base</i>	<i>Mechanism</i>
2°	Less basic than HO <sup>-</sup> : e.g., HS <sup>-</sup> , RS <sup>-</sup> , NH <sub>3</sub> , -CN, RCO <sub>2</sub> <sup>-</sup>	S <sub>N</sub> 2
	HO <sup>-</sup> and more basic: RO <sup>-</sup> , NH <sub>2</sub> <sup>-</sup>	E2
	weak nucleophiles: ROH, H <sub>2</sub> O	S <sub>N</sub> 1 (some E1 on heating)

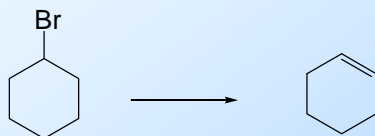
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## Summary

3° substrates only undergo substitution with weakly basic nucleophiles (ROH, H<sub>2</sub>O, RCO<sub>2</sub>H). Stronger bases promote elimination. 1° substrates generally undergo substitution unless the base itself is sterically crowded (e.g., *t*-BuO<sup>-</sup>).

<i>Substrate</i>	<i>Nucleophile/Base</i>	<i>Mechanism</i>
1°	All except <i>t</i> -BuO <sup>-</sup>	S <sub>N</sub> 2
	<i>t</i> -Bu-O <sup>-</sup> (hindered strong base)	E2
Me	all	S <sub>N</sub> 2

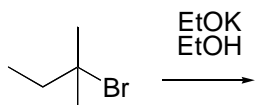
Which of the following reagents results in the most dehydrobromination (elimination) of bromocyclohexane?



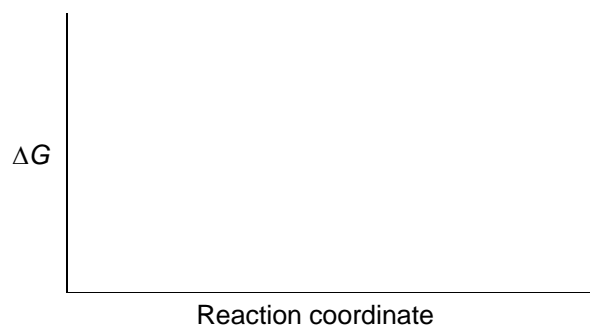
- 1 NaOH
- 2 KO<sup>t</sup>Bu
- 3 NaSH
- 4 NaCN

## STEREOCHEMISTRY AND REGIOCHEMISTRY

### Regiochemistry: Zaitsev Elimination

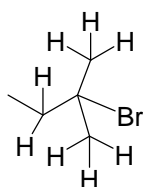
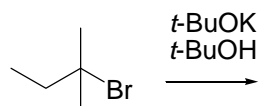


Zaitsev's Rule: \_\_\_\_\_ substituted (stable) alkene is formed

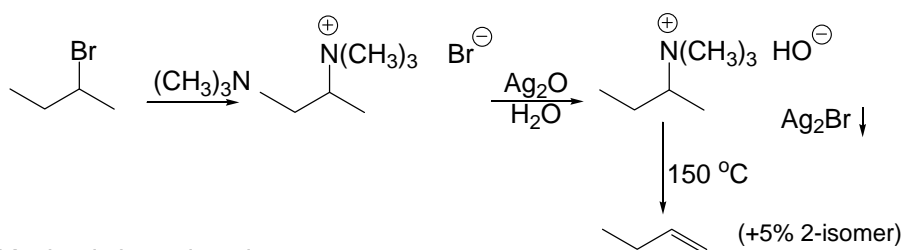


## Anti-Zaitsev Elimination

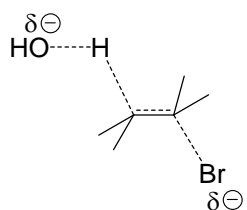
1. Use of bulky bases can lead to formation of “anti-Zaitsev” products



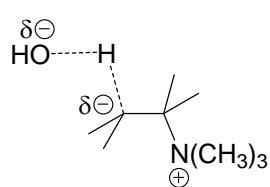
2. Formation of “anti-Zaitsev” products via the Hofmann Elimination



Mechanistic explanation



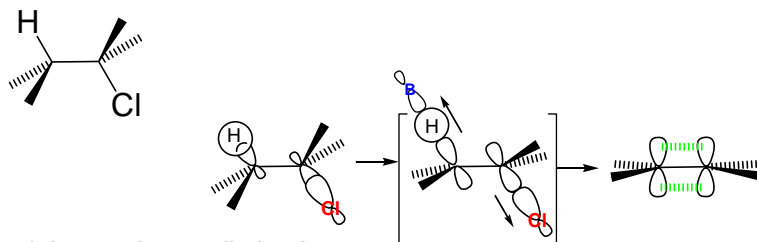
*Concerted E2 of alkyl bromide*  
Developing alkene character in the transition state is stabilized by hyperconjugation, giving Zaitsev product



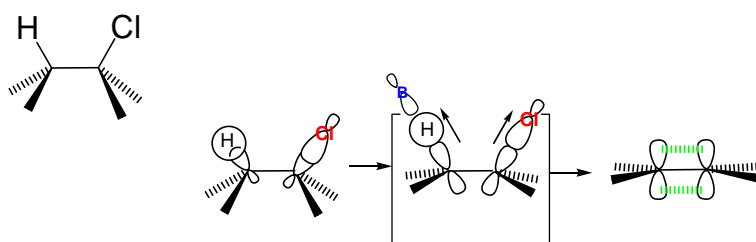
*Hofmann elimination*  
Developing carbanionic character in transition state (facilitated by the  $\text{N}^+$ ) is destabilized by alkyl substituents, giving anti-Zaitsev product

## Orientation of E2 Eliminations

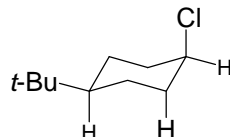
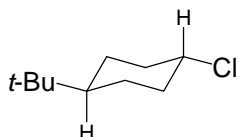
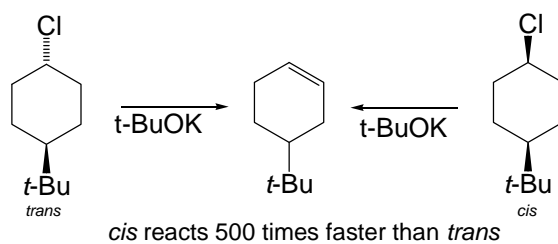
*Antiperiplanar: preferred orientation for elimination*



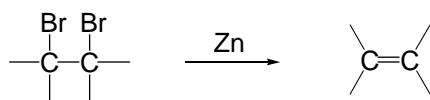
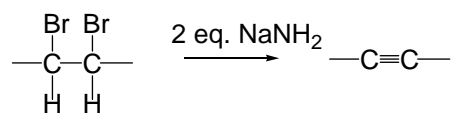
*Synperiplanar: slower elimination*



Explain the observation that *cis*-4-*t*-butyl cyclohexyl chloride undergoes elimination with a strong base 500 times faster than the *trans* isomer

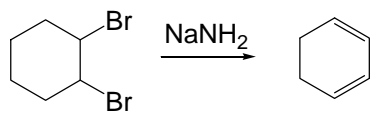


## DEHYDROBROMINATION AND DEBROMINATION OF VICINAL DIBROMIDES



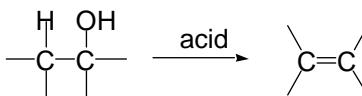
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*Problem.* Why does treatment of 1,2-dibromocyclohexane give 1,3-cyclohexadiene, not an alkyne?



# ACID-PROMOTED DEHYDRATION OF ALCOHOLS

## Acid-Promoted Elimination



Ease of dehydration:

$3^\circ > 2^\circ \gg 1^\circ$

*Proceeds under relatively mild conditions*

85 °C

20% aq. H<sub>2</sub>SO<sub>4</sub>

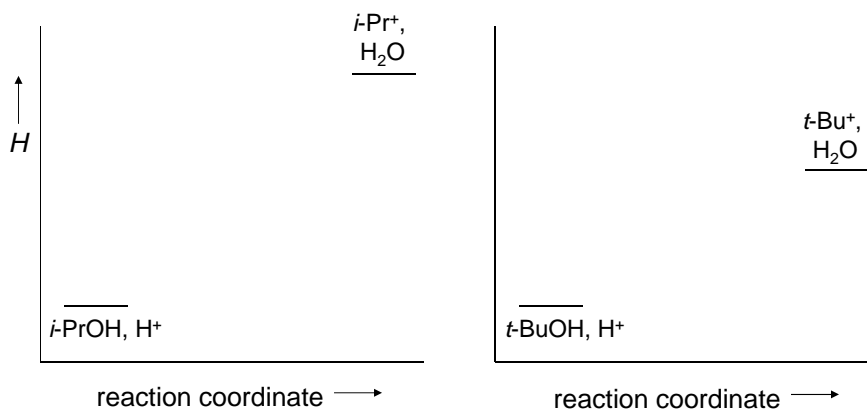
*Requires relatively harsh conditions*

180 °C

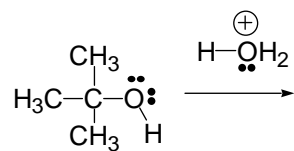
conc. H<sub>2</sub>SO<sub>4</sub>

## Ease of Formation of Carbocations: Kinetics vs. Thermodynamics

Stability of *starting material and products* of a reaction relates to *thermodynamics (equilibrium)*. The relative energy of the *starting material and transition state* relates to the *rate of the reaction (kinetics)*.

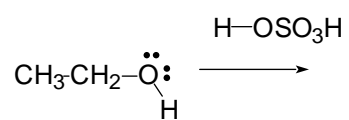


**Mechanism: Dehydration of 2° and 3° Alcohols by E1**

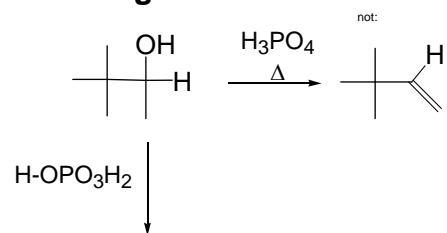


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**Mechanism: Dehydration of 1° Alcohols by E2**

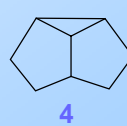
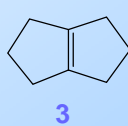
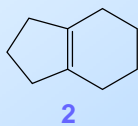
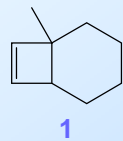
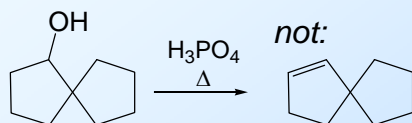


## Rearrangement of Carbocations During Elimination



Carbocations rearrange by hydride or alkyl shifts:  $2^\circ \rightarrow 3^\circ$

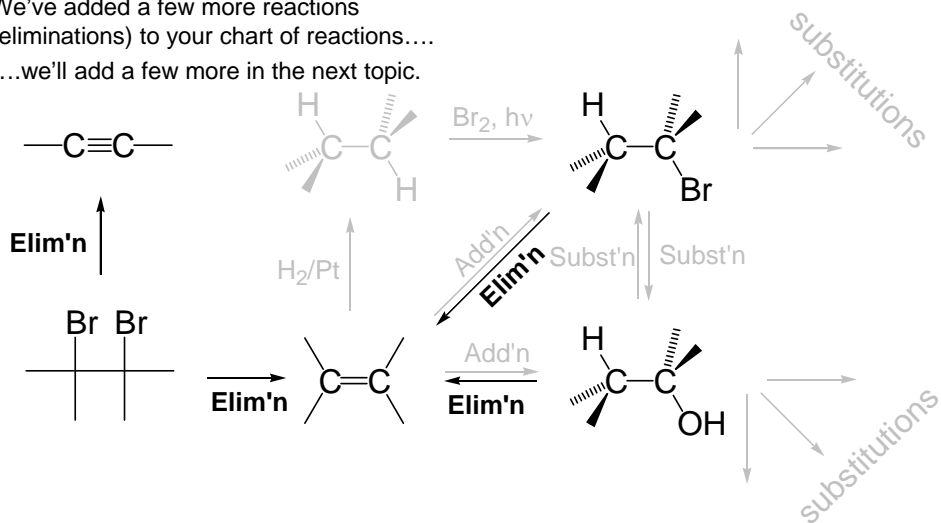
What is the product of the following reaction?





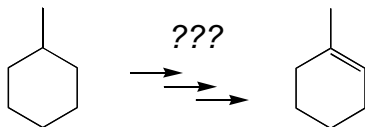
## A SUMMARY OF REACTIONS

We've added a few more reactions  
(eliminations) to your chart of reactions....  
....we'll add a few more in the next topic.



## SYNTHETIC STRATEGIES: TWO (OR MORE) STEP SYNTHESSES

At the end of Topic 6 you were challenged to recognize one-step synthetic transformations. But not all transformations can be achieved in one step. For example, there is no method to dehydrogenate (*i.e.*, remove  $\text{H}_2$ ) alkanes. So how would you bring about the following transformation?



You need to recognize that there is a single intermediate which can:

1. be made from the starting material,
- and 2. be transformed into the desired product

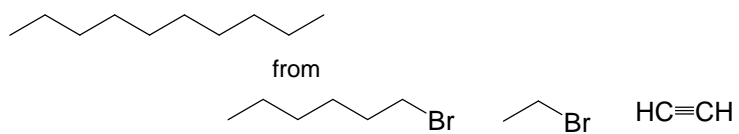


*Problem:* What two-step process can be used to achieve the following overall transformation?

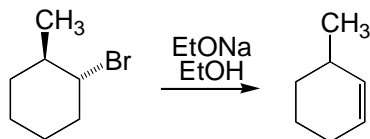


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*Problem:* This process can, of course, be extended to longer sequences of reactions. How could you prepare decane from bromohexane, bromoethane and ethyne?



*Problem:* Reaction of trans-1-bromo-2-methylcyclohexane with sodium ethoxide, a non-bulky base, results in formation of 3-methylcyclohexene, the anti-Zaitzev product. Explain.



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## TOPIC 7

### Types of Questions

- Describe elimination reaction mechanisms
- Predict the products of elimination reactions
- Describe some simple reactions of alkenes (hydrogenation) and alkynes (acidity, hydrogenation)