

Study Guide - Concepts to Understand

Chapter 1: Structure and Bonding

- Orbitals - atomic and molecular
- Hybridization

Chapter 2: Bonding and Molecular Properties

- Electronegativity and dipole moments
- Resonance
- Acids and Bases - Brønsted–Lowry and Lewis definitions

Chapter 3: Alkanes and Cycloalkanes

- Functional groups - know them
- Naming alkanes
- Alkane properties
- Naming cycloalkanes (including cis/trans)

Chapter 4: Stereochemistry (Conformations) of Alkanes and Cycloalkanes

- Alkane conformations (ethane, propane, butane)
- Newman Projections - eclipsed, staggered, gauche, anti
- Strain energy - torsional, angle, steric
- Cycloalkane conformations: cyclopropane – planar
cyclobutane – puckered
cyclopentane – envelope
cyclohexane – chair
- Conformational analysis of substituted cyclohexanes
mono-substituted or multiple substituents

Chapter 5: Overview of Organic Reactions

- Types of organic reactions: addition, elimination, substitution, rearrangement
- Polar, radical, and pericyclic reactions
- Kinetics (reaction rates) and Thermodynamics (equilibria)
- Energy diagrams
- Intermediates and transition states

Chapter 6: Alkenes – Structure and Reactivity

- Degree of Unsaturation: How is it determined? What does it mean?
- Electronic Structure: hybridization, stereochemical consequence (two isomers)
- Alkene naming (including E and Z)
- Alkene stability: Is more substitution good or bad for alkene stability? Why?
- Electrophilic Additions: **mechanism**, regiochemistry (Markovnikov's Rule), reason for regiospecificity
- Carbocation stability: Is more substitution good or bad for carbocation stability? Why?
- Hammond Postulate: What does the transition state more closely resemble?
- Substituent effects on transition states.
- Carbocation rearrangements: 1,2-hydride, and 1,2-alkyl shifts

Chapter 7: Alkenes – Synthesis and Reactions

- Alkene Synthesis:
 - Dehydrohalogenation (strong base [like KOH, NaNH₂], ethanol)
 - Dehydration (H₂SO₄, water, THF)
- Halogen (Br₂ or Cl₂) Addition (X₂, CCl₄)
 - **mechanism** (bromonium, chloronium ion intermediate)
 - anti stereochemistry
- Halohydrin Formation (X₂, H₂O)
 - **mechanism**
 - Markovnikov regiochemistry (Br adds first, ends up on least sub. C)
 - anti stereochemistry
- Hydration
 - Oxymercuration (**1.** Hg(OAc)₂, H₂O, THF **2.** NaBH₄)
 - **mechanism**
 - Markovnikov regiochemistry
 - anti stereochemistry (usually not important - adding H in last step)
 - Hydroboration/Oxidation (**1.** BH₃, THF **2.** H₂O₂, NaOH, H₂O)
 - **mechanism** (of first step only – not H₂O₂, NaOH step)
 - anti-Markovnikov regiochemistry - Why?
 - syn stereochemistry
- Simmons-Smith Reaction - Cyclopropanation
 - Alkene + CH₂I₂ with Zn(Cu) yields cyclopropanated compound
- Hydrogenation (H₂, catalyst)
 - usual catalysts: PtO₂ and Pd(C)
 - syn stereochemistry
 - steric effects on facial selectivity

- Hydroxylation (**1.** OsO₄, pyridine **2.** NaHSO₃, H₂O)
 - 1,2-diol is product (vicinal diol)
 - **intermediate**
 - syn stereochemistry
- Cleavage Reactions
 - 1,2-Diol Cleavage (HIO₄, H₂O, THF)
 - two carbonyl (C=O) compounds formed from diol carbons
 - Ozonolysis (**1.** O₃, CH₂Cl₂ **2.** Zn, CH₃CO₂H, H₂O)
 - two carbonyl (C=O) compounds formed from alkene carbons
 - **intermediates**
 - Potassium Permanganate Cleavage (KMnO₄, H₃O⁺)
 - RR'C=C gives ketone (RR'C=O)
 - RHC=C gives carboxylic acid (RCO₂H)
 - H₂C=C gives CO₂
- Radical Addition of HBr (HBr, peroxides)
 - **mechanism**
 - anti-Markovnikov product – Why?
- Radical stability: Is more substitution good or bad for radical stability? Why?

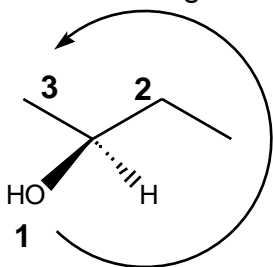
Chapter 8: Alkynes

- Electronic structure - hybridization, π bond strengths
- Alkyne naming
- Preparation – Dehydrohalogenation (strong base [like KOH or NaNH₂], ethanol)
 - from vicinal dihalide or from vinyl halide
- Addition of HX (HX, CCl₄)
 - **mechanism**
 - Markovnikov
 - One equivalent of HX versus excess HX
- Addition of Br₂, Cl₂ (X₂, CCl₄)
 - trans selectivity
 - One equivalent X₂ versus excess X₂
- Hydration
 - Mercuric Ion Addition (HgSO₄, H₂SO₄, H₂O)
 - **mechanism** (first step only – not H₂SO₄ displacement of Hg⁺)
 - Markovnikov formation of enol, tautomerization to ketone
 - terminal alkyne becomes methyl ketone
 - tautomerization mechanism
 - Hydroboration/Oxidation (**1.** BH₃, THF **2.** H₂O₂, NaOH, H₂O)
 - **mechanism** (first step only – not H₂O₂ and NaOH step)
 - anti-Markovnikov formation of enol, tautomerization to carbonyl
 - terminal alkyne becomes aldehyde

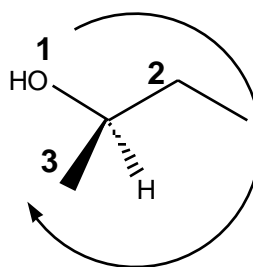
- Reduction
 - Hydrogenation
 - H₂ with regular Pd(C) or PtO₄ yields alkane
 - H₂ with Lindlar's Catalyst yields **cis** alkene (syn addition)
 - Lithium or Sodium Reduction (Na or Li, NH₃)
 - yields **trans** alkene
- Oxidative Cleavage
 - KMnO₄ and Ozonolysis give same products (same reagents/conditions as for alkene cleavages)
 - R-C≡C-H gives RCO₂H and CO₂
- Alkyne Acidity/Alkynes as nucleophiles
 - removal of terminal alkyne H with strong base (NaNH₂)
 - reaction with 1° alkyl halide (electrophile)
 - **mechanism**
 - Terminal alkynes from H-C≡C-H and alkyl halide
 - Internal alkynes from R-C≡C-H and alkyl halide
- Organic Synthesis
 - Work BACKWARDS
 - PRACTICE, PRACTICE, PRACTICE

Chapter 9: Stereochemistry

- Enantiomers - non-superimposable mirror images
- Optical activity - bending of polarized light by chiral molecules
- Diastereomers - stereoisomers that are NOT enantiomers - have inverted stereochemistry at some (not all) chiral centers
- Meso compounds - molecules with chiral (stereogenic) centers that are nonetheless achiral (contain an internal plane of symmetry)
- Racemic mixtures - 50/50 mix of two enantiomers
- Assigning R and S configuration:



"S" enantiomer



"R" enantiomer

When 4th ranked substituent is in the **back**, clockwise = **R**, counterclockwise = **S**

When 4th ranked substituent is in the **front**, reverse the above convention

- Fischer Projections - Rules for manipulation and rules for assigning R, S configuration
- Stereochemistry of some reactions:
 - HBr addition to alkenes – no selectivity
 - X₂ addition to alkenes – anti selectivity

Chapter 10: Alkyl Halides

- Preparation of alkyl halides from alcohols (1°, 2° alcohol: SOCl₂ or PBr₃; 3° alcohol: HX)
- Radical halogenation of alkanes
- Radical allylic bromination (allylic radical stability)
- Making nucleophiles from alkyl halides - organometallic reagents
 - Grignard Reagents – alkyl magnesium compounds
 - Alkyl Lithium Reagents – alkyl lithium compounds
 - Gilman Reagents – diorganocopper reagents
- Organic Synthesis – alkyl halides are electrophiles, and they can be converted into nucleophiles (organometallic reagents)

Chapter 11: Reactions of Alkyl Halides: Nucleophilic Substitutions and Eliminations

- S_N2 reactions
 - Stereochemistry (inversion)
 - Characteristics (polar aprotic solvents, non-hindered substrates, good nucleophiles, good leaving groups)
 - Mechanism - Bimolecular (two molecules involved in rate determining step)
- S_N1 reactions
 - Stereochemistry (loss of stereochemistry in planar intermediate)
 - Characteristics (polar solvent, substrates that yield stable carbocations, nucleophile not important, good leaving group)
 - Mechanism - Unimolecular (one molecule involved in rate determining step)
- E2 reactions
 - Geometric requirement for leaving group and adjacent H (antiperiplanar)
 - Stereochemical consequences of antiperiplanar transition state (E vs. Z)
 - Regioselectivity of eliminations - Zaytsev's Rule (more substituted C=C)
 - E2 reactions and cyclohexane conformations
 - Mechanism – Bimolecular

- E1 Reactions
 - No geometric requirement
 - Stereochemical consequence - planar carbocation intermediate
- When is each type favored? For 1°, 2°, and 3° substrates

Chapter 17: Alcohols

- Naming alcohols
- Properties of alcohols (H-bonding, acidity, basicity, etc.)
- Synthesis of alcohols
 - Hydroboration / Oxidation of alkenes (ch. 7)
 - Oxymercuration of alkenes (ch. 7)
 - Osmium Tetroxide Dihydroxylation of alkenes (ch. 7)
 - Reduction of carbonyl compounds
 - NaBH₄ reduction of aldehydes and ketones to alcohols
 - LiAlH₄ reduction of esters and carboxylic acids to alcohols
 - Addition of a Grignard Reagent to a carbonyl compound (mechanism ch. 19)
- Reactions of Alcohols
 - E1 Elimination of 3° alcohols to alkenes with H₃O⁺ – **mechanism**
 - E2 Elimination of 2° and 3° alcohols with POCl₃ and pyridine – **mechanism**
 - Conversion of 1° and 2° alcohols to alkyl bromides with PBr₃ – **mechanism (S_N2)**
 - Conversion of 1° and 2° alcohols to alkyl chlorides with SOCl₂ – **mechanism (S_N2)**
 - Conversion of 3° alcohols to alkyl halides with HX – **mechanism (S_N1)**
 - Conversion to Tosylates with TosCl – purpose? Think S_N2 stereochemistry
 - Oxidation of 1° alcohols to carboxylic acids with Jones' Reagent (CrO₃, H₂SO₄, H₂O, acetone) – **mechanism (E2)**
 - Oxidation of 1° alcohols to aldehydes with PCC
 - Oxidation of 2° alcohols to ketones with Jones' Reagent or PCC
 - Conversion to Silyl Ether with TMSCl – Protecting Group (removed with acid or tetrabutylammonium fluoride (TBAF))
- Acidity of phenols - including "tuning"
- Synthesis of phenols
 - Alkali fusion (from arylsulfonate)
 - From aryl halide via benzyne intermediate (ch. 16)
 - Hydrolysis of Arenediazonium
- Reactions of phenols
 - Ester formation from acid halide
 - Ether formation via Williamson Synthesis

- Electrophilic Aromatic Substitutions (ch. 16)
- Kolbe-Schmitt carboxylation – **mechanism**
- Oxidation with $(\text{KSO}_3)_2\text{NO}$, H_2O to form quinone
 - and reverse with SnCl_2 , H_2O or NaBH_4
- Claisen rearrangement of allyl phenyl ether to o-allylphenol – **mechanism**

Chapter 18: Ethers

- Naming Ethers
- Synthesis of Ethers
 - Williamson conditions (Alcohol + base (like NaH) + alkyl halide **or** alcohol + Ag_2O + alkyl halide)
 - Alkoxymercuration of alkenes ($\text{Hg}(\text{O}_2\text{CCF}_3)_2$, ROH) – can't make di-3° ether
- Reactions of Ethers
 - Acidic Cleavage – **mechanism**
 - Epoxide formation from alkenes – MCPBA – **mechanism**
 - Epoxide formation from halohydrins – base – **mechanism**
 - Basic / Nucleophilic opening of epoxides – regiochemistry – **mechanism**
 - Acidic opening of epoxides – regiochemistry