

Chapter 6

Ionic Reactions-Nucleophilic Substitution and Elimination Reactions of Alkyl Halides

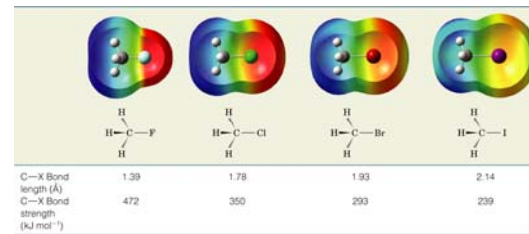
♦ Introduction

→ The polarity of a carbon-halogen bond leads to the carbon having a partial positive charge

→ In alkyl halides this polarity causes the carbon to become activated to substitution reactions with nucleophiles



→ Carbon-halogen bonds get less polar, longer and weaker in going from fluorine to iodine



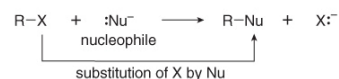
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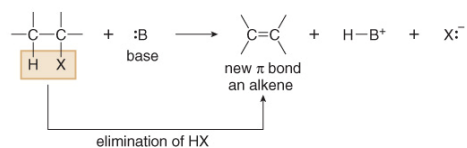
Alkyl Halides and Nucleophilic Substitution

The Polar Carbon-Halogen Bond

♦ Alkyl halides undergo substitution reactions with nucleophiles.



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



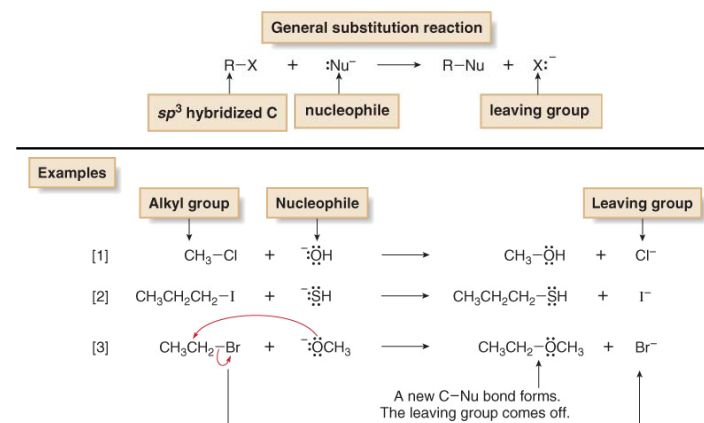
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Alkyl Halides and Nucleophilic Substitution

General Features of Nucleophilic Substitution

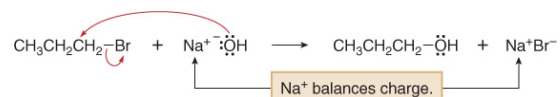
• Three components are necessary in any substitution reaction.



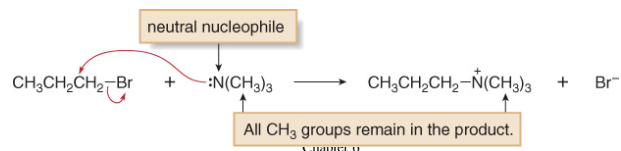
Alkyl Halides and Nucleophilic Substitution

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.

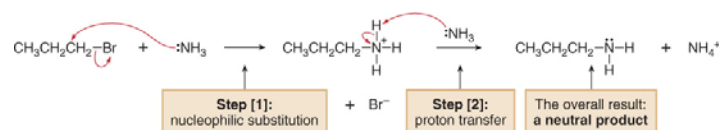


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Alkyl Halides and Nucleophilic Substitution

General Features of Nucleophilic Substitution

- Furthermore, when the substitution product bears a positive charge and also contains a proton bonded to O or N, the initially formed substitution product readily loses a proton in a Brønsted-Lowry acid-base reaction, forming a neutral product.

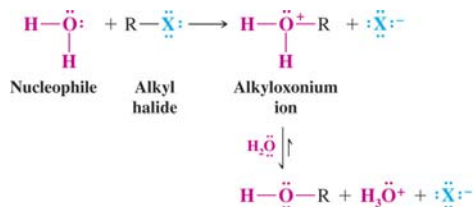


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♦ The Nucleophile

A nucleophile may be any molecule with an unshared electron pair



We'll discuss later what makes a nucleophile strong or weak (good or bad)

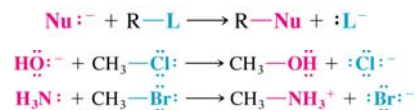
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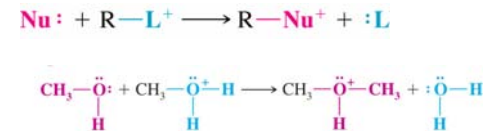
Leaving Groups

A leaving group is a substituent that can leave as a relatively stable entity

It can either leave as an anion....



...or as a neutral molecule



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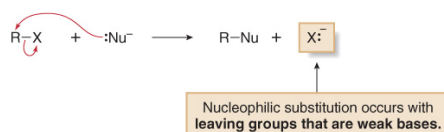
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Alkyl Halides and Nucleophilic Substitution

The Leaving Group

- In a nucleophilic substitution reaction of $R-X$, the $C-X$ bond is heterolytically cleaved, and the leaving group departs with the electron pair in that bond, forming X^- . **The more stable the leaving group X^- , the better able it is to accept an electron pair.**

◆ In comparing two leaving groups, the better leaving group is the weaker base.



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Alkyl Halides and Nucleophilic Substitution

The Leaving Group

TABLE 7.2 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_2O	H_3O^+	-1.7

These molecules undergo nucleophilic substitution. good leaving groups

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Alkyl Halides and Nucleophilic Substitution

The Leaving Group

TABLE 7.3 Poor Leaving Groups for Nucleophilic Substitution

Starting material	Leaving group	Conjugate acid	pK_a
$R-F$	F^-	HF	3.2
$R-OH$	^-OH	H_2O	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

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Neutral molecules as leaving groups

Poor leaving groups can be turned into good leaving groups by **protonation**.

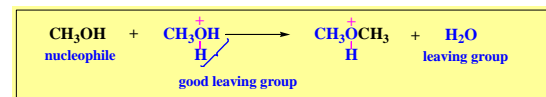


Hydroxide ion is a **poor leaving group** because it is the anion of a **weak acid**, H_2O .

In the presence of a strong acid,



a nucleophilic substitution reaction occurs:



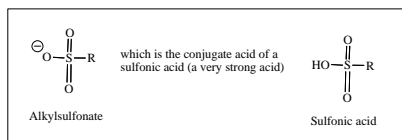
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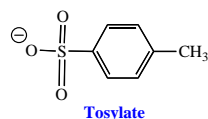
• The Leaving Group

→ The best leaving groups are weak bases which are relatively stable

• Other very weak bases (besides halide ions) which are good leaving groups:



The most common alkylsulfonate is:

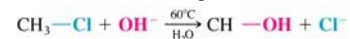


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♦ Kinetics of a Nucleophilic Substitution Reaction: An $\text{S}_{\text{N}}2$ Reaction

→ The initial rate of the following reaction is measured



→ The rate is directly proportional to the initial concentrations of both methyl chloride and hydroxide

Experiment Number	Initial $[\text{CH}_3\text{Cl}]$	Initial $[\text{OH}^-]$	Initial Rate ($\text{mol L}^{-1} \text{s}^{-1}$)
1	0.0010	1.0	4.9×10^{-7}
2	0.0020	1.0	9.8×10^{-7}
3	0.0010	2.0	9.8×10^{-7}
4	0.0020	2.0	19.6×10^{-7}

→ The rate equation reflects this dependence

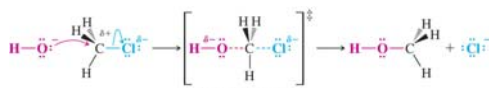
$$\text{Rate} = k[\text{CH}_3\text{Cl}][\text{OH}^-]$$

→ $\text{S}_{\text{N}}2$ reaction: substitution, nucleophilic, 2nd order (bimolecular)

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♦ A Mechanism for the $\text{S}_{\text{N}}2$ Reaction



The negative hydroxide ion brings a pair of electrons to the partially positive carbon from the back side with respect to the leaving group. The chlorine begins to move away with the pair of electrons that bonded it to the carbon.

In the transition state, a bond between oxygen and carbon is partially formed and the bond between carbon and chlorine is partially broken. The configuration of the carbon atom begins to invert.

Now the bond between the oxygen and carbon has formed and the chloride ion has departed. The configuration of the carbon has inverted.

→ A **transition state** is the high energy state of the reaction

• It is an unstable entity with a very brief existence (10^{-12} s)

→ In the transition state of this reaction bonds are partially formed and broken

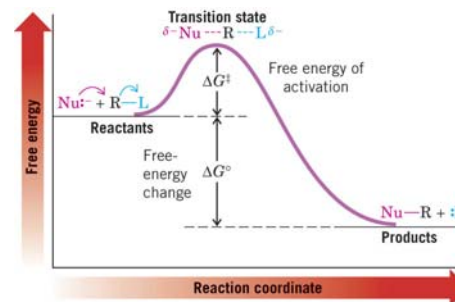
• Both chloromethane and hydroxide are involved in the transition state and this explains why the reaction is second order

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→ An energy diagram of a typical $\text{S}_{\text{N}}2$ reaction

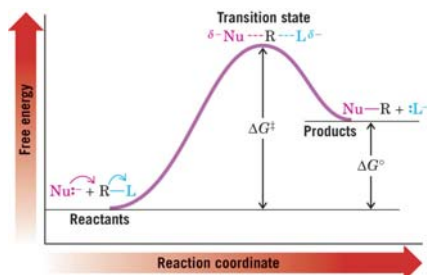
- An energy barrier is evident because a bond is being broken in going to the transition state (which is the top of the energy barrier)
- The difference in energy between starting material and the transition state is the free energy of activation (ΔG^\ddagger)
- The difference in energy between starting molecules and products is the free energy change of the reaction, ΔG°



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→ In a highly endergonic reaction of the same type the energy barrier will be even higher (ΔG^\ddagger is very large)



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→ There is a direct relationship between ΔG^\ddagger and the temperature of a reaction

‣ The higher the temperature, the faster the rate

$$k = k_0 e^{-\Delta G^\ddagger/RT}$$

‣ Near room temperature, a 10°C increase in temperature causes a doubling of rate
‣ Higher temperatures cause more molecules to collide with enough energy to reach the transition state and react

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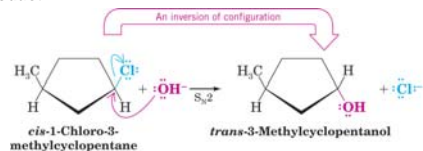
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♦ The Stereochemistry of S_N2 Reactions

→ Backside attack of nucleophile results in an inversion of configuration



→ In cyclic systems a cis compound can react and become trans product



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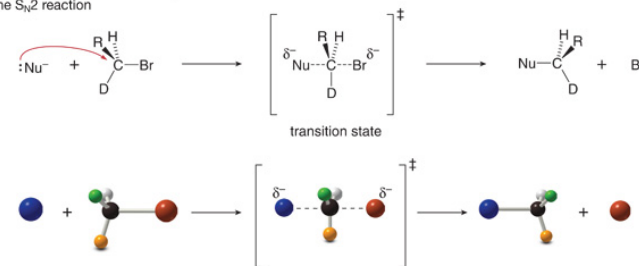
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Alkyl Halides and Nucleophilic Substitution

Mechanisms of Nucleophilic Substitution

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

Figure 7.9 Stereochemistry of the S_N2 reaction



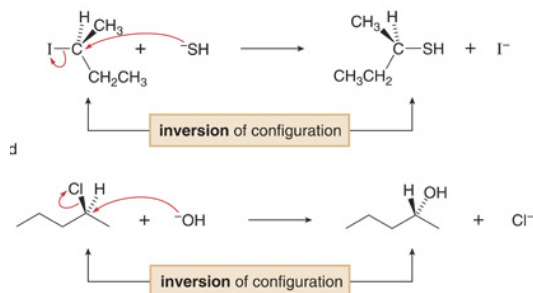
:Nu^- and Br^- are 180° away from each other, on either side of a plane containing R, H, and D.

Alkyl Halides and Nucleophilic Substitution

Mechanisms of Nucleophilic Substitution

Figure 7.10 Two examples of inversion of configuration in the S_N2 reaction

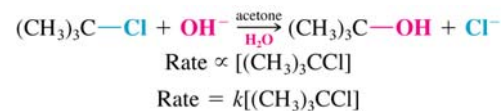
- The bond to the nucleophile in the product is always on the **opposite side** relative to the bond to the leaving group in the starting material.



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♦ The Reaction of *tert*-Butyl Chloride with Hydroxide Ion: An S_N1 Reaction

- \rightarrow *tert*-Butyl chloride undergoes substitution with hydroxide
- \rightarrow The rate is independent of hydroxide concentration and depends only on concentration of *tert*-butyl chloride



$\rightarrow S_N1$ reaction: Substitution, nucleophilic, 1st order (unimolecular)

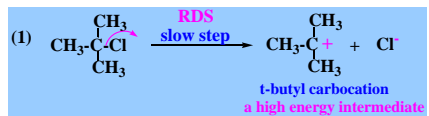
- The rate depends only on the concentration of the alkyl halide
- Only the alkyl halide (and not the nucleophile) is involved in the transition state of the step that controls the rate

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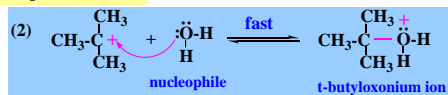
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Mechanism of the S_N1 Reaction (Stepwise)

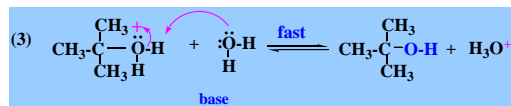
bond heterolysis:



nucleophilic addition:



proton exchange:

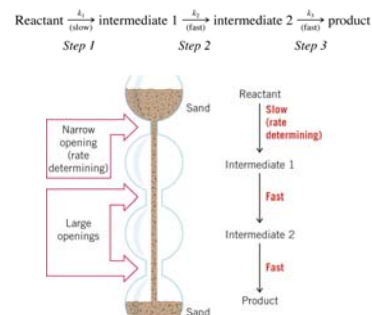


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♦ Multistep Reactions and the Rate-Determining Step

- \rightarrow In multistep reactions, the rate of the slowest step will be the rate of the entire reaction
- \rightarrow This is called the **rate-determining step**
- \rightarrow In the case below $k_1 \ll k_2$ or k_3 and the first step is rate determining



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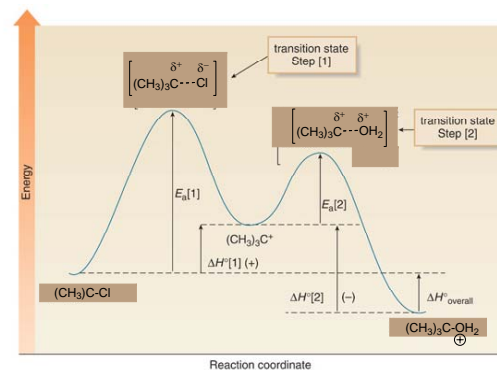
Mechanism of the S_N1 Reaction

Key features of the S_N1 mechanism are that it has **two steps** and involves a **carbocation intermediate**.

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Reaction Energy Diagram: S_N1 Mechanism



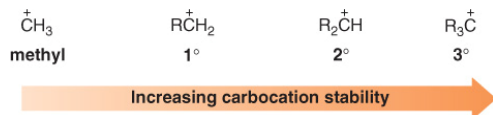
- Since the S_N1 mechanism has two steps, there are two energy barriers.
- Step [1] is rate-determining; $E_a[1] > E_a[2]$.
- In each step only one bond is broken or formed, so the transition state for each step has one partial bond.
- The reaction is drawn with $\Delta H^\circ_{\text{overall}}$ as a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

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Alkyl Halides and Nucleophilic Substitution

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.



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Alkyl Halides and Nucleophilic Substitution

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 more 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.**

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Alkyl Halides and Nucleophilic Substitution

Carbocation Stability

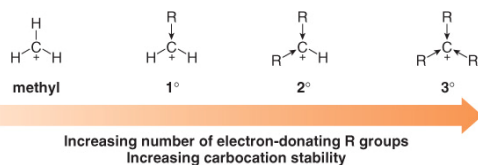
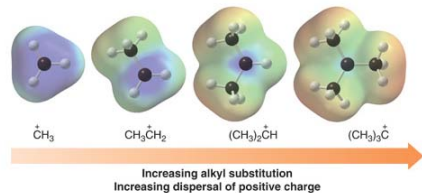


Figure 7.17 Electrostatic potential maps for different carbocations

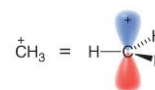


- Dark blue areas in electrostatic potential plots indicate regions low in electron density. As alkyl substitution increases, the region of positive charge is less concentrated on carbon.

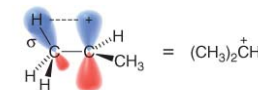
Alkyl Halides and Nucleophilic Substitution

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 large volume, and this stabilizes the carbocation.
- Example: CH₃⁺ cannot be stabilized by hyperconjugation, but (CH₃)₂CH⁺ can.



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

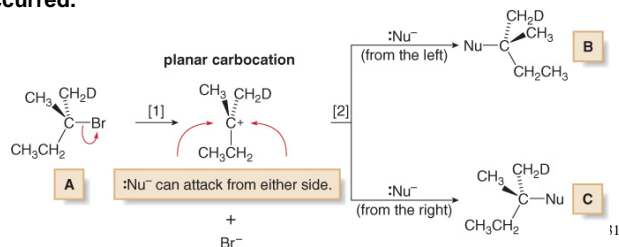


Overlap of the C-H σ bond with the adjacent vacant *p* orbital stabilizes the carbocation.

Alkyl Halides and Nucleophilic Substitution

Stereochemistry of the S_N1 Reaction:

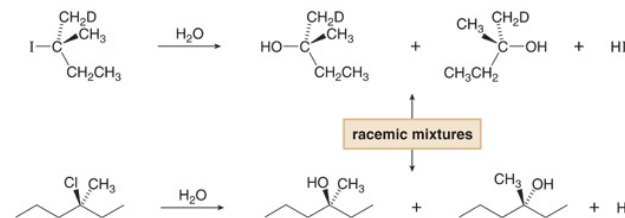
- Loss of the leaving group in Step [1] generates a planar carbocation that is achiral. Attack of the nucleophile in Step [2] can occur on either side to afford two products which are a pair of enantiomers.
- Because there is no preference for nucleophilic attack from either direction, an equal amount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



Alkyl Halides and Nucleophilic Substitution

Mechanisms for Nucleophilic Substitution

Figure 7.16 Two examples of racemization in the S_N1 reaction



- Nucleophilic substitution of each starting material by an S_N1 mechanism forms a **racemic mixture** of two products.
- With H₂O, a neutral nucleophile, the initial product of nucleophilic substitution (ROH₂⁺) loses a proton to form the final neutral product, ROH (Section 7.6).

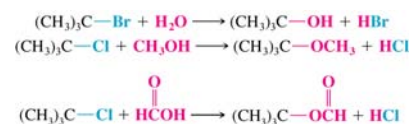
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♦ Solvolysis

→ A molecule of the solvent is the nucleophile in a substitution reaction

⚡ If the solvent is water the reaction is a hydrolysis



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♦ Factors Affecting the Rate of $\text{S}_\text{N}1$ and $\text{S}_\text{N}2$ Reactions

• The Effects of the Structure of the Substrate

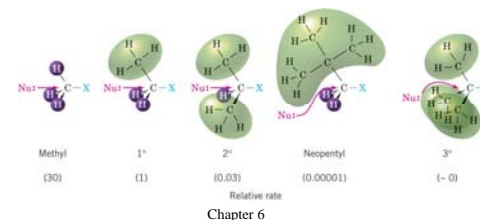
• $\text{S}_\text{N}2$ Reactions

→ In $\text{S}_\text{N}2$ reactions alkyl halides show the following general order of reactivity

Methyl > primary > secondary >> (tertiary — unreactive)

→ Steric hindrance: the spatial arrangement of the atoms or groups at or near a reacting site hinders or retards a reaction

⚡ In tertiary and neopentyl halides, the reacting carbon is too sterically hindered to react



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• $\text{S}_\text{N}1$ reactions

→ Generally only tertiary halides undergo $\text{S}_\text{N}1$ reactions because only they can form relatively stabilized carbocations.

(Secondary substrates can be made to undergo $\text{S}_\text{N}1$ reactions by manipulating other factors which help stabilize the 2° carbocation.)

• The Hammond-Leffler Postulate

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• The Effect of the Concentration of the Nucleophile

• $\text{S}_\text{N}1$ Reaction

→ Rate does not depend on the identity or concentration of nucleophile

• $\text{S}_\text{N}2$ Reaction

→ Rate is directly proportional to the concentration of nucleophile

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THE EFFECT OF THE STRENGTH OF THE NUCLEOPHILE

What Makes a Nucleophile Strong or Weak?

Sometimes, "NUCLEOPHILICITY PARALLELS BASICITY"

- For two nucleophiles with the same nucleophilic atom, the stronger base is the stronger nucleophile

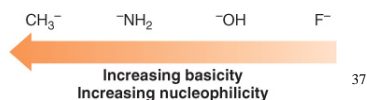


- A negatively charged nucleophile is always a stronger nucleophile than its conjugate acid.

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

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

For second-row elements with the same charge:

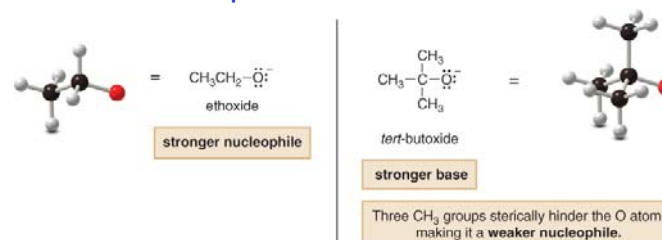


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THE STRENGTH OF THE NUCLEOPHILE

However,

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



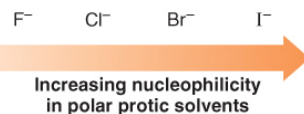
THE STRENGTH OF THE NUCLEOPHILE

Also, nucleophilicity does not always parallel basicity:

- In **polar protic solvents** (defined later).

Nucleophilicity increases down a column of the periodic table as the size of the anion increases. **This opposite to basicity.**

Down a column of the periodic table



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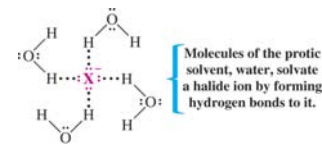
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Solvent Effects on $\text{S}_\text{N}2$ Reactions:

Polar Protic and Aprotic Solvents

→ Polar Protic Solvents

- Polar protic solvents have a hydrogen atom attached to strongly electronegative atoms
- They solvate nucleophiles and make them less reactive



- Larger nucleophilic atoms are less solvated and therefore more reactive in polar protic solvents



- Larger nucleophiles are also more polarizable and can donate more electron density
- Relative nucleophilicity in polar protic solvents:



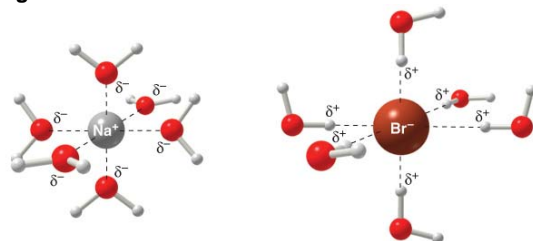
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Effects of Polar Protic and Polar Aprotic Solvents

Nucleophiles in Polar Protic Solvents

- For example, if Br^- is used as a nucleophile in H_2O , the Na^+ cations are solvated by ion-dipole interactions with H_2O molecules, and the Br^- anions are solvated by strong hydrogen bonding interactions. The solvent molecules cluster around the nuclei



Na^+ is solvated by ion-dipole interactions with H_2O .

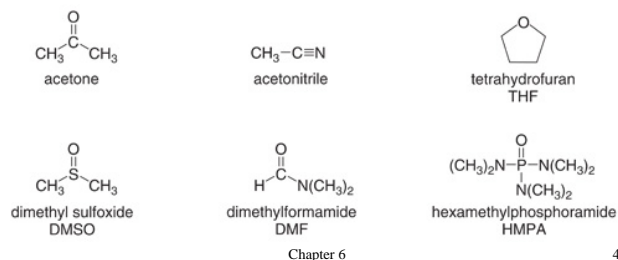
Br^- is solvated by hydrogen bonding with H_2O .

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Effects of Polar Protic and Polar Aprotic Solvents

- Polar aprotic solvents** have no O—H or N—H bonds. Thus, they are incapable of hydrogen bonding. At the same time, however, they exhibit dipole—dipole interactions.

Figure 7.7 Examples of polar aprotic solvents

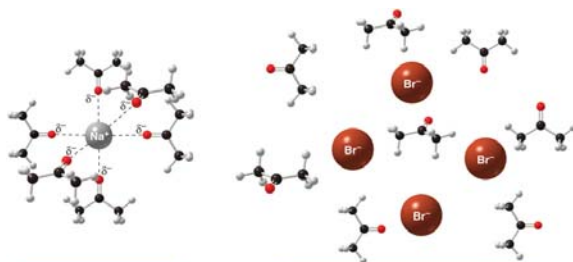


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Nucleophiles in Polar Protic Solvents

Polar aprotic solvents solvate cations by ion—dipole interactions, BUT **anions are not well solvated** because the solvent cannot hydrogen bond to them. These anions are said to be “naked”.



$(\text{CH}_3)_2\text{C}=\text{O}$ 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.

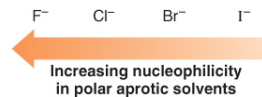
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Effects of Polar Protic and Polar Aprotic Solvents

The result is that -

- in polar aprotic solvents, nucleophilicity does parallel basicity, and the stronger base is indeed the stronger nucleophile.
- Because basicity decreases with size down a column, nucleophilicity decreases as well.

Down a column of the periodic table



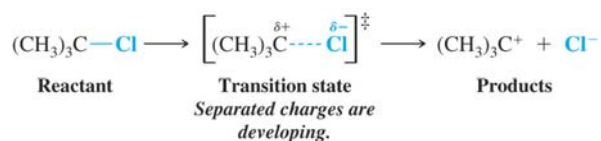
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• **Solvent Effects on S_N1 Reactions:**

The Ionizing Ability of the Solvent

- Polar protic solvents are excellent solvents for S_N1 reactions.
- Polar protic solvents stabilize the carbocation-like transition state leading to the carbocation thus lowering ΔG[‡] (activation energy).
- Water-ethanol and water-methanol mixtures are most common.

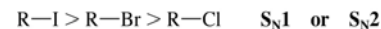


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• **Summary S_N1 vs. S_N2**

→ In both types of reaction alkyl iodides react the fastest because of superior leaving group ability



Factor	S _N 1	S _N 2
Substrate	3° (requires formation of a relatively stable carbocation)	Methyl > 1° > 2° (requires unhindered substrate)
Nucleophile	Weak Lewis base, neutral molecule, nucleophile may be the solvent (solvolysis)	Strong Lewis base, rate favored by high concentration of nucleophile
Solvent	Polar protic (e.g., alcohols, water)	Polar aprotic (e.g., DMF, DMSO)
Leaving group	I > Br > Cl > F for both S _N 1 and S _N 2 (the weaker the base after the group departs, the better the leaving group)	

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Alkyl Halides and Nucleophilic Substitution

Predicting the Likely Mechanism of a Substitution Reaction.

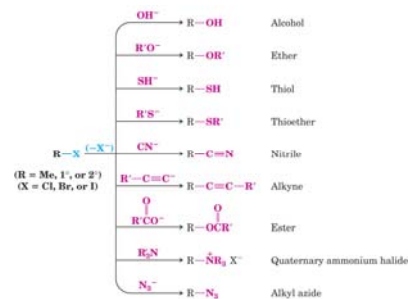
TABLE 7.7 Summary of Factors that Determine the S_N1 or S_N2 Mechanism

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.

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♦ Organic Synthesis: Functional Group Transformations Using S_N2 Reactions



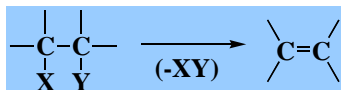
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Elimination Reactions

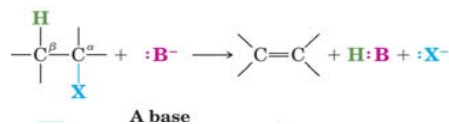
Remember, another major class of organic reactions is **elimination reactions**.

In an elimination reaction, groups X and Y are lost from a larger molecule



When X and Y are on adjacent C's, this is called 1,2-elimination or beta-elimination

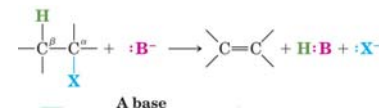
- For example, loss of HX from an alkyl halide produces an alkene. This elimination reaction is called **DEHYDROHALOGENATION**



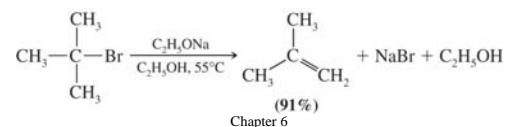
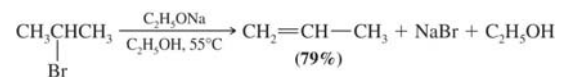
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Elimination Reactions of Alkyl Halides



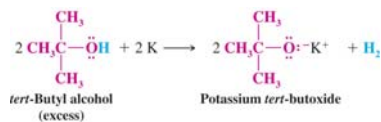
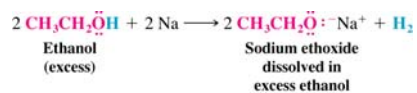
- Useful for the synthesis of alkenes
- Strong bases such as **alkoxides** favor this elimination reaction



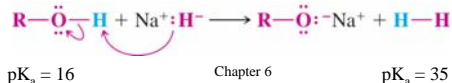
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Alkoxide bases are made from the corresponding alcohols

By adding metallic Na or K to carefully dried alcohol



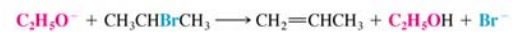
Or by using a stronger base like sodium hydride (NaH)



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Mechanism of Dehydrohalogenation: the E2 Reaction

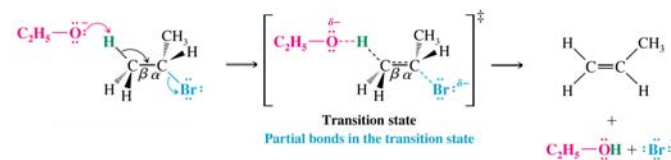
The reaction of isopropyl bromide with sodium ethoxide shows second order kinetics



$$\text{Rate} \propto [\text{CH}_3\text{CHBrCH}_3][\text{C}_2\text{H}_5\text{O}^-]$$

$$\text{Rate} = k[\text{CH}_3\text{CHBrCH}_3][\text{C}_2\text{H}_5\text{O}^-]$$

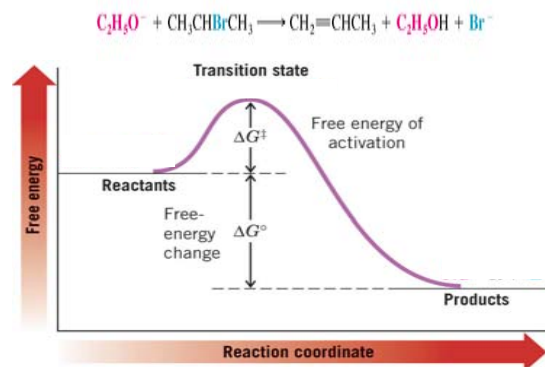
Mechanism:



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Energy diagram of the E2 reaction



Concerted means a single step, with no intermediates – like $\text{S}_{\text{N}}2$

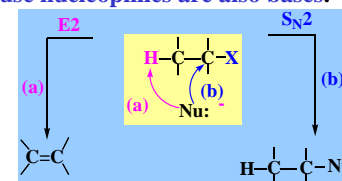
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Substitution versus Elimination

Every time an $\text{S}_{\text{N}}2$ reaction takes place, there will also be some E2 occurring as well.

Why? **Because nucleophiles are also bases.**



$$\text{Rate} = k_{\text{elim}} [\text{RX}] [\text{Nu}^-] \quad \text{Rate} = k_{\text{sub}} [\text{RX}] [\text{Nu}^-]$$

However, this competition depends on the structure of RX and choice of base.

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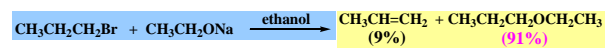
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♦ Substitution versus Elimination

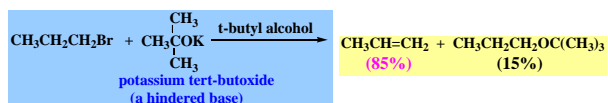
• $\text{S}_{\text{N}}2$ VERSUS E2

→ PRIMARY SUBSTRATE

¶ If the base is small, $\text{S}_{\text{N}}2$ is favored because approach at carbon is unhindered



¶ If the base is bulky, E2 is favored because approach at carbon is hindered

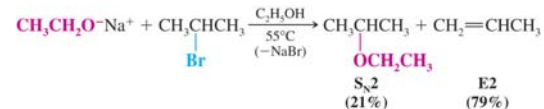


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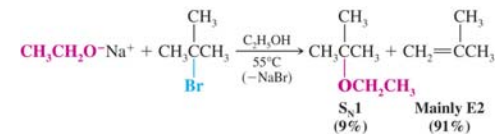
→ SECONDARY SUBSTRATE

¶ Approach to carbon is sterically hindered and E2 ELIMINATION IS FAVORED, especially if the base is strong.



→ TERTIARY SUBSTRATE

¶ Approach to carbon is extremely hindered and ELIMINATION PREDOMINATES.



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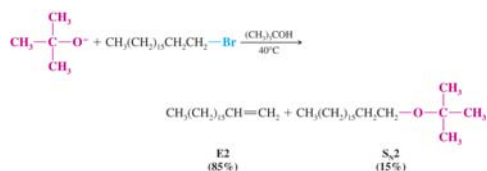
→ EFFECT OF TEMPERATURE

Increasing temperature favors elimination over substitution

→ EFFECT OF THE SIZE OF THE BASE/NUCLEOPHILE

Large, sterically hindered bases favor elimination because they cannot directly approach the carbon closely enough to react in a substitution

Potassium *tert*-butoxide is an extremely bulky base and is routinely used to favor E2 reaction

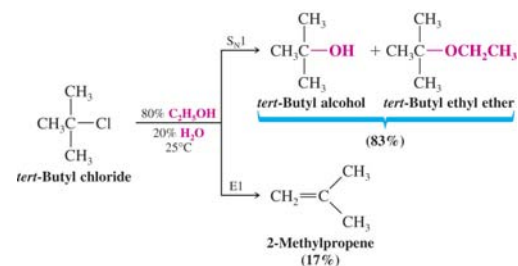


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♦ Elimination can also follow first order kinetics: the E1 REACTION

The E1 reaction competes with the S_N1 reaction and likewise goes through a carbocation intermediate

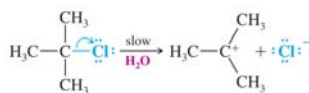


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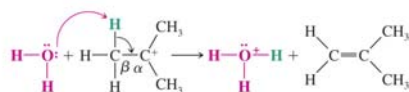
Mechanism for E1

Step 1



Slow step is ionization of C-Cl bond, aided by solvent

Step 2



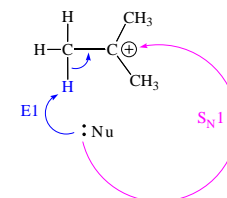
Water can act as nucleophile (S_N1) OR as base (E1)

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Mechanism for E1

In other words, there are **two competing pathways** that a carbocation can take:

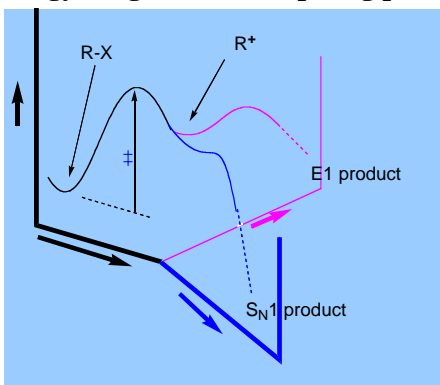


1. The nucleophile bonds to the carbocation carbon giving the S_N1 product.
OR
2. The nucleophile acts as a base and removes the β proton giving the E1 product.

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Free Energy Diagram for competing pathways



Once the carbocation forms, it can go two different ways to give the S_N1 product and the E1 product.

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◆ Overall Summary

Factor	S_N1	S_N2
Substrate	3° (requires formation of a relatively stable carbocation)	Methyl > 1° > 2° (requires unhindered substrate)
Nucleophile	Weak Lewis base, neutral molecule, nucleophile may be the solvent (solvolysis)	Strong Lewis base, rate favored by high concentration of nucleophile
Solvent	Polar protic (e.g., alcohols, water)	Polar aprotic (e.g., DMF, DMSO)
Leaving group	I > Br > Cl > F for both S_N1 and S_N2 (the weaker the base after the group departs, the better the leaving group)	

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Overall Summary of Substitution/Elimination Effect of Substrate Structure

	S_N1	S_N2	E1	E2
CH_3X	—	yes, very fast	—	—
RCH_2X	—	mostly	—	but hindered bases give mostly alkenes
$\begin{array}{c} R' \\ \\ RCHX \end{array}$	very little	mostly S_N2 with weak bases	very little	strong bases promote E2
$\begin{array}{c} R' \\ \\ R-CX \\ \\ R'' \end{array}$	very favorable	none	always competes with S_N1	strong bases promote E2 path

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Alkyl Halides and Nucleophilic Substitution

Predicting the Likely Mechanism of a Substitution Reaction.

TABLE 7.7 Summary of Factors that Determine the S_N1 or S_N2 Mechanism

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CH_3X RCH_2X (1°)	S_N2	Favored by <ul style="list-style-type: none"> strong nucleophiles (usually a net negative charge) polar aprotic solvents
R_3CX (3°)	S_N1	Favored by <ul style="list-style-type: none"> weak nucleophiles (usually neutral) polar protic solvents
R_2CHX (2°)	S_N1 or S_N2	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, H_2O and CH_3OH are polar protic solvents that favor the S_N1 mechanism, whereas acetone [$(CH_3)_2C=O$] and DMSO [$(CH_3)_2S=O$] are polar aprotic solvents that favor the S_N2 mechanism.

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