Synthesis of Alkenes I

Reading: Wade chapter 7, sections 7-9- 7-11
Study Problems: 7-38, 7-39, 7-40, 7-41, 7-45, 7-46, 7-48, 7-53

Key Concepts and Skills:

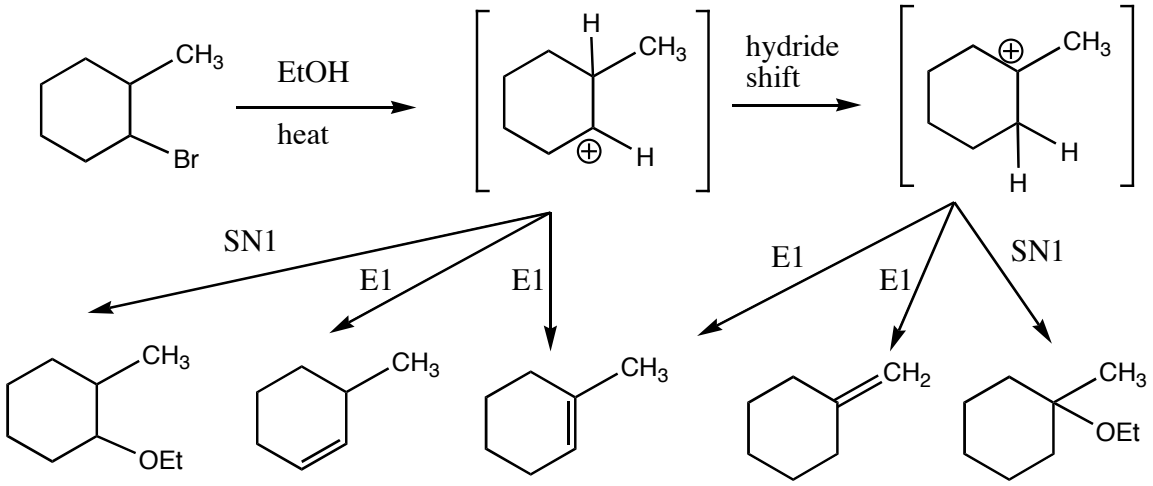
- Predict the products of dehydrohalogenation of alkyl halides, dehalogenation of dibromides, and dehydration of alcohols, including major and minor products.
- Propose mechanisms for dehalogenation, dehydrohalogenation, and dehydration reactions.
- Predict and explain the stereochemistry of E2 eliminations to form alkenes. Predict the products of E2 reactions on cyclohexene systems.

Lecture Topics:

I. Synthesis of alkenes *via* E1 and E2 mechanisms

A. Unimolecular Elimination (E1)

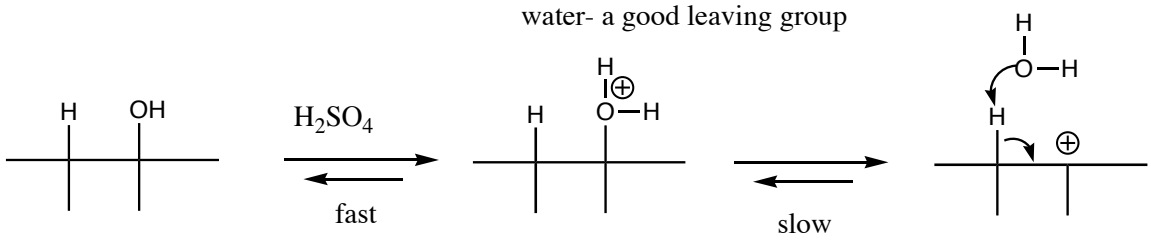
•The E1 reaction is a first-order process that has the same slow step as the SN1 reaction ➔ a rate-limiting ionization step to produce an intermediate carbocation.
• E1 reaction usually takes place in a good ionizing solvent like alcohols and water *without a strong nucleophile or base present*.
•The alkyl halide substrate is usually a 2° or a 3° halide
•The carbocation intermediate can undergo a deprotonation by a weak base to form an alkene or it may undergo substitution by that weak base acting as a nucleophile.
• Rearrangements are common when carbocations are intermediates



5 products!

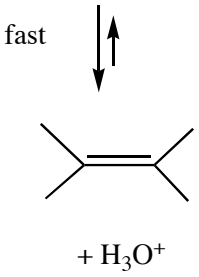
B. Dehydration of alcohols

Dehydration of alcohols is an acid-catalyzed reversible process occurring by an E1 mechanism with a carbocation intermediate

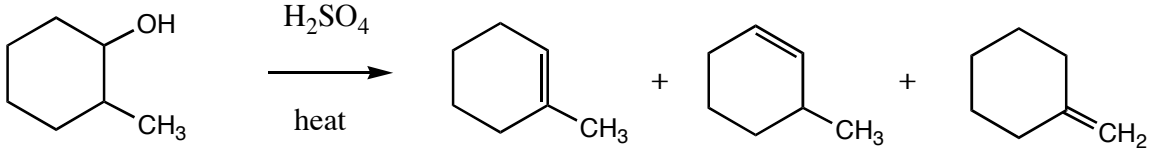


Reverse process, hydration of alkenes, provides a practical synthesis of alcohols

To drive the equilibrium in the direction of alkene production, less volatile alkene is distilled from reaction mixture to shift equilibrium



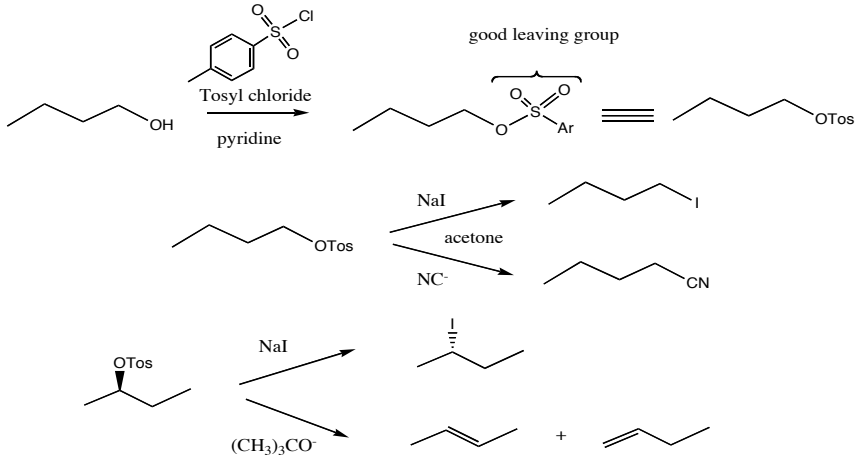
•again, rearrangements are possible, since carbocations are intermediates:



C. E2 elimination

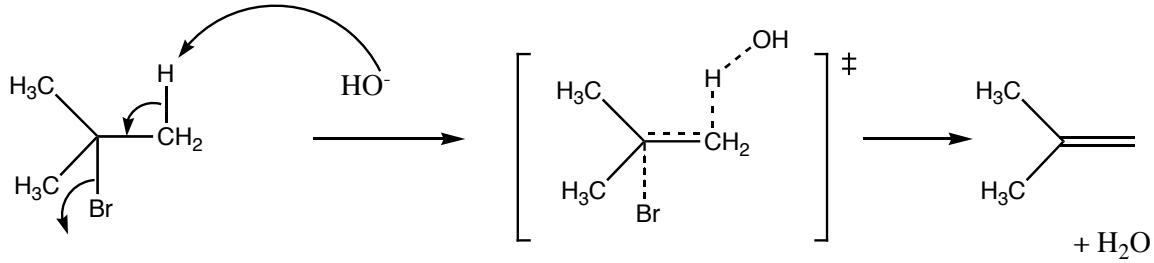
E2 elimination provides a more practical synthesis of alkenes.

• alcohols can be used either as precursors of alkyl halides via their aryl and alkane sulfonates, which are good leaving groups. Alternatively, alkane/aryl sulfonates can be used in place of alkyl halides for SN2 and E2 reactions



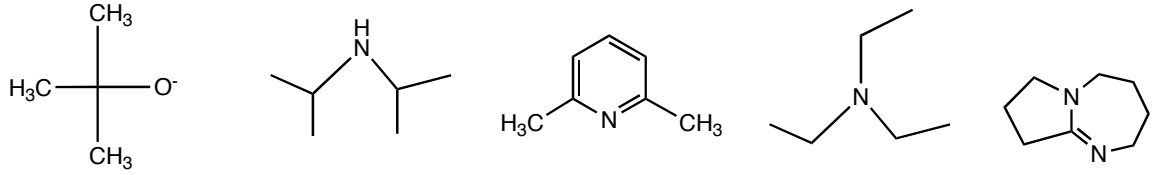
• Alkyl halides must be poor SN2 substrates (2° or 3°) for E2 elimination to predominate.

• Concerted mechanism: **strong** base abstracts a proton from a neighboring carbon atom as the leaving group departs; excellent yields are obtained with bulky halides:

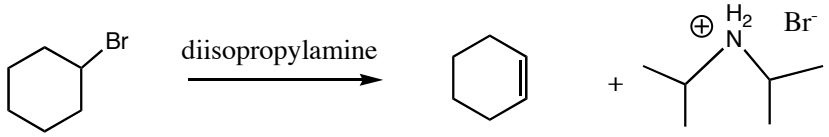


•For 2° halides which are prone to SN2 substitution, a bulky base can minimize the amount of substitution; large alkyl groups hinder its approach to carbon, yet it can still attack a proton

E2 bases:



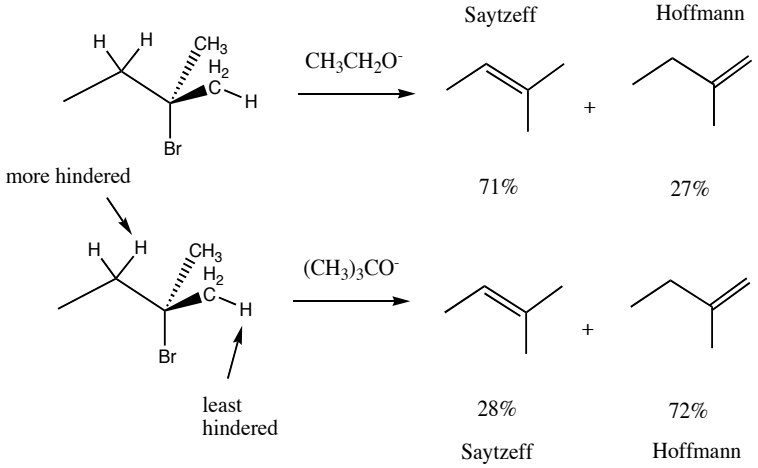
t-butoxide ion | diisopropyl amine | 2,6-lutidine | triethyl amine | DBU



Thus, bulky bases can abstract protons, but are too large to undergo SN2 substitution

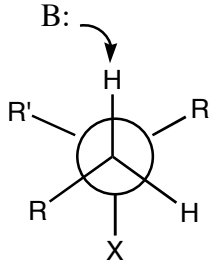
D. Dehydrohalogenation: Saytzeff vs. Hoffman elimination

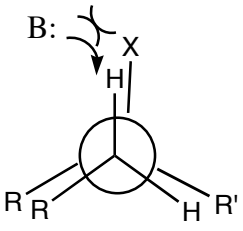
Steric hindrance on an alkyl halide substrate will prevent abstraction of the proton leading to the most highly substituted alkene (Saytzeff product) when a bulky base is used. In this case, the Hoffman product (less highly-substituted alkene) predominates.



E. E2 eliminations are stereospecific

•E2 elimination requires a coplanar arrangement of orbitals in the transition state. Remember: anti coplanar arrangement is lower in energy than syn-coplanar arrangement due to both steric and electrostatic repulsion.





steric and electrostatic repulsion

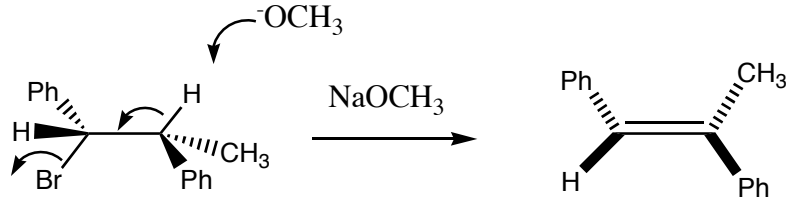
180° anti H-X

staggered
low energy conformer

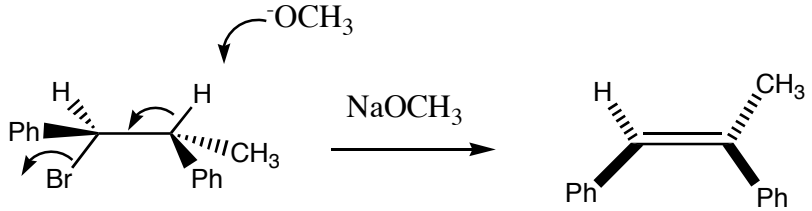
0° syn H-X

eclipsed
high-energy conformer

• E2 elimination is stereospecific: different isomers of the starting materials produce different isomers of products:



S R trans phenyl

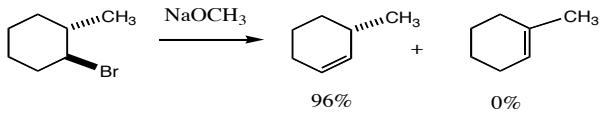


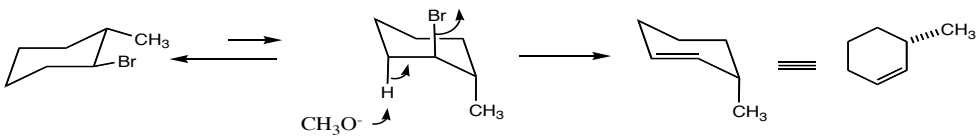
R R cis phenyl

F. E2 reactions in cyclohexanes

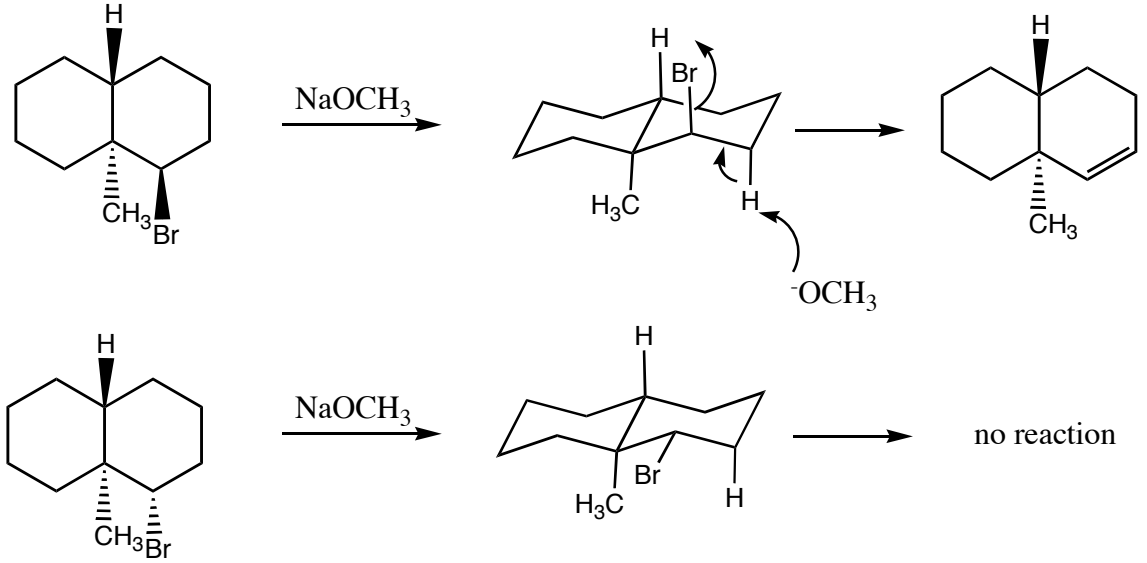
A trans-diaxial arrangement of H-X is preferred for elimination, which means that both H and X must be axial on the chair.

Example:



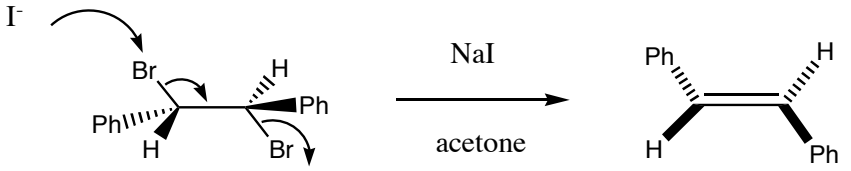


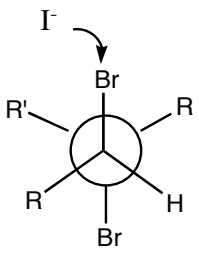
Trans-decalin ring systems are rigid and therefore cannot undergo a ring flip. Explain why the anti bromo-methyl isomer below can undergo elimination, while the syn-bromomethyl isomer cannot:



G. Dehalogenation of Vicinal Dihalides

Dehalogenation of vicinal dihalides by iodide ion occurs stereospecifically and concertedly via an E2 mechanism. An anti-coplanar arrangement of both bromine atoms is required:

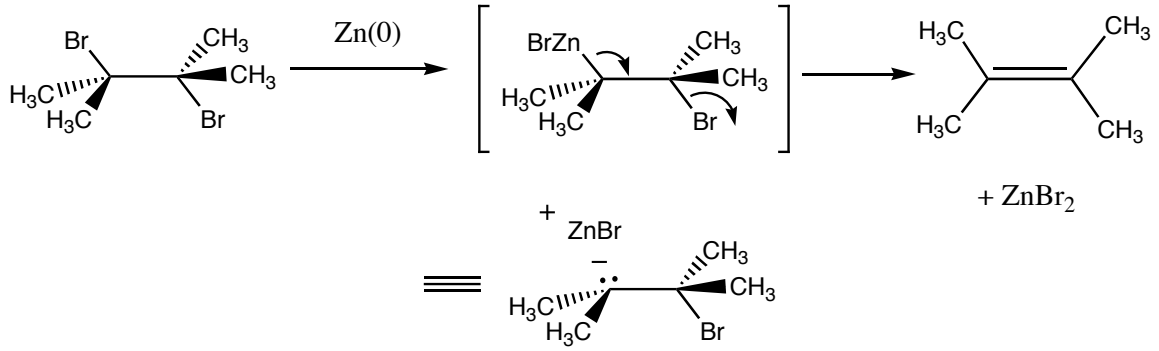




180° anti Br-Br

staggered

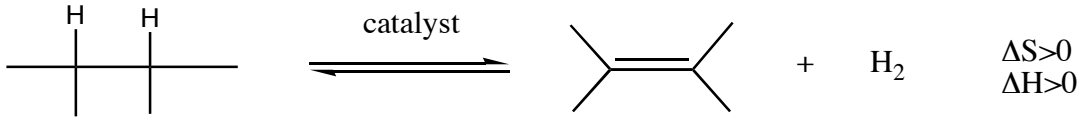
Reduction of vicinal dibromides by zinc metal proceeds by way of oxidative insertion of Zn(0) into a C-Br bond, producing an organozinc species which undergoes dehalogenation:



H. Dehydrogenation of Alkanes

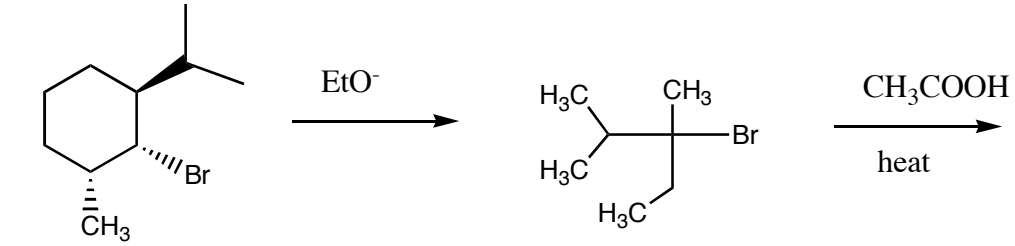
Dehydrogenation of alkanes is an entropically favored but enthalpically disfavored process

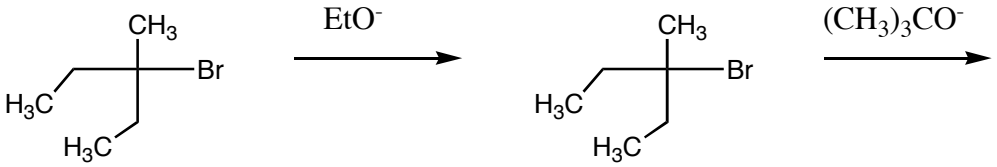
Thus, at room temperature, the reverse reaction predominates; at 500°C, however, the forward reaction takes place to give an industrial synthesis of alkenes.



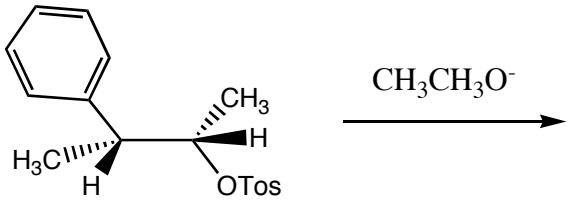
Additional Problems for practice:

1.) Predict the major alkene product from each of the following eliminations:





2.) Show the structure and stereochemistry of the alkenes that result from elimination of the following 3-phenyl-2 butanol tosylates:



2R, 3S

2R, 3R $\xrightarrow{CH_3CH_3O^-}$

2S, 3R $\xrightarrow{CH_3CH_3O^-}$

2S, 3S $\xrightarrow{CH_3CH_3O^-}$

3.) Optically active 2-butanol slowly racemizes on standing in dilute sulfuric acid. Propose a mechanism to account for this observation

4) Account for the different outcomes when menthyl chloride is subjected to the following conditions: