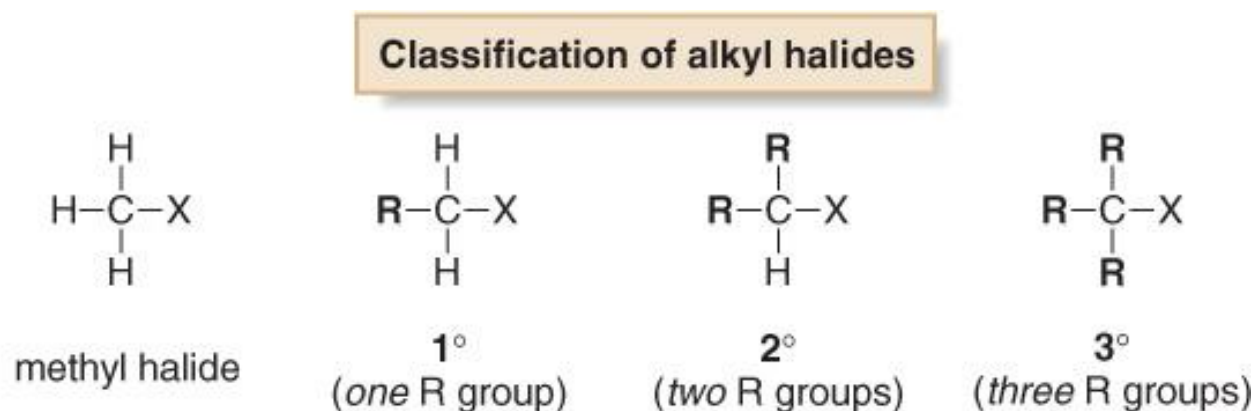
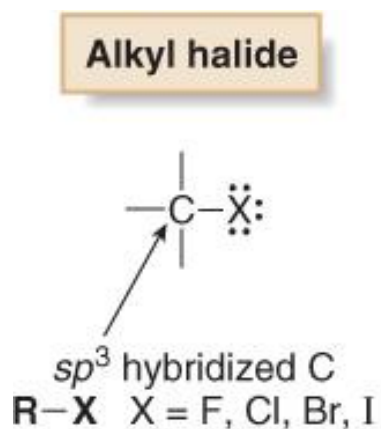


Alkyl Halides and Nucleophilic Substitution

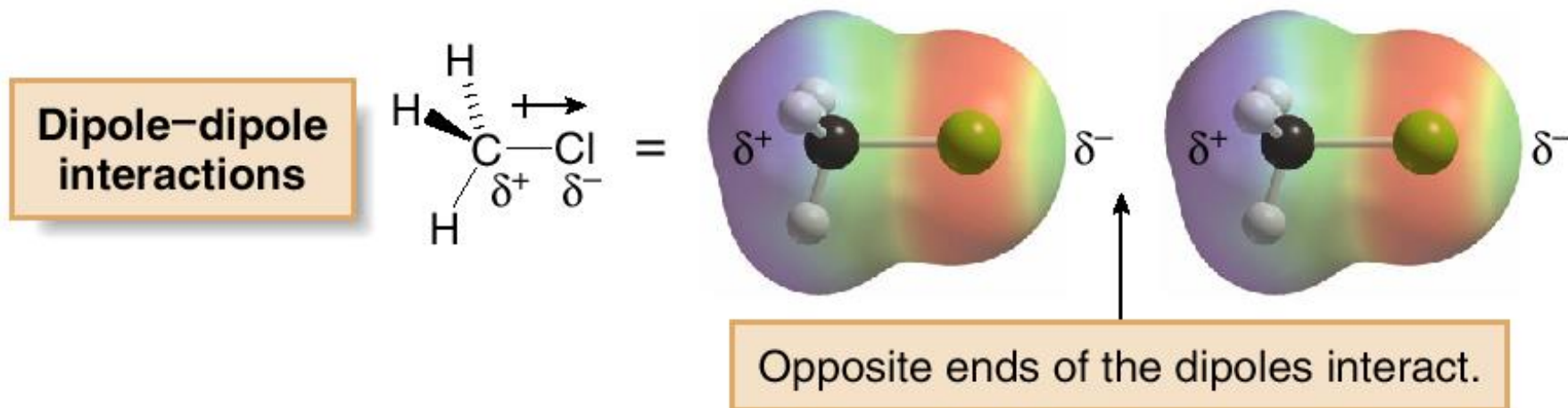
Introduction to Alkyl Halides:

- **Alkyl halides** are organic molecules containing a halogen atom bonded to an sp^3 hybridized carbon atom.
- Alkyl halides are classified as **primary** (1°), **secondary** (2°), or **tertiary** (3°), depending on the number of carbons bonded to the carbon with the halogen atom.
- The halogen atom in halides is often denoted by the symbol “X”.



Physical Properties:

- Alkyl halides are weak polar molecules. They exhibit dipole-dipole interactions because of their polar C—X bond, but because the rest of the molecule contains only C—C and C—H bonds, they are incapable of intermolecular hydrogen bonding.

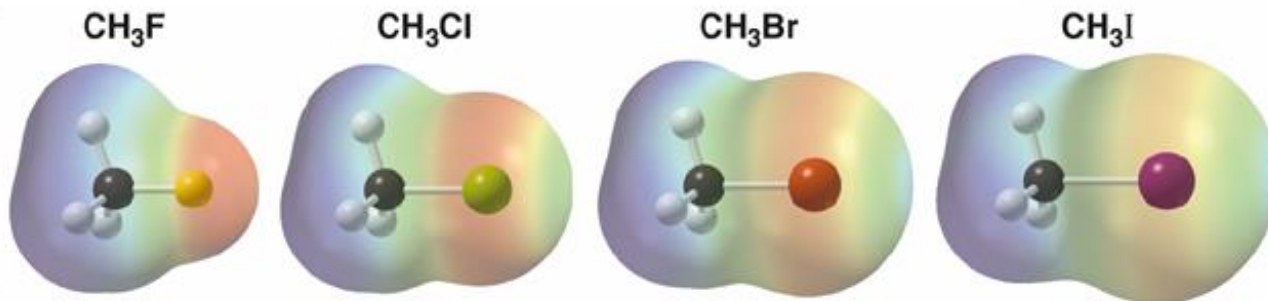
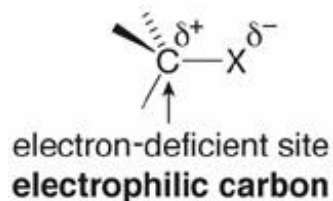


The Polar Carbon-Halogen Bond

- The electronegative halogen atom in alkyl halides creates a polar C—X bond, making the carbon atom electron deficient.

Electrostatic potential maps of four halomethanes (CH₃X)

General structure



- The polar C—X bond makes the carbon atom *electron deficient* in each CH₃X molecule.

Nucleophile (Nucleophile = “seeks a nucleus” Nucleus = + charge)

Lewis Bases – any species that has a lone pair of electrons.

The electrons can be used to make a new bond to an electron deficient species.

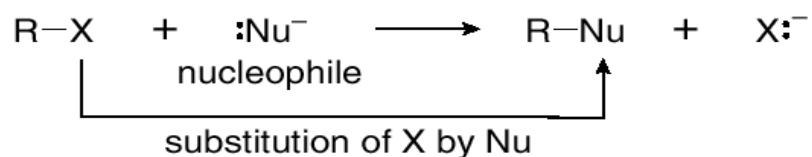
Nucleophilic substitution and elimination reactions Generally speaking, there are two things that can happen when a nucleophile ("Nu:-") encounters an alkyl halide:

The replacement of one of the groups (leaving group,) bonded to a carbon, by a electron-rich reagent, nucleophile, such as I⁻ or HO⁻

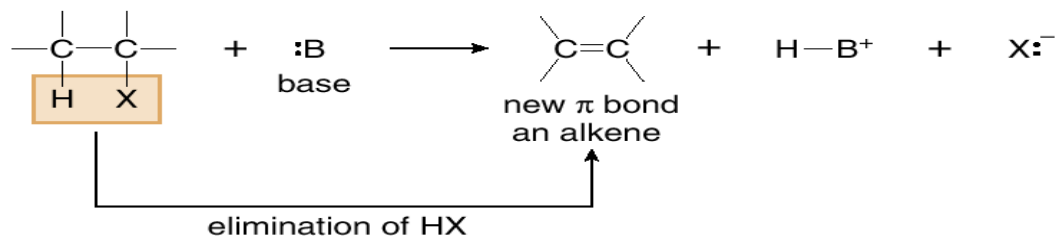
An electron-rich reagent, Nu, bonds to an H as HX is removed in a *elimination reaction*.

Nucleophile can act as a base, inducing "dehydrohalogenation" of the alkyl halide and producing an alkene.

- Alkyl halides undergo substitution reactions with nucleophiles.



- Alkyl halides undergo elimination reactions with Brønsted–Lowry bases.

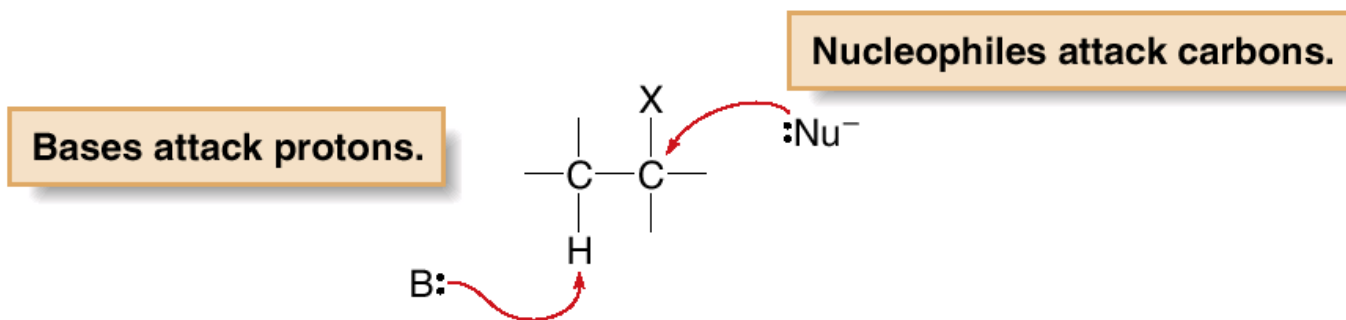


Alkyl Halides and Nucleophilic Substitution

The Nucleophile:

- **Nucleophiles and bases are structurally similar: both have a lone pair or a π bond. They differ in what they attack.**

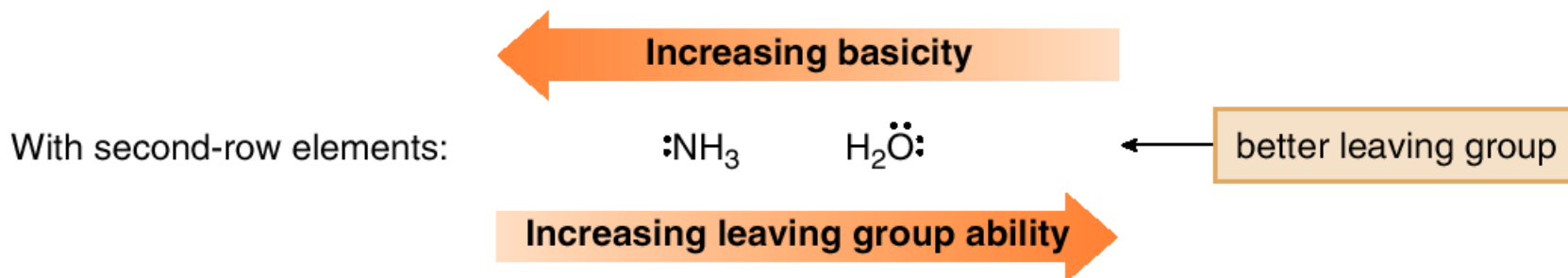
- Bases attack protons. Nucleophiles attack other electron-deficient atoms (usually carbons).



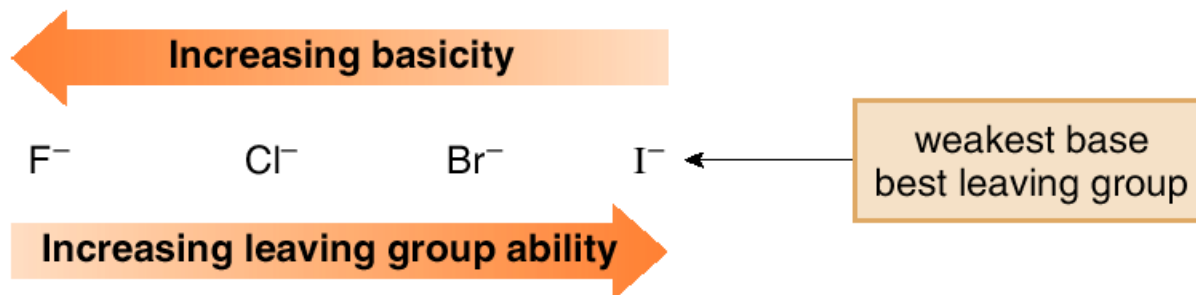
The Leaving Group (a review of basicity):

- There are periodic trends in leaving group ability:

- Left-to-right across a row of the periodic table, basicity *decreases* so leaving group ability *increases*.



- Down a column of the periodic table, basicity *decreases* so leaving group ability *increases*.



The Leaving Group:

Poor leaving groups for Nucleophilic Substitution

Starting material	Leaving group	Conjugate acid	pK _a
R-F	F ⁻	HF	3.2
R-OH	⁻ OH	H ₂ O	15.7
R-NH ₂	⁻ NH ₂	NH ₃	38
R-H	H ⁻	H ₂	35
R-R	R ⁻	RH	50

These molecules do *not* undergo nucleophilic substitution.

poor leaving groups

Strong bases

The Leaving Group

Good leaving groups for Nucleophilic Substitution

Starting material	Leaving group	Conjugate acid	pK_a
R-Cl	Cl^-	HCl	-7
R-Br	Br^-	HBr	-9
R-I	I^-	HI	-10
R-OH ₂ ⁺	H ₂ O	H ₃ O ⁺	-1.7

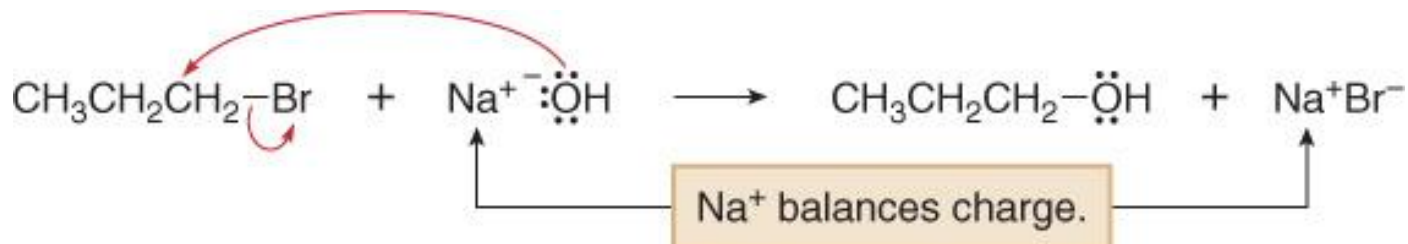
These molecules undergo nucleophilic substitution.

good leaving groups

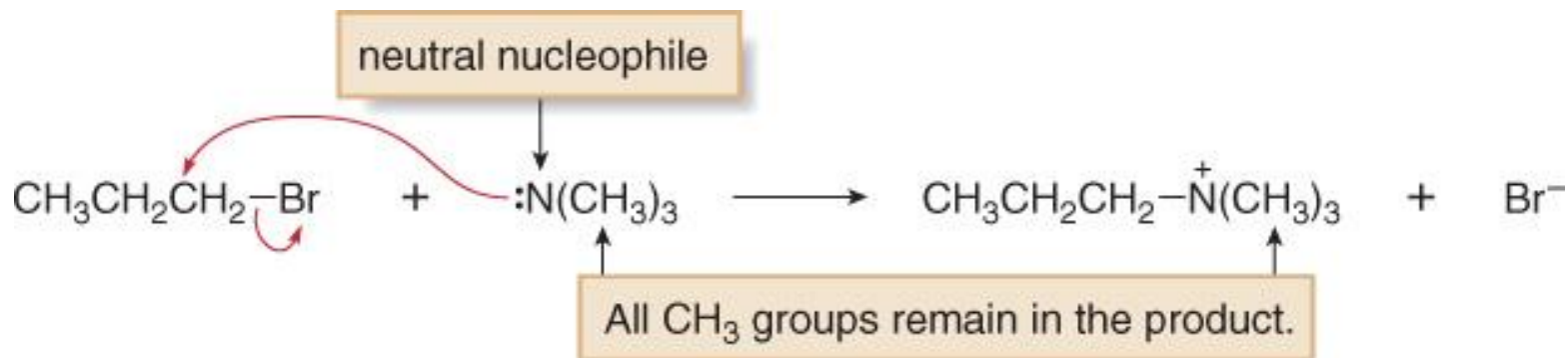
Weak bases

General Features of Nucleophilic Substitution:

- Negatively charged nucleophiles like HO^- and HS^- are used as salts with Li^+ , Na^+ , or K^+ counterions to balance the charge. Since the identity of the counterion is usually inconsequential, it is often omitted from the chemical equation.



- When a neutral nucleophile is used, the substitution product bears a positive charge.



The Nucleophile:

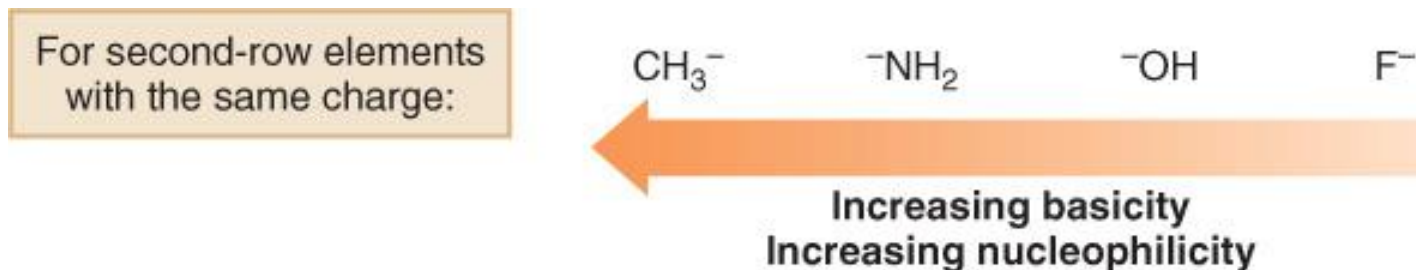
- Nucleophilicity parallels basicity in three instances:
 1. For two nucleophiles with the same nucleophilic atom, the stronger base is the stronger nucleophile.

The relative nucleophilicity of HO^- and CH_3COO^- , two oxygen nucleophiles, is determined by comparing the $\text{p}K_a$ values of their conjugate acids ($\text{H}_2\text{O} = 15.7$, and $\text{CH}_3\text{COOH} = 4.8$). HO^- is a stronger base and stronger nucleophile than CH_3COO^- .

2. A negatively charged nucleophile is always a stronger nucleophile than its conjugate acid.

HO^- is a stronger base and stronger nucleophile than H_2O .

3. Right-to-left-across a row of the periodic table, nucleophilicity increases as basicity increases:



Common Nucleophiles:

	Negatively charged nucleophiles			Neutral nucleophiles	
Oxygen	${}^{-}\text{OH}$	${}^{-}\text{OR}$	$\text{CH}_3\text{COO}^{-}$	H_2O	ROH
Nitrogen	N_3^{-}			NH_3	RNH_2
Carbon	${}^{-}\text{CN}$	$\text{HC}\equiv\text{C}^{-}$			
Halogen	Cl^{-}	Br^{-}	I^{-}		
Sulfur	HS^{-}	RS^{-}		H_2S	RSH

In the left box, all are strong nucleophiles except chloride and acetate which are medium.

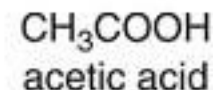
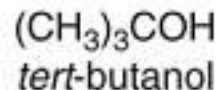
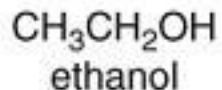
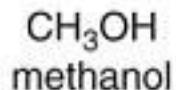
In the right box, HOH and ROH are weak, the others medium.

Solvent effect on the Nucleophile:

Polar protic solvent has a hydrogen atom attached to a strongly electronegative element (e.g. oxygen) that forms hydrogen bonds. **-Polar protic** solvent solvate cations and anions effectively while **aprotic solvents** do not solvate anions to any appreciable extend.

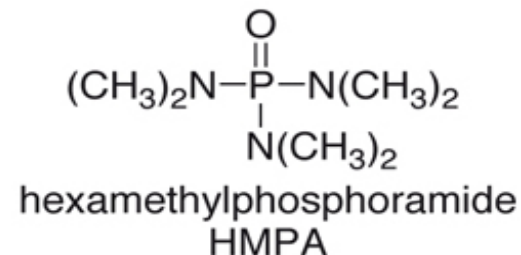
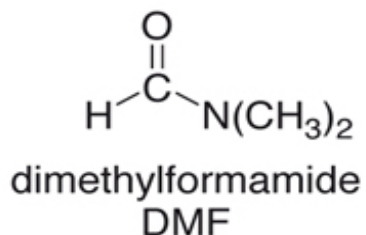
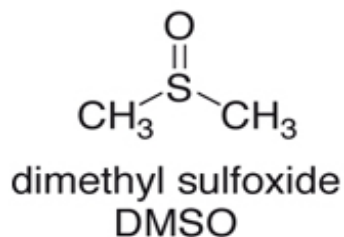
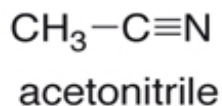
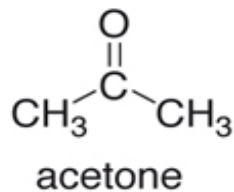
-Polar protic solvents are more suitable for S_N1 reactions, while **aprotic solvents** are used for S_N2 reactions

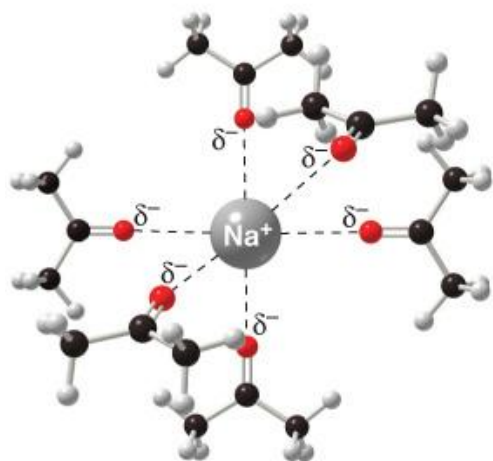
Example of polar protic solvents



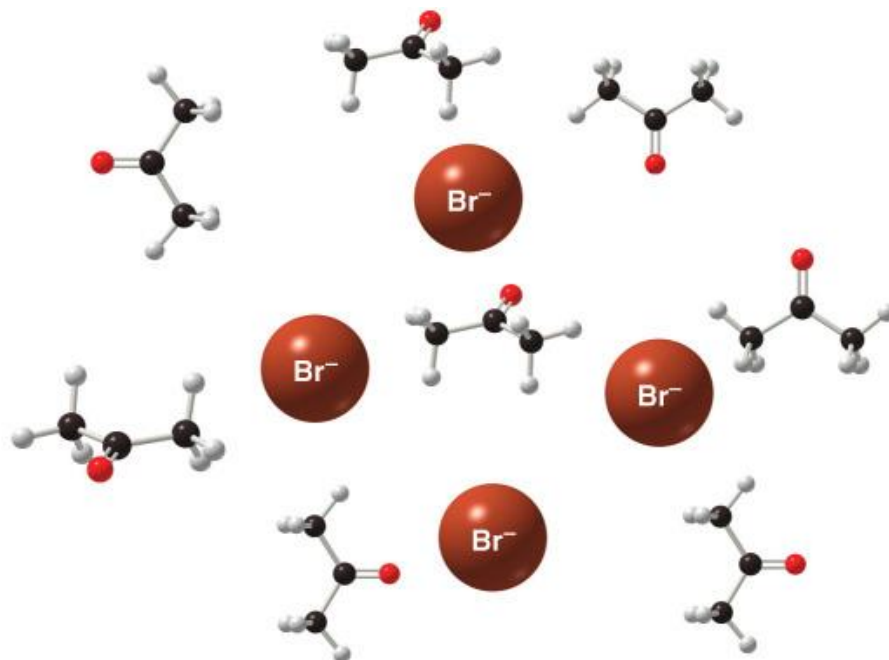
- Polar aprotic solvents are those solvents whose molecules do not have a hydrogen atom that's attached to an atom of an electronegative element. **Polar aprotic solvents** also exhibit dipole—dipole interactions, but they have no O—H or N—H bonds. Thus, they are incapable of hydrogen bonding.

Examples of polar aprotic solvents





$(\text{CH}_3)_2\text{C}=\text{O}$ solvates Na^+ well by ion-dipole interactions.

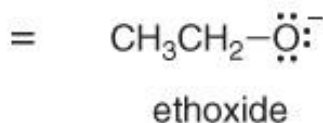
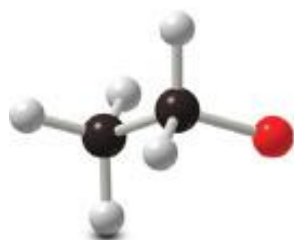


Br^- anions are surrounded by solvent but not well solvated by the $(\text{CH}_3)_2\text{C}=\text{O}$ molecules.

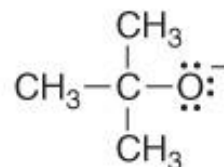
- In polar aprotic solvents, nucleophilicity parallels basicity, and the stronger base is the stronger nucleophile.
- Because basicity decreases as size increases down a column, nucleophilicity decreases as well. F highest nucleophilicity and I lowest

The Nucleophile:

- Nucleophilicity does not parallel basicity when steric hindrance becomes important.
- **Steric hindrance** is a decrease in reactivity resulting from the presence of bulky groups at the site of a reaction.
- Steric hindrance decreases nucleophilicity but not basicity.
- Sterically hindered bases that are poor nucleophiles are called **nonnucleophilic bases**.



stronger nucleophile



tert-butoxide

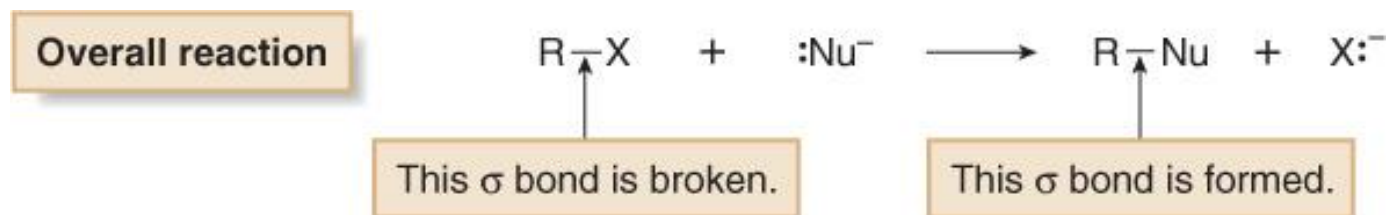
stronger base



Three CH_3 groups sterically hinder the O atom, making it a **weaker nucleophile**.

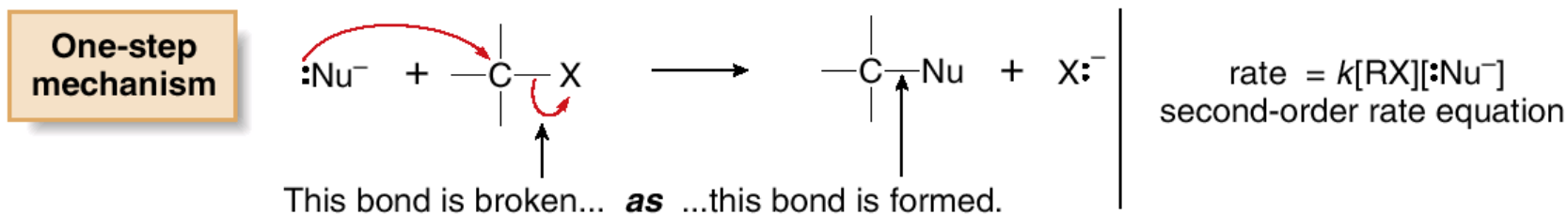
Mechanisms of Nucleophilic Substitution:

In a nucleophilic substitution:



But what is the order of bond making and bond breaking? In theory, there are three possibilities.

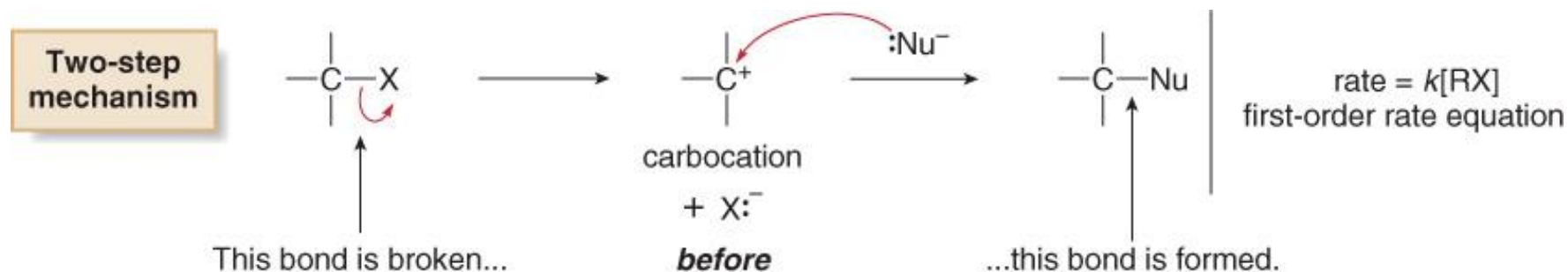
[1] Bond making and bond breaking occur at the same time.



In this scenario, the mechanism is comprised of one step. In such a bimolecular reaction, the rate depends upon the concentration of both reactants, that is, the rate equation is second order.

Mechanisms of Nucleophilic Substitution:

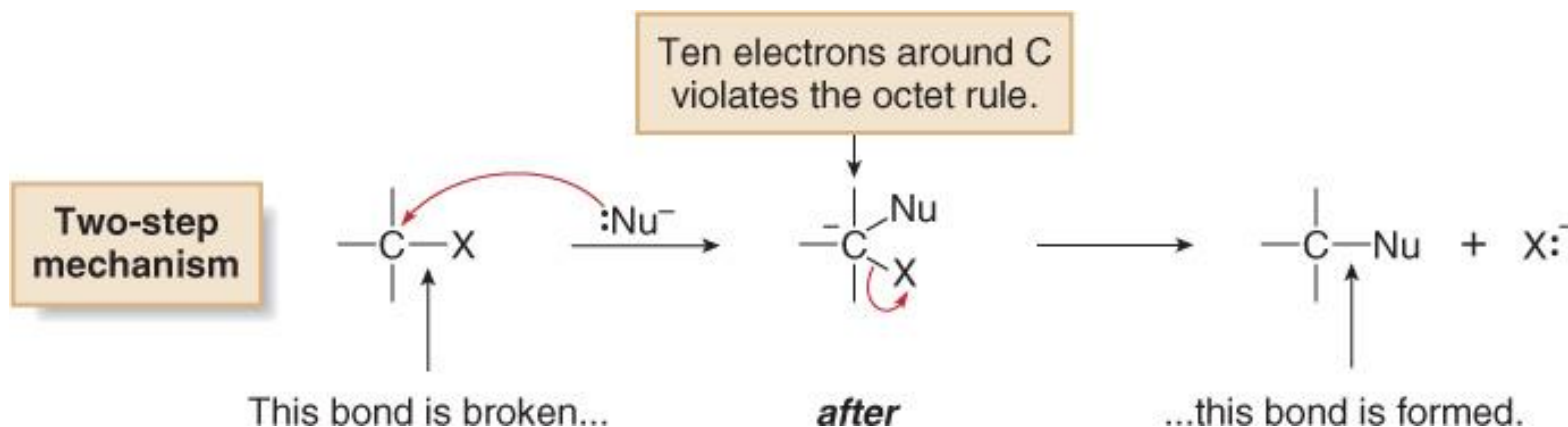
[2] Bond breaking occurs before bond making.



In this scenario, the mechanism has two steps and a carbocation is formed as an intermediate. Because the first step is rate-determining, the rate depends on the concentration of RX only; that is, the rate equation is first order.

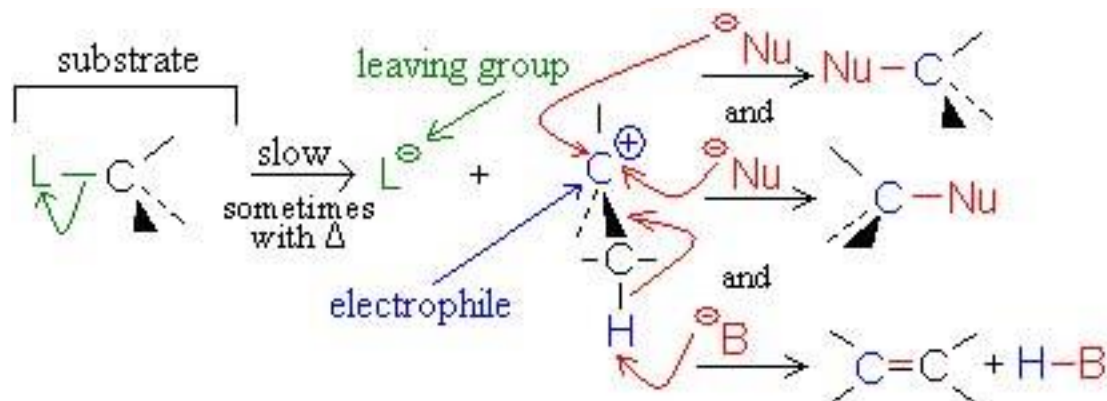
Mechanisms of Nucleophilic Substitution:

[3] Bond making occurs before bond breaking.



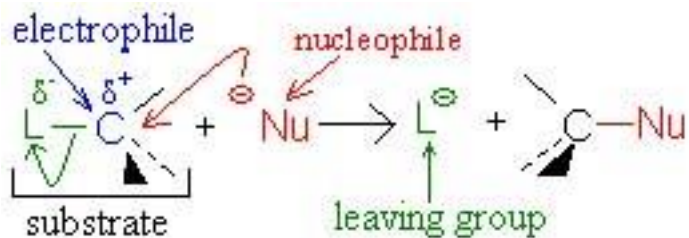
This mechanism has an inherent problem. The intermediate generated in the first step has 10 electrons around carbon, violating the octet rule. Because two other mechanistic possibilities do not violate a fundamental rule, this last possibility can be disregarded.

$S_N1/E1$

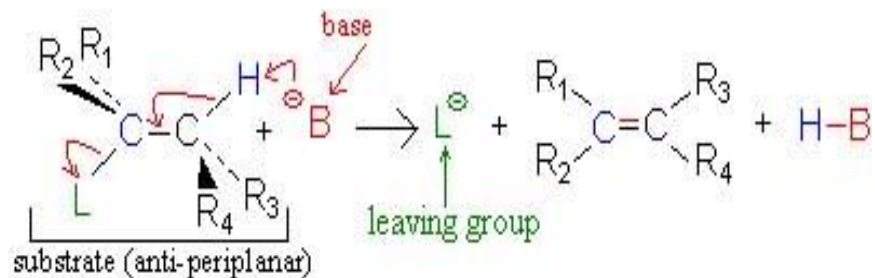


S_N1 and $E1$ have identical rate determining steps, so they generally occur simultaneously and have the same properties.

S_N2



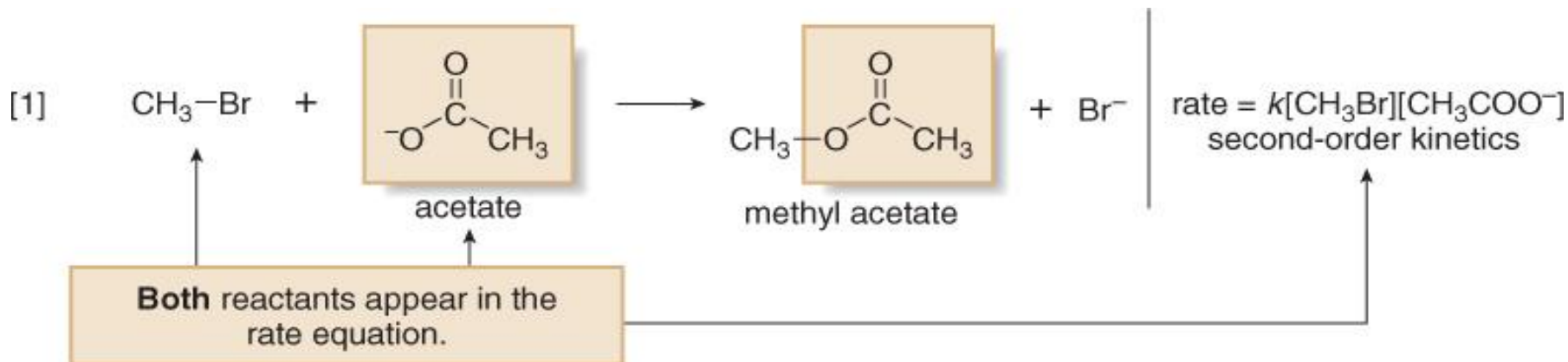
$E2$



Kinetics

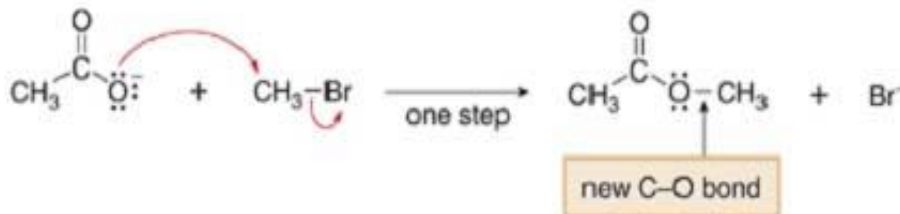
- If two molecules must come together in order for a reaction to take place, then the rate at which that reaction occurs will depend on the concentrations of both of these species. If this reaction is the slowest step (i.e., the "rate-determining step") in a series of steps leading to an overall transformation, or if it is the only step in the reaction, then that reaction will exhibit "bimolecular" or "second-order" kinetics.
- Both the S_N2 and E2 reactions exhibit bimolecular kinetics. That is, these reactions have "rate laws" that show the direct dependence of the reaction rate on the concentrations of both the alkyl halide and the nucleophile:
 - $\text{rate} = k[\text{RX}][\text{Nu}^-]$
- S_N1 and E1 reactions exhibit "unimolecular" kinetics, for which the rate depends only on the concentration of the alkyl halide, and not at all on the nucleophile. The different rate law for these reactions implies that they proceed by a different mechanism.

Mechanisms of Nucleophilic Substitution: S_N2 reaction



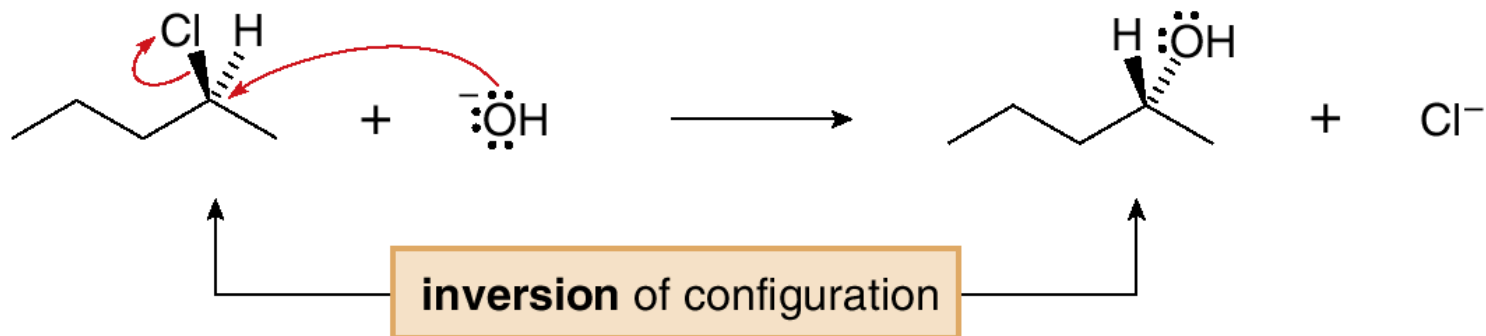
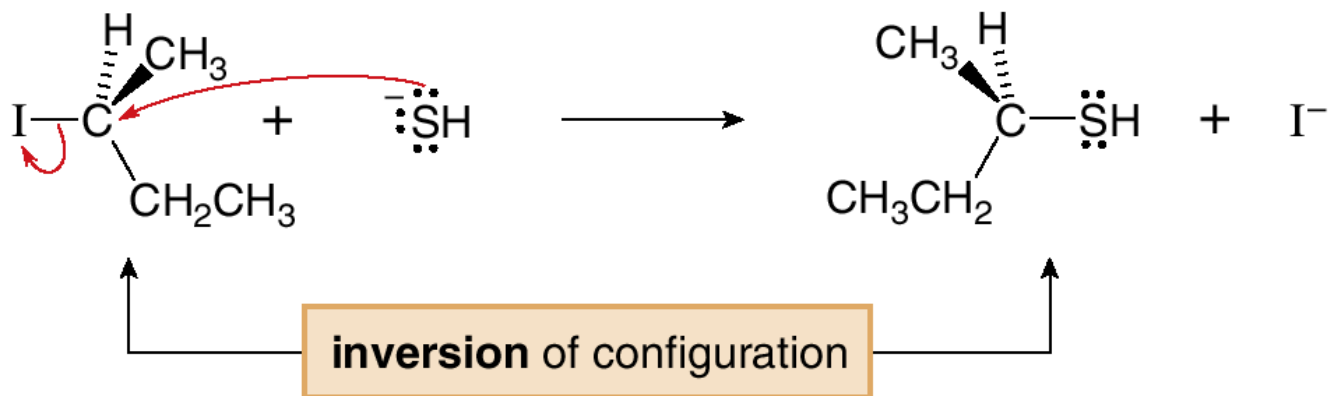
Kinetic data show that the rate of reaction depends on the concentration of both reactants, which suggests a bimolecular reaction with a one-step mechanism. This is an example of an S_N2 (substitution nucleophilic bimolecular) mechanism.

One step The C-Br bond breaks as the C-O bond forms.

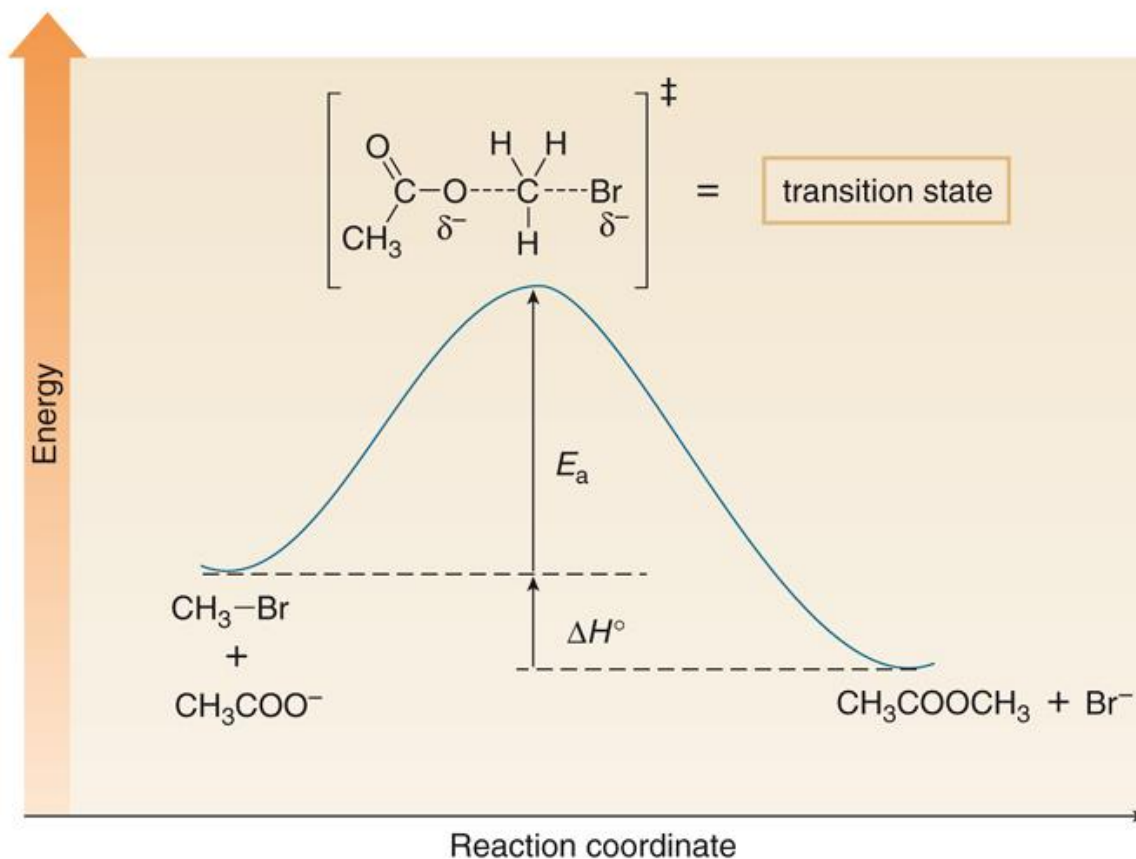
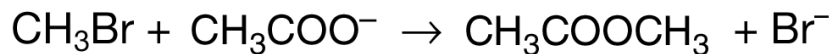


examples of S_N2 inversion of configuration: **The Walden Inversion.**

- The bond to the nucleophile in the product is always on the **opposite side** relative to the bond to the leaving group in the starting material.



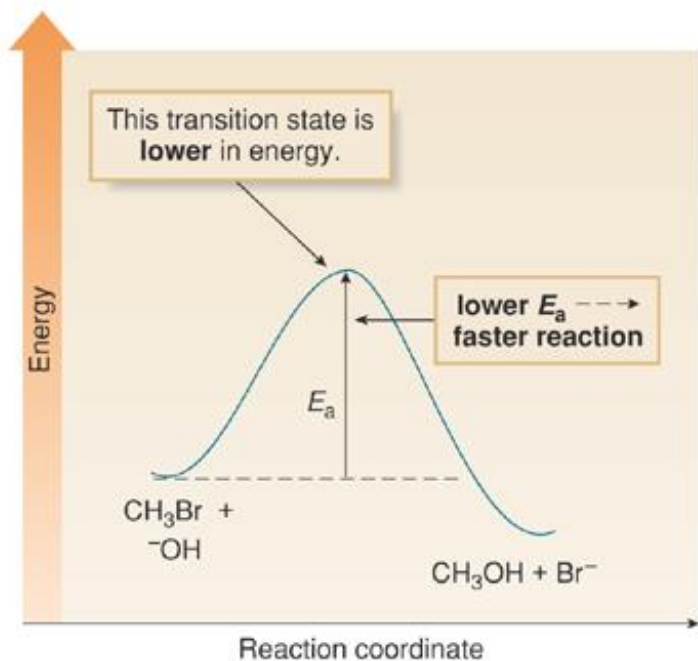
An energy diagram for the S_N2 reaction:



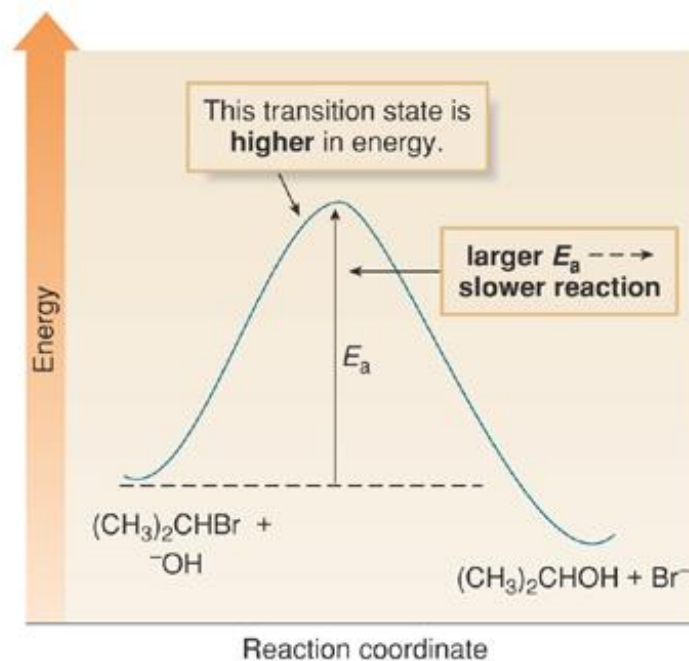
- In the transition state, the C–Br bond is partially broken, the C–O bond is partially formed, and both the attacking nucleophile and the departing leaving group bear a partial negative charge.

- The higher the E_a , the slower the reaction rate. Thus, any factor that increases E_a decreases the reaction rate.

Two energy diagrams depicting the effect of steric hindrance in S_N2 reactions



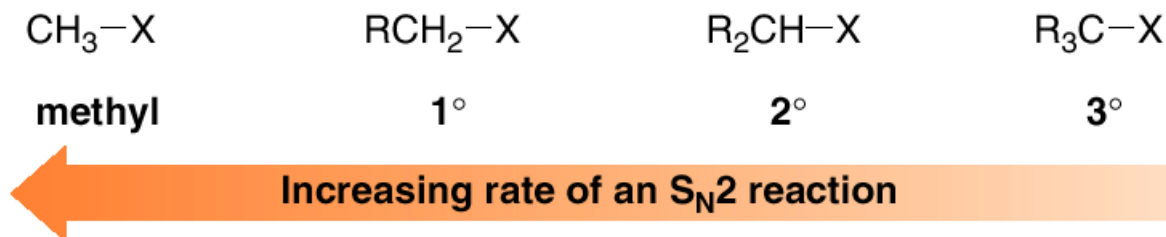
- CH_3Br is an unhindered alkyl halide. The transition state in the S_N2 reaction is lower in energy, making E_a lower and increasing the reaction rate.



- $(\text{CH}_3)_2\text{CHBr}$ is a sterically hindered alkyl halide. The transition state in the S_N2 reaction is higher in energy, making E_a higher and decreasing the reaction rate.

Mechanisms of Nucleophilic Substitution:

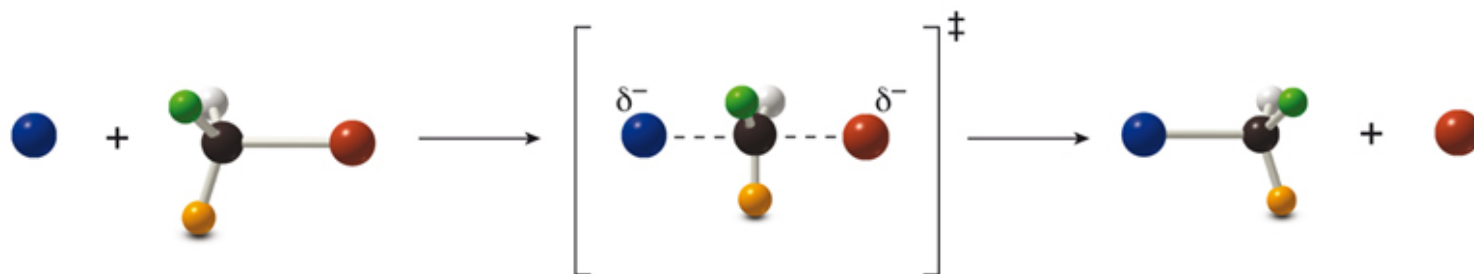
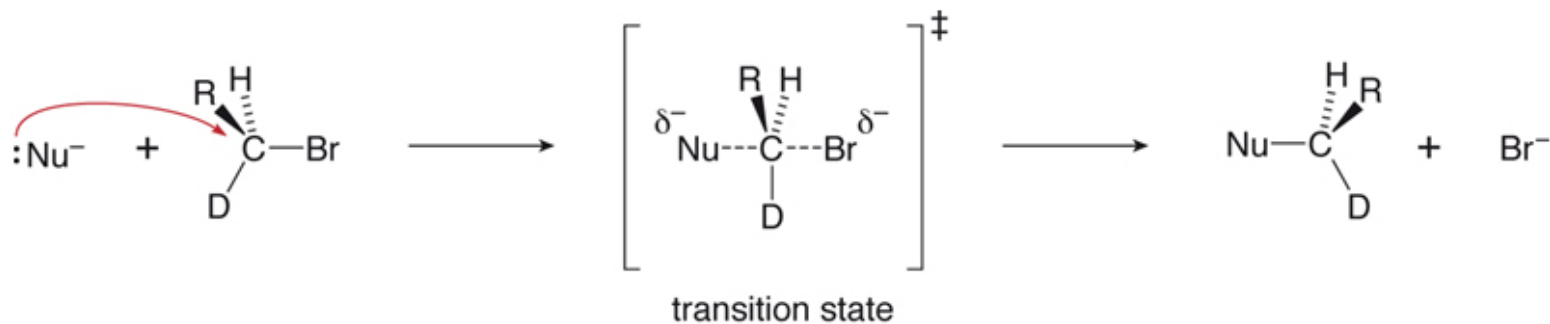
- As the number of R groups on the carbon with the leaving group *increases*, the rate of an S_N2 reaction *decreases*.



- Methyl and 1° alkyl halides undergo S_N2 reactions with ease.
- 2° Alkyl halides react more slowly.
- 3° Alkyl halides do not undergo S_N2 reactions. This order of reactivity can be explained by steric effects. Steric hindrance caused by bulky R groups makes nucleophilic attack from the backside more difficult, slowing the reaction rate.

- All S_N2 reactions proceed with backside attack of the nucleophile, resulting in inversion of configuration at a stereogenic center.

Stereochemistry of the S_N2 reaction



:Nu⁻ and Br⁻ are 180° away from each other, on either side of a plane containing R, H, and D.

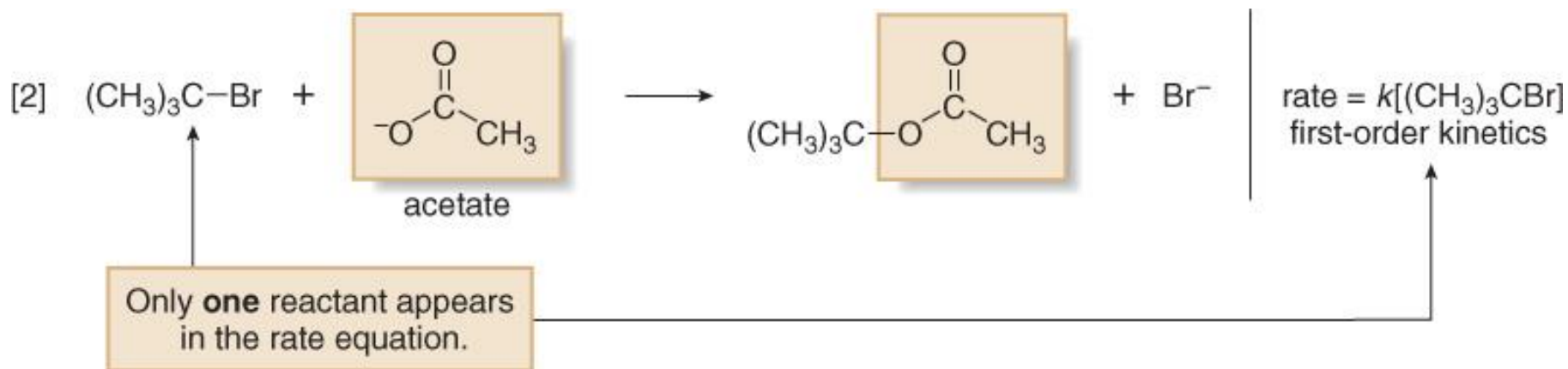
Factors influencing the rate of S_N2 reactions

There are four factors that influence the rate of S_N2 reactions:

1. the substrate (alkyl halide) structure
2. the nucleophile
3. the leaving group
4. the solvent

Characteristics of S_N2 reactions

Characteristic	Result
Kinetics	<ul style="list-style-type: none">• Second-order kinetics; rate = $k[\text{RX}][:\text{Nu}^-]$
Mechanism	<ul style="list-style-type: none">• One step
Stereochemistry	<ul style="list-style-type: none">• Backside attack of the nucleophile• Inversion of configuration at a stereogenic center
Identity of R	<ul style="list-style-type: none">• Unhindered halides react fastest.• Rate: $\text{CH}_3\text{X} > \text{RCH}_2\text{X} > \text{R}_2\text{CHX} > \text{R}_3\text{CX}$

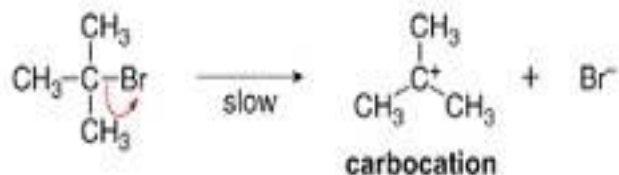


Kinetic data show that the rate of reaction [2] depends on the concentration of only the alkyl halide. This suggests a two-step mechanism in which the rate-determining step involves the alkyl halide only. This is an example of an $\text{S}_{\text{N}}1$ (substitution nucleophilic unimolecular) mechanism.

- mechanism $\text{S}_{\text{N}}1$ indicates a **substitution, nucleophilic, unimolecular** reaction, described by the expression rate = $k[\text{R-LG}]$. This implies that the rate determining step of the mechanism depends on the decomposition of a single molecular species.
- This pathway is a multi-step process with the following characteristics:
 - step 1: slow loss of the leaving group, **LG**, to generate a carbocation intermediate,

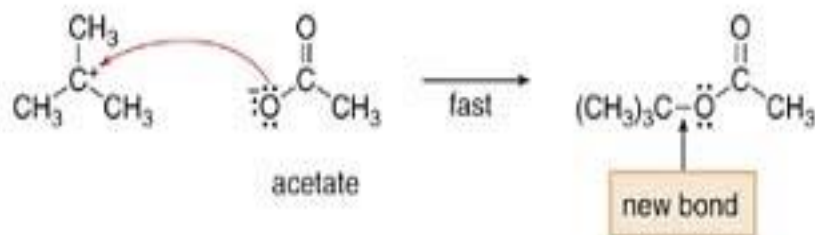
The mechanism of an S_N1 reaction would be drawn as follows: Note the curved arrow formalism that is used to show the flow of electrons.

Step [1] The C-Br bond is broken.



- **Heterolysis of the C-Br bond** forms an intermediate **carbocation**. This step is rate-determining because it involves only bond cleavage.

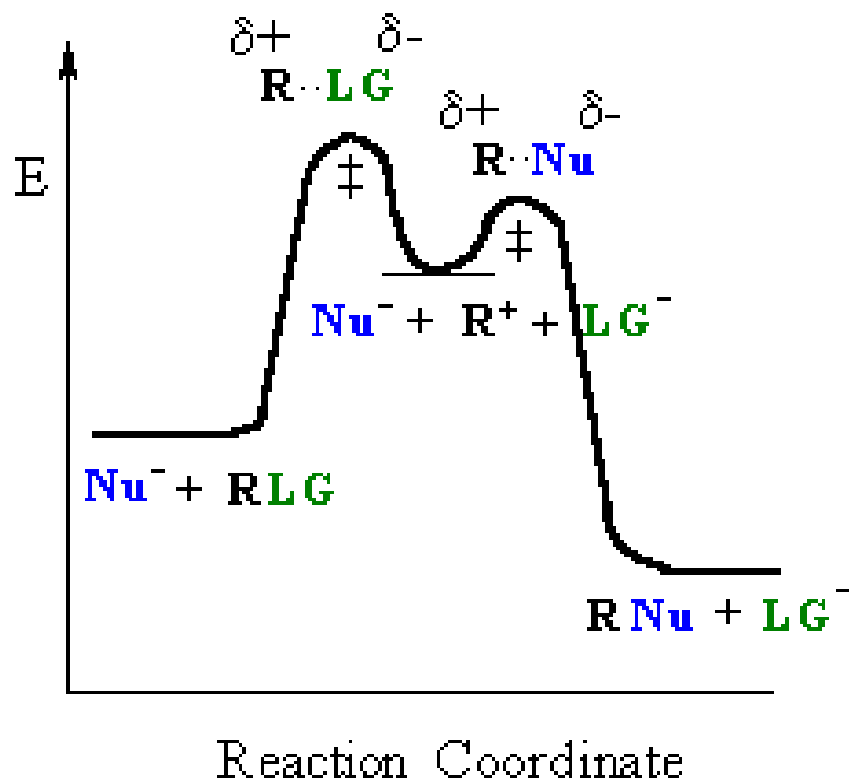
Step [2] The C-O bond is formed.



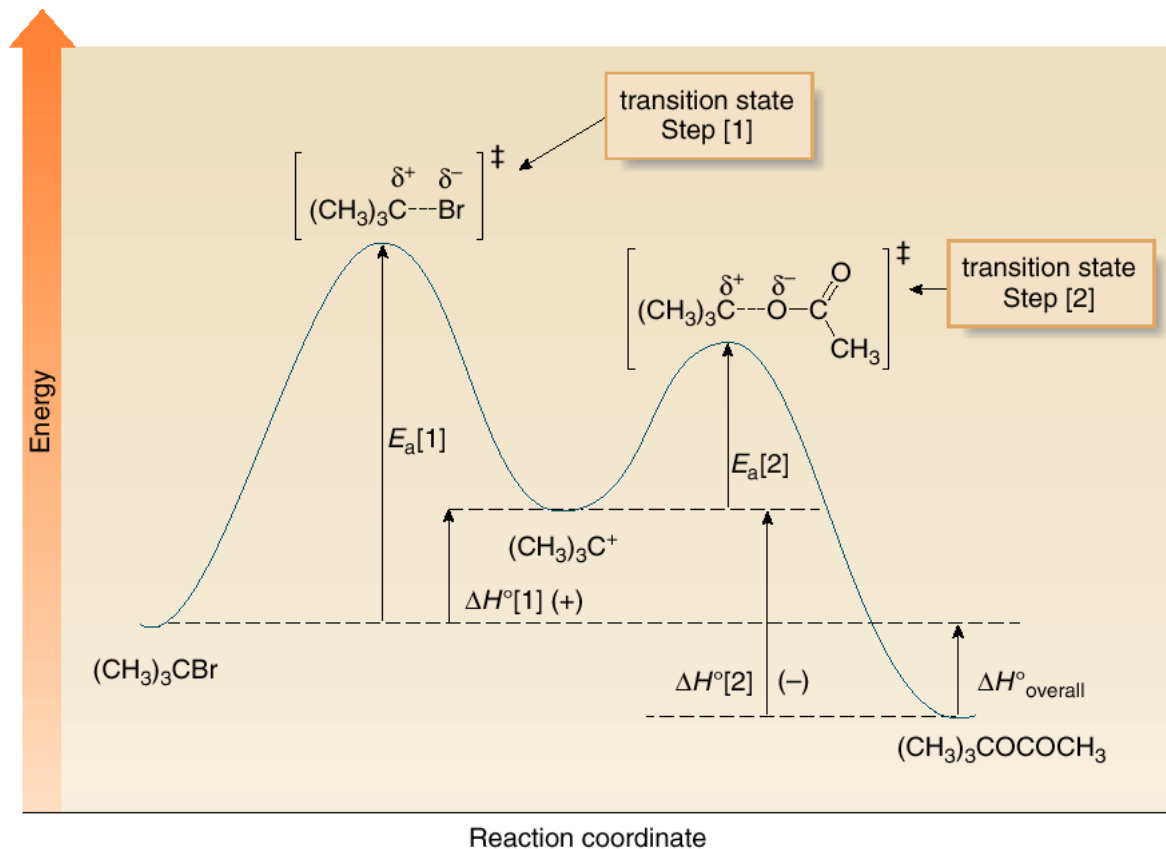
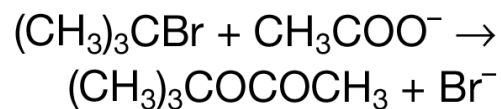
- **Nucleophilic attack of acetate** on the carbocation forms the new C-O bond in the product. This is a **Lewis acid-base reaction**; the nucleophile is the Lewis base and the carbocation is the Lewis acid. Step [2] is *faster* than Step [1] because no bonds are broken and one bond is formed.

Key features of the S_N1 mechanism are that it has two steps, and carbocations are formed as reactive intermediates.

Multi-step reactions have intermediates and a several transition states (TS). In an SN1 there is loss of the leaving group generates an intermediate carbocation which is then undergoes a rapid reaction with the nucleophile..

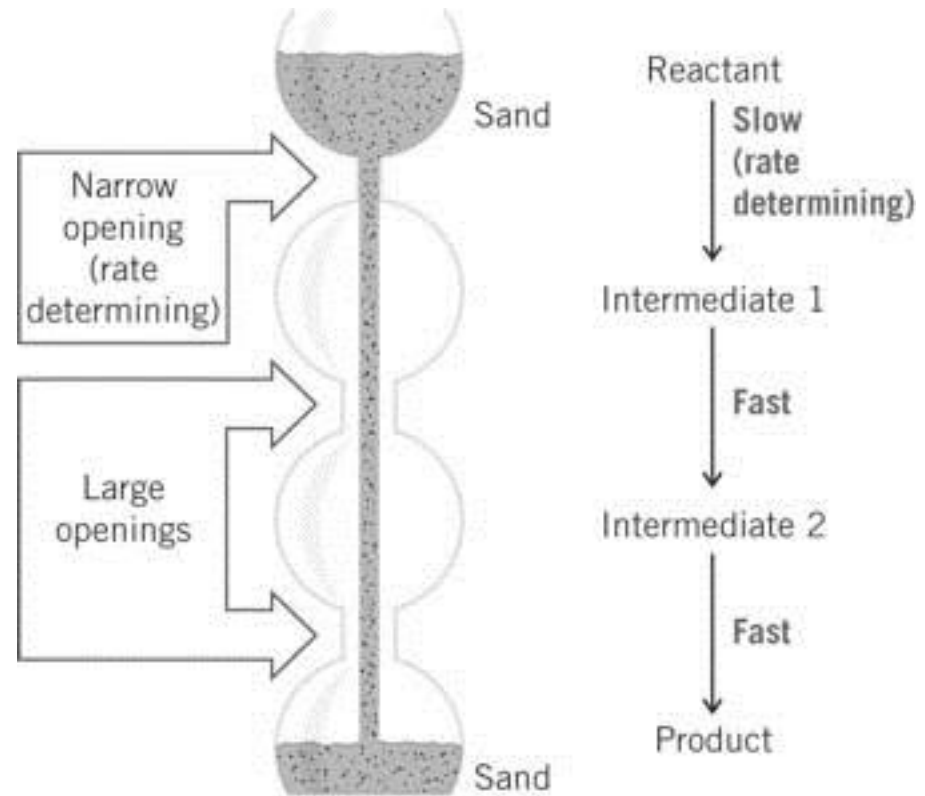
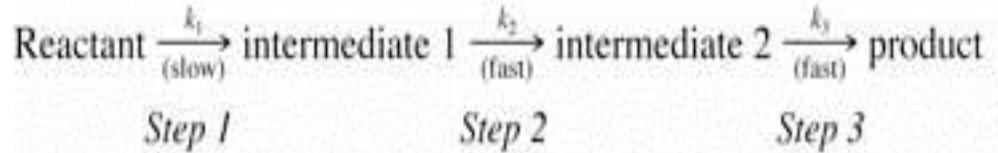


An energy diagram for the S_N1 reaction:



- Since the S_N1 mechanism has two steps, there are two energy barriers.
- $E_a[1] > E_a[2]$ since Step [1] involves bond breaking and Step [2] involves bond formation.
- In each step only one bond is broken or formed, so the transition state for each step has one partial bond.
- The reaction is drawn with $\Delta H^\circ_{\text{overall}}$ as a negative value, since the products are lower in energy than the starting materials.

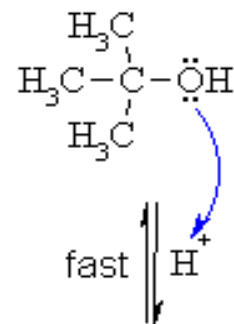
In multistep reactions, the rate of the slowest step will be the rate of the entire reaction. This is called the rate determining step. In the case to the right, $k_1 \ll k_2$ or k_3 and the first step is rate determining.



SN1 MECHANISM FOR REACTION OF ALCOHOLS WITH HBr

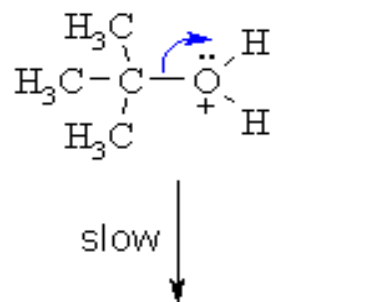
Step 1:

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.



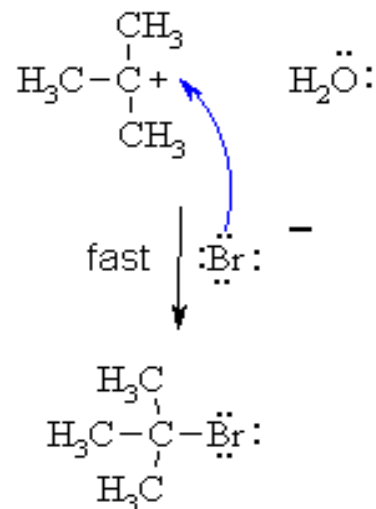
Step 2:

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)



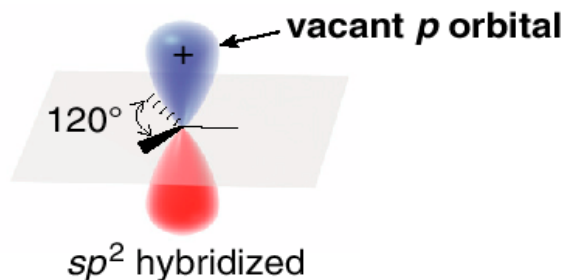
Step 3:

Attack of the nucleophilic bromide ion on the electrophilic carbocation creates the alkyl bromide.

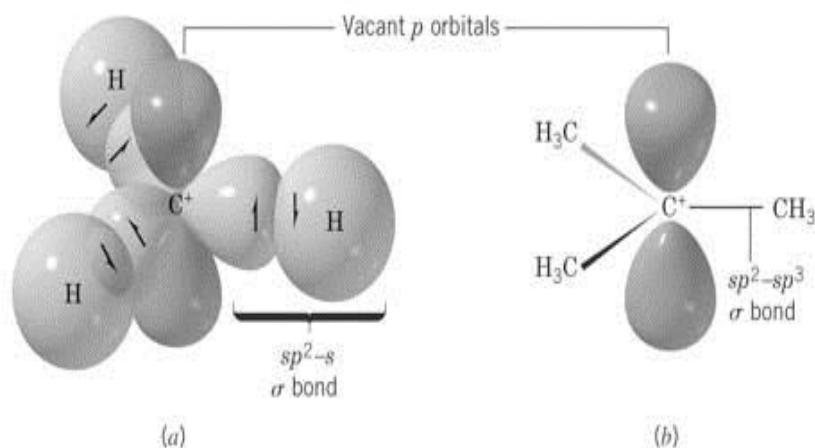


To understand the stereochemistry of the S_N1 reaction, we must examine the geometry of the carbocation intermediate.

A trigonal planar carbocation



- A carbocation (with three groups around C) is sp² hybridized and trigonal planar, and contains a vacant p orbital extending above and below the plane.

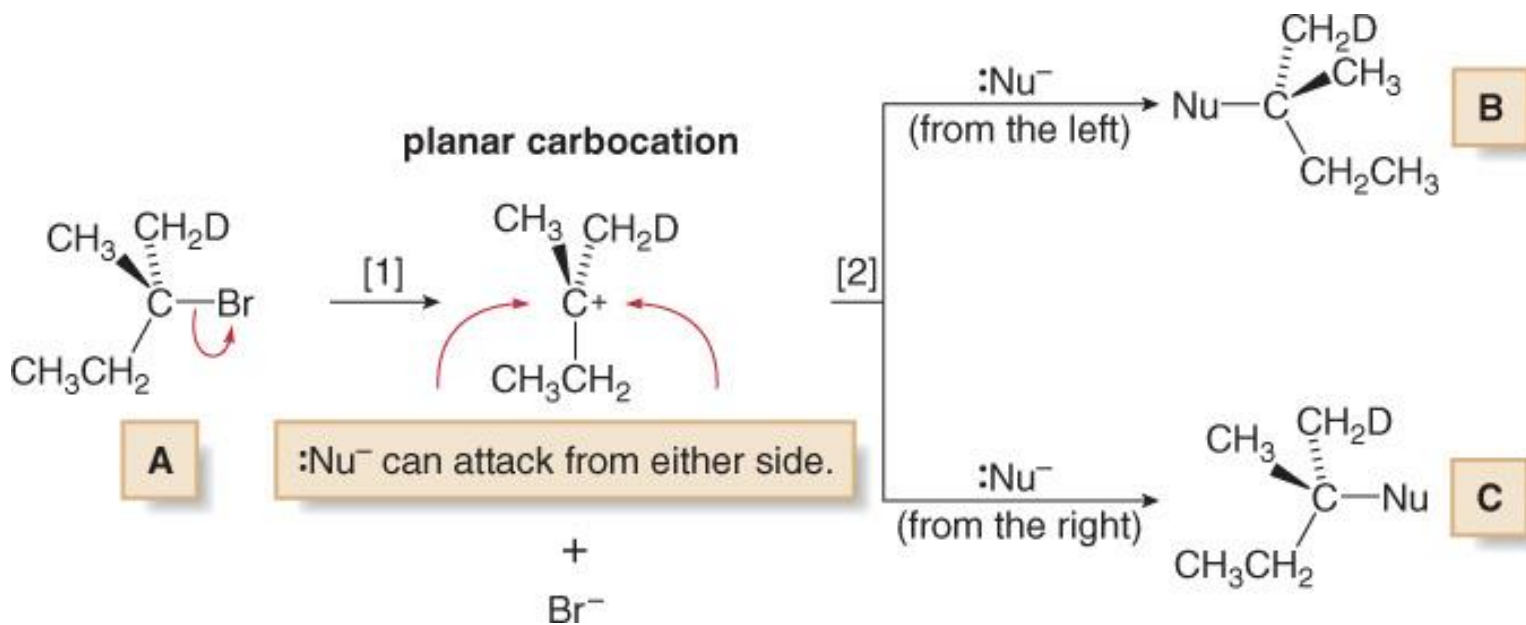


The more highly substituted a carbocation is, the more stable it is.

The more stable a carbocation is, the easier it is to form.

3^o > 2^o > 1^o > methyl

- Loss of the leaving group in Step [1] generates a planar carbocation that is achiral. In Step [2], attack of the nucleophile can occur on either side to afford two products which are a pair of enantiomers.
- Because there is no preference for nucleophilic attack from either direction, an equal amount of the two enantiomers is formed called a racemic mixture. We say that **racemization** has occurred. (transformation of of optically active compound to a racemic mixture)



components of the reaction influence the reaction pathway:

- **R-** Reactivity order : $(\text{CH}_3)_3\text{C}^- > (\text{CH}_3)_2\text{CH}^- > \text{CH}_3\text{CH}_2^- > \text{CH}_3^-$

In an SN1 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 SN1 reaction will be. Since a carbocation intermediate is formed, there is 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 substituent 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 SN1 is breaking the **C-LG** bond. Therefore, there is a very strong dependence on the nature of the leaving group, the better the leaving, the faster the SN1 reaction will be.

Nu

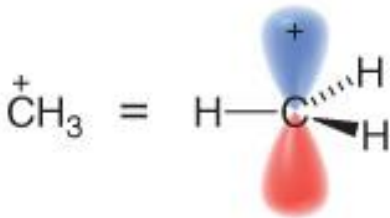
Since the nucleophile is not involved in the rate determining step, the nature of the nucleophile is unimportant in an SN1 reaction. However, the more reactive the nucleophile, the more likely an SN2 reaction becomes.

Carbocation Stability:

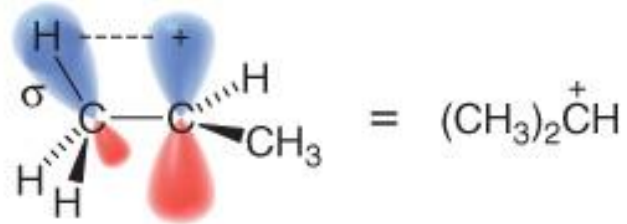
- The order of carbocation stability can be rationalized through **inductive effects** and **hyperconjugation**.
- **Inductive effects** are electronic effects that occur through σ bonds. Specifically, the inductive effect is the pull of electron density through σ bonds caused by electronegativity differences between atoms.
- Alkyl groups are **electron donating** groups that stabilize a positive charge. Since an alkyl group has several σ bonds, each containing electron density, it is more polarizable than a hydrogen atom, and better able to donate electron density.
- In general, the greater the number of alkyl groups attached to a carbon with a positive charge, the more stable will be the cation.

Carbocation Stability:

- The order of carbocation stability is also a consequence of hyperconjugation.
- **Hyperconjugation** is the spreading out of charge by the overlap of an empty p orbital with an adjacent σ bond. This overlap (hyperconjugation) delocalizes the positive charge on the carbocation, spreading it over a larger volume, and this stabilizes the carbocation.
- **Example: CH_3^+ cannot be stabilized by hyperconjugation, but $(\text{CH}_3)_2\text{CH}^+$ can.**



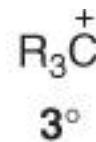
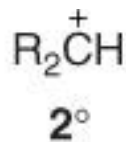
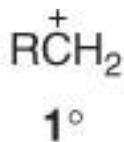
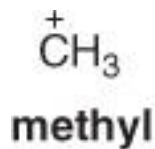
This carbocation has no opportunity for orbital overlap with the vacant p orbital.



Overlap of the $\text{C}-\text{H}$ σ bond with the adjacent vacant p orbital stabilizes the carbocation.

Carbocation Stability:

- The effect of the type of alkyl halide on S_N1 reaction rates can be explained by considering carbocation stability.
- Carbocations are classified as **primary (1°)**, **secondary (2°)**, or **tertiary (3°)**, based on the number of R groups bonded to the charged carbon atom. As the number of R groups increases, carbocation stability increases.

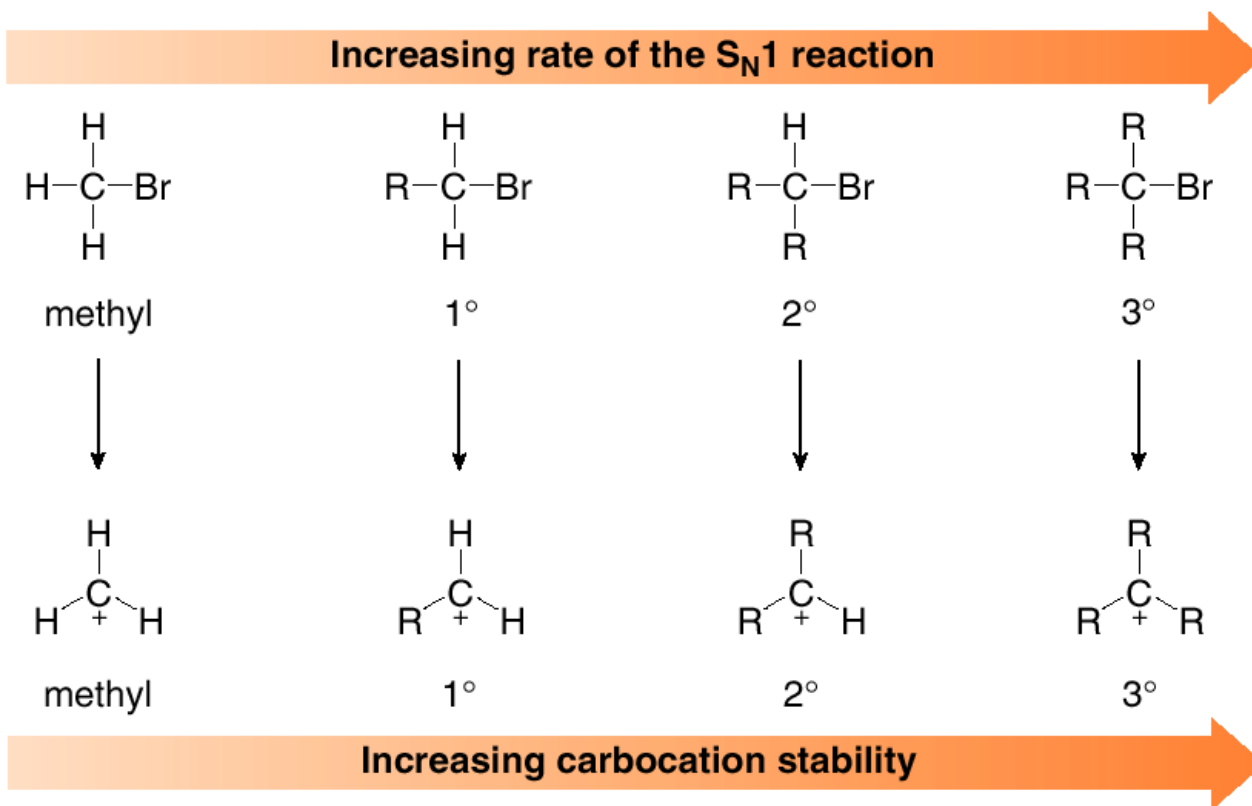


Increasing carbocation stability



Carbocation Stability:

- The rate of an S_N1 reaction *increases* as the number of R groups on the carbon with the leaving group *increases*.
- The stability of a carbocation *increases* as the number of R groups on the positively charged carbon *increases*.



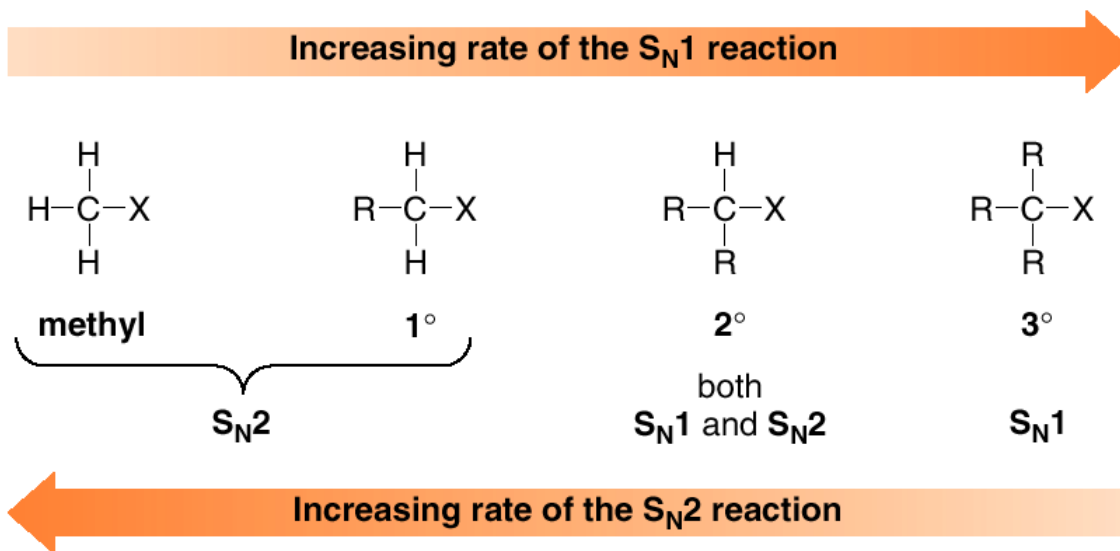
Characteristics of S_N1 reactions

Characteristic	Result
Kinetics	<ul style="list-style-type: none">• First-order kinetics; rate = $k[\text{RX}]$
Mechanism	<ul style="list-style-type: none">• Two steps
Stereochemistry	<ul style="list-style-type: none">• Trigonal planar carbocation intermediate• Racemization at a single stereogenic center
Identity of R	<ul style="list-style-type: none">• More substituted halides react fastest.• Rate: $\text{R}_3\text{CX} > \text{R}_2\text{CHX} > \text{RCH}_2\text{X} > \text{CH}_3\text{X}$

Substrate in predicting SN1 vs SN2 mechanisms:

- Four factors are relevant in predicting whether a given reaction is likely to proceed by an S_N1 or an S_N2 mechanism:
The most important is the structure of the alkyl halide.

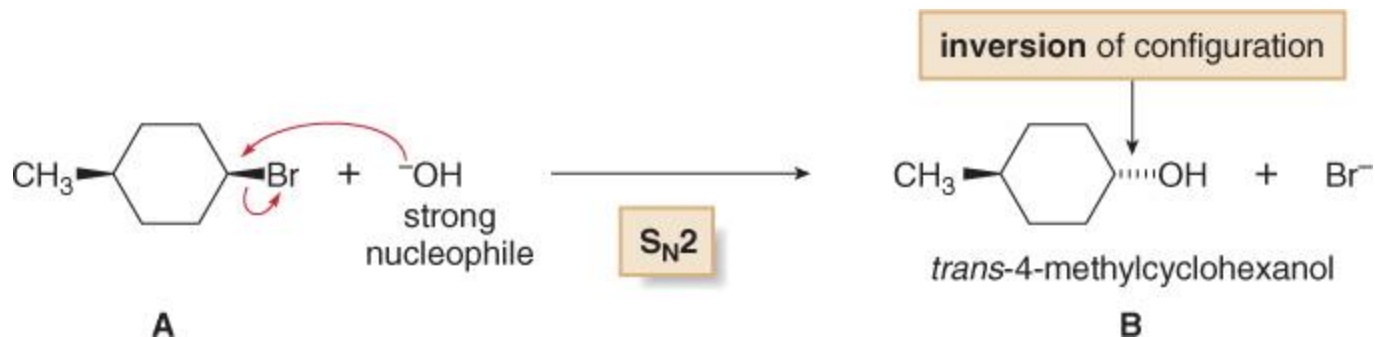
- Increasing alkyl substitution favors S_N1.
- Decreasing alkyl substitution favors S_N2.



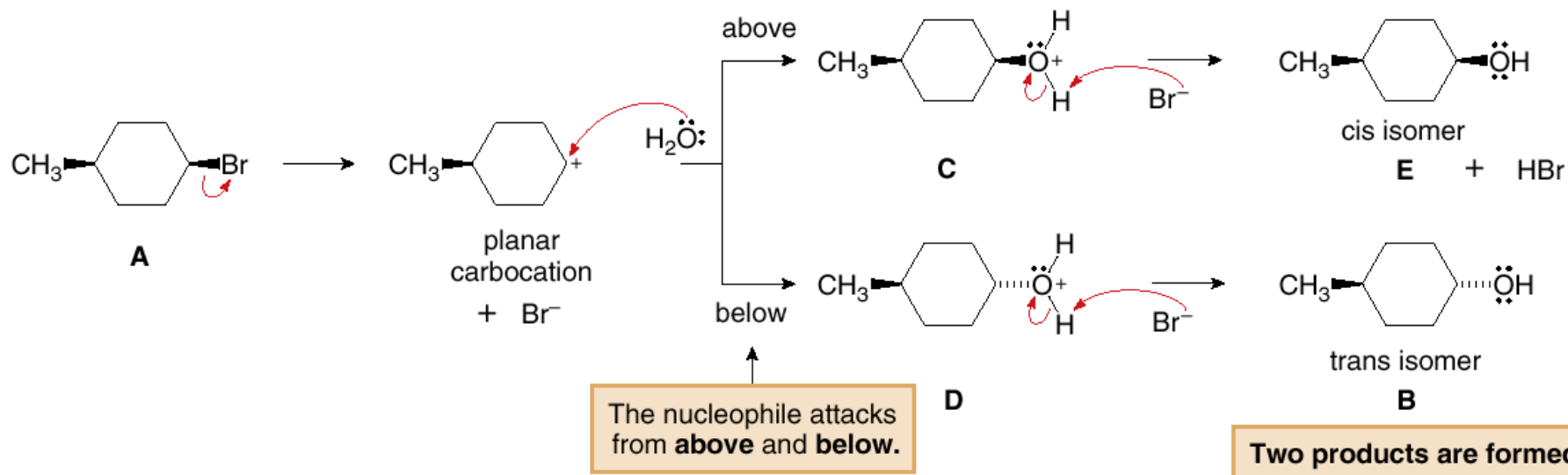
- Methyl and 1° halides (CH₃X and RCH₂X) undergo S_N2 reactions only.
- 3° Alkyl halides (R₃CX) undergo S_N1 reactions only.
- 2° Alkyl halides (R₂CHX) undergo both S_N1 and S_N2 reactions. Other factors determine the mechanism.

Nucleophile in predicting SN1 vs SN2 mechanisms:

- The strong nucleophile favors an S_N2 mechanism.



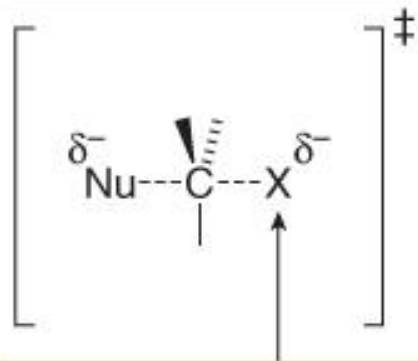
- The weak nucleophile favors an S_N1 mechanism.



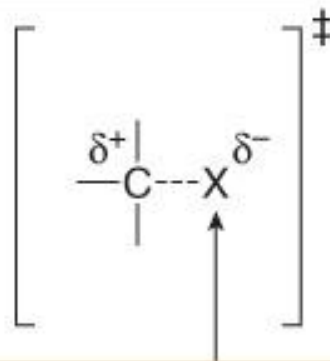
Leaving Group in predicting SN1 vs SN2 mechanisms:

- **The leaving group is the third factor.** A better leaving group increases the rate of both S_N1 and S_N2 reactions.

Transition state of the S_N2 mechanism



Transition state of the rate-determining step of the S_N1 mechanism



A better leaving group is more able to accept the negative charge.

R-F

R-Cl

R-Br

R-I



Increasing leaving group ability
Increasing rate of S_N1 and S_N2 reactions

Solvent in predicting SN1 vs SN2 mechanisms:

- **The nature of the solvent is a fourth factor.**
- **Polar protic solvents like H₂O and ROH favor S_N1 reactions because the ionic intermediates (both cations and anions) are stabilized by solvation.**
- **Polar aprotic solvents favor S_N2 reactions because nucleophiles are not well solvated, and therefore, are more nucleophilic.**

Factors in predicting SN1 vs SN2 mechanisms:

Nucleophile:

SN1 Nucleophilic strength not important

SN2 Needs a strong nucleophile

Substrate:

SN1 $3^\circ > 2^\circ$

SN2 $\text{CH}_3 > 1^\circ > 2^\circ$

Solvent:

SN1 Enhanced by more polar solvent

SN2 Enhanced by less polar solvent

Leaving Group:

SN1 Good LG important to form C^+

SN2 Not as important but enhances reaction

Results of SN1 vs SN2 mechanisms:

Kinetics:

SN1 rate = $k[\text{RX}]$

SN2 rate = $k[\text{RX}][\text{Nu:}]$

Stereochemistry:

SN1 both inversion and retention (racemic)

SN2 inversion only

Rearrangements:

SN1 rearrangements common

SN2 rearrangements not possible

Factors in predicting SN1 vs SN2 mechanisms:

Alkyl halide	Mechanism	Other factors
CH ₃ X RCH ₂ X (1°)	S _N 2	Favored by <ul style="list-style-type: none">• strong nucleophiles (usually a net negative charge)• polar aprotic solvents
R ₃ CX (3°)	S _N 1	Favored by <ul style="list-style-type: none">• weak nucleophiles (usually neutral)• polar protic solvents
R ₂ CHX (2°)	S _N 1 or S _N 2	The mechanism depends on the conditions. <ul style="list-style-type: none">• Strong nucleophiles favor the S_N2 mechanism over the S_N1 mechanism. For example, RO⁻ is a stronger nucleophile than ROH, so RO⁻ favors the S_N2 reaction and ROH favors the S_N1 reaction.• Protic solvents favor the S_N1 mechanism and aprotic solvents favor the S_N2 mechanism. For example, H₂O and CH₃OH are polar protic solvents that favor the S_N1 mechanism, whereas acetone [(CH₃)₂C=O] and DMSO [(CH₃)₂S=O] are polar aprotic solvents that favor the S_N2 mechanism.

Correlation of Structure and Reactivity for Substitution and Elimination Reactions

Halide Type	S_N1	S_N2	E1	E2
RCH_2X (primary)	Does not occur	Highly favored	Does not occur	Occurs when strong bases are used
R_2CHX (secondary)	Can occur with benzylic and allylic halides	Occurs in competition with E2 reaction	Can occur with benzylic and allylic halides Occurs in competition with S_N2 reaction	Favored when strong bases are used
R_3CX (tertiary)	Favored in hydroxylic solvents	Does not occur	Does not occur	Favored when bases are used

(as a function of RX Structure)

In general, substrates react in the following way:

RCH₂X
(primary)

Mostly S_N2 substitution

R₂CHX
(primary)

S_N2 substitution with nonbasic nucleophiles
E2 elimination with strong bases

R₃CX
(primary)

Mostly E2 elimination
(S_N1 substitution and E1 elimination in nonbasic solvents)

So what you need to take home is, that if it's a strong base (such as H_2N^- , R-O^- , or OH^-) the reaction will most likely be elimination. If the reactant is a good nucleophile, but a poor base then substitution is a safe bet.

Protic, highly polar solvents favor $\text{S}_{\text{N}}1$ and E1, while aprotic, polar solvents will be found in $\text{S}_{\text{N}}2$ reactions. Following these simple tips will get you through the vast majority of nucleophilic substitution and beta elimination reactions.

Molecules synthesized from R-X by the SN2 reaction

	Nucleophile (:Nu ⁻)	Product	Name
Oxygen compounds	^-OH	R-OH	alcohol
	$^-OR'$	R-OR'	ether
	$\begin{array}{c} O \\ \\ ^-O-C-R' \end{array}$	$\begin{array}{c} O \\ \\ R-O-C-R' \end{array}$	ester
Carbon compounds	^-CN	R-CN	nitrile
	$^-C\equiv C-H$	R-C≡C-H	alkyne
Nitrogen compounds	N_3^-	R-N ₃	azide
	$:NH_3$	R-NH ₂	amine
Sulfur compounds	^-SH	R-SH	thiol
	$^-SR'$	R-SR'	sulfide

↑
products of nucleophilic substitution