

Week 9

Nucleophilic Substitutions and Elimination

9.1 Nucleophilic Substitutions (cont.)

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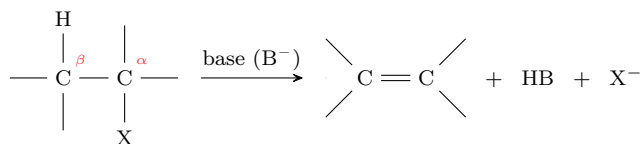
- Choosing between the mechanisms (cont.).

4. Solvent.

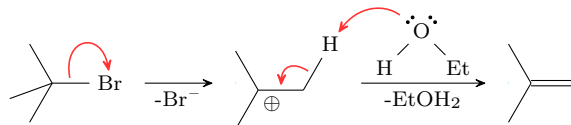
- Critical for borderline cases.
 - The solvent is important for dissolving things/providing an environment for the reaction.
 - There are two types of solvents: **protic** and **aprotic**.
 - We need to know all of the common solvents (a table will be uploaded).
 - Key difference between protic and aprotic solvents.
 - Protic solvents can do hydrogen bonding with anions (LGs), stabilizing them.
 - Aprotic solvents cannot do this.
 - Protic solvents can stabilize X^- , easing the self-ionization step in S_N1 .
 - Protic solvents stabilize both the nucleophile and LG in S_N2 .
 - With the nucleophile retarded, the rate of S_N2 goes down.
 - In an aprotic solvent, the nucleophile is even more reactive.
 - Take-home message: For secondary alkyl halides (the borderline cases), protic solvents promote S_N1 and aprotic solvents promote S_N2 .
- **Protic** (solvent): A solvent with an acidic proton.
 - **Aprotic** (solvent): A solvent without an acidic proton.
 - If you see a nucleophilic substitution-type reaction with just one compound surrounding the arrow, assume it is both the nucleophile *and* the solvent.
 - **Allylic** (carbocation): A carbocation on a carbon adjacent to an alkene.
 - Extra stable due to resonance stabilization.

9.2 β -Elimination

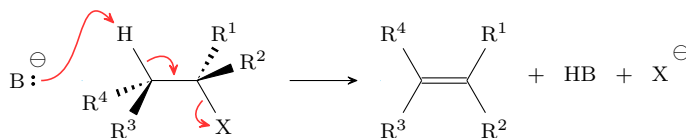
- β -elimination is a form of dehydrohalogenation.
- General form.



- Mechanisms.



(a) E1.



(b) E2.

Figure 9.1: Elimination mechanisms.

- **E1:** Unimolecular elimination.

- Not a clean reaction — E1 and S_N1 often happen together.
- They will not ask us to tell which pathway is more favored.
- Features.
 1. Tertiary alkyl halides are favored (secondary sometimes).
 2. Protic solvents are needed.
 3. We need a weak base/poor nucleophile.
 4. Selectivity: Determined by the alkene stability; we favor forming the more stable alkene (as per **Zaitsev's Rule**).
- E1 is not a useful reaction to prepare alkenes from alkyl halides since we get a mixture of products and there are selectivity issues.

- **Zaitsev's Rule:** More substituted alkenes are more stable.

- For secondary carbons, $cis < trans < geminal$ in terms of stability.
- Since sp^2 is more electronegative than sp^3 and R is an EDG, more R groups can provide more electrons to stabilize the sp^2 carbons.

- **E2:** Bimolecular elimination.

- Often very selective, and you can make it very selective.
 - The lack of a carbocation intermediate and the fact that it's a concerted mechanism both contribute to the higher yield.
- In order to realize E2, the conformation *must* adopt **anti-periplanar geometry**.
 - E2 is a stereospecific reaction.

- **Anti-periplanar geometry:** Two groups of importance are opposite each other and lie in the same plane.

- Consider the H and X in Figure 9.1b.

- Example: Consider *cis*-1-chloro-2-isopropylcyclohexane in solution with MeONa and MeOH.

- Only the more stable cyclohexane conformation (with Cl axial and Pr^i equatorial) has hydrogens anti to the chlorine.
 - Both of these hydrogens will undergo E2 elimination with the chlorine, and the trisubstituted product will be the major product (as per Zaitsev's rule).
 - However, if we use *t*-butoxide instead of methoxide, the disubstituted product would be the major product due to sterics.
- Example: Consider *trans*-1-chloro-2-isopropylcyclohexane in solution with MeONa and MeOH.
 - Since the less stable conformation is the reactive one, the reaction will still go, but it will be very slow.
- Take-home summary: For E2, the first priority is anti-periplanar, and then Zaitsev.