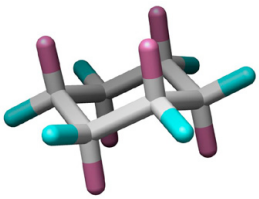


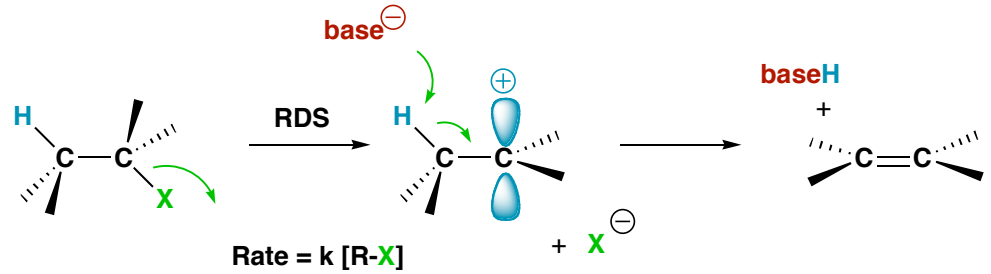
Chem 341 • Organic Chemistry I

Lecture Summary 32 • November 09, 2007

Chapter 11 - Reactions of Alkyl Halides: Nucleophilic Substitutions and Eliminations

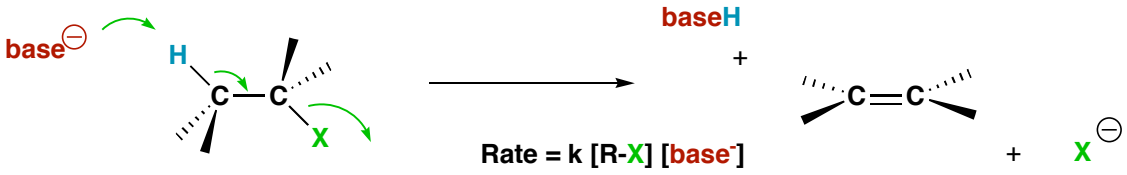
Elimination reactions

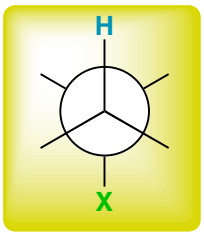
Elimination reactions often compete with substitution reactions. In an elimination a base removes a proton from a carbon adjacent to a leaving group and the electrons form a new double bond with loss of the leaving group. According to "Zaitsev's rule", the more substituted double bond is formed preferentially. The energy barrier to form the more stable product is lower than that to form the less stable product.



E2 Elimination

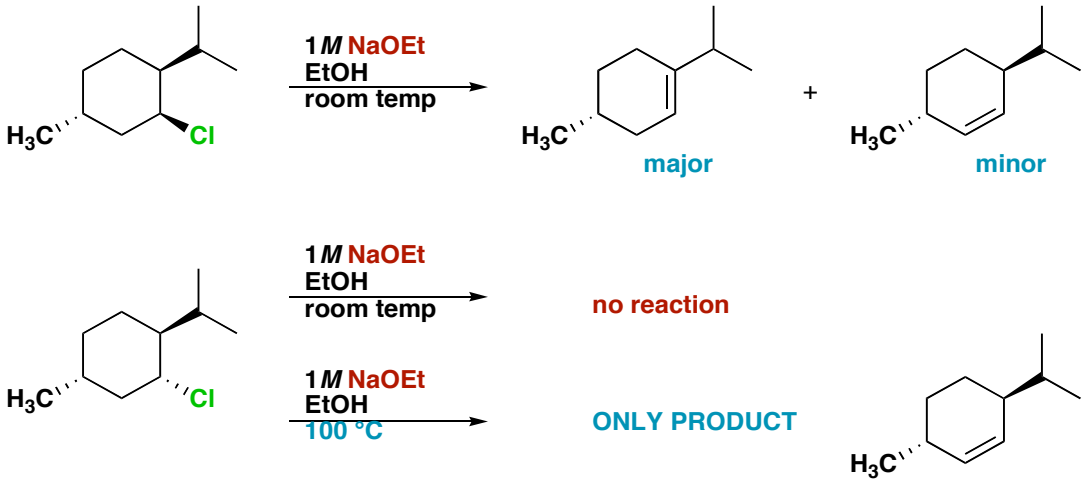
If the elimination reaction takes place in a single step, this is called an E2 elimination. Similar to a S_N2 substitution reaction, the rate of the reaction depends on two species; the substrate AND the base. Thus, the rate expression indicates the reaction is bimolecular. In this mechanism, a number of bonds are forming and breaking at the same time. The base-H bond and the new double bond are beginning to form, while the C-H bond and the C-X bond is breaking. Everything happens in a single operation. In order for an E2 elimination to take place, the bonds that are breaking must be aligned in the same plane (periplanar) and be 180° apart (anti). If this geometry cannot be adopted, the E2 elimination will not take place under most normal conditions.



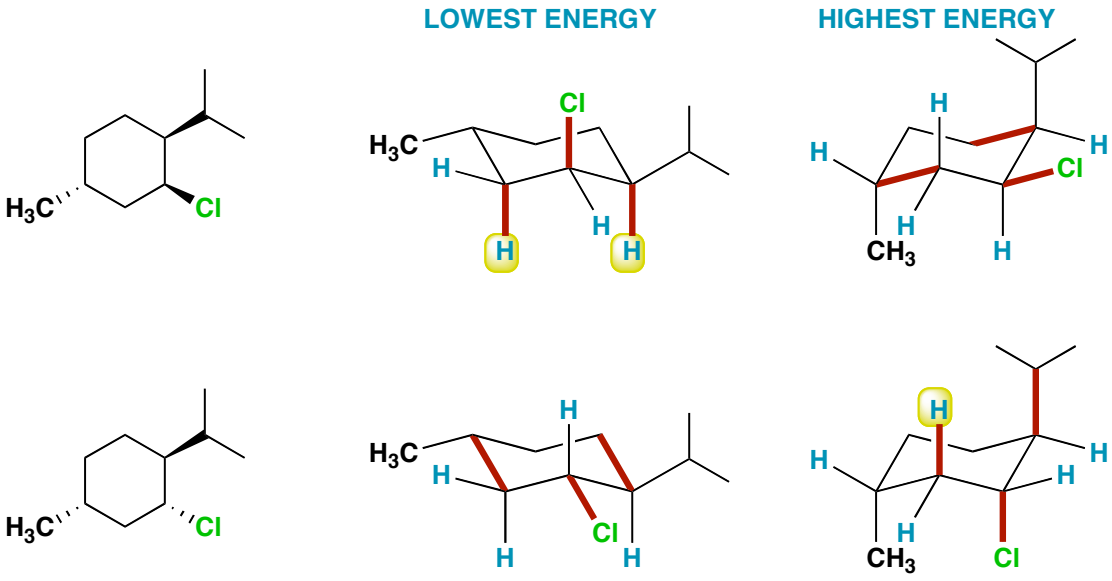


Hydrogen and leaving group must be antiperiplanar for elimination to take place.

The requirement for antiperiplanar alignment is readily apparent in the substitution of cyclohexane derivatives. The E2 elimination can only take place if the leaving group is in an axial position. Only then could you have the possibility of a hydrogen on the adjacent carbon aligned 180° from the departing leaving group. Any equatorial position would place the leaving group bond antiperiplanar only to other C-C bonds of the ring. As shown below, one diastereomer of the chlorocyclohexane eliminates readily at room temperature while the other requires heat to get the reaction to proceed. This is simply due to the requirement of placing the chloride in the axial position. In the top diastereomer, the lowest energy conformation of the ring puts the chlorine axial. In the bottom diastereromer, the axial chloride is the less stable conformation and heat is required to get the ring flip to occur.

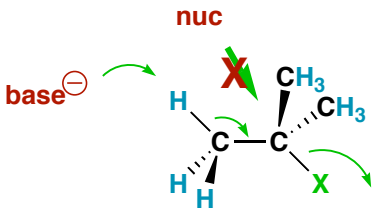


In the chair conformations below, I have highlighted the anti-periplanar bonds with red bold lines. Notice in the first isomer, the lower energy conformation has two hydrogens (indicated in yellow) that could eliminate in an E2 reaction. In the bottom isomer, the only possibility for an E2 elimination occurs from the highlighted H in the higher energy conformation. Thus, the reaction requires heat and affords only the less substituted double bond.



E2 Elimination Characteristics - Substrate

Unlike the S_N2 substitution, an E2 elimination can occur readily form a tertiary substrate. Since the base does not need to approach the crowded carbon, but only the relatively unhindered hydrogen on an adjacent carbon, the sterics around the leaving group don't matter. Primary, secondary and tertiary substrates all undergo E2 elimination reactions. The only requirement, as discussed above, is that there be a hydrogen antiperiplanar on an adjacent carbon.



Tertiary substrates will work just fine in an E2 elimination.

E2 Elimination Characteristics - Base

The other important feature of an E2 reaction is the base. A strong base is usually required. Strong bases are not necessarily the best nucleophiles. The best bases are things like hydroxide (NaOH), alkoxides (NaOR), or amides ($NaNH_2$).

E2 Elimination Characteristics - Leaving Groups

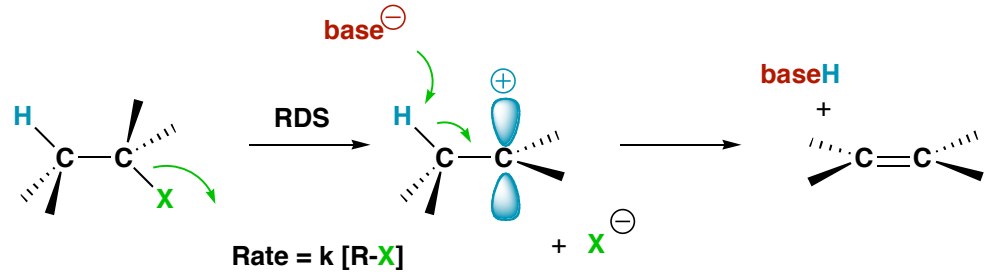
Since the leaving group is departing in the reaction, it is important just like in the S_N2 reaction. Better leaving groups that form more stable anions are best for elimination reactions.

E2 Elimination Characteristics - Solvent

Polar solvents are required to dissolve the reagents. Aprotic solvents are great for E2. Protic solvents also work well in strongly basic conditions. Note that in any strongly basic media, even if it is a protic solvent, you cannot form carbocations. E2 eliminations will compete successfully with strong base before any carbocation could be formed.

E1 Elimination

If the elimination reaction takes place in a two step process, this is called an E1 elimination. Similar to a S_N1 substitution reaction, the rate of the reaction depends on how easily a carbocation can be formed. Thus, the rate expression indicates the reaction is unimolecular. There is no requirement for antiperiplanar alignment of a hydrogen with the leaving group as the hydrogen is not taken off in the rate determining step. Once the carbocation is formed, an adjacent hydrogen can align with the p-orbital and be taken off. Since the base is not involved in the RDS, it's strength is less important than that for an E2 elimination. Usually E1 and S_N1 pathways are in competition with each other and a mixture is often formed.



E1 Elimination Characteristics - Substrate

Exactly like the S_N1 reaction, the E1 reaction depends on easily forming a carbocation. Thus, 3° will work best and secondary allylic substrates can react. Secondary is slower and primary is very unlikely.

E1 Elimination Characteristics - Base

Strong bases are not required. Weaker bases will work just fine.

E1 Elimination Characteristics - Leaving Groups

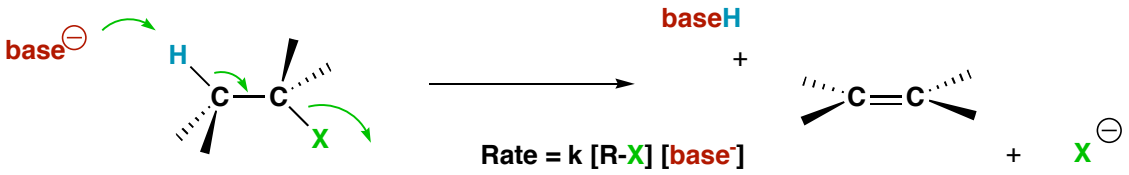
Since the leaving group is departing in the reaction, it is important just like in the S_N1 reaction. Better leaving groups that form more stable anions are best for elimination reactions.

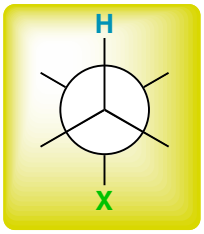
E2 Elimination Characteristics - Solvent

Polar protic solvents are best. Polar solvents help to stabilize the carbocation intermediate and protic solvents help to stabilze the leaving group anion.

Summary of Substitution and Elimination Reactions

Sometimes it is difficult to tell what mechanism will be the predominant pathway in a reaction. Usually the most important factor is the substrate. For competing elimination reactions, the base strength (vs. nucleophile) is key.



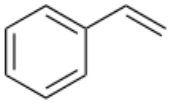


Hydrogen and leaving group must be antiperiplanar for elimination to take place.

Quiz of the day

Q: What is the product of the following reaction sequence?

1:



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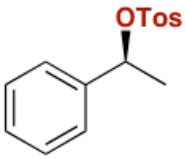
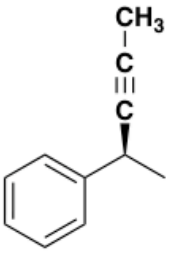


3:



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