Chapter-1
Bonding and Isomerism

Organic chemistry is the chemistry of carbon compounds.

Chemical Bonding

Ionic Bonding

$$Na\cdot + \cdot\ddot{Cl}: \longrightarrow Na^+ + :\ddot{Cl}:^-$$

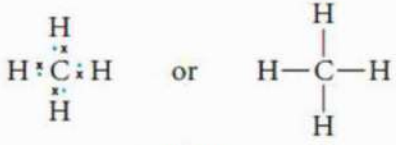
sodium atom — chlorine atom — sodium cation — chloride anion

Covalent Bonding

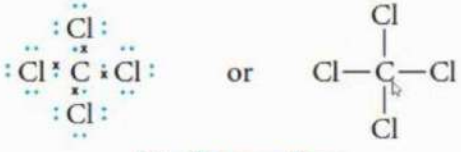
$$H\cdot + H\cdot \longrightarrow H:H + \text{heat}$$

hydrogen atoms — hydrogen molecule

Carbon and the Covalent Bond

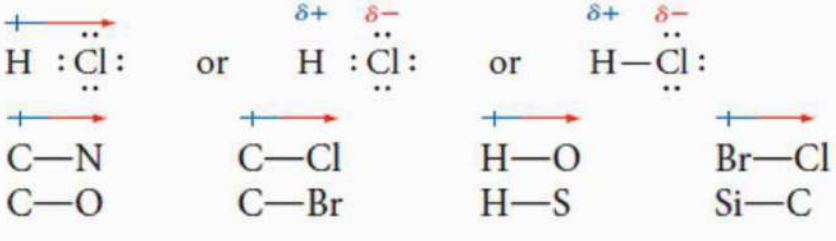


methane



tetrachloromethane
(carbon tetrachloride)

Polar Covalent Bonds



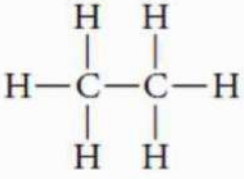
C—N
C—O

C—Cl
C—Br

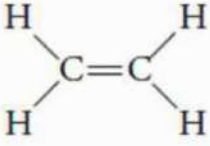
H—O
H—S

Br—Cl
Si—C

Carbon–Carbon Single and Multiple Covalent Bonds



ethane

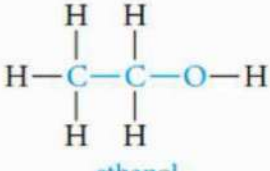


ethene
(ethylene)

ethyne
(acetylene)

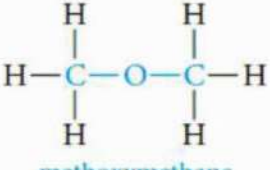
Isomerism

Molecules that have the same kinds and numbers of atoms but different arrangements are called **isomers**.



ethanol
(ethyl alcohol)
bp 78.5°C

and



methoxymethane
(dimethyl ether)
bp −23.6°C

Structural Formula

Condensed formula | Line angle formula | Three dimensional formula

1. Condensed formula

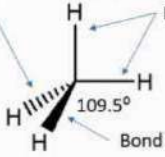
Sometimes these formulas are abbreviated even further. For example, they can be printed on a single line in the following ways:

2. Line angle Formula

3. Three dimensional formula

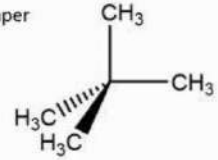
Bond behind the plane of the paper

Bond in the same plane of the paper



Bond out of the plane of the paper

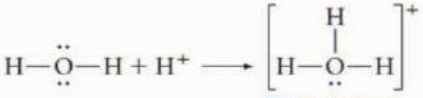
methane



2,2-dimethylpropane
Neopentane

Formal Charge

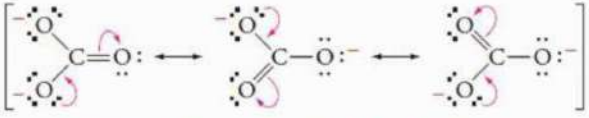
Formal charge = valence es – ½ bonding es – unshared es



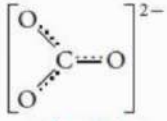
hydronium ion

Resonance Structures

They are equivalent structures for the same molecule and differ from one another only in the arrangement of the electrons.



three equivalent structures for the carbonate ion



carbonate ion
resonance hybrid

Classification According to Functional Group

Table 1.6 The Main Functional Groups

	Structure	Class of compound	Specific example
A. Functional groups that are a part of the molecular framework		alkane	$CH_3—CH_3$
		alkene	$CH_2=CH_2$
		alkyne	$HC\equiv CH$
		arene	
B. Functional groups containing oxygen			
1. With carbon–oxygen single bonds		alcohol	CH_3CH_2OH
		ether	$CH_3CH_2OCH_2CH_3$

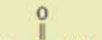
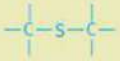
(continued)

Table 1.6 continued

	Structure	Class of compound	Specific example
*2. With carbon–oxygen double bonds**		aldehyde	$CH_2=O$
		ketone	
3. With single and double carbon–oxygen bonds		carboxylic acid	
		ester	
*C. Functional groups containing nitrogen***		primary amine	$CH_3CH_2NH_2$
		nitrile	$CH_2=CH—C\equiv N$

(continued)

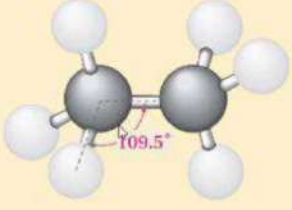
Table 1.6 continued

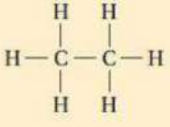
	Structure	Class of compound	Specific example
D. Functional group with oxygen and nitrogen		primary amide	
E. Functional group with halogen		alkyl or aryl halide	CH_3Cl
F. Functional groups containing sulfur[f]		thiol (also called mercaptan)	CH_3SH
		thioether (also called sulfide)	$(CH_2{=}CHCH_2)_2S$

Chapter-2
Alkanes and Cycloalkanes; Conformational and Geometric Isomerism

The Structures of Alkanes

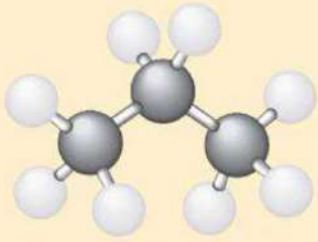
ethane

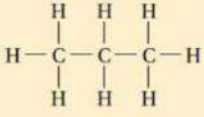




or CH_3CH_3

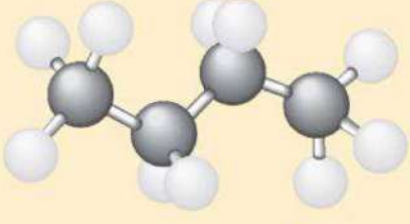
propane

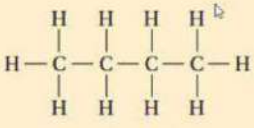




or $CH_3CH_2CH_3$

butane





or $CH_3CH_2CH_2CH_3$

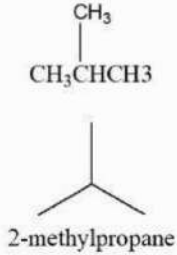
Table 2.1 Names and Formulas of the First Ten Unbranched Alkanes

Name	Number of carbons	Molecular formula	Structural formula	Number of structural isomers
methane	1	CH_4	CH_4	1
ethane	2	C_2H_6	CH_3CH_3	1
propane	3	C_3H_8	$CH_3CH_2CH_3$	1
butane	4	C_4H_{10}	$CH_3CH_2CH_2CH_3$	2
pentane	5	C_5H_{12}	$CH_3(CH_2)_3CH_3$	3
hexane	6	C_6H_{14}	$CH_3(CH_2)_4CH_3$	5
heptane	7	C_7H_{16}	$CH_3(CH_2)_5CH_3$	9
octane	8	C_8H_{18}	$CH_3(CH_2)_6CH_3$	18
nonane	9	C_9H_{20}	$CH_3(CH_2)_7CH_3$	35
decane	10	$C_{10}H_{22}$	$CH_3(CH_2)_8CH_3$	75

Structural isomers of butane

$CH_3CH_2CH_2CH_3$

butane



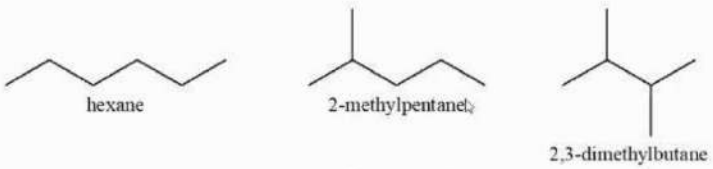
2-methylpropane

Total # of isomers of butane = 2

Structural isomers of pentane (C_5H_{12})

pentane | 2-methylbutane | neopentane

Structural isomers of hexane (C_6H_{14})



hexane | 2-methylpentanel | 2,3-dimethylbutane

2,2-dimethylbutane | 3-methylpentane

Total # of isomers of hexane = 5

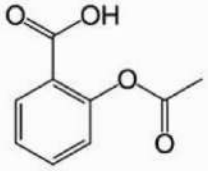
Nomenclature of Organic Compounds

IUPAC[1] names

internationally recognized systems of nomenclature

Common names

names that were usually based on source or use of compounds.

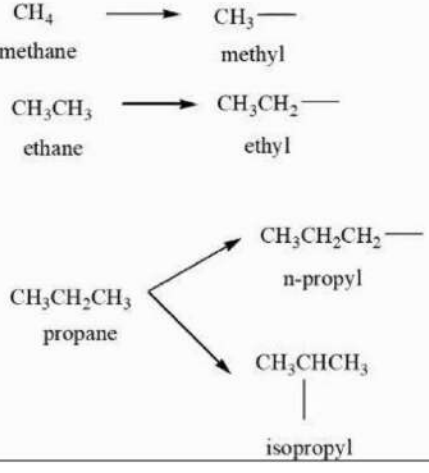


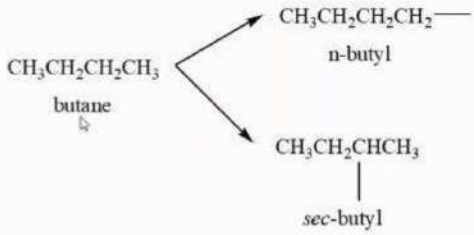
acetylsalicylic acid (IUPAC name)
aspirin (common name)

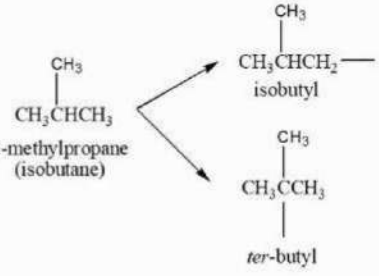
[1]IUPAC is the abbreviation of International Union of Pure and Applied Chemistry

IUPAC Rules for Naming Alkanes

Names of alkyl halogen substituents

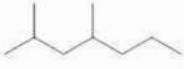




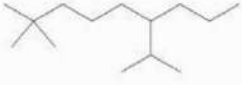


Halogen substituents are named by changing the *-ine* ending of the element to *-o*.

F—	Cl—	Br—	I—
fluoro-	chloro-	bromo-	iodo-



2,4-dimethylheptane

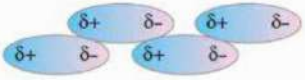


6-isopropyl-2,2-dimethylnonane

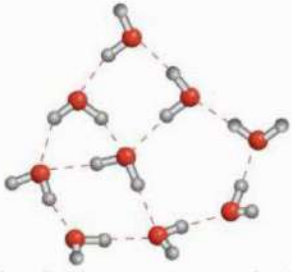
The only prefix that is used when putting substituents in alphabetical order is "iso". The prefixes sec- and tert- are not used in determining alphabetical order.

Physical Properties of Alkanes

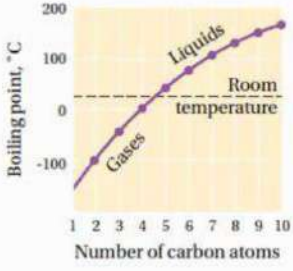
- ❑ Alkanes are insoluble in water.
- ❑ Alkanes have lower boiling points for a given molecular weight than most other organic compounds.



van der Waals attractions between alkanes molecules

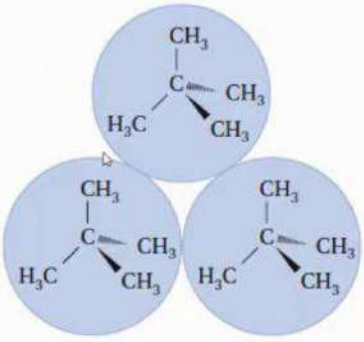


H-bonding between water molecules

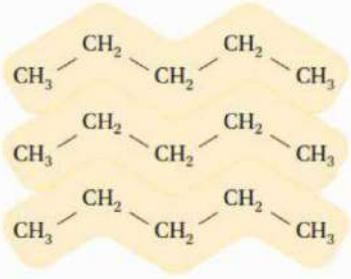


Name	Formula	Boiling point, °C
pentane	$CH_3CH_2CH_2CH_2CH_3$	36
2-methylbutane (isopentane)	$CH_3CHCH_2CH_3$ (CH₃ branch)	28
2,2-dimethyl-propane (neopentane)	$CH_3-C(CH_3)_2-CH_3$	10

Pentane, isopentane and neopentane are isomers because they have the same molecular formula (C_5H_{12})



2,2-dimethylpropane
bp 10°C

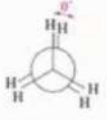


pentane
bp 36°C

Conformations of Alkanes

Conformations are **stereoisomers**, isomers in which the atoms are connected in the same order but are arranged differently in space. Simply they are formed as a result of the free rotation about the C-C single bond.

eclipsed

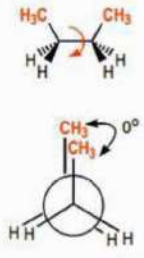


Newman

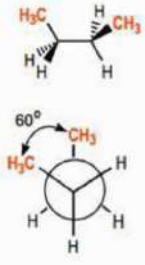
staggered

Newman

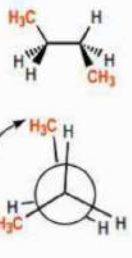
Conformations of Butane



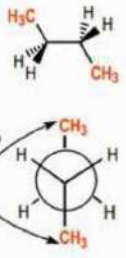
Totally eclipsed conformation.
Dihedral angle = 0°



Gauche conformation.
Dihedral angle = 60°



Eclipsed conformation.
Dihedral angle = 120°



Anti conformation.
Dihedral angle = 180°

Cycloalkane Nomenclature and Conformation

Cycloalkanes are named by placing the prefix *cyclo-* before the alkane name that corresponds to the number of carbon atoms in the ring. The structures and names of the first six unsubstituted cycloalkanes are as follows:

cyclopropane
bp −32.7°C

cyclobutane
bp 12°C

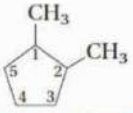
cyclopentane
bp 49.3°C

cyclohexane
bp 80.7°C

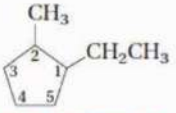
cycloheptane
bp 118.5°C

cyclooctane
bp 149°C

methylcyclopentane

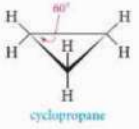


1,2-dimethylcyclopentane

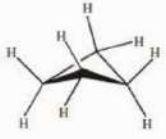


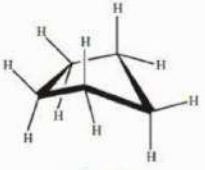
1-ethyl-2-methylcyclopentane

Conformations of cycloalkanes

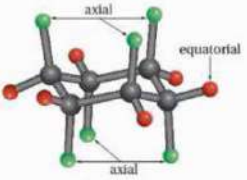


cyclopropane

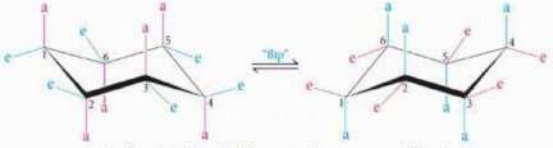




C—C—C angle	cyclobutane	cyclopentane
for planar molecule	90°	108°
observed experimentally	88°	105°



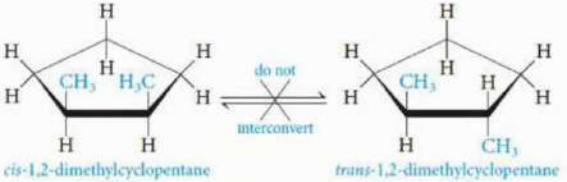
ball-and-stick model



Axial bonds (red) in the left structure become equatorial bonds (red) in the right structure when the ring "flips."

cyclohexane

Cis–Trans Isomerism in Cycloalkanes



cis-1,2-dimethylcyclopentane
bp 99°C

trans-1,2-dimethylcyclopentane
bp 92°C

Reactions of Alkanes

1. Combustion Reaction

A. Complete combustion

$$\underset{\text{methane}}{CH_4} + 2\,O_2 \longrightarrow CO_2 + 2\,H_2O + \text{heat (212.8 kcal/mol)}$$

$$\underset{\text{butane}}{C_4H_{10}} + \tfrac{13}{2}\,O_2 \longrightarrow 4\,CO_2 + 5\,H_2O + \text{heat (688.0 kcal/mol)}$$

B. Incomplete combustion

$$CH_4 + O_2 \longrightarrow \underset{\text{formaldehyde}}{CH_2O} + H_2O$$

$$2\,C_2H_6 + 3\,O_2 \longrightarrow 2\,\underset{\text{acetic acid}}{CH_3CO_2H} + 2\,H_2O$$

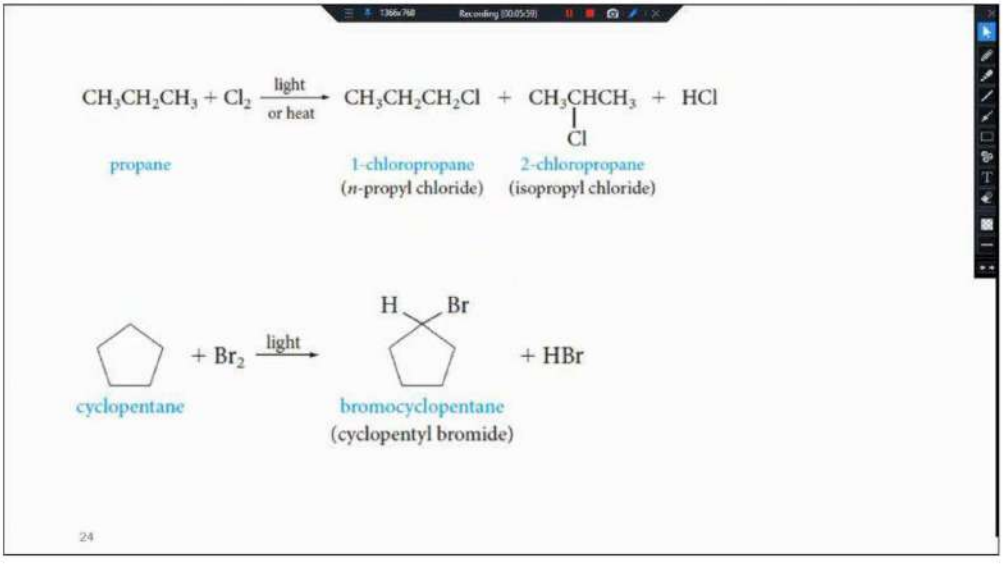
2. Halogenation Reaction

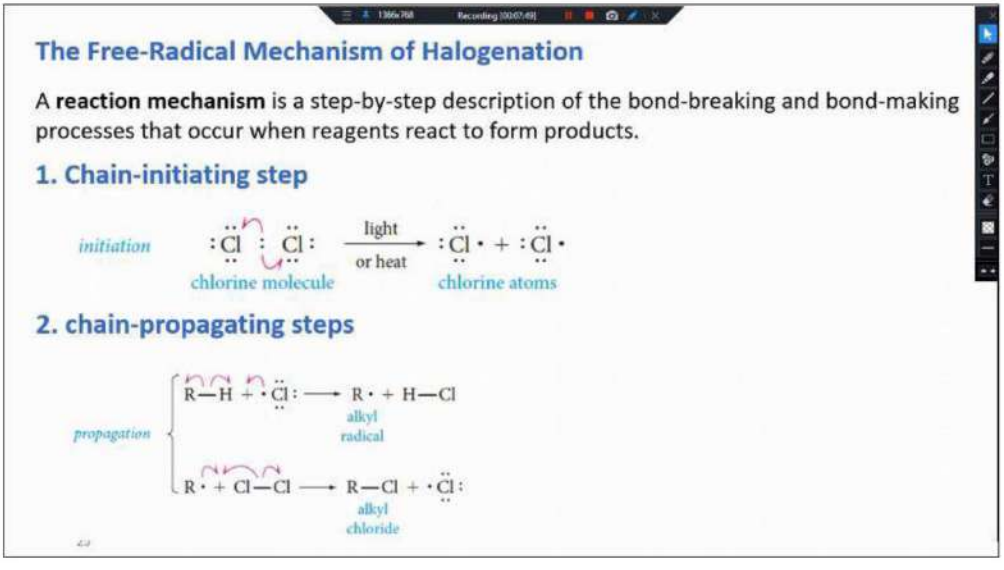
$$R{-}H + Cl{-}Cl \xrightarrow[\text{heat}]{\text{light or}} R{-}Cl + H{-}Cl$$

$$R{-}H + Br{-}Br \xrightarrow[\text{heat}]{\text{light or}} R{-}Br + HBr$$

$$\underset{\text{methane}}{CH_4} + Cl{-}Cl \xrightarrow[\text{or heat}]{\text{sunlight}} \underset{\substack{\text{chloromethane}\\ \text{(methyl chloride)}\\ \text{bp } -24.2^\circ C}}{CH_3Cl} + HCl$$

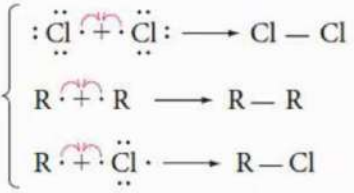
$$CH_3Cl \xrightarrow{Cl_2} \underset{\substack{\text{dichloromethane}\\ \text{(methylene chloride)}\\ \text{bp } 40^\circ C}}{CH_2Cl_2} \xrightarrow{Cl_2} \underset{\substack{\text{trichloromethane}\\ \text{(chloroform)}\\ \text{bp } 61.7^\circ C}}{CHCl_3} \xrightarrow{Cl_2} \underset{\substack{\text{tetrachloromethane}\\ \text{(carbon tetrachloride)}\\ \text{bp } 76.5^\circ C}}{CCl_4}$$





3. Chain-terminating steps

termination



Chapter-3
Alkenes and alkynes: Structure and chemical reactions

Definition Classification

Unsaturated hydrocarbons that contain a carbon–carbon double bond are called alkenes; those with a carbon–carbon triple bond are alkynes.* Their general formulas are

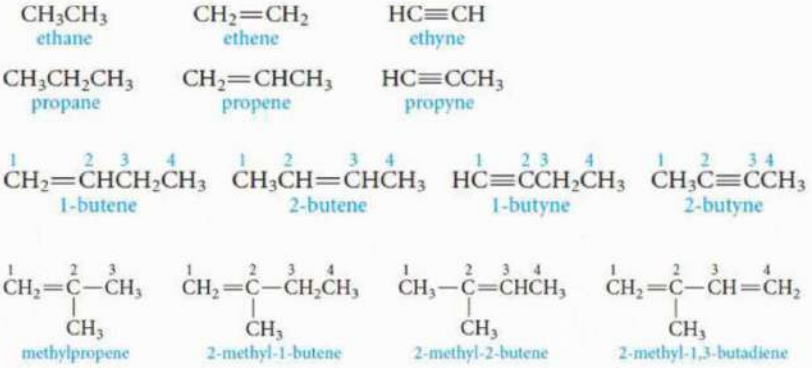
C_nH_{2n} alkenes C_nH_{2n-2} alkynes

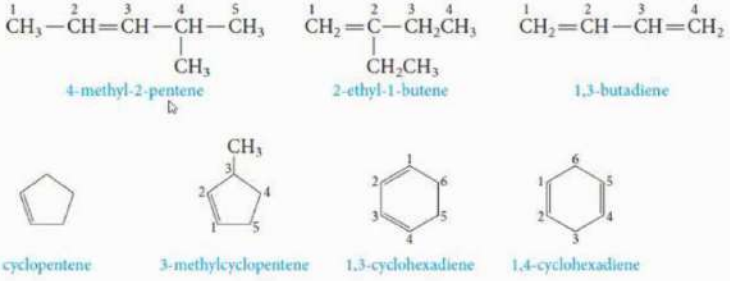
C=C=C
C=C=C=C
cumulated

C=C−C=C
C=C−C≡C
conjugated

C=C−C−C=C
C≡C−C−C−C≡C
nonconjugated (isolated)

Nomenclature





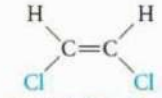
$CH_2{=}CH{-}$
vinyl
(ethenyl)

$CH_2{=}CHCl$
vinyl chloride
(chloroethene)

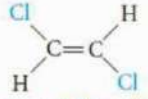
$CH_2{=}CH{-}CH_2{-}$
allyl
(2-propenyl)

$CH_2{=}CH{-}CH_2Cl$
allyl chloride
(3-chloropropene)

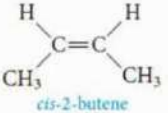
Cis–Trans Isomerism in Alkenes



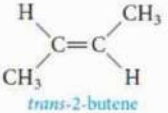
cis-1,2-dichloroethene



trans-1,2-dichloroethene



cis-2-butene

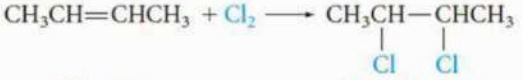


trans-2-butene

5

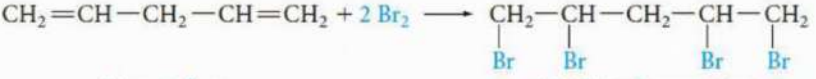
Addition Reactions of Alkenes

1. Addition of Halogens



2-butene
bp 1–4°C

2,3-dichlorobutane
bp 117–119°C



1,4-pentadiene
bp 26.0°C

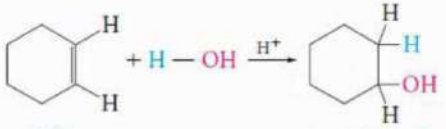
1,2,4,5-tetrabromopentane
mp 85–86°C

6

2. Addition of Water

$$CH_2{=}CH_2 + H{-}OH \xrightarrow{H^+} \underset{\displaystyle H}{\overset{\displaystyle CH_2{-}CH_2}{|\quad\quad|}}{}_{\displaystyle \quad OH} \qquad (\text{or } CH_3CH_2OH)$$

ethanol



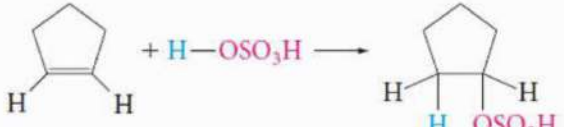
cyclohexene
bp 83.0°C

cyclohexanol
bp 161.1°C

3. Addition of Acids

$$CH_2{=}CH_2 + H{-}Cl \longrightarrow \underset{\displaystyle H}{\overset{\displaystyle CH_2{-}CH_2}{|\quad\quad|}}{}_{\displaystyle \quad Cl} \qquad (\text{or } CH_3CH_2Cl)$$

ethene — hydrogen chloride — chloroethane (ethyl chloride)

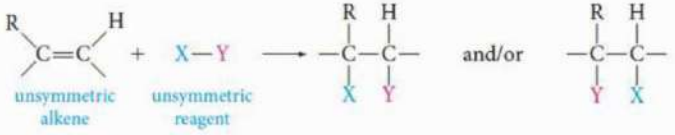


cyclopentene — sulfuric acid — cyclopentyl hydrogen sulfate

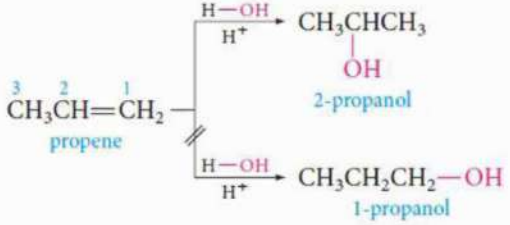
Mechanism of Electrophilic Addition to Alkenes

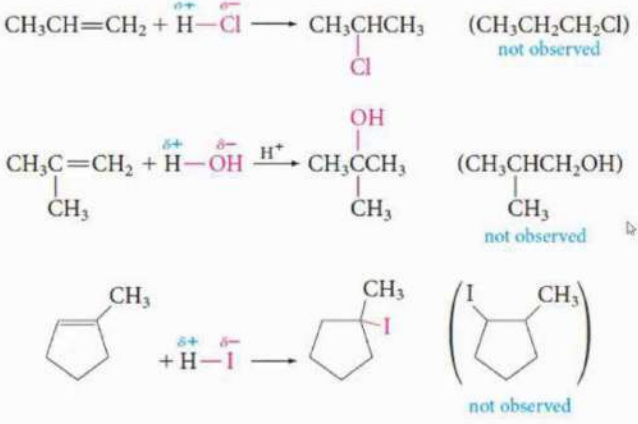
Table 3.2 Classification of Reagents and Alkenes by Symmetry with Regard to Addition Reactions

	Symmetric	Unsymmetric
Reagents	Br—Br Cl—Cl H—H	H—Br H—OH H—OSO_3H
Alkenes	$CH_2=CH_2$	$CH_3CH=CH_2$
	mirror plane	not a mirror plane



Markovnikov's Rule





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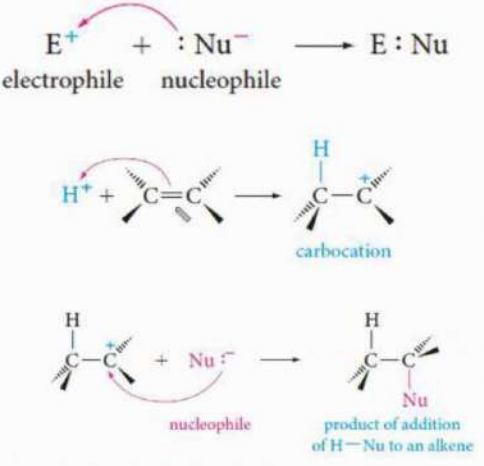

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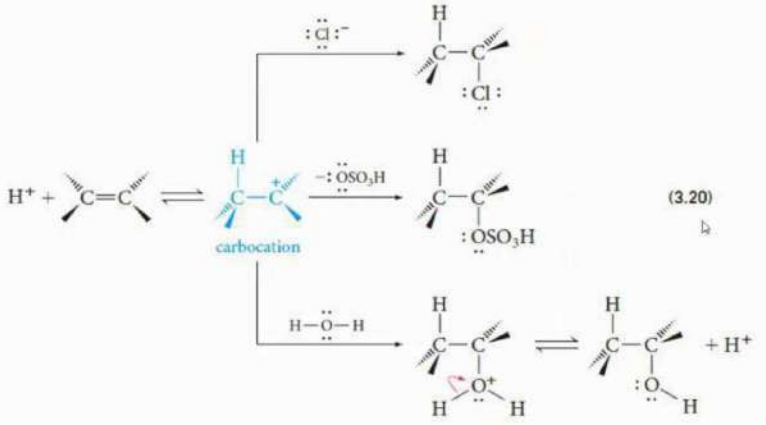

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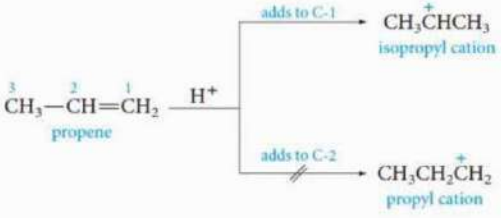
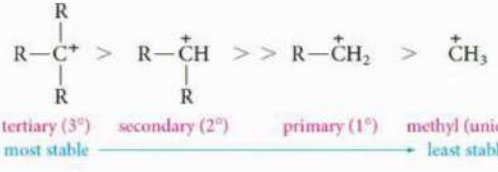
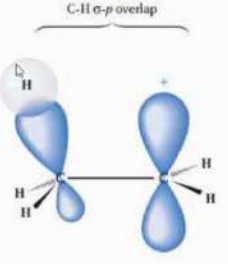
Explanation of Markovnikov's Rule







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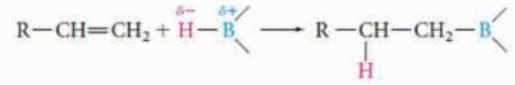
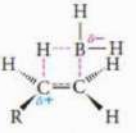
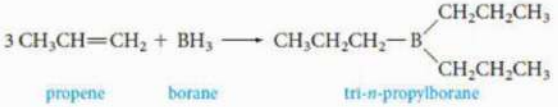
4. Hydroboration-Oxidation of Alkenes (two-step alcohol synthesis)

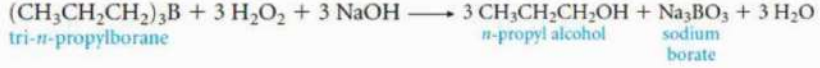




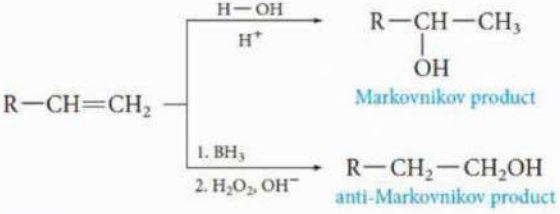
transition state for hydroboration



propene borane tri-*n*-propylborane

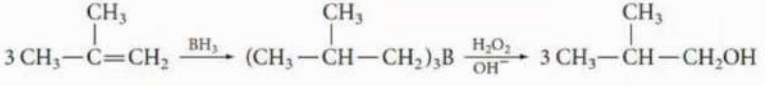


tri-*n*-propylborane *n*-propyl alcohol sodium borate

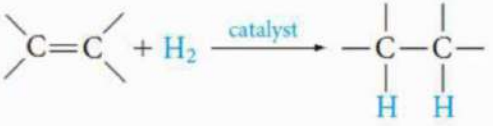


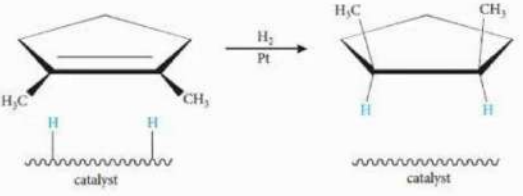
Markovnikov product

anti-Markovnikov product



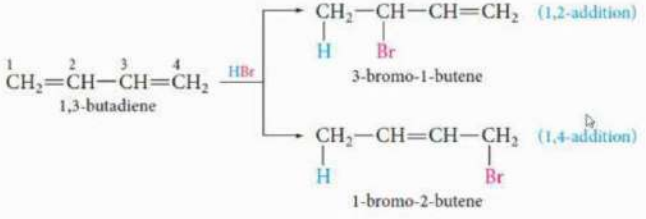
5. Addition of Hydrogen

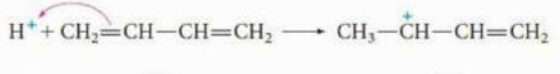


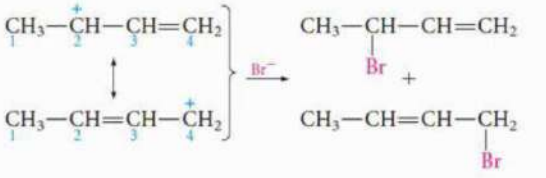


6. Additions to Conjugated Systems

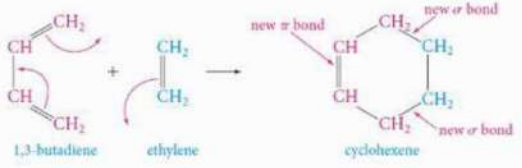
6.1 Electrophilic Additions to Conjugated Dienes

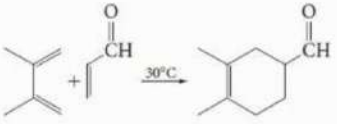


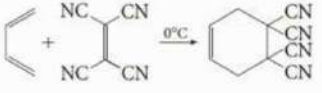




6.2 Cycloaddition to Conjugated Dienes: The Diels–Alder Reaction







7. Free-Radical Additions; Polyethylene

$$CH_2{=}CH_2 \xrightarrow[1000\ atm,\ >100^\circ C]{ROOR} {+}CH_2{-}CH_2{+}_n$$

ethylene — polyethylene (n = several thousand)

$$R{-}O{-}O{-}R \xrightarrow{heat} 2\,R{-}O\cdot$$

organic peroxide — two radicals

$$RO\cdot + CH_2{=}CH_2 \longrightarrow RO{-}CH_2{-}\dot{C}H_2$$

catalyst radical — a carbon-centered free radical

$$ROCH_2\dot{C}H_2 \xrightarrow{CH_2=CH_2} ROCH_2CH_2CH_2\dot{C}H_2 \xrightarrow{CH_2=CH_2} ROCH_2CH_2CH_2CH_2CH_2\dot{C}H_2 \text{ and so on}$$

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8. Oxidation of Alkenes

8.1 Oxidation with Permanganate; a Chemical Test

$$3\ \text{alkene} + 2\,K^+MnO_4^- + 4\,H_2O \longrightarrow 3\ \text{a glycol (OH OH)} + 2\,MnO_2 + 2\,K^+OH^-$$

alkene — potassium permanganate (purple) — a glycol — manganese dioxide (brown-black)

© Leslie Crase

Hexane does not react with purple $KMnO_4$ (left); cyclohexene (right) reacts, producing a brown-black precipitate of MnO_2.

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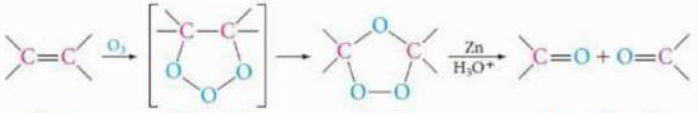
8.2 Ozonolysis of Alkenes



alkene — molozonide — ozonide — two carbonyl groups

$$CH_2{=}CHCH_2CH_3 \xrightarrow[2.\ Zn,\ H^+]{1.\ O_3} CH_2{=}O + O{=}CHCH_2CH_3$$

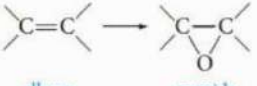
1-butene → formaldehyde + propanal

$$CH_3CH{=}CHCH_3 \xrightarrow[2.\ Zn,\ H^+]{1.\ O_3} 2\ CH_3CH{=}O$$

2-butene → 2 ethanal

8.3 Other Alkene Oxidations

Various reagents can convert alkenes to epoxides (eq. 3.47).



alkene — epoxide

(3.47)

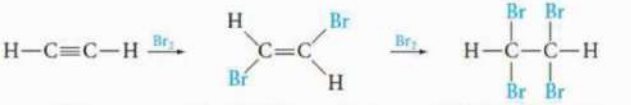
This reaction and the chemistry of epoxides are detailed in Chapter 8.

Like alkanes (and all other hydrocarbons), alkenes can be used as fuels. Complete combustion gives carbon dioxide and water.

$$C_nH_{2n} + \tfrac{3n}{2}\,O_2 \longrightarrow nCO_2 + nH_2O \qquad (3.48)$$

Addition Reactions of Alkynes

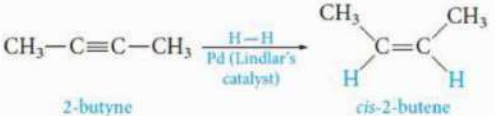
1. Addition of Halogens



ethyne — *trans*-1,2-dibromoethene — 1,1,2,2-tetrabromoethane

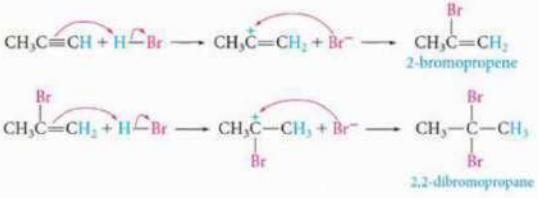
2. Addition of Hydrogen

With an ordinary nickel or platinum catalyst, alkynes are hydrogenated all the way to alkanes. However, a special palladium catalyst (called **Lindlar's catalyst**) can control hydrogen addition so that only 1 mole of hydrogen adds.

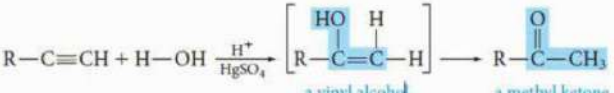


2-butyne, bp 27°C — *cis*-2-butene, bp 3.7°C

3. Addition of Acids

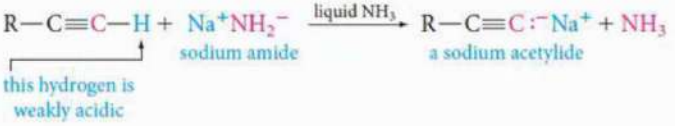


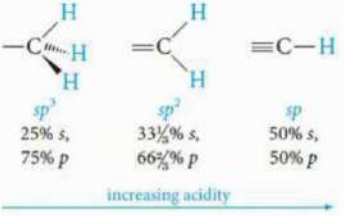
4. Addition of Water



a vinyl alcohol, or enol — a methyl ketone

5. Acid-base reaction





Chapter-4
Aromatic Compounds

Some Facts About Benzene

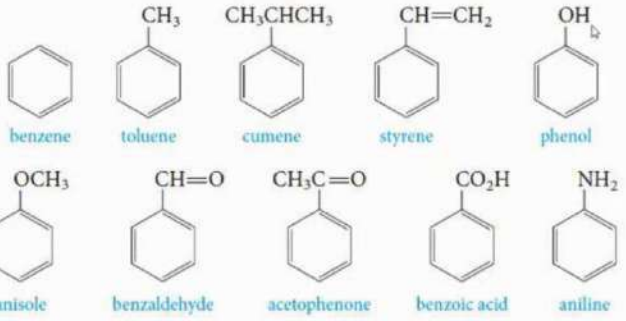
Benzene is a resonance hybrid of these two contributing structures.

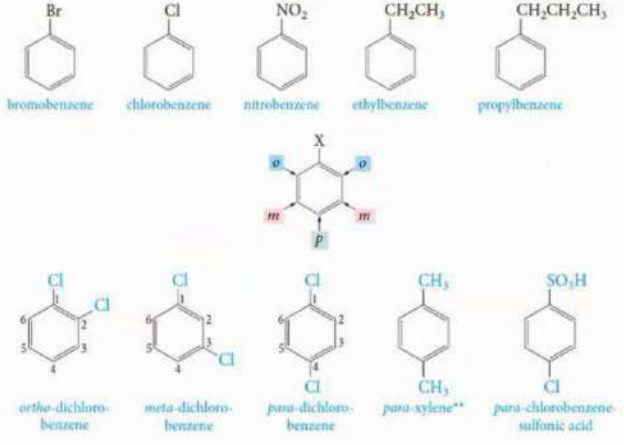
Properties:
colorless liquid
bp 80°C
mp 5.5°C

Figure 4.1
Ball-and-stick and space-filling models of benzene.

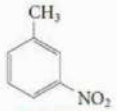
Nomenclature of Aromatic Compounds

Some common names accepted by IUPAC

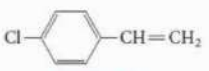




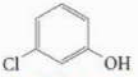
o-bromochlorobenzene



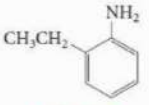
m-nitrotoluene



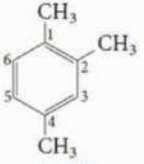
p-chlorostyrene



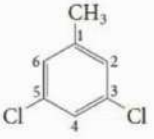
m-chlorophenol



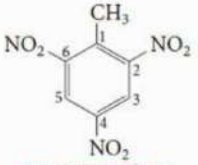
o-ethylaniline



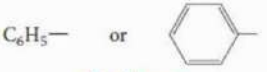
1,2,4-tri-methylbenzene



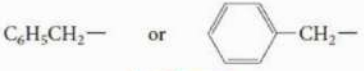
3,5-dichlorotoluene



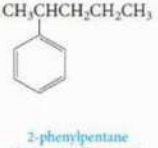
2,4,6-trinitrotoluene (TNT)



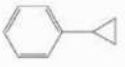
phenyl group



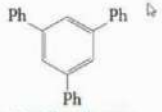
benzyl group



2-phenylpentane (or 2-pentylbenzene)

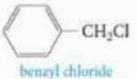


phenylcyclopropane (or cyclopropylbenzene)

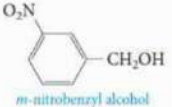


1,3,5-triphenylbenzene

biphenyl



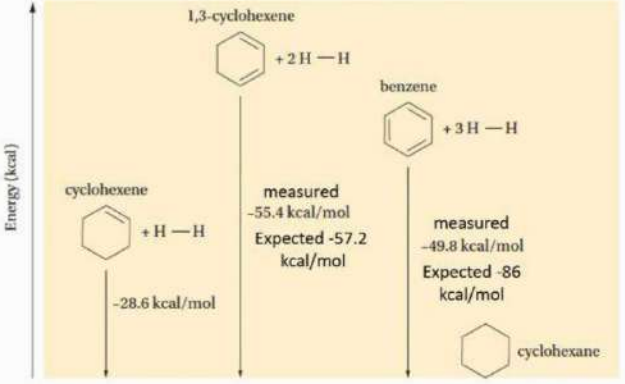
benzyl chloride



m-nitrobenzyl alcohol

The Resonance Energy of Benzene

Figure 4.3
Comparison of heat released by the hydrogenation of cyclohexene, 1,3-cyclohexadiene, and benzene to produce cyclohexane.

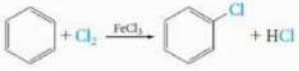


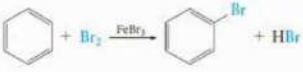
Stabilization energy, or **resonance energy**, is the difference between the actual energy of the real molecule (the resonance hybrid) and the calculated energy of the most stable contributing structure.

7

Electrophilic Aromatic Substitution Reactions

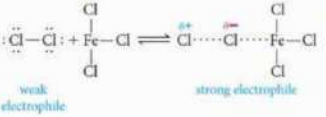
1. Chlorination Reactions



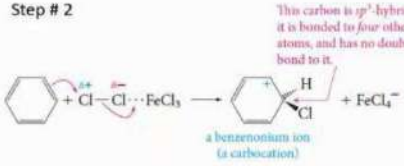


Mechanism

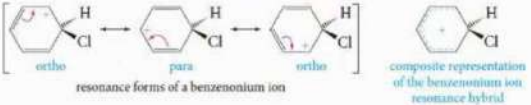
Step # 1



Step # 2

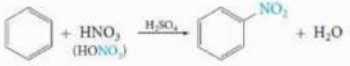


Step # 3

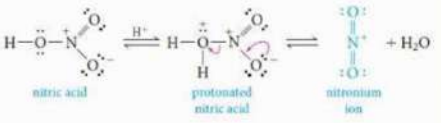


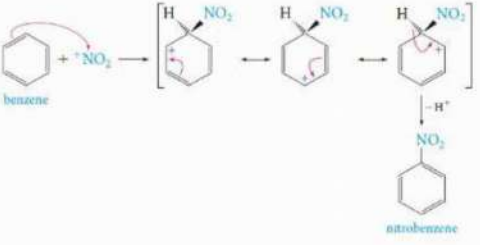
8

2. Nitration Reaction



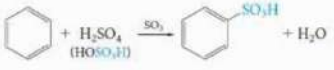
Mechanism





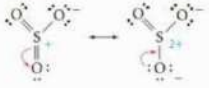
9

3. Sulfonation Reaction



Mechanism

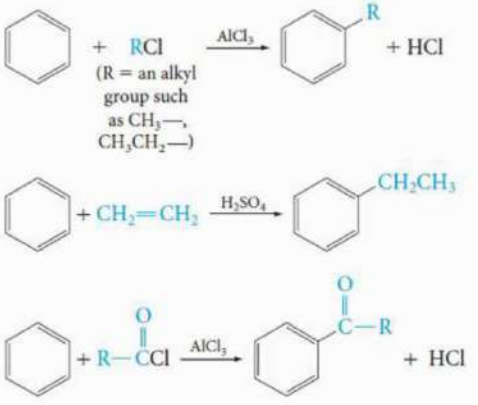
*Sulfuric acid provides a proton catalyst as shown in the following equilibrium:



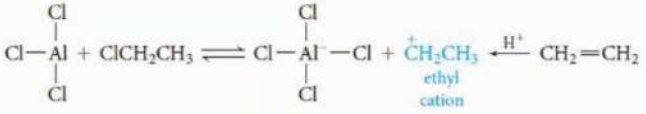
Example:

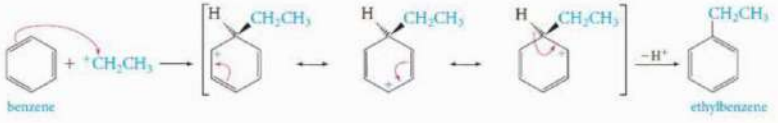
10

4. Alkylation and Acylation

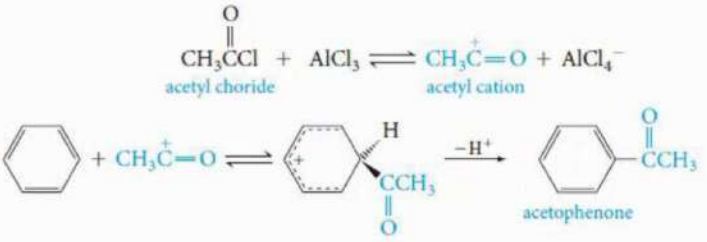


Mechanism of Alkylation

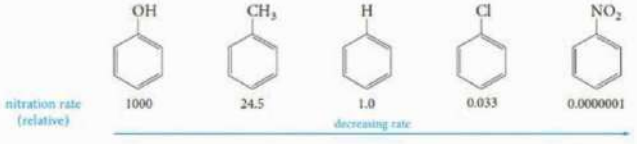




Mechanism of Acylation



Ring-Activating and Ring-Deactivating Substituents



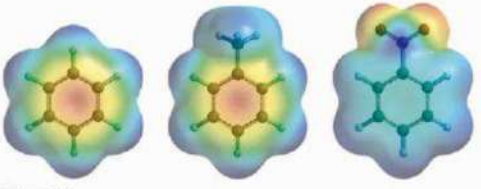


Figure 4.6
Electrostatic potential maps of benzene (left), toluene (middle), and nitrobenzene (right). The pi electron clouds in benzene and toluene are electron-rich (red), while the pi electron cloud in nitrobenzene is electron-deficient (blue).

Ortho,Para-Directing and Meta-Directing Groups

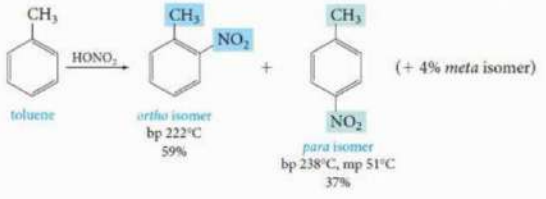


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Table 4.1 Directing and Activating Effects of Common Functional Groups (Groups are Listed in Decreasing Order of Activation)

	Substituent group	Name of group	
Ortho,Para-Directing	$-\ddot{N}H_2$, $-\ddot{N}HR$, $-\ddot{N}R_2$	amino	Activating
	$-\ddot{O}H$, $-\ddot{O}CH_3$, $-\ddot{O}R$	hydroxy, alkoxy	
	$-\ddot{N}H\overset{\ddot{O}:}{\overset{\|}{C}}-R$	acylamino	
	$-CH_3$, $-CH_2CH_3$, $-R$	alkyl	
	$-\ddot{F}:$, $-\ddot{C}l:$, $-\ddot{B}r:$, $-\ddot{I}:$	halo	Deactivating
Meta-Directing	$-\overset{:O:}{\overset{\|}{C}}-R$	acyl, carboxy	
	$-\overset{:O:}{\overset{\|}{C}}-\ddot{O}H$		
	$-\overset{:O:}{\overset{\|}{C}}-\ddot{N}H_2$	carboxamido, carboalkoxy	
	$-\overset{:O:}{\overset{\|}{C}}-\ddot{O}R$		
	$-\overset{:O:}{\overset{\|}{\underset{:O:}{\overset{\|}{S}}}}-\ddot{O}H$	sulfonic acid	
	$-C\equiv N:$	cyano	
	$-\overset{:O:}{\overset{\|}{N}}=\overset{:O:}{\overset{\|}{O}}$	nitro	

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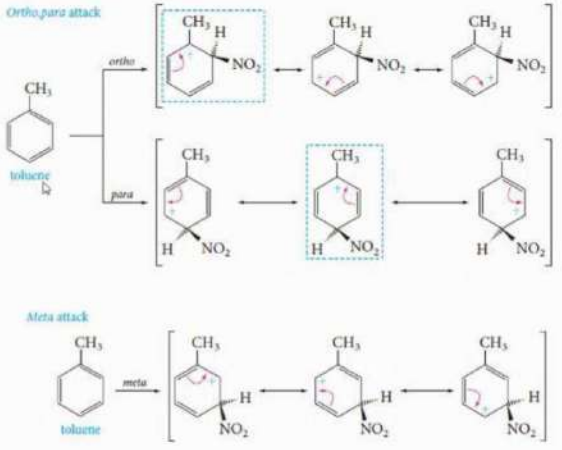
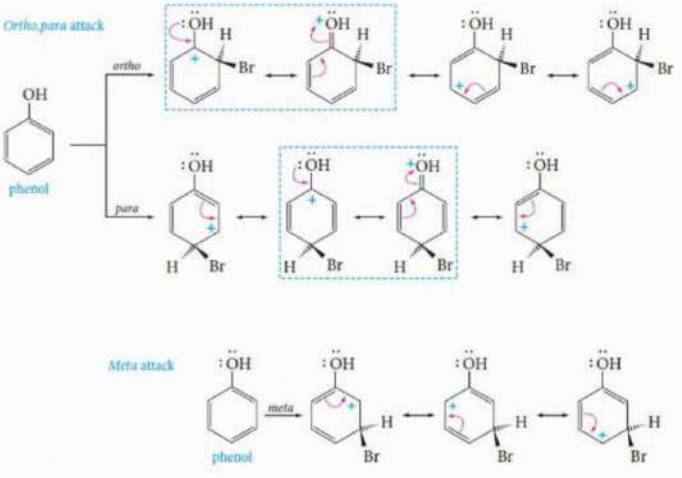
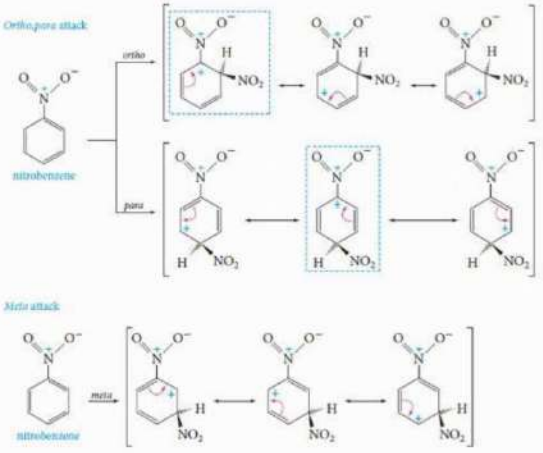
1. Ortho,Para-Directing Groups





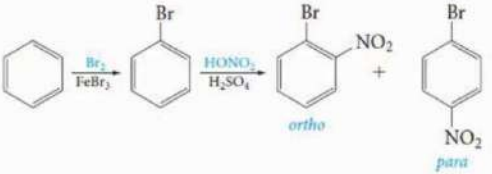
2. Meta-Directing Groups

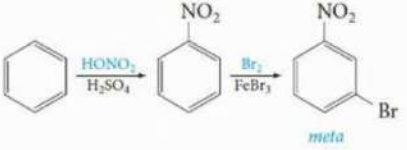


Specificity of Halogens

In all *meta*-directing groups, the atom connected to the ring carries a full or partial positive charge and will therefore withdraw electrons from the ring. *All* meta-*directing groups are therefore ring-deactivating groups.* On the other hand, ortho,para-*directing groups in general supply electrons to the ring and are therefore ring activating.* With the halogens (F, Cl, Br, and I), two opposing effects bring about the only important exception to these rules. *Because they are strongly electron withdrawing, the halogens are ring deactivating; but because they have unshared electron pairs, they are* ortho,para *directing.*

The Importance of Directing Effects in Synthesis



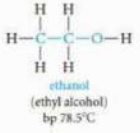


Chapter-5
Stereoisomerism

Isomers

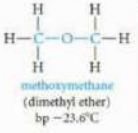
Constitutional Isomers

They have different connectivity.



ethanol
(ethyl alcohol)
bp 78.5°C

and



methoxymethane
(dimethyl ether)
bp −23.6°C

Stereoisomers

They have the same connectivity.

Enantiomers

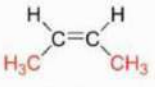
They are mirror images of each other.

Diastereomers

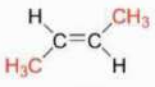
They are **NOT** mirror images of each other.

Your hands are mirror images of each other.

Diastereomers

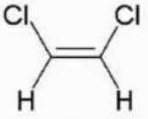


cis-2-butene

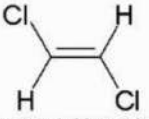


trans-2-butene

mirror



cis-2,3-dichloro-2-butene



trans-2,3-dichloro-2-butene

mirror

Diastereomers are not mirror images of each other.

Your hands are mirror images of each other.

Enantiomers (Chiral molecules)

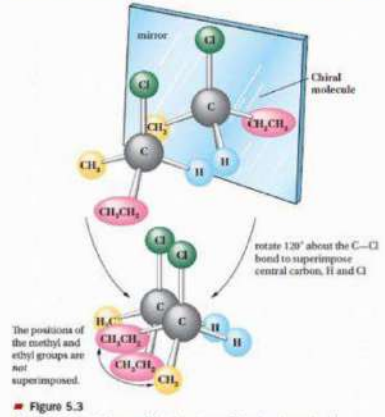
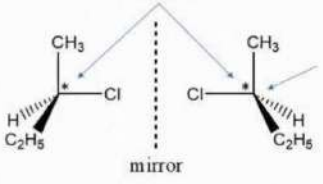


Figure 5.3
Model of 2-chlorobutane and its mirror image. The mirror image is *not* superimposable on the original molecule. The two forms of 2-chlorobutane are enantiomers.

Your hands are mirror images of each other.

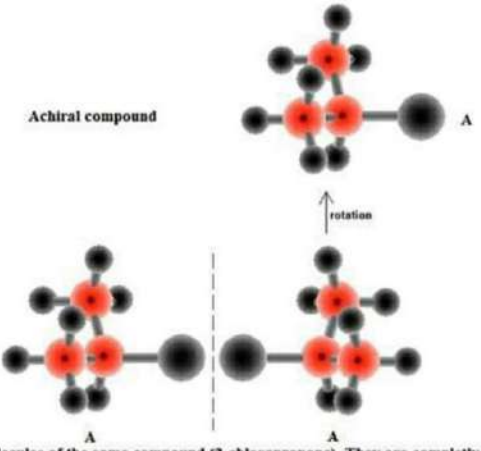
Chiral (stereogenic) center



Tow enentiomers of 2-chlorobutane

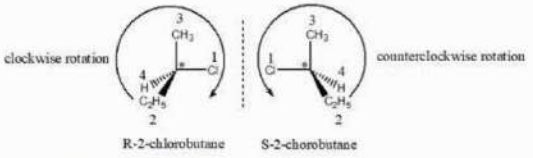
They are mirror images of each other.

Achiral molecule

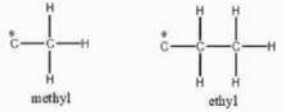


No chiral center; three molecules of the same compound (2-chloropropane). They are completly superimposed.

Configuration and the R-S System



Giving priority (methyl versus ethyl)

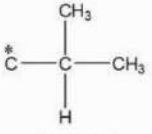


1st set of atoms:	C	C
Atomic number:	6	6
2nd set of atoms:	H,H,H	C,H,H
Atomic number:	3	8

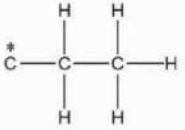
Ethyl group has higher priority than methyl group.

6

Giving priority (isopropyl versus ethyl)



isopropyl



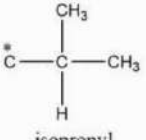
ethyl

1st set of atoms:	C	C
Atomic number:	6	6
2nd set of atoms:	C,C,H	C,H,H
Atomic number:	13	8

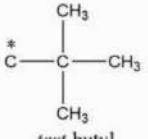
Isopropyl group has higher priority than ethyl group.

7

Giving priority (isopropyl versus *tert*-butyl)



isopropyl



tert-butyl

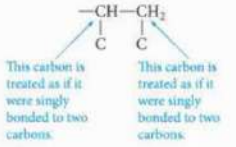
1st set of atoms:	C	C
Atomic number:	6	6
2nd set of atoms:	C,C,H	C,C,C
Atomic number:	13	18

***Tert*-butyl group has higher priority than Isopropyl group.**

8

In case of multiple bonds, priority is given as follows:

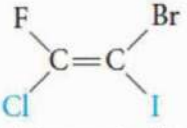
Multiple bonds are treated as if they were an equal number of single bonds. For example, the vinyl group —CH=CH_2 is counted as



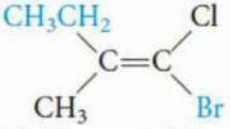
Similarly,

and

The E-Z Convention for *Cis–Trans* Isomers



(*Z*)-1-bromo-2-chloro-2-fluoro-1-iodoethene



(*E*)-1-bromo-1-chloro-2-methyl-1-butene

Polarized Light and Optical Activity

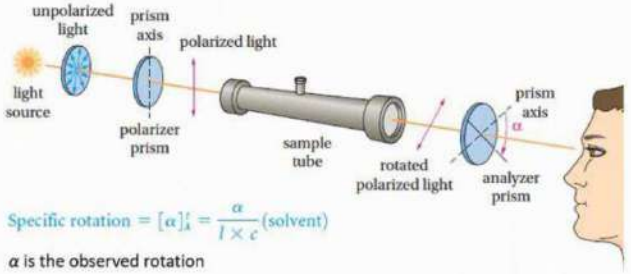


Figure 5.9
Diagram of a polarimeter.

$$\text{Specific rotation} = [\alpha]_\lambda^t = \frac{\alpha}{l \times c}(\text{solvent})$$

α is the observed rotation

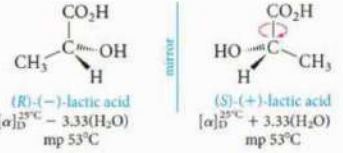
l is the length of the sample tube in *decimeters*

c is the concentration in *grams per milliliter*

t is the temperature of the solution

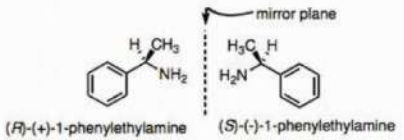
λ is the wavelength of light (For sodium vapor lamp, λ = 589.3 nm)

Examples:



(*R*)-(−)-lactic acid
$[\alpha]_D^{25°C}$ − 3.33(H_2O)
mp 53°C

(*S*)-(+)-lactic acid
$[\alpha]_D^{25°C}$ + 3.33(H_2O)
mp 53°C

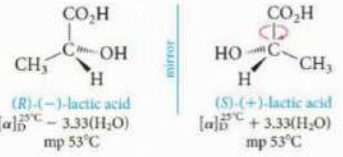


(*R*)-(+)-1-phenylethylamine (*S*)-(-)-1-phenylethylamine

Definition:
Racemic mixture: A 1:1 mixture of a pair of enantiomers. Therefore, it will not rotate the plane of polarization (optical activity = zero).

Properties of Enantiomers

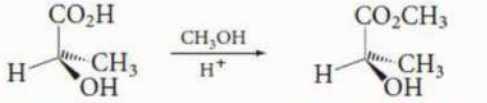
1. Enantiomers have identical achiral properties, such as melting point, boiling point, density, and various types of spectra. Their solubilities in an ordinary, achiral solvent are also identical. However, *enantiomers have different chiral properties,* one of which is the *direction* in which they rotate plane-polarized light (clockwise or counterclockwise).



(*R*)-(−)-lactic acid
$[\alpha]_D^{25°C}$ − 3.33(H_2O)
mp 53°C

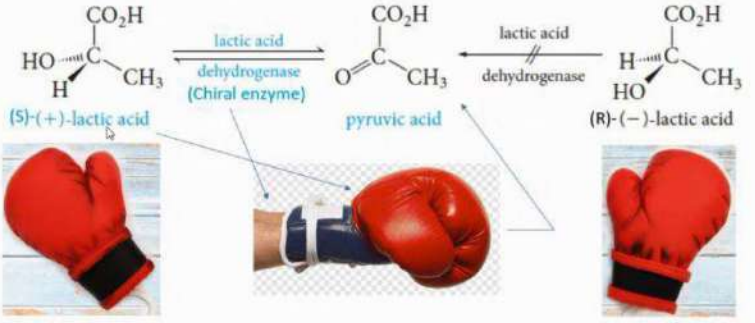
(*S*)-(+)-lactic acid
$[\alpha]_D^{25°C}$ + 3.33(H_2O)
mp 53°C

2. There is no obvious relationship between configuration (R or S) and sign of rotation (+ or -).



(*R*)-(−)-lactic acid (*R*)-(+)-methyl lactate

3. Enantiomers often behave differently in a biological setting because these properties usually involve a reaction with another chiral molecule.



Imagine that the chiral enzyme is your left hand which fits best with the left-handed boxing glove (S-lactic acid) and not with the right-handed boxing glove (R-lactic acid).

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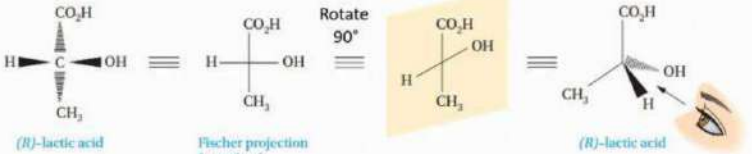
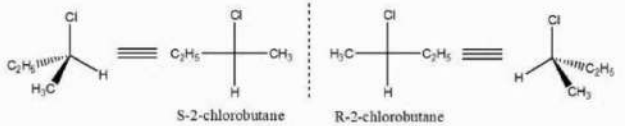
Enantiomers differ in many types of biological activity. One enantiomer may be a drug, whereas its enantiomer may be ineffective. For example, only (−)-adrenaline is a cardiac stimulant; (+)-adrenaline is ineffective. One enantiomer may be toxic, another harmless. One may be an antibiotic, the other useless. One may be an insect sex attractant, the other without effect or perhaps a repellant. Chirality is of paramount importance in the biological world.

(R)-(-)-adrenaline

Fischer Projection Formulas



(*R*)-lactic acid | Fischer projection formula of (*R*)-lactic acid | (*R*)-lactic acid



S-2-chlorobutane | R-2-chlorobutane

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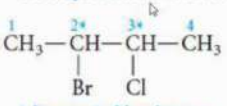
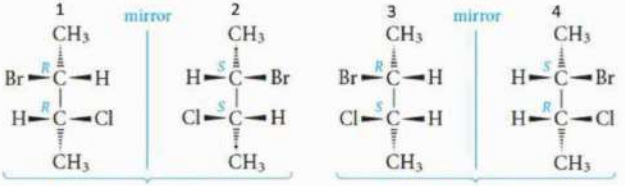
Compounds with More Than One Stereogenic Center; Diastereomers



2-bromo-3-chlorobutane



(2R,3R)-2-bromo-3-chlorobutane | (2S,3S)-2-bromo-3-chlorobutane | (2R,3S)-2-bromo-3-chlorobutane | (2S,3R)-2-bromo-3-chlorobutane

Maximum # of stereoisomers = $2^n = 2^2 = 4$, where n = # of stereogenic centers

Maximum # of pairs of enantiomers = $2^n/2 = 4/2 = 2$ pairs of enentiomers

Some relationships:

1-2 and 3-4 are pairs of enantiomers (they are mirror images of each other)

1-3, 1-4, 2-3, and 2-4 are pairs of diastereomers (they are ***NOT*** mirror images of each other)

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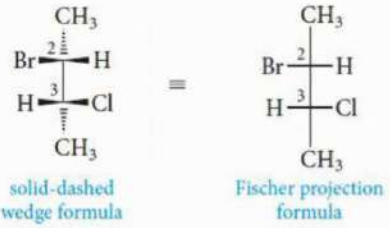
Representation of a molecule with two stereogenic centers using Fisher projection formula



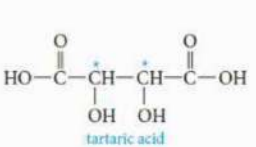
solid-dashed wedge formula

Fischer projection formula

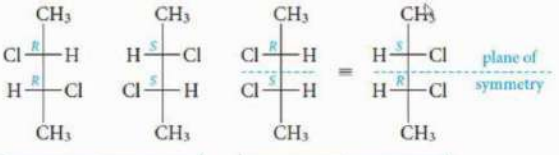
(2R,3R)-2-bromo-3-chlorobutane

Meso Compounds

A *meso* compound: is an achiral diastereomer of a compound with stereogenic centers. Its stereogenic centers have opposite configurations. Also, they have a plane of symmetry that is perpendicular to the plane of the paper and bisects the central C-C bond. Being achiral, *meso* compounds are optically inactive.



tartaric acid



enantiomers, chiral

identical, achiral a *meso* form

Configuration	(*R*,*R*)	(*S*,*S*)	*meso* (*R*,*S*)
$[\alpha]_D^{20}$ (H_2O)	+12	−12	0
Melting point, °C	170	170	140

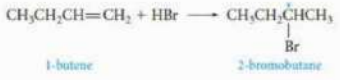
Notice that the total # of stereoisomers of tartaric acid = 3, therefore it does ***NOT*** obey the above-mentioned 2^n rule. Why? Because it has a meso form.

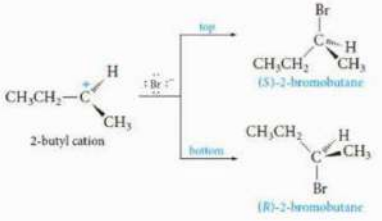
Enantiomers Versus Diastereomers; Chiral and Achiral Properties

There is an important, fundamental difference between enantiomers and diastereomers. Because they are mirror images, enantiomers differ *only* in mirror-image (chiral) properties. They have the same achiral properties, such as melting point, boiling point, and solubility in ordinary solvents. Enantiomers cannot be separated from one another by methods that depend on achiral properties, such as recrystallization or distillation. On the other hand, diastereomers are *not* mirror images. They may differ in *all* properties, whether chiral or achiral. As a consequence, diastereomers may differ in melting point, boiling point, and solubility, not only in direction but also in the number of degrees that they rotate plane-polarized light—in short, they behave as two different chemical substances.

Stereochemistry and Chemical Reactions

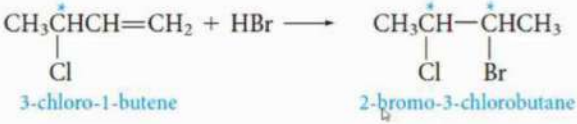
Example 1



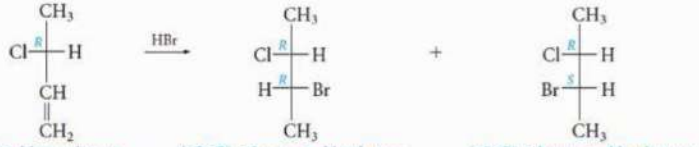


Stereochemistry and Chemical Reactions

Example 2

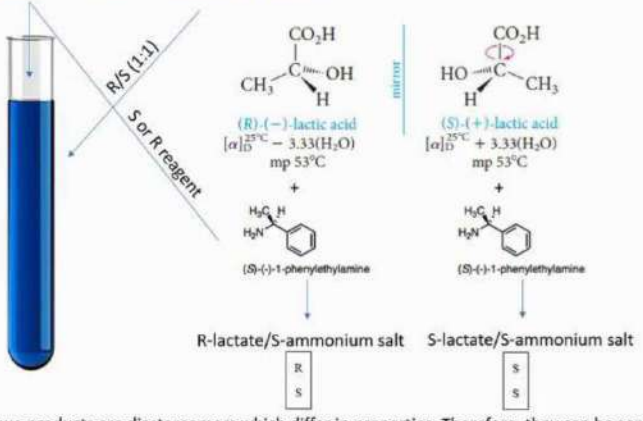


3-chloro-1-butene　　2-bromo-3-chlorobutane



(*R*)-3-chloro-1-butene　　(2*R*,3*R*)-2-bromo-3-chlorobutane　　(2*S*,3*R*)-2-bromo-3-chlorobutane

Resolution of a Racemic Mixture



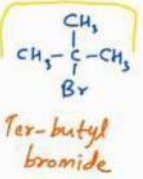
The two products are diastereomers which differ in properties. Therefore, they can be separated by ordinary achiral methods, such as distillation or recrystallization.

Chapter-6
Organic Halogen Compounds; Substitution and Elimination Reactions

larger surface area

$CH_3-CH_2-CH_2-CH_2-Br$

n-butyl bromide



Tert-butyl bromide

Nucleophilic Substitution

$$HO^- + CH_3CH_2-Br \xrightarrow{H_2O} CH_3CH_2-OH + Br^-$$

ethyl bromide → ethanol

Classification of Nucleophiles

Oxygen nucleophiles

1.	HO^-	hydroxide
2.	RO^-	alkoxide
3.	HOH	water
4.	ROH	alcohol
5.	$R-C(=O)-O^-$	carboxylate

Nitrogen nucleophiles

6.	NH_3	ammonia
7.	RNH_2	primary amine
8.	R_2NH	secondary amine
9.	R_3N	tertiary amine

Sulfur nucleophiles

10.	HS^-	hydrosulfide
11.	RS^-	mercaptide
12.	R_2S	thioether

Halogen nucleophiles

13.	I^-	iodide

Carbon nucleophiles

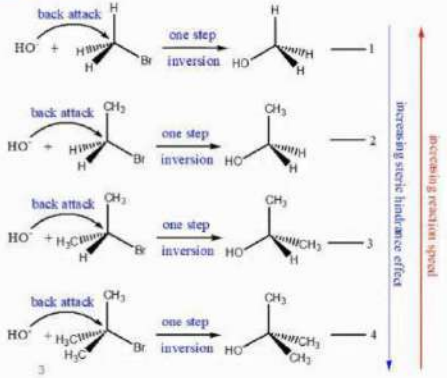
14.	$^-:C\equiv N:$	cyanide
15.	$^-:C\equiv CR$	acetylide

Nucleophilic Substitution Mechanisms

1. S_N2 Mechanism

The **S_N2 mechanism** is a one-step process in which the bond to the leaving group begins to break as the bond to the nucleophile begins to form.

Examples



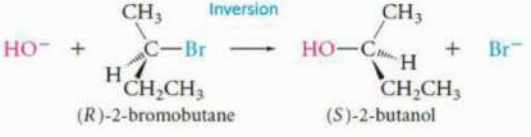
In S_N2 mechanism,
methyl halide > 1° alkyl halide > 2° alkyl halide > 3° alkyl hali

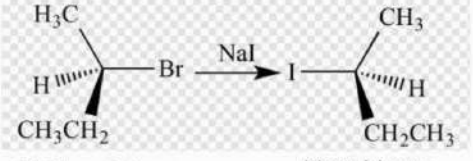
Increasing steric hindrance effe

Low steric effect → High steric effect

Rate of reaction = K [HO^-][alkyl halide]
That is why we have the number 2 in the abbreviation (S_N2).
That is, the reaction rate depends on the concentration of both reactants.

When inversion is important and attracts our attention?!!

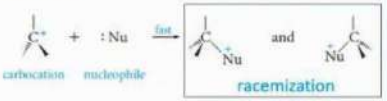




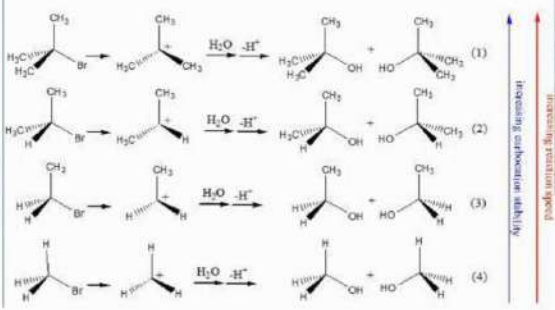
2. S_N1 Mechanism

Step # 1

Step # 2



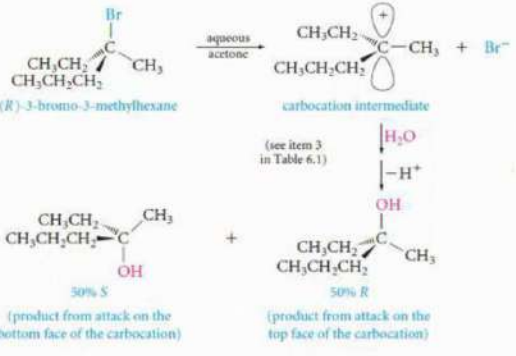
Examples



In S_N1 mechanism,
3° alkyl halide > 2° alkyl halide > 1° alkyl halide > methyl halide

Rate of reaction = K [alkyl halide]
That is why we have the number 1 in the abbreviation (S_N1).
That is, the reaction rate depends on the concentration of ***ONLY*** one reactant (alkyl halide).

When racemization is important and attracts our attention?!!



Your hands can be considered as a racemic mixtur

The final product is a racemic mixture. Therefore, it is optically inactive.

S_N2 versus S_N1

In S_N2 mechanism,
One step mechanism
Inversion takes place.
Rate of reaction = K [Nu][alkyl halide]
methyl halide > 1° alkyl halide > 2° alkyl halide > 3° alkyl halide

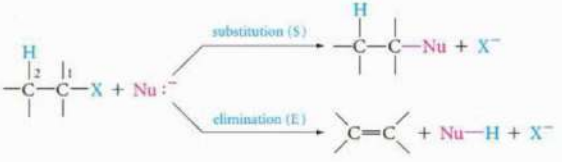
In S_N1 mechanism,
Two step mechanism
Racemization takes place.
Rate of reaction = K [alkyl halide]
3° alkyl halide > 2° alkyl halide > 1° alkyl halide > methyl hali

Table 6.2 Comparison of S_N2 and S_N1 Substitutions

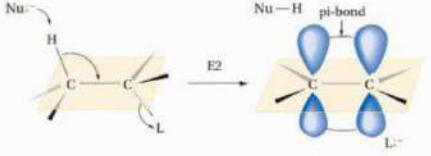
Variables	S_N2	S_N1
Halide structure		
Primary or CH_3	Common	Rarely*
Secondary	Sometimes	Sometimes
Tertiary	Rarely	Common
Stereochemistry	Inversion	Racemization
Solvent	Rate is retarded by polar protic solvents and increased by polar aprotic solvents	Because the intermediates are ions, the rate is increased by polar solvents
Nucleophile	Rate depends on nucleophile concentration; mechanism is favored when the nucleophile is an anion	Rate is independent of nucleophile concentration; mechanism is more likely with neutral nucleophiles

9

Dehydrohalogenation, an Elimination Reaction; the E2 and E1 Mechanisms

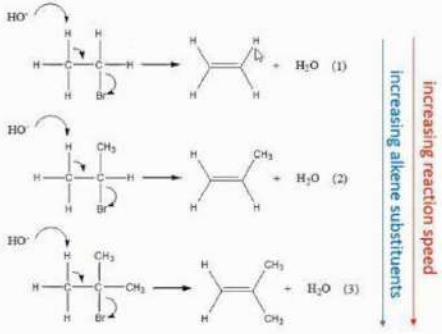


E2 mechanism



11

E2 mechanism

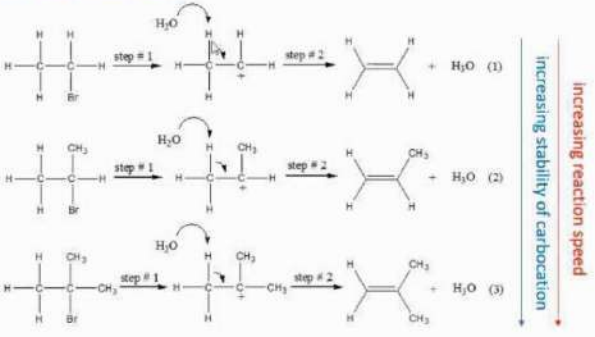


In E2 mechanism,
3° alkyl halide > 2° alkyl halide > 1° alkyl halide

Rate of reaction = K [HO⁻][alkyl halide]
That is why we have the number 2 in the abbreviation (E2).
That is, the reaction rate depends on the concentration of bo
reactants.

12

E1 mechanism



In E2 mechanism,
3° alkyl halide > 2° alkyl halide > 1° alkyl halide

Rate of reaction = K [alkyl halide]
That is why we have the number 1 in the abbreviation (E1).
That is, the reaction rate depends on the concentration of both
reactants.

13

E2 versus E1

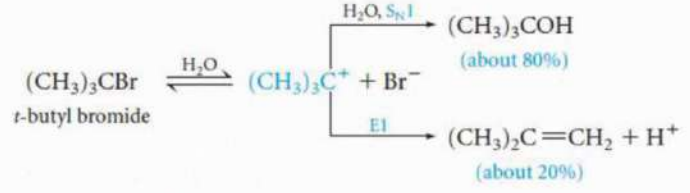
In E2 mechanism,
One step mechanism
Rate of reaction = K [Nu][alkyl halide]
3° alkyl halide > 2° alkyl halide > 1° alkyl halide

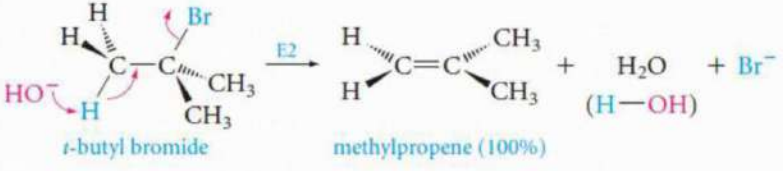
In E1 mechanism,
Two step mechanism
Rate of reaction = K [alkyl halide]
3° alkyl halide > 2° alkyl halide > 1° alkyl halide

Notice that alkyl halides have the same reactivity toward **E2** and **E1**. That is, 3° alkyl halide > 2° alkyl halide > 1° alkyl halide.
Why?? The reasons have been discussed before.

Substitution and Elimination in Competition

Tertiary Halides





Substitution and Elimination in Competition

Primary Halides

Small-sized nucleophile

$CH_3CH_2CH_2CH_2Br$ (1-bromobutane)

$CH_3CH_2O^-\ Na^+$ in ethanol → $CH_3CH_2CH_2CH_2OCH_2CH_3$ + $CH_3CH_2CH{=}CH_2$

butyl ethyl ether (S_N2; 90%) — 1-butene (E2; 10%)

$(CH_3)_3C{-}O^-\ K^+$ in *t*-butyl alcohol → $CH_3CH_2CH_2CH_2OC(CH_3)_3$ + $CH_3CH_2CH{=}CH_2$

butyl *t*-butyl ether (S_N2; 15%) — 1-butene (E2; 85%)

large-sized nucleophile

Substitution and Elimination in Competition

Secondary Halides

CH_3CHCH_3 (Br) 2-bromopropane

$CH_3CH_2S^-\ Na^+$ strong nucleophile → CH_3CHCH_3 (SCH_2CH_3) (S_N2)

CH_3CH_2OH weak nucleophile → CH_3CHCH_3 (OCH_2CH_3) + $CH_3CH{=}CH_2$

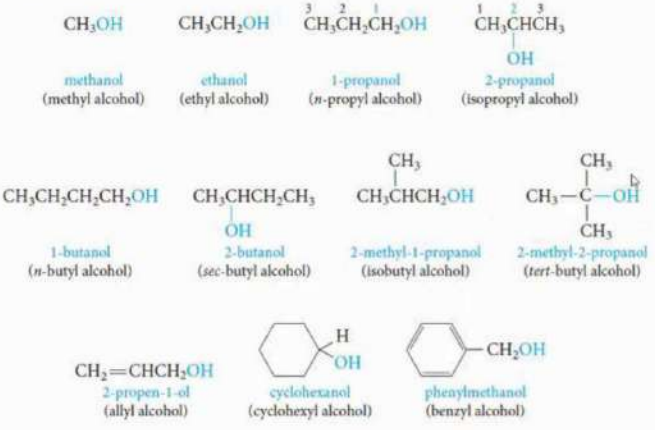
(S_N1; major) (E1; minor)

$CH_3CH_2O^-\ Na^+$ strong base → CH_3CHCH_3 (OCH_2CH_3) + $CH_3CH{=}CH_2$

(S_N2; minor) (E2; major)

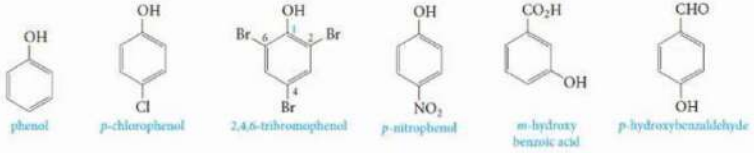
Chapter-7
Alcohols, Phenols, and Thiols

Nomenclature of Alcohols



Classification of Alcohols

Nomenclature of Phenols



Hydrogen Bonding in Alcohols and Phenols

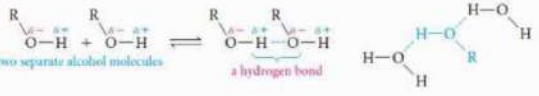
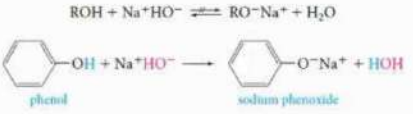
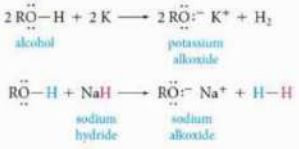


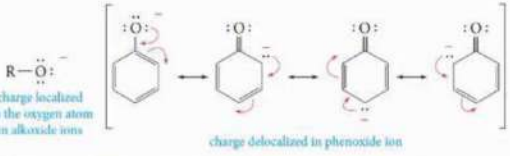
Table 7.1 Boiling Point and Water Solubility of Some Alcohols

Name	Formula	bp, °C	Solubility in H_2O g/100 g at 20°C
methanol	CH_3OH	65	completely miscible
ethanol	CH_3CH_2OH	78.5	completely miscible
1-propanol	$CH_3CH_2CH_2OH$	97	completely miscible
1-butanol	$CH_3CH_2CH_2CH_2OH$	117.7	7.9
1-pentanol	$CH_3CH_2CH_2CH_2CH_2OH$	137.9	2.7
1-hexanol	$CH_3CH_2CH_2CH_2CH_2CH_2OH$	155.8	0.59

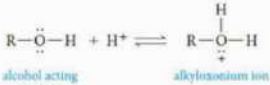
The Acidity of Alcohols and Phenols







The Basicity of Alcohols and Phenols



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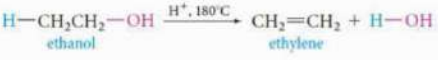
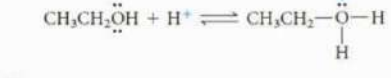
Reactions of Alcohols

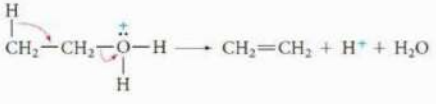
1. Dehydration reaction

Dehydration of primary alcohols



E2 dehydration mechanism





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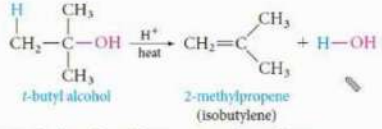
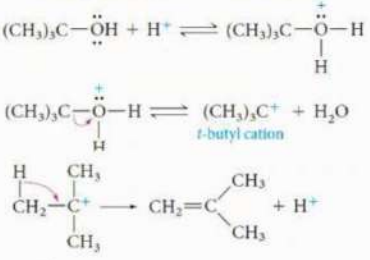
Dehydration of tertiary alcohols



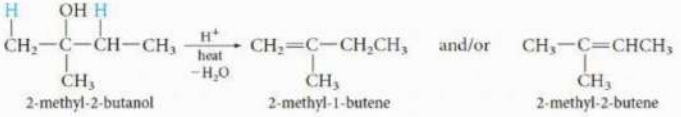
t-butyl alcohol — 2-methylpropene (isobutylene)

E1 dehydration mechanism



The ease of alcohol dehydration is 3° > 2° > 1° (the same as the order of carbocation stability).

Sometimes a single alcohol gives two or more alkenes.



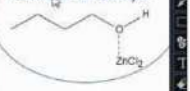
2-methyl-2-butanol — 2-methyl-1-butene — 2-methyl-2-butene

2. Reaction with Hydrogen Halides

The ease of reaction with HX is 3° > 2° > 1° (the same as the order of carbocation stability).

$$\underset{\text{alcohol}}{R{-}OH} + H{-}X \longrightarrow \underset{\text{alkyl halide}}{R{-}X} + H{-}OH$$

Lewis acid catalyst

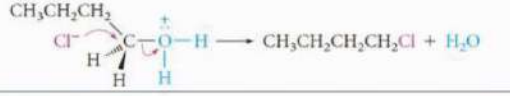


$$\underset{\text{1-butanol}}{CH_3CH_2CH_2CH_2OH} + H{-}Cl \xrightarrow[\text{several hours}]{\text{heat, } ZnCl_2} \underset{\text{1-chlorobutane}}{CH_3CH_2CH_2CH_2{-}Cl} + H{-}OH$$

S_N2 mechanism

$$CH_3CH_2CH_2CH_2{-}\ddot{O}H + H^+ \rightleftharpoons CH_3CH_2CH_2CH_2{-}\overset{+}{O}(H){-}H$$

slow reaction



S_N1 mechanism

$$\underset{t\text{-butyl alcohol}}{(CH_3)_3COH} + H{-}Cl \xrightarrow[15\text{ min}]{rt} \underset{t\text{-butyl chloride}}{(CH_3)_3C{-}Cl} + H{-}OH$$

$$(CH_3)_3C^+ + Cl^- \xrightarrow{fast} (CH_3)_3CCl$$

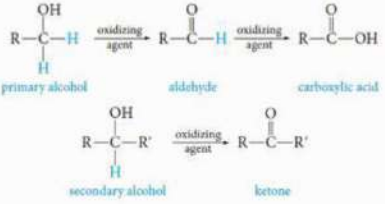
fast reaction

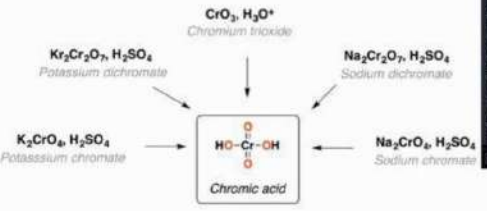
3. Reaction with Thionyl Chloride and Phosphorus Halides; Preparation of Alkyl Halides from Alcohols

$$3\,ROH + \underset{\substack{\text{phosphorus}\\\text{halide}}}{PX_3} \longrightarrow 3\,RX + H_3PO_3\,(X = Cl \text{ or } Br)$$

Both of these methods are used mainly with primary and secondary alcohols, whose reaction with hydrogen halides is slow.

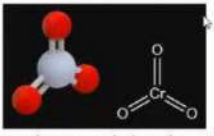
4. Oxidation of Alcohols to Aldehydes, Ketones, and Carboxylic Acids



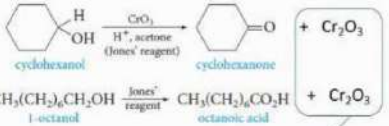


Chromic acid is often made "in situ" (that is, in the reaction flask) through the addition of acid to sources of chromium (such as chromate salts). The large number of possible chromium sources (and acids!) can make this confusing, but it is chromic acid that is the active reagent.

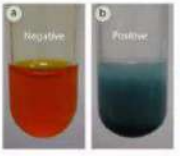
Reaction of a primary alcohol, secondary alcohol, and aldehyde with the chromic acid reagent; Chromic Acid (Jones) Test



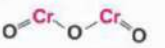
Chromium (VI) oxide
orange



3° alcohol gives negative test



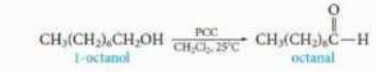
orange Blue-green

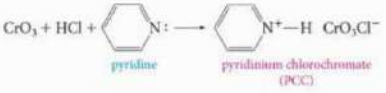


Chromium (III) oxide

Negative (a) and positive (b) results for the chromic acid test.

How to stop the oxidation of primary alcohols at the aldehyde stage?
By using mild oxidizing agents, such as PCC.





13

Alcohols with More Than One Hydroxyl Group

ethylene glycol
(1,2-ethanediol)
bp 198°C

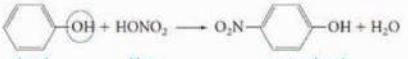
glycerol (glycerine)
(1,2,3-propanetriol)
bp 290°C (decomposes)

sorbitol
(1,2,3,4,5,6-hexanehexaol)
mp 110–112°C

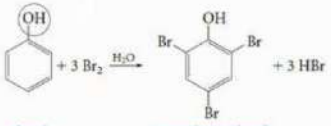
14

Aromatic Substitution in Phenols

The ring activating group (OH) gives phenol the ability to react under mild conditions.

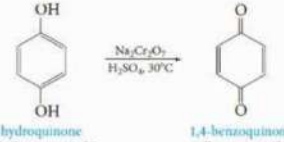


phenol — dilute nitric acid — *p*-nitrophenol



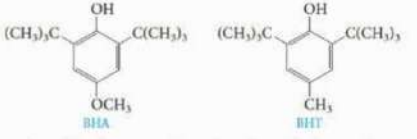
phenol — 2,4,6-tribromophenol

Oxidation of Phenols



hydroquinone
colorless, mp 171°C
(1,4-dihydroxybenzene)

1,4-benzoquinone
yellow, mp 116°C

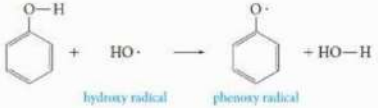


BHA — butylated hydroxyanisole

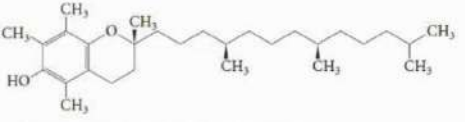
BHT — butylated hydroxytoluene

Food antioxidants

Phenols as Antioxidants



hydroxy radical — phenoxy radical



Vitamin E (a-tocopherol) is a natural phenolic antioxidant that protects the body against free radicals

Thiols

Naming

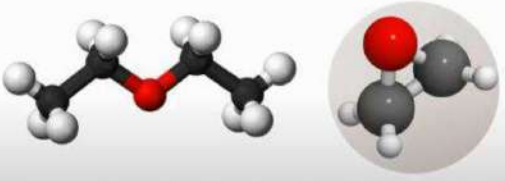
methanethiol (methyl mercaptan) | 1-butanethiol (*n*-butyl mercaptan) | thiophenol (phenyl mercaptan)

Preparation

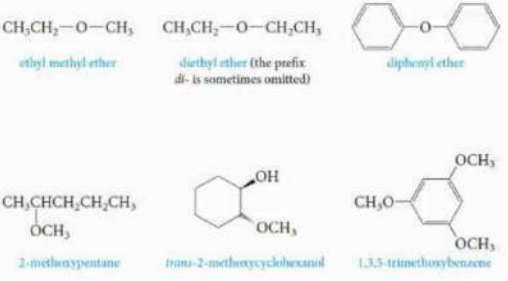
Thiols are more acidic than alcohols. The pK_a of ethanethiol, for example, is 10.6 whereas that of ethanol is 15.9. Hence, thiols react with aqueous base to give thiolates.

a sodium thiolate

Chapter-8
Ethers and Epoxides



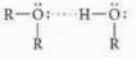
Nomenclature of Ethers



Physical Properties of Ethers

Table 8.1 Properties of Alcohols, Ethers, and Hydrocarbons of Similar Molecular Weight

Compound	Formula	bp	mol wt	Water solubility (g/100 mL, 20°C)
1-butanol	$CH_3CH_2CH_2CH_2OH$	118°C	74	7.9
diethyl ether	$CH_3CH_2{-}O{-}CH_2CH_3$	35°C	74	7.5
pentane	$CH_3CH_2{-}CH_2{-}CH_2CH_3$	36°C	72	0.03

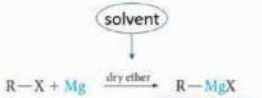


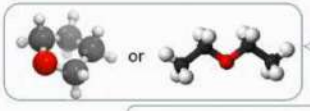
The general inertness, coupled with the fact that most organic compounds are ether-soluble, makes ethers excellent solvents in which to carry out organic reactions.

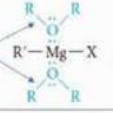
Ethers as Solvents; inertness of ethers

Ethers are relatively inert compounds. They do not usually react with dilute acids, with dilute bases, or with common oxidizing and reducing agents. They do not react with metallic sodium—a property that distinguishes them from alcohols. This general inertness, coupled with the fact that most organic compounds are ether-soluble, makes ethers excellent solvents in which to carry out organic reactions.

Ethers are also used frequently to extract organic compounds from their natural sources. Diethyl ether is particularly good for this purpose. Its low boiling point makes it easy to remove from an extract and easy to recover by distillation. It is highly flammable, however, and must not be used if there are any flames in the laboratory.





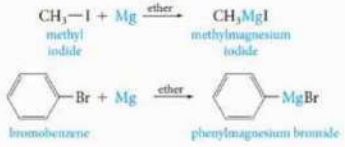


Acting as a Lewis base, ether stabilizes a Grignard reagent.

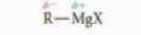
Stabilization of Mg through coordinate to ether molecules

Organometallic Compounds; Carbanions

1. Grignard Reagent

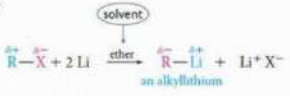


Grignard Reagents are considered to be strong bases (carbanions)



Organometallic Compounds; Carbanions

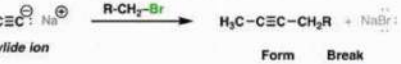
2. Organolithium Compounds



3. Acetylides

Acetylide ions are strong bases and good nucleophiles

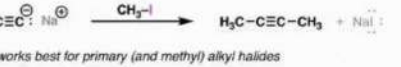
Notably useful: They can perform an S_N2 reaction with alkyl halides



Acetylide ion

Form	Break
C–C	C–Br

Specific Example:



Note: works best for primary (and methyl) alkyl halides

Preparation of Ethers

1. By Condensation of Alcohols

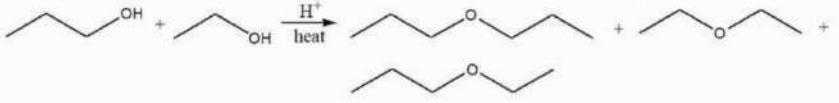
$$\underset{\text{ethanol}}{CH_3CH_2OH} + HOCH_2CH_3 \xrightarrow[140^\circ C]{H_2SO_4} \underset{\text{diethyl ether}}{CH_3CH_2OCH_2CH_3} + H_2O$$

Note:

$$\underset{\text{ethanol}}{H{-}CH_2CH_2{-}OH} \xrightarrow{H^+,\ 180^\circ C} \underset{\text{ethylene}}{CH_2{=}CH_2} + H{-}OH$$

The above-mentioned reactions provide a good example of how important it is to control reaction conditions and to specify them in equations.

Disadvantages of this method: the condensation of different alcohols leads to a mixture of different ethers.



2. Williamson Synthesis; Preparation of Symmetric and Asymmetric Ethers

$$2\,ROH + 2\,Na \longrightarrow 2\,RO^-Na^+ + H_2$$

$$RO^-Na^+ + R'{-}X \longrightarrow ROR' + Na^+X^-$$

Which alkyl halides work best?

- The Williamson Ether synthesis is an S_N2 reaction
- Methyl and primary alkyl halides are best, since they have the least steric hindrance

Since the second step is an S_N2 reaction, it works best if R′ in the alkyl halide is primary and not well at all if R′ is tertiary.

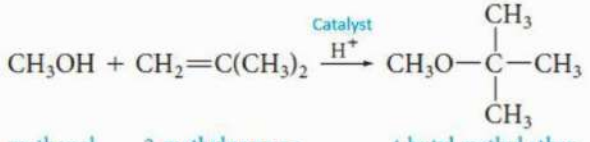
Advantages of this method: it leads ONLY to one ether product.

Methyl halides: work well

Primary alkyl halides: work well

Preparation of Ethers

3. Acid catalyzed Addition of Alcohols to Alkenes

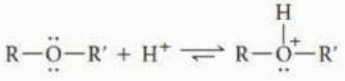


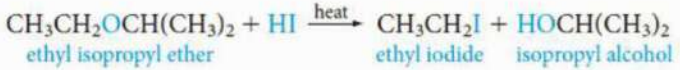
methanol — 2-methylpropene — *t*-butyl methyl ether

Asymmetric ether

The reaction follows Markovinicov's rule

Reactions of Ethers; Cleavage of Ethers





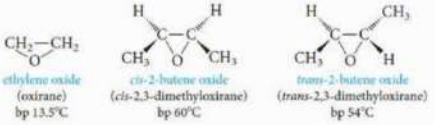
ethyl isopropyl ether — ethyl iodide — isopropyl alcohol

t-butyl phenyl ether — phenol — *t*-butyl alcohol (and $(CH_3)_2C{=}CH_2$)

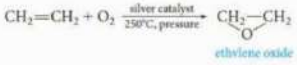
Acid catalyzed reaction

Epoxides (Oxiranes)

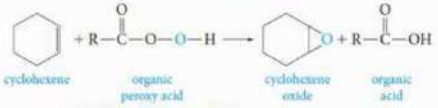
Nomenclature



Preparation of Epoxides



This method is suitable only for ethylene oxide.

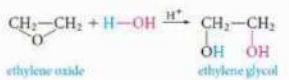


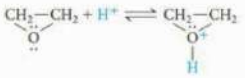
This method is suitable for all other epoxides.

good oxidizing agent

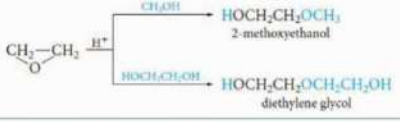
Reactions of Epoxides; Ring Opening Reaction

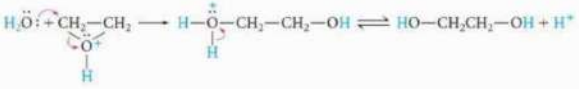
1. Acid-catalyzed ring opening



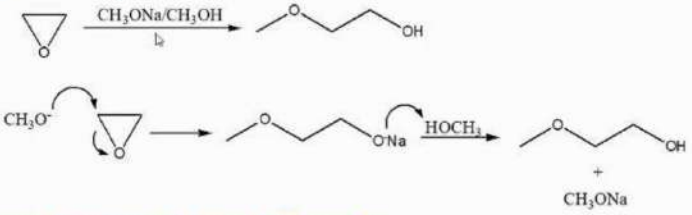


Other nucleophiles add to epoxides in a similar way.

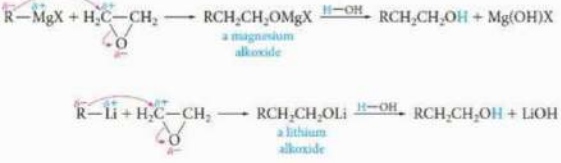




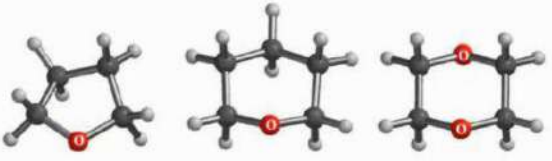
2. Base-catalyzed ring opening

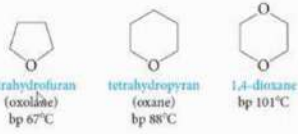


3. Ring opening by using Grignard Reagents



Cyclic Ethers



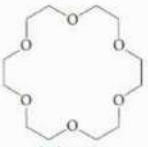


tetrahydrofuran (oxolane) bp 67°C	tetrahydropyran (oxane) bp 88°C	1,4-dioxane bp 101°C

They are useful solvent that not only dissolve many organic compounds but are miscible with water.

Crown Ethers

They are cyclic ethers have a crownlike shape.

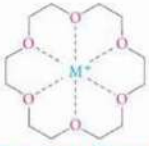


[18]crown-6
mp 39–40°C

[15]crown-5
(liquid)

[12]crown-4

Molecular Recognition (Host–Guest Chemistry)



M+ complexed in [18]crown-6

X⁻

Cavity diameter	2.6–3.2 Å
Ion diameter	
Na^+	1.90 Å
K^+	2.66 Å
Cs^+	3.34 Å

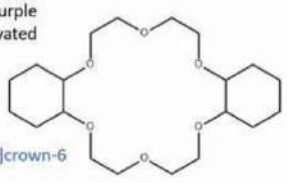
Only this ion achieves a snug fit.

Phase Transfer catalysis

However, if some dicyclohexyl[18]crown-6 is dissolved in the benzene, it is possible to extract the potassium permanganate from the water into the benzene! The resulting "purple benzene," containing free, essentially unsolvated permanganate ions, is a powerful oxidizing agent.*

Benzene layer

aqueous solution (layer) of $KMnO_4$

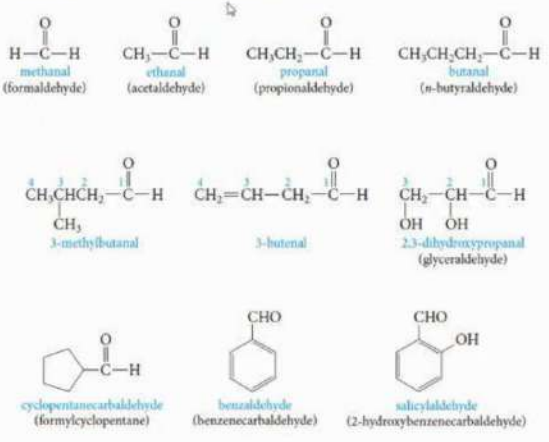


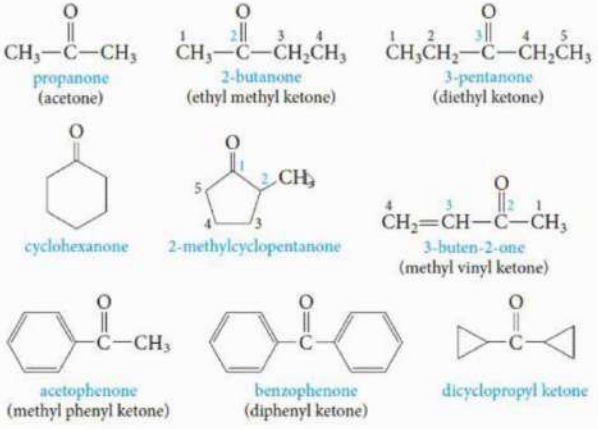
dicyclohexyl[18]crown-6

Chapter-9
Aldehydes and Ketones

Cinnamaldehyde

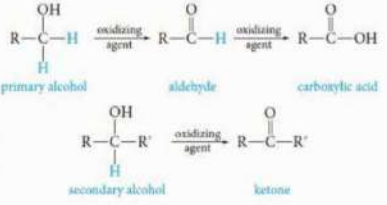
Nomenclature of Aldehydes and Ketones

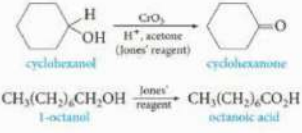




Synthesis of Aldehydes and Ketones

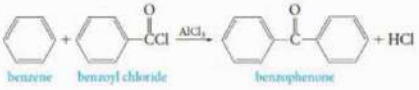
1. By Oxidation of Alcohols





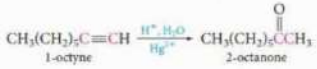
Synthesis of Aldehydes and Ketones

2. By Friedel-Craft Acylation of Aromatic Compounds



benzene benzoyl chloride benzophenone

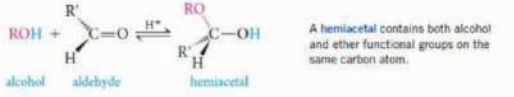
3. By Hydration of Terminal Alkynes



1-octyne 2-octanone

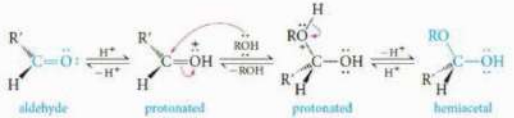
Reactions of Aldehydes and Ketones; Nucleophilic Addition to Carbonyl Groups

1. Addition of Alcohols: Formation of Hemiacetals and Acetals



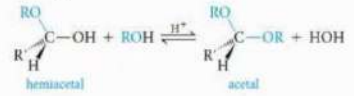
alcohol aldehyde hemiacetal

A hemiacetal contains both alcohol and ether functional groups on the same carbon atom.

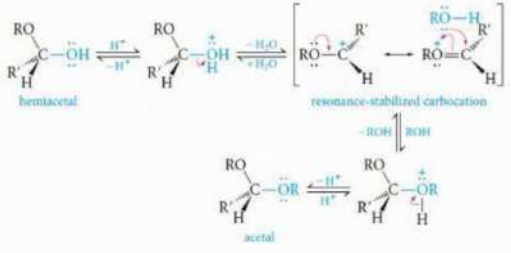


aldehyde protonated aldehyde protonated hemiacetal hemiacetal

In the presence of *excess alcohol*, hemiacetals react further to form acetals.



An **acetal** has two ether functional groups on the same carbon atom.



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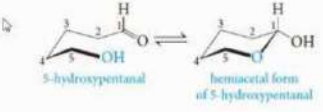
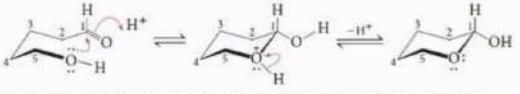
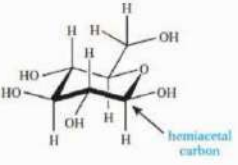
Intramolecular Nucleophilic Addition; Cyclic Hemiacetal



In a **cyclic hemiacetal**, the ether functional group is cyclic.



For example, glucose is an important carbohydrate that exists as a cyclic hemiacetal.



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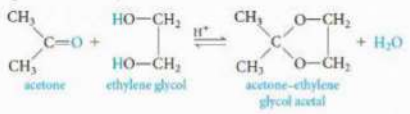
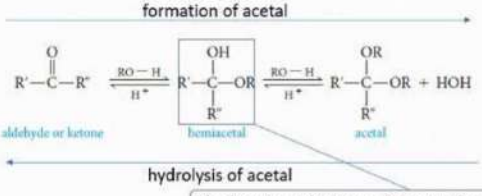
Ketones also form acetals. If, as in the following example, a glycol is used as the alcohol, the product will be cyclic.

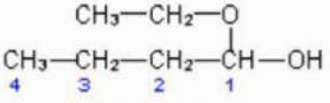


To summarize, aldehydes and ketones react with alcohols to form, first, hemiacetals and then, if excess alcohol is present, acetals.

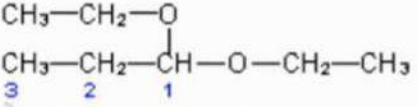


The hemiacetal intermediate usually cannot be isolated.

Nomenclature of hemiacetals and acetals



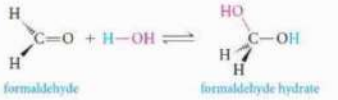
1-Ethoxybutan-1-ol
Butanal ethyl hemiacetal



1,1-Diethoxypropane
Propanal diethyl acetal

Reactions of Aldehydes and Ketones; Nucleophilic Addition to Carbonyl Groups

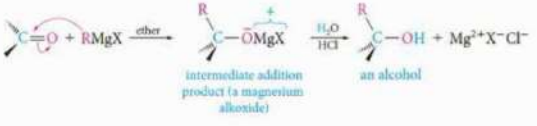
2. Addition of Water; Hydration of Aldehydes and Ketones



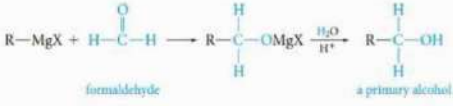
Chloral hydrate (trichloroacetaldehyde hydrate) is used in medicine as sedative.

Reactions of Aldehydes and Ketones; Nucleophilic Addition to Carbonyl Groups

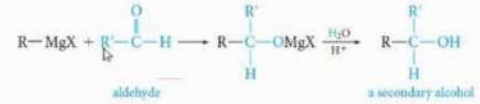
3. Addition of Grignard reagents



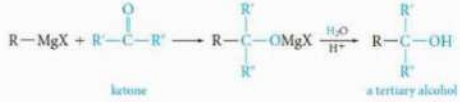
Formaldehyde gives primary alcohols.

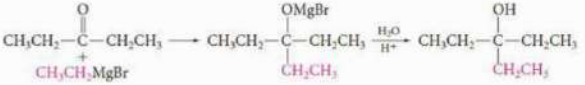


Other aldehydes give secondary alcohols.



Ketones give tertiary alcohols.





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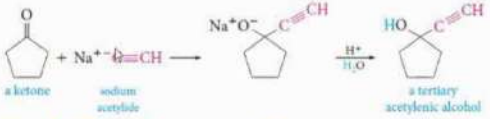
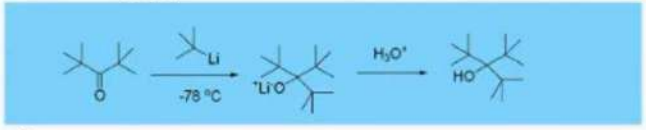
Reactions of Aldehydes and Ketones; Nucleophilic Addition to Carbonyl Groups

4. Addition of Acetylides



5. Addition of organolithium compounds



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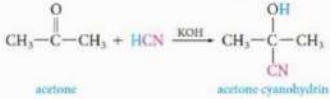
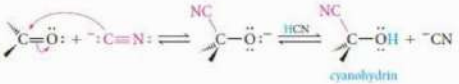
Reactions of Aldehydes and Ketones; Nucleophilic Addition to Carbonyl Groups

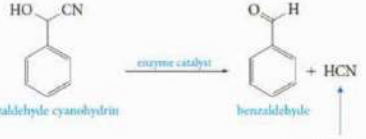
5. Addition of Hydrogen Cyanide; Cyanohydrins

Cyanohydrins are compounds with a hydroxyl and a cyano group attached to the same carbon.



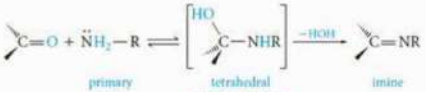


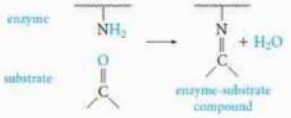
Cyanohydrin chemistry plays a central role in the defense system of *Apheloria corrugata*.



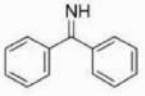
Reactions of Aldehydes and Ketones; Nucleophilic Addition to Carbonyl Groups

6. Addition of Nitrogen Nucleophiles





biochemical reaction

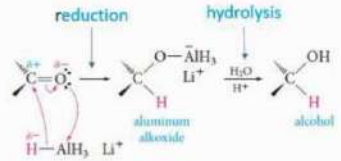


Benzophenone imine

Reactions of Aldehydes and Ketones

7. Reduction reaction

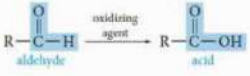
The most common metal hydrides used to reduce carbonyl compounds are lithium aluminum hydride ($LiAlH_4$) and sodium borohydride ($NaBH_4$).



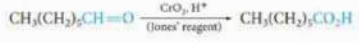
Because a carbon–carbon double bond is not readily attacked by nucleophiles, it remains intact during the course of the reaction.

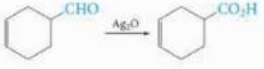
Reactions of Aldehydes and Ketones

8. Oxidation reaction

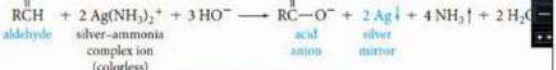


Because the reaction occurs easily, many oxidizing agents, such as $KMnO_4$, CrO_3, Ag_2O, and peracids (RCOOOH), will work.



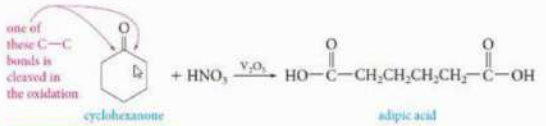


Tollens' silver mirror test: A laboratory test that distinguishes aldehydes from ketones takes advantage of their different ease of oxidation. In the this test, the silver–ammonia complex ion is reduced by aldehydes (but not by ketones) to metallic silver.*



Tollens' silver mirror test

Ketones also can be oxidized, but require special oxidizing conditions.



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Reactions of Aldehydes and Ketones

9. Aldol Condensation

Introduction to Aldol Condensation

A. Keto–Enol Tautomerism

Aldehydes and ketones may exist as an equilibrium mixture of two forms, called the **keto form** and the **enol form**. The two forms differ in the location of a proton and a double bond.

An α-hydrogen is attached to the α-carbon atom, the carbon atom adjacent to a carbonyl group.

This type of structural isomerism is called tautomerism (from the Greek *tauto*, the same, and *meros*, part). The two forms of the aldehyde or ketone are called **tautomers**.

Notice that tautomers are ***NOT*** resonance structures.

Tautomers of acetone.

Most simple aldehydes and ketones exist mainly in the keto form. Why?

keto form is more stable than the enol form because the C=O plus C-H bond energy present in the keto form is greater than the C=C plus O-H bond energy of the enol form.

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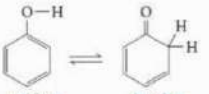
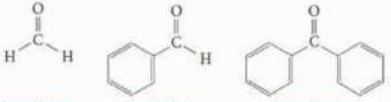
Some molecules, however, exist mainly in enol form—the *phenols*. *Why? The driving force for this phenomenon is the tendency of aromatic ring to keep its aromaticity by delocalization of electrons over its surface.*



enol form of phenol ⇌ keto form of phenol

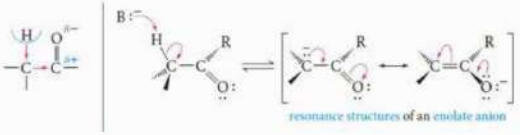
Aromatic system More stable	Non aromatic system Less stable

Carbonyl compounds that do not have an α-hydrogen cannot form enols and exist only in the keto form. Examples are



formaldehyde benzaldehyde benzophenone

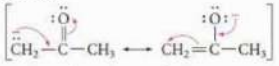
B. Acidity of α-Hydrogens; the Enolate Anion



resonance structures of an enolate anion

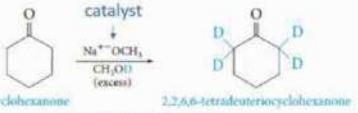
An enolate anion is formed by removal of the α-hydrogen of a ketone or aldehyde.

Example:



enolate anion of acetone

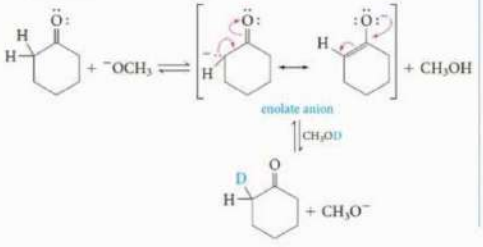
C. Nucleophilicity of Enolate Anions

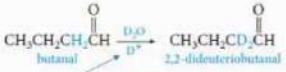


cyclohexanone — 2,2,6,6-tetradeuteriocyclohexanone

base catalyzed reaction

Mechanism

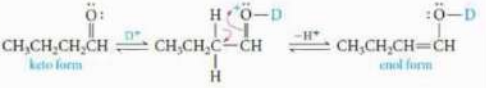




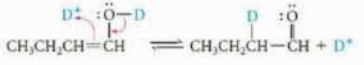
acid catalyzed reaction

Catalyst: it might be deuterated hydrochloric acid (DCl)

Mechanism



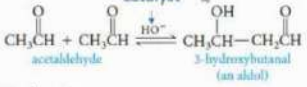
In the reversal of these equilibria, the enol then adds D^+ at the α-carbon.



Repetition of this sequence results in exchange of the other α-hydrogen.

Reactions of Aldehydes and Ketones

9. Aldol Condensation

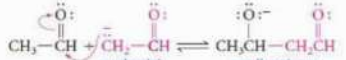


An enolate anion adds to the carbonyl group of an aldehyde or ketone in an **aldol condensation**. An **aldol** is a 3-hydroxyaldehyde or 3-hydroxyketone.

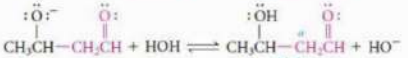
Mechanism

Step 1.

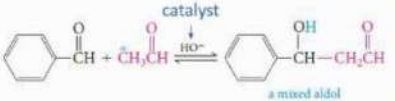
Step 2.



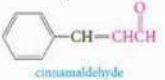
Step 3.



Mixed Aldol Condensation

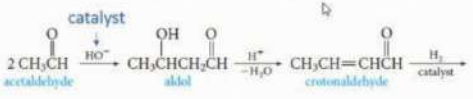


heat
$-H_2O$



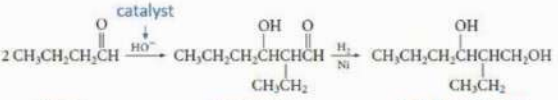
Commercial Syntheses via the Aldol Condensation

Aldols are useful in synthesis of many commercial organic compounds



acetaldehyde aldol crotonaldehyde

butanal 1-butanol

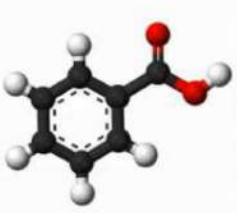


butanal butanal aldol 2-ethylhexane-1,3-diol

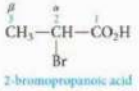
mosquito repellent

The aldol condensation is also used in nature to build up (and, in the case of *reverse* aldol condensations, to break down) carbon chains.

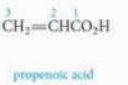
Chapter-10
Carboxylic Acids and Their Derivatives



Nomenclature of Acids

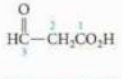


2-bromopropanoic acid
(α-bromopropionic acid)

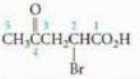


propenoic acid
(acrylic acid)

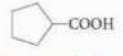
3-hydroxybutanoic acid
(β-hydroxybutyric acid)



3-oxopropanoic acid



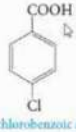
2-bromo-4-oxopentanoic acid



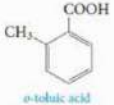
cyclopentanecarboxylic acid

trans-3-chlorocyclobutanecarboxylic acid

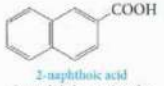
benzoic acid
(benzenecarboxylic acid)



p-chlorobenzoic acid
(4-chlorobenzenecarboxylic acid)



o-toluic acid
(2-methylbenzenecarboxylic acid)



2-naphthoic acid
(2-naphthalenecarboxylic acid)

butanedioic acid

butynedioic acid

maleic acid
(*cis*-2-butenedioic acid)

and

fumaric acid
(*trans*-2-butenedioic acid)

an acyl group

formyl
(methanoyl)

acetyl
(ethanoyl)

propanoyl

benzoyl

phthalic acid

isophthalic acid

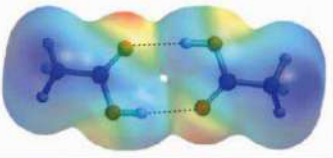
terephthalic acid

Physical Properties of Acids

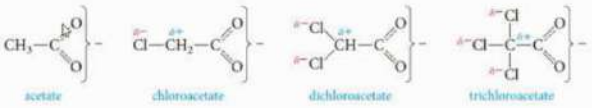
Table 10.3 Physical Properties of Some Carboxylic Acids

Name	bp, °C	mp, °C	Solubility, g/100 g H_2O at 25°C
formic acid	101	8	miscible (∞)
acetic acid	118	17	
propanoic acid	141	−22	
butanoic acid	164	−8	
hexanoic acid	205	−1.5	1.0
octanoic acid	240	17	0.06
decanoic acid	270	31	0.01
benzoic acid	249	122	0.4 (but 6.8 at 95°C)

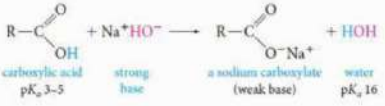
Hydrogen bonding



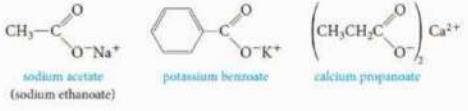
Effect of Structure on Acidity; the Inductive Effect



Conversion of Acids to Salts



Naming of carboxylates

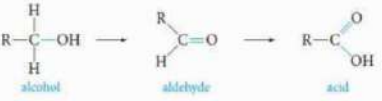


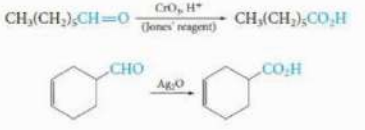
5

Preparation of Acids

1. Oxidation of Primary Alcohols and Aldehydes

The most commonly used oxidizing agents for these purposes are potassium per manganate ($KMnO_4$), chromic acid anhydride (CrO_3), nitric acid (HNO_3), and, with aldehydes only, silver oxide (Ag_2O).

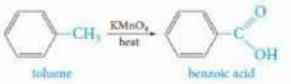




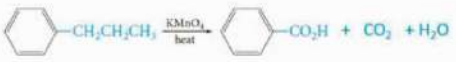
6

Preparation of Acids

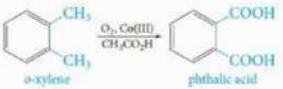
2. Oxidation of Aromatic Side Chains



toluene benzoic acid



p-xylene terephthalic acid

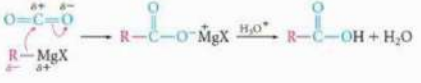


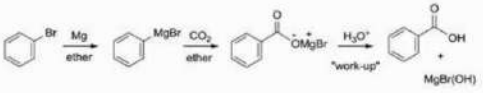
o-xylene phthalic acid

If no C—H bond is in the benzylic position, however, the aromatic ring is oxidized, although only under severe reaction conditions.

Preparation of Acids

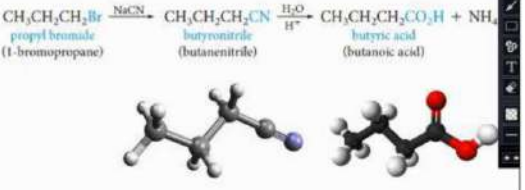
Reaction of Grignard Reagents with Carbon Dioxide



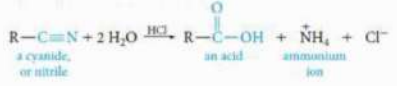


Preparation of Acids

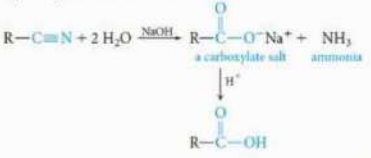
Hydrolysis of Cyanides (Nitriles)



Hydrolysis is acidic media

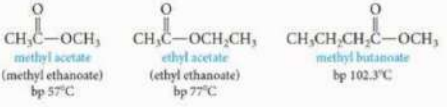


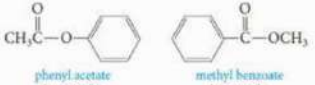
Hydrolysis is basic media



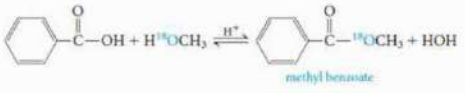
Carboxylic Acid Derivatives

Esters



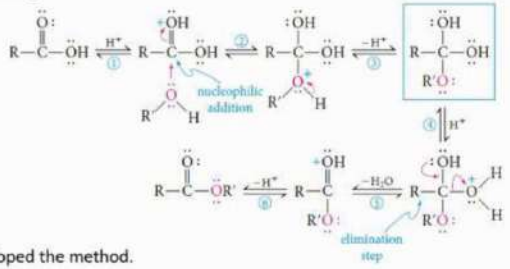


Preparation of Esters; Fischer* Esterification



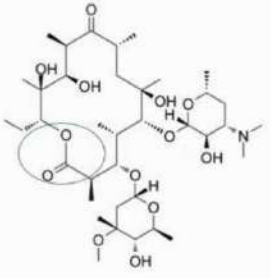
Nucleophilic acyl substitution is substitution of another group for the —OH group of a carboxylic acid.

Mechanism; isotopic labeling



* The scientist who developed the method.

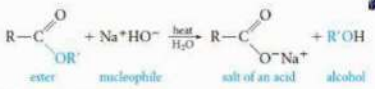
Lactones (cyclic esters)



antibiotic

Saponification of Esters

This type of reaction is used to make soaps from fats. That is why it is called saponification of esters.

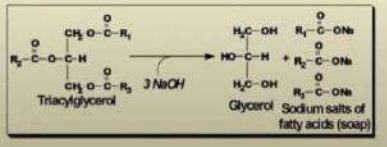


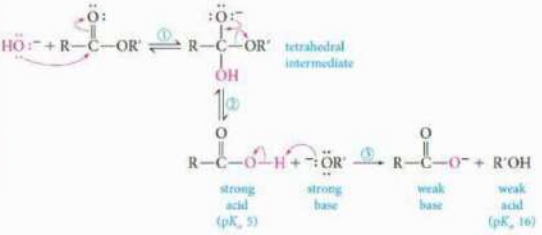
Nucleophilic acyl substitution is substitution of another group for the —OH group of a carboxylic acid.

Saponification is the hydrolysis of an ester with a base.

Saponification

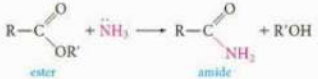
Alkaline hydrolysis produces glycerol and salts of fatty acids (soaps). Soaps cause emulsification of oily material this help easy washing of the fatty materials.



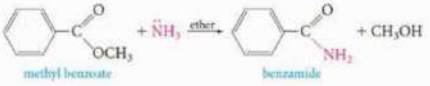


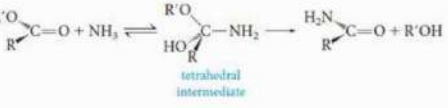
Ammonolysis of Esters

Ammonia converts esters to amides.

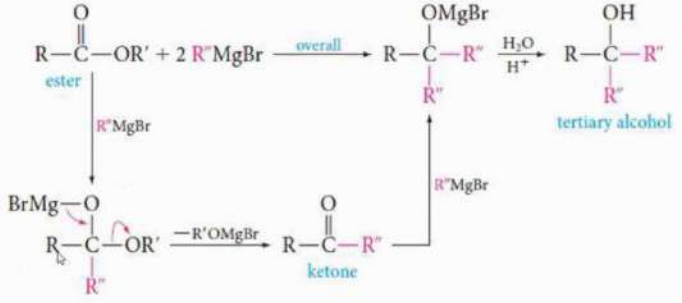


For example,

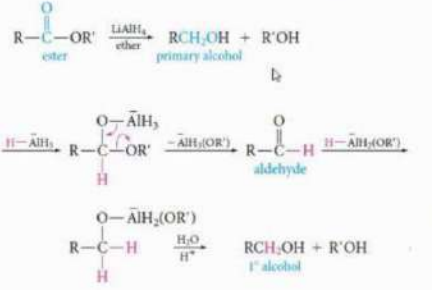


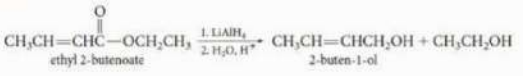


Reaction of Esters with Grignard Reagents



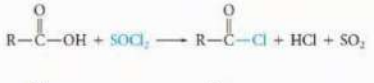
Reduction of Esters

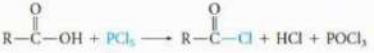




Acyl Halides

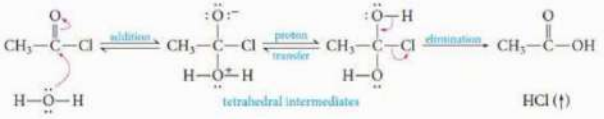
Synthesis





Reactions

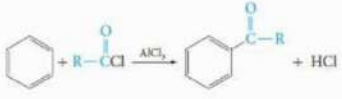
Hydrolyzed by water



Acyl halides react rapidly with alcohols to form esters.

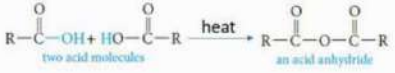
Acyl halides react rapidly with ammonia to form amides.

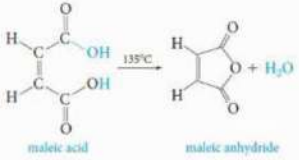
Acyl halides are used to synthesize aromatic ketones, through Friedel–Crafts acylation of aromatic rings

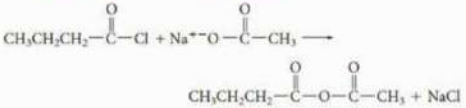


Acid Anhydrides

Synthesis



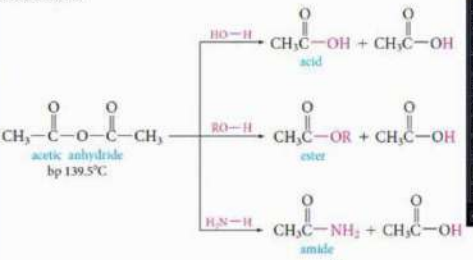


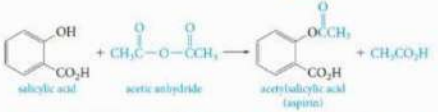


butanoic ethanoic anhydride

Mixed anhydrides are prepared from two different carboxylic acids.

Reactions

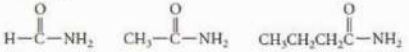


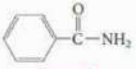


analgesic and antipyretic drug

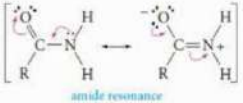
Amides

Naming



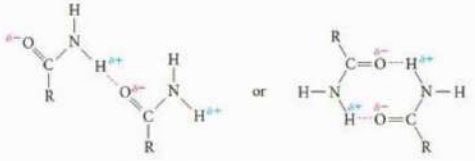


Resonance structures



amide resonance

H-bonding



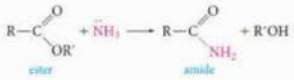
Amides are highly polar and form strong hydrogen bonds.

Physical properties

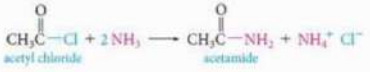
Alkyl substitution on the nitrogen lowers the boiling and melting points by decreasing the hydrogen-bonding possibilities

Synthesis of amides

Ammonia converts esters to amides.

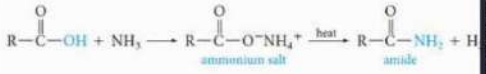


Acyl halides react rapidly with ammonia to form amides.



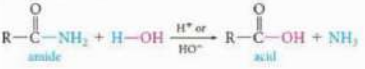
Ammonia reacts with acid anhydrides to from amides.

Amides can also be prepared by heating the ammonium salts of acids.

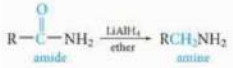


Reactions of amides

Hydrolysis by water



Reduction reaction

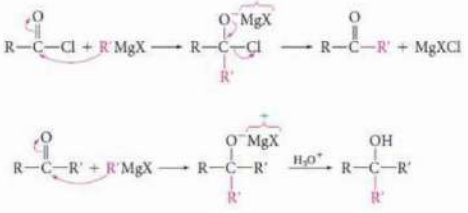


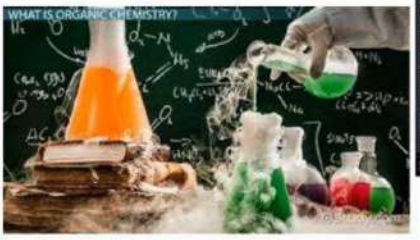
Urea is a special amide, a diamide of carbonic acid. A colorless, water-soluble, crystalline solid, urea is the normal end product of protein metabolism. An average adult excretes approximately 30 g of urea in his or her urine daily. Urea is produced commercially from carbon dioxide and ammonia, mainly for use as a fertilizer.

Definition

A blood urea nitrogen (BUN) test analyzes the level of urea through the detection of the nitrogen within the esolecule. High levels of urea within the blood can be a sign that certain body systems are not functioning properly, especially the kidneys.

Prediction new nucleophilic acyl substitution reactions

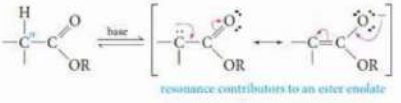




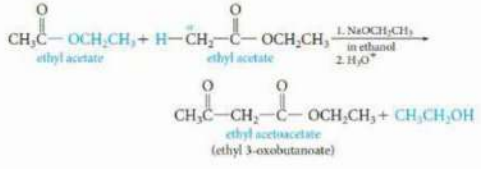
The α-Hydrogen of Esters; the Claisen Condensation

Is a reaction by which two esters molecules are condensed. It resembles the aldol condensation of aldehydes and ketones.

The α-hydrogens of an ester are weakly acidic and can be removed by a *strong base*. The product is an **ester enolate**.



An **ester enolate** is the anion formed by removing the α-hydrogen of an ester.



Mechanism of Claisen Condensation

The Claisen condensation takes place in three steps.

Step 1. $CH_3C(=O)OCH_2CH_3 + Na^+ {}^-OCH_2CH_3 \rightleftharpoons$

sodium ethoxide

$Na^+ {}^-CH_2C(=O)OCH_2CH_3 + CH_3CH_2OH$

ester enolate

Step 2. $CH_3C(=O)OCH_2CH_3 + {}^-CH_2C(=O)OCH_2CH_3 \rightleftharpoons$

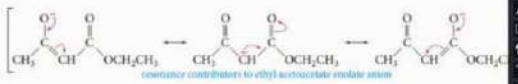
$CH_3C(O^-)(OCH_2CH_3)CH_2C(=O)OCH_2CH_3 \rightleftharpoons CH_3C(=O)CH_2C(=O)OCH_2CH_3 + {}^-OCH_2CH_3$

β-keto ester

Step 3. $CH_3C(=O)CH_2C(=O)OCH_2CH_3 + {}^-OCH_2CH_3 \longrightarrow$

$CH_3C(=O)\bar{C}HC(=O)OCH_2CH_3 + CH_3CH_2OH$

enolate ion of a β-keto ester



resonance contributors to ethyl acetoacetate enolate anion

To complete the Claisen condensation, the solution is acidified, to regenerate the β-keto ester from its enolate anion.

Claisen Condensation as synthetic tool

$2\,CH_3C(=O)OCH_2CH_3 \xrightarrow[NaOCH_2CH_3]{\text{Claisen}} CH_3C(=O)CH_2C(=O)OCH_2CH_3 \xrightarrow{NaBH_4} CH_3CH(OH)CH_2C(=O)OCH_2CH_3 \xrightarrow[-H_2O]{H^+}$

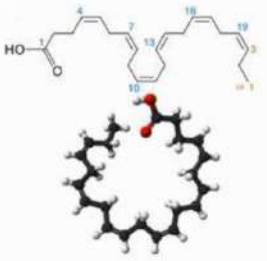
ethyl acetate — ethyl acetoacetate — ethyl 3-hydroxybutanoate

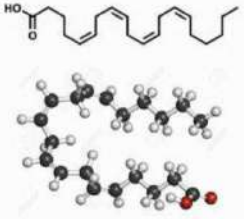
$CH_3CH{=}CHC(=O)OCH_2CH_3 \xrightarrow[Pt]{H_2} CH_3CH_2CH_2C(=O)OCH_2CH_3$

ethyl 2-butenoate — ethyl butanoate

In this way, the acetate chain is lengthened by two carbon atoms. Nature makes use of a similar process, catalyzed by various enzymes, to construct the long-chain carboxylic acids that are components of fats and oils.

Both omega-3 and omega-6 fatty acids help maintain healthy skin.





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Prof. Dr. Hussein Alhendawi

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