

CHMC42H3

Organic Synthesis

Course Outline

LEC01: Fri 9:00-11:00, HW 215.

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Office Hours (S-507 A): Mon 1-2, Wed 1-2 and Fri 12-2

Required Text Books:

Francis A. Carey and Richard J. Sundberg, Advanced Organic Chemistry, 4th ed., Part B: Reactions and Synthesis, Plenum Press.

Method of Evaluation:

Lab Marks- 25%

Midterm Test- 30%

Final Exam- 45%

Lecture 1. Enolates and Enamines

- Review (Stereochemistry, NMR, IR and Mass spectroscopy)
- Generation of Carbon Nucleophiles by Deprotonation
- Regioselectivity in Enolate Formation
- Kinetic Control vs Thermodynamic Control Reactions
- Alkylation of Enolates
- Decarboxylation of β -ketoacids and Malonic Acids
- Silyl Enol Ethers
- Stereoselectivity in Enolate Formation
- Generation and Alkylation of Dianions
- Ambident Nucleophiles
- Intramolecular Alkylation of Enolates
- Alkylation of Esters, Lactones and Nitriles
- Enamines and Imine Anions
- Conjugate Addition or Michael Reaction

Lecture 2. Reactions of Carbon Nucleophiles with Carbonyl Groups

- Aldol Condensation
- Mixed Aldol Condensation
- Intramolecular Aldol Condensation and Robinson Annulation
- Mannich Bases

- Claisen Condensation
- Dieckmann Condensation
- Wittig Reaction
- Sulfur Ylides and Related Nucleophiles
- Reactions of Carbonyl Compounds with α -Trimethyl Silyl Carbanions
- Reactions of Ylide
- Reactions of Sulfur Ylides
- Darzen Reaction

Lecture 3. Functional Group Interconversion by Nucleophilic Substitution

- Alkyl Halides
- Nitriles
- Azides
- Alkylation of Amines and Amides
- The Classical Gabriel Procedure for Synthesis of Amines
- Transformation of Functional Groups by Nucleophilic Substitution
- Nucleophilic Cleavage of Carbon-Oxygen Bonds in Ether and Esters
- Cleavage of Methyl Ethers and Esters by Trimethyl Iodide
- Cleavage of Ethers by Boron Trifluoride
- Preparation of Reactive Reagents for Acylation
- Preparation of Ester
- Synthesis of Amides

Lecture 4. Electrophilic Additions to Carbon-Carbon Multiple Bonds

- Addition of Hydrogen Halides
- Synthesis Via Mercuration
- Addition of Halogen to Alkenes
- Iodolactonization
- Additions to Allenes and Alkynes
- The Addition of HCl, HBr and HI to Allenes
- Ketones by Hydration of Alkynes
- Addition at Double Bonds via Organoboranes
- Reactions of Organoboranes
- Replacement of Boron atom by an Amino Group
- Enantioselective Hydroboration
- Hydroboration of Alkynes
- Addition of Bromine to Vinylborane

Lecture 5. Reduction of Carbonyl and Other Functional Groups

- Stereochemistry of Hydrogenation and Some Alkenes
- Hydrogenolysis
- Reduction of Carbonyl Compounds
- Reduction of Other Functional Groups by Hydride Donors
- Conversion of Epoxides and Alcohols

- Hydrogen Atom Donors
- Dissolving-Metal Reduction
- Birch Reduction
- Reductive Carbon-Carbon
- Reductive Deoxygenation of Carbonyl Groups
- Shapiro Reaction

Lecture 6. Cycloaddition, Unimolecular Rearrangements and Thermal Eliminations

- Diels-Alder Addition
- Enantioselective Diels-Alder Reaction
- The Diels-Alder Reaction: Dienes
- Stereospecificity
- Intramolecular Diels-Alder Reactions
- The Essential Characteristics of the Diels-Alder Cycloaddition
- [2+2] Cycloaddition and Other Reactions Leading to Cyclobutanes
- Intramolecular [2+2] Photochemical Cycloaddition Reaction of Dienes
- Photochemical Cycloaddition Reactions of Enones and Alkenes
- Photochemical Cycloaddition Reactions of Carbonyl Compounds with Alkenes
- [3,3] Sigmatropic Rearrangements: Cope and Claisen Rearrangement
- Cope Rearrangement of 1,5-Dienes
- Claisen Rearrangement
- Ene Reactions
- Decomposition of Cyclic Azo Compounds
- Photochemical and Thermal Decomposition of Cyclic Azo Compounds

Lecture 7. Organometallic Compounds of Group I and II Metals

- Synthesis of Grignard Reagents
- Preparation of Organo Metallic Reagents
- Organolithium Compounds by Metalation
- Preparing Organolithium by Metal-Metal Exchange
- Reactions of Organolithium and Organomagnesium Compounds
- Reactions with Carbonyl Compounds
- Synthetic Procedure Involving Grignard Reagents
- Organozinc Compounds
- 'Condensation of α -Halocarbonyl Compounds Using Zinc – The Reformatsky Reaction
- Organocadmium

Lecture 8. Reactions Involving Highly Reactive Electron-Deficient Intermediates

- Rearrangement of Carbocations
- Fragmentation Reactions
- Generation of Carbenes
- Addition Reactions

- Nitrenes and Related Intermediates
- Aromatic Substitution Reactions
- Nitration
- Halogenation

Lecture 9. Reactions Involving Highly Reactive Electron-Deficient Intermediates

- Friedel-Crafts Alkylations
- Friedel-Crafts Acylation Reaction
- Formylation with Carbon Monoxide
- Formylation with Hydrogen Cyanide
- Acylation with Nitriles
- Nucleophilic Aromatic Substitution
- Aromatic Diazonium Ions as Synthetic Intermediates
- Substitution by the Elimination-Addition Mechanism
- Substitution by the $S_{RN}1$ Mechanism

Lecture 10. Oxidations

- Oxidations with Cr(VI)
- Addition of Oxygen at Carbon-Carbon Double Bonds
- Epoxides from Alkenes and Peroxidic Reagents
- Anti-Hydroxylation
- Nucleophilic and Solvolytic Ring Opening of Epoxides
- Ozonolysis
- Glycol cleavage
- Bayer-Villiger Oxidation

Lecture 11. Protective Groups

- Hydroxyl-Protective Groups
- Alcoholysis
- Methoxymethyl and Methoxyethoxymethyl Protecting Groups
- Amine Protecting Groups
- T-Butoxy Carbonyl Group
- Carbonyl Protecting Groups
- Synthetic Equivalent Groups

Lecture 12. Stereoselective Synthesis

- Hydroboration
- Epoxidation
- Sharpless Epoxidation
- Additions to Carbonyl Bonds
- Models for Acyclic Substrates
- The Chelation Effect
- Nonchelating Polar Effects