HALOALKANES

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Preparation of Haloalkanes

- From
  - Alkanes
  - Alkenes
  - Alcohols
  - Carboxylic Acids (Hundsdicker Reaction)
  - Halide Exchange Method
    - » Finkelstein Reaction
    - » Swarts Reaction

Physical Properties of Alkyl Halides:

- Boiling point
- Solubility in water

Effect of Structure on Boiling Point

	$CH_3CH_2CH_3$	CH_3CH_2F
Molecular weight	44	48
Boiling point, ℃	-42	-32
Dipole moment, D	0	1.9

Boiling point increases with increasing number of halogens

Compound	Boiling Point
• CH_3Cl	-24°C
• CH_2Cl_2	40°C
• $CHCl_3$	61°C
• CCl_4	77°C

Even though CCl_4 is the only compound in this list without a dipole moment, it has the highest boiling point.

Induced dipole-induced dipole forces are greatest in CCl_4 because it has the greatest number of Cl atoms. Cl is more polarizable than H.

PHYSICAL PROPERTIES

Boiling point Increases with molecular size due to increased van der Waals' forces

	M_r	bp / ℃
chloroethane	**64.5**	**13**
1- chloropropane	**78.5**	**47**
1-bromopropane	**124**	**71**

Boiling point also increases for "straight" chain isomers.

Greater branching = lower inter-molecular forces

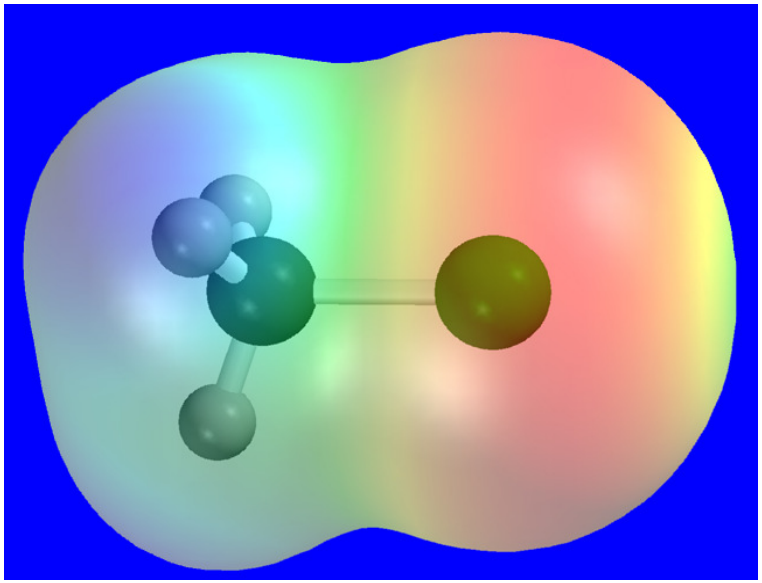
		bp/℃
1-bromobutane	**$CH_3CH_2CH_2CH_2Br$**	**101**
2-bromobutane	**$CH_3CH_2CHBrCH_3$**	**91**
2-bromo -2-methylpropane	**$(CH_3)_3CBr$**	**73**

Solubility in water

- Alkyl halides are insoluble in water.

- Methanol, ethanol, isopropyl alcohol are completely miscible with water.

μ = 1.9 D



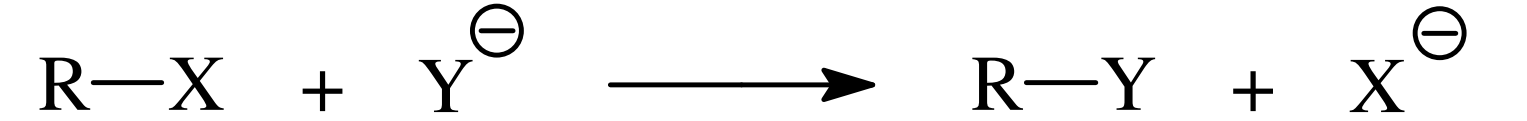
Chemical Properties

I. Nucleophilic Aliphatic Substitution
   A. Mechanisms of nucleophilic substitution
      1. S_N2 mechanism
      2. S_N1 mechanism
   B. Factors influencing S_N1 and S_N2 reactions
      1. Nucleophile
      2. Substrate structure
      3. Leaving group
      4. Solvent

II. Elimination
   A. Mechanisms of elimination
      1. E2 mechanism
      2. E1 mechanism

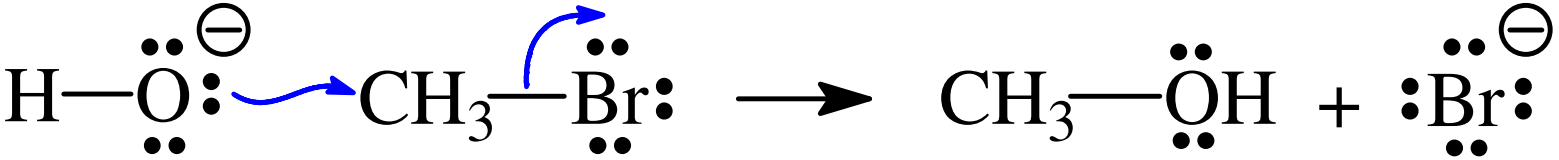
III. Reaction with Active metals

I. Nucleophilic Aliphatic Substitution

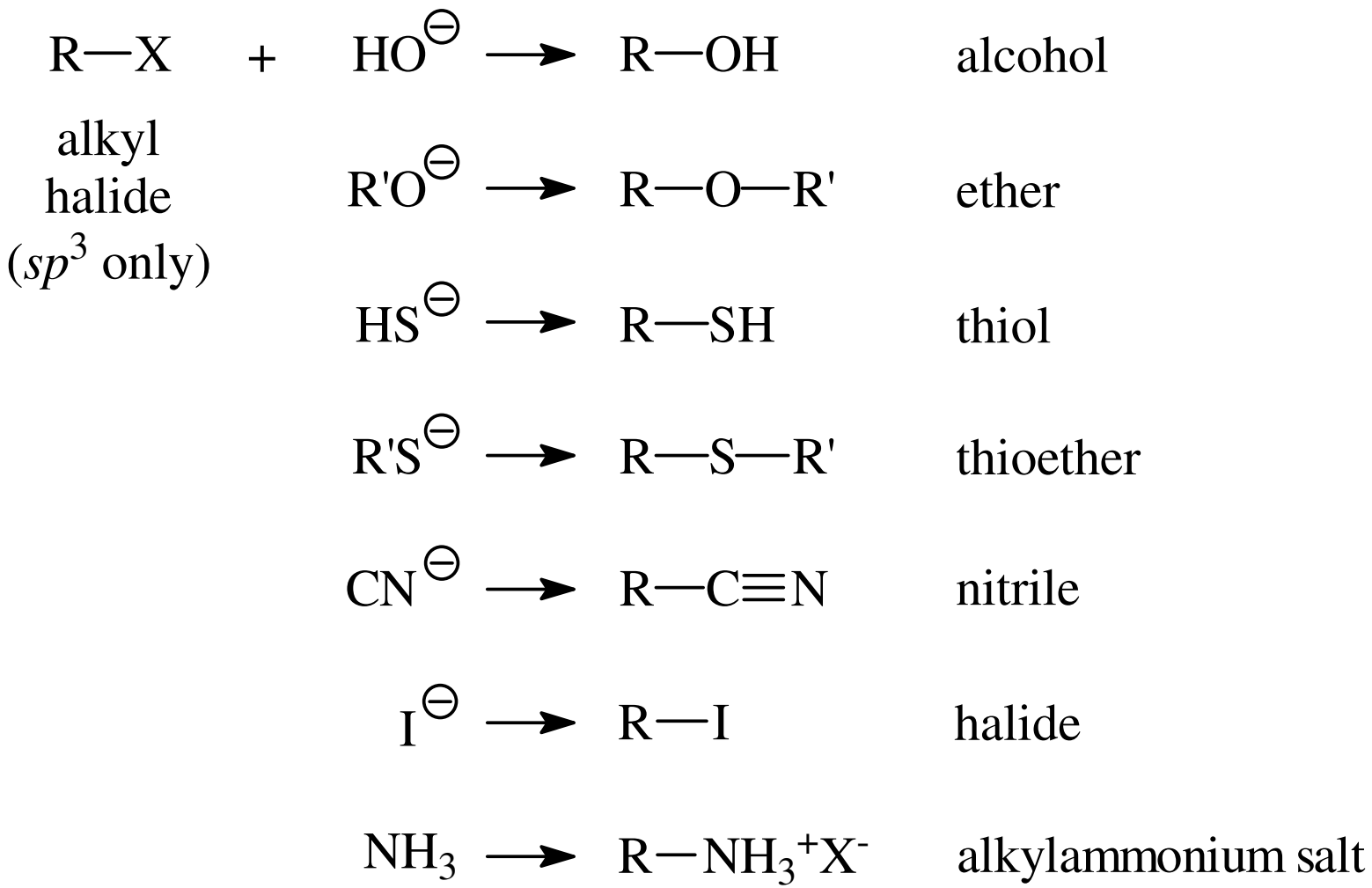


substrate nucleophile product leaving group

e.g.,



I. Nucleophilic Aliphatic Substitution

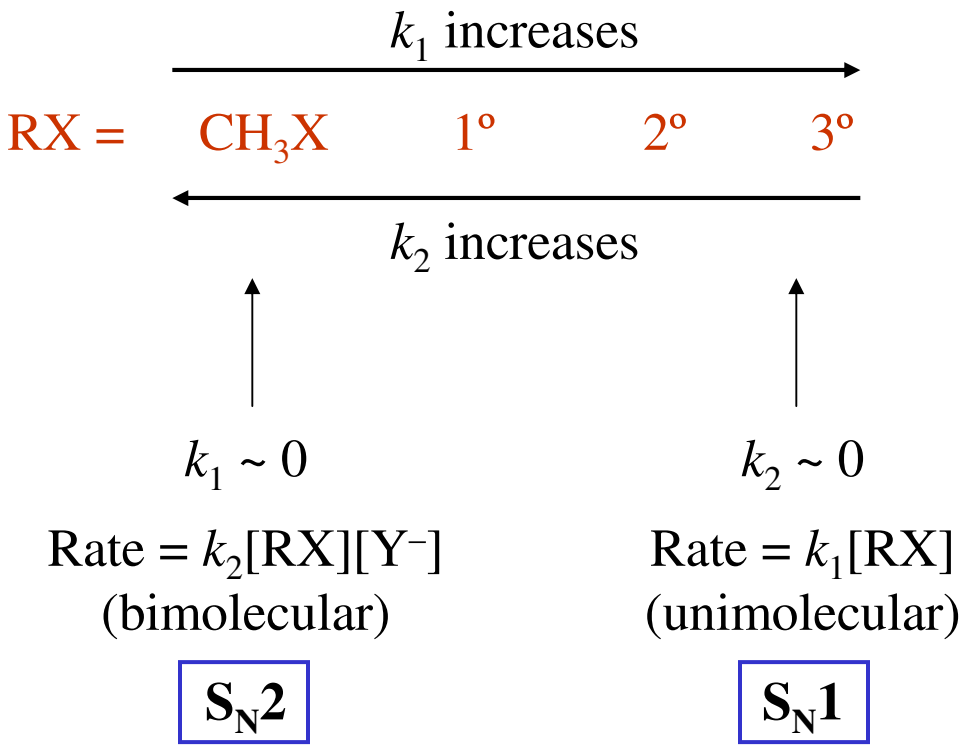


Nucleophilic Aliphatic Substitution

B. Mechanisms of nucleophilic substitution

Two mechanisms:

General: Rate = k_1[RX] + k_2[RX][Y^-]



Nucleophilic Aliphatic Substitution

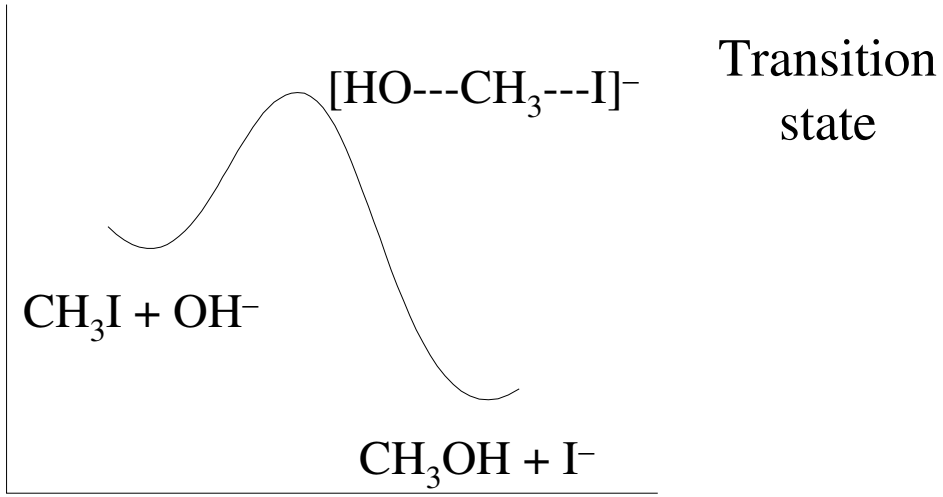
1. S_N2 mechanism

e.g., $CH_3I + OH^- \rightarrow CH_3OH + I^-$

find: Rate = $k[CH_3I][OH^-]$, *i.e.*, **bimolecular**

$\therefore$ both CH_3I and OH^- involved in RDS

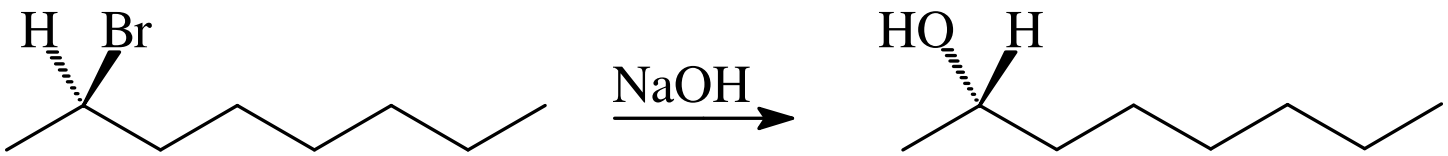
$\Rightarrow$ **concerted, single-step mechanism**:



Nucleophilic Aliphatic Substitution

1. S_N2 mechanism

Stereospecific reaction:



(*R*)-(–)-2-bromooctane

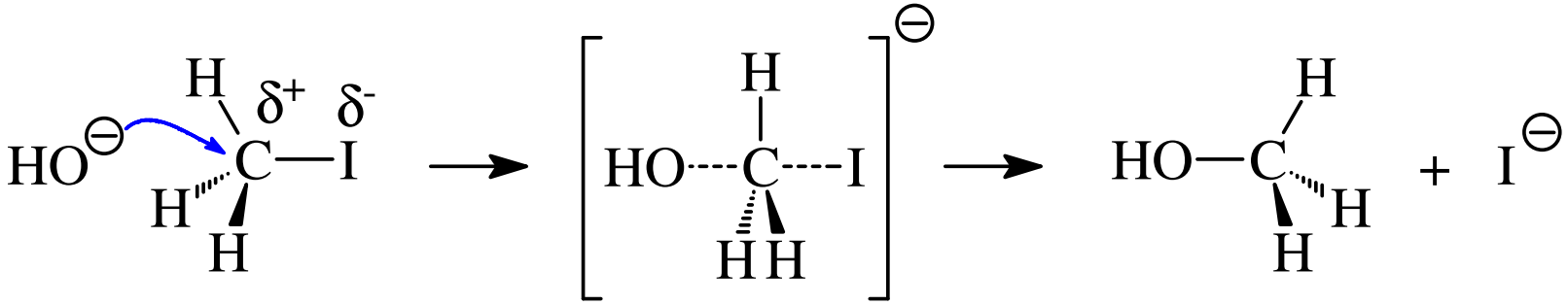
(*S*)-(+)-2-octanol

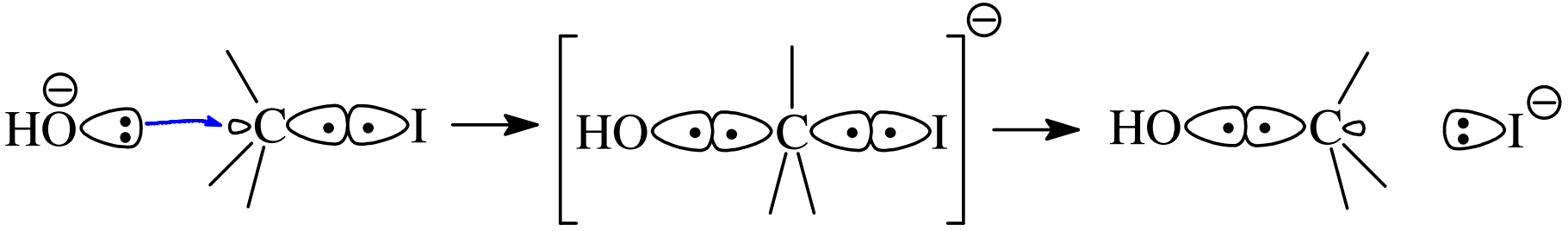
Reaction proceeds with
inversion of configuration.

Nucleophilic Aliphatic Substitution

1. S_N2 mechanism

back-side attack: inversion of configuration





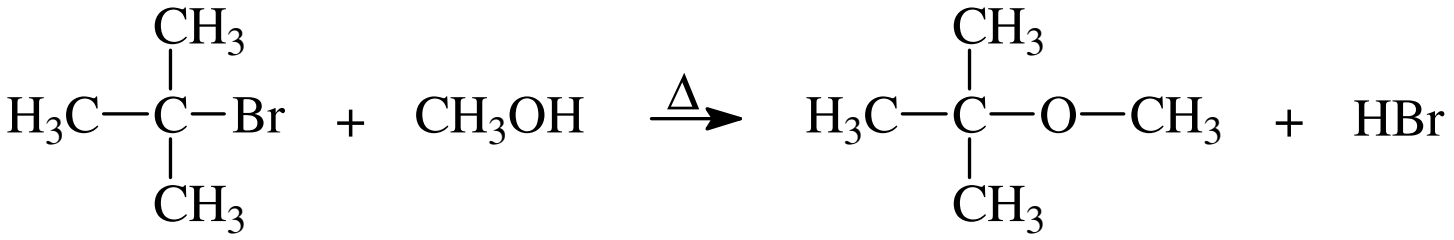
sp^3 sp^2 sp^3

high energy TS

II. Nucleophilic Aliphatic Substitution

2. S_N1 mechanism

e.g.,

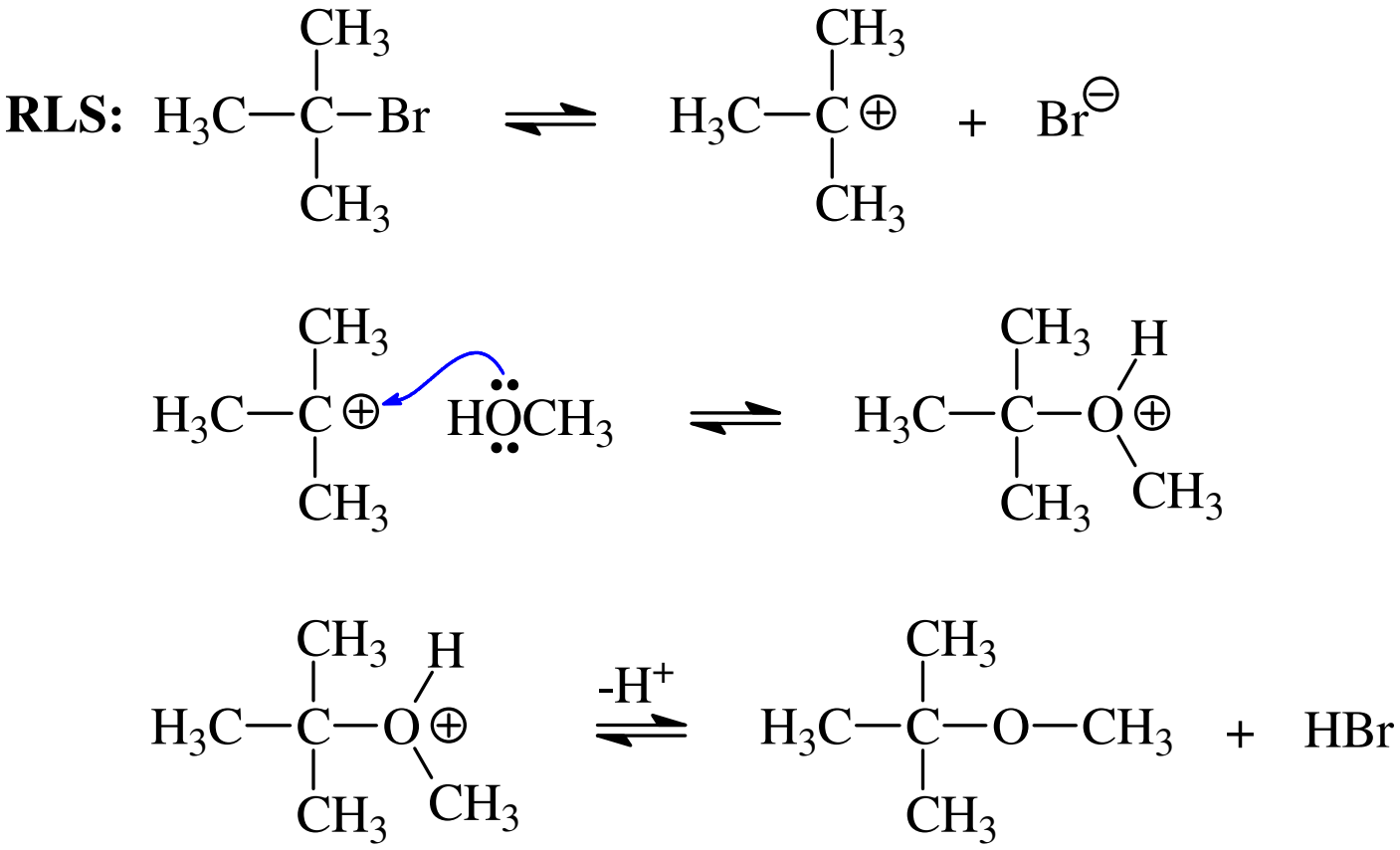


Find: Rate = $k[(CH_3)_3CBr]$ **Unimolecular**

$\therefore$ RDS depends only on $(CH_3)_3CBr$

II. Nucleophilic Aliphatic Substitution

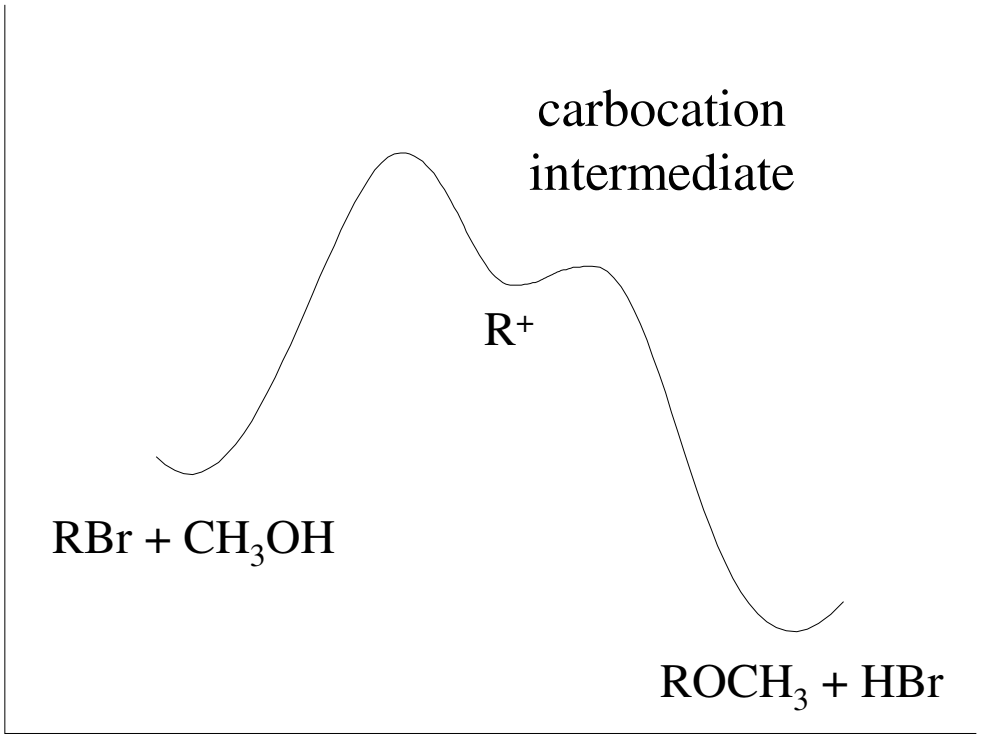
2. S_N1 mechanism



II. Nucleophilic Aliphatic Substitution

2. S_N1 mechanism

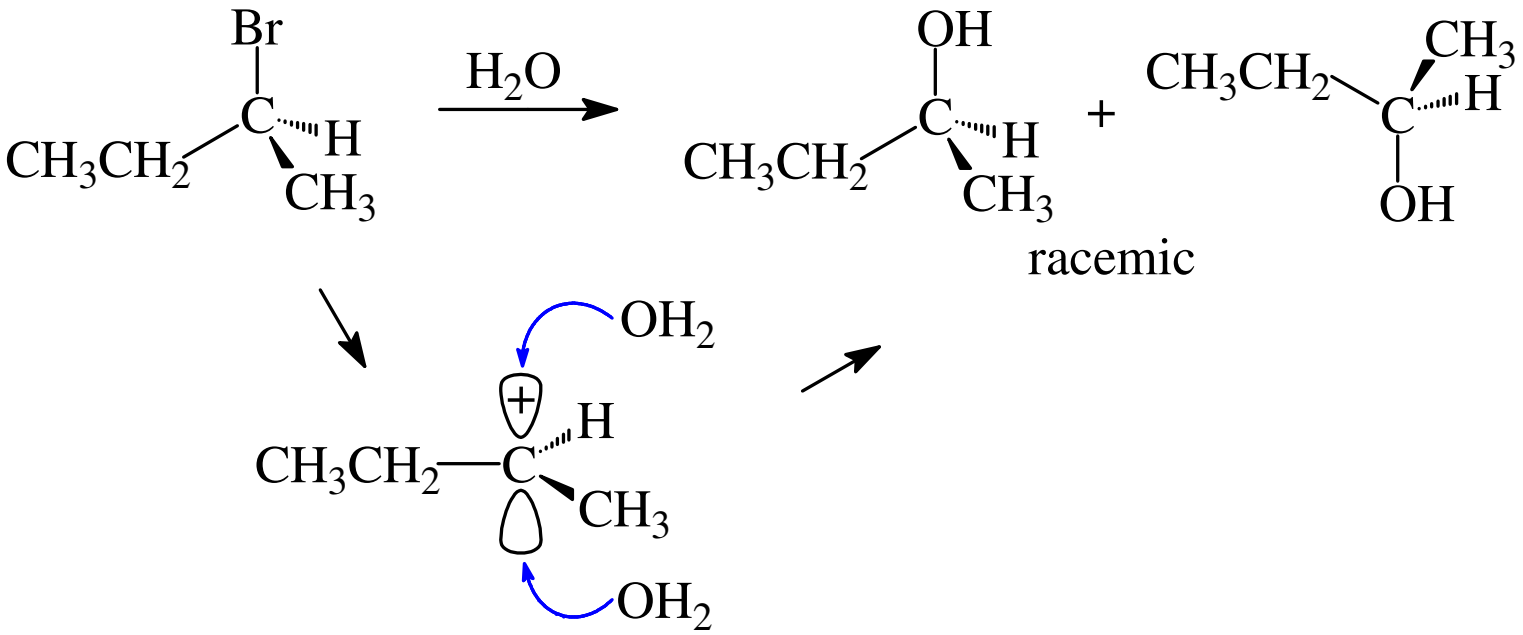
Two-step mechanism:



II. Nucleophilic Aliphatic Substitution

2. S_N1 mechanism

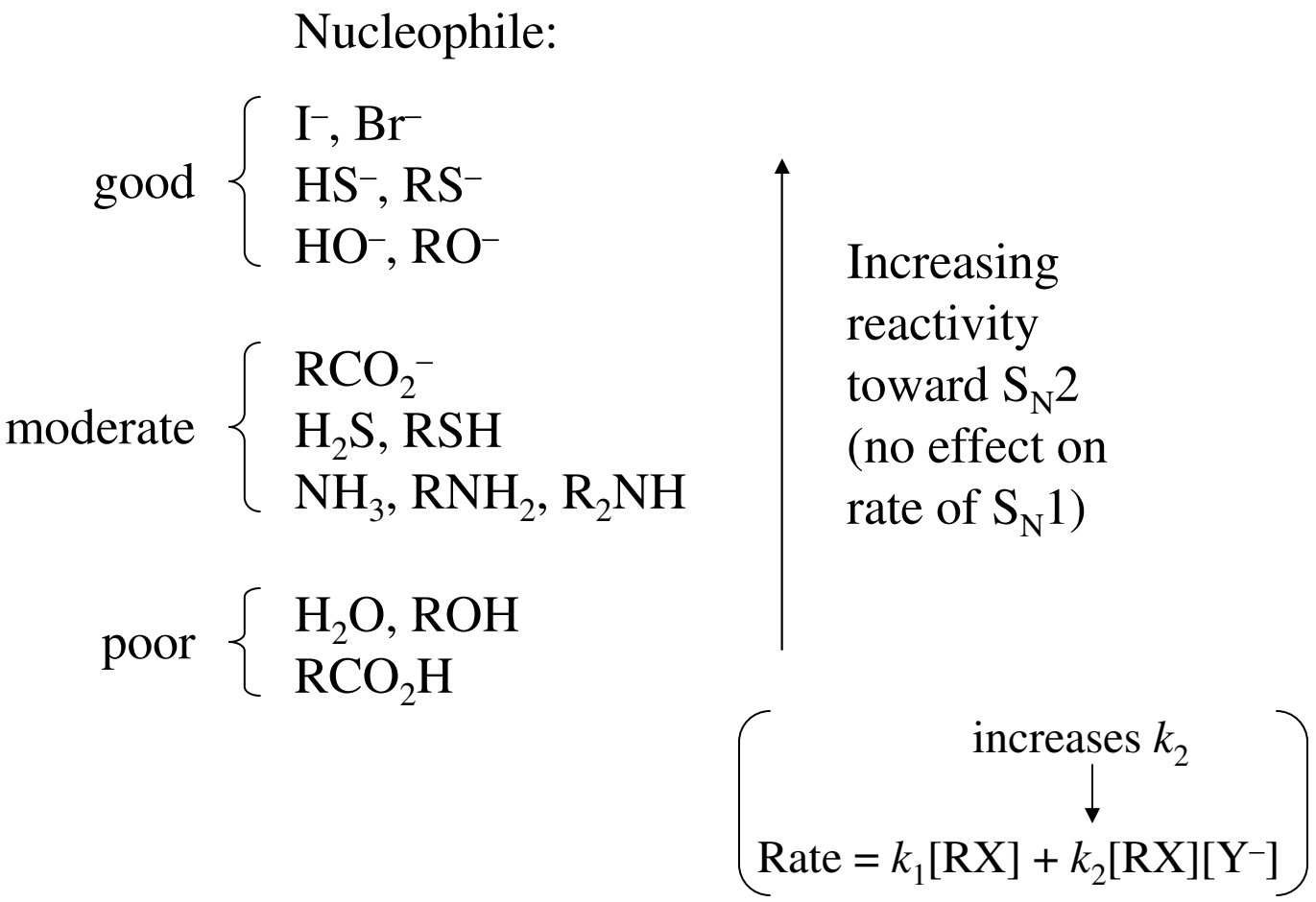
stereochemistry: **stereorandom**



sp^2, trigonal **planar**, achiral
(optically inactive)

C. Factors influencing S_N1 and S_N2 reactions

1. Nucleophile



C. Factors influencing S_N1 and S_N2 reactions

2. Substrate structure

S_N2 mechanism: governed by **steric factors**

- **steric hindrance** = hindrance to back side attack on the carbon by the nucleophile owing to the size of the groups on that carbon
- less steric hindrance $\Rightarrow$ faster rate of S_N2

S_N1 mechanism: governed by **electronic effects**

- more stable cation $\Rightarrow$ faster rate of S_N1

C. Factors influencing S_N1 and S_N2 reactions

2. Substrate structure

S_N2 mechanism: **steric effects**

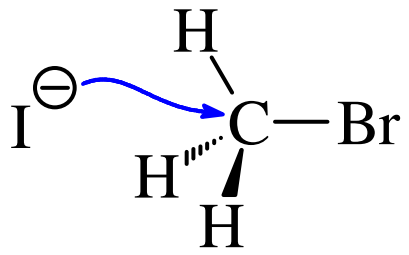
e.g., R–Br + I^- → R–I + Br^- (S_N2)

	Compound	Rel. Rate
methyl	CH_3Br	150
1° RX	CH_3CH_2Br	1
2° RX	$(CH_3)_2CHBr$	0.008
3° RX	$(CH_3)_3CBr$	~0

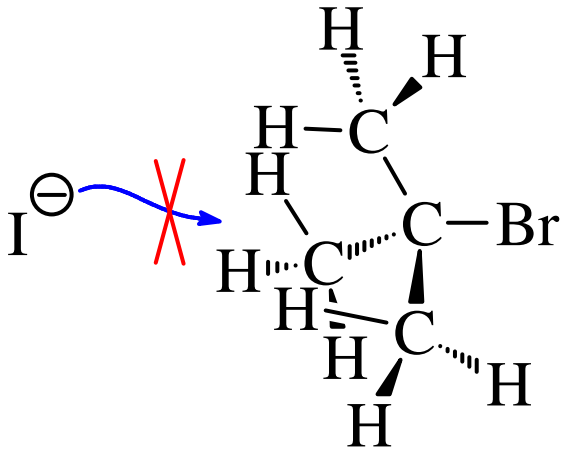
↓ increasing **steric hindrance**

C. Factors influencing S_N1 and S_N2 reactions

2.Substrate structure



minimal steric hindrance



maximum steric hindrance

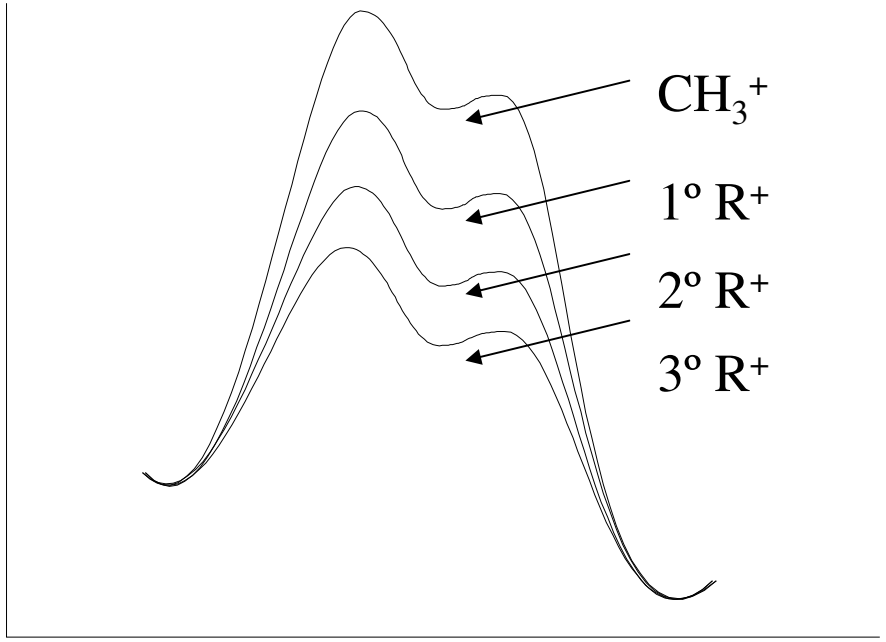
C. Factors influencing S_N1 and S_N2 reactions

2. Substrate structure

S_N1 mechanism: **electronic effects**

R^+ stability: 3º > 2º >> 1º > CH_3^+

R-X reactivity toward S_N1: 3º > 2º >> 1º > CH_3X

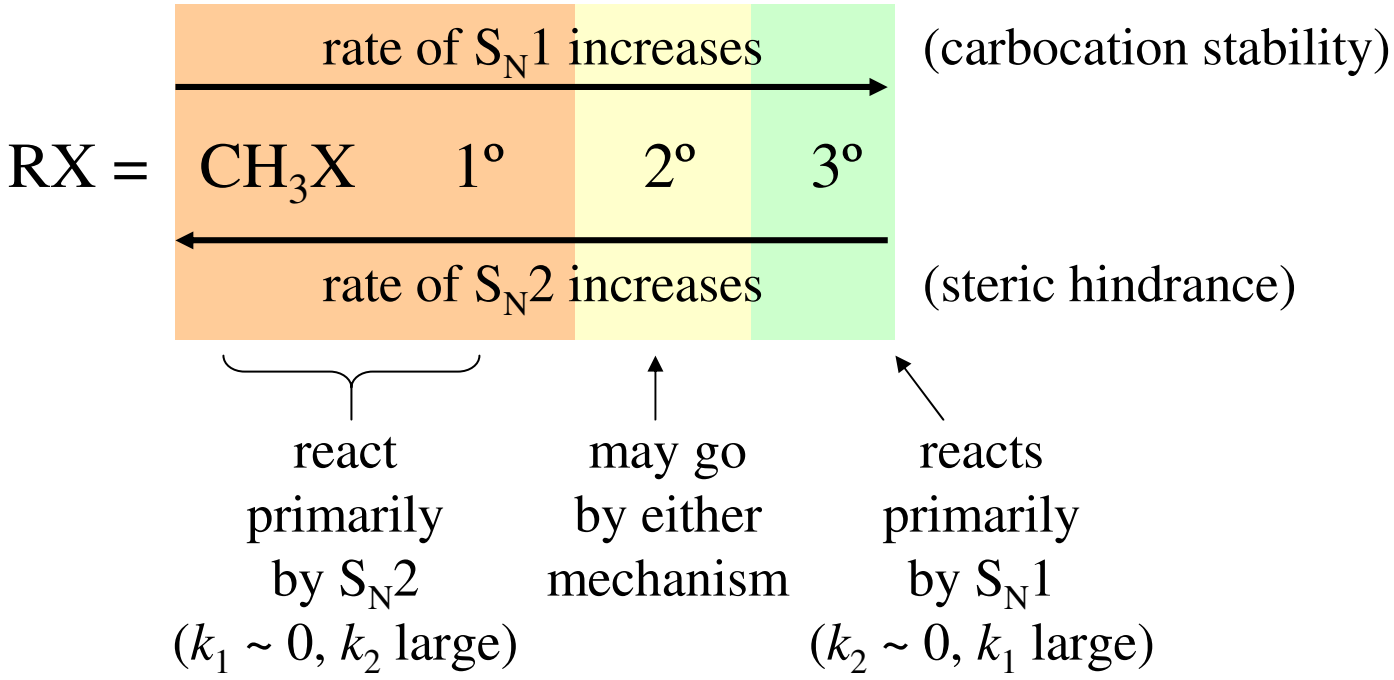


C. Factors influencing S_N1 and S_N2 reactions

2. Substrate structure

Summary:

Rate = k_1[RX] + k_2[RX][Nu]

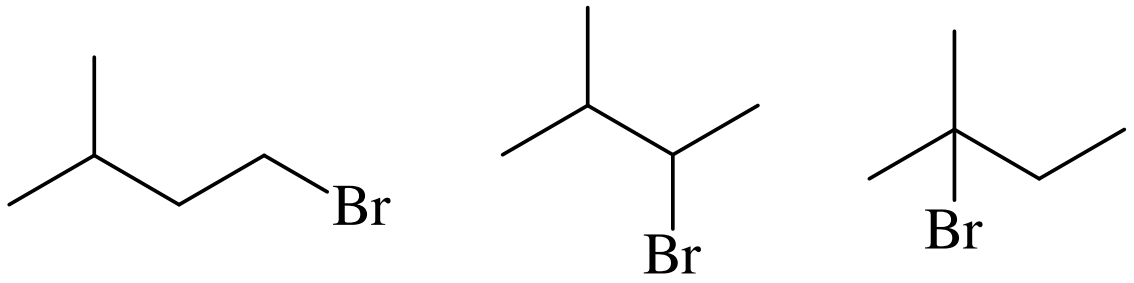


C. Factors influencing S_N1 and S_N2 reactions

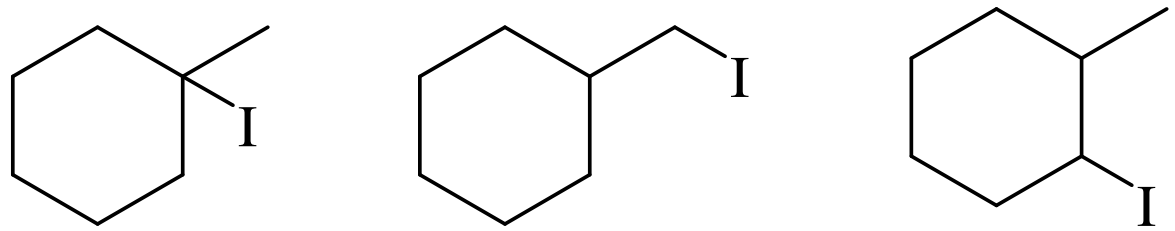
2. Substrate structure

Which compound in each group would react fast by S_N2? Which by S_N1?

a)



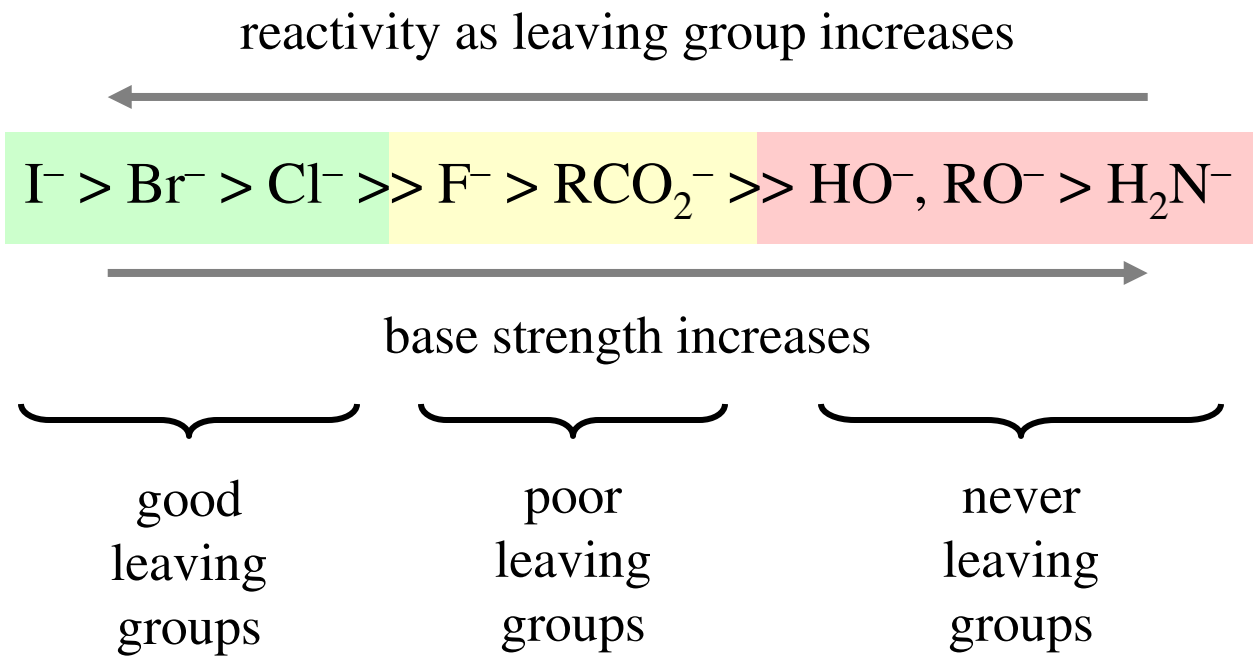
b)



C. Factors influencing S_N1 and S_N2 reactions

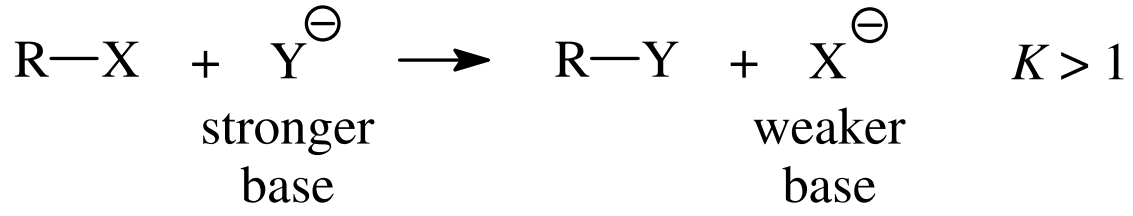
3. Leaving group

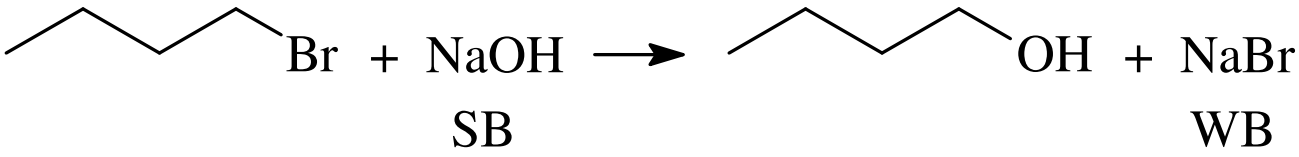
weaker base = better leaving group

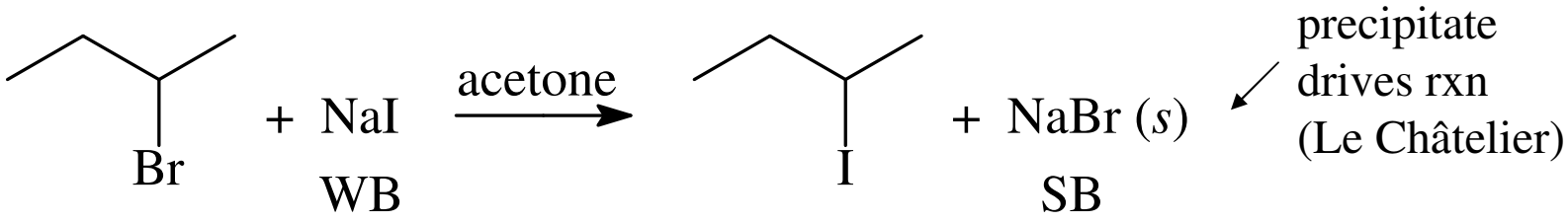


C. Factors influencing S_N1 and S_N2 reactions

3. Leaving group







C. Factors influencing S_N1 and S_N2 reactions

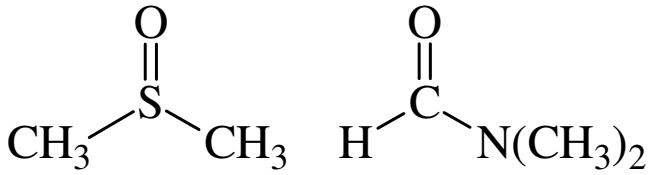
4. Solvent

nonpolar aprotic: hexane, benzene

moderately polar aprotic: ether, acetone, ethyl acetate

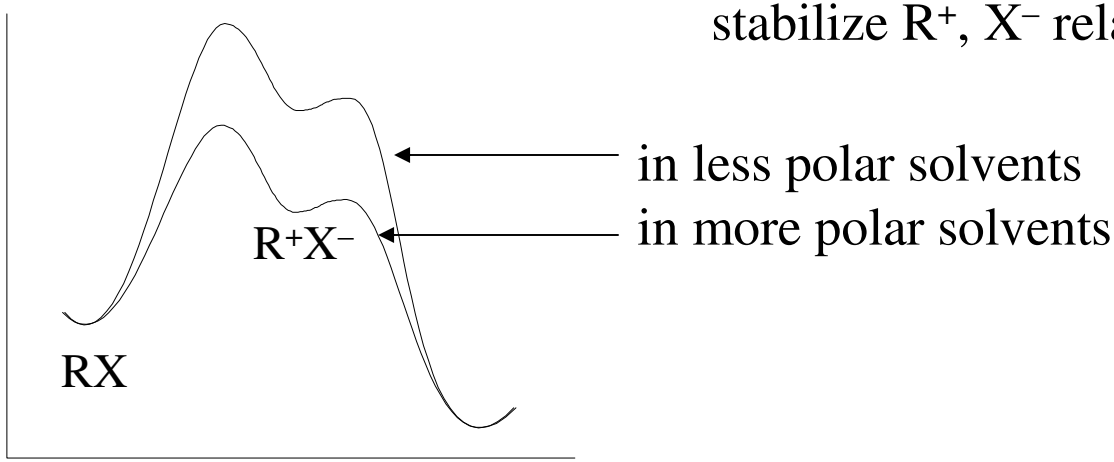
polar protic: H_2O, ROH, RCO_2H

polar aprotic: DMSO DMF acetonitrile



S_N1 mechanism promoted by **polar protic solvents**

stabilize R^+, X^- relative to RX



C. Factors influencing S_N1 and S_N2 reactions

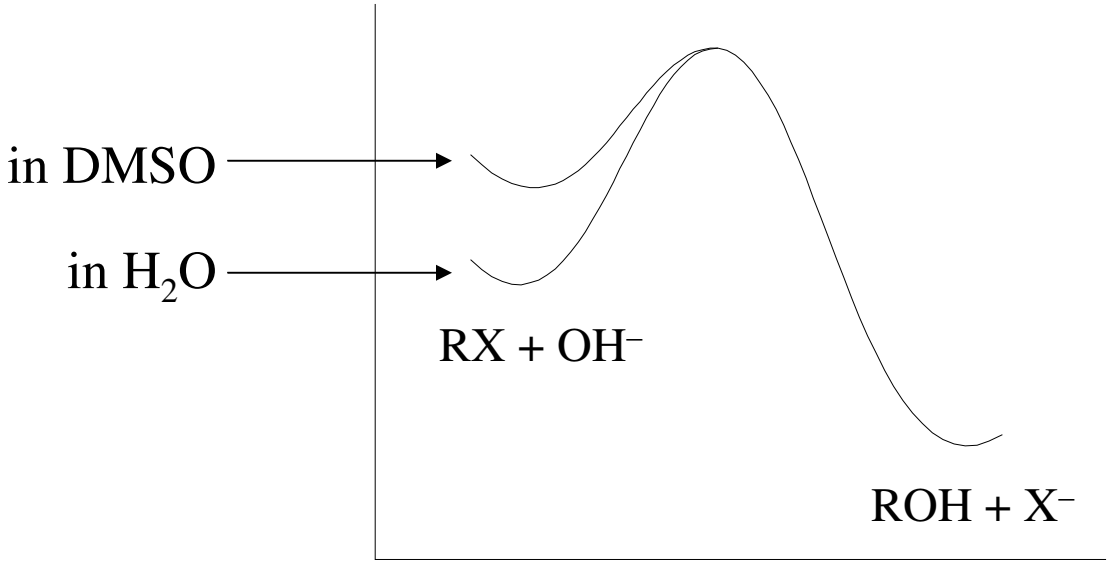
4. Solvent

S_N2 mechanism promoted by moderately polar & polar **aprotic** solvents

destabilize Nu^-s, make them more nucleophilic

e.g., OH^- in H_2O: strong H-bonding to water makes OH^- less reactive

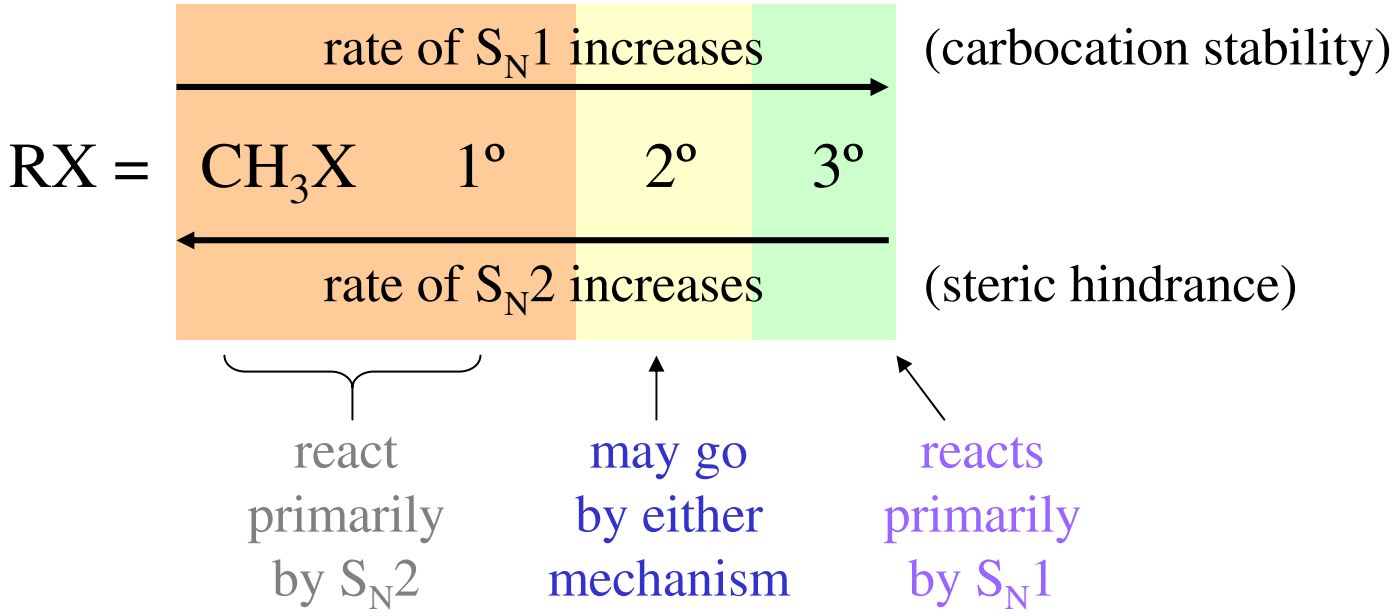
OH^- in DMSO: weaker solvation makes OH^- more reactive (nucleophilic)



II. Nucleophilic Aliphatic Substitution

C. Factors influencing S_N1 and S_N2 reactions

5. Summary



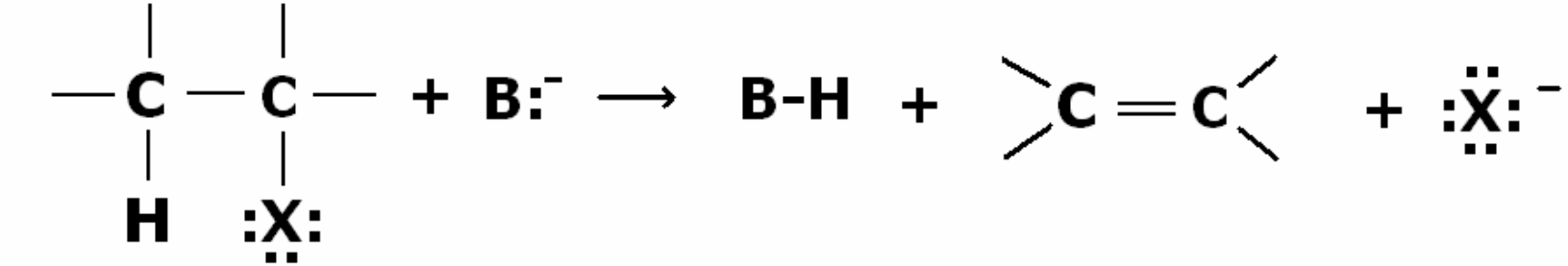
S_N2 promoted good nucleophile (Rate = k_2[RX][Nu])
-usually in polar aprotic solvent

S_N1 occurs in absence of good nucleophile (Rate = k_1[RX])
-usually in polar protic solvent (solvolysis)

S_N1 and S_N2 Reactions

	S_N1	S_N2
Substrate	3°>2°>1°	CH_3X>1°>2°>3°
Nucleophile	Unimportant, but usually weak	Strong and unhindered
Leaving group	Excellent	Better than nucleophile
Solvent	Polar and ionizing	Polar aprotic
Rate	=k[RX]	=k[RX][Nuc:-]
Carbocation intermediate?	Yes	No
Stereochemistry	mix	Inversion of configuration
Rearrangement	~H, ~ CH3 possible	No rearrangements

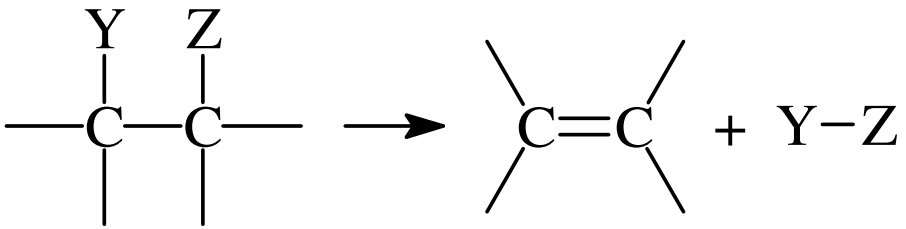
Elimination



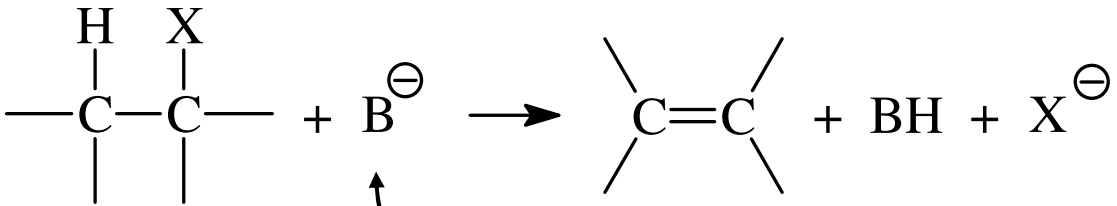
B:$^-$ is a species acting as a base.

Since HX is lost, this particular reaction is called a dehydrohalogenation.

II. Elimination



Elimination reaction
β-elimination or
1,2-elimination

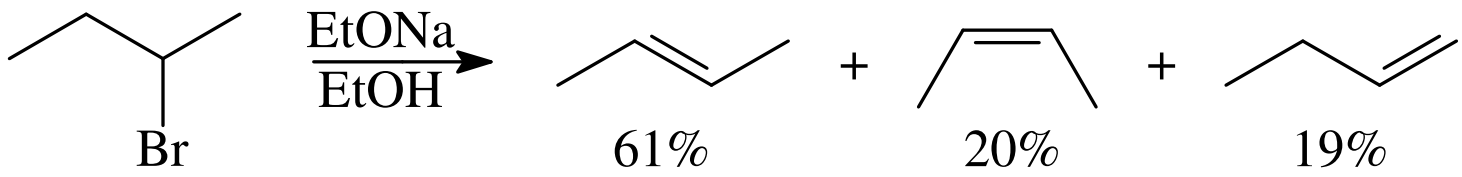


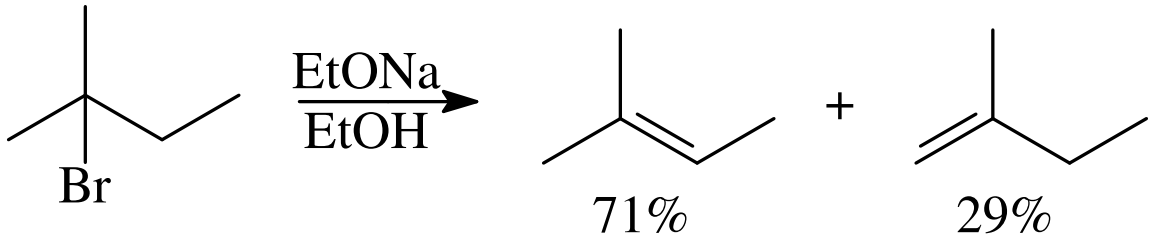
dehydrohalogenation

strong base, usually HO^- or RO^-

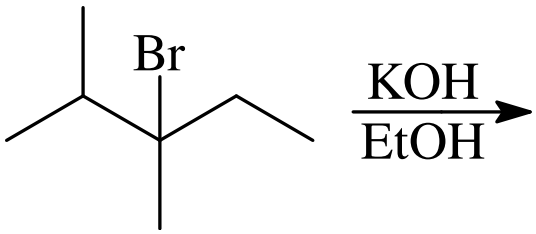
II. Elimination

Follows the **Zaitsev rule** **(Saytzeff)**:the more stable alkene predominates
(more substituted alkene; more trans than cis)





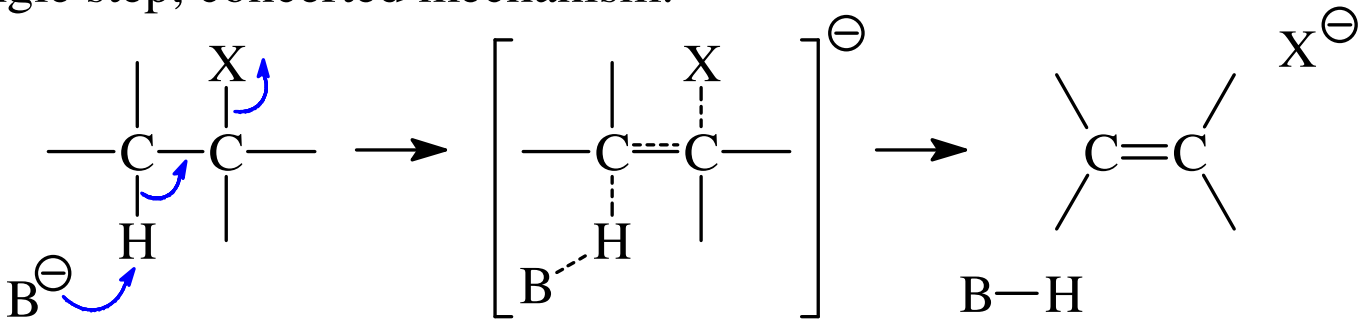
What would be the product distribution from the following reaction?



A. Mechanisms of elimination

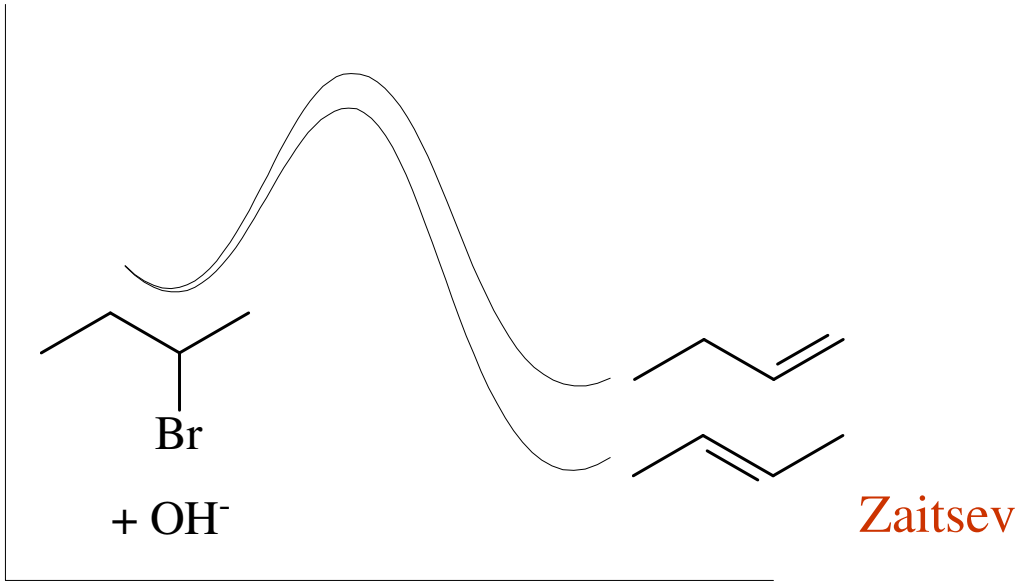
1. E_2 mechanism

Single step, concerted mechanism:



bimolecular

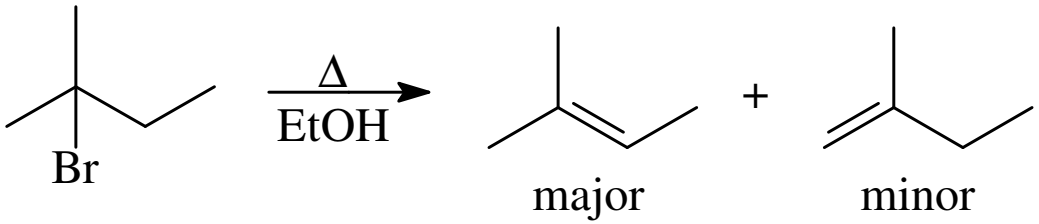
Rate = k[RX][B^-]



Mechanisms of elimination

2. E_1 mechanism

Occurs in the absence of a strong base:



Rate = k[RBr] **unimolecular** (no involvement from B^-)

Reactivity: RI > RBr > RCl > RF (RDS involves R–X breaking)

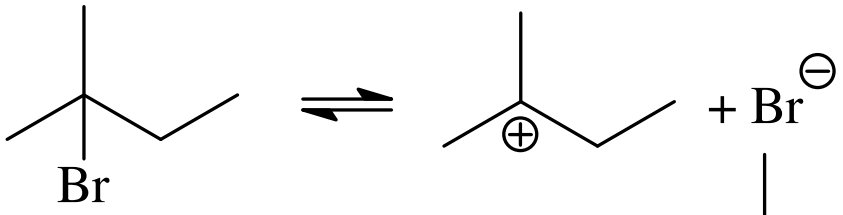
and: 3° > 2° > 1° (RDS invloves R^+)

Elimination

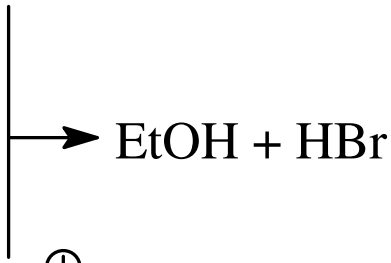
2. E_1 mechanism

Two step mechanism:

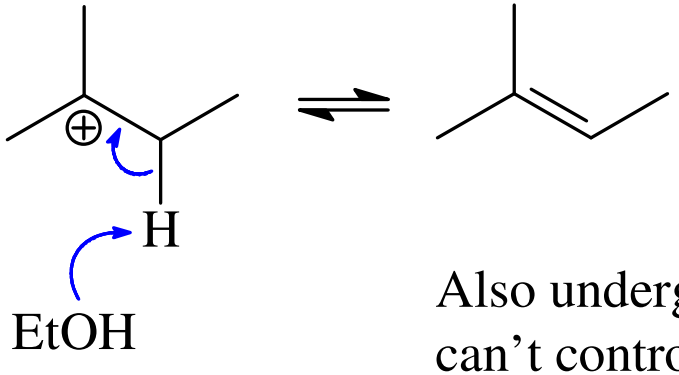
Step 1:
(**RLS**)



unimolecular



Step 2:



Also undergoes S_N1 reaction;
can't control the ratio of S_N1 to E1.

Bimolecular Reactions: S_N2 and E2 (usually the preferred way)

- require a good nucleophile or a strong base
- promoted by polar aprotic solvents

Substrate	Good Nu, Weak B I^-, Br^-, Cl^-, RS^-, R_3N	Good Nu, Strong B HO^-, RO^-, H_2N^-
1°	S_N2	mostly S_N2
2°	S_N2	mostly E2
3°	no reaction	E2

ELIMINATION v. SUBSTITUTION

The products of reactions between haloalkanes and OH^- are influenced by the solvent

SOLVENT	ROLE OF OH^-	MECHANISM	PRODUCT
WATER	NUCLEOPHILE	SUBSTITUTION	ALCOHOL
ALCOHOL	BASE	ELIMINATION	ALKENE

Modes of attack

Aqueous soln — OH^- attacks the slightly positive carbon bonded to the halogen.
OH^- acts as a nucleophile

Alcoholic soln — OH^- attacks one of the hydrogen atoms on a carbon atom adjacent the carbon bonded to the halogen.

OH^- acts as a base (A BASE IS A PROTON ACCEPTOR)

Both reactions take place at the same time but by varying the solvent you can influence which mechanism dominates.

C. Reaction With Metals

- Wurtz Reaction
- Frankland Reaction
- Reaction with Magnesium