

OUTLINE OF CHEMISTRY 341 NOTES (Prof. Walker)

0. INTRODUCTION: Review Of Concepts From General Chemistry

0.1. Atomic & Molecular Structure

- 0.1.1. The atom
- 0.1.2. s and p orbitals
- 0.1.3. Bonding
 - ionic & covalent
- 0.1.4. Polarity of bonds
- 0.1.5. Formal charges
- 0.1.6. Resonance hybrids
 - definition
 - judging major/minor
 - common types: C=Y, aromatic, C=Y+, allylic
- 0.1.7. Structural formulae
 - condensed
 - line-angle

0.2. Acidity and Basicity

- 0.2.1. Bronsted-Lowry acids/bases
 - acid = H⁺ donor, base = H⁺ acceptor
 - conjugate acids/bases
 - effect of electronegativity, atom size, bond strength, resonance
- 0.2.2. Lewis acids/bases
 - Lewis acid = e- pair acceptor = electrophile
 - Lewis base = e- pair donor = nucleophile

I. MOLECULAR STRUCTURE & PROPERTIES

I.1. Molecular Orbitals

- I.1.1. Combining atomic orbitals, σ and π bonding
 - s + s, s + p, p + p => σ , and p + p side-on => π
 - antibonding orbitals (σ^* , π^*)
 - energy diagrams
 - double & triple bonds
 - s can rotate, p can not
- I.1.2. Hybrid orbitals
 - sp hybrid, structure of ethyne (acetylene), triple bond ($1\sigma + 2\pi$)
 - sp² hybrid, structure of ethene, double bond ($1\sigma + 1\pi$)
 - sp³ hybrid, structure of methane, ethane, single bond (σ only, no π)

I.2. Basic Isomerism

- I.2.1. Structural Isomerism
- I.2.2. Stereoisomers

I.3. Intermolecular Forces

- I.3.1. Comparison of attractive forces
 - Ionic, dipole-dipole, London forces

I.4. Functional Groups

II. ALKANES

II.1. Introduction

- Definition & examples

II.2. Nomenclature

- II.2.1. Simple alkanes
- II.2.2. Simple alkyl groups
- II.2.3. Complex alkanes
- II.2.4. Properties & uses of alkanes
- II.2.5. Angle strain in cycloalkanes

II.3. Conformations

- II.3.1. Ethane
- II.3.2. Propane
- II.3.3. Butane
 - Totally eclipsed, gauche, eclipsed, anti
- II.3.4. Cyclopropane, cyclobutane, cyclopentane
- II.3.5. Cyclohexane
 - Chair (major form), chair, half-chair, twist-boat
 - Two chairs possible
 - Axial & equatorial positions
- II.3.6. Monosubstituted cyclohexanes
 - Bigger groups "prefer" to be equatorial
- II.3.7. Disubstituted cyclohexanes
 - More stable form has bigger groups equatorial

III. FREE RADICAL HALOGENATION OF ALKANES

III.1. What is a Free Radical?

III.2. How Do Free Radicals React?

- Initiation: Radicals formed
- Propagation: A cycle in which reactants go to product, and the initial radical reacts & re-forms
- Termination: Any two radicals combine

III.3. Halogenation of Alkanes

- III.3.1. Methane
- III.3.2. More complex alkanes (e.g. propane)
 - Radical stability ($3^\circ > 2^\circ > 1^\circ$) determines product composition.
- III.3.3. Summary

IV. PHYSICAL ORGANIC CHEMISTRY

IV.1. Introduction

- Thermodynamics (mainly reversible rxns, how *far* rxns go)
- Kinetics (mainly irreversible rxns, how *fast* rxns go)

IV.2. Thermodynamics

IV.2.1. Equilibrium

IV.2.2. Energy & entropy

- $\Delta G^\circ = \Delta H^\circ - T\Delta S^\circ$ so entropy becomes more important as we increase temp.
- Predicting ΔH for rxns using bond dissociation energy

IV.3. Reaction Coordinate Diagrams

- Transition state, ΔH , activation energy

IV.4. Kinetics

IV.4.1. Reaction mechanisms

- Rate determining step (rate for this determines rate for overall rxn)
- Hammond's postulate

IV.4.2. Reaction order

IV.4.3. Radical halogenation revisited.

- Hammond's postulate explains how stability of intermed. radical affects course of rxn.

IV.5. Reactive Intermediates

IV.5.1. Carbocations (R^+)

IV.5.2. Free radicals ($R\cdot$)

IV.5.3. Carbanions (R^-)

IV.5.4. Carbenes

V. STEREOCHEMISTRY

V.1. Chirality

- Definitions
- How to test for chirality (quick way- mirror plane => achiral)
- Cyclohexanes: treat as if flat (unless on Triton!)
- Nitrogen lone pair flips at RT so achiral, sulfur & phosphorus don't so can be chiral

V.2. Physical Properties of Enantiomers

- V.2.1. General physical properties (identical)
- V.2.2. Optical activity
 - Specific rotation α , opposite for enantiomer

V.3. Nomenclature (R/S)

V.4. Molecules With Multiple Chiral Centers

- If all centers inverted, these are enantiomers
- If not all centers inverted, these are diastereomers
- If chiral centers present but overall molecule achiral, then MESO

V.5. Stereochemistry of Reactions

- V.5.1. Reactions at a single chiral carbon atom
 - Retention, inversion or racemization
 - Racemization occurs whenever rxn has an achiral intermediate (radical, carbocation)
- V.5.2. Reactions which form a new chiral carbon atom
 - Achiral starting material => racemic product (unless chiral agent used)
- V.5.3. Reactions which do not involve the chiral carbon atom
 - If no bonds broken to chiral carbon, configuration is unaffected

V. 6. Separating enantiomers

- Chromatography
- Classical resolution

VI. ALKYL HALIDES

VI.1. Introduction

- Classes, uses

VI.2. Nomenclature

VI.3. Structure & Properties

VI.4. Preparation of Alkyl Halides

VI.4.1. Free radical halogenation of alkanes & alkenes

- Basic reaction covered in sections III & IV of notes

- Use of NBS, particularly with alkenes

VI.4.2. Preparation from alkenes & alkynes (see later, VIII.3.1.1, IX.3.1.3)

VI.4.3. From alcohols

- 1°, 2° use PX_3 , 3° use HX

VI.5. Reactions of Alkyl Halides

- mainly nucleophilic substitutions or eliminations

VI.5.1. Conversion to alcohols (nucl. substitn)

VI.5.2. Reduction to alkanes (nucl. substitn)

VI.5.3. Dehydrohalogenation (elimination)

VII. NUCLEOPHILIC SUBSTITUTION

VII.1. Overview of Nucleophilic Substitution

VII.2. Physical Chemistry for S_N2 Reactions

VII.3. Physical Chemistry for S_N1 Reactions

VII.4. Factors Affecting Rate of Nucleophilic Substitution Reactions

VII.4.1. Nucleophile strength (S_N2 only)

- Charge, electronegativity, size of atom, steric hindrance, solvent effects

VII.4.2. Leaving group ability (both S_N1 and S_N2)

- Good leaving group is electron-withdrawing, stable, polarizable, breaks weak bond

- Solvent effects

- Examples of good leaving groups: halide, sulfonates, phosphates (biol.)

VII.4.3. Substrate (both S_N1 and S_N2)

- Steric crowding, carbocation stability mean S_N2 has $3^\circ < 2^\circ < 1^\circ$, S_N1 $1^\circ < 2^\circ < 3^\circ$

- Rearrangements possible with S_N1 (see VII.5.)

VII.5. Rearrangements (S_N1 only)

- H-shift, alkyl shift

VIII. ALKENES

VIII.1. Introduction

VIII.1.1. Structure

- 120° bond angles, geometric isomers

VIII.1.2. Nomenclature for alkenes

VIII.1.3. Uses

VIII.1.4. Stability

- Conjugation and alkyl groups stabilize the DB
- Steric crowding and small ring (angle) strain destabilize the DB

VIII.2. Preparation of Alkenes

VIII.2.1. Dehydrohalogenation of alkyl halides

VIII.2.1.1. E2 Elimination

- Uses a strong base such as NaOCH₃ or KOH
- 3° fastest but 1° still OK
- Anti Rule, Saytseff's Rule (unless hindered (KO^tBu), then Hofmann)

VIII.2.1.2. E1 Elimination

- Occurs with weak bases such as H₂O
- 3° fastest, never 1°
- No specific stereochem, but Saytseff's Rule applies

VIII.2.2. Dehydration of alcohols

- Follows E1 mechanism
- Reversible (see VIII.3.1.2)

VIII.2.3. Dehalogenation of *vic*-dibromides

VIII.2.4. Wittig reaction- next semester!

VIII.2.5. Reduction of alkynes

- Alkynes typically made from acetylide salts + 1° alkyl halides
- Na/liq. NH₃ gives trans, H₂/Lindlar gives cis isomer

VIII.3. Reactions of Alkenes

VIII.3.1. Addition Reactions

- Opposite of elimination

VIII.3.1.1. Addition of hydrogen halides

- Follows Markovnikov's Rule

VIII.3.1.2. Hydration of alkenes using acid

- Follows Markovnikov's Rule, but may lead to rearrangements. Reverse of VIII.2.2.
- Also see VIII.3.1.5.

VIII.3.1.3. Addition of bromine (Br₂) or chlorine (Cl₂) to give *vic*-dibromides

- Reverse of VIII.2.3.
- Anti addition is observed, due to halonium ion intermediate

VIII.3.1.4. Halohydrin formation

- Goes via same intermediate as VIII.3.1.3., so gives anti addition
- Follows Markovnikov's Rule
- Nucleophile in 2nd step may be water or ROH
- Works with Cl₂, Br₂ and I₂

VIII.3.1.5. Oxymercuration-demercuration of alkenes

- Higher yield than the equivalent reaction VIII.3.1.2.
- Also works with ROH, to make an ether

VIII.3.1.6. Anti-Markovnikov Reactions

- (A) Hydroboration-oxidation: Makes anti-Mv. alcohols
- (B) HBr in presence of ROOR/heat gives anti-Mv alkyl bromides

[VIII.3.1. Addition Reactions of alkenes, contd.]

VIII.3.1.7. Hydrogenation of alkenes

- Addition is *syn*

VIII.3.1.8. Addition of carbenes & carbenoids (NOT ON EXAM)

VIII.3.1.9. Epoxidation of alkenes

- MCPBA forms epoxide *syn*

- HCOOOH forms anti-dihydroxy compound (c.f. VIII.3.1.10)

VIII.3.1.10. Syn-dihydroxylation

VIII.3.2. Oxidative cleavage of alkenes

VIII.3.2.1. Ozonolysis/reduction

IX. ALKYNES

IX.1. Introduction

IX.1.1. Structure & Properties

IX.1.2. Nomenclature

IX.1.3. Acidity of terminal alkynes

IX.2. Preparations of Alkynes

IX.2.1. Alkylation of acetylide salts (also see VIII.2.5.)

- This is the only C-C bond forming reaction learnt this semester

IX.2.2. Double dehydrohalogenation of dihalides

IX.3. Reactions of Alkynes

IX.3.1. Additions to alkynes

IX.3.1.1. Hydrogenation/reduction (also see VIII.2.5.)

IX.3.1.2. Addition of Br₂ or Cl₂

IX.3.1.3. Addition of HBr or HCl

IX.3.1.4. Hydration of alkynes

- Products tautomerize to C=O

- Hg²⁺/H₂SO₄ gives Mv. product (a ketone)

- Si₂BH then OH⁻/H₂O₂ gives anti Mv. product (an aldehyde)

IX.3.2. Oxidative cleavage