BarCharts,Inc.® WORLD'S #1 ACADEMIC OUTLINE

Quick Study® ACADEMIC

ORGANIC CHEMISTRY

REACTIONS

FEATURES OF AN ORGANIC REACTION

Mechanism: Describes the overall reaction using a series of simple steps.

Stoichiometry: Calculate reactant and product masses using the balanced equation and molar masses.

Kinetics: The study of the reaction rate and mechanism.

Theoretical yield: Mass of product given by a complete reaction;

%yield=100%x(product mass)÷(theoretical yield).

Equilibrium: Reaction does not proceed to completion, instead, it reaches a balanced state of forward and reverse reactions.

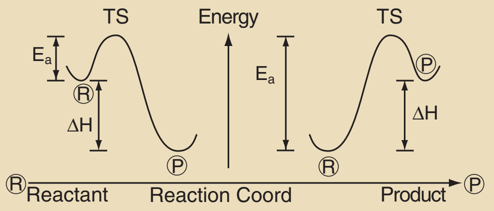
Major reaction types:

- Acid
- Base
- Oxidation Reduction
- Condensation
- Substitution (SN1, SN2)
- Ionic Reaction
- Elimination (E1, E2)
- Cyclization
- Hydrolysis
- Addition
- Radical reaction

Important named reactions:

- **Diels Alder:** form cyclic alkene
- **Friedel-Crafts:** add acyl or akyl group
- **Grignard:** add alkyl or aryl group
- **Wolf-Kirschner, Clemmenson:** reduce ketone to alkane
- **Wittig:** convert aldehyde/ketone to alkene

KINETICS AND REACTION MECHANISM



Transition state (TS): Maximum on the reaction-coordinate curve: the least stable intermediate.

Activation Energy (E_a): Energy of the TS relative to the reactant. The change in enthalpy (ΔH) is < 0 for **exothermic**; > 0 for **endothermic**.

Hammond-Leffler postulate: The TS is more like the reactant or product that is closer in energy; *endothermic* TS is like the product, *exothermic* TS is like the reactant.

Kinetic vs. thermodynamic control: ΔG and ΔH describe Thermodynamic Stability.

- If ΔG is large and negative (**exergonic**), the product formation is likely controlled by "thermodynamics." Large Keq corresponds to a large amount of product, relative to reactant.
  - A large E_a may give rise to "kinetic" control; the energy of the TS controls the reaction, instead of the product-reactant thermodynamics.

Solvent effects: A solvent may stabilize an intermediate, decreasing E_a and increasing the rate of the reaction. Charged-complexes are stabilized by polar solvents.

ORGANIC ACID AND BASE

Acid:

- Electron-pair acceptor (Lewis acid)
- Proton donor (Bronsted-Lowry acid); example: carboxylic acid

Base:

- Electron-pair donor (Lewis base)
- Proton acceptor (Bronsted-Lowry base); example: *amine*

Factors enhancing *acid* strength (HA):

- Weaker H-A bond
- Greater electronegativity of "A"
- Inductive effect of substituent on "A" (electron withdrawal enhances transfer).
- More "s" character in hybrid orbital (s-orbital is lower in energy than p-orbital)
- Resonance stabilized conjugate base (A^-)

Factors enhancing *base* strength:

- Reverse of acid-strength guidelines
  A base is a nucleophile; Electronic effects which shift electron density to the atom with the lone-pair increases base-strength.

ALKANE $-\overset{|}{\underset{|}{C}}-\overset{|}{\underset{|}{C}}-$

Properties:

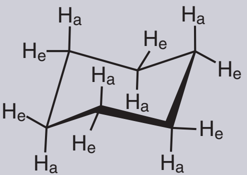
- Hydrocarbon
- Weak intermolecular forces
- Non-cyclic: general formula C_nH_{2n+2}
- Tetrahedral C-C-C (109°)

Nomenclature:

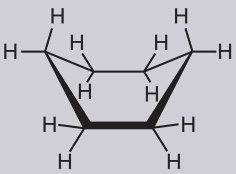
- Add "-ane" to prefix
- Locate substituent by position #
- Haloalkane: substitute halide for -H

Cycloalkane: (C_nH_{2n})

- Bicyclic - two fused or bridged rings
- n = 3: **cyclopropane**: (highly strained)
- n = 4: **cyclobutane**: (some flexiblity)
- n = 5: **cyclopentane**: (slight puckering)
- n = 6: **cyclohexane**: *chair* - stable conformer; *boat* - less stable; *Axial* position: "perpendicular" to ring; *Equatorial* position: in ring "plane" (see H_a and H_e in chair diagram below)
- Cis - two substituents in *up* position
- Trans - *one* up and *one* down



Chair



Boat

Synthesis:

- Hydrogenate alkene or alkyne (H_2, Pt catalyst)
- Free-radical reaction of alkene
- Reduce haloalkane (Zn, H^+)
- Friedel-Crafts alkylation

Reaction:

- Combustion: alkane + O_2 => CO_2 + H_2O
- Halogenation to haloalkane (Cl_2/Br_2, light or heat)

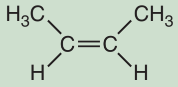
ALKENE >C=C<

Properties: Similar to alkane; non-polar, flammable

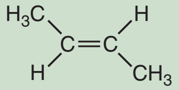
Nomenclature:

- Add -ene to prefix; Use # to denote C=C position
- **Isolated** C-C=C-C-C=C; **cumulative** -C=C=C-
- Polyunsaturated fatty acid: 2 or more C=C
- Allene: adjacent C=C=C
- Vinyl group: H_2C=CH-
- Methylene group: H_2C=
- Allyl group: H_2C=CH-CH_2-
- Vinyl halide: halide replaces -H on >C=C<
- Conjugated: alternate C-C and C=C (resonance)
- Alkadiene, 2 conjugated C=C; example: butadiene; s-cis and s-trans (rotate about C-C bond)
- Alkatriene, 3 conjugated C=C
- Annulene: conjugated monocyclic compound; example: [6] annulene = benzene
- Aromatic cyclic ions: cyclopentadiene anion, cycloheptatriene cation (6 electrons)

Isomers: no free rotation of C=C



(*Z*)-2-Butene
cis-2-butene



(*E*)-2-Butene
trans-2-butene

- E/Z; prioritize groups by atomic weight (Z - higher priority groups on the same side)
- For noncyclic: cis is less stable (steric hindrance). For cyclic, cis more stable.
- **Hofmann Rule:** Form the least-substituted alkene
- **Markovnikof Addition:** H adds to C with most -H's
- **Zaitsev Elimination:** Form alkene with more substitution

Synthesis:

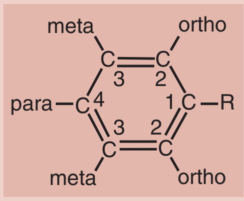
- Dehydrate alcohol (H^+, heat) (elimination)
- Dehydrohalogenate haloalkane (base, heat)
- Dehalogenate vic dihalide (Zn, acetic acid)
- Hydrogenate alkyne:
  - syn, Z/cis-isomer (H_2,P-2 catalyst)
  - anti, E/trans-isomer (Li, NH_3, -78°C)
- Wittig, aldehyde/ketone + phosphorous ylide

Reaction:

- Combustion (O_2)
- Hydrate to 2°/3° alcohol (H^+, H_2O); 1° from ethene; can rearrange (Markovnikov)
- Hydrate to alcohol; hydroborate/oxidize ($THF/B_2H_6,H_2O_2/OH^-$) (syn, anti-Markovnikov)
- Oxymercurate-demercurate to alcohol
- Hydrohalogenate (HX) (Markovnikov)
- Halogenate (Br_2/Cl_2), vic dihaloalkane (X_2,CCl_4; anti)
- Halohydrin (X_2, H_2O; anti-addition)
- Hydroxylate to form a 1,2-diol ($KMnO_4$, cold OH^-; syn addition)
- Oxidize to carboxylic acid (KMnO4, hot OH^-)
- Ozonolyze to ketone (O_3; Zn, H_2O)
- Hydrogenate to alkane (Pt, H_2; syn-addition)
- Free radical polymerization
- Alkadiene Reaction
  - allylic halogenation (Cl_2, heat)
  - Diels-Alder: cycloalkene from diene + alkene/alkyne

BENZENE/ARENE

Properties: insoluble in water, miscible with non-polar organic solvents.



Nomenclature:

- **Aromatic** (or arene): Denote substituent using group name and ring position; ortho (1,2), meta (1,3), para (1,4);
- examples: benzene C_6H_6; phenol, Ar-OH (carbolic acid, hydroxybenzene, benzenol); aniline Ar-NH_2; toluene, Ar-Me (methyl benzene); xylene, dimethyl benzene
- **Fused rings:** naphthalene, $C_{10}H_8$ (2 edge-sharing rings)
- **Aryl or Phenyl group:** Ar- (remove H from benzene)
- **Aryl halide:** halogen replaces an H atom; Ar-X
- **Alkenyl benzene:** Ar-C=C<
- **Benzyl:** Ar-CH_2-

Synthesis: Dehydrogenate cyclohexane (sulfur+ heat)

General Reaction:

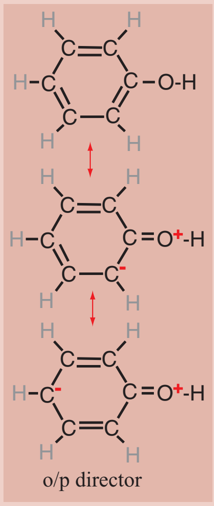
- Combustion (similar to alkane)
- Birch reduction => 1,4 cyclohexadiene (Na, NH_3, EtOH)
- Hydrogenate to cyclohexane (H_2, Pt)

Electrophilic substitution:

- Alkylation: Ar-R (*Friedels-Craft*, RCl, $AlCl_3$)
- Nitration: Ar-NO_2 (HNO_3, H_2SO_4)
- Halogenation: Ar-Br (Br_2, $FeBr_3$)
  - Ar-Cl (Cl_2, $FeCl_3$)
  - Ar-I (I_2, HNO_3)
- Acylation: Ar-CR=O (RCOCl, $AlCl_3$)
- Sulfonation: Ar-SO_3H (SO_3, H_2SO_4)

Reactivity of substituted benzene:

- A substituent alters the ring electronic structure.
- **Activating group:** More reactive than benzene; add electrons to the ring, stabilize the arenium cation
- **Deactivating group:** Less reactive; pull electrons from the ring, destabilize the arenium cation
- **Ortho/para-director:**
  - substituent tends to activate the ring (except for -X); electron density donated to ring creates "-" center on o/p sites, o/p isomers are preferred
  - examples: -NR_2, -OH, -R, -OR, -X (halogen)
- **Meta-director:**
  - substituent tends to deactivate the ring; electron density withdrawn from the ring creating "+" center on o/p site, m- preferred reaction site.
  - examples: -NO_2, -CN, -COOH, -SO_3H, -COOR, -CHO, -CRO



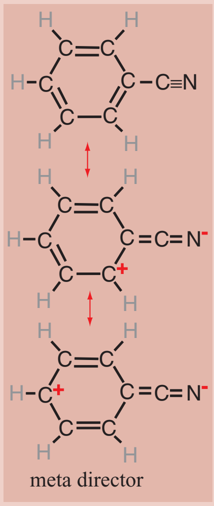
o/p director

Reactivity of di-substituted benzene:

- Directing effects may be cooperative; e.g. "o/p" plus "m" at 1,4 positions
- Otherwise: consider steric effects; activating group tends to dominate deactivating group.

Reaction of alkyl substituted benzene:

- Toluene to benzoic acid: ($KMnO_4$, OH^-, heat, H^+)
- Chlorinate -Me of Toluene (Cl_2)



meta director

ALKYNE -C≡C-

Properties:

- Hydrocarbon, at least 1 C ≡ C triple bond
- Properties similar to alkane or alkene
- Linear R"-C≡C-R'

Nomenclature:

- Add **-yne** to prefix
- Number denotes position of triple bond; example: ethyne (acetylene) C_2H_2

Synthesis:

- $CaC_2 + H_2O$ => $Ca(OH)_2 + C_2H_2$
- Dehydrohalogenate vic-haloalkene ($NaNH_2$, liq NH_3)
- Alkylate terminal alkyne ($NaNH_2$, liq NH_3; R-X)

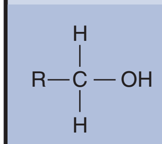
Reaction:

- Addition: hydrogenate to alkane (H_2, Pt or Ni)
  - syn to cis/Z alkene (H_2/Ni_2B P-2 catalyst)
  - anti to trans/E alkene (Li, Liq NH_3)
  - haloalkene to gem-dihalide (HX) (Markovnikov)
  - halogenate to haloalkene or haloalkane (X_2)
- Ozonolyze to carboxylic acid (O_3, H_2O)
- Oxidize to carboxylic acid ($KMnO_4$, OH^-; H^+)

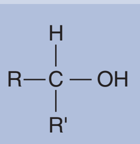
ALCOHOL R-OH

Properties:

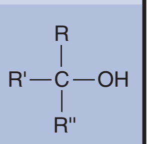
- Low molecular weight are water-soluble
- H-bonding, polar
- RO-H acidic proton
- Resonance stabilized ArO^- or RO^-



Primary (1°) alcohol



Secondary (2°) alcohol



Tertiary (3°) alcohol

Nomenclature:

- Prefix + "anol"; example: methanol Me-OH (methyl alcohol)
- **Cyanohydrin**: -OH and -CN
- Halohydrin: -OH and halogen
- Diol or glycol (two -OH); **gem-diol**: 1,1 diol; **vic-diol**: 1,2 diol

Synthesis:

- Hydrate alkene (H_2O, H^+)
- Hydroborate/oxidize alkene (THF:BH_3; H_2O_2, OH^-)
- Hydrogenate aldehyde (H_2/Ni or Pt catalyst)
- Hydrolyze 1o alkyl halide (water, OH^-)
- Reduce aldehyde, ester, ketone or carboylic acid
- Ethanol: Ferment sugar or starch
- Methanol: CO + H_2, catalyst; Pyrolyze cellulose
- Hydrolyze ester (water, acid)
- Dehydrate ether (H_2SO_4, low heat)
- Grignard (RMgX): formaldehyde => 1˚ alcohol; aldehyde => 2˚ alcohol; ketone => 3˚ alcohol
- Synthesis of Glycol from Ketone/aldehyde: (HIO_4 or $Pb(OAc)_4$; H_2SO_4 + heat)
  - oxidize alkene: ($KMnO_4$: cis) (H_2O_2, formic acid: trans)
  - hydrolyze epoxide (H_2O, H_2SO_4)

Reaction:

- Oxidize 1˚ to aldehyde (CuO, heat) or 2˚ to ketone ($KMnO_4$,H^+)
- Oxidize 1˚ to carboxylic acid ($KMnO_4$,H^+)
- Dehydrate to alkene; Zaitsev's rule; rate 3˚>2˚>1˚ (hot H_2SO_4, or Al_2O_3)
- Dehydrate to ether (H_2SO_4, lower temperature)
- Oxidize to ketone (2˚ alcohol) (H_2CrO_2)
- Form haloalkane (HX; substitution)

AROMATIC ALCOHOL Ar-OH

Properties:

- The most common is Phenol, Ar-OH
- Acidic hydrogen, ArO-H; pK_a=9.9
- Ring substituent alters acidity
- Benzendiol, HO-Ar-OH; para, hydroquinone; ortho, catechol; meta, resorcinol

Reaction of Phenol:

- Electrophilic substitution: o-p director
- Hydrogenate to cyclohexane (H_2, catalyst)
- Form ester (acid anhydride or acid chloride)

Synthesis of Phenol:

- Electrophilic aromatic substitution
- Williamson reaction, phenyl ether (NaOH, RCH_2X)
- Arenediazonium salt intermediate: Ar-NH_2 + HONO => Ar-N_2^+ + Cu_2O, H_2O => Ar-OH
- Benezene + propene => cumene; oxidation/acid => phenol + acetone
- Aryl halide (Ar-X) + NaOH, heat and acid
- Ar-OR + HI/HBr, heat

HALOALKANE/ ALKENE/ARENE R-X

Nomenclature:

- Halogen (X = fluorine, chlorine, bromine or iodine) replaces -H on hydrocarbon group
- Denote halogen in the name; example: Chloromethane: Cl-Me; chlorobenzene Ar-Cl

Synthesis: alcohol (ROH) + HX

Reaction:

- Dehydrohalogenate to alkene (often rearranges)
- Hydrolyze 1˚ alkyl halide to alcohol (RX + OH^-)

HALOHYDRIN X-R-R'-OH

Synthesis: Alkene + X_2, H_2O

Reaction:

- Halohydrin + ROH => β hydroxy ether
- Halohydrin + RNH_2 => β hydroxy amine
- Halohydrin + RSH => β hydroxy sulfide

ETHER R"-O-R'

Properties:

- Polar, hydrogen bonding
- Oxygen lone-pair is a nucleophile
- Flammable liquid

Nomenclature:

- R"-O-R', "R R' ether" or "alkoxy alkane";
- Example: diethyl ether, common solvent: Et-O-Et
- **Alkoxy** group, -OR (O-Me, methoxy; O-Et, ethoxy)
- Oxa-: substitute an -O- for a -CH_2-
- Cyclic ether: tetrahydrofuran (THF)
- **Epoxide** or **oxirane**: 3-member ring
- **Dioxane**: cyclic double ether
- **Peroxide**: R-O-O-R' ; -O-O- single-bond

Synthesis:

- Williamson synthesis (R'I + NaOR)
- Dehydrate 1° alcohol (H_2SO_4, heat)
- Epoxidation: alkene + peroxyacid
- Halohydrin + ROH => hydroxy ether

Reaction:

- Hydrolyze to alcohol (H+ or OH-)
- Autoxidize to peroxide (oxygen in air); EXPLOSIVE HAZARD!

Epoxide reaction:

- Hydrolyze 1,2 glycol (acid, H^+)
- Hydrolyze to 1,2 glycol (base, OH^- or OR^-)
- *Grignard* + epoxide => 1° alcohol

ALDEHYDE & KETONE >C=O

Properties:

- Polar $>C^{+}=O^{-}$; low molecular weight are water-soluble
- Main chemical difference: ketone is harder to oxidize than aldehyde.

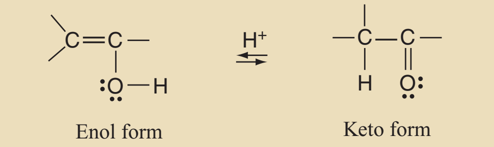
Aldehyde nomenclature (RCHO):

- Prefix+"anal";
- Example: HCHO, methanal (formaldehyde); MeCHO, ethanal (acetaldehyde); Ar-CHO, benzaldehyde

Ketone nomenclature (RR'CO):

- Prefix +"anone," also "R,R' ketone";
- Example: 2-propanone (acetone or dimethyl ketone);
- Diketone: 2 >C=O groups
- Acyl group: RC=O or Ar-C=O
- Ketene: C=C=O
- Ketal: RR'C(OR)(OR);
- Acetal: RHC(OR)(OR)
- Hemiacetal: RHC(OH)(OR)
- Diketone: R' -CO-CH2-CO-R

Keto-enol tautomerism:



- Nucleophile attacks >C=C< of enol-form
- Acidic α-H, -CH*-CHO can form resonance stabilized carbanion (especially for diketone).
- Racemization via keto-enol: chiral ketone => achiral enol => achiral ketone

Synthesis:

- Oxidize alcohol: aldehyde from 1° (Cu, heat); ketone from 2° (H_2CrO_4)
- *Grignard*: nitrile (RCN) + R'MgX => RCR'O
- Reduce RCO_2R' ($i\text{-}Bu_2AlH$)
- Reduce RCN ($i\text{-}Bu_2AlH$)
- Ozonolyze alkene (O_3, H_2O_2)
- *Friedel-Craft* acylation: Ar-H + RCOCl ($AlCl_3$)

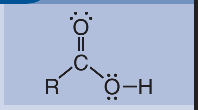
General Reaction:

- *Wittig*, form alkene (phosphorous ylide)
- Form Oxime (>C=N-OH) (hydroxyl amine)
- Reduce to alcohol (Metal hydride, $LiAlH_4$)
- *Wolff-Kishner*: >C=O to $>CH_2$ (N_2H_4, base, heat)
- *Clemmenson* reduction, >C=O to $>CH_2$ (Zn(Hg), HCl)
- Hydrogenate to ROH (H_2, metal; $NaBH_4$, H^+; $LiAlH_4$, H^+)
- Oxidize to RCOOH (peroxyacid)
- Form cyanohydrin (HCN)
- Form imine (>C=N-R) (1° amine)
- Aldol condensation, >CH=O + COOH => >C=C-CH=O
- Nucleophilic attack: RCHO + H-Nu => R-C(OH)-N]
- Hemiacetal/ketal formation: ROH + $R'_2C=O$ => $R'_2C(OH)(OR)$
- Formation of acetal (R'OH, HCl)
- Reductive amination: aldehyde or ketone => amine (amine or ammonia, H_2, Rh)

Specific Reaction:

- Acetaldehyde to gem-diol (H_2O, H^+ or OH^- catalyst)
- Synthesis of acetaldehyde (C_2H_2, Hg^{2+}, H^+, H_2O)
- Oxidize aldehyde to RCOOH: Ag_2O,OH^- or $Ag(NH_3)_2^+$; *Tollen's* reagent, ketone is not oxidized
- Haloform, methyl ketone (X_2, OH^-)
- Halogenate -H of ketone (X_2, H^+ or OH^-)

CARBOXYLIC ACID



Properties:

- Organic acid, resonance stabilizes dissociation
- Soluble in water; H-bonding, acid strength given by pKa

Nomenclature:

- Prefix+"oic acid";
- Examples: HCOOH, **methanoic acid** (formic acid) Me-COOH, **ethanoic** acid (acetic acid), Ar-COOH, **benzoic** acid (benzenecarboxylic acid) **oxalic** acid (dicarboxylic acid, HOOC-COOH) **malonic** acid (HOOC-CH_2-COOH)
- **Fatty acid**, "R" long hydrocarbon (aliphatic) chain

Derivatives:

- Ester
- Amide
- Acyl chloride
- Amino acid
- Acid anhydride: RCO-O-CO-R
- Peroxyacid: R-CO_3H

Synthesis:

- Oxidize 1° alcohol ($K_2Cr_2O_7$, OH^-)
- Oxidize aldehyde (Ag_2O, H^+)
- Oxidize alkene ($KMnO_4$, OH^-, heat, H^+)
- Ozonolyze alkene (O_3, H_2O_2)
- Hydrolyze nitrile or acyl chloride (H^+, H_2O)
- Acid anhydride + water
- Grignard and carbonation (RMgX + CO_2, H^+)
- Benzoic acid: oxidize 1°/2°alkylbenzene ($KMnO_4$,OH^-, heat, H^+)
- From methyl ketone (Ar-CO-CH_3) (X_2, OH^-, H^+)

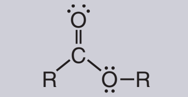
Reaction:

- Form acyl chloride ($SOCl_3$, PCl_3 or PCl_5)
- Reduce to alcohol ($LiAlH_4$)
- Neutralize with a base, form a salt
- Esterification: (R'OH, H^+)
- Reduce to ketone ($Ba(OH)_2$, heat)
- Decarboxylate keto acid to ketone (heat)
- α halo acid: (X_2, P, H_2O): HVZ (Hell-Volhard-Zelinski)
- α hydroxy acid from halo acid (OH^-; H^+)
- α amino acid from halo acid (NH_3 or amine)

Carbonic acid and derivatives:

- Carbonic acid: H_2CO_3 or HO-CO-OH
- Carbonyl dichloride (phosgene), Cl-CO-Cl; toxic gas
- Phosgene + EtOH => diethylcarbonate, EtO-CO-OEt
- Phosgene + NH_3 => H_2N-CO-NH_2 (urea)
- Phosgene + ROH => RO-CO-Cl (alkyl chloroformate)
- RO-CO-Cl + RNH_2 => RO-CO-NHR (urethane, carbamates)

ESTER



Properties:

- Derive from carboxylic acid; polar, weak H-bonding; pleasant or fruity odor

Nomenclature:

- Denote "alcohol" component with "-yl" suffix, acid with "-oate" or "-ate" suffix.
- Examples: Me-CO-O-Eth, ethyl acetate (ethanol+acetic acid);
- Lactone: cyclic ester

Synthesis:

- Esterification: ROH+R'COOH=>R'COOR (acid)
- Acid chloride (RCOCl) + R'OH
- R-CN + R'OH (H^+)
- Acid anhydride + alcohol => ester + carboxylic acid
- Aromatic ester: phenol + carboxylic anhydride
- β-keto ester: Claisen condensation from ethyl acetate (NaOEt, HCl)
- Transesterification: R'COOR + R"OH => R'COOR" + ROH (H^+, heat)

ESTER *continued*

Reaction:

- Acid-catalyzed hydrolysis
- Saponification: base-catalyzed hydrolysis
- Three fatty acids + ethylene glycol => triglyceride
- Grignard to 3° alcohol (R"MgX + R-COOR')
- Reduce to 1° alcohol (H_2, Ni)
- Form amide (RCOOR + 1°/2° amine)
- Pyrolyze to alkene and carboxylic acid

Lactone: Cyclic ester

- Intramolecular esterfication of δ-hydroxy acid (H^+)
- Hydrolyze δ/γ lactone to δ/γ hydroxy acid (OH^-, H^+)

AMINE RR'R"N

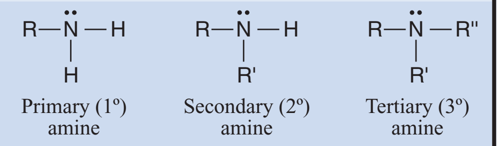
Properties:

- Substituted ammonia; polar, water soluble; >N-H forms H-bonds
- **Organic base:** strength denoted by pKb
- **Structure:** distorted pyramid (AX_3E)

Nomenclature:

- "R1 R2 R3 amine"
- Example: Me-NH_2, methyl amine; Ar-NH_2, phenylamine (aniline, amino benzene)

Types of amines:



Primary (1°) amine · Secondary (2°) amine · Tertiary (3°) amine

- Quaternary ammonium salt (4°) NR`R'R"R cation (no lone-pair)

Synthesis:

- **1°:** aminate haloalkane: $RCH_2X + NH_3$
  - reduce nitrile, RCN ($LiAlH_2$) or (H_2, Ni)
  - reduce nitroalkane, RNO_2 ($LiAlH_4$)
  - reduce oxime (Na, EtOH)
  - from aldehyde/ketone (NH_3, H^+)
- **2°:** haloalkane + 1° amine aldehyde/ketone + R'NH_2 (H^+)
- **3°:** haloalkane + 2° amine reduce amide ($LiAlH_4$, H_2O) aldehyde/ketone + R'R"NH (H^+)
- Aromatic Amine: Ar-NO_2 => Ar-NH_2 (H_2, catalyst; Fe, HCl, OH^-)

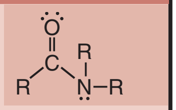
Reaction of amine:

- React as a base: amine + H^+ => R_3NH^+
- Nucleophilic N lone-pair
- Amine + sulfonyl chloride => sulfonamide
  - amide formation: 1° + R'COCl => R'CO-NHR
  - 1° + CH_3COOOH => R-NO_2
  - amide formation: 2° + RCOCl
  - **Cope Elimination**: oxidize 3° amine to tertiary ammonium oxide (R_3N^+-O^-), heat produces RHC=CH_2
- Ar-NH_2: o-p director, electrophilic aromatic substitution
- Ar-NH_2: nucleophilic aromatic substitution:
  Step 1: Ar-NH_2 + cold nitrous acid => Ar-N_2^+ (diazonium salt, unstable)
  Step 2: Depends on substitution:
  + Cu_2O, Cu^{2+}, H_2O => Ar- OH
  + CuCl => Ar-Cl
  + CuCN => Ar-CN
  + H_3PO_2 => Ar-H

Hofmann elimination:

- Quaternary ammonium hydroxide => alkene (heat)

AMIDE

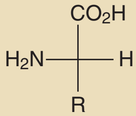


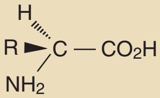
Nomenclature:
- Example: Me-CO-NH_2, acetamide
- Cyclic amide (lactam): N of amide forms ring with β, γ or δ carbon;
  - β forms 4 membered ring; γ forms a 5 membered ring, δ form a 6 membered ring.
  - Observed in amino acids

Synthesis:
- Nitrile hydrolysis (R-CN + H_2O, conc. H_2SO_4)
- Acyl chloride + 1°/2° amine or ammonia
- Pyrolysis of ammonium salt + RCOOH
- Ammonolysis of ester: 1° or 2° amine + ester
- Polyamide => polypeptide => protein

Reaction:
- Reduce to amine ($LiAlH_4$)
- Hydrolyze to acid (H_2O, H^+ or OH^-)
- Dehydrate to nitrile, RCN (P_4O_{10}, heat)
- *Hofmann* Reaction: Form 1° amine (NaOBr)
- *Grignard* (R˜MgX) to ketone, R-CO-R˜
- Form aldehyde and 2° amine ($LiAlH_2(OEt)_2$)
- Nucleophilic substitution; Form R-CO-Nu + amine

AMINO ACID





Properties:
- Basic (-NH_2) and acidic (-COOH) functionality
- Chiral isomers
- **Zwitterion:** self-ionization of amino acid to produce COO^- and -NH_3^+
- Isoelectric point, pH which produces equal + and - charges

Nomenclature:
- Common name based on "R" group; examples: glycine (-H), alanine (-CH_3)

Synthesis:
- Gabriel synthesis: RCH_2COOH + Br_2, PCl_3, NH_3

Reaction:
- Lactam formation (cyclic amide)
- Polypeptide formation (peptide bond); dehydration: R-NH_2 and HO-R' moieties
- Protein, amino acid polymer

OTHER NITROGEN-COMPOUNDS

Nitrile: R-C≡N:

example: H_3C-CN; methane nitrile

Synthesis:
- Haloalkane + NaCN
- Aldehyde/ketone => cyanohydrin (CN^-, H^+)
- Dehydrate amide (P_4O_{10}, heat)

Reaction:
- Hydrolyze to carboxylic acid (acid, heat)
- Hydrolyze to carboxylate (base, heat)
- Reduce to 1° amine (Raney Ni; $LiAlH_4$)
- Form aldehyde (DIBAL-H $(i\text{-}Bu)_2AlH$, H_2O)
- Form ketone (*Grignard* reagent or R-Li, H^+)

Imine: >C=N-R

Synthesis: Aldehyde/ketone + 1° amine (H^+)

Reaction: Intermediate in amination of aldehyde/ketone

NITROGEN *continued*

Imide: R-CO-NH-CO-R'

Synthesis:
- Dehydration, amide + carboxylic acid

Oxime: >C=NOH

Synthesis:
- aldehyde/ketone + hydroxylamine

Reaction:
- oxime to 1° amine (Na, EtOH)

ORGANIC POLYMER

-M- M -M - M - M -

Monomers (M) bond to form a high molecular weight compound.

Factors which influence properties: chain length, branching vs. linear, nature of the monomer, density, interchain bonds, hydrophobic and hydrophilic interactions.
- Examples:
  - PE (polyethylene)
  - PS (polystyrene)
  - HDPE (high density polyethylene)
  - LDPE (low density polyethylene)
  - PET (polyethylene teraphthalate)

Synthesis:
- Free-radical synthesis: ethylene => PE; styrene => PS (radical initiation)
- Condensation:
  - HO-R-OH+HO-R'-OH => HO-R-R'-OH + H_2O
  - Example: ethylene glycol and teraphthalic acid => PET

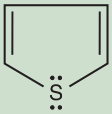
Reaction:
- Hydrolysis of polymer (reverse of condensation)
- Cross-link adjacent polymer chains or segments

SULFUR CHEMISTRY

Sulphur Compounds

• Thiol:	R-SH
• Sulfide or Thioether:	R-S-R'
• Disulfide:	R-S-S-R'
• Thiol ester:	R-CO-SR'
• Sulfoxide:	R-S-OR'
• Sulfone:	R-SO_2-R'
• Thiophenol:	Ar-SH
• Thioketone:	R-CS-R'
• Sulfonic acid:	R-SO_3H
• Sulfinic Acid:	R-SO_2H
• Hydrogen sulfate:	R-OSO_3H

Thiophene, Heterocyclic sulphur compound

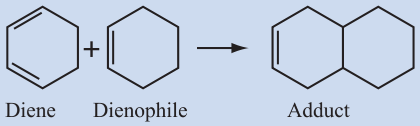


Synthesis:
- Thiol: From alkyl bromide/iodide (KOH, H_2S)
- Thiol: RCH_2X + NaSH => RCH_2SH (EtOH, heat)
- Thiol ester: Acyl chloride + thiol
- Alkyl hydrogen sulfate (Alkene + cold conc. H_2SO_4)
- Thiol: Alkene + H_2S (H_2SO_4, heat) (Markovnikoff addition)
- Thiol: Alkene+H_2S (peroxide or UV) (Anti-Markovnikoff addition)

Reaction:
- Form sulfide from thiol (NaOH, R'CH_2X)
- Form disulfide from thiol (I_2 or H_2O_2)
- Oxidize thiol to form sulfonic acid, RSO_3H, (HNO_3)
- Desulfurization of thiol to alkane (H_2, Ni)
- Sulfonate benzene (SO_3, conc. H_2SO_4)

CYCLIZATION: SYNTHESIS OF A CYCLIC COMPOUND

Synthesis:
- Diels-Alder: diene + dienophile + heat => adduct



- Freund-Gustavson: 3-membered ring from 1,3 dihalide (EtOH, Zn, heat)
- [2,2] cycloaddition of alkenes giving cyclobutane adduct (two alkenes, photochemical reaction)

Reaction of cyclic compound:
- Retro-Diels-Alder: thermally decompose cycloalkene
- Reduce aromatic to symmetric 1,4 cycloalkene (Li or Na, EtOH, Liq NH_3) (Birch)
- Small ring is strained, may decompose to linear chain
- Epoxide ring opening reaction

METAL REACTION

Organometallic:
- Carbon atom bonded to a metal atom
- Types of bonding:
  - ionic bond, Na,K; R^--M^+
  - partial covalent, Mg, Li; R electrophilic character
  - covalent, Pb, Sn, Hg; R-M

Grignard reagent:
- Strong base gives R electrophilic character:
  - Li + R-Br => R-Li
  - RX + Mg => RMgX
  - ArX + Mg => ArMgX

Organoborane:
- Boron hydride, B_nH_m example: diborane, B_2H_6
- **Synthesis:**
  - Hydroboration: Alkene + Boron hydride syn addition
- **Reaction:**
  - Organoborane => alcohol (H_2O_2/OH^-)
  - R-B< => R-H (acetic acid; addition of H)

Organolithium: R-Li

Synthesis:
- Li + haloalkane (R-X or Ar-X) (cold, Et_2O)

Organomagnesium: RMgX or ArMgX
- *Grignard*: RX + Mg (Et_2O); R behaves as R^-

Organocopper: R-Cu
- Add R- to C=C of unsaturated carbonyl

Organolead/mercury:
- Stable compound, VOLATILE AND TOXIC
- Tetraethyl lead (anti-knock agent in gasoline)

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Note: Due to the condensed nature of this chart, use as a quick reference guide, not as a replacement for assigned course work. The reaction reagents are noted for illustrative purposes only; this should not serve as guide for lab experiment procedures.

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