

ORGANIC CHEMISTRY

I. OVERVIEW

- **Organic Chemistry:** the study of organic compounds
→ Contains (C, H, O, N, P, S, X (F, Cl, Br, I))

Carbon Properties

- **Catenation:** ability to form chains
- **Isomerism:** two or more compounds with the same molecular formula but different structure
- **Stability:** following the octet rule
- **Hybridization:** mixing of 2 or more non-equivalent atomic orbitals to form a new set of equivalent or *degenerate* hybrid orbitals
→ E.g., sp^3 , sp^2 , sp
→ There are 3 main groups of geometries of organic molecules

Geometries of Organic Compounds

- **sp^3 /tetrahedral shape**
→ configuration of alkanes
- **sp^2 /trigonal planar shape**
→ configuration of alkenes
- **sp /linear shape**
→ configuration of alkynes

II. CLASSIFICATION OF ORGANIC COMPOUNDS

Hydrocarbons

Aliphatic Hydrocarbons

- **Saturated:** usually alkanes
→ Contains only single bonds
- **Unsaturated:** alkenes (double bonds), alkynes (triple bonds)
- **Cyclic alkanes:** occurs when electrons are removed and the structure connects to itself, instead of forming terminal ends

Aromatic Hydrocarbons

- Also known as polyaromatic hydrocarbons or arenes
- Prototype: benzene
- Most are polycyclic benzenoids/polyaromatic HC
→ Benzene rings that are fused together
→ Examples: benzene, naphthalene, anthracene
- Benzo[α]pyrene undergoing phase I (functionalization) → diol epoxide derivatives or BPDE (carcinogenic component) → generate free radicals

- From automobile exhaust, charcoal, tar in cigarettes
- NTK: Breast cancer is not smoking-dependent

Hydrocarbon Derivatives

Halogen-containing

- Alkyl halides (H-X)
- Aryl halides (Ar-X)
- Examples:
→ Propellants in aerosols (CFCs)
→ Insecticides (DDT)
→ Non-stick pans (Teflon)

Sulfur-containing

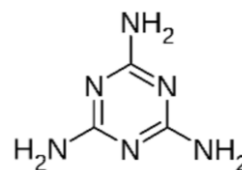
- **Thiols** (R-SH)
→ Analog of alcohols
 - Cysteine
→ Odor of flatulence, garlic odor, "rotten egg" odor
- **Thioethers** (R-S-R)
→ Methionine

Phosphorus-containing

- **Phosphates**
→ ATP, Glucose-6-phosphate
- **Organophosphates**
→ Pesticides: Malathion, Parathion
→ Nerve agents: Sarin, Tabun, Soman

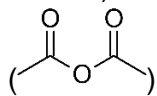
Nitrogen-containing

- Amines ($-NH_2$)
- Nitriles ($R-C\equiv N$) – cyano
- Nitro ($R-NO_2$)
- Heterocyclic nitrogen compounds
→ Pyrimidine, Purine, Alkaloids
→ Melamine
 - Adulterant in milk
 - "as high apparent protein content"
 - Total N-content measured by Kjeldahl method



- Melaware – polymerized melamine
 - Causes kidney stones or renal failure in babies

Oxygen-containing

- Alcohols/phenols (ROH and ArOH) - Hydroxyl
- Ethers (R-O-R) - Alkoxy
- Aldehydes and ketones (RCHO and RCOR) - Carbonyl
- Carboxylic acids (COOH) - Carboxyl
- Carboxylic derivatives
 - Esters (RCOOR)
 - Amides (RCONH₂)
- Anhydride 
- Acyl halides (RC=O X)

III. ISOMERISM

- Existence of two or more compounds of the same molecular formula but different structures
- Differences are based on:
 - Order of bonding
 - Spatial orientation
 - Arrangement of atoms in space
 - NTK: Racemic mixtures involve atoms of equal quantity of S & R isomers
 - Some isomers are more active
 - 40 mg of (S)-isomer omeprazole was discovered to be more potent than 40 mg of omeprazole

Classification of Isomers

- Structural or Constitutional isomers
 - Chain
 - Position of substituents
 - Functional
- Stereoisomers
 - Geometric (cis/trans) - substituents containing double bonds
 - Conformational
 - Optical or configurational (using polarimeter for determination)

Structural Isomers

Chain Isomers

- Branching exhibited, also in the ability to form chains
 - C_NH_(2N+2)
 - Ex. C₄H₁₀ - CH₃CH₂CH₂CH₃
 - Based on the formula, it can be n-butane if straight chain
 - Can be isobutane or 2-methyl propane if one of the methyl groups is placed or connected to C-2, making the structure symmetrical (iso)

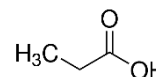
- NTK: Naming of the longest alkane chain (parent chain)
 - Place "n-" prefix if normal/straight chain

Position Isomers

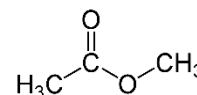
- Differences in the position of a multiple bond
 - Ex. C₄H₈ - alkene w/ 1 double bond
 - Can be named as:
 - 1-butene (CH₂=CHCH₂CH₃)
 - 2-butene (CH₃CH=CHCH₃)
- Differences in the position of a substituent of a functional group
 - Ex. C₃H₇Br
 - Can be named as:
 - 1-bromopropane
 - 2-bromopropane
- Disubstituted benzenes
 - Occurs in positions:
 - Ortho- (1,2-)
 - Meta- (1,3-)
 - Para- (1,4-)

Functional Isomers

- Similarities in molecular formula but difference in functional group formed
- Examples:
 - Alcohols and ethers as functional isomers
 - C₂H₆O can be:
 - Ethanol (CH₃CH₂OH)
 - Methyl ether (CH₃OCH₃)
 - Aldehydes and ketones as functional isomers
 - C₃H₆O can be:
 - Propanal
 - Propanone/ acetone
 - Carboxylic acids and esters as functional isomers
 - C₃H₆O₂ can be:
 - Propanoic acid



- Methyl ethanoate or methyl acetate



Index of Hydrogen Deficiency (IHD)

$$IHD = \frac{2C + 2 - H - X + N}{2}$$

IHD = 0 → saturated

IHD = 1 → double bond or cyclic

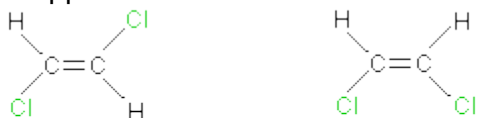
IHD = 2 → triple bond

- Benzene: IHD = 4

Stereoisomers

Geometric Isomers

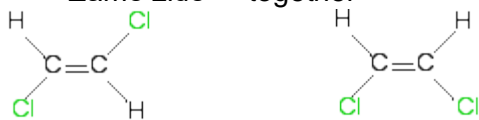
- Occurs in:
 - Double bonds
 - Cyclic structures
- Types of Geometric Isomers
 - Cis/trans isomerism – disubstituted alkene; same substituents
 - Cis = functional groups are on the same side
 - Trans = functional groups are on the opposite side



trans-1,2-dichloroethene

cis-1,2-dichloroethene

- E/Z isomerism – tri-/tetra-substituted alkenes; same priority
 - E = “entgegen”
 - ✱ “KEbElaan” – opposite side
 - Z = “zusammen”
 - ✱ “Zame zide” – together



(E)-1,2-dichloroethene

(Z)-1,2-dichloroethene

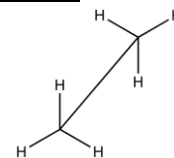
- Prioritization according to the Cahn-Ingold-Prelog Sequence
 - ↑ atomic # → ↑ priority

Conformational Isomers

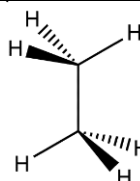
- Results from the different ways an atom can flex and bend due to:
 - Rotation along a single bond
 - Occurs in acyclic and open chain
 - Ex. Ethane (CH₃CH₃)
 - Ring flipping
 - Occurs in cyclic structures
 - Ring strain from angle strain and torsional strain
- Factors affecting rotation and stability**
 - Torsional energy (TE)
 - Energy needed to resist a conformation
 - ↑ TE → ↓ stability
 - TE of eclipsed > TE of staggered
 - Steric effect / “crowding”
 - Bulky groups
 - Crowding = ↓ stability

- Graphical Representations of Conformational Isomers

→ Saw horse formula

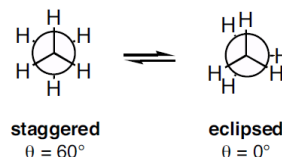


→ Perspective (dash and wedge) formula

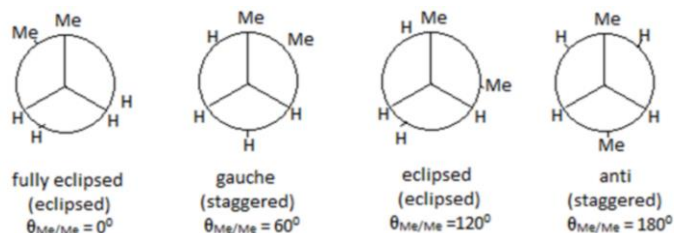


→ Newman projection formula

- Eclipsed
- Staggered – more stable



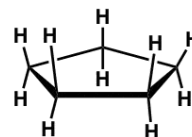
- Conformation of butane
 - Stability: anti > gauche > E₂ > E₁



- Factors affecting ring strains

- Angle strain
- Torsional strain
- Examples

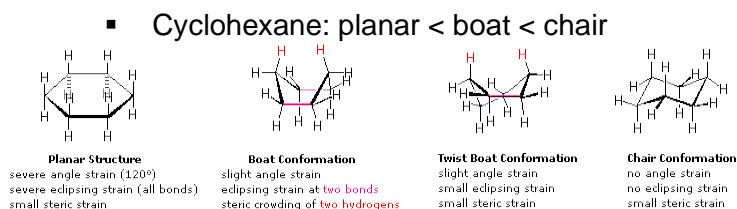
- Cyclobutane: planar < butterfly (less strain)
- Cyclopentane: planar < envelope



"Flat" cyclopentane



"Envelope" cyclopentane



Optical Isomers

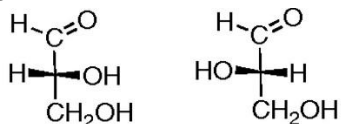
- Optical activity: ability of a compound to rotate a plane-polarized light either to the right or to the left
 - Uses a polarimeter
- Structural requirement for optical activity
 - Chiral center/ stereogenic C – carbon with 4 different groups or substituents
 - No symmetry element
- Dextrorotatory** = d/(+); to the right
- Levorotatory** = l/(-); to the left
- Types

	Forms mirror images?	Super-imposable?
Enantiomers	Yes	No
Diastereomers	No	No
Mesocompounds - same compounds - optically inactive (since these are symmetrical)	Yes	Yes

Two Systems to Designate Configuration

→ D & L system

- Common in biochemistry especially in sugar and amino acids
- Orientation of hydroxyl (-OH) at chiral center



D-Glyceraldehyde

L-Glyceraldehyde

→ R & S system

- R/rectus – right (clockwise)
- L/sinister – left (counterclockwise)

Determination of R, S through Cahn-Ingold-Prelog Sequence



→ Examine the atoms attached to the central carbon. Prioritize these atoms according to atomic number.

- Hydrogen is the lowest possible priority substituent and must be placed at the back
- Draw an arrow from the highest priority to the second and then the third priority substituents

- In a structure, a counterclockwise direction, the configuration at stereocenter is considered S ("Sinister" → Latin= "left").
- If, however, the arrow points clockwise then the stereocenter is labeled R ("Rectus" → Latin= "right").

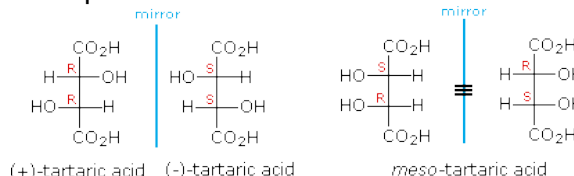
• NTK:

- Wedges indicate coming towards the viewer.
- Dashes indicate pointing away from the viewer.

• Racemic mixture

- Equal amount/ concentration of R & S or d & l isomers
- Optically inactive
- Examples of isomers which produce difference side effects:
 - R-thalidomide → sedative, hypnotic
 - S-thalidomide → teratogenic (i.e. Phocomelia, Amelia)

• Example: Tartaric acid



→ From L-R: I, II, III, IV

- Mesocompounds: III and IV
- Diastereoisomers: II and III
- Stereoisomers: I and II

IV. HC: ALIPHATIC

Alkanes, Alkenes, and Alkynes

Alkanes	Alkenes	Alkynes
$C_nH_{(2n+2)}$	$C_nH_{(2n)}$	$C_nH_{(2n-2)}$
Saturated hydrocarbons	Unsaturated hydrocarbons	Unsaturated hydrocarbons
Single bond (sp^3)	Double bonds (sp^2)	Triple bonds (sp)
Reactions are essentially inert	Most reactive among the three	
Aka Paraffins	Aka Olefins	
Suffix = "+ane"	Suffix = "+ene"	Suffix = "+yne"
IUPAC naming: Root word + "-ane"	IUPAC naming: Position of the double bond + root word + "-ene"	IUPAC naming: Position of the triple bond + root word + "-yne"

- # of carbons and root word
 - 1 – meth-
 - 2 – eth-
 - 3 – para-
 - 4 – but-
 - 5 – pent-

Chemical Reactions

Alkanes

- Essentially inert under most conditions
- Types
 - Displacement
 - Addition
 - Elimination
 - Rearrangement
 - Reduction-oxidation
- Combustion**
 - Redox reaction
 - $C_nH_{2n+2} \xrightarrow{\text{complete}} CO_2(g) + H_2O(l)$
 - $C_nH_{2n+2} \xrightarrow{\text{incomplete}} CO_2 + H_2O + CO + C \text{ (soot)}$
 - Will be based on the present O_2 supply
- Halogenation**
 - Free radical substitution
 - $CH_3CH_3 + X_2(Cl_2 \text{ or } Br_2) \xrightarrow{UV \text{ or } \Delta} CH_3CH_2X + HX$
(alkyl halide)
 - Example:
 - $CH_4 + Cl_2 \xrightarrow{UV \text{ or } \Delta} CH_3Cl + HCl$
 - Will also form and proceed to other products (usually low due to the concept of limiting reagents)
 - CH_2Cl_2
 - $CHCl_3$
 - CCl_4

REVIEW: Chain Reaction Mechanism

- Chain initiation** – free radical formation (unpaired electrons) through homolytic cleavage
 - $Cl_2 \xrightarrow{UV} 2Cl$
- Chain propagation**
 - $CH_4 + Cl \rightarrow CH_3 + HCl$
 - $CH_3Cl_2 \rightarrow CH_3Cl + Cl$
 - $CH_4 + Cl_2 \rightarrow CH_3Cl + HCl$
- Chain termination**
 - $2Cl \rightarrow Cl_2$
 - $CH_3 + Cl \rightarrow CH_3Cl$
 - $CH_3 + CH_3 \rightarrow CH_3 - CH_3$

Alkenes

- More reactive due to more diffused electrons
 - Greater instance of reactivity
- Addition of Hydrogen: Catalytic Hydrogenation
- Principle involved: electrophilic addition reaction

REVIEW: Types of Organic Reagents

- Electrophiles (E^+)**
 - Electro-loving
 - Electron pair acceptor
 - (+) reagents
- Nucleophiles (Nu^-)**
 - Electron-rich
 - Electron pair donor
 - (-) reagents

REVIEW: Markonikov's Rule

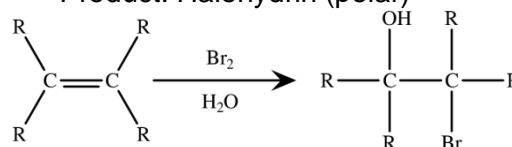
- H adds to carbon with greater # of H substituents (less substituted carbon)
- X adds to carbon with lesser # of H substituents (more substituted carbon)
 - Based on stability of carbonation intermediate

Alkenes: Electrophilic Addition Reaction

- Addition of Halogen: Halogenation**
 - Reagent: $X_2 + CHCl_3$ or CCl_4
 - Product: Alkyl halide vicinal (nonpolar)

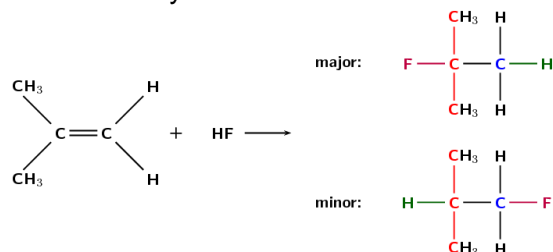


- Reagent: $X_2 + H_2O$
 - Product: Halohydrin (polar)



- Addition of Hydrohalogen (HX): Hydrohalogenation

→ Product: Alkyl halide

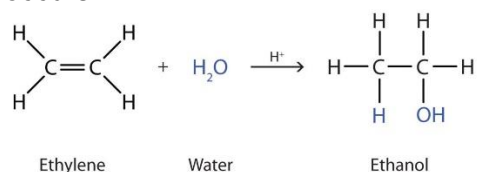


- Hydration

→ Addition of water (as a nucleophile)

→ Initially no reaction

- But upon exposure to acid, reaction occurs



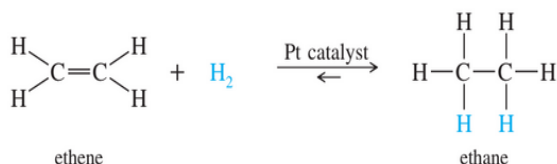
Alkenes: Reduction-Oxidation

- Reduction

→ Removal of O₂ or addition of H

→ Hydrogenation

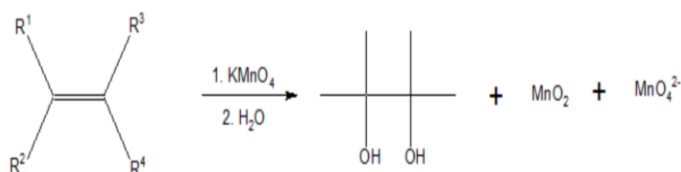
- Used in the production of margarine
 - Fixed oils and unsaturated FAs will produce saturated FAs (solid form) upon exposure to an acidic environment



- Oxidation

→ Hydroxylation

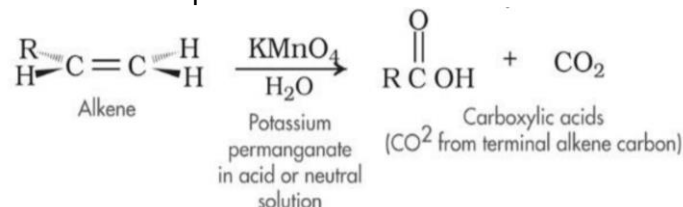
- Formation of "glycol" + brown precipitate (MnO₂) in basic/neutral condition
- Also called vicinal diol
- Must occur in basic environment and cold temperatures
- Alternative catalyst: Osmium tetroxide
- Principle behind Bayer's test for unsaturation (VR: brown precipitate)



→ Oxidative Cleavage

- If performed in acidic condition

- Results to a colorless solution (from the products, Mn ions)
- Products of alkene + MnO₄
 - If there is CH₂ = CO₂ will be produced
 - If there is RCH = RCHOH will be produced
 - If there is RCHR = RR'CO will be produced



Alkynes

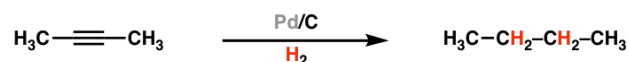
- Via electrophilic addition reactions

→ Since alkynes are electron rich (1 □, 2 □ bonds),

- Reduction to alkenes

→ A continuous reaction that proceeds to forming alkanes

- In the presence of an acid environment
- Catalysts: Pd, Pt, Ni

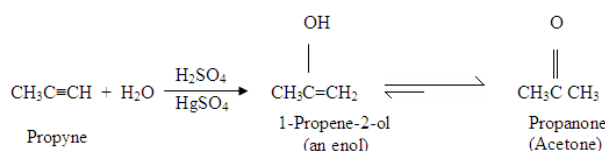


→ If only the alkene form is desired, used Lindlar's reagent as the catalyst

- Electrophilic addition

→ Hydration

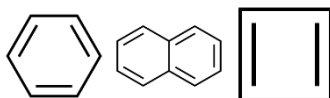
- Addition of H₂O with H₃O⁺ medium and HgSO₄ as the catalyst
- Product: Enol, but will undergo rearrangement called "Keto-enol Tautomerism"



V. HC: AROMATIC

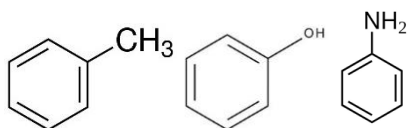
Aromaticity

- Benzene and its derivatives
- Criteria for aromaticity:
 - Cyclic
 - Flat or planar – sp^2 hybridization (trigonal planar)
 - Conjugated alternating double bonds
 - Follows Huckel's Rule
 - $4n + 2$ = number of π electrons (where $n = 0, 1, 2, 3$, any integer)
- Examples (from L-R): **benzene** (6 π e-s), **naphthalene** (10 π e-s), **cyclobutadiene** (anti-aromatic compound following "4n rule")



IUPAC Nomenclature

- Substituted substitute + benzene
- Examples (from L-R): **methylbenzene** (toluene), **hydroxybenzene** (phenol), **aminobenzene** (aniline)

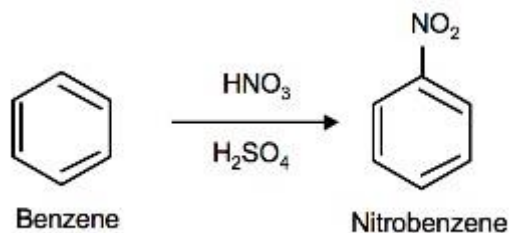


Chemical Reactions

- Principal Involved: Electrophilic Aromatic Substitution

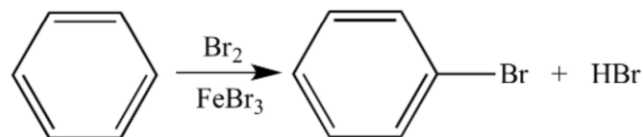
Nitration

- Reagents: concentrated HNO_3 + concentrated H_2SO_4
- Electrophile: NO_2^+ (nitronium ion)
- Product: nitrobenzene



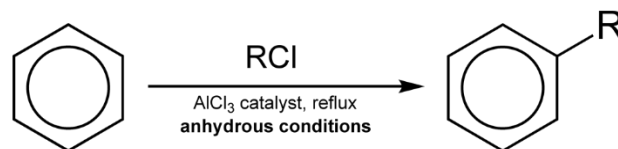
Halogenation

- Reagents: X_2 (Cl_2 , Br_2) + FeX_3 ($FeCl_3/FeBr_3$) as a Lewis acid catalyst
- Electrophile: X^+ (halonium ion)
- Product: acyl halide (such as bromobenzene or chlorobenzene)



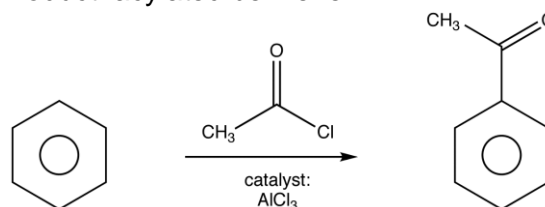
Friedel-Craft's Alkylation

- Reagents: $R-Cl$ + $AlCl_3$ as a Lewis acid catalyst
- Electrophile: R^+ (carbonium ion or carbocation or carbonium ion)
- Product: alkylated benzene



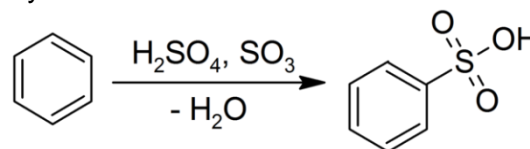
Friedel-Craft's Acylation

- Reagents: $R-C(=O)Cl$ (acid-Cl) + $AlCl_3$ as a Lewis acid catalyst
- Electrophile: $R-C^+=O$ (acylium ion)
- Product: acylated benzene



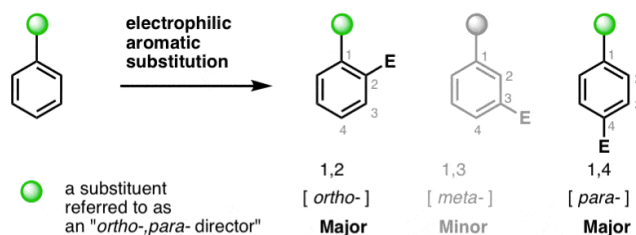
Sulfation

- Reagents: SO_3 + concentrated H_2SO_4 (fuming sulfuric acid)
- Electrophile: sulfonium ion
- Product: acylated benzene
- Only reversible reaction

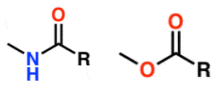


Effects of Substituents

Pattern 1: *ortho*- and *para*- products are major; *meta* product is minor



- Ortho- and Para-directing Activators
 - Strongly activating: -OH, -OR, -NH₂, -NHR, -NR₂



- Moderately activating:
 - Weakly activating: -R, -benzene, -CH=CH₂
- Meta-directing Deactivators
 - Strongly deactivating: -NO₂, -NR₃, -SO₃H, -CN
 - Moderately deactivating: -CHO, -COR, -COOH, -COX
- Ortho- and Para-directing Deactivators
 - Weakly deactivating: halogens (F, Cl, Br, I)

VI. HC DERIVATIVES: ALCOHOLS

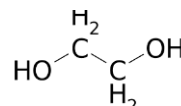
- Functional group: -OH, -COH (carbinol)

IUPAC Nomenclature

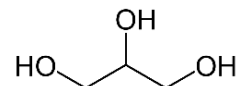
- Position of -OH + root word + -ol
- Examples:
 - CH₃OH – methanol
 - CH₃CH₂OH – ethanol
 - CH₃CH₂CH₂OH – 1-propanol

Classification

- **Based on number of R groups attached to C-OH**
 - Primary alcohol – 1 R group
 - Ethanol
 - Secondary alcohol – 2 R groups
 - Isopropyl alcohol
 - Tertiary alcohol – 3 R groups
 - 2-methyl-2-propanol or tertbutyl alcohol
- **Based on number of OH groups**
 - Monohydric – 1 -OH group
 - Dihydric – 2 -OH groups
 - Example: ethylene glycol or 1,2-ethanediol



- Trihydric – 3 -OH groups
 - Example: glycerol/glycerin or 1,2,3-propanetriol



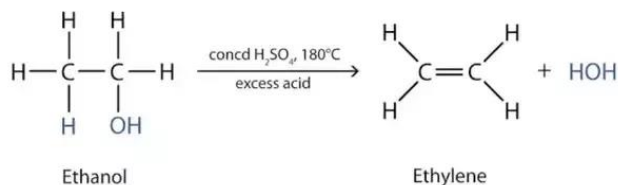
- Polyhydric (such as carbohydrates – glucose, fructose, galactose)

Chemical Reactions

- Principal Involved: Electrophilic Aromatic Substitution

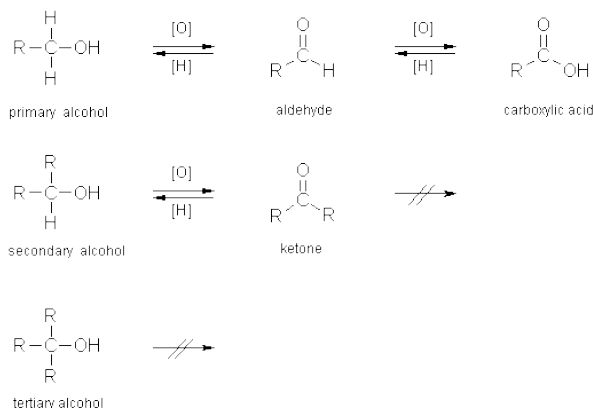
Dehydration

- Removal of H₂O
- Principle: elimination



Oxidation

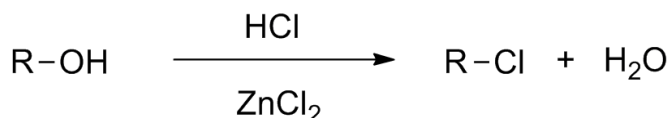
- Oxidizing agent: K₂Cr₂O₇
- Tertiary alcohol has no hydrogen on the carbon atom → no reaction



Qualitative Tests

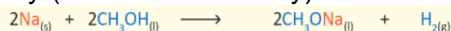
Lucas Test

- Test to differentiate alcohols
- Reagent: concentrated HCl + ZnCl₂
- Visible result: formation of immiscible layer (non-polar alkyl halide)
- Reactivity: tertiary > secondary > primary > CH₃OH



Reaction with Active Metals (Na)

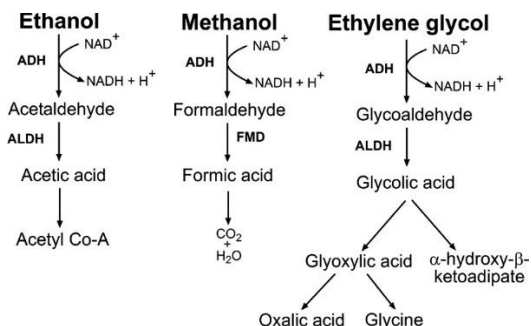
- Principle involved: electrophilic substitution
- Visible result: bubble formation (H₂)
- Reactivity: methanol > primary > secondary > tertiary (not much reactivity)



REVIEW: Common Names of Alcohols

- Methanol – wood alcohol
- Ethanol – grain alcohol
- Isopropyl – rubbing alcohol
- Ethylene glycol – “antifreeze” humectant

Clinical Correlates



Ethanol

- Acetaldehyde produces the “hangover effect”
- Disulfiram inhibits aldehyde dehydrogenase

Methanol

- Accumulation of formic acid or methanoic acid can lead to metabolic acidosis and destroys the optic nerve (blindness)
- Treatment
 - 50% ethanol (as competitive inhibitor)
 - Fomepizole (inhibits alcohol dehydrogenase)
 - NaHCO₃ (treatment of metabolic acidosis and reversal of damage to the optic nerve)
 - Hemodialysis (as last resort)

Ethylene Glycol

- Oxalic acid chelates with Ca²⁺ precipitating CaC₂O₄ → nephrotoxicity

VII. HC DERIVATIVES: ETHERS

- Functional group: alkoxy substituents
- Properties
 - Relatively inert
 - Good organic solvents
 - Highly flammable with low flash points
- Examples:
 - Monobenzene – depigmenting agent
 - Eugenol – active components in clove and oil (Zn-eugenol cement)

Classification

Open-Chain Ethers

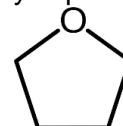
- Symmetrical – same R groups
 - Dimethylether (methoxymethane) CH₃OCH₃
 - Diethylether (ethoxyethane as inhalational anesthetic) CH₃CH₂OCH₂CH₃
- Mixes ethers – different R groups
 - Ethylmethyl ether (methoxyethane) CH₃OCH₂CH₃

Cyclic Ethers

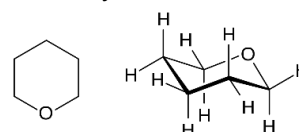
- Epoxides/ oxyranes/ oxycyclopropanes
 - Ether oxygen is a part of a 3-membered ring system
 - Ethylene oxide as gas sterilant (MOA: alkylation)

With More than 3 members

- Furanose or oxacyclopentane



- Pyranose or oxacyclohexane



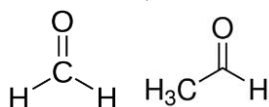
VIII. HC DERIVATIVES: ALDEHYDES AND KETONES

- Functional group: carbonyl

Classification

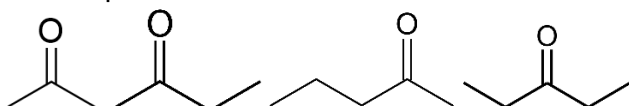
Aldehyde

- RCHO with terminal carbonyl group
- Suffix: -al
- Examples (from L-R)
 - Methanal or formaldehyde
 - Ethanal or acetaldehyde



Ketone

- Nonterminal carbonyl group
- Suffix: -one
- Examples (from L-R)
 - Propanone (acetone)
 - Butanone
 - 2-pentanone
 - 3-pentanone

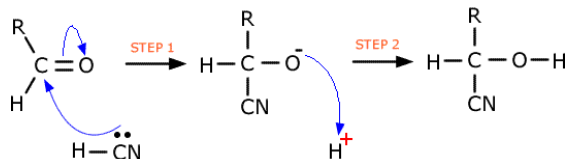


Chemical Reactions

- Principal Involved: Nucleophilic acyl addition

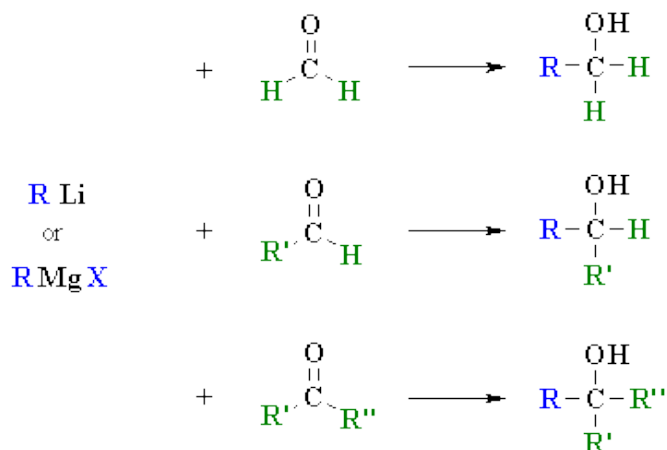
Reaction with HCN

- Product: cyclohydrin (precursor of amino acids)



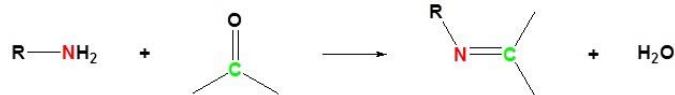
Reaction with Grignard Reagent (RMgX)

- Nucleophile: R⁽⁻⁾ carbanion
- Product: alcohol

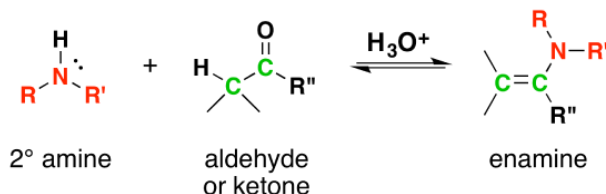


Reaction with Amines

- Involves elimination of water
- With primary amines → imines



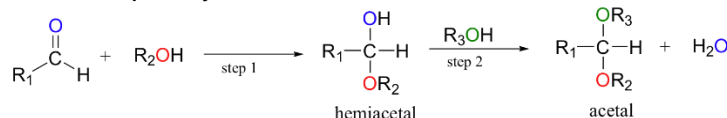
- With secondary amines → enamines



- With tertiary amines → no reaction

Reaction with Alcohols

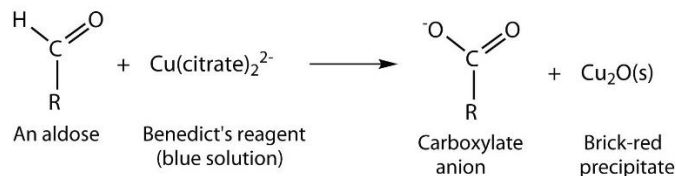
- Hemiacetal/hemiketal and acetal/ketal formation
- Example: cyclization of monosaccharides



Qualitative Tests

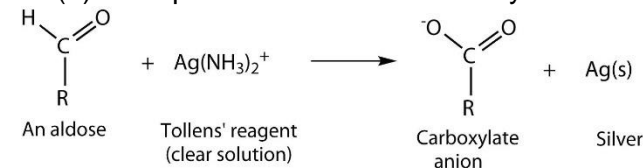
Benedict's Test

- Test for reducing sugar
- (+) for aliphatic aldehydes and alpha-hydroxy-ketones only



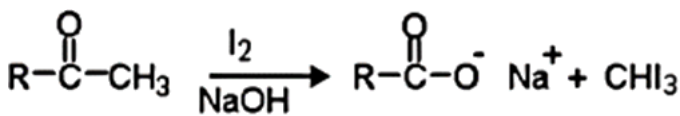
Tollen's Test/Silver Mirror Test

- Test to distinguish aldehydes and ketones
- Tollen's reagent ammoniacal silver nitrate
- (+) for aliphatic and aromatic aldehydes



Iodoform Test

- Reaction of I₂ and KI
- Test for presence of methylketone



Examples

Aldehydes

- Formaldehyde/formalin: embalming fluid through polymerization of tissues
→ Poison: hardening of tissues
→ Antidote: ammonia (converts formalin to methanamine)
- Benzaldehyde: "oil of bitter almond" as flavoring agent
- Vanillin: flavoring agent
- Retinal: from retinaldehyde as visual pigment
- Chloral hydrate: "KO" drug; precursor of insecticide (DDT)

Ketones

- Acetone: semi-polar for nail polish remover
- Chloracetophenone: lacrimating agent as a component of tear gas
- Muscone: produced from musk (deer) as a sex attractant or pheromones; used as fixative in perfumes
→ Grandisol: pheromone from bees
→ Muscalure: pheromone from mosquitoes

IX. HC DERIVATIVES: CARBOXYLIC ACIDS

- Functional group: -COOH (carboxyl group)
→ Terminal functional group
 - R-COOH
 - Ar-COOH
- Suffix: -oic acid
- Examples:
 - HCOOH: Methanoic acid/ formic acid → formica = ants
 - CH₃COOH: Ethanoic acid/ acetic acid

Chemical Reactions

- **Salt formation/ Neutralization**
→ $R - COOH + NaOH \rightarrow R - COO^{(-)}Na^{(+)} + H_2O$
- **Conversion to Functional Derivatives**
 - To acid/acyl halides
 - $R - COOH + SOCl_2 \rightarrow R - COCl$
(thionyl chloride) (acyl/acyl chloride)
 - To esters (esterification)
 - $R - COOH + R' - OH \xrightarrow{H^+} R - COOR' + H_2O$
 - To amides
 - $R - COOH + NH_3 \xrightarrow{x} R - CO NH_2 \rightarrow R - COO^{(-)}NH_4^{(+)}$
 - $R - COOH + SOCl_2 \xrightarrow{(1)} R - COCl + NH_3 \xrightarrow{(3)} R - CONH_2$
- **Reduction**
→ $R - COOH \xrightarrow{LiAlH_4} RCH_2OH$ (1° alcohol)

Examples

- Benzoic acid – antifungal agent
→ Na benzoate – Preservative for juices
→ Na benzoate + salicylic acid = Whitfield's ointment (antifungal agent)
- Salicylic acid – keratolytic agent
→ Destroys skin keratin
- Acetyl salicylic acid (ASA) – aspirin
→ COX inhibitor
→ Analgesic, antiplatelet, anti-inflammatory

X. HC DERIVATIVES: CARBOXYLIC ACID DERIVATIVES

Acyl/Acid Chlorides

- Suffix: -oic acid → -oyl chloride
- Reaction: Hydrolysis (very reactive)
- Example
 - $\text{CH}_3\text{-COCl}$: ethanoyl chloride (acetyl chloride)
 - $\text{R-COCl} + \text{H}_2\text{O} \rightarrow \text{R-COOH} + \text{HCl}$
 - $\text{CH}_3\text{-COCl} + \text{H}_2\text{O} \rightarrow \text{CH}_3\text{-COOH} + \text{HCl}$

Acid Anhydrides

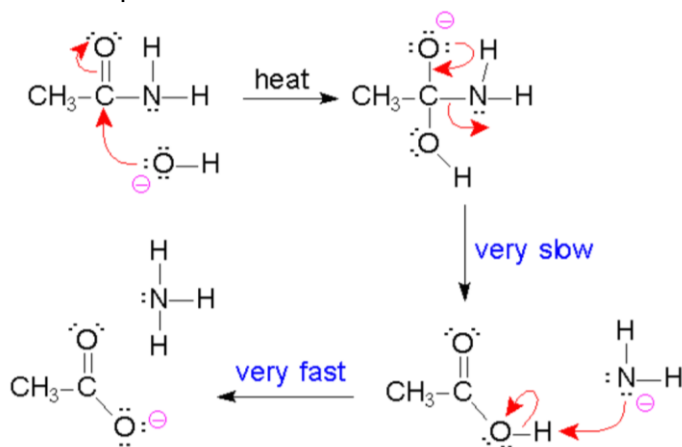
- Suffix: -oic acid → -oic anhydride
- Reaction: Hydrolysis (very reactive)
- Example:
 - $\text{CH}_3\text{-COO-COCH}_3$ ethanoic anhydride (acetic anhydride)
 - $\text{CH}_3\text{-COO-COH} + \text{H}_2\text{O} \rightarrow \text{CH}_3\text{COOH} + \text{HCOOH}$
- Formation of ethanoic methanoic anhydride (acetic formic anhydride)
 - $\text{R-COO-COR} + \text{H}_2\text{O} \rightarrow 2 \text{R-COOH}$

Esters

- Suffix: -oic acid → -oate
- Reaction: Hydrolysis (very reactive)
- Example:
 - $\text{CH}_3\text{-COOCH}_2\text{CH}_3$ ethyl ethanoate (ethyl acetate)
 - $\text{R-COOR} + \text{H}_2\text{O} \rightarrow \text{R-COOH} + \text{R'-OH}$
 - $\text{ASA} + \text{H}_2\text{O} \rightarrow \text{Salicylic acid} + \text{acetic acid}$
 - Dry granulation
 - Direct compression

Amides

- Suffix: -oic acid → -amide
- Reaction: Hydrolysis
- Example:



Examples

- Reactivity: acid chlorides > anhydrides > esters
= acids > amides

Local anesthetics

→ Esters

- Short-duration
- Metabolized in the plasma via pseudocholinesterases

→ Amides (e.g., lidocaine)

- Long-duration
- Metabolized in the liver through amidases

Nicotinamide/niacinamide

- Nicotinic acid (niacin)
- Vitamin B3 supplement
- Prevent pellagra (deficiency of vitamin B3)
 - Pellagra: dermatitis, diarrhea, dementia, death

Sulfonilamide

- Sulfur analogue of an amide
- Parent compound of sulfonamides

XI. HC DERIVATIVES: AMINES

Classification

Aliphatic Amines

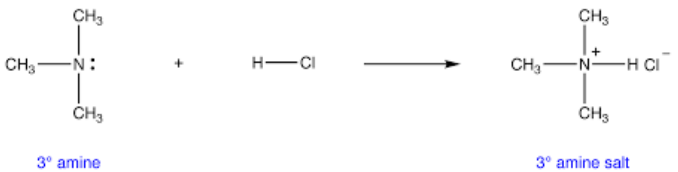
- IUPAC Nomenclature: alkyl + amine
- R – electron-donating group (steric/ crowding effect)
- Lewis base is an electron pair donor (availability of lone pairs to be donated = basicity)
 - Basicity: secondary > tertiary > primary > NH_3

Aromatic Amines

- Basicity: aliphatic amines > aromatic > amides

Chemical Reactions

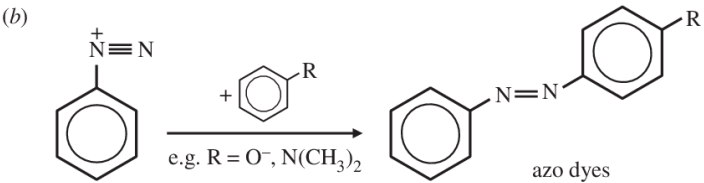
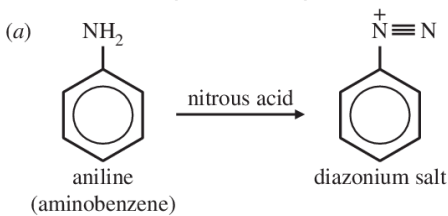
- **Salt formation/neutralization**



- **Diazotization**

→ Aniline produces diazonium salt (using concentrated HCl in ice bath 0 to 5 degrees Celsius)

- With aromatic compounds (or coupling): produces azo dyes
- With water: produces phenol and N_2



Examples

- Beta-adrenergic agonist
→ Salbutamol, terbutaline
- Catecholamines
→ NE, Epi, Dopamine
- Pseudoephedrine, phenylpropanolamine
- Amphetamine, methamphetamine