Chapter 7: Part 1:
Substitution Reactions - SN2

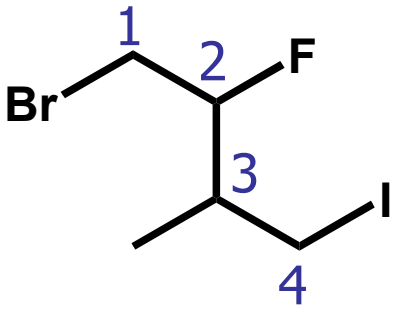
Today Chapter 7 (7.1-7.4)

1. Alkyl Halides
2. Substitution and Elimination Reactions
3. The SN2 Mechanism
4. Inversion of Configuration/ Stereochemistry
5. Factors Affecting SN2 Reactions
    1. The Leaving Group
    2. The Nucleophile
    3. Steric Hindrance
    4. The Solvent

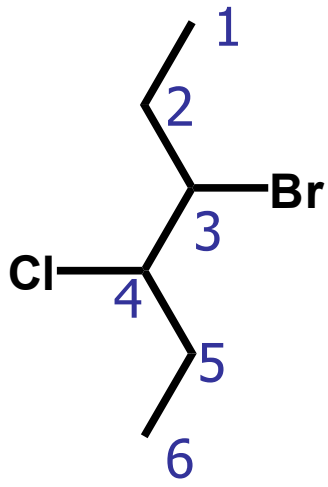
Naming Alkyl Halides

1. The prefixes fluoro, chloro, bromo, iodo are used to indicate presence of halogens.
2. They are treated in same manner as alkyl substituents.
3. Find longest chain, name it as parent chain

   (PRIORITY goes to a double or triple bond if present)
4. Number from end nearest any substituent (alkyl or halogen)
5. IF <u>two Halides</u> are Equally Distant from Ends of Chain → begin at the end nearer to the substituent whose name comes first in the alphabet



1-bromo-2-fluoro-4-iodo-3-methylbutane



3-bromo-4-chlorohexane

Substitution and Elimination Reactions

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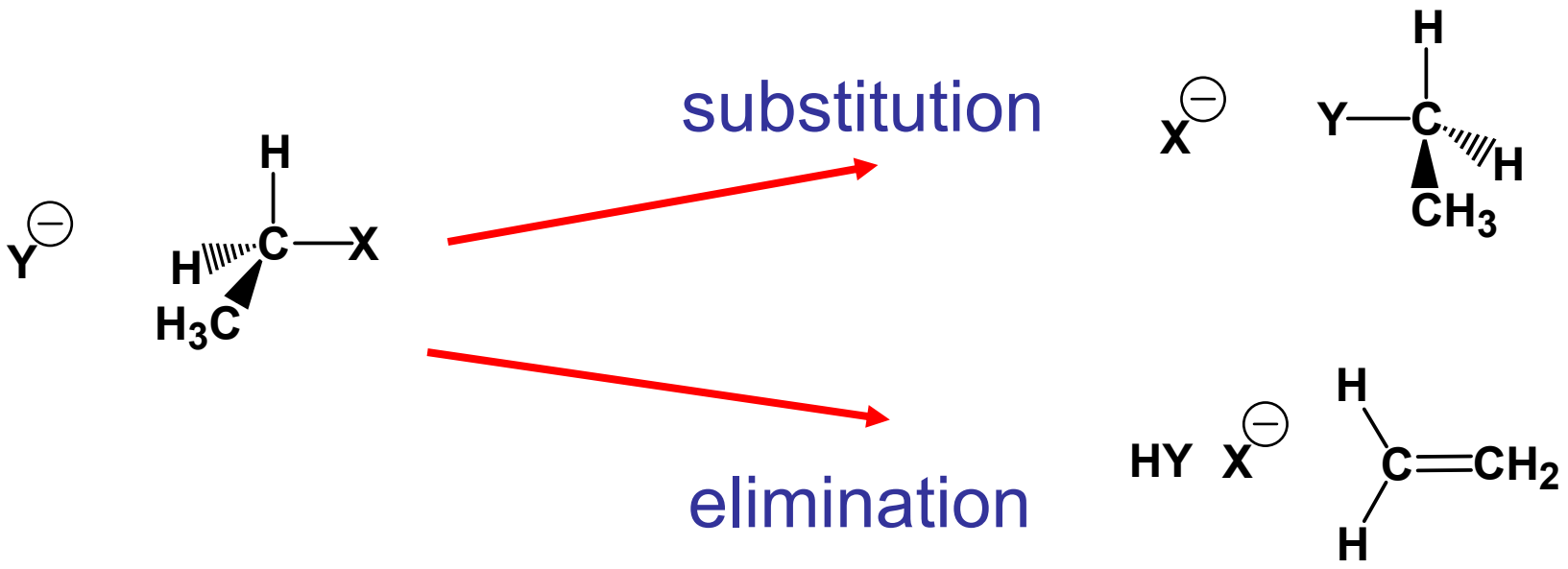
- 2 kinds of reactions - Substitution and Elimination
- Key to this - understanding the factors which determine which mechanism predominates and which products form.

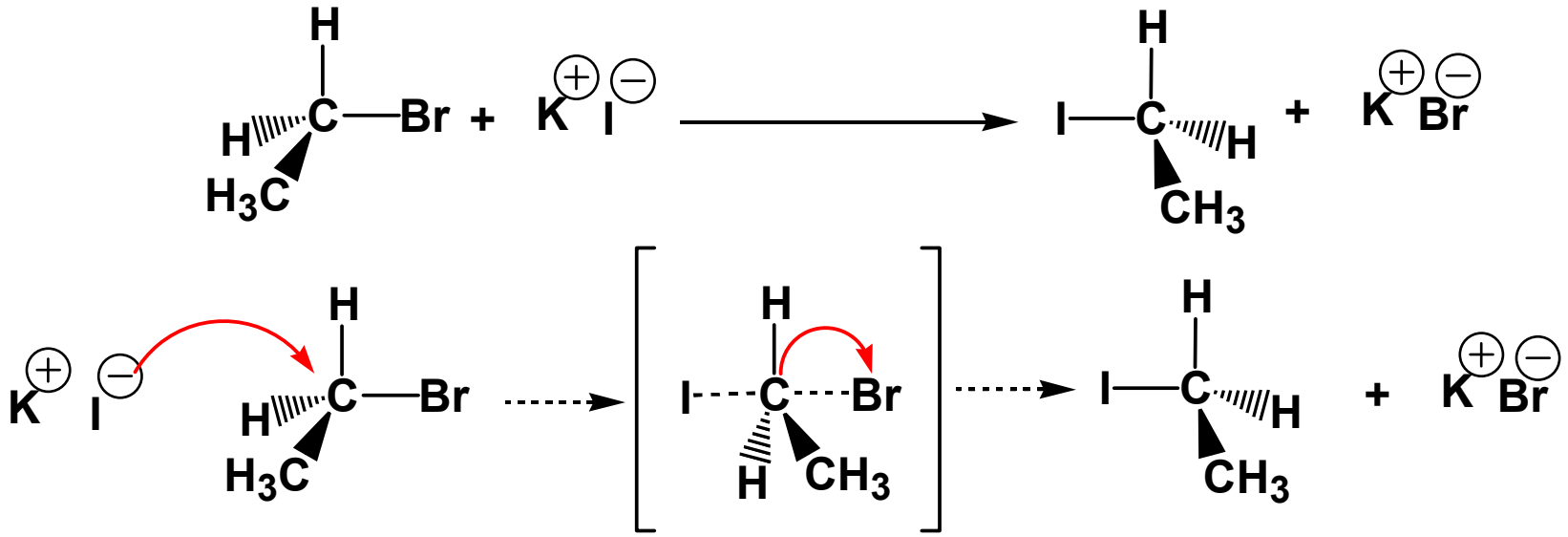


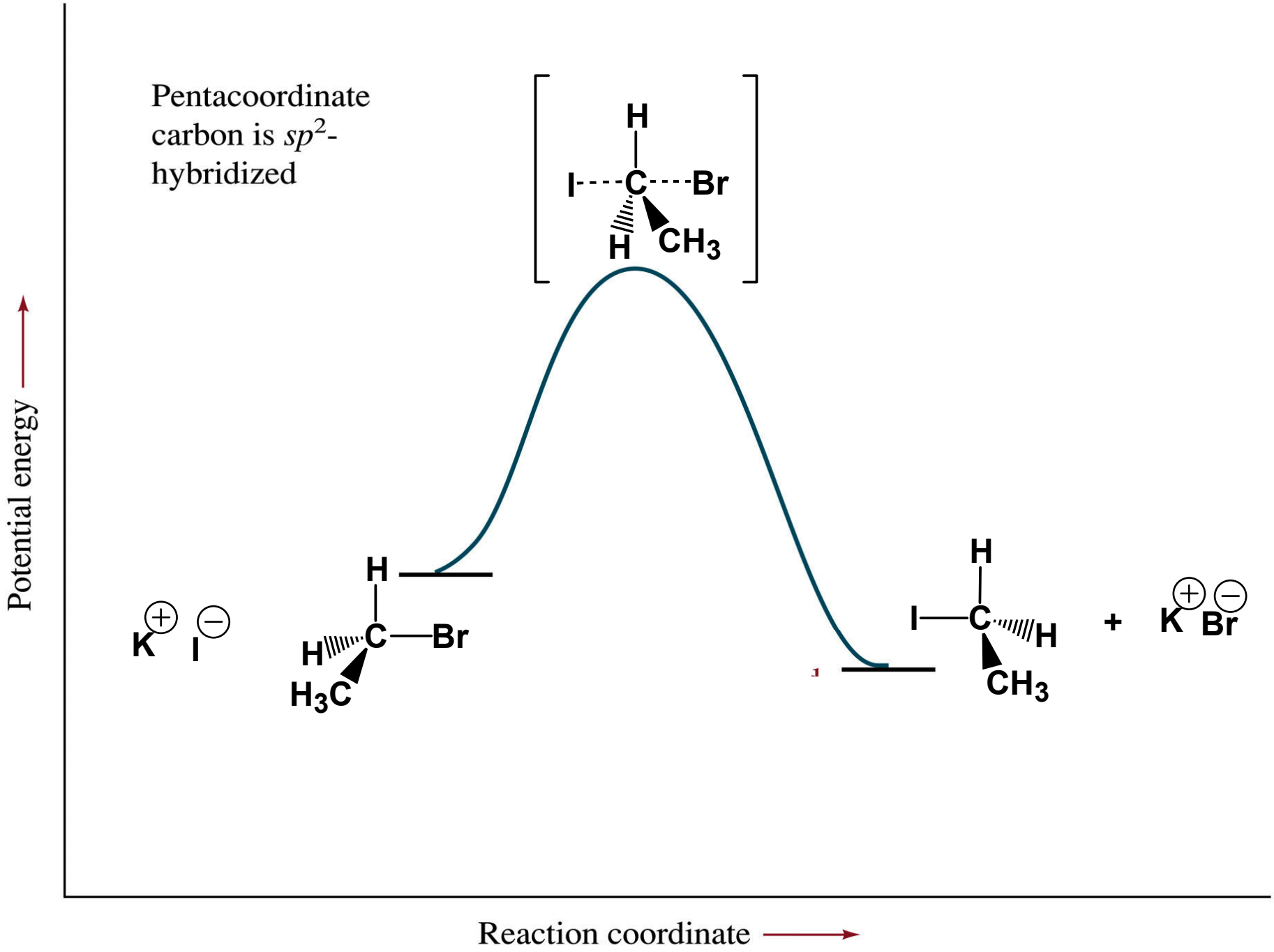
The atom or group that is substituted or eliminated in these reactions is called a leaving group

The SN2 reaction:

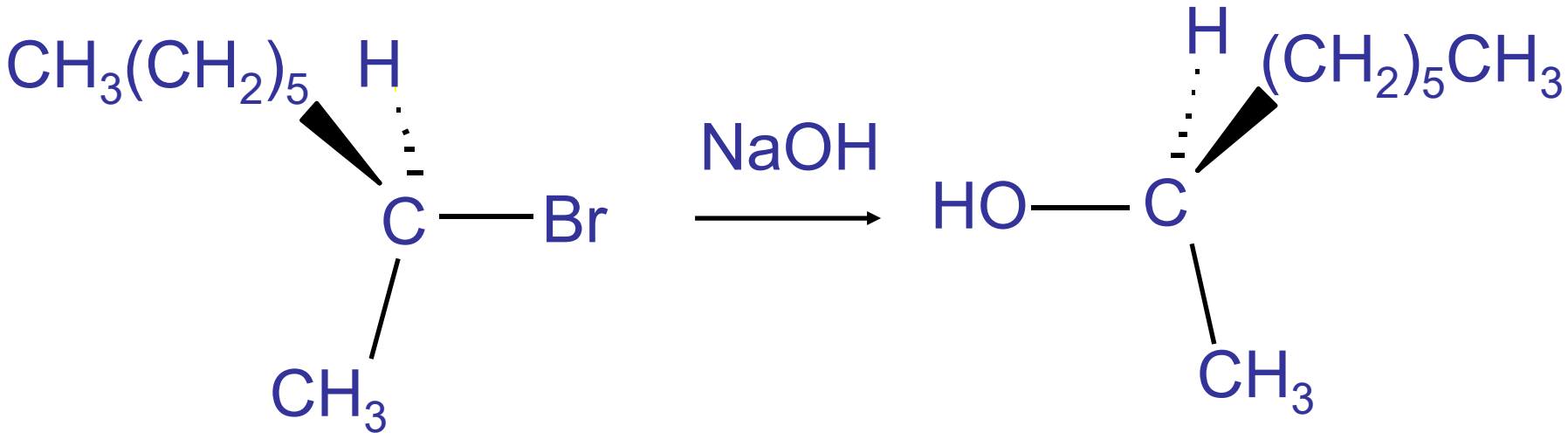
Substitution Nucleophilic *Bimolecular*

The SN2 is a mechanism in which a nucleophile attacks the back side of a carbon ejecting a leaving group.




Pentacoordinate carbon is sp^2-hybridized
H
I
C
Br
H
CH_3
Potential energy
Reaction coordinate
K
I
H
H
C
Br
H_3C
H
I
C
H
CH_3
+
K
Br

Stereospecific Reaction



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

(*R*)-(–)-2-Octanol

Inversion of Configuration

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

Because a nucleophile substitutes for the halogen, these reactions are known as nucleophilic substitution reactions

The reaction mechanism which predominates depends on the following factors:

1. The Leaving Group
2. The Nucleophile
3. The Solvent
4. Steric Hindrance

Remember-

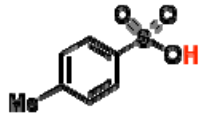
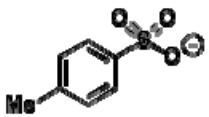
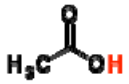
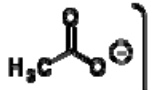
- nucleophile is a Lewis base or *electron-pair donor*
- substrate is usually an alkyl halide

S_N2 Reactions Are Affected by the Leaving Group

•Leaving Group	Relative Rate	Conjugate acid of leaving group	pK_a of conj. acid
• F^-	10^{-5}	HF	3.5
• Cl^-	1	HCl	-7
• Br^-	10	HBr	-9
• I^-	10^2	HI	-10
• H_2O	10^1	H_3O^+	-1.7
•$CF_3SO_2O^-$	10^8	CF_3SO_2OH	-6

The weaker the base, the better it is as a leaving group
The better the leaving group – the faster the reaction.

A pKa table is a handy guide to leaving groups

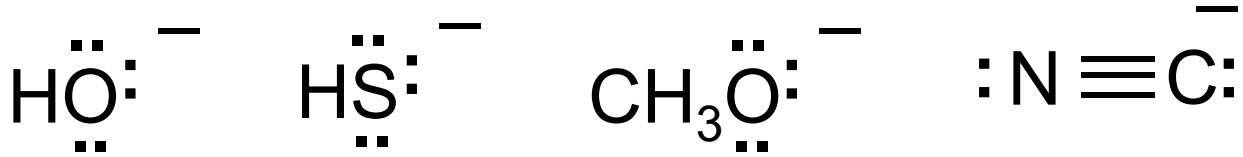
Functional group / Example		pKa	Conjugate base	
Hydroiodic acid	HI	−10	$I^{\ominus}$	Excellent leaving groups (extremely weak bases)
Hydrobromic acid	HBr	−9	$Br^{\ominus}$	
Hydrochloric acid	HCl	−6	$Cl^{\ominus}$	
Sulfuric acid	H_2SO_4	−3	$HSO_4^{\ominus}$	
Sulfonic acids	 (tosic acid)	−3		
Hydronium ion	$H_3O^{\oplus}$	−1.7	H_2O	
Hydrofluoric acid	H–F	3.2	$F^{\ominus}$	Exception: $F^{\ominus}$ is typically an extremely poor leaving group (forms strong bonds)
Carboxylic acids		4		Moderate leaving groups (weak bases)
Protonated amines	$NH_4^{\oplus}\ Cl^{\ominus}$	9-11	NH_3	
Water	HO–H	16	$HO^{\ominus}$	Poor leaving groups (strong bases)
Alcohols	CH_3O–H	16-18	$CH_3O^{\ominus}$	
Amine	NH_3	~35	$NH_2^{\ominus}$	Extremely poor leaving groups (very strong bases)
Hydrogen	H–H	42	$H^{\ominus}$	
Alkane		~60		

A single organic product was obtained when 1-bromo-3-chloropropane was allowed to react with one molar equivalent of sodium cyanide in aqueous ethanol. What was this product?

Br is a better leaving group than Cl

Nucleophilicity. What is a Nucleophile? What Makes a Good One?

The nucleophiles described earlier have all been anions.



Not all nucleophiles are anions. Many are neutral.

All nucleophiles, however, are Lewis bases.

The term *solvolysis* refers to a nucleophilic substitution in which the nucleophile is the solvent.

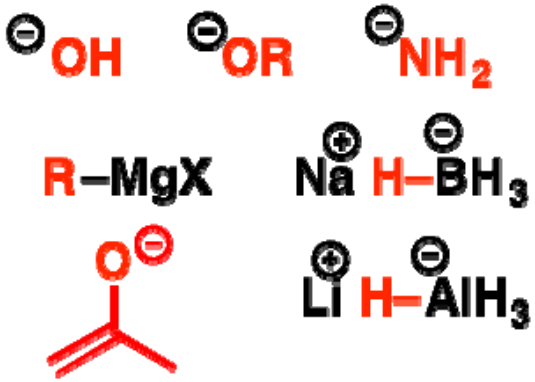
Nucleophilicity

Rank	Nucleophile	Relative rate
•strong	I^-, HS^-, RS^-	$>10^5$
•good	Br^-, HO^-,	10^4
•	RO^-, CN^-, N_3^-	
•fair	NH_3, Cl^-, F^-, RCO_2^-	10^3
•weak	H_2O, ROH	1
•very weak	RCO_2H	10^{-2}

Anionic vs. Neutral nucleophiles

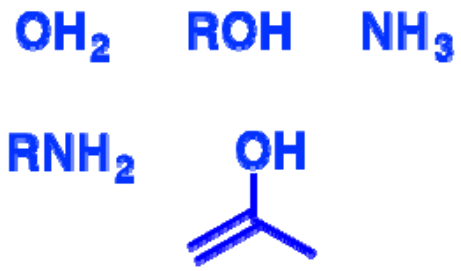
(In reactions with aldehydes, ketones, and carboxylic acid derivatives)

Anionic nucleophiles



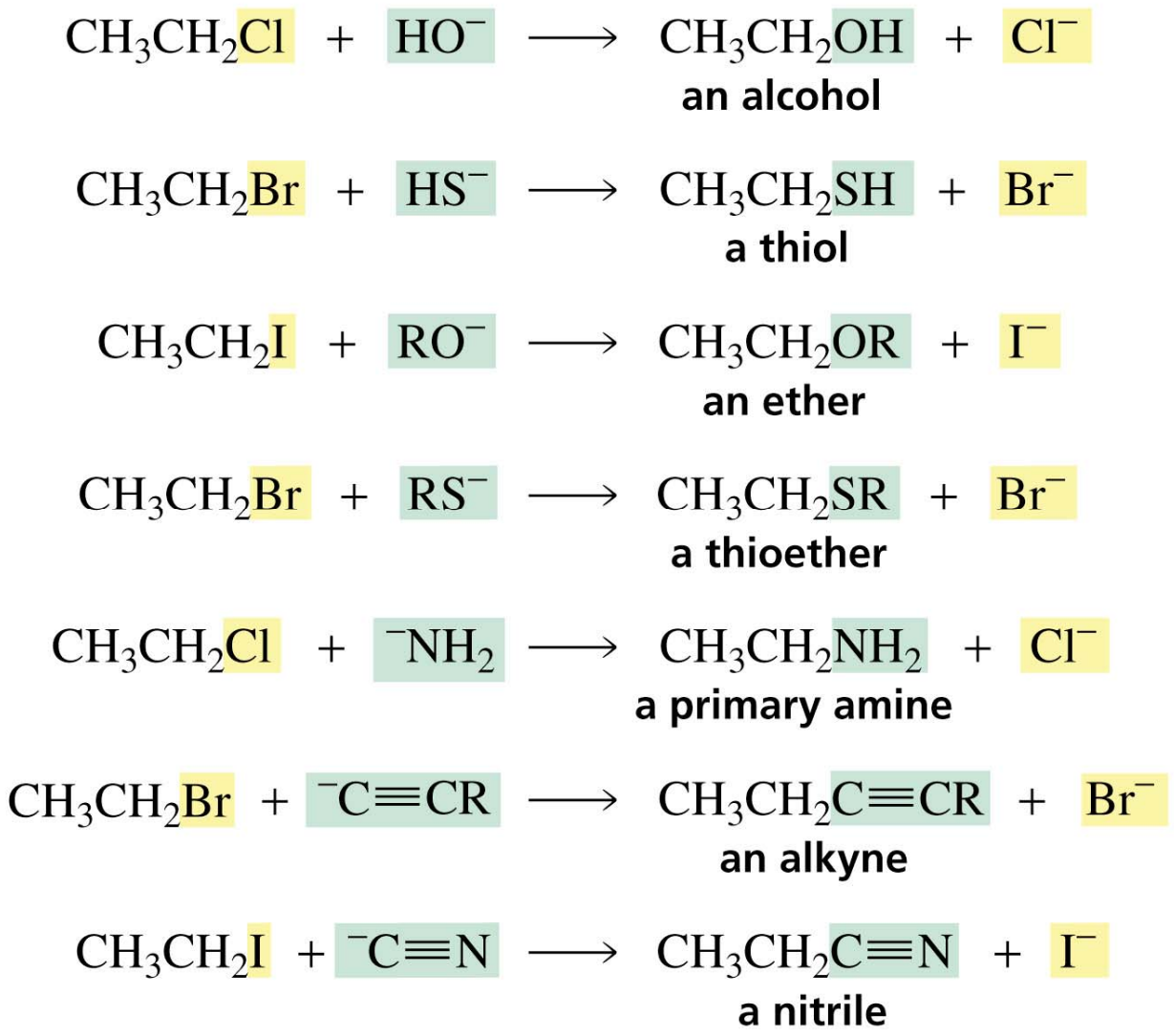
- No acid catalysis (incompatible)
- Can be reversible, depending on basicity.
- Mechanism can involve sequential 1,2-addition / 1,2-elimination steps
- Last step is usually "add acid"

Neutral nucleophiles



- Accelerated by acid catalysis: acid promotes 1,2-addition and 1,2-elimination
- Equilibria - generally reversible
- Addition/elimination steps alternate with proton transfer
- Last step is usually "deprotonate"

An S_N2 reaction proceeds in the direction that allows the strongest base to displace the weaker base



S_N2 Reactivity versus Type of Solvent

S_N2 Reaction Rates Increase in Polar Aprotic Solvents

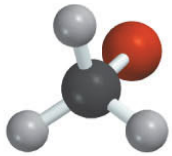
$$CH_3CH_2CH_2CH_2Br + N_3^-$$

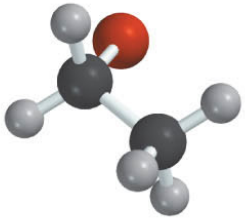
•Solvent	Type	Relative rate
•CH_3OH	polar protic	1
•H_2O	polar protic	7
•DMSO	polar aprotic	1300
•DMF	polar aprotic	2800
•Acetonitrile	polar aprotic	5000

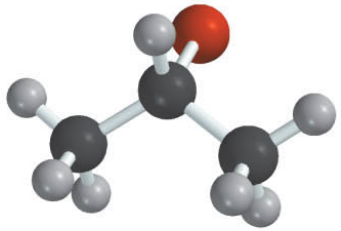
Least crowded–
most reactive

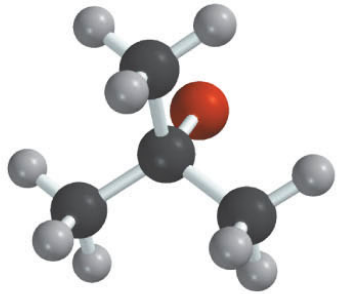
Increasing Reactivity

Most crowded–
least reactive







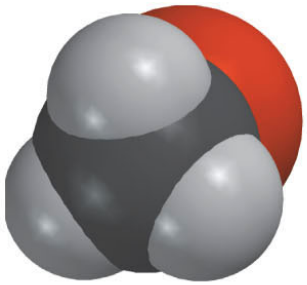


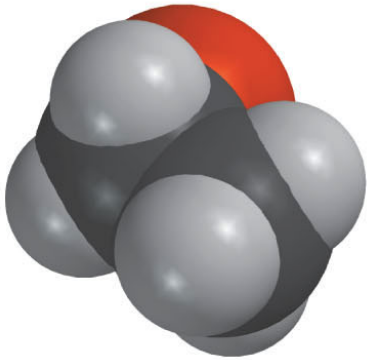
CH_3Br

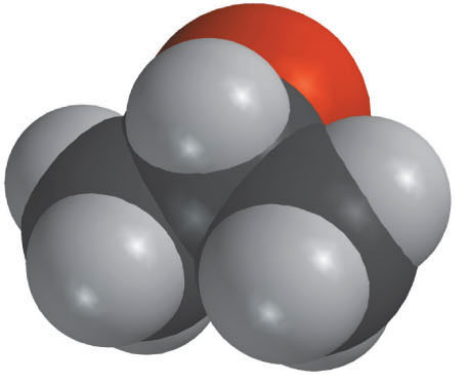
CH_3CH_2Br

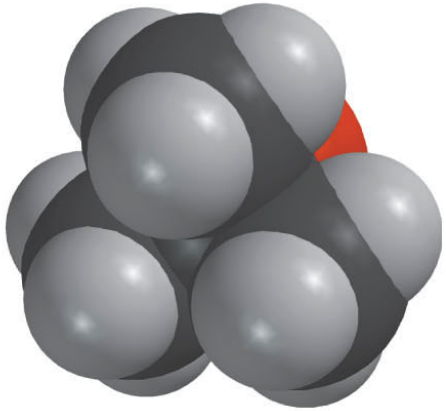
$(CH_3)_2CHBr$

$(CH_3)_3CBr$









In an SN2 reaction: A bulky substituent in the alkyl halide reduces the reactivity of the alkyl halide: steric hindrance

Summary of SN2

1. Best with 1^{o} alkyls with good leaving groups.
2. Helped by polar aprotic solvents.
3. Using good highly polarized species as nucleophiles helps.
4. Crowding at the carbon that bears the leaving group slows the rate of bimolecular nucleophilic substitution.

For Next Time….

WEDNESDAY Chapter 7: Alkenes and Eliminations (7.5-7.8)
FRIDAY Chapter 7: Unimolecular Reactions (7.9-7.10)
NEXT MONDAY Chapter 7: Putting it all together 7.11

Suggested Homework Problems Chapter 6
#4, 7, 11, 17, 24, 26, 28, 34-36

Suggested Homework Problems Chapter 7

#1,3,5,16, 18, 21, 37, 41, 47, 48, 54, 56, 60, 62-65, 70, 76