

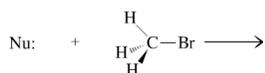
## The S<sub>N</sub>2 Mechanism of Nucleophilic Substitution

mechanism of the S<sub>N</sub>2 reaction



Bimolecular Reaction

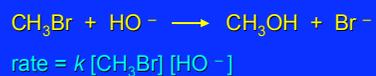
Click "React" to begin S<sub>N</sub>2 reaction.



React

## Kinetics

Many nucleophilic substitutions follow a second-order rate law.



What is the reaction order of each starting material?

What can you infer on a molecular level?

What is the overall order of reaction?

## Bimolecular mechanism

one step  
concerted

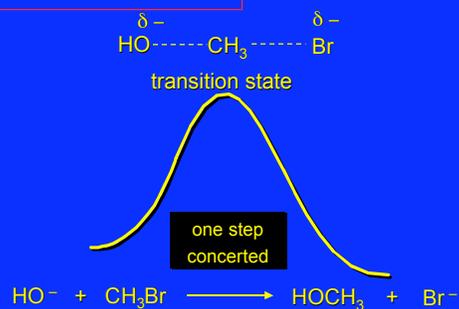


## Bimolecular mechanism

one step  
concerted

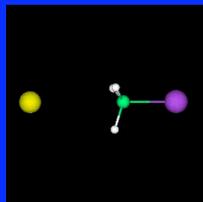


### Bimolecular mechanism



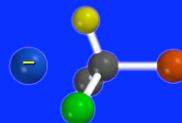
### Stereochemistry of S<sub>N</sub>2 Reactions

### Generalization



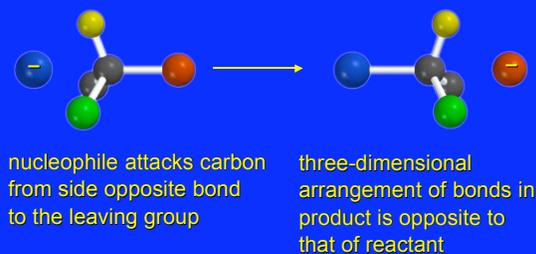
Nucleophilic substitutions that exhibit second-order kinetic behavior are stereospecific and proceed with inversion of configuration.

### Inversion of Configuration

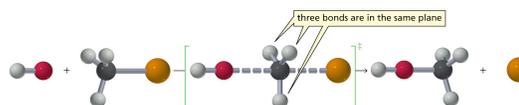


nucleophile attacks carbon from side opposite bond to the leaving group

### Inversion of Configuration



*Inversion of configuration (Walden inversion) in an S<sub>N</sub>2 reaction is due to back side attack*



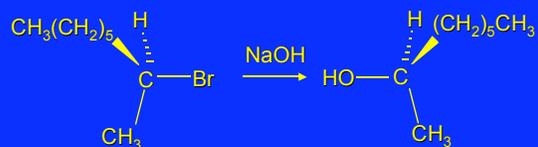
### Stereospecific Reaction

A stereospecific reaction is one in which stereoisomeric starting materials give stereoisomeric products.

The reaction of 2-bromooctane with NaOH (in ethanol-water) is stereospecific.



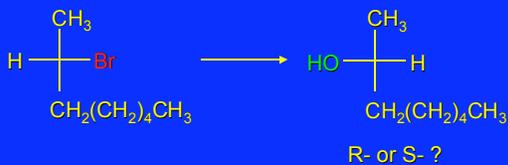
### Stereospecific Reaction



(S)-(+)-2-Bromooctane

(R)-(-)-2-Octanol

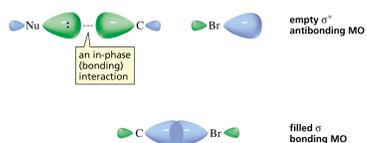
- 1) Draw the Fischer projection formula for (+)-S-2-bromooctane.
- 2) Write the Fischer projection of the (-)-2-octanol formed from it by nucleophilic substitution with inversion of configuration.



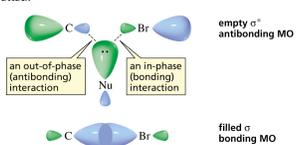
A conceptual view of  $S_N2$  reactions

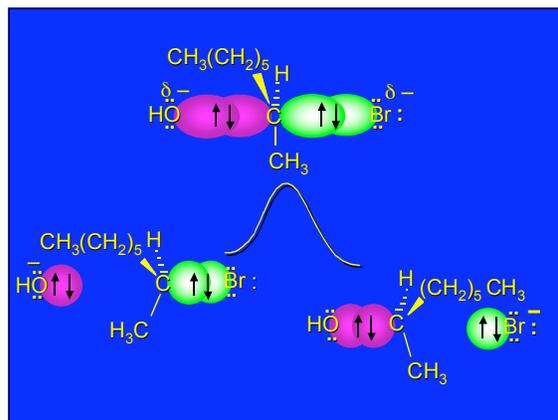
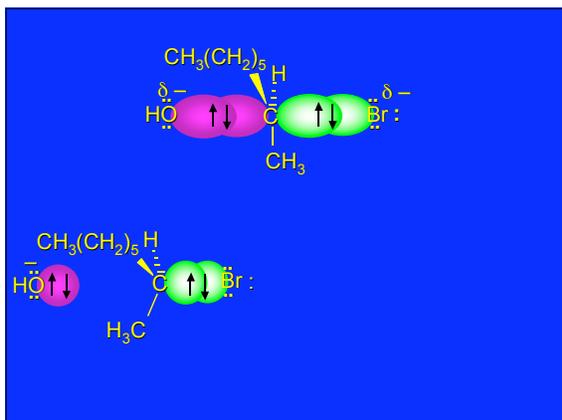
### Why does the nucleophile attack from the back side?

#### a. Back-side attack



#### b. Front-side attack





Steric Effects in  $S_N2$  Reactions

**Crowding at the Reaction Site**

The rate of nucleophilic substitution by the  $S_N2$  mechanism is governed by steric effects.

Crowding at the carbon that bears the leaving group slows the rate of bimolecular nucleophilic substitution.

**Reactivity toward substitution by the  $S_N2$  mechanism**

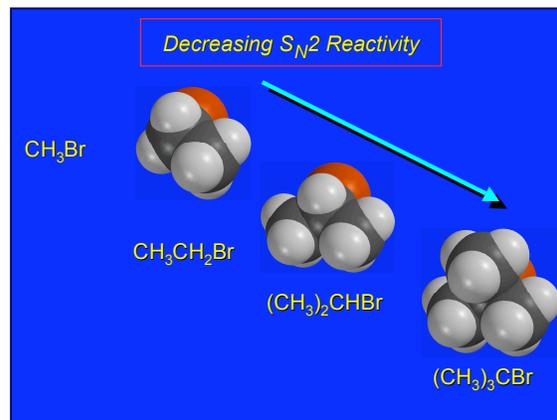
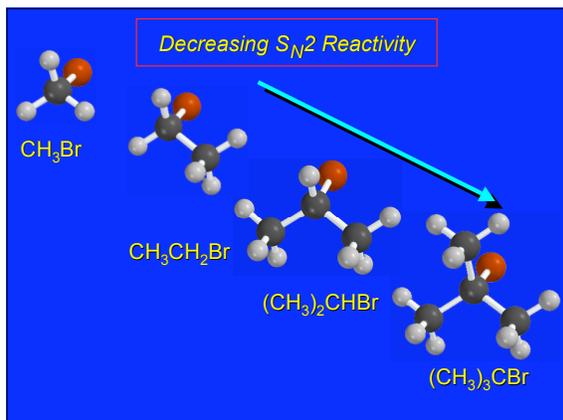
$$RBr + LiI \rightarrow RI + LiBr$$

Alkyl bromide	Class	Relative rate
$CH_3Br$	Methyl	221,000
$CH_3CH_2Br$	Primary	1,350
$(CH_3)_2CHBr$	Secondary	1
$(CH_3)_3CBr$	Tertiary	too small to measure

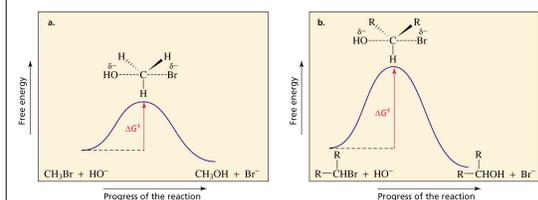
*A bulky substituent in the alkyl halide reduces the reactivity of the alkyl halide: steric hindrance*

relative reactivities of alkyl halides in an  $S_N2$  reaction

most reactive  $\left\{ \text{methyl halide} > 1^\circ \text{ alkyl halide} > 2^\circ \text{ alkyl halide} > 3^\circ \text{ alkyl halide} \right\}$  least reactive



Reaction coordinate diagrams for (a) the  $S_N2$  reaction of methyl bromide and (b) an  $S_N2$  reaction of a sterically hindered alkyl bromide



Crowding Adjacent to the Reaction Site

The rate of nucleophilic substitution by the  $S_N2$  mechanism is governed by steric effects.

Crowding at the carbon adjacent to the one that bears the leaving group also slows the rate of bimolecular nucleophilic substitution, but the effect is smaller.

Effect of chain branching on rate of  $S_N2$  substitution



Alkyl bromide	Structure	Relative rate
Ethyl	CH <sub>3</sub> CH <sub>2</sub> Br	1.0
Propyl	CH <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub> Br	0.8
Isobutyl	(CH <sub>3</sub> ) <sub>2</sub> CHCH <sub>2</sub> Br	0.036
Neopentyl	(CH <sub>3</sub> ) <sub>3</sub> CCH <sub>2</sub> Br	0.00002