

9.6 Elimination from Substituted Cyclohexanes

- Elimination from cyclic compounds follows the same stereochemical rules as elimination from open-chain compounds.
- For the anti-periplanar geometry, the two groups that are being eliminated from a cyclic compound must be *trans* to one another.
- For six-membered rings, the groups being eliminated will be anti-periplanar only if both are in axial positions.
- The more stable conformer of chlorocyclohexane does not undergo E2 reaction, because the chloro substituent is in an equatorial position.
- The rate constant of the reaction is given by $k'K_{eq}$, so the reaction is faster if K_{eq} is large.
- When a substituted cyclohexane undergoes an E1 reaction, the two groups do not have to be in axial position.
- Must check the possibility of a carbocation rearrangement.

9.7 A Kinetic Isotope Effect Can Help Determine a Mechanism

- Deuterium kinetic isotope effect: the ratio of the rate constant observed for a compound containing hydrogen to the rate constant observed for an identical compound in which one or more of the hydrogens has been replaced by deuterium, an isotope of hydrogen.
- **Deuterium kinetic effect:** $= k_H/k_D$ = rate constant for H-containing reactant/ rate constant for D-containing reactant.
- The chemical properties of deuterium and hydrogen are similar, but a C-D bond is about 1.2 kcal/mol stronger than a C-H bond. So it is more difficult to break C-D bond than a corresponding C-H bond.
- The deuterium kinetic isotope effect for elimination of HBr from 1-bromo-2phenylethane is 7.1. It is due to the difference in energy to break a C-H bond compared with a C-D bond.
- Since the deuterium kinetic isotope effect is greater than unity, *we can tell that the C-H (or C-D) bond must be broken in the rate-determining step*: It is consistent with the mechanism proposed for an E2 reaction.

9.8 Competition Between Substitution and Elimination

- Ways to predict the product of reactions.
 1. One must decide whether the reaction conditions favor $S_N2/E2$ or $S_N1/E1$ reaction. If the reactant is primary alkyl halide, it undergoes only $S_N2/E2$ reactions.
 2. If the reactant is a secondary or a tertiary alkyl halide, it may undergo either $S_N2/E2$ or $S_N1/E1$ reaction, depending on the reaction conditions.
 3. $S_N2/E2$ reactions are favored by a high concentration of a good nucleophile/strong base. Whereas $S_N1/E1$ reactions are favored by a poor nucleophile/weak base.
 4. Now decide how much of the product will be the substitution product and how much will be the elimination product. The relative amounts of substitution and elimination products will depend on whether the alkyl halide is primary. Secondary, or tertiary, and on the nature of the nucleophile/base.
- The negatively charged species can act as a nucleophile and attack the back side of the α -carbon to form the substitution product, or it can act as a base and remove a β -hydrogen, leading to the elimination product. So the two reactions compete with each other. The relative reactivities of alkyl halides for S_N2 and E2 reactions are shown in.

Table 11.5 Relative Reactivities of Alkyl Halides			
In an S_N2 reaction:		In an S_N1 reaction:	
$1^\circ > 2^\circ > 3^\circ$		$3^\circ > 2^\circ > 1^\circ$	
In an E2 reaction:		In an E1 reaction:	
$3^\circ > 2^\circ > 1^\circ$		$3^\circ > 2^\circ > 1^\circ$	

- Because a primary alkyl halide is the most reactive in an S_N2 reaction and the least reactive in an E2 reaction, so the substitution product is the major one.
- If either the primary alkyl halide or the nucleophile/base is sterically hindered, the nucleophile will have difficulty getting to the back side of the α -carbon, so the elimination product is the major one.
- The relative amounts of substitution product and elimination product for a secondary alkyl halide depends on the base strength and the bulk of the nucleophile/base. The stronger and bulkier the base, the greater the percentage of the elimination product. A weak base encourages substitution over elimination.
- A tertiary alkyl halide is the least reactive of the alkyl halides in an S_N2 reaction and the most reactive in an E2 reaction (Table 9.5). Only the elimination product is formed when a tertiary alkyl halide reacts with a nucleophile/base under $S_N2/E2$ conditions.
- In $S_N1/E1$ reactions, the alkyl halides have the same intermediate, carbocation, and the products are both substitution and elimination product.
- Primary alkyl halides do not undergo $S_N1/E1$ reactions because primary carbocations are too unstable to be formed.

9.10 Consecutive E2 Elimination Reactions

- Alkyl dihalides can undergo two consecutive dehydrohalogenations, giving products that contain two double bonds.
- The first dehydrohalogenation follows Zaitsev's rule, but the second one does not, because a conjugated diene is more stable than an isolated diene.
- If the two halogens are on the same carbon or on adjacent carbons, the two consecutive E2 dehydrohalogenations can result in the formation of a triple bond.
- The vinyl halide intermediates are relatively unreactive, so a very strong base, such as NH_2^- , is needed for the second elimination.

9.11 Intermolecular Versus Intramolecular Reactions

- Some molecules are bifunctional with two functional groups on one molecule, so the two functional groups can react with each other.
 1. Intermolecular reaction takes place between two molecules generating dimmer or polymers.
 2. Intramolecular reaction takes place in a single molecule generating a cyclic compound.
- Which reaction is more likely to occur, an intermolecular reaction or an intramolecular reaction? => It depends on the concentration of the bifunctional molecule and the size of the ring that will be formed in the intramolecular reaction.
- The intramolecular reaction has an advantage, because the reacting groups are close by each other, so they don't need to diffuse through the solvent to find a group with which to react. Therefore, a low concentration of reactant favors an intramolecular reaction because the two functional groups have a better chance of finding one another.
- The size of the ring that is formed is very important: If the intramolecular reaction forms a five- or six-membered ring, it will be highly favored over the intermolecular reaction because five- and six-membered rings are stable and easily formed. Three- and four-membered rings are strained, so they are less stable than five- and six-membered rings and less easily formed.
- Three-membered ring compounds are formed more easily than four-membered ring compounds. To form a cyclic ether, the nucleophilic oxygen atom must be oriented so that it can attack the back side of the carbon bonded to the halogen. .