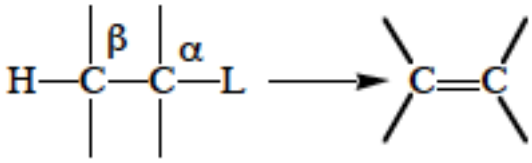
12AL Experiment 12 (3 days): Elimination Reactions

***Instructor Note: Day 1 (half of the class; 2-methyl-1-cyclohexanol); Day 2 (other half of the class; 4-methyl-1-cyclohexanol); Day 3 (everyone to finish up). Limited Macro Simple Distillation equipment & experiments are individually performed.**

Safety: Proper lab goggles/glasses must be worn (even over prescription glasses). Wear gloves – use safety when working with phosphoric acid. As always, ask where organic waste containers are located in the lab.

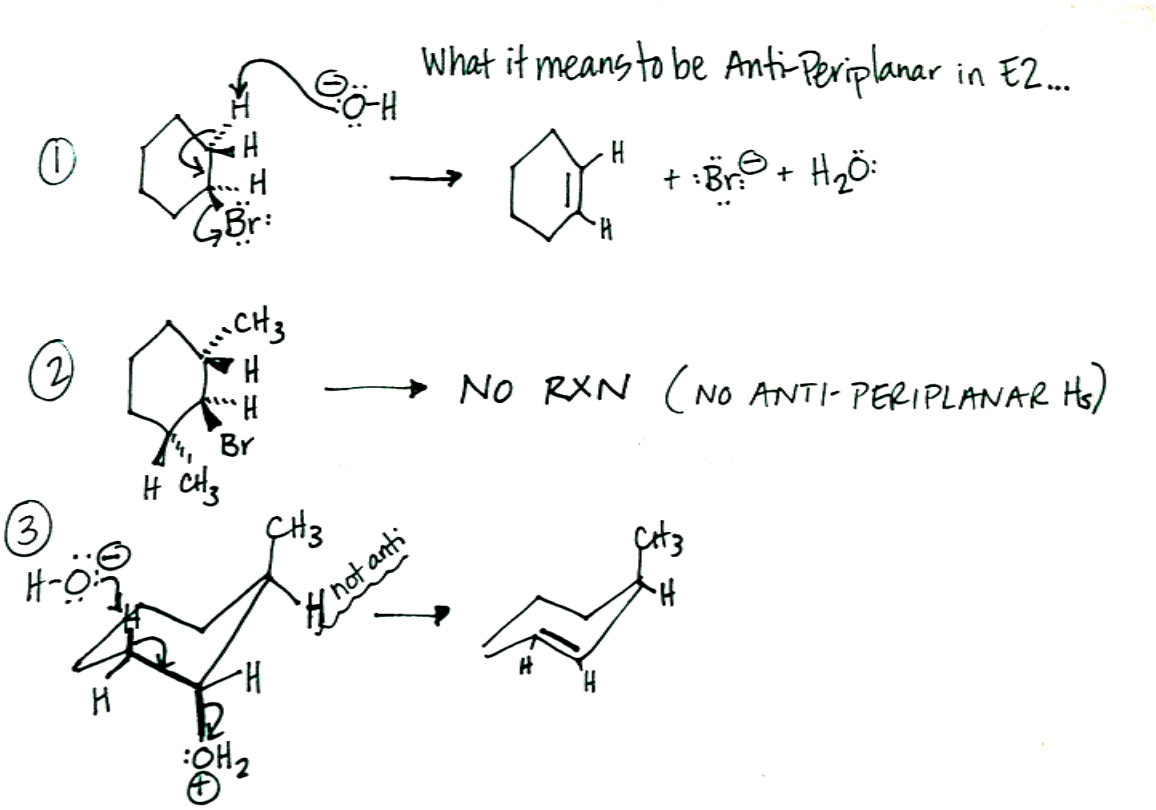
Background:

Elimination reactions are those in which a molecule loses an atom or groups of atoms, usually from adjacent carbons, often resulting in a new π bond. Eliminations are very useful reactions in syntheses – reactive alkenes and alkynes can be produced. Eliminations compete with Nucleophilic Substitution reactions and sometimes you obtain a mixture of both substitution and elimination products.



- β-elimination (most common elimination reaction)

There are two types of elimination reactions: E2 and E1. An E2 reaction is a bimolecular, concerted, one-step mechanism in which a *strong base* (& polar aprotic solvent) attacks the beta-H that is *anti-periplanar* to a moderate-good leaving group. These reactions are more <u>likely to occur before an SN2</u> reaction because the attacking nucleophile feels less repulsion when approaching the *anti-periplanar* H atom on the beta-carbon. In an SN2, the nucleophile attacks the carbon to which the leaving group is bonded – although the SN2 proceeds through a backside attack to minimize steric hindrance, there is still some repulsion unlike the E2 mechanism.



Often, more than one alkene product is possible – there may be two beta-H atoms that are *anti-periplanar* to the leaving group. But because energy is the driving force of all reactions and life itself, the major product to form will be the alkene that is the most stable (lowest energy) and/or the mechanism will proceed through the lowest energy route possible.

- *Trans* more stable than *cis* (steric hindrance)

- *Internal* pi bonds more stable than *terminal* pi bonds (review hyperconjugation)

- *More substituted* alkene more stable (Zaitsev's Rule: more highly branched alkene is more stable – hyperconjugation)

However, when the attacking nucleophile is strong, but overly large, like tert-butoxide, or if the leaving group is very bulky, like amines NR_3, the less substituted alkene is found to be the major product.

- Hofmann orientation: Less substituted alkene is major when base/leaving group is extremely large

Like SN2, primary and secondary reactants undergo E2 reactions, with secondary reactants being able to undergo E1 if the conditions for E2 are not met (*strong base*, polar aprotic solvent).

An E1 reaction is a unimolecular, two-step mechanism, in which the first step is the slow, rate-determining step that forms a carbocation as the *moderate-good leaving group leaves*; followed by the attack of *any beta-H atom* resulting in an alkene. Like SN1 that also is two-steps and has a carbocation intermediate, the E1 also does NOT depend on the strength of the attacking nucleophile (& prefers a polar protic solvent). It is extremely difficult to prevent E1 and SN1 reactions from occurring simultaneously – generally a mixture of products is seen. And as seen before, it is important to watch out for carbocation shifting within a mechanism!

So how do you decide between E2 or E1?

- If a *strong base* is used, it is quick to attack in the case of primary and secondary reactants.

- If a strong base is NOT used, reactants that can form stable, low energy carbocations (2˚, or 1˚ allylic) generally will undergo E1.

- 3˚ will always follow an E1 pathway.

And how do you decide between SN1, E1, SN2, and E2?

- Concerted mechanisms (E2, S_N2) before carbocation mechanisms (E1, S_N1)

- E2 before S_N2 (base/nuc moves past β-hydrogen atoms before approaching carbon bearing leaving group. *Exception*: Primary alkyl halides: consider S_N2 before E2)

Material adapted from: http://www.chem.ucla.edu/harding/lecsups/elim30.pdf

Today you will be performing an elimination of an alcohol, otherwise known as a *dehydration*. You will drive the reversible reaction forward, by drawing off the alkene product as it is formed through simple distillation. Alcohols are considered poor leaving groups as the oxygen atom of the OH forms a strong sigma bond to the similarly sized carbon atom (review strengths of leaving groups etc..). In order for the elimination to proceed, a strong acid catalyst is used to protonate the alcohol creating an unhappy positive-charged oxygen atom which weakens the carbon-oxygen bond (R-OH → $R\text{-}OH_2^+$). You will prove your synthesis of an alkene through IR spectroscopy.

Objective: 1. To successfully synthesize a pure alkene from an alcohol. 2. To practice E1 and E2 reactions & their mechanisms. 3. To understand the requirements for E1 and E2 reactions and how they compete with SN1 and SN2 reactions. 4. Use IR spectroscopy to prove synthesis.

Procedure:

1. Carefully set up a Macro Simple Distillation apparatus, using a hot/stir plate. Remember, never let go of a piece of glassware until it is securely clamped and lightly lubricate all glass joints with glycerol.

2. Measure out 5.0 mL of 2-methyl-1-cyclohexanol (day 1 students) OR 5.0 mL of 4-methyl-1-cyclohexanol (day 2 students) into the smallest macro round-bottom flask available.

3. Add 1.4 mL of 85% phosphoric acid to the flask as well.

4. Check out a stir bar from your instructor and add to the flask too.

5. Have two small 10-20mL beakers ready as your collection containers. You will be collecting two separate fractions.

5. Begin heating once the water is circulating in the condenser.

6. HEAT GENTLY while stirring. Any alkenes synthesized in this lab all have boiling points much lower than the alcohol reactants; in fact, 50-70 degrees lower. Therefore, it should be relatively easy to collect pure alkenes with the first few milliliters collected.

*Collect 1-2 mL of distillate, then switch collection beakers, and collect another 1-2 mL of distillate.

7. For each separate fraction, add 1.5 mL of 5% aqueous sodium bicarbonate to neutralize any phosphoric acid that made its way over.

8. For each separate fraction, use a plastic pipette to collect the top organic alkene layer.

9. For each separate alkene fraction, add a *teeny tiny amount of anhydrous powder to dry any remaining water droplets you did not separate. *TINY TINY – you don't have much liquid to work with and you don't want to cover up your alkene liquid in powder!

10. Run an IR on your alkene liquids (don't pipette any powder into IR) – choose the best IR to print out. Remember, there should be no 3400cm^{-1} alcohol stretch present!

11. Attach a completely analyzed IR to your postlab – all bonds and wavenumbers in your alkene product should be labeled in the appropriate positions on the spectrum.

12AL Prelab Experiment 12: Elimination Reactions

1. Complete the following questions about elimination reactions:

E2

What does the 2 in E2 represent?

How many molecules are involved in slow step?

How many steps in mechanism?

List what occurs in the mechanism:

What does the nucleophile attack?

Are E2 rxns dependent on the strength of nucleophile?

What type of nucleophile is required? (& give an example)

What type of product do you form?

What type of reactant(s) undergo E2?

E1

What does the 1 in E1 represent?

How many molecules are involved in slow step?

How many steps in mechanism?

List what occurs in the mechanism:

What does the nucleophile attack?

Are E1 rxns dependent on the strength of nucleophile?

What type of product do you form?

What type of reactant(s) undergo E1?

2. Draw the low energy chair conformation of trans-2-methyl-1-cyclohexanol and label as low energy. Perform a ring flip to form the high energy chair conformation and label as high energy.

3. What product will be more abundant and explain why for the given reaction:

2-bromobutane + tert-butoxide → 1-butene and 2-butene

4. What is Zaitsev's Rule?

5. Alcohols are catalyzed with acid in order to create a better leaving group (R-OH → $R\text{-}OH_2^+$). The alcohol functional group (OH) is a poor leaving group. Why?

12AL Postlab Experiment 12: Elimination Reactions

1. Have you attached your completely analyzed IR?

2. What chemical reaction occurred when you added sodium bicarbonate? (show the balanced reaction; you don't have to show a mechanism)

3. For your given reactant undergoing an E1 dehydration (2-methyl-1-cyclohexanol or 4-methyl-1-cyclohexanol), you had a mixture of cis and trans isomers. Give the structure(s) of the major product(s) formed if you separated out your reactants:

   a. Product(s) from the cis isomer reactant?

   b. Product(s) from the trans isomer reactant?

4. Given the following: Cis 2-methyl-1-cyclohexanol + H_3O^+
(high energy chair conformation for mechanism)

a. What type of elimination reaction will the molecule undergo & why?

b. Perform the appropriate mechanism – be neat & clear, showing all arrows, charges, structures, etc…

5. Given the following: N,N-trimethyl-2-pentanamine + NaOH

a. What type of elimination reaction will the molecule undergo & why?

b. Perform the appropriate mechanism – be neat & clear, showing all arrows, charges, structures, etc…

6. Indicate the type of elimination the following will undergo AND show the major product(s) for the following reactions:

a. 1-bromohexane + $NaOCH_3$

b. 2-chlorohexane + NaOH

c. 2-chlorohexane + $NaOC(CH_3)_3$

d. *trans*-2-methyl-1-bromocyclopentane + KOH

e. *cis*-2-methyl-1-bromocyclopentane + KOH

f. *cis*-2-methyl-1-bromocyclopentane + H_2O