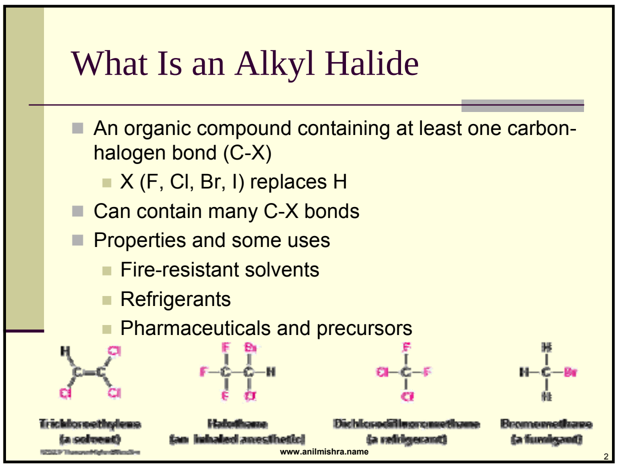


What Is an Alkyl Halide

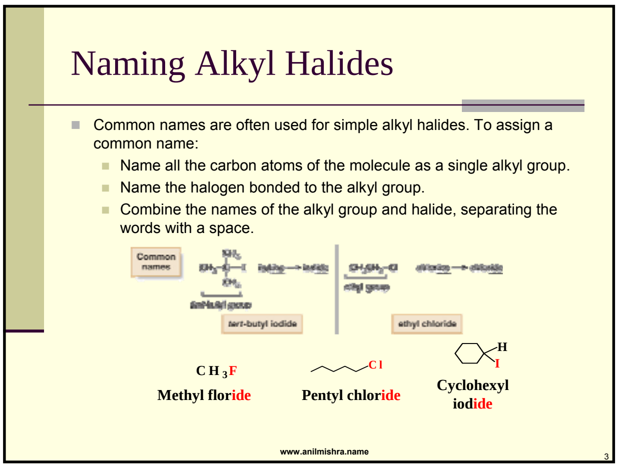
- An organic compound containing at least one carbon-halogen bond (C-X)
  - X (F, Cl, Br, I) replaces H
- Can contain many C-X bonds
- Properties and some uses
  - Fire-resistant solvents
  - Refrigerants
  - Pharmaceuticals and precursors

Trichloroethylene (a solvent)

Halothane (an inhaled anesthetic)

Dichlorodifluoromethane (a refrigerant)

Bromomethane (a fumigant)



Naming Alkyl Halides

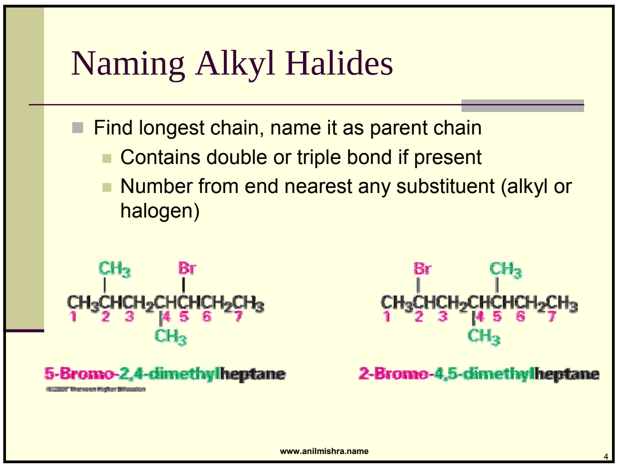
- Common names are often used for simple alkyl halides. To assign a common name:
  - Name all the carbon atoms of the molecule as a single alkyl group.
  - Name the halogen bonded to the alkyl group.
  - Combine the names of the alkyl group and halide, separating the words with a space.

CH_3F

Methyl floride

Pentyl chloride

Cyclohexyl iodide

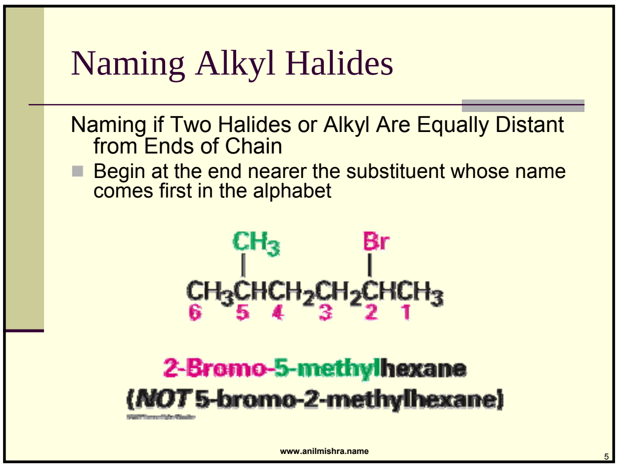


Naming Alkyl Halides

- Find longest chain, name it as parent chain
  - Contains double or triple bond if present
  - Number from end nearest any substituent (alkyl or halogen)

5-Bromo-2,4-dimethylheptane

2-Bromo-4,5-dimethylheptane



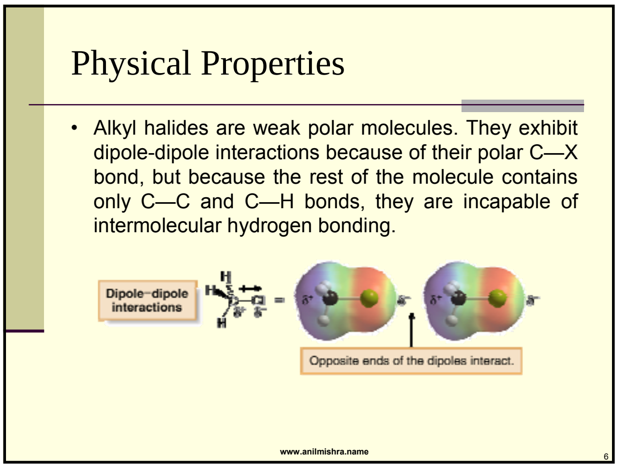
Naming Alkyl Halides

Naming if Two Halides or Alkyl Are Equally Distant from Ends of Chain

- Begin at the end nearer the substituent whose name comes first in the alphabet

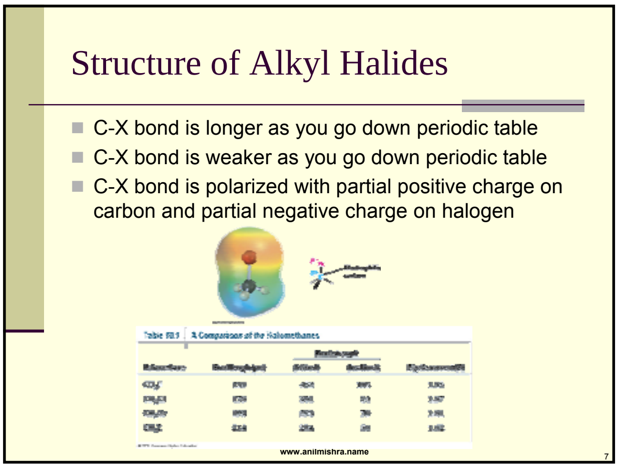
2-Bromo-5-methylhexane

(*NOT* 5-bromo-2-methylhexane)



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.



Structure of Alkyl Halides

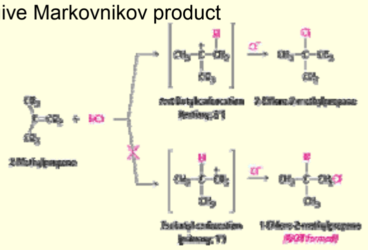
- C-X bond is longer as you go down periodic table
- C-X bond is weaker as you go down periodic table
- C-X bond is polarized with partial positive charge on carbon and partial negative charge on halogen

A Comparison of the Halomethanes

Preparing Alkyl Halides

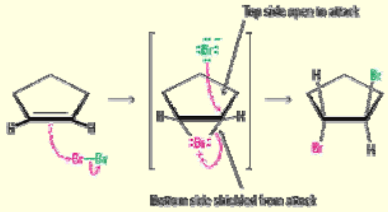
From Alkenes

- Alkyl halide from addition of HCl, HBr, HI to alkenes to give Markovnikov product



Preparing Alkyl Halides

- Alkyl dihalide from *anti* addition of bromine or chlorine



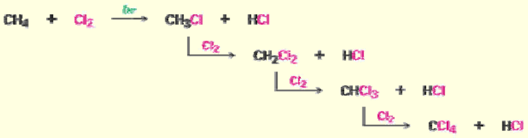
Preparing Alkyl Halides

From Alkanes:

- Radical Halogenation
- Alkane + Cl_2 or Br_2, heat or light replaces C-H with C-X but gives mixtures
  - Hard to control
  - Via free radical mechanism
- It is usually not a good idea to plan a synthesis that uses this method—multiple products

Preparing Alkyl Halides

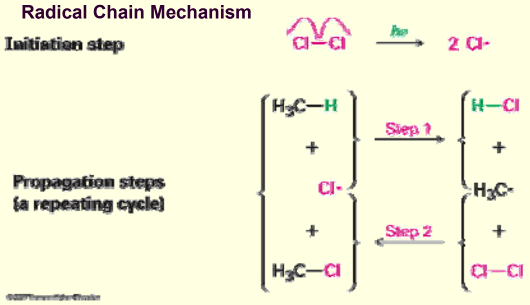
Radical Chain Mechanism



$$CH_4 + Cl_2 \xrightarrow{h\nu} CH_3Cl + HCl$$
$$\xrightarrow{Cl_2} CH_2Cl_2 + HCl$$
$$\xrightarrow{Cl_2} CHCl_3 + HCl$$
$$\xrightarrow{Cl_2} CCl_4 + HCl$$

Preparing Alkyl Halides

Radical Chain Mechanism



Preparing Alkyl Halides

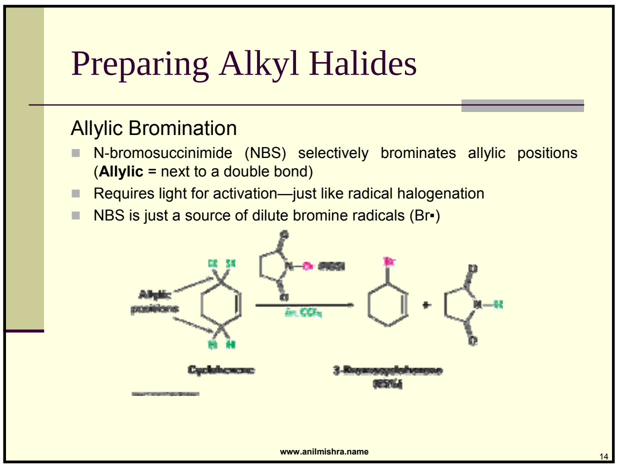
Radical Chain Mechanism

Termination steps

$$H_3C\cdot + \cdot CH_3 \longrightarrow H_3C{-}CH_3$$
$$Cl\cdot + \cdot CH_3 \longrightarrow Cl{-}CH_3$$
$$Cl\cdot + \cdot Cl \longrightarrow Cl{-}Cl$$

Overall reaction

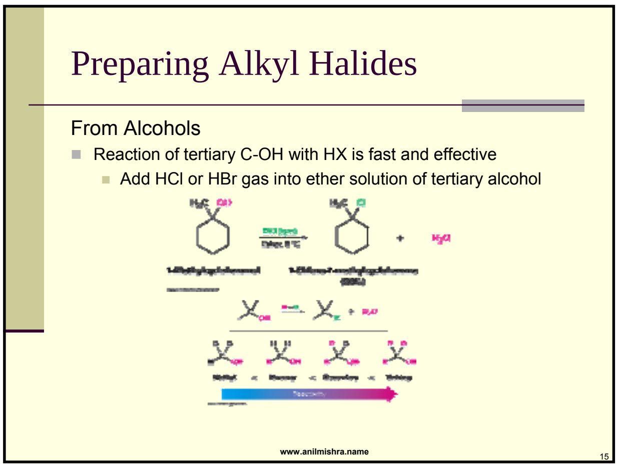
$$CH_4 + Cl_2 \longrightarrow CH_3Cl + HCl$$



Preparing Alkyl Halides

Allylic Bromination

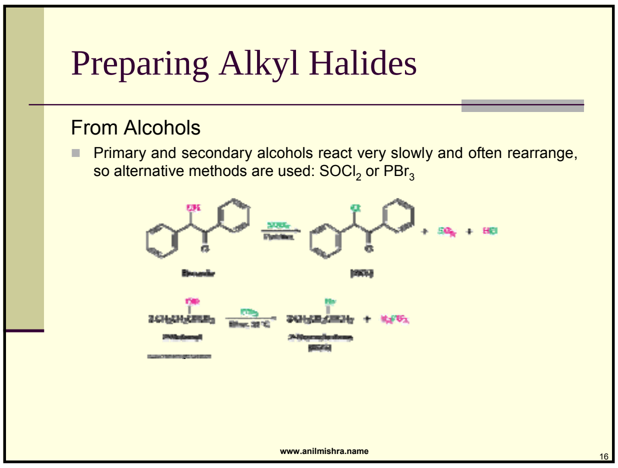
- N-bromosuccinimide (NBS) selectively brominates allylic positions (**Allylic** = next to a double bond)
- Requires light for activation—just like radical halogenation
- NBS is just a source of dilute bromine radicals (Br•)



Preparing Alkyl Halides

From Alcohols

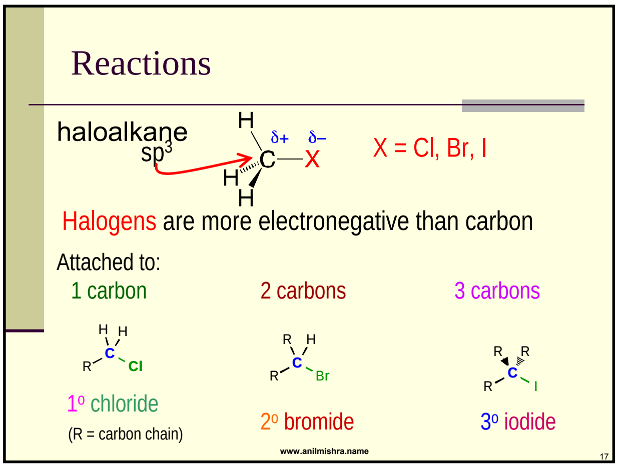
- Reaction of tertiary C-OH with HX is fast and effective
  - Add HCl or HBr gas into ether solution of tertiary alcohol



Preparing Alkyl Halides

From Alcohols

- Primary and secondary alcohols react very slowly and often rearrange, so alternative methods are used: $SOCl_2$ or PBr_3



Reactions

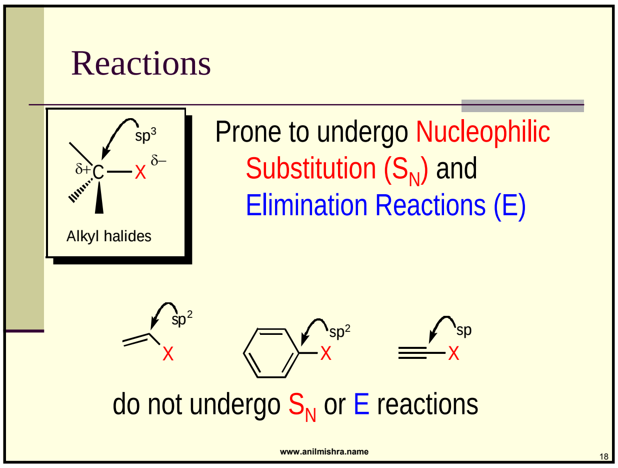
haloalkane

X = Cl, Br, I

Halogens are more electronegative than carbon

Attached to:

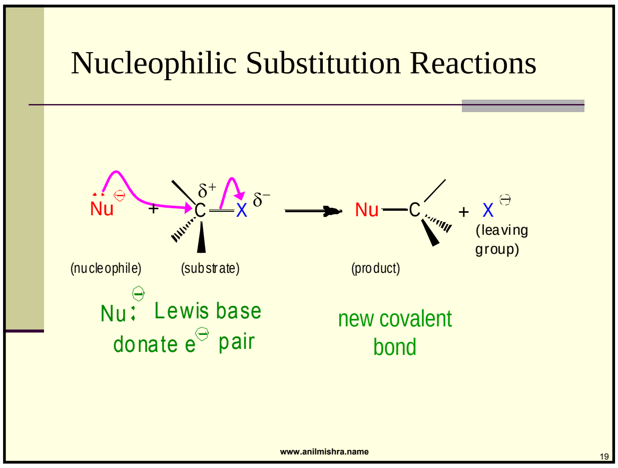
1 carbon	2 carbons	3 carbons
1° chloride (R = carbon chain)	2° bromide	3° iodide



Reactions

Prone to undergo Nucleophilic Substitution (S_N) and Elimination Reactions (E)

do not undergo S_N or E reactions



Nucleophilic Substitution Reactions

Nu:⊖ Lewis base donate e⊖ pair

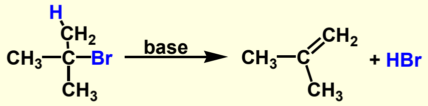
new covalent bond

Reactions

- Alkyl halides (R-X) undergo two types of reactions :
  - ***Substitution*** reactions
  - ***Elimination*** reactions

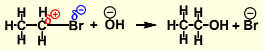
Reactions

- In an ***elimination*** reaction, the elements of H-X are ***eliminated*** from R-X
  - The product is very often an alkene.



Reactions

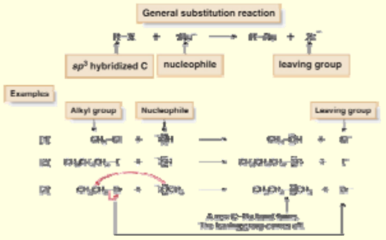
- In a ***substitution*** reaction, the X group in R-X is ***replaced*** by a different group, e.g. **R-X→R-OH +X$^{\ominus}$**
- This is a ***nucleophilic substitution*** or nucleophilic displacement reaction on which OH displaces Br.



- The C-Br bond is polar, and the carbon ($\delta^{\oplus}$) is susceptible to attack by an anion or any other ***nucleophile***.
  - **$^{\ominus}$OH** is the ***nucleophile***
    - Species which "loves nuclei" or has an affinity for positive charges
  - **Br$^{\ominus}$** is the ***leaving group***

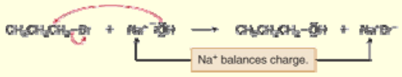
Reactions

- General Features of Nucleophilic Substitution
- Three components are necessary in any substitution reaction.

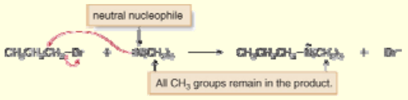


Reactions

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

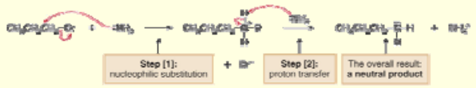


- **When a neutral nucleophile is used, the substitution product bears a positive charge.**



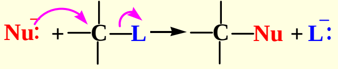
Reactions

- **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.**



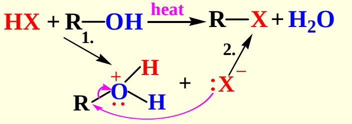
Nucleophilic Substitution

General type of the reaction:



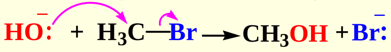
$$\overset{-}{Nu:} + -\underset{|}{\overset{|}{C}}-L \longrightarrow -\underset{|}{\overset{|}{C}}-Nu + \overset{-}{L:}$$

Ex. The reaction of ROH with HX



$$HX + R-OH \xrightarrow{heat} R-X + H_2O$$

The reaction of alkyl halides with sodium hydroxide:



$$\overset{-}{HO:} + H_3C-Br \longrightarrow CH_3OH + \overset{-}{Br:}$$

$:X^-$ and $\overset{-}{HO:}$ are nuclophiles

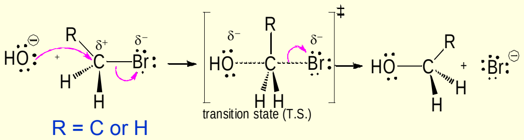
Mechanism

- Chemists propose two limiting mechanisms for nucleophilic displacement
  - a fundamental difference between them is the timing of bond breaking and bond forming steps

Nucleophilic Substitution Reactions

Two types of mechanisms

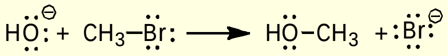
- 1st type: S_N2 (concerted mechanism)



transition state (T.S.)

R = C or H

S_N2 Reaction:



$$H\ddot{O}:^{\ominus} + CH_3-Br: \longrightarrow HO-CH_3 + :Br:^{\ominus}$$

The rate(speed) of reaction is directly proportional to the concentration of either reactant.

When the concentration of either reactant is doubled, the rate of reaction doubles.

Rate *dependant on* $[CH_3Br][OH^-]$

Rate = $k[CH_3Br][OH^-]$

second order rx - bimolecular

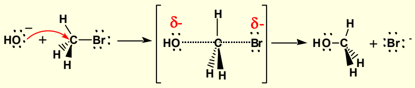
Mechanism

- At one extreme, the two processes take place simultaneously; designated S_N2
  - S = substitution
  - N = nucleophilic
  - 2 = bimolecular
    - Two species are involved in the rate-determining step
  - rate = k[haloalkane][nucleophile]

S_N2 Reaction:

Bimolecular Nucleophilic Substitution

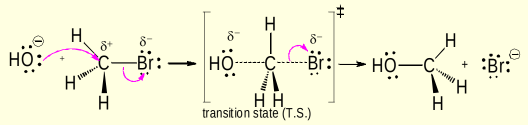
- both reactants are involved in the transition state of the rate-determining step
- the nucleophile attacks the reactive center from the side opposite the leaving group



Transition state with simultaneous bond breaking and bond forming

S_N2 Reaction:

A Mechanism for the S_N2 Reaction

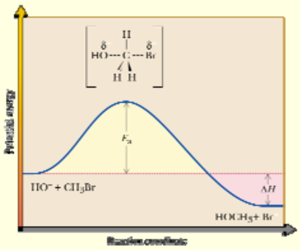


second order rx - **s**ubstitution **n**ucleophilic **bi**molecular

S_N2

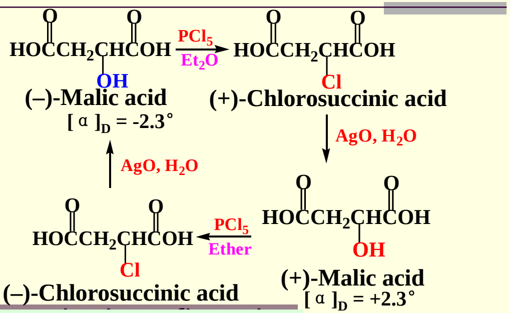
S_N2

- An energy diagram for an S_N 2 reaction
  - there is one transition state and no reactive intermediate



Nucelophilic Substitution

Paul Walden made a remarkable discovery:



Inversion in configuration

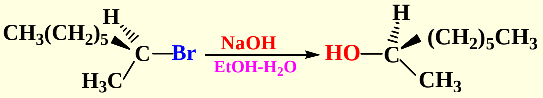
Paul Walden
1863-1957

Born 14 July 1863; died 24 January 1957. Paul Walden was a Latvian chemist who, while teaching at Riga, discovered the Walden inversion, a reversal of stereochemical configuration that occurs in many reactions of covalent compounds (1896). Due to this discovery, Walden's name is mentioned almost in all textbooks on organic chemistry published throughout the world.

Walden revealed autoracemization and put the foundations to electrochemistry of nonaqueous solutions. Walden is also known for Walden's rule, which relates the conductivity and viscosity of nonaqueous solutions.

Stereochemistry of S_N2 Reactions

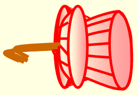
- The substitution by SN2 mechanism is **stereoselective** and proceeds with **inversion of conjugation** at carbon that bears the leaving group.



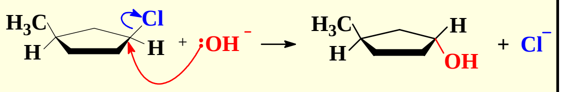
(S)-(+)-2-Bromooctane **(R)-(-)-2-Octanol**

Stereochemistry of S_N2 Reactions

Like an umbrella in the gale



An inversion of configuration

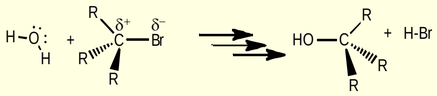


SN1 Reaction

- In the other limiting mechanism, bond breaking between carbon and the leaving group is entirely completed before bond forming with the nucleophile begins. This mechanism is designated S_N1 where
  - S = substitution
  - N = nucleophilic
  - 1 = unimolecular
    - only one species is involved in the rate-determining step
  - rate = k[haloalkane]

SN1 Reaction

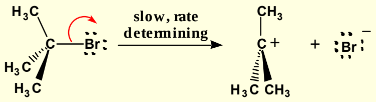
- 2nd type: S_N1 (stepwise mechanism)



S_N1 Reaction

Unimolecular Nucleophilic Substitution

- S_N1 is illustrated by the solvolysis of *tert*-butyl bromide
  - Step 1: ionization of the C-X bond gives a carbocation intermediate

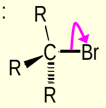


A carbocation intermediate; carbon is trigonal planar

S_N1 Reaction

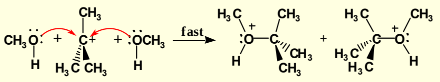
2nd type: S_N1 (stepwise mechanism)

Step (1):



S_N1 Reaction

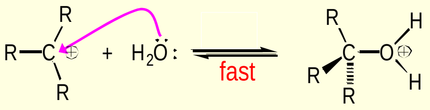
- Step 2: reaction of the carbocation (an electrophile) with methanol (a nucleophile) gives an oxonium ion



S_N1 Reaction

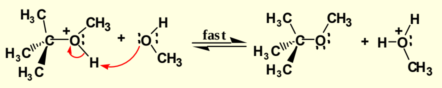
2nd type: S_N1 (stepwise mechanism)

Step (2)



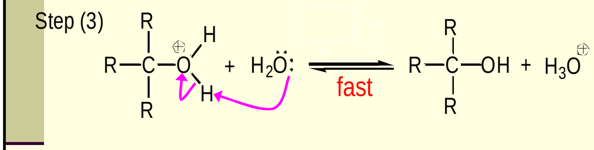
S_N1 Reaction

- Step 3: proton transfer completes the reaction



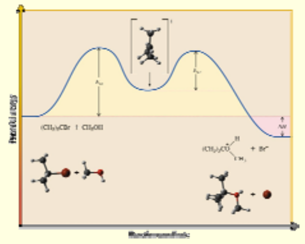
S_N1 Reaction

2nd type: S_N1 (stepwise mechanism)



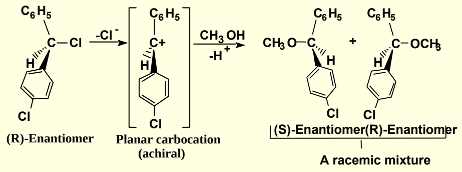
S_N1 Reaction

- An energy diagram for an S_N1 reaction



S_N1 Reaction

- For an S_N1 reaction at a stereocenter, the product is a racemic mixture
- the nucleophile attacks with equal probability from either face of the planar carbocation intermediate

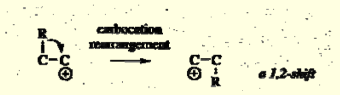


Summary of S_N1 and S_N2

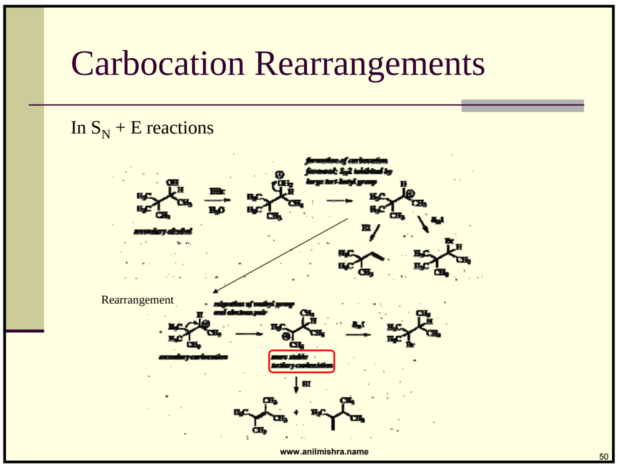
Type of Haloalkane	S_N2	S_N1
Methyl CH_3X	S_N2 is favored.	S_N1 does not occur. The methyl cation is so unstable that it is never observed in solution.
Primary RCH_2X	S_N2 is favored.	S_N1 does not occur. Primary carbocations are so unstable that they are never observed in solution.
Secondary R_2CHX	S_N2 is favored in aprotic solvents with good nucleophiles.	S_N1 is favored in protic solvents with poor nucleophiles.
Tertiary R_3CX	S_N2 does not occur because of steric hindrance around the substitution center.	S_N1 is favored because of the ease of formation of tertiary carbocations.
Substitution at a stereocenter	Inversion of configuration. The nucleophile attacks the stereocenter from the side opposite the leaving group.	Racemization. The carbocation intermediate is planar, and attack by the nucleophile occurs with equal probability from either side.

Carbocation Rearrangements

- The driving force of rearrangements is
  - To form a more stable carbocation !!!
- Happens often with secondary carbocations
  - More stable tertiary carbocation



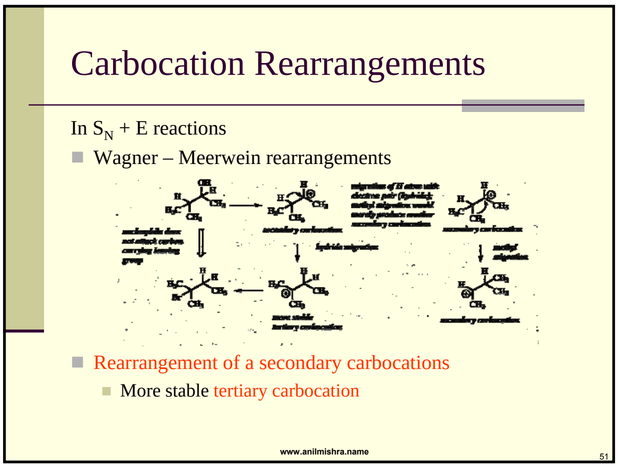
Also 1,3- and other shifts are possible



Carbocation Rearrangements

In S_N + E reactions

Rearrangement



Carbocation Rearrangements

In S_N + E reactions

- Wagner – Meerwein rearrangements

- Rearrangement of a secondary carbocations
  - More stable tertiary carbocation