

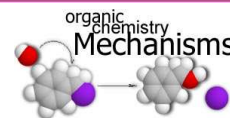
CHEM 344

ORGANIC REACTION MECHANISM

FOR CHEMISTRY' STUDENTS, COLLEGE OF SCIENCE

PRE-REQUISITES COURSE; CHEM 241

CREDIT HOURS; 2 (2+0+0)



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Elimination Reactions

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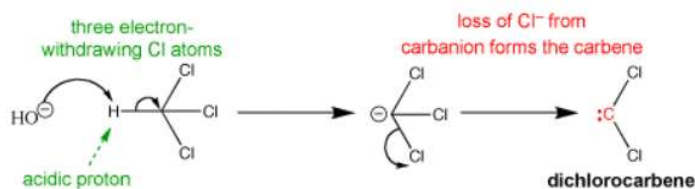
ELIMINATION REACTIONS

TYPES OF ELIMINATION REACTIONS

- **Elimination reactions**, are those reactions in which hydrogen along with a leaving group will be eliminated.
- **Elimination reactions** are used for the generation of double and triple bonds from a saturated compounds.
- **Based on the position of eliminating groups, elimination reactions are classified as:**

- **α -Elimination**

Both groups are lost from the same atom to give a carbene.



Unstable species are formed, which undergo further reactions.

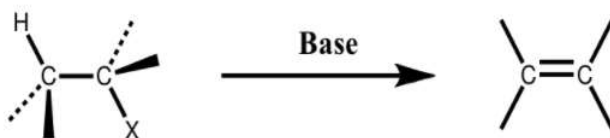
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ELIMINATION REACTIONS

TYPES OF ELIMINATION REACTIONS

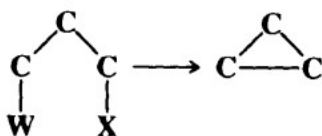
- **β -Elimination**

Both groups are lost from the two adjacent carbon atoms to give alkene.



- **γ -Elimination**

A three-membered ring is formed



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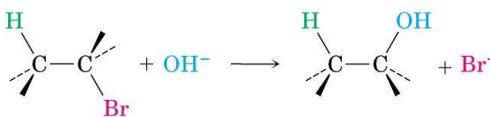
ELIMINATION REACTIONS

B-ELIMINATIONS

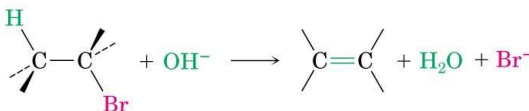
- β -elimination proceeds through two mechanisms;
 - E2 biomolecular elimination reactions
 - E1 unimolecular elimination reactions
- E2 & E1 mechanism differ in the *timing of bond cleavage and bond formation*, analogous to the S_N^2 & S_N^1 mechanisms
- E2 & S_N^2 reactions have some features in common, as do E1 & S_N^1 reactions.



Substitution



Elimination



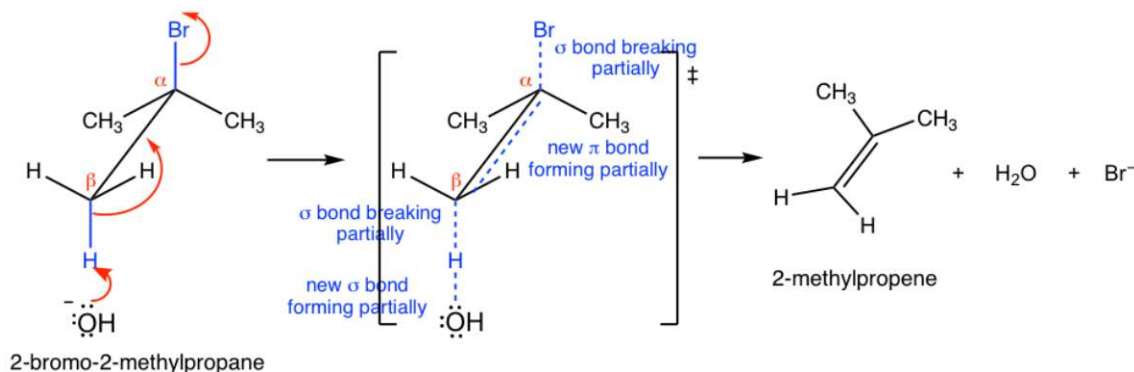
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E2 REACTION

REACTION MECHANISM

- E2 reaction is a **single step** elimination, with a **single transition state**



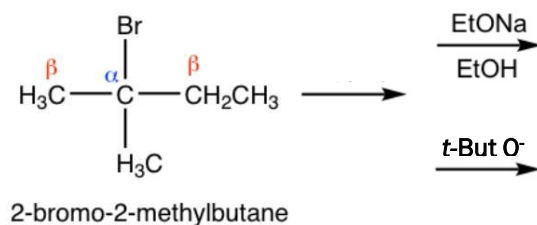
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E2 REACTION

REGIOSELECTIVITY OF E2 REACTION:

For alkyl halides, if there are *different β -carbons* in the substrate, then the elimination reaction may yield *more than one products*.

- **Example:** Dehydrohalogenation of 2-bromo-2-methylbutane can produce two products, *2-methyl-2-butene* and *2-methyl-1-butene*



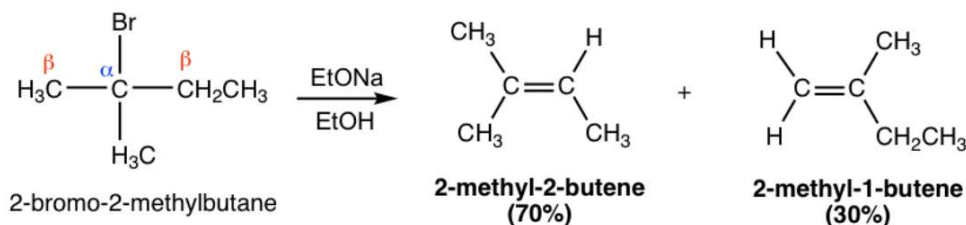
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E2 REACTION

REGIOSELECTIVITY OF E2 REACTION:

Zaitsev's Rule

When *small base, such as OH^- , CH_3O^- , EtO^-* , is applied, the elimination products can be predicted by *Zaitsev's rule*, i.e. the major product is the more stable product - the one with the *more substituted double bond*.



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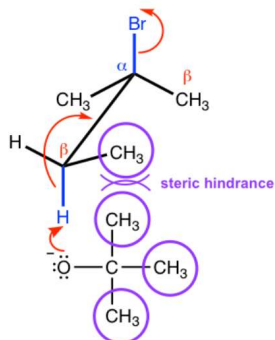
E2 REACTION

REGIOSELECTIVITY OF E2 REACTION:

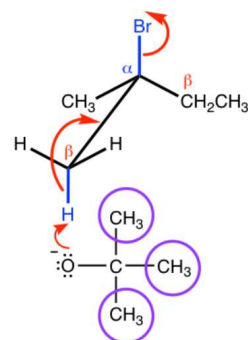
Hofmann's Rule

If a *bulky base such as t-BuOK*, is applied in the elimination, the reaction favors the formation of *less substituted double bond*.

This is mainly because of *Steric Hindrance*.



pathway (a): bulky base t-BuO⁻ is more hindered



pathway (b): bulky base t-BuO⁻ is less hindered

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E2 REACTION

REACTION KINETICS

- The E2 reaction is a *concerted process* (one step reaction), with a *bimolecular rate-determining step*.

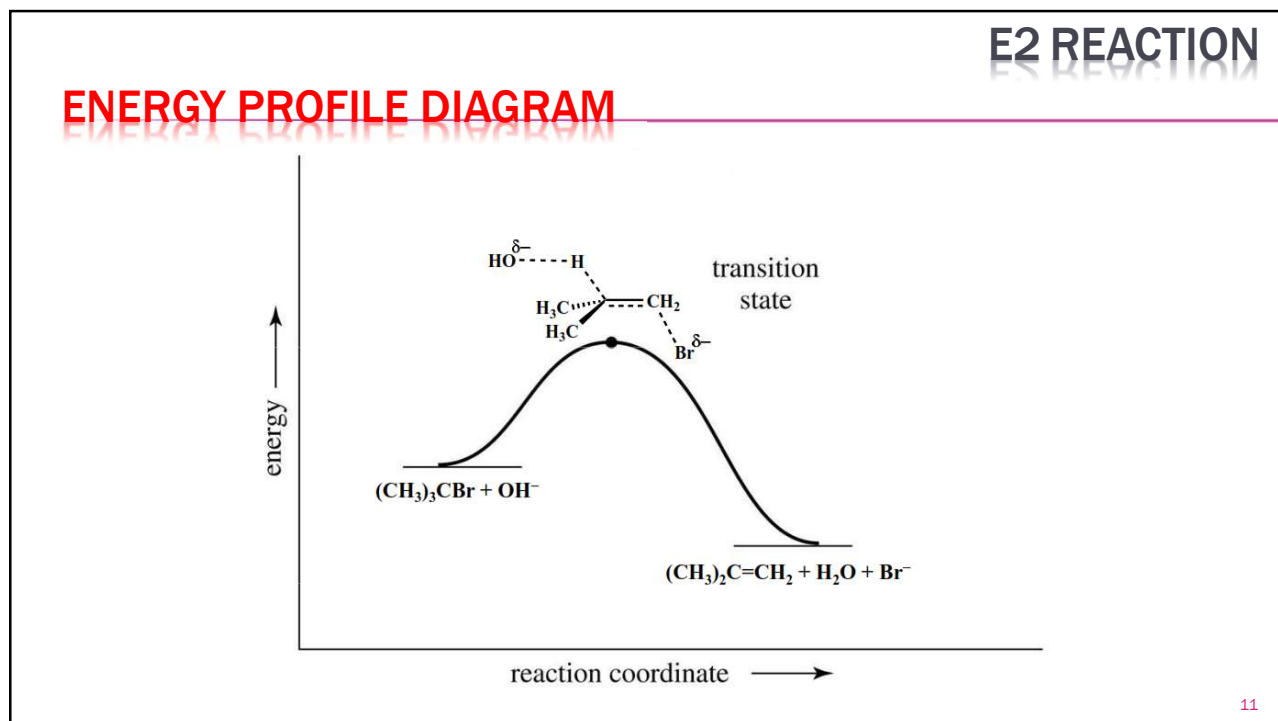
"*Concerted*" means that the formation of a double bond, and departure of the leaving group (X⁻ and H⁺) all occur in one step.

- The reaction rate is *second order*, because it's influenced by both the *alkyl halide* and *the base* (bimolecular).

$$\text{Rate} = k [\text{R-X}][\text{B:}]$$

- Reaction goes faster with *stronger base* and *better leaving group*.

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E2 REACTION

FACTORS AFFECTING THE RATE OF E2 REACTION

- **E2 & S_N² reactions** have some features in common in how the identity of the *base*, the *leaving group* and the *solvent affect the rate*.
- The rate of the E2 reaction increases with
 - the *strong, negatively charged bases* like ⁻OH and ⁻OR.
 - the *Polar aprotic solvents*
 - the *better the leaving group*.
- Rate of reaction follows the order,

most reactive → RI > RBr > RCl > RF ← least reactive

- Alkyl iodides are the most reactive
- alkyl fluorides the least reactive

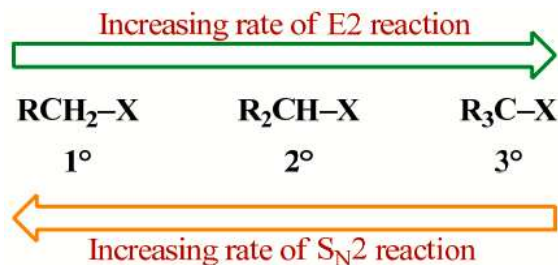
} because weaker bases are better leaving groups

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E2 REACTION

FACTORS AFFECTING THE RATE OF E2 REACTION

- The S_N^2 and E2 mechanisms differ in how the **R group** affects the reaction rate.
As the number of R groups on the carbon with the leaving group increases, the rate of the E2 reaction increases.



- In the transition state;

- The double bond is partially formed.

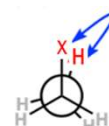
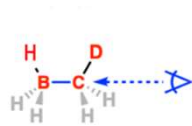
Thus, the transition state for a more substituted alkene is lower in energy, reducing the activation energy for the reaction and making the reaction faster.

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E2 REACTION

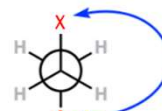
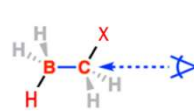
STEREOCHEMISTRY

- The H being abstracted and the leaving group must be in the same plane

Dihedral angle: 0° 

Syn periplanar:
the H and X
are eclipsed
dihedral angle = 0°

Anti periplanar:
the H and X are
anti staggered
dihedral angle = 180°

Dihedral angle: 180°

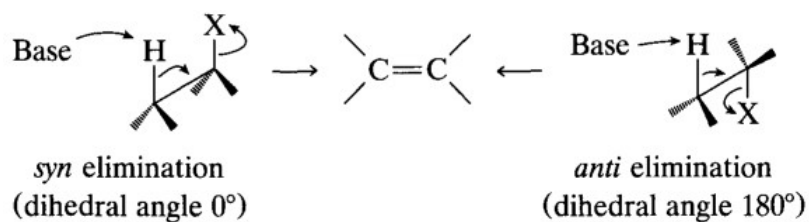
- Staggered conformation has a lower potential energy
- Whereas eclipsed conformation has the maximum potential energy.

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E2 REACTION

STEREOCHEMISTRY

- The term **anti elimination** means that the proton and leaving group depart from opposite sides of the bond, which then becomes a double bond.
- The term **syn elimination** means that they depart from the same side.



- **E2 reactions** are highly stereospecific and **anti elimination** is preferred over syn elimination
 - In **anti E substrate** has staggered conformation while that of in **syn** is eclipsed.

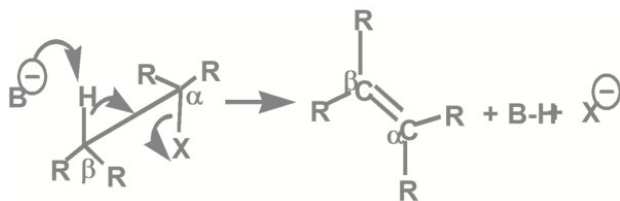
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E2 REACTION

STEREOCHEMISTRY

Anti Elimination in E2

- **Antiperiplanar**; the H and X groups must be anti to each other and be in the same plane with each other and the carbon atoms to which they are attached.



- The **anti-position** allows the transition state of the reaction is in the more stable staggered conformation (helps to lower down the energy level of the transition state and speed up the reaction).

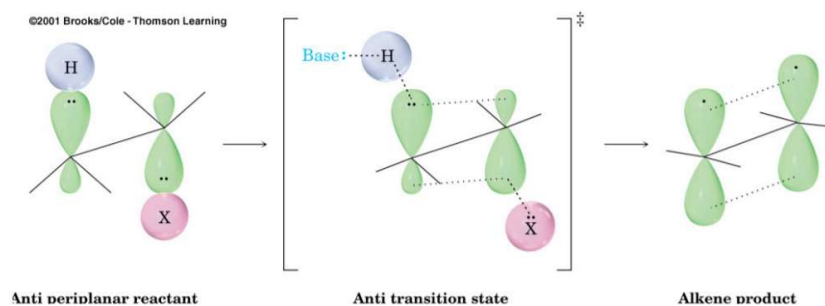
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E2 REACTION

STEREOCHEMISTRY

Anti Elimination in E2

- **Antiperiplanar** allows orbital overlap and minimizes steric interactions



- In the periplanar conformation, the orbitals are already aligned for π -bond formation

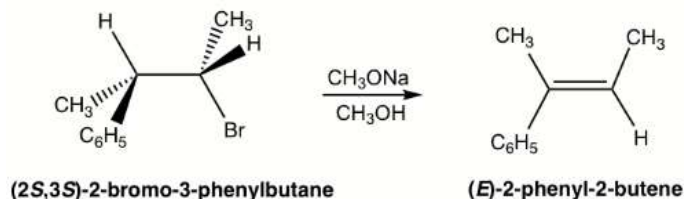
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E2 REACTION

STEREOCHEMISTRY

Anti Elimination in E2

- **E2 reactions** are stereoselective, resulting in the formation of *trans-double bonds* preferably.
- **Example**; the elimination of (2*S*,3*S*)-2-bromo-3-phenylbutane produces the *E* isomer specifically, not the *Z* isomer at all.



This is because when H is in anti-position to the leaving group Br, the whole compound is in staggered conformation, and the other groups retain their relative position in elimination that leads to the *E* isomer.

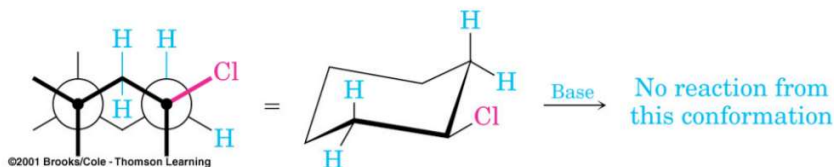
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E2 REACTION

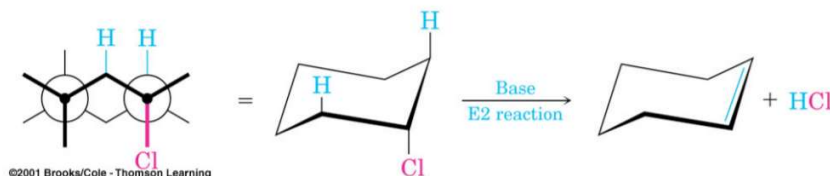
STEREOCHEMISTRY

E2 Elimination with Halocyclohexane Reactants

Equatorial chlorine: H and Cl are not anti periplanar



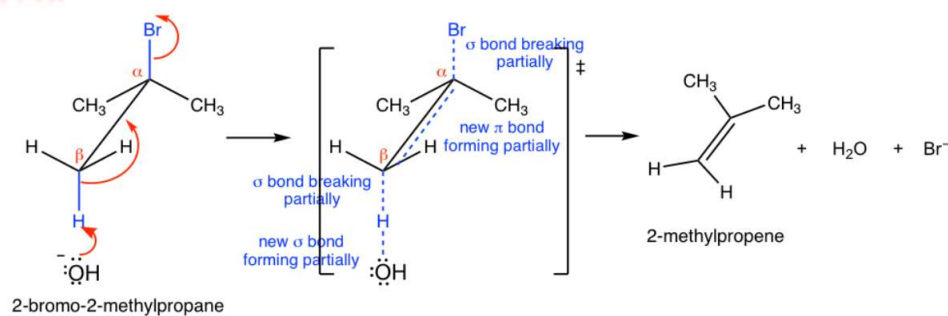
Axial chlorine: H and Cl are anti periplanar



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E2 REACTION

SUMMARY



○ **Reaction is:**

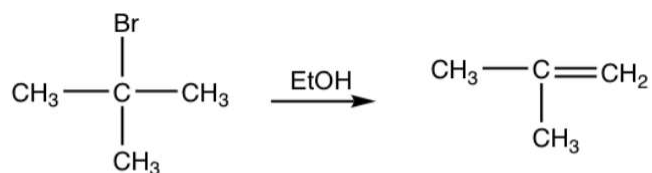
- Stereospecific (Anti-periplanar geometry preferred, Syn-periplanar geometry possible)
- Concerted - all bonds form and break at the same time
- Bimolecular - rate depends on concentration of both base and substrate
- Favored by strong bases

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E1 REACTION

REACTION

- When *t*-butyl bromide reacts with ethanol, small amount of elimination products obtained via E1 mechanism.



Reaction Rate = $k \times [(\text{CH}_3)_3\text{Br}]$ first-order reaction

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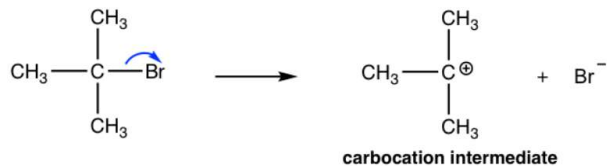
E1 REACTION

REACTION MECHANISM

- The overall elimination involves two steps:

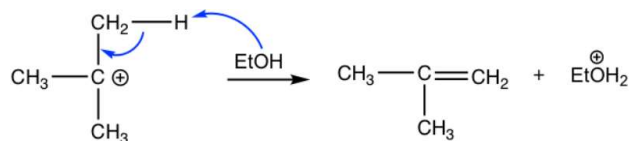
Step 1: Cleavage of C-Br bond **slowly** to form the carbocation intermediate.

Spontaneous dissociation of the tertiary alkyl bromide yields carbocation intermediate in a slow, rate-determining step



Step 2: base (Et-OH) removes H from β -carbon, and double bond produced.

Loss of a neighboring H⁺ in a fast step yields the neutral alkene product. The electron pair from the C-H bond goes to form the alkene π -bond.

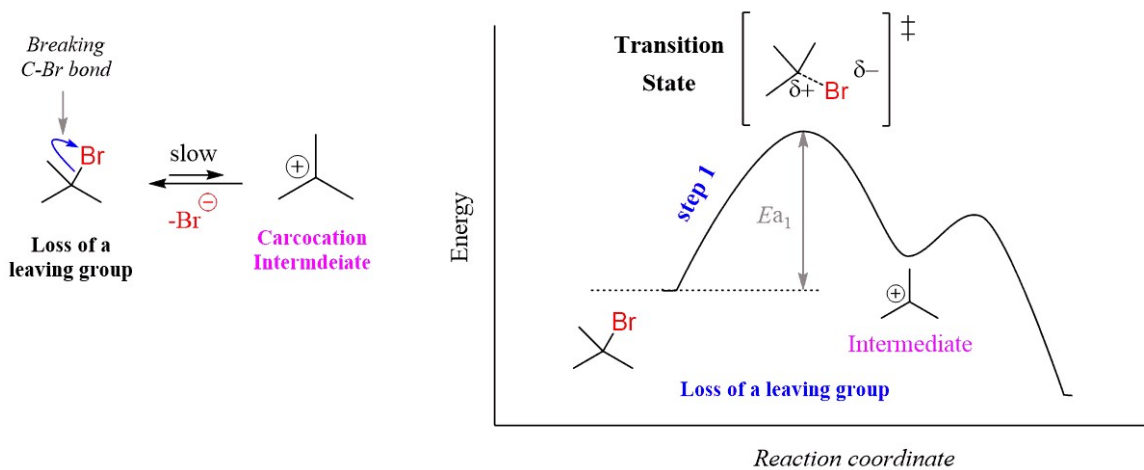


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E1 REACTION

ENERGY PROFILE DIAGRAM

The energy diagram showing the first step of the E1 mechanism

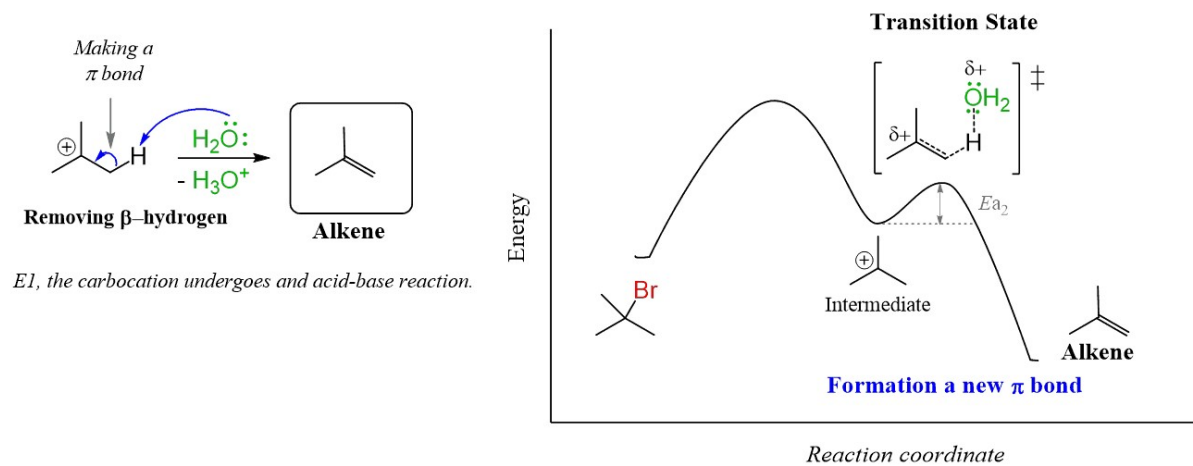


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E1 REACTION

ENERGY PROFILE DIAGRAM

The energy diagram showing the formation of the π bond



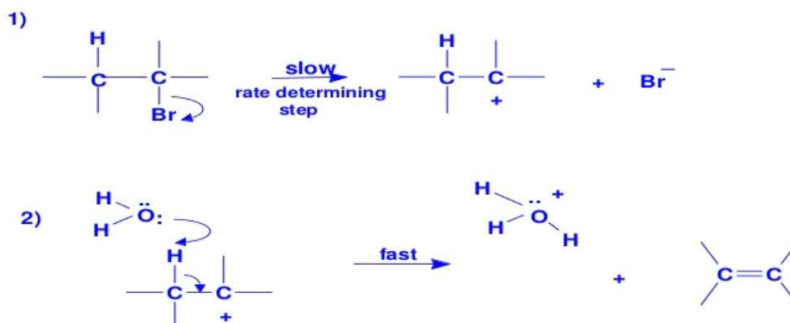
E1, the carbocation undergoes an acid-base reaction.

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E1 REACTION

REACTION KINETICS

- E1 reactions follow first order (unimolecular) kinetics.
- Rate = $k [R-X]$
- The solvent helps to stabilize the carbocation, but it does not appear in the rate law



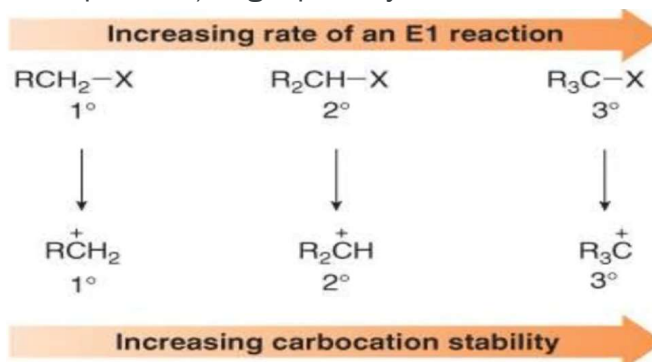
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E1 REACTION

FACTORS AFFECTING THE RATE OF E1 REACTION

1) Substrate Effect

- The order of the reactivity of the alkyl groups is: Tertiary > Secondary > Primary
- This is because the rate-determining step is the formation of carbocation and the stability of these ions increases; Tertiary > Secondary > Primary
- It is hard (but not impossible) to get primary carbocations are not stable.



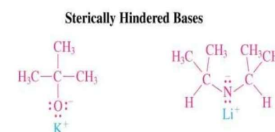
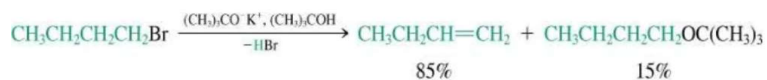
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E1 REACTION

FACTORS AFFECTING THE RATE OF E1 REACTION

2) Base Effect

- Bulky bases favor elimination



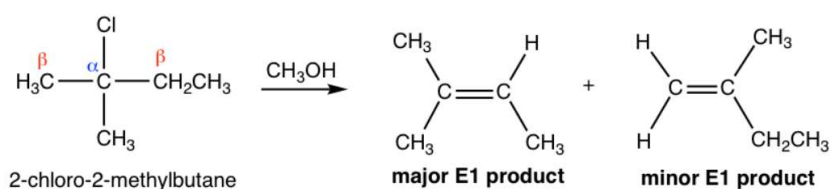
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E1 REACTION

FACTORS AFFECTING THE RATE OF E1 REACTION

3) Orientation of Elimination: Zaitsev's Rule

- E1 reactions follow **Zaitsev's rule**
- The major product should be the product that is the most highly substituted.

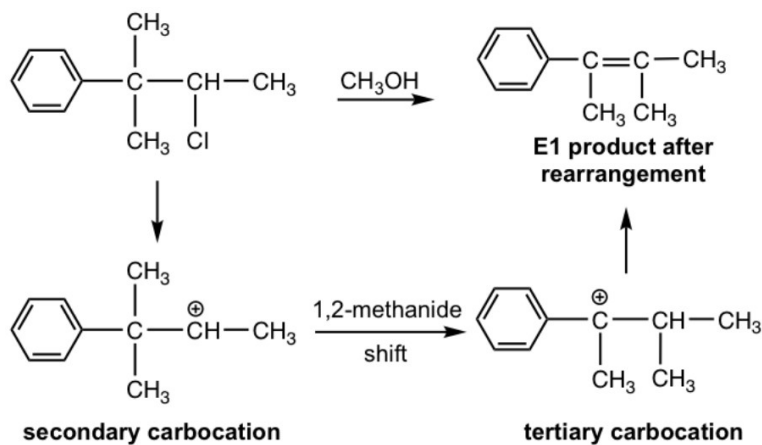


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E1 REACTION

REARRANGEMENTS

- Since E1 reaction involves a carbocation intermediate, the carbocation rearrangement might occur if such rearrangement leads to a more stable carbocation.

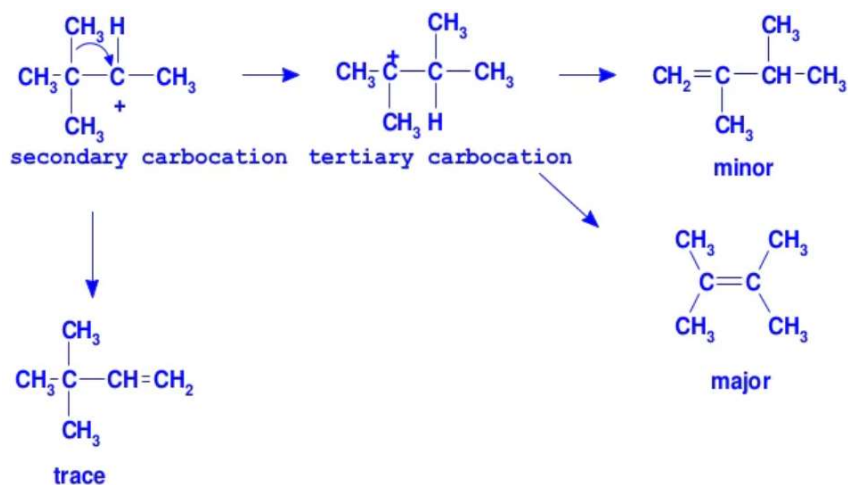


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E1 REACTION

REARRANGEMENTS

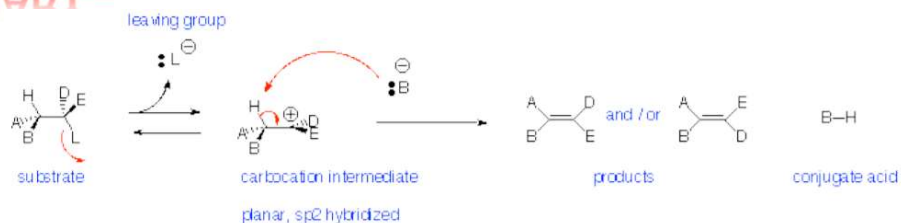
- Alkyl groups and hydrogen can migrate in rearrangement reactions to give the more stable intermediate carbocations.



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E1 REACTION

SUMMARY



○ Reaction is:

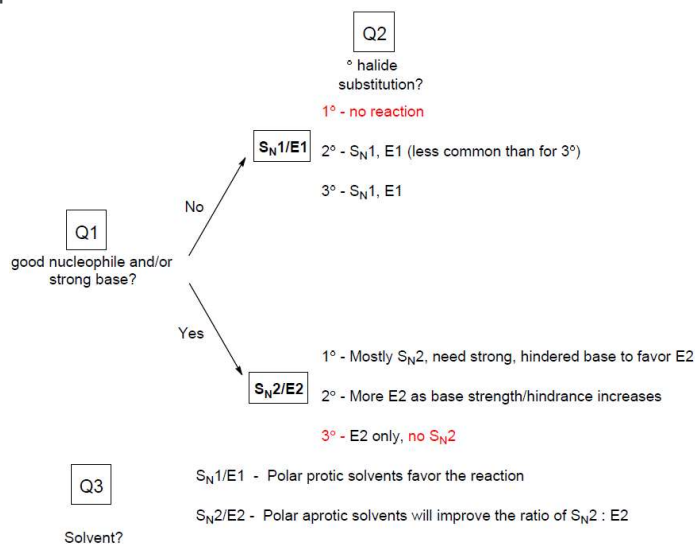
- Non-stereospecific- follows Zaitsev (Saytseff) Rule
- Non-concerted - has carbocation intermediate - favoured for tertiary leaving groups
- Unimolecular - rate depends on concentration of only the substrate
- Does NOT occur with primary alkyl halides (leaving groups)
- Strong acid can promote loss of OH as H₂O or OR as HOR if tertiary or
- conjugated carbocation can be formed

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SUBSTITUTION or ELIMINATION

SUBSTITUTION / ELIMINATION FLOWCHART

- Ask these three questions:



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SUBSTITUTION or ELIMINATION

SUMMARY OF ALKYL HALIDES AND S_N^1 , S_N^2 , E1 AND E2 MECHANISMS

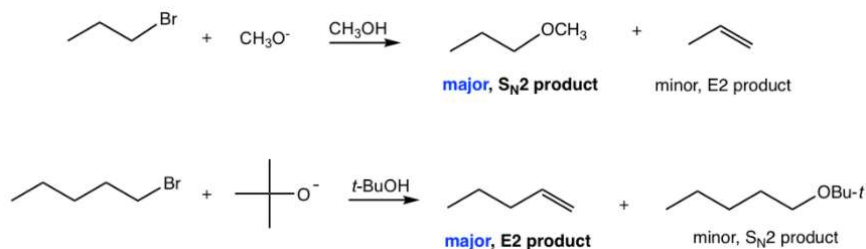
Alkyl halide type	Reaction with		Mechanism
$1^\circ \text{RCH}_2\text{X}$	<ul style="list-style-type: none"> • Strong nucleophile • Strong bulky base 	→	S_N2
		→	E2
$2^\circ \text{R}_2\text{CHX}$	<ul style="list-style-type: none"> • Strong base and nucleophile • Strong bulky base • Weak base and nucleophile; 	→	S_N2 and E2
		→	E2
		→	S_N1 and E1
$3^\circ \text{R}_3\text{CX}$	<ul style="list-style-type: none"> • Weak base and nucleophile • Strong base 	→	S_N1 and E1
		→	E2

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COMPARISON and COMPETITION BETWEEN S_N^1 , S_N^2 , E1 & E2

STRUCTURAL NATURE OF A SUBSTRATE (PRIMARY, SECONDARY OR TERTIARY)

- **Methyl substrate** only go with S_N2 reaction,
- **Primary (1°) substrates**
 - cannot go with any unimolecular reaction, (e.g. no S_N^1 /E1),
because primary carbocations are too unstable to be formed.
 - S_N^2 is the predominant pathway when **good nucleophile** is used; Cl^- , Br^- , I^- , RS^- , N_3^- , CN^- , RCO_2^- .
 - **E2** becomes the major reaction when **big bulky base/nucleophile** is used; $t\text{-BuO}^-$ and LDA



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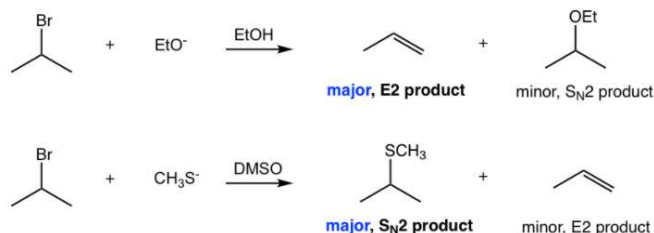
COMPARISON and COMPETITION BETWEEN S_N^1 , S_N^2 , E1 & E2

STRUCTURAL NATURE OF A SUBSTRATE (PRIMARY, SECONDARY OR TERTIARY)

o Secondary (2°) substrates

- It is most complicated or challenging because all the pathways are possible.
- **E2**: favored by a **strong base**; ^-OH , RO^- (R: small size alkyl group), NH_2^-
- **S_N^2** : favored by a **good nucleophile (relatively weaker base)**; Cl^- , Br^- , I^- , RS^- , N_3^- , CN^- , RCO_2^- .
- **S_N^1 /E1**: It is hard to separate S_N^1 and E1 completely apart, because they both go through **carbocation intermediates**, and are favored by **poor nucleophile/weak base**; H_2O or ROH (solvolysis).

S_N^1 and E1 usually occur together for secondary substrates, and increasing the reaction temperature favors E1 over S_N^1 .



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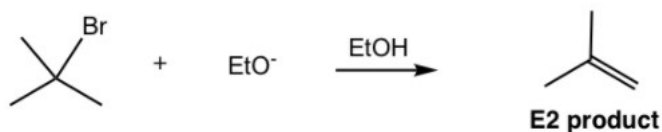
COMPARISON and COMPETITION BETWEEN S_N^1 , S_N^2 , E1 & E2

STRUCTURAL NATURE OF A SUBSTRATE (PRIMARY, SECONDARY OR TERTIARY)

o Tertiary (3°) substrates

- do not go with S_N^2 reactions because of **steric hindrance**.
- **E2** reaction is the choice when **strong base** applied; ^-OH , RO^- (R: small size alkyl group), NH_2^-
- **S_N^1 /E1** pathway with neutral condition (**poor nucleophile/weak base**); H_2O or ROH (solvolysis).

E1 always combine together with S_N^1 , and it is almost impossible to avoid the substitution product.



NOTES:

- The relative stronger bases have the stronger tendency to act as base.
- The relative weaker base, with small size and good polarizability, have the better tendency to act as nucleophile.
- Bulky bases, such as $t-BuO^-$ and LDA, always favor E2 and generate elimination products that follow Hofmann rule, because they are too big to do back-side attack in S_N^2 .

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