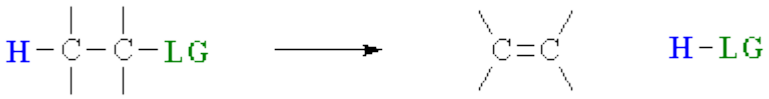
Elimination reactions



Elimination reactions are important as a method for the preparation of alkenes.
The term "***elimination***" describes the fact that a small molecule is lost during the process.
A **1,2-elimination** indicates that the atoms that are lost come from adjacent C atoms.
The two most important methods are:

- Dehydration (-H_2O) of alcohols, and
- Dehydrohalogenation (-HX) of alkyl halides.

There are three fundamental events in these elimination reactions:

1. removal of a proton
2. formation of the CC π bond
3. breaking of the bond to the leaving group

Depending on the relative timing of these events, different mechanisms are possible:

- Loss of the **LG** to form a carbocation, removal of H^+ and formation of C=C bond : E1 reaction
- Simultaneous H^+ removal, C=C bond formation and loss of the **LG** : E2 reaction
- Removal of H^+ to form a carbanion, loss of the **LG** and formation of C=C bond (E1cb reaction)

In many cases the elimination reaction may proceed to alkenes that are constitutional isomers with one formed in excess of the other. This is described as **regioselectivity**.

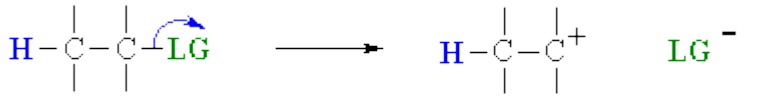
Zaitsev's rule, based on the dehydration of alcohols, describes the preference for eliminations to give the highly substituted (more stable) alkene, which may also be described as the **Zaitsev product**. The rule is not always obeyed, some reactions give the anti-Zaitsev product.

Similarly, eliminations often favour the more stable trans-product over the cis-product (**stereoselectivity**)

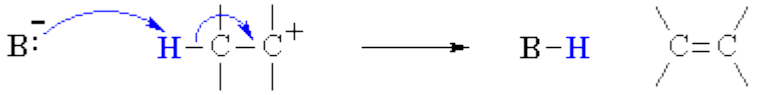
E1 mechanism

E1 indicates a ***elimination***, ***unimolecular*** reaction, where rate = k [**R-LG**].
This implies that the rate determining step of the mechanism depends on the decomposition of a single molecular species.

Overall, this pathway is a multi-step process with the following two critical steps:



loss of the leaving group, LG, to generate a carbocation intermediate, then



loss of a proton, H^+, from the carbocation to form the π-bond

Lets look at how the various components of the reaction influence the reaction pathway:

R-

Reactivity order : $(CH_3)_3C$- > $(CH_3)_2CH$- > CH_3CH_2- > CH_3-

In an E1 reaction, the rate determining step is the loss of the leaving group to form the intermediate carbocation. The more stable the carbocation is, the easier it is to form, and the faster the E1 reaction will be. Some students fall into the trap of thinking that the system with the less stable carbocation will react fastest, but they are forgetting that it is the generation of the carbocation that is rate determining.

Since carbocation intermediates are formed during an E1, there is always the possibility of rearrangements (*e.g.* 1,2-hydride or 1,2-alkyl shifts) to generate a more stable carbocation. This is usually indicated by a change in the position of the alkene or a change in the carbon skeleton of the product when compared to the starting material.

-LG

The only event in the rate determining step of the E1 is breaking the **C-LG** bond. Therefore, there is a very strong dependence on the nature of the leaving group, the better the leaving group, the faster the E1 reaction will be. In the acid catlaysed reactions of alcohols, the -OH is protonated first to give an oxonium ion, providing the much better leaving group, a water molecule (see scheme below).

B

Since the base is not involved in the rate determining step, the nature of the base is unimportant in an E1 reaction. However, the more reactive the base, the more likely an E2 reaction becomes.

Selectivity

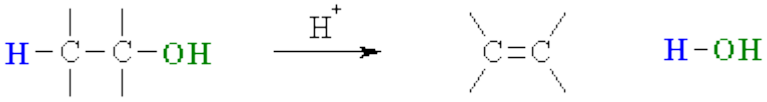
E1 reactions usually favour the more stable alkene as the major product : more highly substituted and trans- > cis-

This E1 mechanistic pathway is most common with:

- good leaving groups
- stable carbocations
- weak bases.

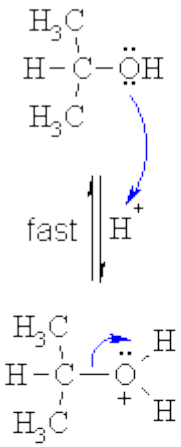
A typical example is the acid catalysed dehydration of 2^o or 3^o alcohols.

E1 MECHANISM FOR ALCOHOLS

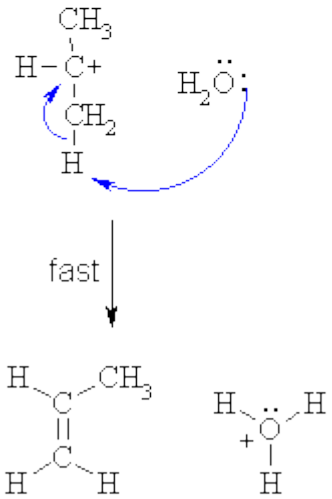


Step 1:
An acid/base reaction. Protonation of the alcoholic oxygen to make a better leaving group. This step is very fast and reversible. The lone pairs on the oxygen make it a Lewis base.

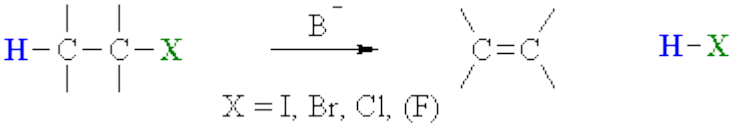
Step 2:
Cleavage of the C-O bond allows the loss of the good *leaving group*, a neutral water molecule, to give a carbocation intermediate. This is the rate determining step (bond breaking is endothermic)



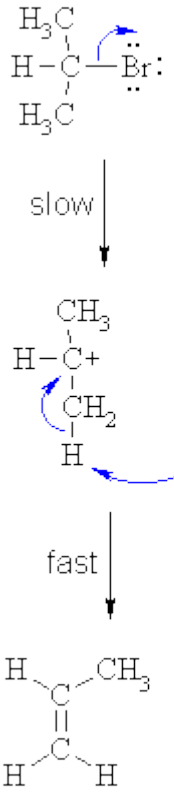
Step 3:
An acid/base reaction. Deprotonation by a base (a water molecule) from a C atom adjacent to the carbocation center leads to the creation of the C=C



E1 MECHANISM FOR ALKYL HALIDES



Step 1:
Cleavage of the polarised C-X bond allows the loss of the good *leaving group*, a halide ion, to give a carbocation intermediate. This is the rate determining step (bond breaking is endothermic)



Step 2:
An acid/base reaction. Deprotonation by a base (here an alkoxide ion) from a C atom adjacent to the carbocation center leads to the creation of the C=C

E2 mechanism

E2 indicates an ***elimination***, ***bimolecular*** reaction, where rate = k [**B**][**R-LG**].
This implies that the rate determining step involves an interaction between these two species, the base and the organic substrate.

This pathway is a concerted process with the following characteristics:

Simultaneous removal of the proton, H^+, by the base, loss of the leaving group, **LG**, and formation of the π-bond

Let's look at how the various components of the reaction influence the reaction pathway:

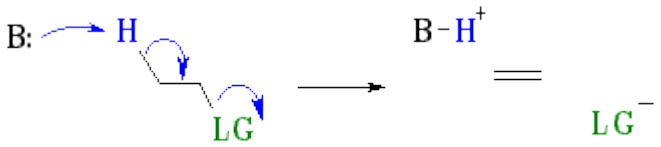
Effects of R-
In an E2 reaction, the reaction transforms 2 sp^3 C atoms into sp^2 C atoms. This moves the substituents further apart decreasing any steric interactions. So more highly substituted systems undergo E2 eliminations more rapidly. This is the same reactivity trend as seen in E1 reactions.

-LG
The **C-LG** bond is broken during the rate determining step, so the rate does depend on

the nature of the leaving group.
However, if a leaving group is too good, then an E1 reaction may result.

B
Since the base is involved in the rate determining step, the nature of the base is very important in an E2 reaction.
More reactive bases will favour an E2 reaction.

Stereochemistry
E2 reactions occur most rapidly when the **H**-**C** bond and **C**-**LG** bonds involved are co-planar, most often at 180^{o} or antiperiplanar. This sets up the σ bonds that are broken in the correct alignment to become the π bond. More details ?



Selectivity
The outcome of E2 reactions is controlled by the stereochemical requirements described above. Where there is a choice, the more stable alkene will be the major product.

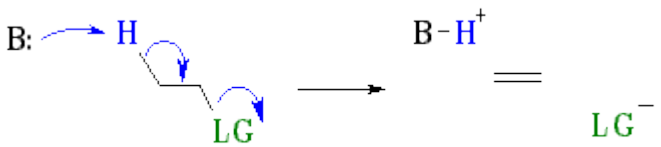
The E2 pathway is most common with:

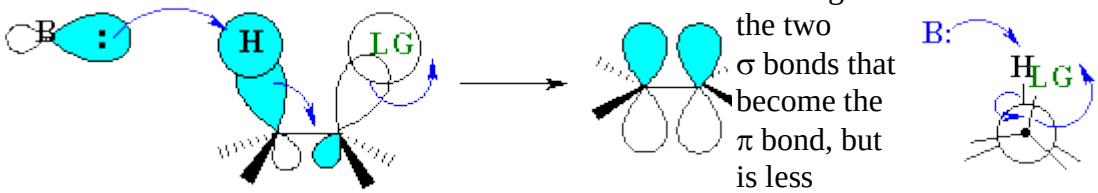
- high concentration of a strong base
- poorer leaving groups
- **R**-**LG** that would not lead to stable carbocations (when the E1 mechanism will occur).

A typical example is the dehydrohalogenation of alkyl halides using KOtBu / tBuOH

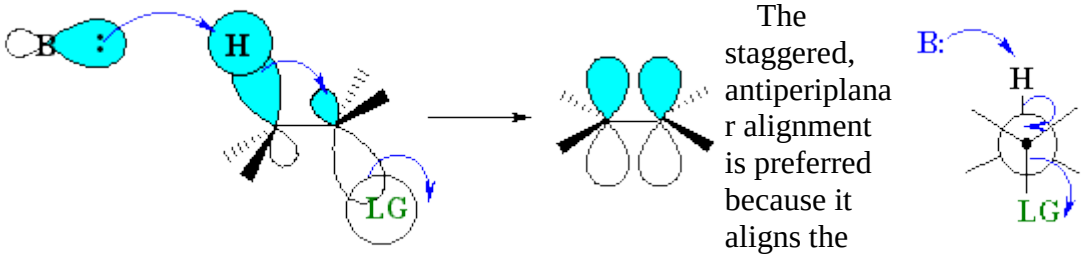
E2 Stereochemistry

E2 reactions occur most rapidly when the **H**-**C** bond and **C**-**LG** bonds involved are co-planar, most often at 180^{o} with respect to each other. This is described as an **antiperiplanar conformation**. This conformation positions the σ bonds that are being broken in the correct alignment to become the π bond.





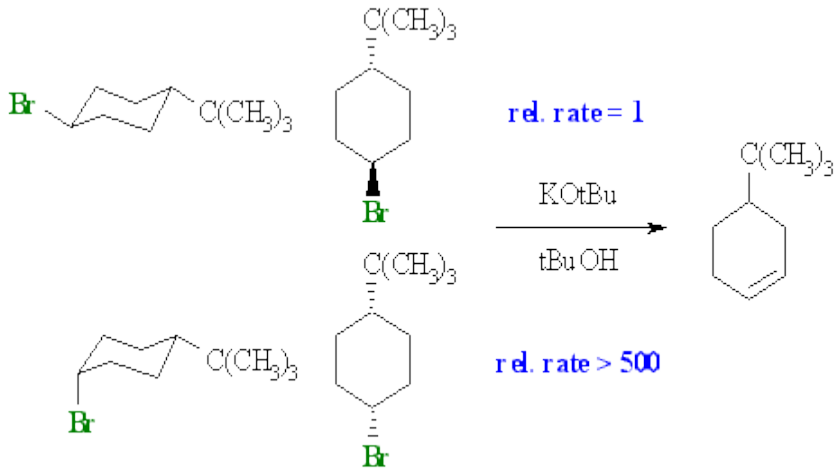
The eclipsed, synperiplanar alignment also aligns the two σ bonds that become the π bond, but is less favourable than the antiperiplanar arrangement.



The staggered, antiperiplanar alignment is preferred because it aligns the two σ bonds that become the π bond.

Synperiplanar arrangments where the angle between the **H**-**C** bond and **C**-**LG** is 0^{o} are also known, usually in systems that are either inflexible rings or intramolecular eliminations.
These alignments are example of a **stereoelectronic effect** because they involve the specific spatial postioning of the bonds (electrons) in order for the process to occur.

Implications:



The cis- isomer undergoes elimination over 500 times faster than the trans-isomer.

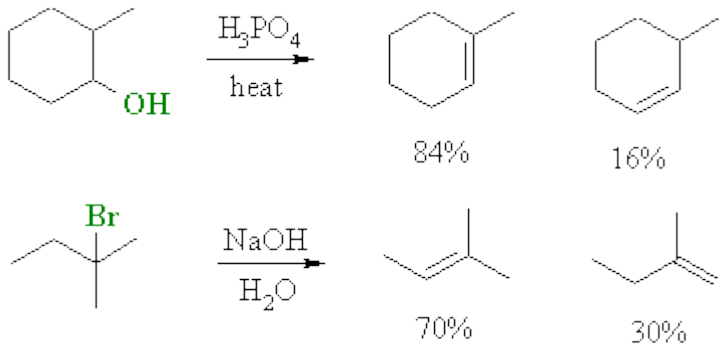
In the cyclic system, in order for the preferred antiperiplanar arrangement favoured by E2 reactions, the **C**-**H** and **C**-**LG** bonds both need to be axial.

Recall that in chapter 3 that we learnt that the t-butyl group has a strong preference for the equatorial position on cyclohexanes and acts as a "lock". In the trans isomer, this means that the **-Br** is also equatorial and is therefore anti to **C-C** bonds, not **C-H**. Since the cyclohexane is locked it cannot ring flip into the geometry required for the E2 and elimination is slow.
In contrast, in the cis isomer, the **-Br** is axial and is anti to 2 **C-H** bonds and the E2 occurs rapidly. Use the CHIME images below to show the antiperiplanar bonds if you need to.

Selectivity

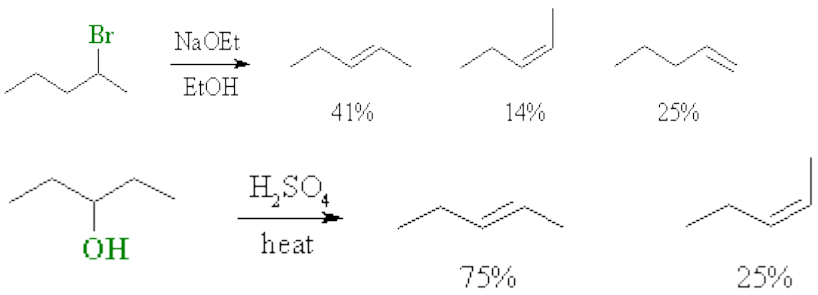
In many cases elimination reactions may proceed to alkenes that are isomeric but with one formed in excess of the other.

Rgioselectivity (products are constitutional isomers):



Zaitsev's rule, based on experiment observations of the dehydration of alcohols, expresses the preference for eliminations to give the highly substituted (**more stable**) alkene, which may also be described as the **Zaitsev product**.
The rule is not always obeyed, some reactions give the anti-Zaitsev product which is sometimes described as the Hoffman product. (Hoffman studied the elimination of ammonium salts)
Care is needed with E2 eliminations of cyclic systems since the antiperiplanar alignment of the **C-H** and **C-LG** bonds can dictate that the anti-Zaitsev products dominate.

Stereoselectivity (products are stereoisomers)



Similarly, eliminations often favour the **more stable** *trans*-product over the *cis*-product.