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

![Diagram of E1 reaction]

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

5 products!
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.

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.

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:

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:

\[
\begin{align*}
\text{BrZn} & \quad \text{CH}_3 \\
\text{Br} & \quad \text{CH}_3 \\
\text{H}_3\text{C} & \quad \text{H}_3\text{C} \\
\text{H}_3\text{C} & \quad \text{H}_3\text{C}
\end{align*}
\]

\[+ \text{ZnBr}_2\]

\[
\begin{align*}
\text{H}_3\text{C} & \quad \text{CH}_3 \\
\text{H}_3\text{C} & \quad \text{CH}_3 \\
\text{H}_3\text{C} & \quad \text{H}_3\text{C} \\
\text{H}_3\text{C} & \quad \text{H}_3\text{C}
\end{align*}
\]

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.

\[
\begin{align*}
\text{H}_3\text{C} & \quad \text{CH}_3 \\
\Delta S > 0 \\
\Delta H > 0
\end{align*}
\]

Additional Problems for practice:

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

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\begin{align*}
\text{EtO}^- & \quad \text{heat} \\
\text{H}_3\text{C} & \quad \text{CH}_3 \\
\text{H}_3\text{C} & \quad \text{Br} \\
\text{CH}_3 & \quad \text{H}_3\text{C} \\
\text{CH}_3 & \quad \text{Br}
\end{align*}
\]

\[
\begin{align*}
\text{EtO}^- & \quad \text{heat} \\
\text{H}_3\text{C} & \quad \text{CH}_3 \\
\text{H}_3\text{C} & \quad \text{Br} \\
\text{CH}_3 & \quad \text{H}_3\text{C} \\
\text{CH}_3 & \quad \text{Br}
\end{align*}
\]

\[
\begin{align*}
\text{EtO}^- & \quad \text{heat} \\
\text{H}_3\text{C} & \quad \text{CH}_3 \\
\text{H}_3\text{C} & \quad \text{Br} \\
\text{CH}_3 & \quad \text{H}_3\text{C} \\
\text{CH}_3 & \quad \text{Br}
\end{align*}
\]
2.) Show the structure and stereochemistry of the alkenes that result from elimination of the following 3-phenyl-2 butanol tosylates:

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\[
\begin{align*}
\text{2R, 3S} & \quad \text{CH}_3\text{CH}_3\text{O}^- \\
\text{2R, 3R} & \quad \text{CH}_3\text{CH}_3\text{O}^- \\
\text{2S, 3R} & \quad \text{CH}_3\text{CH}_3\text{O}^- \\
\text{2S, 3S} & \quad \text{CH}_3\text{CH}_3\text{O}^- 
\end{align*}
\]
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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:

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\[
\begin{align*}
\text{NaOEt} \quad \text{EtOH, 100°C} & \quad \text{H}_3\text{C}\text{Cl} \\
\text{EtOH} \quad \text{160°C} & \quad \text{H}_3\text{C} \\
\end{align*}
\]
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