

Elimination and Substitution Reactions

Lecture in Organic Chemistry

By

Doctoral students

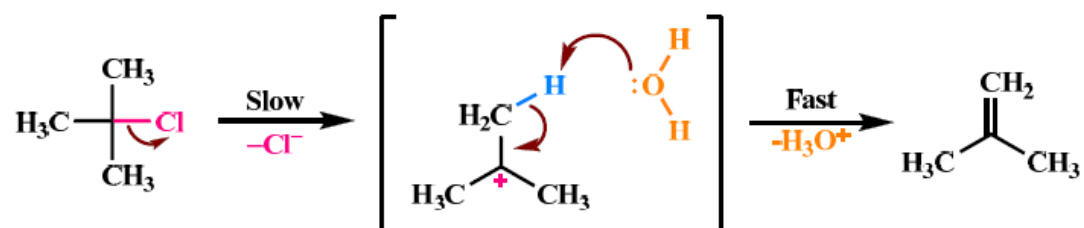
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Elimination Reactions – E1 Reaction:

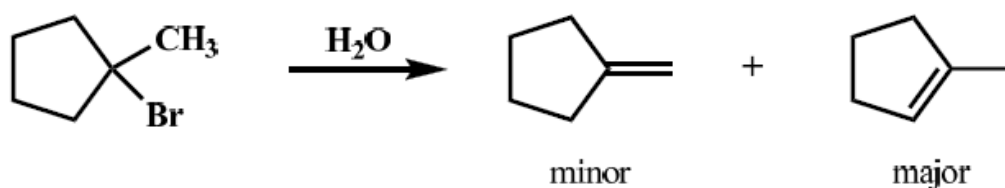
The E1 Mechanism



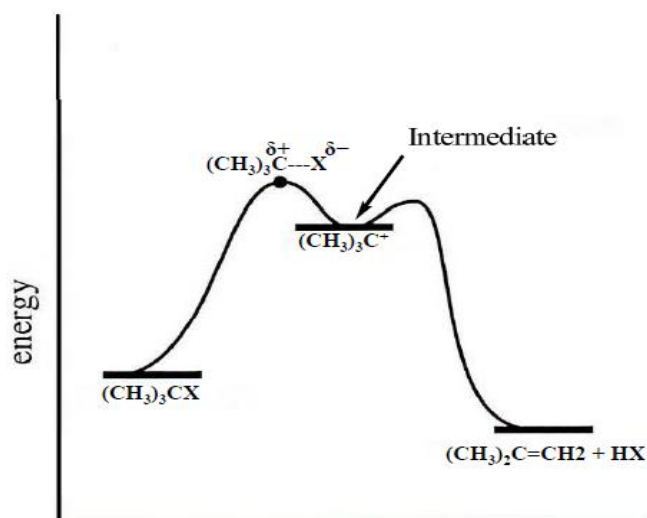
The E1 reaction proceeds via a two-step mechanism: the bond to the leaving group breaks first before the π bond is formed. The slow step is unimolecular, involving only the alkyl halide. It exhibits first-order kinetics,

$$\text{rate} = k[(\text{CH}_3)_3\text{CCl}]$$

E1 reactions also are regioselective and follow Zaitsev rule

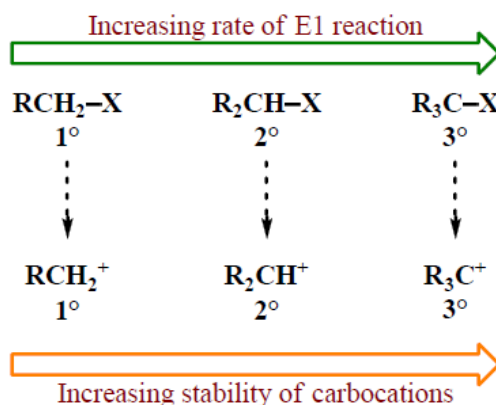


Energy Profile for an E1 Reaction



Factors Affecting the Rate of an E1 Reaction

The rate of an E1 reaction increases as the number of R groups on the carbon with the leaving group increases.



The strength of the base usually determines whether a reaction follows the E1 or E2 mechanism. Strong bases like OH^- and OR^- favor E2 reactions, whereas weaker bases like H_2O and ROH favor E1 reactions.

Characteristics of an E1 Reaction

Kinetics – First order

Mechanism – Two steps

Identity of R group – More substituted halides react faster

Rate: $R_3CX > R_2CHX > RCH_2X$

Strength of the base – Favored by weaker bases such as H_2O and ROH

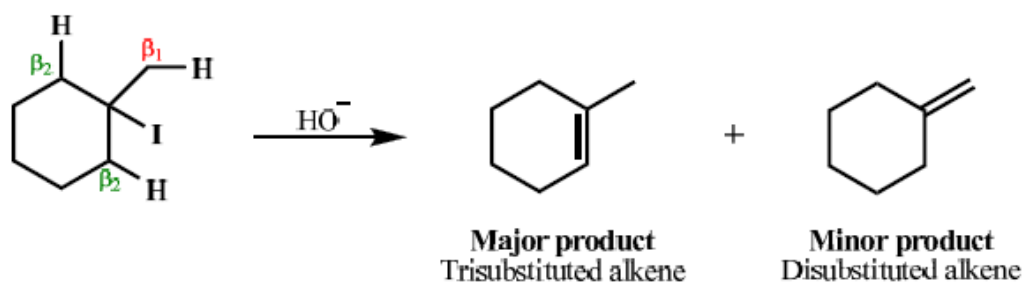
Leaving group – Better leaving group leads to faster reaction rates.

Just as in S_N1 reactions, the rate determining step involves the $C-X$ bond cleavage

Type of solvent – Favored by polar protic solvents, which can stabilize the ionic intermediates

The Zaitsev (Saytseff) Rule

When alkyl halides have two or more different β carbons, more than one alkene product is formed. In such cases, the major product is the more stable product—the one with the more substituted double bond. This phenomenon is called the Zaitsev rule

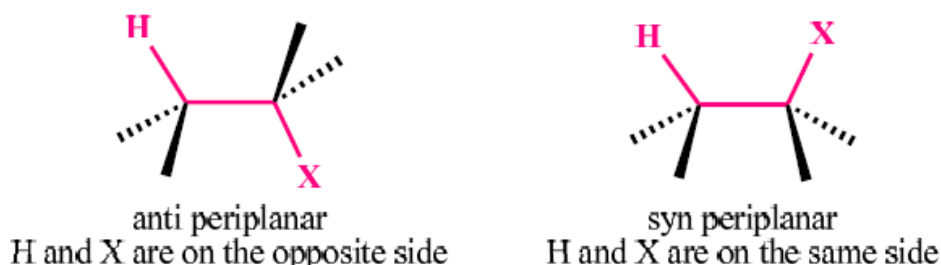


The Zaitsev product or the more substituted alkene product is more stable than the less substituted product. The stability of the more substituted alkene is a result of number of different contributing factors, including hyperconjugation. Each alkyl

group that can involve in hyperconjugation with the double bond stabilizes it by approximately 6 kcal/mol.

Stereochemistry of the E2 Reaction

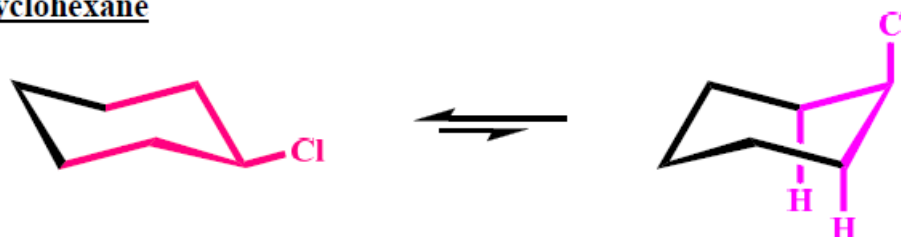
The transition state of an E2 reaction consists of four atoms from the substrate (one hydrogen atom, two carbon atoms, and the leaving group, X) aligned in a plane. There are two ways for the C—H and C—X bonds to be coplanar.



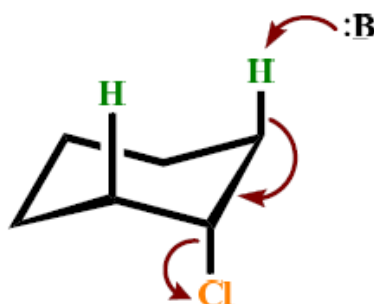
E2 elimination occurs most often in the anti periplanar geometry. This arrangement allows the molecule to react in the lower energy staggered conformation, and allows the incoming base and leaving group to be further away from each other. The anti periplanar geometry also allows direct interaction between the bonding electrons of C—H bond and the anti-bonding orbital of the C—X bond.

E2 Reactions in 6-Membered Rings

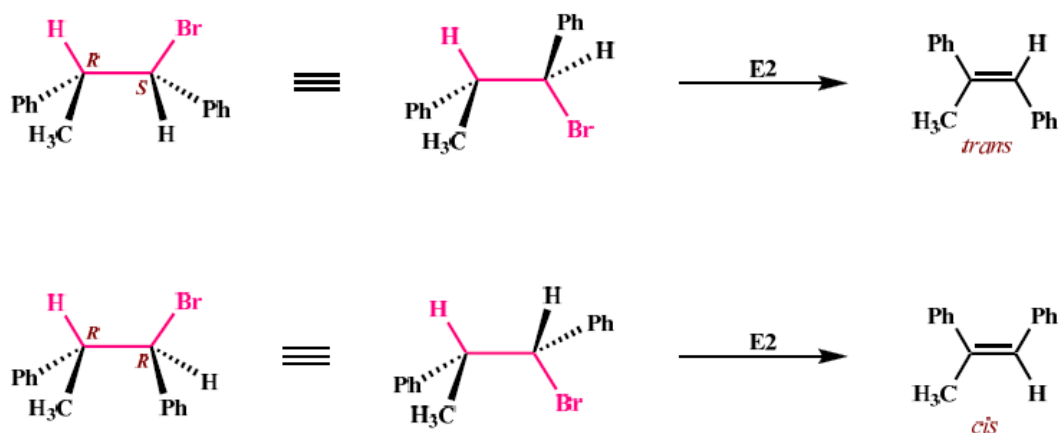
The stereochemical requirement of an anti periplanar geometry in an E2 reaction has important consequences for compounds containing six-membered rings.

Chlorocyclohexane

For E2 elimination, the C—Cl bond must be anti periplanar to the C—H bond on a β carbon, and this occurs only when the H and Cl atoms are both in the axial position. The requirement for trans-diaxial geometry means that elimination must occur from the less stable conformer.

**Stereospecificity in E2 reactions**

Diastereomeric starting compounds yield diastereomeric products after an E2 reaction



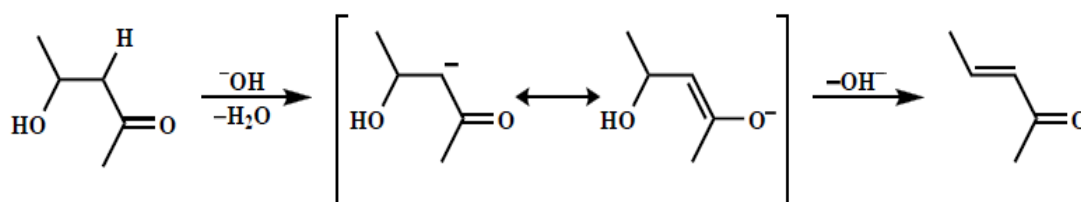
E1cB Reaction

An elimination reaction that happens when a compound bearing a poor leaving group and an acidic hydrogen is treated with a base.

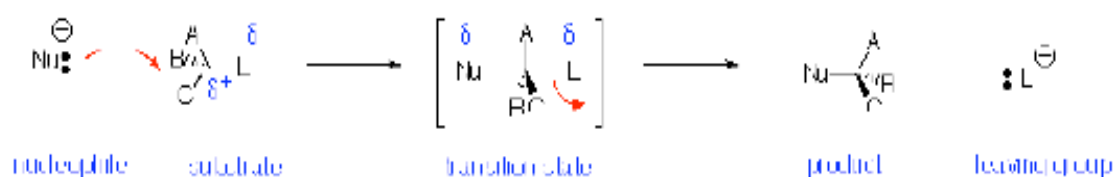


E1cB stands for **E**limination **U**nimolecular **c**onjugate **B**ase. The reaction is unimolecular from the conjugate base of the starting compound, which in turn is formed by deprotonation of

the starting compound by a suitable base. The electron withdrawing group (EWG) can be a carbonyl group (keto, aldehyde, ester), a nitro group, an electron deficient aromatic group etc. Dehydration of aldol is the most common E1cB reaction.



Nucleophilic Substitution Reactions - S_N2 Reaction:



• Reaction is:

- * Stereospecific (Walden Inversion of configuration)
- * Concerted - all bonds form and break at same time
- * Bimolecular - rate depends on concentration of both nucleophile and substrate

• Substrate:

- * Best if **primary** (one substituent on carbon bearing leaving group)
- * works if secondary, fails if tertiary

• Nucleophile:

- * Best if more reactive (i.e. more anionic or more basic)

• Leaving Group: Best if more stable (i.e. can support negative charge well):

- * TsO^- (very good) $> \text{I}^- > \text{Br}^- > \text{Cl}^- > \text{F}^-$ (poor)

* RF , ROH , ROR , RNH_2 are NEVER Substrates for $\text{S}_{\text{N}}2$ reactions

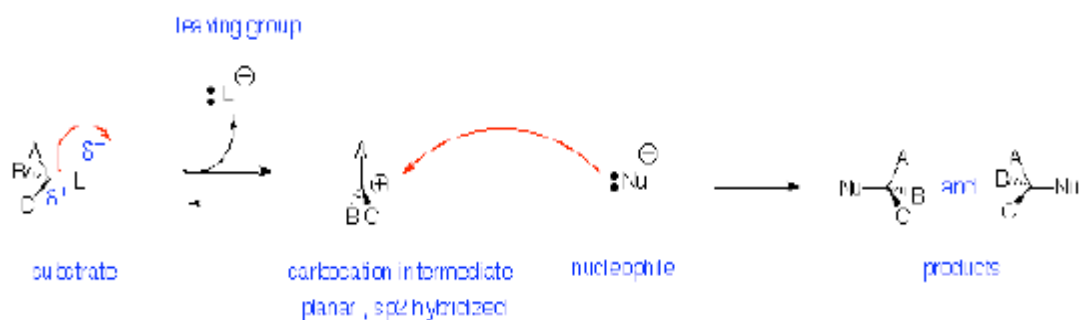
* Leaving Groups on double-bonded carbons are never replaced by $\text{S}_{\text{N}}2$ reactions

• Solvent: Polar Aprotic (i.e. no OH) is best.

* For example dimethylsulfoxide (CH_3SOCH_3), dimethylformamide

($\text{HCON}(\text{CH}_3)_2$), acetonitrile (CH_3CN).

* Protic solvents (e.g. H_2O or ROH) deactivate nucleophile by hydrogen bonding but can be used in some case

Nucleophilic Substitution Reactions – $\text{S}_{\text{N}}1$ Reaction:**• Reaction is:**

*Non-stereospecific (attack by nucleophile occurs from both sides)

* Non-concerted - has carbocation intermediate

*Unimolecular - rate depends on concentration of only the substrate

• **Substrate:**

* Best if tertiary or conjugated (benzylic or allylic) carbocation can be formed as leaving group departs

* never primary

• **Nucleophile:**

* Best if more reactive (i.e. more anionic or more basic)

• **Leaving Group:**

* Same as S_N2

* best if more stable (i.e. can support negative charge well)

* Examples: TsO^- (very good) $> \text{I}^- > \text{Br}^- > \text{Cl}^- > \text{F}^-$ (poor)

* However, tertiary or allylic ROH or ROR' can be reactive under strongly acidic conditions to replace OH or OR

• **Solvent:**

* Same as S_N2

* Polar Aprotic (i.e. no OH) is best

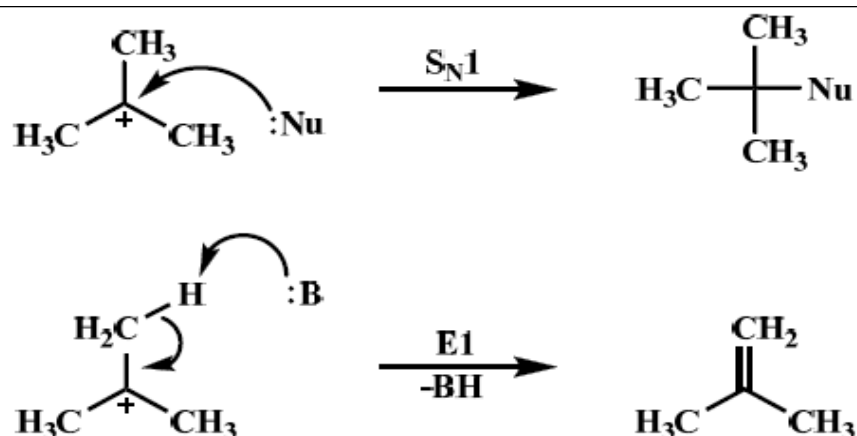
* Examples: dimethylsulfoxide (CH_3SOCH_3), DMF ($\text{HCON}(\text{CH}_3)_2$), acetonitrile (CH_3CN).

* Protic solvents (e.g. H_2O or ROH) deactivate but can be used in some cases

S_N1 and E1 Reactions

S_N1 and E1 reactions have exactly the same first step—formation of a carbocation.

They differ in what happens to the carbocation.



Since in both the reactions, the rate determining steps are the same, they cannot be individually controlled.

Because $E1$ reactions often occur with a competing S_N1 reaction, $E1$ reactions of alkyl halides are much less useful than $E2$ reactions.

S_N1 , S_N2 , $E1$ or $E2$

3° Alkyl Halides

With strong bases: $E2$ elimination occurs

With weak nucleophiles or bases: A mixture of products from S_N1 and $E1$ reactions

1° Alkyl Halides

With strong nucleophiles: Substitution occurs by an S_N2 mechanism

With strong sterically hindered bases: Elimination occurs by an $E2$ mechanism

2° Alkyl Halides

With strong bases and nucleophiles: A mixture of S_N2 and $E2$ reaction products are formed

With strong sterically hindered bases: Elimination occurs by an E2 mechanism

With weak nucleophiles or bases: A mixture of S_N1 and E1 products results

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