CHEM 263 (edition 10)

MODULE 7: Hydrogenation of alkenes and Alkynes
Text Sections: 7.13-7.15

MODULE 8: Alkenes and Alkynes II: Addition reactions
Addition reactions of alkenes
  - How to understand addition to alkenes
Electrophilic addition of hydrogen halides to alkenes: Mechanism and Markovnikov’s Rule
    - theoretical explanation of Markovnikov’s rule
    - modern statement of Markovnikov’s rule
    - regioselective reactions
    - exception to Markovnikov’s rule
Stereochemistry of the ionic addition to an alkene
Addition of water to alkenes: Acid-catalyzed hydration
  - mechanism
  - rearrangements
Alcohols from alkenes through oxymercuration-demercuration: Markovnikov’s addition
  - Regioselectivity of oxymercuration-demercuration
  - Mechanism of oxymercuration
Alcohols from alkenes through hydroboration-oxidation: Anti-Markovnikov’s syn hydration
Hydroboration: Synthesis of alkylboranes
  - mechanism of hydroboration
  - stereochemistry of hydroboration
Oxidation and hydrolysis of alkylboranes
  - regiochemistry and stereochemistry of alkylborane oxidation and hydrolysis
Summary of alkene hydration methods
Electrophilic addition of bromine and chlorine to alkenes
  - mechanism of halogen addition
  - stereospecific reactions
Halohydrin formation
Oxidation of alkenes: Syn 1,2-dihydroxylation
  - mechanism for syndihydroxylation of alkenes
Oxidative cleavage of alkenes
  - cleavage with hot basic potassium permanganate
  - cleavage with ozone
Electrophilic addition of bromine and chlorine to alkynes
Addition of hydrogen halides to alkynes
Oxidative cleavage of alkynes
How to plan a synthesis: some approach and examples
  - retrosynthetic analysis
  - disconnections, synths, and synthetic equivalents
  - stereochemical considerations
  - Hydrogenation of Alkenes and Alkynes.

Text Sections: 8.1-8.3, 8.5-8.10, 8.12-8.14, 8.16-8.21

MODULE 9: Nuclear Magnetic Resonance Spectroscopy
Nuclear Magnetic Resonance (NMR) spectroscopy
  - chemical shift
  - integration of signal area
  - coupling (signal splitting)
How to interpret proton NMR spectra
Nuclear Spin: The origin of the signal
Detecting the signal: Fourier transform NMR spectrometers
Shielding and deshielding of protons
The chemical shift
  - PPM and the δ scale
Chemical shift equivalent and nonequivalent protons
  - Homotopic and heterotopic atoms
  - Enantiotopic and diastereotopic hydrogen atoms
Signal splitting: Spin-spin coupling
  - Vicinal coupling
  - Splitting tree diagrams and the origin of signal splitting
- Coupling constants-recognizing splitting patterns
- The dependence of coupling constants on dihedral angle
- Complicating features
- Analysis of complex integrations
Proton NMR spectra and rate processes
Interpretation of $^{13}$C NMR Spectra
One Peak for each Magnetically Distinct Carbon Atom
$^{13}$C Chemical Shift
Off-resonance Decoupled Spectra
DEPT $^{13}$C Spectra

**Text Sections:** 9.1-9.11

**Homework Chapter 9:** 6, 7, 9, 23, 25, 26, 30, 31, 39, 40, 42, 44, 50, 51

**MODULE 10: Radical Reactions**
Introduction: How radicals forms and how they react
- Production of radicals
- Reactions of radicals
Homolytic bond dissociation energy ($\Delta H^\circ$)
- How to use homolytic bond dissociation energies to calculate heat of reaction
- How to use homolytic bond dissociation energies to determine the relative stabilities of radical
Reactions of alkenes with halogens
- Multiple halogen substitution
- Lake of chlorine selectivity
Chlorination of methane: Mechanism of reaction
- Activation energies
- Reaction of methane with other halogens
Halogenation of higher alkanes
- Selectivity of bromine
The geometry of alkyl radicals
Reactions that generate tetrahedral chirality centers
- Generation of a second chirality center in a radical halogenations
Radical addition to alkenes: The anti-Markovnikov addition of hydrogen bromide
- Summary of Markovnikov versus anti-Markovnikov addition of HBr to alkenes.

**Text Sections:** 10.1-10.9

**Homework Chapter 10:** 2, 14, 16, 22, 24, 25, 27, 32, 33

**MODULE 11: Alcohols and Ethers**
Structure and Nomenclature
- nomenclature of alcohols
- nomenclature of ethers
Physical Properties of Alcohols and Ethers
Synthesis of Alcohols from Alkenes
Reactions of Alcohols
Alcohols as Acids
Conversion of Alcohols into Alkyl Halides
Alkyl Halides from the Reaction of Alcohols with Hydrogen Halides
- mechanism of the reactions of alcohols with HX
Alkyl halides from the reaction of alcohols with PB$_3$ or SOCl$_2$
Tosylate, mesylates, and triflates: Leaving group derivatives of alcohols
Synthesis of Ethers
- ethers by intermolecular dehydration of alcohols
- the Williamson Ether Synthesis of ethers
- synthesis of ethers by Alkoxymercuration-demercuration.
Reactions of Ethers
- ether cleavage
Epoxides
- synthesis of epoxides: epoxidation
- stereochemistry of epoxidation
Reactions of epoxides
- acid-catalyzed ring opening of an epoxide
- base-catalyzed ring opening of an epoxide
Anti 1,2-dihydroxylation of Alkenes via Epoxides
Summary of reactions of alkenes, alcohols, and ethers
- how alkenes can be used in synthesis


Homework: Chapter 11: 2, 3, 4, 6, 9, 13, 14, 17, 18, 19, 20, 25, 26, 27, 28, 29, 30, 32, 33, 38, 40, 43, 44, 45, 46, 48.

MODULE 12. Alcohols from Carbonyl Compounds: Oxidation-reduction and Organometallic compounds

Structure of the Carbonyl group
- reactions of Carbonyl Compounds with Nucleophiles
Oxidation-reduction Reactions in Organic Chemistry
- oxidation states in organic chemistry
Alcohols by Reduction of Carbonyl Compounds
- lithium aluminum hydride
- sodium borohydride
- overall summary of LiAlH₄ and NABH₄ reactivity
Oxidation of alcohols
- oxidation of primary alcohols to aldehyde
- oxidation of primary alcohols to carboxylic acids
- oxidation of secondary alcohols to ketones
- mechanism of chromate oxidations
- a chemical test for primary and secondary alcohols
- spectroscopic evidence for alcohols
Organometallic Compounds
Preparation of organolithium and organomagnesium compounds
- organolithium compounds
- Grignard reagents
Reactions of organolithium and organomagnesium compounds
- reactions with compounds containing acidic hydrogen atoms
- reactions of Grignard reagents with epoxides
- reactions of Grignard reagents with carbonyl compounds
Alcohols from Grignard Reagents
How to plan a Grignard synthesis
Restrictions on the use of Grignard reagents
The use of lithium reagents
The use of sodium alkynides

Text Sections: 12.1 – 12.8.

Homework: Chapter 12: 3, 4, 5, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 19, 26, 27, 28, 29, 30, 32, 33.

MODULE 14: Aromatic Compounds
Nomenclature of Benzene Derivatives

Text Sections: 14.2

MODULE 15: Reactions of aromatic Compounds
Electrophilic Aromatic Substitution Reactions
A General Mechanism for Electrophilic aromatic substitution
Reactions of Benzenes
- halogenation
- nitration
- sulfonation
- Friedel-Crafts alkylation
- Friedel-Crafts Acylation
- limitation of Friedel-Craft reactions
Synthetic Applications of Friedel-Crafts Acylations: The Clemmensen Reduction
Substituents can affect both the reactivity of the ring and the orientation of the incoming group
- how do substituents affect reactivity?
- ortho-para directing groups and meta-directing groups
- electron-donating and electron-withdrawing substituents
- ortho-para directors
- deactivating groups: Meta directors
- halo substituents: Deactivating ortho-para directors
- classification of substituents

How substituents affect electrophilic aromatic substitution: A closer look
- reactivity: The effect of electron-releasing and electron-withdrawing groups
- inductive and resonance effects: Theory of orientation
- meta-directing groups
- ortho-para-directing groups
- ortho-para direction and reactivity of alkylbenzene

Reactions of the Side Chain of Alkylbenzenes:
- benzylic radicals and cations
- halogenations of the side chain: Benzylic radicals
- oxidation of the side chain

Alkenylbenzenes:
- stability of conjugated alkenylbenzenes
- addition reaction to the double bond of alkenylbenzenes

Synthetic Applications
- use of protecting and blocking groups
- orientation in substituted benzenes

Allylic and Benzylic Halides in Nucleophilic Substitution Reactions

Text Sections: 15.1-15.15

Homework: Chapter 15: 3, 4, 5, 6, 7, 8, 9, 14, 15, 16, 17, 18, 24, 30, 31, 32, 33, 34, 35, 36, 37, 38, 44.

MODULE 16: Aldehydes and Ketones. Nucleophilic Addition to the Carbonyl Group

Nomenclature of Aldehydes and Ketones
Physical Properties
Synthesis of aldehydes:
- aldehyde by oxidation of 1° alcohols
- aldehydes by ozonolysis of alkene
- aldehydes by reduction of acyl chlorides, esters, and nitriles

Synthesis of ketones:
- ketones from alkenes, arenes, and 2° alcohols
- ketones from nitriles

Nucleophilic Addition to the Carbon-oxygen Double Bond
- relative reactivity of aldehydes versus ketones
- reversibility of nucleophilic addition to the carbon-oxygen double bond
- addition products can undergo further reactions

The addition of alcohols: Hemiacetals and acetics
- hemiacetals
- acetals
- acetals are used as protecting groups

The addition of primary and secondary amines
- oximes and hydrazones

The addition of hydrogen cyanide: Cyanohydrins

The addition of Ylides: The Wittig reaction
- how to plan a Wittig synthesis

Oxidation of aldehydes
Tollen’s test (silver mirror test)

Spectroscopic properties of aldehydes and ketones.
Summary of aldehyde and ketone addition reactions


Homework: Chapter 16: 1, 3, 4, 5, 6, 10, 12, 13, 16, 17, 19, 20 (a-i), 22(a-e, no b), 26(a-d), 29, 30(a-g), 31, 32, 33, 35(a, b, d), 46, 47.

MODULE 17: Carboxylic Acids and their Derivatives

Introduction
Nomenclature and physical Properties
- carboxylic acids
- carboxylate salts
- acidity of carboxylic acids
- dicarboxylic acids

Carboxylic acid Derivatives:
- esters
- carboxylic anhydrides
- acyl chlorides
Spectroscopic Properties of Acyl Compounds
- $^1$H NMR
- IR spectra

Preparation of Carboxylic acids by:
- oxidation of alkenes
- oxidation of aldehydes and primary alcohols
- oxidation of alkylbenzene
- hydrolysis of cyanohydrins and other nitriles
- carbonation of Grignard reagents

Acyl substitution: Nucleophilic Addition – Elimination at the Acyl carbon
- relative reactivity of acyl compounds

Acyl chlorides
- synthesis of acyl chloride using thionyl chloride

Synthesis of esters: Fischer esterification
- mechanism of the esterification reaction

Text Sections: 17.1 – 17.7. (no 17.3 (4), and 17.5 A, 17.6)
Homework: Chapter 17: 1, 3, 4, 5, 6, 7, 18, 19, 28, 29, 31, 33(a, c), 35, 36, 37.

MODULE 20: Amines
Nomenclature of Amines
- arylamines

Physical Properties and structure of amines
- basicity of amine : Amine salts
- basicity of arylamines
- amines versus amides
- solubility of amines in aqueous acid

Preparation of amines
- through nucleophilic substitution reactions
- the Gabriel synthesis
- preparation of aromatic amines through reduction of nitro compounds
- preparation of primary, secondary, and tertiary amines through reductive amination
- preparation of primary, secondary, or tertiary amines through reduction of nitriles, oximes, and amides

Spectroscopic analysis of Amines
Text Sections: 20.1(A) – 20.3(A-E, no B, F), 20.4, 20.11
Homework: Chapter 20: 4, 5, 7(a,b, e), 10, 19(a-c), 22(a-f), 46.