



CHEMISTRY

53rd and 54th Class, 22-11-2021

Dr. K. Ananthanarayanan
Associate Professor (Research)
Department of Chemistry
Room No 319, 3rd Floor, Raman Research Park

Email : ananthak@srmist.edu.in

Phone : 9840154665



Last class..

- ☐ Absolute configuration – CIP rules



Last class..

- ☐ Organic reactions
- ☐ Reactions of alkyl halides, S_N2 reaction

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In this class..

- ☐ Elimination reactions – E1 and E2
- ☐ Predicting the reaction pathway

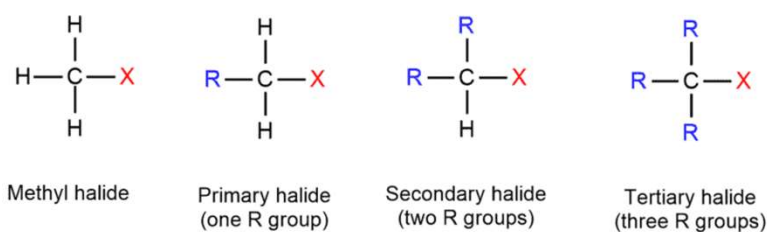
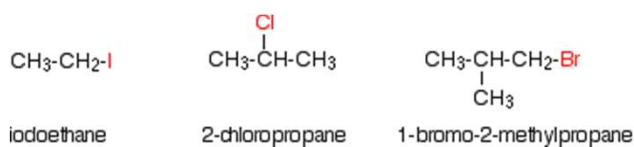
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Alkyl halides



Alkyl halides are compounds in which one or more hydrogen atoms in an alkane have been replaced by halogen atoms (fluorine, chlorine, bromine or iodine).



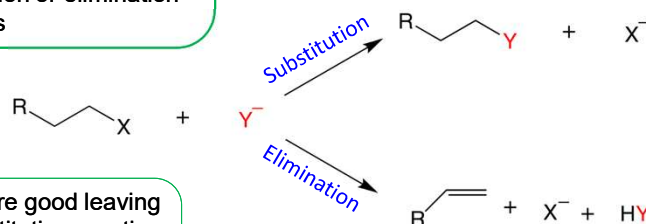
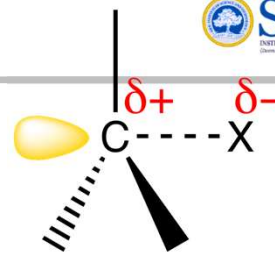
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Organic reactions



Organic compounds with an electronegative atom or an electron-withdrawing group bonded to a sp^3 carbon undergo substitution or elimination reactions



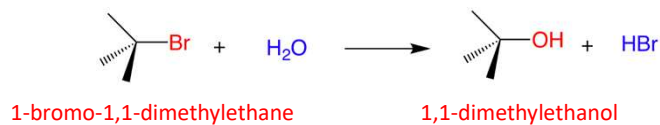
Halide ions are good leaving groups. Substitution reaction on these compounds are easy and are used to get a wide variety of compounds



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Substitution Reactions With Halides



Rate law:

$$\text{rate} = k [\text{1-bromo-1,1-dimethylethane}]$$

If concentration of (1) is doubled, the rate of the reaction is doubled.

If concentration of (2) is doubled, the rate of the reaction is **not** doubled.

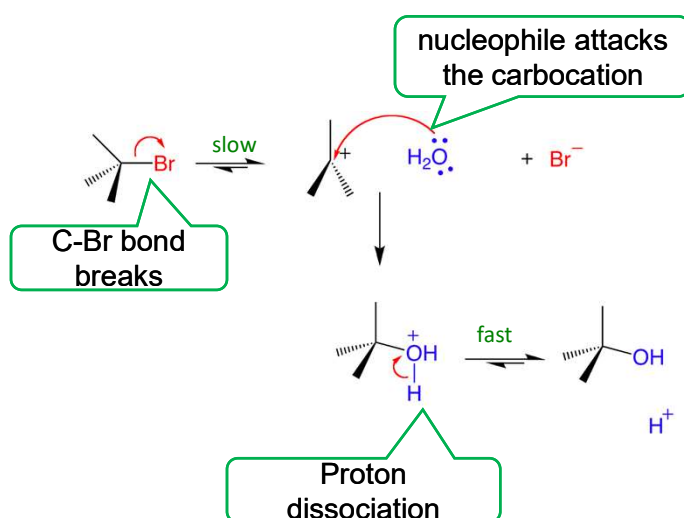
this reaction is an example of a

S_N1 reaction.
S stands for **substitution**
N stands for **nucleophilic**
1 stands for **unimolecular**

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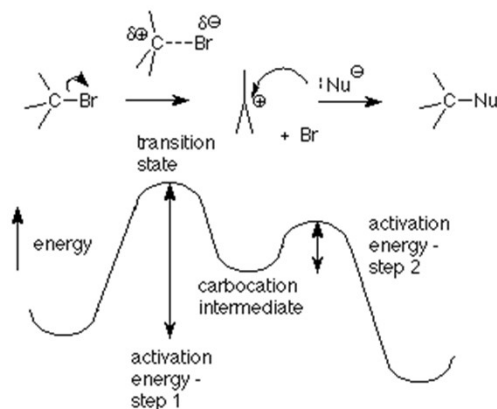
Mechanism of S_N1 Reaction



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Mechanism of S_N1 reaction



The only reactant that is undergoing **change in the first (rate-determining) step is the alkyl halide**, so we expect such reactions would be **unimolecular** and follow a first-order rate equation. Hence the name **S_N1**

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Mechanism

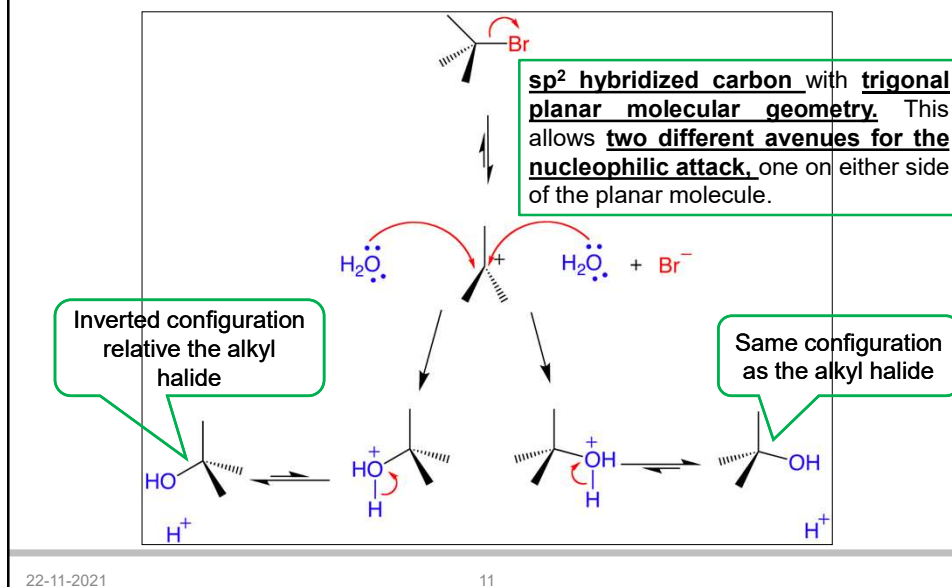


- ☐ The energy **required to break this bond comes from random collisions with the solvent** without the solvent reacting.
- ☐ The **activation energy for the first step is higher than for the second step.**
- ☐ Once a molecule is through the first step, it can react rapidly in the second step. **We call the step which is slowest the "rate determining step."** Notice that the rate determining step for this reaction **doesn't involve the nucleophile.**
- ☐ That means that **changing the concentration of the nucleophile doesn't affect the rate.**
- ☐ First order reaction, and the rate law includes only one reactant: **Rate = k[RX]**

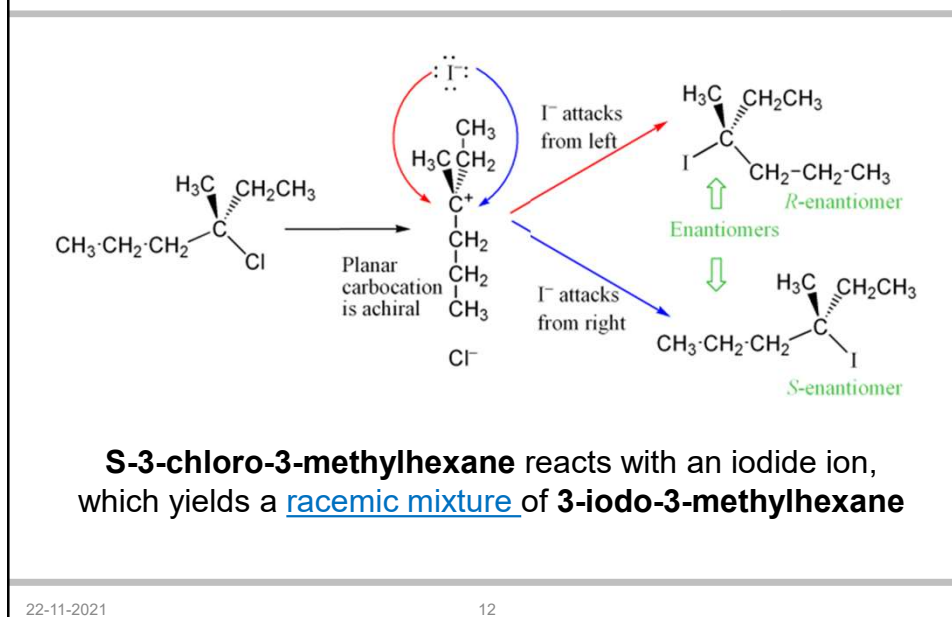
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Mechanism of S_N1 Reaction



3-chloro-3-methylhexane reacts with an iodide ion



Mechanism of S_N1 Reaction, rates



The rate of reaction depends on the concentrations of the alkyl halide only.

When the methyl groups of 1-bromo-1,1-dimethylethane are replaced with hydrogens the reaction rate slow down.

The reaction of an alkyl halide in which the halogen is bonded to an assymmetric center leads to the formation of two stereoisomers

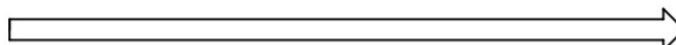
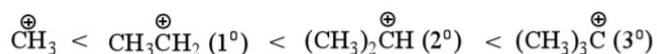
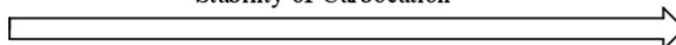
Alkyl halide	Relative rate
	≈ 0 *
	≈ 0 *
	12
	1 200 000

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Stability of Carbocation



Order of Reactivity of alkyl halide towards S_N1

- ☐ Since the rate of **reaction depends on the ionization of C-X (carbon halogen) bond in alkyl halide** to form carbocation.
- ☐ More **stable the carbocation formed, faster is the reaction.**

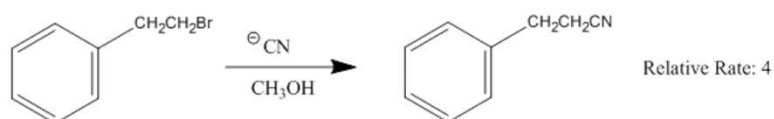
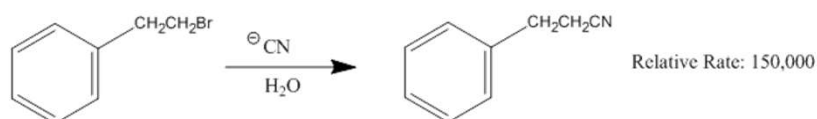
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Mechanism of S_N1 Reaction, rates



Solvent	Dielectric Constant	Relative Rate
• CH ₃ CO ₂ H • CH ₃ OH • H ₂ O	• 6 • 33 • 78	• 1 • 4 • 150,000



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Effect of solvent



- ☐ Polar protic solvents **speed up the rate** of the unimolecular substitution reaction because the **large dipole moment of the solvent helps to stabilize the transition state**.
- ☐ The highly positive and highly negative parts interact with the substrate to **lower the energy of the transition state**.
- ☐ Since the **carbocation is unstable**, anything that can stabilize this even a little will speed up the reaction.
- ☐ Examples of **polar protic solvents** are: acetic acid, isopropanol, ethanol, methanol, formic acid, water, etc.

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Effect of leaving group



Excellent	• TsO^- • NH_3
Very Good	• I^- • H_2O
Good	• Br^-
Fair	• Cl^-
Poor	• F^-
Very Poor	• OH^- • NH_2^-

- ❑ $\text{S}_{\text{N}}1$ reaction speeds up with a good leaving group. This is because the leaving group is involved in the rate-determining step.
- ❑ A good leaving group wants to leave so it breaks the C-Leaving group bond faster.
- ❑ Once the bond breaks, the carbocation is formed and the faster the carbocation is formed, the faster the nucleophile can come in and the faster the reaction will be completed.

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Factors affecting $\text{S}_{\text{N}}1$ reaction



Two factors affect the rate of a $\text{S}_{\text{N}}1$ reaction:

- The ease with which the leaving group dissociate from the carbon
- The stability of the carbocation

The more substituted the carbocation is the more stable it is and therefore the easier it is to form.

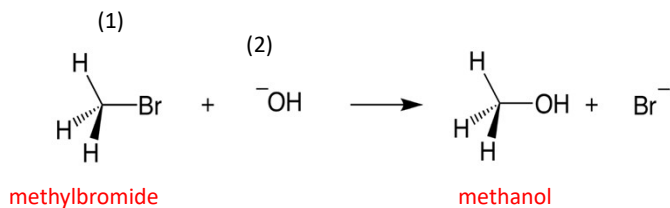
The reactivity of the nucleophile has no effect on the rate of a $\text{S}_{\text{N}}1$ reaction

The weaker base is the leaving group, the less tightly it is bonded to the carbon and the easier it is to break the bond.

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Substitution Reaction with Halides



If concentration of (1) is doubled, the rate of the reaction is doubled.

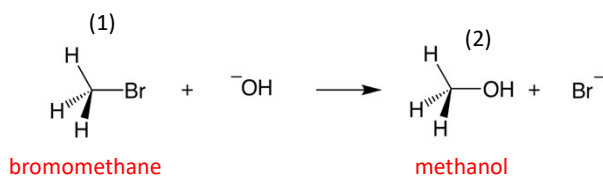
If concentration of (1) **and** (2) is doubled, the rate of the reaction quadruples.

If concentration of (2) is doubled, the rate of the reaction is doubled.

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Substitution Reaction with Halides



Rate law:

$$\text{rate} = k [\text{bromoethane}][\text{OH}^-]$$

this reaction is an example of a $\text{S}_{\text{N}}2$ reaction.

S stands for **substitution**

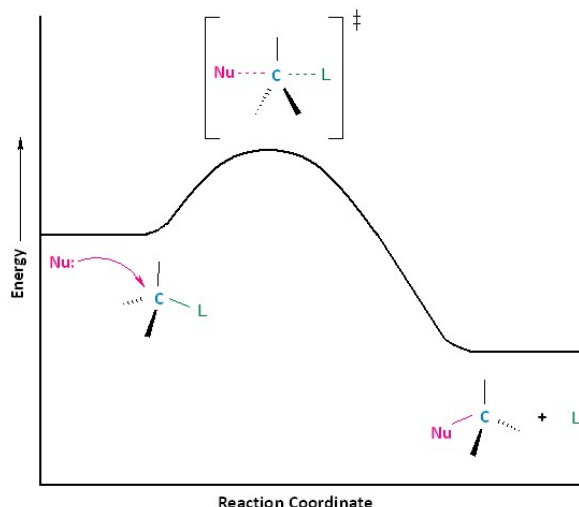
N stands for **nucleophilic**

2 stands for **bimolecular**

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Mechanism of S_N2 Reaction



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Mechanism



- ☐ Energy required to reach the transition state comes from the **energy with which the nucleophile and the alkyl halide collide.**
- ☐ The requirement for a collision also means that the **frequency with which the nucleophile and the alkyl halide collide** is important. This frequency is primarily controlled by **concentration.**
- ☐ Overall, the **rate depends on the concentration of both reactants**, and the reaction is said to be second order. This can be summarized in the rate equation or rate law.

$$\text{Rate} = k[\text{RX}][\text{Nu}^-]$$

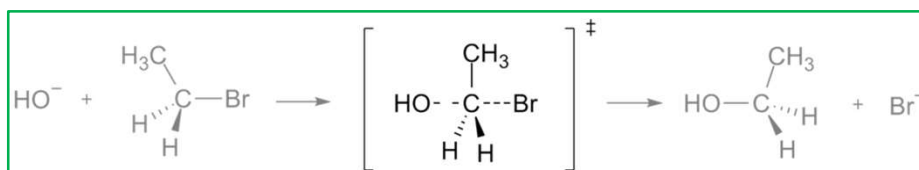
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Mechanism of S_N2 Reaction



Hughes and Ingold proposed the following mechanism:



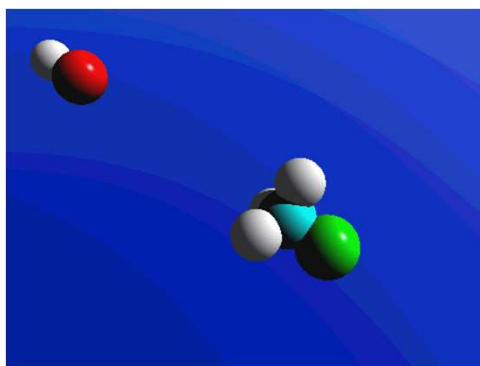
Transition state

Increasing the concentration of either of the reactant makes their collision more probable.

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Mechanism of S_N2 Reaction



A consequence of the concerted, bimolecular nature of the S_N2 reaction is that the **nucleophile must attack from the side of the molecule opposite to the leaving group**. This geometry of reaction is called back side attack.

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Mechanism of S_N2 Reaction

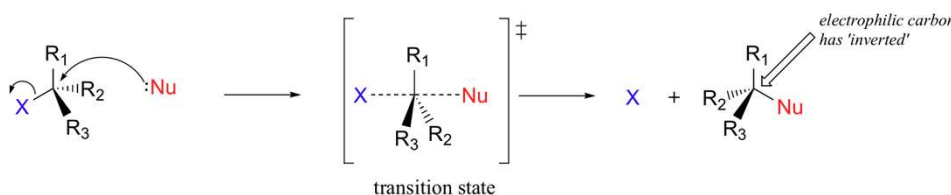


- ❑ **Breaking of the C–X bond and the formation of the new bond** (often denoted **C–Y or C–Nu**) occur **simultaneously**
- ❑ Transition state in which a carbon under nucleophilic attack is pentacoordinate, and **approximately sp² hybridised**
- ❑ The nucleophile **attacks the carbon at 180°** to the leaving group, since this provides the **best overlap between the nucleophile's lone pair and the C–X σ* antibonding orbital**
- ❑ The leaving group is then pushed off the opposite side and the product is formed **with inversion of the tetrahedral geometry at the central atom**

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Mechanism of S_N2 Reaction

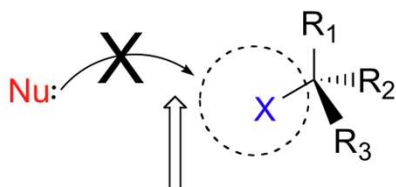


- ❑ The result of this backside attack is that the **stereochemical configuration at the central carbon inverts** as the reaction proceeds. In a sense, the molecule is turned inside out.
- ❑ At the transition state, **the electrophilic carbon and the three 'R' substituents all lie on the same plane.**

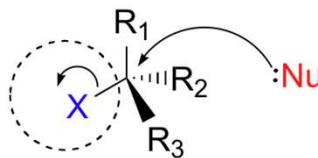
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Mechanism of S_N2 Reaction



*nucleophilic attack is blocked
from the front side . . .*



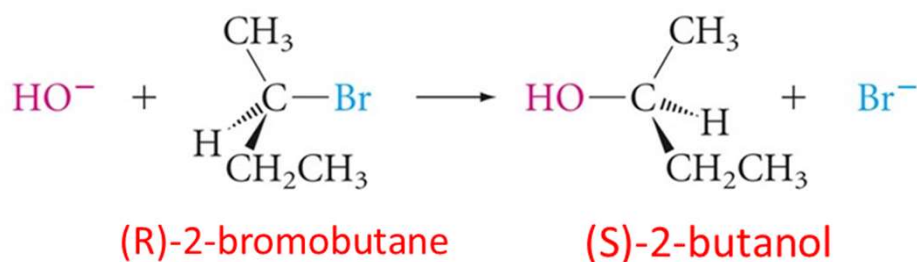
. . .so attack occurs from the back side

- ❑ The nucleophile, **being an electron-rich species**, must attack the electrophilic carbon from the **back side** relative to the location of the leaving group.
- ❑ Approach from the front side simply doesn't work: the leaving group - which is also an **electron-rich group - blocks the way**.

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Mechanism of S_N2 Reaction



Inversion of configuration

Substrate under nucleophilic attack is chiral, then this often leads to inversion of configuration (stereochemistry), called a **Walden inversion**

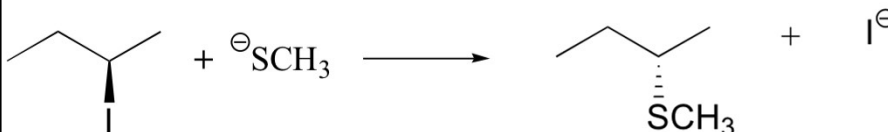
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Mechanism



- Predict the structure of the product in this S_N2 reaction. Be sure to specify stereochemistry.



The leaving group (I) was pointing out of the plane of the page, while the nucleophile (CH_3S^-) attacks from behind, and ends up pointing into the plane of the page.

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Mechanism of S_N2 Reaction, rates



The rate of reaction depends on the **concentrations of both reactants**.

When the hydrogens of bromomethane are replaced with **methyl groups** the **reaction rate slow down**.

The reaction of an alkyl halide in which the halogen is bonded to an **asymmetric centre** leads to the **formation of only one stereoisomer**

Alkyl halide	Relative rate
	1200
	40
	1
	≈ 0

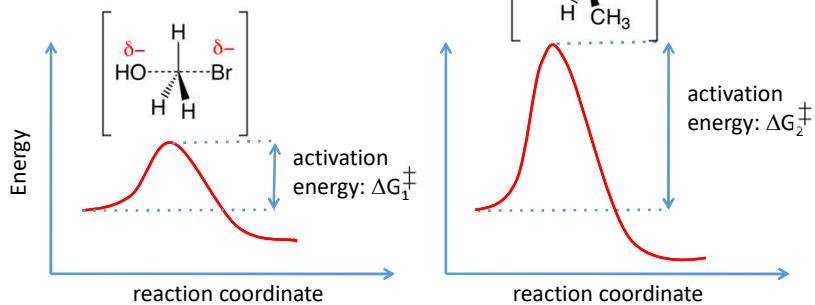
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Mechanism of S_N2 Reaction



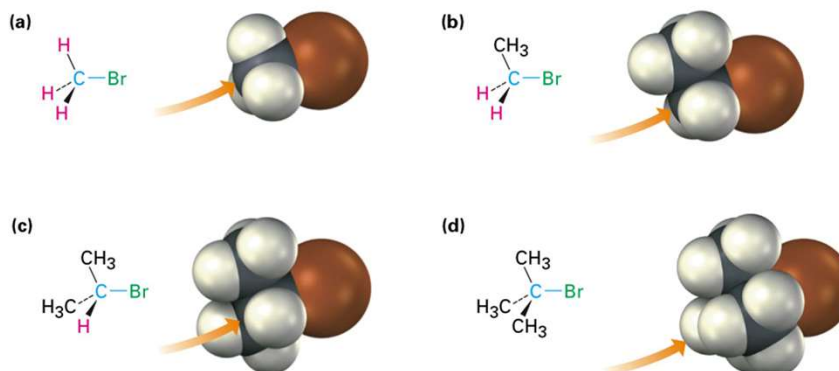
Steric effect



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Mechanism of S_N2 Reaction



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Factors affecting S_N2 reactions



The leaving group

	relative rates of reaction
$\text{HO}^- + \text{RCH}_2\text{I} \longrightarrow \text{RCH}_2\text{OH} + \text{I}^-$	30 000
$\text{HO}^- + \text{RCH}_2\text{Br} \longrightarrow \text{RCH}_2\text{OH} + \text{Br}^-$	10 000
$\text{HO}^- + \text{RCH}_2\text{Cl} \longrightarrow \text{RCH}_2\text{OH} + \text{Cl}^-$	200
$\text{HO}^- + \text{RCH}_2\text{F} \longrightarrow \text{RCH}_2\text{OH} + \text{F}^-$	1

The nucleophile

In general, for halogen substitution the **stronger the base the better the nucleophile**.

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Factors Affecting S_N2 Reactions, Solvent



Example - Protic Solvent



Example - Aprotic Solvent

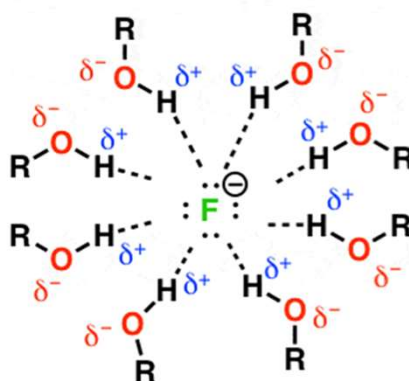


The use of **protic solvents** (those, such as water or alcohols, with hydrogen-bond donating capability) **decreases the power of the nucleophile**, because of strong **hydrogen-bond interactions between solvent protons and the reactive lone pairs on the nucleophile**.

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Role of solvent



- Partial **positive charges on hydrogen are attracted to the partial negative charges** on the electronegative atoms.
- Hydrogen bonding solvents **surround negatively charged ions like a jacket.**
- Nucleophiles are made less nucleophilic! The **propensity to form hydrogen bonds is highest for small, highly electronegative ions such as fluorine and decreases as ions get larger** (and the charge is more diffuse).

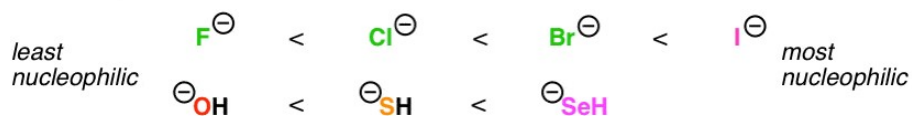
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Role of solvent, protic solvents



Recall that the order of nucleophilicity in polar protic solvents **increases** going **down** the periodic table:



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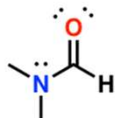
Role of solvent, aprotic solvents



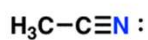
Polar aprotic solvents cannot hydrogen-bond with nucleophiles



Acetone



N,N-Dimethylformamide (DMF)



Acetonitrile (CH_3CN)

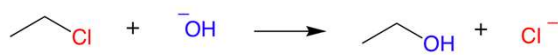


Dimethyl sulfoxide (DMSO)

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$\text{S}_{\text{N}}2$ Reactions With Alkyl Halides



an alcohol



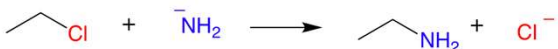
a thiol



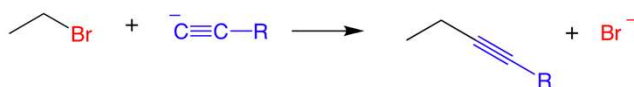
an ether



a thioether



an amine



an alkyne



a nitrile

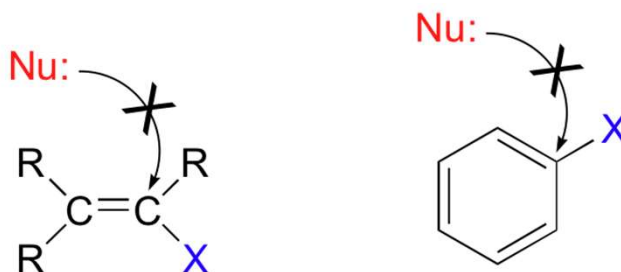
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No reaction – Why ?



- ❑ Nucleophilic substitutions as a rule occur at **sp³-hybridized carbons, and *not* where the leaving group is attached to an sp²-hybridized carbon::**



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- ❑ Bonds on sp²-hybridized carbons are inherently shorter and stronger than bonds on sp³-hybridized carbons, meaning that it is **harder to break the C-X bond in these substrates.**
- ❑ In addition, **sp² carbons are more electronegative, and therefore less electrophilic (δ⁺) than sp³ carbons.**
- ❑ S_N2 reactions of this type are unlikely also because the (hypothetical) **electrophilic carbon is protected** from nucleophilic attack by **electron density in the pi bond.**
- ❑ S_N1 reactions are highly unlikely, because the resulting **carbocation intermediate, which would be sp-hybridized, would be very unstable.**

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Summary, Comparison S_N1 & S_N2



S_N1	S_N2
A two-step mechanism	A one-step mechanism
A unimolecular rate-determining step	A bimolecular rate-determining step
Products have both retained and inverted configuration relative to the reactant	Product has inverted configuration relative to the reactant
Reactivity order: $3^\circ > 2^\circ > 1^\circ > \text{methyl}$	Reactivity order: $\text{methyl} > 1^\circ > 2^\circ > 3^\circ$

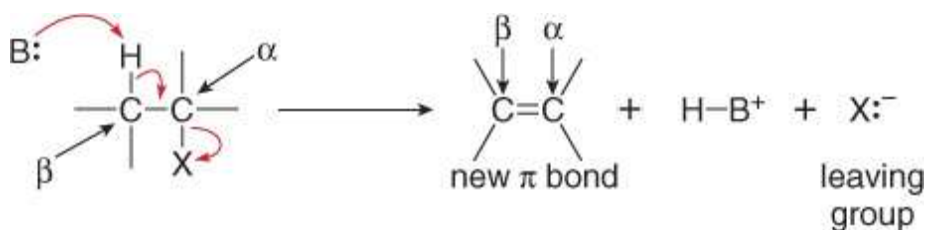
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Elimination Reaction



- ❑ Elimination reactions involve the loss of elements from the starting material to form a new π bond in the product
- ❑ Removal of the elements **HX** is called **dehydrohalogenation**
- ❑ Dehydrohalogenation is an example of β elimination
- ❑ Generalized mechanism is shown



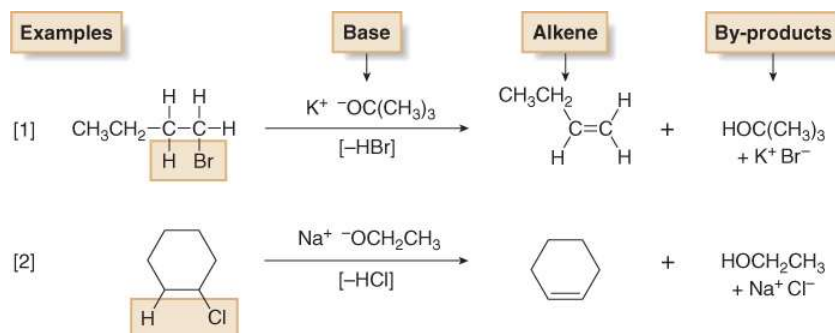
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Elimination Reactions, examples



In both reactions a **base removes the elements of an acid, HX**, from the organic starting material



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Elimination Reactions, bases used



- ❑ The most common bases used in elimination reactions are negatively charged **oxygen compounds, such as HO^- and its alkyl derivatives, RO^- , called alkoxides**

Common Bases Used in Dehydrohalogenation

$\text{Na}^+ \text{ } ^-\text{OH}$	sodium hydroxide
$\text{K}^+ \text{ } ^-\text{OH}$	potassium hydroxide
$\text{Na}^+ \text{ } ^-\text{OCH}_3$	sodium methoxide
$\text{Na}^+ \text{ } ^-\text{OCH}_2\text{CH}_3$	sodium ethoxide
$\text{K}^+ \text{ } ^-\text{OC(CH}_3)_3$	potassium <i>tert</i> -butoxide

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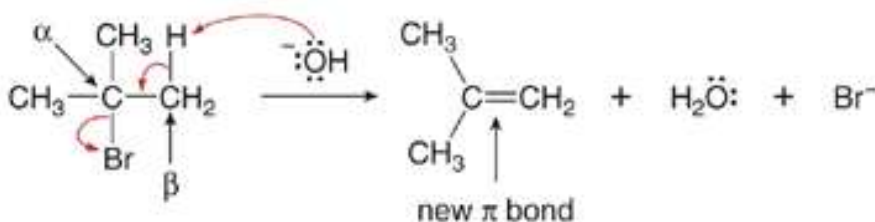
Mechanisms of Elimination

- ❑ There are two mechanisms of elimination—E2 and E1, just as there are two mechanisms of substitution, S_N2 and S_N1
- ❑ **E2 mechanism—bimolecular elimination**
- ❑ **E1 mechanism—unimolecular elimination**
- ❑ The E2 and E1 mechanisms **differ in the timing of bond cleavage and bond formation**, analogous to the S_N2 and S_N1 mechanisms
- ❑ E2 and S_N2 reactions have some features in common, as do E1 and S_N1 reactions

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E2 reaction, mechanism



- The base :OH^- removes a proton from the β carbon, forming H_2O (a by-product).
- The electron pair in the β C–H bond forms the new π bond.
- The leaving group Br^- comes off with the electron pair in the C–Br bond.

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E2 reaction, mechanism



❑ The **most common mechanism** for dehydrohalogenation is the E2 mechanism

❑ It exhibits **second-order kinetics**, and both the alkyl halide and the base appear in the rate equation, i.e.,

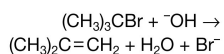
$$\text{rate} = k[(\text{CH}_3)_3\text{CBr}][^-\text{OH}]$$

❑ The reaction is **concerted**—all bonds are broken and formed in a single step

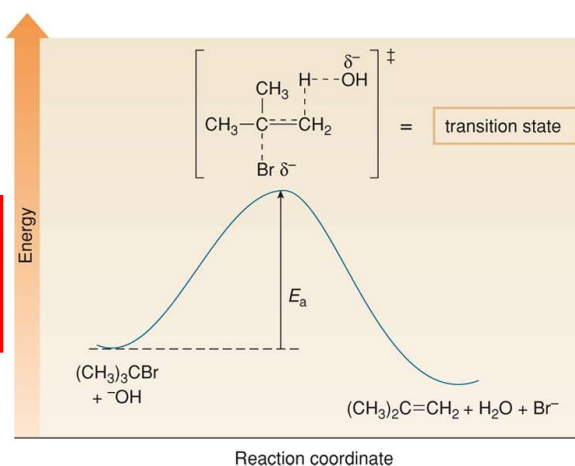
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E2 reaction, transition state



- In the transition state, the C–H and C–Br bonds are partially broken, the O–H and π bonds are partially formed, and both the base and the departing leaving group bear a partial negative charge.



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E2 reaction, rate dependence on base



- ❑ There are close parallels between E2 and S_N2 mechanisms in how the identity of the **base, the leaving group and the solvent affect the rate**
- ❑ The base appears in the rate equation, so the rate of the E2 reaction increases as the strength of the base increases
- ❑ E2 reactions are generally run with strong, negatively charged bases like ⁻OH and ⁻OR.

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E2 reaction, order of reactivity



Order of reactivity
of RX:

R-F

R-Cl

R-Br

R-I

- Because the bond to the leaving group is partially broken in the transition state, the better the leaving group the faster the E2 reaction.

Order of reactivity
of RX:

R-F

R-Cl

R-Br

R-I

Increasing leaving group ability
Increasing rate of the E2 reaction

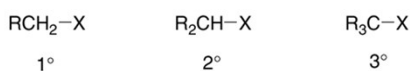
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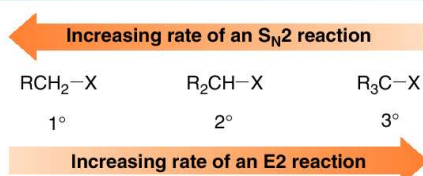
E2 reaction, order of reactivity



- The S_N2 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.



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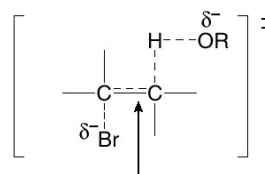
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E2 reaction, order of reactivity



- ❑ The increase in E2 reaction rate with increasing alkyl substitution can be rationalized in terms of transition state stability.
- ❑ In the transition state, the **double bond is partially formed**. Thus, increasing the stability of the double bond with alkyl substituents stabilizes the transition state (i.e., **lowers E_a , which increases the rate of the reaction**).

Transition state for an E2 reaction with an alkoxide ^-OR as base

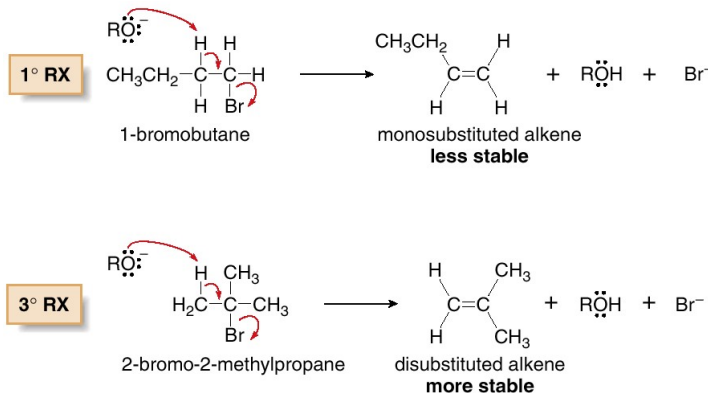


The double bond is partially formed.

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E2 reaction, order of reactivity



- ☐ Increasing the number of R groups on the carbon with the leaving group forms more highly substituted, more stable alkenes in E2 reactions.
- ☐ In the reactions below, since the disubstituted alkene is more stable, the **3° alkyl halide reacts faster than the 1° alkyl halide.**

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Alkene stability



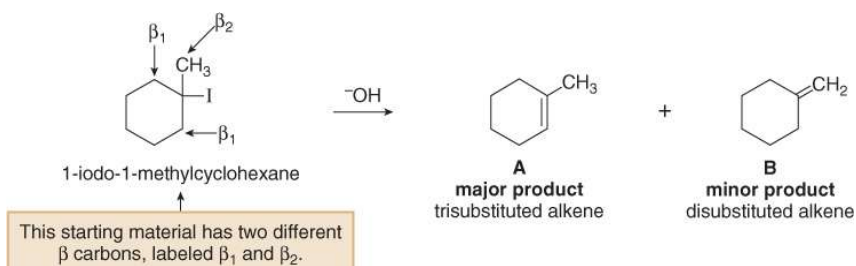
- ☐ **Saytzeff's Rule:** The **more highly substituted an alkene is, the more stable it is.** In other words, **alkyl groups attached to the double bonded carbons stabilize the alkene.**
- ☐ The **two probable factors** responsible for the stabilizing effect of alkyl groups to the double bond are the **contribution of electron density to the pi bond by the alkyl groups,** and the **increased separation of bulky groups from one another (120° bond angle) in alkenes.**
- ☐ In general, **trans isomers are more stable than cis isomers because of decreased steric interactions.**

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The Zaitsev (Saytzeff) Rule

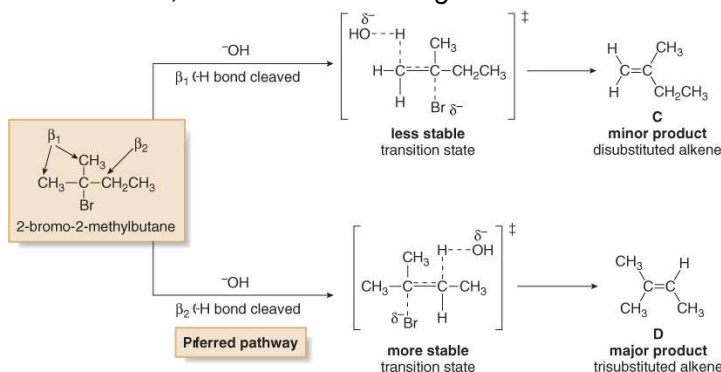
- ❑ Recall that when **alkyl halides have two or more different β carbons**, **more than one alkene product** is formed
- ❑ When this happens, one of the products usually predominates
- ❑ The **major product is the more stable product**—the one with the more substituted double bond
- ❑ This phenomenon is called the Zaitsev rule



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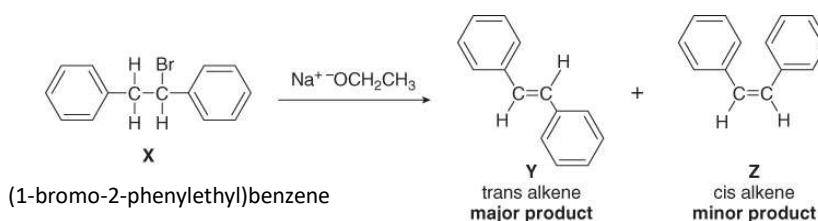
- ❑ The Zaitsev rule: the major product in β elimination has the more substituted double bond
- ❑ A reaction is **regioselective** when it yields **predominantly or exclusively one constitutional isomer** when more than one is possible. Thus, the E2 reaction is regioselective



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- ❑ When a mixture of stereoisomers is possible from a dehydrohalogenation, the major product is the more stable stereoisomer
- ❑ A reaction is **stereoselective** when it forms **predominantly or exclusively one stereoisomer** when two or more are possible.
- ❑ The E2 reaction is stereoselective because one stereoisomer is formed preferentially



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Characteristics of E2 Elimination

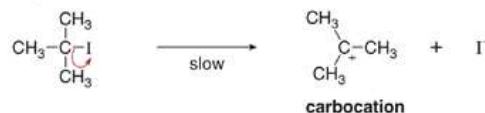
Kinetics	• Second order
Mechanism	• One step
Identity of R	• More substituted halides react fastest
	• Rate: $\text{R}_3\text{CX} > \text{R}_2\text{CHX} > \text{RCH}_2\text{X}$
Base	• Favored by strong bases
Leaving group	• Better leaving group \rightarrow faster reaction
Solvent	• Favored by polar aprotic solvents

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Mechanisms of Elimination—E1

Step [1] The C–I bond is broken.



Step [2] A C–H bond is cleaved and the π bond is formed.



- **Heterolysis of the C–I bond** forms an intermediate **carbocation**. This is the same first step as the S_N1 mechanism. It is responsible for the first-order kinetics because it is rate-determining.

- A **base** (such as H_2O or I^-) **removes a proton from a carbon adjacent to the carbocation** (a β carbon). The electron pair in the C–H bond is used to form the new π bond.

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Mechanisms of Elimination—E1

❑ The **dehydrohalogenation of $(CH_3)_3CI$ with H_2O** to form $(CH_3)_2C=CH_2$ can be used to illustrate the second general mechanism of elimination, the E1 mechanism.

❑ An E1 reaction exhibits first-order kinetics:

$$\text{rate} = k[(CH_3)_3CI]$$

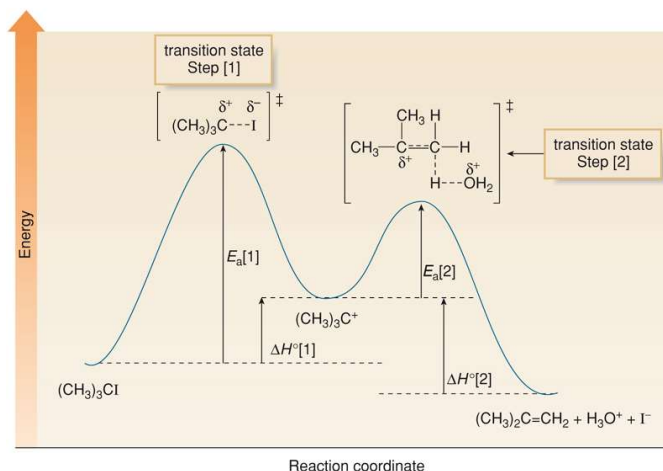
❑ **The E1 reaction proceeds via a two-step mechanism:** the bond to the leaving group breaks first before the π bond is formed. The slow step is **unimolecular**, involving only the alkyl halide.

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Figure 8.6
 Energy diagram
 for an E1 reaction:
 $(\text{CH}_3)_3\text{CI} + \text{H}_2\text{O} \rightarrow$
 $(\text{CH}_3)_2\text{C}=\text{CH}_2 + \text{H}_3\text{O}^+ + \text{I}^-$

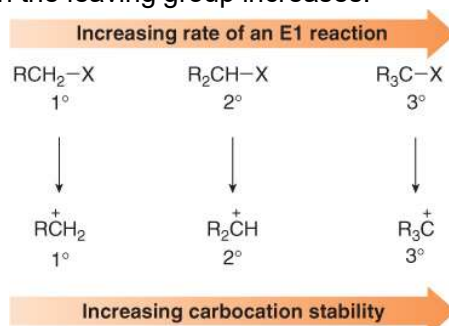
- Since the E1 mechanism has two steps, there are two energy barriers.
- Step [1] is rate-determining; $E_a[1] > E_a[2]$ making the transition state for Step [1] higher in energy.



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

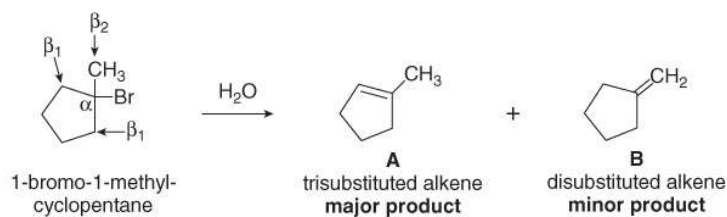


- ❑ The strength of the base usually determines whether a reaction follows the E1 or E2 mechanism. **Strong bases like OH^- and OR^- favor E2 reactions, whereas weaker bases like H_2O and ROH favor E1 reactions.**

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- ❑ **E1 reactions are regioselective**, favoring formation of the more substituted, more stable alkene.
- ❑ **Zaitsev's rule** applies to E1 reactions also.



two different β carbons
labeled β_1 and β_2

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Characteristics of E1 Elimination

Kinetics	<ul style="list-style-type: none"> • First order
Mechanism	<ul style="list-style-type: none"> • Two steps
Identity of R	<ul style="list-style-type: none"> • More substituted halides react fastest • Rate: $R_3CX > R_2CHX > RCH_2X$
Base	<ul style="list-style-type: none"> • Favored by weaker bases such as H_2O and ROH
Leaving group	<ul style="list-style-type: none"> • A better leaving group makes the reaction faster because the bond to the leaving group is partially broken in the rate-determining step.
Solvent	<ul style="list-style-type: none"> • Polar protic solvents that solvate the ionic intermediates are needed.

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Mechanisms of Elimination—E1

- ❑ The E1 and E2 mechanisms both **involve the same number of bonds broken and formed.**

- ❑ The only difference is timing. In an E1, **the leaving group comes off before the β proton is removed, and the reaction occurs in two steps.**

- ❑ In an E2 reaction, **the leaving group comes off as the β proton is removed, and the reaction occurs in one step.**

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Table 9.1 Summary of Elimination Mechanisms

	E1	E2
Mechanism	Two steps $R-L \longrightarrow R^+ \longrightarrow \text{alkene}$	One step $R-L + B^- \longrightarrow \text{alkene} + BH + L^-$
Kinetics	First order rate = $k[RL]$	Second order rate = $k[RL][B^-]$
Competes with	S_N1	S_N2
Stereochemistry	No preferred conformation	Anti-periplanar elimination (<i>trans</i> -diaxial in cyclohexanes)
Regiochemistry	Zaitsev's rule: favors more highly substituted alkene	Zaitsev's rule: favors more highly substituted alkene (Hofman elimination follows Hofman's rule: favors less highly substituted alkene)
	Conjugated always preferred	Conjugated always preferred
Competition with Substitution	Some E1 always accompanies S_N1	E2 favored by strong bases, steric hindrance, and higher temperatures

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When is the Mechanism E1 or E2?

- The **strength of the base** is the most important factor in determining the mechanism for elimination. **Strong bases favor the E2 mechanism. Weak bases favor the E1 mechanism.**

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Table 8.4 A Comparison of the E1 and E2 Mechanisms

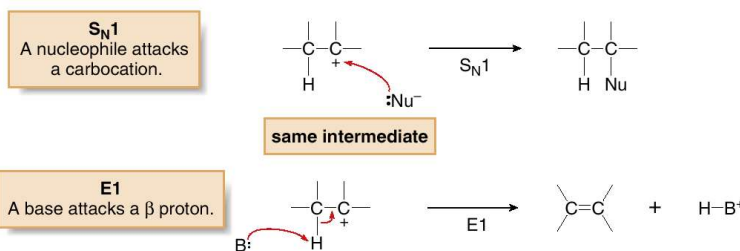
E2 mechanism	<ul style="list-style-type: none"> Much more common and useful. Favored by strong, negatively charged bases, especially OH^- and OR^-. The reaction occurs with 1°, 2°, and 3° alkyl halides. Order of reactivity: $\text{R}_3\text{CX} > \text{R}_2\text{CHX} > \text{RCH}_2\text{X}$.
E1 mechanism	<ul style="list-style-type: none"> Much less useful because a mixture of $\text{S}_\text{N}1$ and E1 products usually results. Favored by weaker, neutral bases, such as H_2O and ROH. This mechanism does not occur with 1° RX because they form highly unstable 1° carbocations.

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$\text{S}_\text{N}1$ and E1 Reactions

- $\text{S}_\text{N}1$ and E1 reactions have exactly the same first step—formation of a carbocation. They differ in what happens to the carbocation.



- In an $\text{S}_\text{N}1$ reaction, a nucleophile attacks the carbocation, forming a substitution product.
- In an E1 reaction, a base removes a proton, forming a new π bond.

- Because E1 reactions often occur with a competing $\text{S}_\text{N}1$ reaction, E1 reactions of alkyl halides are much less useful than E2 reactions.

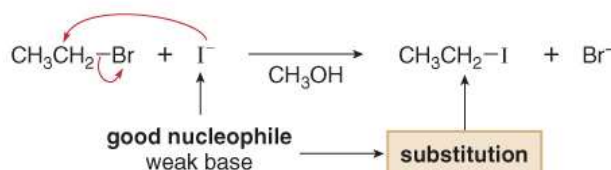
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Predicting the Mechanism from the Reactants—S_N1, S_N2, E1 or E2.



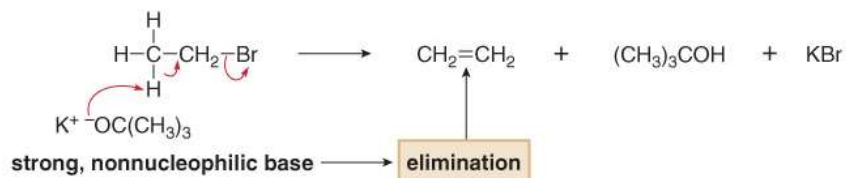
- **Good nucleophiles that are weak bases favor substitution over elimination**—Certain anions generally give products of substitution because they are good nucleophiles but weak bases. These include I[−], Br[−], HS[−], [−]CN, and CH₃COO[−].



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- **Bulky nonnucleophilic bases favor elimination over substitution**—KOC(CH₃)₃ is **too sterically hindered to attack** tetravalent carbon, but are **able to remove a small proton, favoring elimination over substitution**.



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General rules

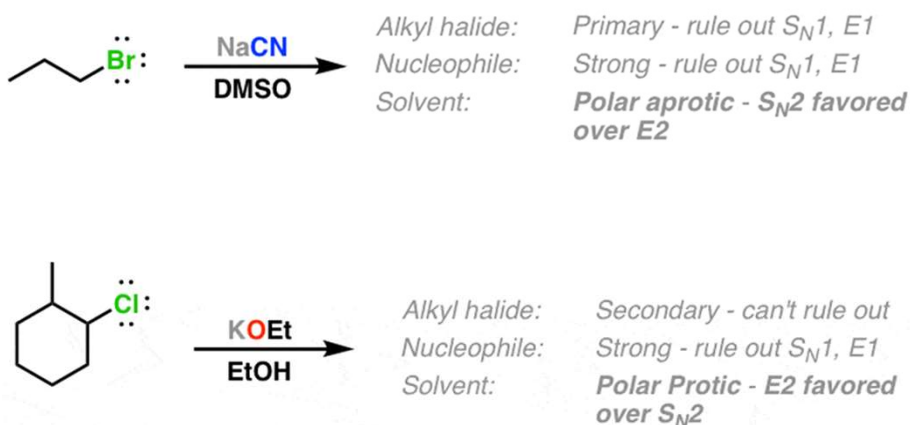


- ❑ For **Primary Carbons**, rule Out The **S_N1 and E1**. For **Tertiary Carbons**, rule out The **S_N2**
- ❑ If you see a **charged nucleophile/base**, you can **rule out carbocation formation (i.e. rule out $S_N1/E1$)**. In other words, the reaction will be **$S_N2/E2$** .
- ❑ If you **don't see a charged species present**, you're likely looking at a reaction that will go through a **carbocation (i.e. an S_N1 or E1)**.
- ❑ **Polar protic solvents tend to favor elimination (E2)** over substitution (S_N2). **Polar aprotic solvents tend to favor substitution (S_N2)** relative to elimination (E2)
- ❑ When **carbocations** are formed, at **low temperatures, the S_N1 pathway** will dominate over the E1 pathway. At **higher temperatures, more E1** products will be formed.

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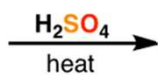
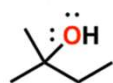
Examples



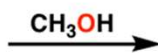
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Examples



Alkyl halide: Tertiary - rule out S_N2
 Nucleophile: Neutral - rule out S_N2 , E2
 Solvent: Polar Protic
 Temperature: **Heat: E1 favored over S_N1**

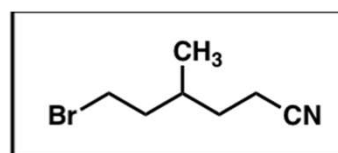
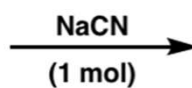
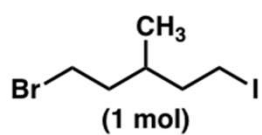


Alkyl halide: Tertiary - rule out S_N2
 Nucleophile: Neutral - rule out S_N2 , E2
 Solvent: Polar Protic
 Temperature: **No heat: S_N1 favored over E1**

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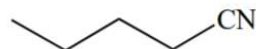
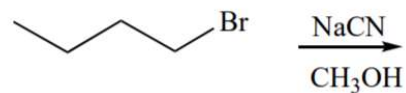
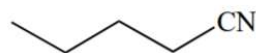
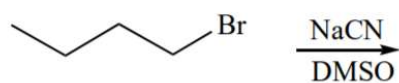
Examples



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Which will undergo faster reaction?

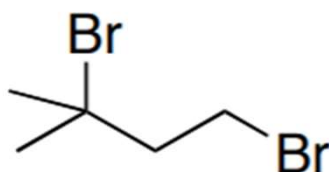


S_N2 reactions are faster in polar aprotic solvents like DMSO

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Examples

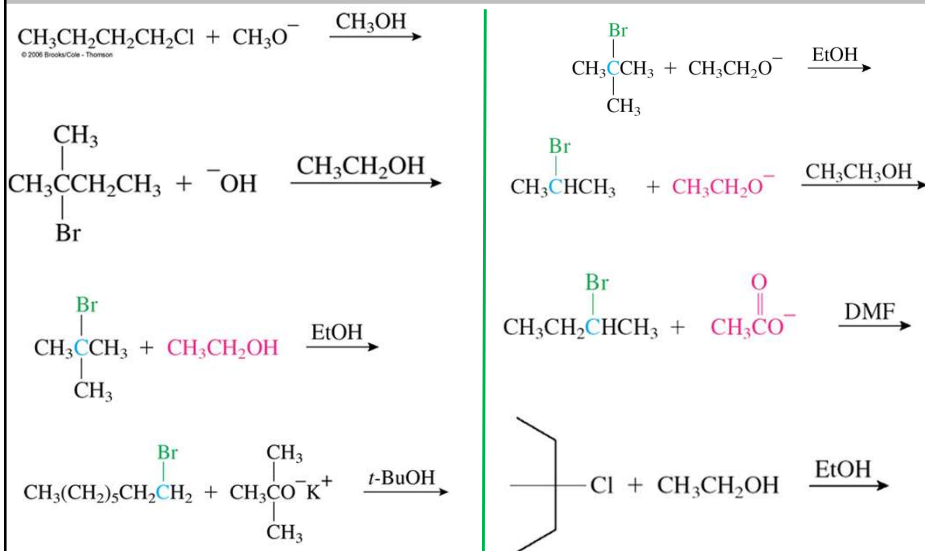


For the above dibromo alkane determine which position will react faster (be more reactive) under S_N1 and S_N2 conditions. Explain your answer.

3° fastest under S_N1 because carbocation
1° fastest under S_N2 because unhindered

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Problems - S_N1, S_N2, E1 or E2 ??

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Thank you all for your attention

Information presented here were collected from various sources – textbooks, articles, manuscripts, internet and newsletters. All the researchers and authors of the above mentioned sources are greatly acknowledged.