

Course Topic Summary

Chapter 12: Mass Spectrometry and Infrared Spectroscopy

- Uses of Mass Spec (obtaining molecular formula, fragmentation patterns)
- Use of IR to determine functional groups

Chapter 13: Nuclear Magnetic Resonance Spectroscopy

- Four pieces of info from ^1H NMR:
 - 1) Number of types of H (# of signals)
 - 2) Number of each type of H (integration)
 - 3) Number of neighboring H (coupling patterns – N+1 rule)
 - 4) Electronic environment of each type of H (chemical shift – how deshielded)
- ^{13}C NMR – including DEPT experiments (determines H substitution on C)
- Determining molecular structure from spectroscopic data

Chapter 14: Conjugated Dienes and Ultraviolet Spectroscopy

- Conjugated diene - two C=C separated by one C–C
- Stability (orbital overlap, molecular orbitals)
- Electrophilic Additions to conjugated dienes – 1,2 and 1,4 addition
- Allylic carbocation stability
- Kinetic (cold) vs. Thermodynamic (hot) control
- Diels-Alder reactions – good dienophiles, stereoselectivity (endo)
- UV Spectroscopy ($\pi \rightarrow \pi^*$)

Chapter 15: Benzene and Aromaticity

- Structure and stability of benzene (resonance and molecular orbital explanations)
- Aromaticity rules (Hückel $4n+2$ rule)

Chapter 16: Chemistry of Benzene: Electrophilic Aromatic Substitution

- Halogenation of benzene rings (Lewis Acid catalyst needed, e.g. FeBr_3) **Mech**
- Nitration of benzene rings (Lewis Acid catalyst needed – H_2SO_4) **Mech**
- Sulfonation of benzene rings (no Lewis acid) **Mech**

- Friedel–Crafts Alkylations (Lewis Acid catalyst needed, e.g. AlCl_3) **Mech**
- Problems with F–C Alkylations

- Friedel–Crafts Acylations (Lewis Acid catalyst needed, e.g. AlCl_3) **Mech**
- Reduction of F–C acylation products to give alkylated benzenes
- Activation (strong and weak) and Deactivation (strong and weak) of Benzene rings
- Substituent effects and regioselectivity of Electrophilic Aromatic Substitutions (ortho, para directors and meta directors)

- Substituent effects are cumulative
- Better activators direct better (strong better than weak and both better than deactivator)
- Nucleophilic Aromatic Substitution reactions – Activating and Deactivating substituents are reversed. **Mech**
- Making phenol from aryl halides (benzyne intermediate) **Mech**
- KMnO_4 oxidations of alkyl benzenes to carboxylic acids
- Benzylic Brominations – analogous to allylic brominations
- Reduction of benzene compounds
 - benzene to cyclohexane with H_2 and Rh/C
 - NO_2 to NH_2 with H_2 and Pd/C
 - ArCOR to ArCH_2R with: H_2 , Pd/C and heat
 - or
 - Wolff-Kishner (NH_2NH_2 , KOH, water)
 - or
 - Clemmensen Reduction (Zn(Hg) , HCl, heat)
 - or
 - Make thioketal, reduce (1: CH_3SH , BF_3 2: Raney Ni)

Chapter 19: Ketones and Aldehydes

- Naming Aldehydes and Ketones
- Synthesis of Aldehydes and Ketones
 - Aldehydes from Hydroboration of terminal alkynes
 - Ketones from Mercuric Ion Hydration of terminal alkynes
 - Ketones and aldehydes from alkene cleavage reactions (ozonolysis, potassium permanganate)
 - Oxidation of alcohols with PCC (1° or 2° alcohols) or Jones' Reagent (2° alcohols)
 - Friedel-Crafts Acylations of benzene compounds
 - Reduction of Esters with DIBAL (diisobutylaluminum hydride)
 - Ketone from acid chloride and Gilman Reagent (R_2CuLi)
- Reactions of Aldehydes and Ketones
 - Oxidation of aldehydes to carboxylic acids – Jones Reagent **or** Tollens' Reagent (Ag_2O , NH_4OH , H_2O , EtOH) **or** by cleavage with 1) KMnO_4 , H_2O , NaOH 2) H_3O^+
 - Addition of water to aldehydes or ketones under acidic *or* basic conditions to form geminal diols – **mechanisms**
 - Cyanohydrin formation with HCN – **mechanism**
 - Conversion of cyanohydrin to 1° amine with 1) LiAlH_4 and 2) water
 - Conversion of cyanohydrin to carboxylic acid under acidic or basic conditions
 - Grignard Additions to aldehydes and ketones – **mechanism**
 - Hydride Reductions of aldehydes and ketones to alcohols with 1) NaBH_4 2) water – **mechanism**
 - Addition of 1° amines to aldehydes or ketones to form imines - **mechanism**
 - Addition of 2° amines to aldehydes or ketones to form enamines – **mechanism**

- Reduction of ketones or aldehydes to alkanes with hydrazine – Wolff-Kishner Reaction (H_2NNH_2 , KOH) – **mechanism**
- Reduction of ketones or aldehydes to alkanes with Zn(Hg) , H_3O^+ (Clemmensen reduction)
- Acetal formation from aldehydes or ketones with ROH and acid – **mechanism**
- Wittig Reaction – **mechanism**
- Conjugate (1, 4) Additions to α,β -unsaturated ketones and aldehydes – amines or copper (Gilman's or Grignard's with CuI) nucleophiles – **mechanism**

Chapter 20: Carboxylic Acids

- Naming Carb. Acids, Acid Halides, Anhydrides, Amides, Esters, Nitriles
- Acidity of Carb. Acids - fine tuning with electron withdrawing/donating groups
- Substituted Benzoic Acids - acidity and correlation to benzene reactivity in Electrophilic Aromatic Substitution reactions
- Synthesis of Carb. Acids
 - KMnO_4 cleavage of alkyl benzenes
 - KMnO_4 cleavage of alkenes
 - Jones Oxidation of 1° alcohols and aldehydes (CrO_3 , H_2SO_4 , acetone)
 - Ag_2O Oxidation of aldehydes (Ag_2O , NH_4O)
 - Acidic or basic hydrolysis of nitriles - **mechanism** (chapter 21)
 - Grignard addition to CO_2 – **mechanism**
- Reactions of Carboxylic Acids
 - LiAlH_4 Reduction to 1° alcohols (1. LiAlH_4 2. H^+)
 - BH_3 Reduction to 1° alcohols (1. BH_3 2. H^+) (selective for carb. acids)

Chapter 21: Carboxylic Acid Derivatives – Acyl Substitutions

- Reactivity trend (acid halides > anhydride > ester > amide)
- Synthesis of Acid Halides:
 - Thionyl chloride (SOCl_2) reaction of carb. acid to make acid chloride - **mechanism**
 - Phosphorous tribromide (PBr_3) reaction of carb. acid to make acid bromide
- Reactions of Acid Halides
 - Treatment with H_2O and pyridine to make carb. acid – **mechanism**
 - Treatment with 1° or 2° amine and pyridine to make amide – **mechanism**
 - Treatment with 1) LiAlH_4 and 2) H^+ to form 1° alcohol – **mechanism**
 - Treatment with Grignard reagent to give 3° alcohol – **mechanism**
 - Treatment with Gilman (R_2CuLi) to form ketone
 - Treatment with alcohol and pyridine to form ester – **mechanism**
- Synthesis of Acid Anhydrides from Acid Halide and Carboxylic Acid
- Reactions of Acid Anhydrides – same as Acid Halide reactions (unsymmetrical anhydrides give product mixtures)
- Other formation of Ester: Fischer Esterification (carb. acid + alcohol) – **mechanism**

- Reactions of Esters
 - Hydrolysis to alcohol and carb. acid under acidic **or** basic conditions – **mechanisms**
 - Treatment with 1° or 2° amine to form amide – **mechanism**
 - Treatment with LAH to give 1° alcohol – **mechanism**
 - Treatment with DIBAL to give aldehyde
 - Treatment with Grignard or alkyl lithium to give 3° alcohol – **mechanism**
- Reactions of Amides
 - Hydrolysis to carb. acid and amine under acidic **or** basic conditions – **mechanisms**
 - Reduction with LAH to form amine – **mechanism**
- Formation of Nitriles
 - Via S_N2 pathway – CN⁻ attack of 1° alkyl halide – **mechanism**
 - Via 1° amide with thionyl chloride (SOCl₂) – **mechanism**
- Reactions of Nitriles
 - Hydrolysis to carb. acid and ammonia under acidic **or** basic conditions – **mechanisms**
 - Reduction with 1) LAH and 2) water to form 1° amine
 - Reduction with 1) DIBAL and 2) water to form aldehyde
 - Reaction with 1) Grignard reagent and 2) H⁺ to form ketone

Chapter 22: Carbonyl Alpha Substitution

- Ketone / Enol equilibrium
- Enol Halogenation with X₂ and acetic acid – **mechanism**
- Hell-Volhard-Zelinski α-Bromination of Carboxylic Acids with 1) PBr₃, Br₂ and 2) water
- α-Hydrogen acidity
- Haloform reaction: Treatment of methyl ketone with X₂ and NaOH to give carb. acid and CHX₃
- Malonic Ester Synthesis – **mechanism**
- Acetoacetic Ester Synthesis – **mechanism**

Other enolate alkylations (S_N2) – **mechanism**

Chapter 23: Carbonyl Condensation Reactions

- Aldol Condensation - ketone/aldehyde as nucleophile and electrophile – **mechanism**
- Aldol condensation vs. α-Substitution (base strengths: LDA vs. ⁻OH)
- Dehydration (elimination) of aldol product to form α,β-unsaturated ketone/aldehyde – **mechanism**
- Mixed Aldol – when do we get only one product? – **mechanism**
- Intramolecular Aldol – cyclization reaction – **mechanism**
- Claisen Condensation – Aldol type reaction with esters – **mechanism**
- Mixed Claisen – when do we get only one product? – **mechanism**
- Dieckman Cyclization (Intramolecular Claisen) – **mechanism**
- Michael Addition - enolate attacks α,β-unsaturated carbonyl compound (1,4-addition) – **mechanism**

- Good Michael Donors: stable enolates (eg diethyl malonate)
- Good Michael Acceptors: α,β -unsaturated aldehydes, ketones, esters, nitriles, amides, nitro compounds
- Robinson Annulation - Michael Addition followed by Aldol Condensation

Chapter 24: Amines

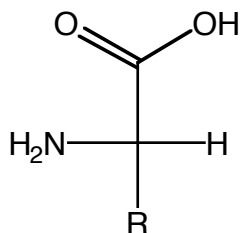
- Naming
- Basicity of amines - fine tuning with electron withdrawing/donating groups
- Synthesis of amines
 - Azide synthesis - **mechanism**
 - Gabriel synthesis - **mechanism**
 - Reduction of amides
 - Reduction of nitriles
 - Reductive amination - (**imine formation ch. 19**)
 - Hoffman Rearrangement of amide – **mechanism**
 - Curtius Rearrangement of acyl azide – **mechanism**
- Reactions of amines
 - Amides from amine and acid chloride
 - Hoffman Elimination (makes non-Saytsev alkene)
- Basicity of arylamines, including “tuning”
- Synthesis of arylamines
 - From aromatic nitro compounds
- Reactions of arylamines
 - Normal Electrophilic Aromatic Substitution reactions (very reactive) (ch.16)
 - Conversion to amide to avoid polyadditions

Chapter 25: Carbohydrates

- Classification - aldose vs. ketose, tri, tetra, etc.
- D,L sugars
- Know names and structures for D-aldotriose through D-aldohexoses (15 sugars)
- Hemiacetal formation - pyranose, furanose forms - alpha (trans) and beta (cis) forms – **mechanism (chapter 19)**
- Chair conformations and Haworth Projections
- Ester formation
- Ether formation
- Glycoside formation (acetal)
- Reduction to alditol
- Oxidation to aldonic acids
- Oxidation to aldaric acids
- Kiliani-Fischer chain lengthening
- Wohl Degradation
- Disaccharide linkages (usually 1, 4')

Chapter 26 – Amino Acids, Peptides, and Proteins

- Structure of Amino Acids
 - 20 common naturally occurring Amino Acids – page 1058
 - All are α -Amino Acids (amino group is alpha to the carboxy group)
 - 19 of 20 Amino Acids are 1° amines (proline is only 2°)
 - 19 of 20 are chiral (glycine is not) due to chiral center at α position – only one form found naturally – L enantiomer based on carbohydrate nomenclature



- 15 of 20 are neutral amino acids – side chain (R) has no NH_2 or CO_2H groups
 - 3 of 20 are basic (R contains NH_2 group) – lysine, arginine, histidine
 - 2 of 20 are acidic (R contains CO_2H group) – glutamic acid, aspartic acid
- Zwitterions
 - Amino acids are basic and acidic – undergo intramolecular acid/base reaction to form neutral dipolar ion – zwitterion
 - Acid / base behavior of zwitterions is “reversed”
- Isoelectric Point – the pH at which an amino acid has a neutral charge
- Electrophoresis – using isoelectric point differences among amino acids to separate them
- Synthesis of α Amino Acids
 - From carboxylic acids via α -bromination followed by Gabriel amine synthesis
 - Strecker Synthesis – imine formation from aldehyde, nucleophilic attack by CN^- , hydrolysis of nitrile to carboxylic acid
 - Reductive Amination of α -keto acid with NH_3 and NaBH_4
 - Amidomalonate Synthesis – analogous to Malonic Ester
- Resolution of Racemic Amino Acids
 - Make diastereomeric salt and separate as usual
 - Make use of enzyme like carboxypeptidase
- Peptides – chain of amino acids shorter than 50 units
 - Amide linkages between amino acids (remember pi character of C–N bond)
 - Sulfide cross-links
- Peptide structure determination
 - Automated amino acid analysis
 - Sequence determination by Edman Degradation (cleavage from amino end), with help from partial hydrolysis for large peptides or proteins
 - Trypsin cleaves only at carboxy side of lysine and arginine (basic AAs)
 - Chymotrypsin cleaves at carboxy side of phenylalanine, tyrosine, and tryptophan (R groups contain benzene ring)
 - Carboxypeptidase cleavage from carboxy end
- Peptide synthesis
 - BOC protecting groups for amino ends
 - Put on with di-t-butyl dicarbonate

- Removed with TFA (trifluoroacetic acid)
- Ester protecting groups for carboxy ends
 - Put on with alcohol and acid
 - Removed under saponification (basic hydrolysis) conditions
- DCC coupling reagent - **mechanism**
- Classification of Proteins
 - Simple vs. Conjugated
 - Fibrous vs. Globular
- Protein Structure – primary, secondary, tertiary, quaternary
 - Common secondary structures – α -helix; β -pleated sheet

Chapter 28: Nucleic Acids – DNA, RNA

- Nucleosides – sugar plus amine base connected at 1' position of sugar
- Sugar for RNA is ribose
- Sugar for DNA is deoxyribose (no OH group at 2' position)
- DNA has four possible bases:
 - two purines – adenine and guanine
 - two pyrimidines – cytosine and thymine
- RNA has four possible bases – substitute uracil for thymine
- Nucleotides contain nucleoside plus a phosphate group at the 5' position of sugar (all nucleotides shown on page 1141)
- DNA contains nucleotides linked at 3' and 5' positions by phosphate groups
- By convention, DNA chains are described from 5' end (phosphate) to 3' end (hydroxy)
- Base pairing
 - Adenine and Thymine form strong hydrogen bonds only to each other
 - Guanine and Cytosine form strong hydrogen bonds only to each other
- DNA secondary structure
 - Two strands of DNA form a double helix
 - Oriented in opposite directions (one is 5' to 3', other is 3' to 5')
 - Nucleotides are ordered so that hydrogen bonds form between complimentary base pairs (Where A occurs in one, T must be in the other; where G occurs in one, C must be in the other)
 - Example DNA primary structure:
 - 5' end → AGGCTATCG ← 3' end
 - 3' end → TCCGATAGC ← 5' end