Contents

Chemistry 220B Section One

Spring 2006

Instructor: Piotr Kaszynski, SC 7636, phone/fax: 322-3458,
E-mail: piotr.kaszynski@vanderbilt.edu
Class hours: T, TH 9:35-10:50 room SC 4309
Textbook: *Organic Chemistry, Sixth Edition* J. McMurry,
purchase of the accompaning study guide (*Organic Chemistry Study Guide and Solution Manual*) is strongly recommended
Office Hours: T 2-3, TH 3-4, or by appointment.

General Description

Chemistry 220B is built on foundation laid in CHEM 220A. We will study the preparation, basic characteristics, and chemical transformations of several important functional groups. This should give you the basis for the study of polyfunctional compounds in living organisms, research laboratories, or industry.

Date	**Topic**	**Chapter**
Jan 12, 17	Introduction and Review of Chapter 14	
Jan 19, 24	Benzene and Aromaticity	15
Jan 26, 31	Electrophilic Aromatic Substitution	16
Jan 31	*Review session 6:00-7:00 pm in 4309*	
Feb 2	**Exam 1** (Thursday)	
Feb 7, 9	Alcohols and Phenols	17
Feb 14	Ethers, Epoxides, Thiols, and Sulfides	18
Feb 16, 21	Aldehydes and Ketones	19
Feb 23	Carboxylic Acids and Nitriles	20
Feb 24	*Review session 6:00-7:00 pm in 4309*	
Feb 28	**Exam 2** (Tuesday)	
Mar 2	Carboxylic Acid Derivatives	21
	SPRING BREAK!	
Mar 14	Carboxylic Acid Derivatives (*cont*)	21
Mar 16, 21	Carbonyl α-Substitution Reactions	22
Mar 21	*Review session 6:00-7:00 pm in 4309*	
Mar 23	**Exam 3** (Thursday)	
Mar 28, 30	Carbonyl Condensation Reactions	23
Apr 4, 6	Amines	24
Apr 11, 13	Carbohydrates	25
Apr 17	*Review session 6:00-7:00 pm in 4309*	
Apr 18	**Exam 4** (Tuesday)	
Apr 20	Amino Acids, Peptides, and Proteins	26
Apr 25	Lipids and Nucleic Acids	27,28
May 4	**Final Exam**, Tuesday 9:00 am	

Homework

Textbook problems will be assigned but not graded. Answers will be posted when not available in the Study Guide. Working the problems is essential to learning Organic Chemistry.

Grading

Final grades will be awarded in accordance with the policies delineated in the undergraduate catalog. There will be four "in-class" 50 min exams (100 points each) and one comprehensive final exam (200 points). The final grade will be based on a total of 600 points.

Any questions you may have about an exam grade must be discussed with me within two class days after the test is returned.

Exams

No make up exams nor alternate exam final will be offered because they cannot be made of equal difficulty. If an hour exam is missed, the grade will be 0 unless the absence is determined by me to be excused in advance. For those who do not miss an exam and those whose absence is excused: if one half of the final exam grade is better than one of the exams, it will replace the worst exam grade. The course cannot be passed when more than one exam is missed. An excused absence from the final exam can be obtained only from the Dean's office, otherwise a grade M will be given in accordance with University policy.

Getting Help

Get help early if you need it! Falling behind in organic chemistry is no fun and can impede your future progress in the course because the material builds on itself. Special help sessions are scheduled before each exam, and a couple of practice exams will be available for study purposes. Remember, there is more material to study than last semester.

I encourage you to see me during my office hours to get help with questions and problems. Other sources of help include your lab instructor, lab TA, other organic texts, and your fellow students.

Honor Code

All aspects of the Vanderbilt honor code apply to this course. You must legibly write and sign the Vanderbilt Honor Pledge on every exam. Students are encouraged to work together on problems and to study in groups. Exams, however, must be taken on an individual basis with no external aids other than those specifically permitted in advance by the instructor.

Overall Goals of Chem 220B

- Learn the structure of organic molecules
- Learn general reactivity of organic functional groups
- Learn general mechanisms of organic reactions and formulate e- pushing representations for the mechanistic steps
- Learn the language of organic chemistry

Typical Organic Exam Format

5 sections

- Review, nomenclature, and terminology
- General knowledge
- Mechanisms
- Synthesis

Chapter 14 Review

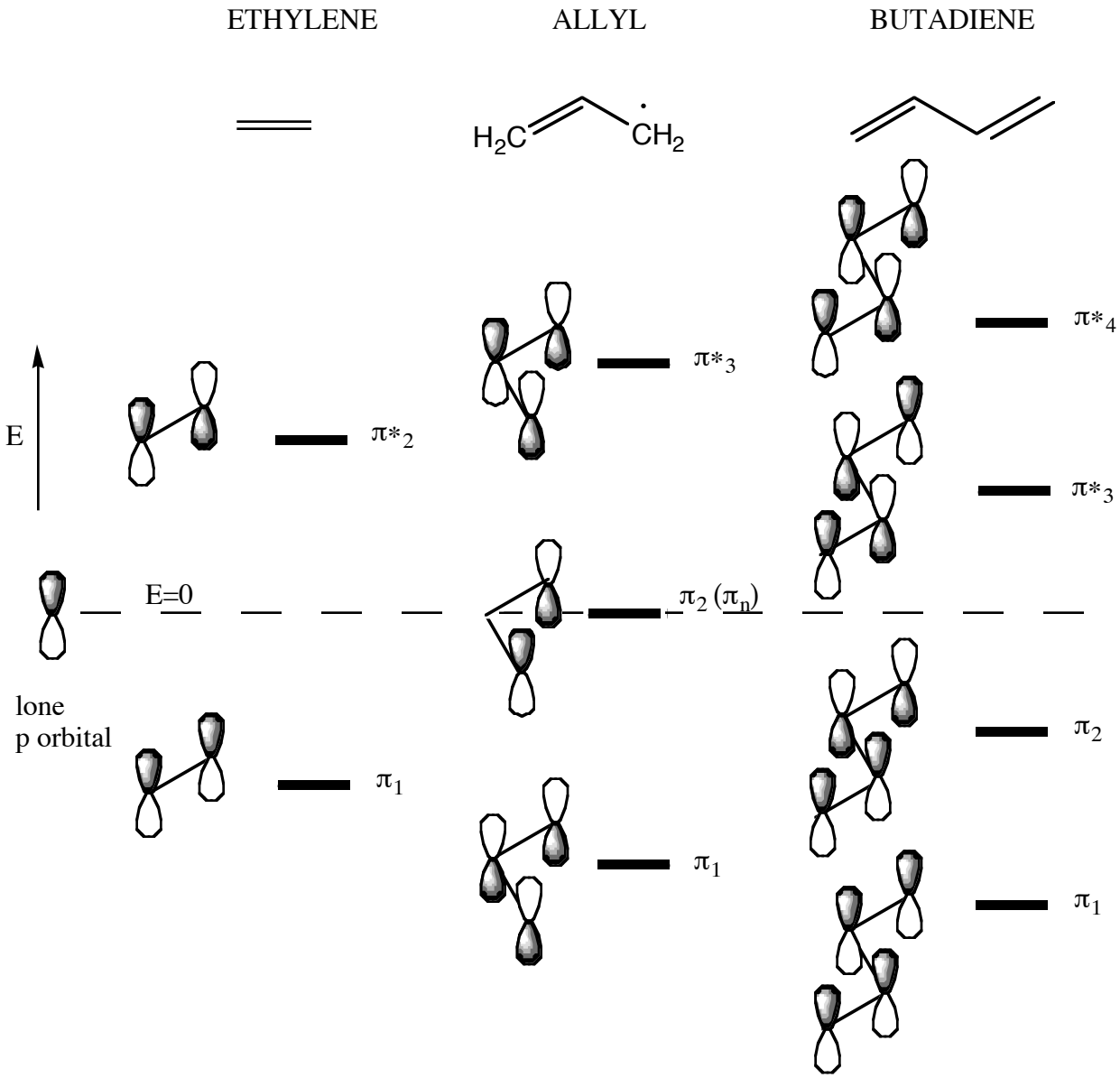
Conjugated Dienes and UV Spectroscopy

I. Conjugated dienes
- A. Structure: Atomic Hybridization and π Conjugation

II. Other Conjugated Systems
- A. π Molecular Orbitals of Simple Linear Conjugated Systems
  1. Ethene
  2. Allyl
  3. Butadiene
- B. Identification of HOMO and LUMO and Their Significance
  1. UV-vis Absorption in Relation to Electronic Excitation
  2. Diels-Alder Reaction

Problem:
Draw the π MO's for pentadienyl cation showing their relative energies, labels, spatial propertis, and electron population. The UV-vis absorption for the cation would involve ___ to ___ transition.

Orbital interaction scheme and hints for forming MO's from AO's



Note:

1. π MO's are symmetrically placed about a defined "zero E" line, that of an isolated *p* orbital

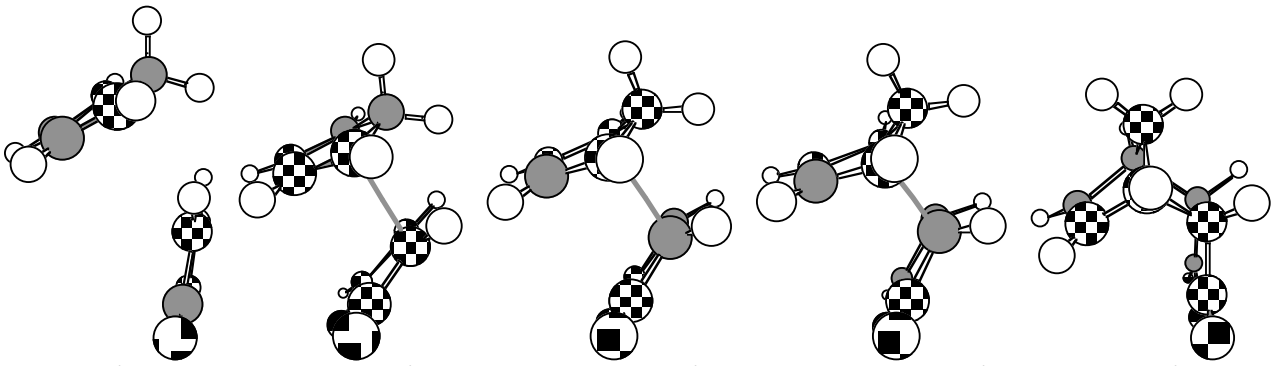
2. Number of *p* AO's is equal to number of p MO's

3. For linear π-conjugated systems, th lowest E orbital is completely bonding (all AO's "in-phase") and has 0 nodes. The number of nodes increases by 1 for each higher energy orbital with the highest E orbital being totally antibonding (all AO's "out-of-phase")

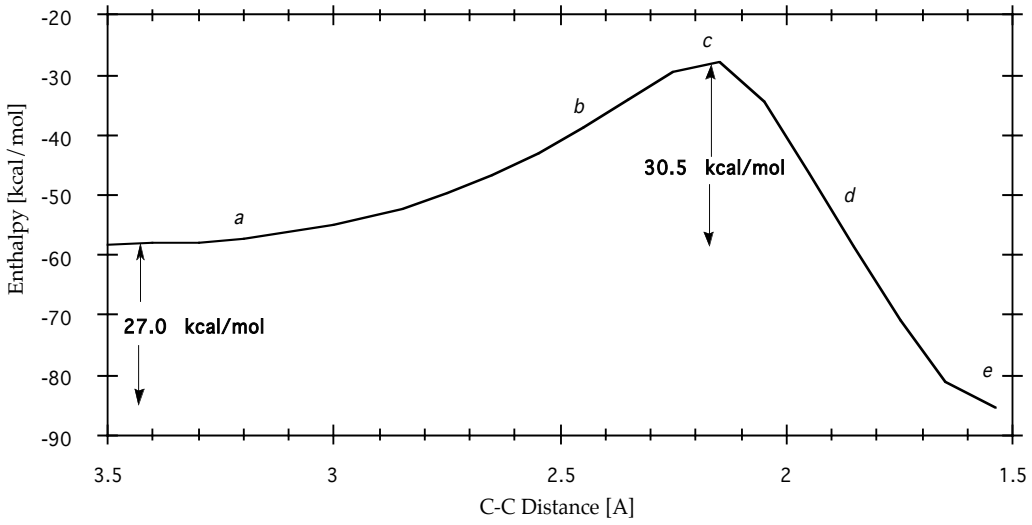
4. Nodes are symmetrically distributed in the orbital chain

5. MO energy spacing decreases as the number of conjugated *p* orbitals increases

Diels-Alder Reaction Path: Cyclopentadiene and maleic anhydride



a: d=3.20 Å *b*: d=2.45 Å *c*: d=2.15 Å *d*: d=1.85 Å *e*: d=1.54 Å



(PM3/MOPAC 6.0)

Chapter 15 Lecture Outline

Benzene and Aromaticity

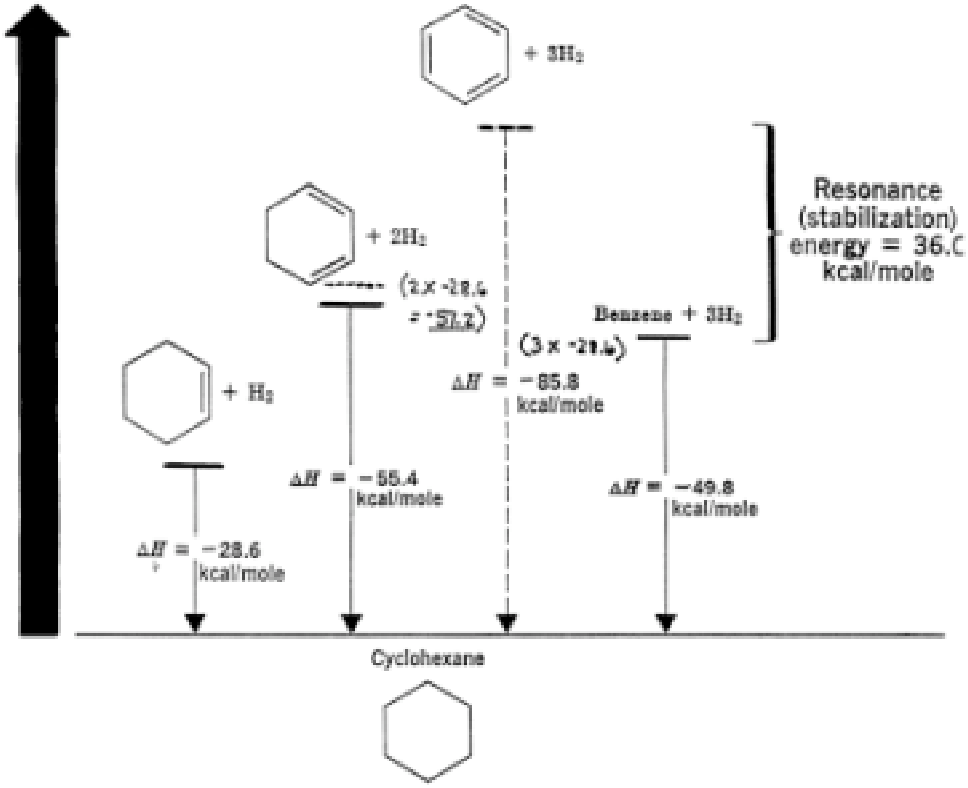
Problems: 1, 2, 3a-d, 4, 8, **10-14**, 17-21, **23**, 25, **27**, 28, **29**, 30, 31, 33-36, **38**, **39**, 40, 41, 43-45ab, **46**, 47, 48

I. Benzene and Derivatives
- A. Benzene Structure
- B. Nomenclature
- C. Reactivity of Benzene

II. Aromaticity
- A. π MO's of Benzene and Other Cyclic π Systems
- B. Hückel 4n+2 Rule

III. Other Aromatic Systems
- A. Aromatic Ions
- B. Heterocyclic Aromatics
- C. Polycyclic Aromatics (Benzenoid Compounds)

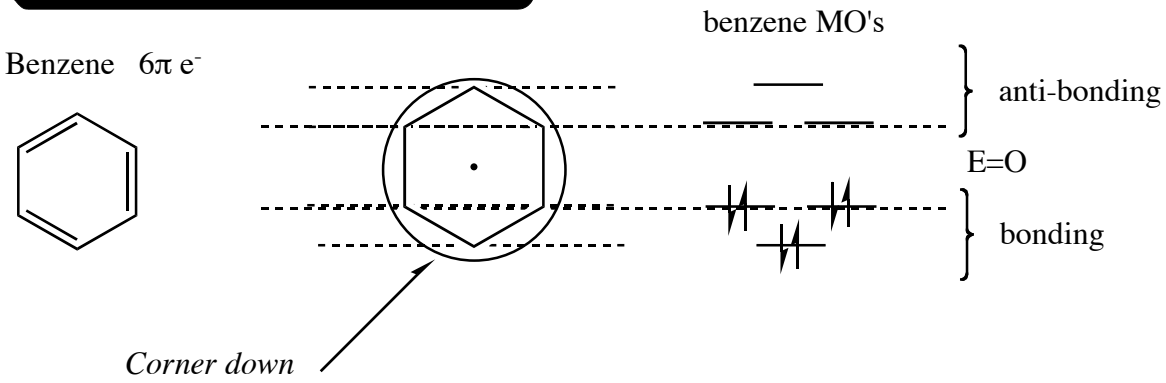
IV. Spectroscopy
- A. ^{1}H NMR
- B ^{13}C NMR
- C. IR



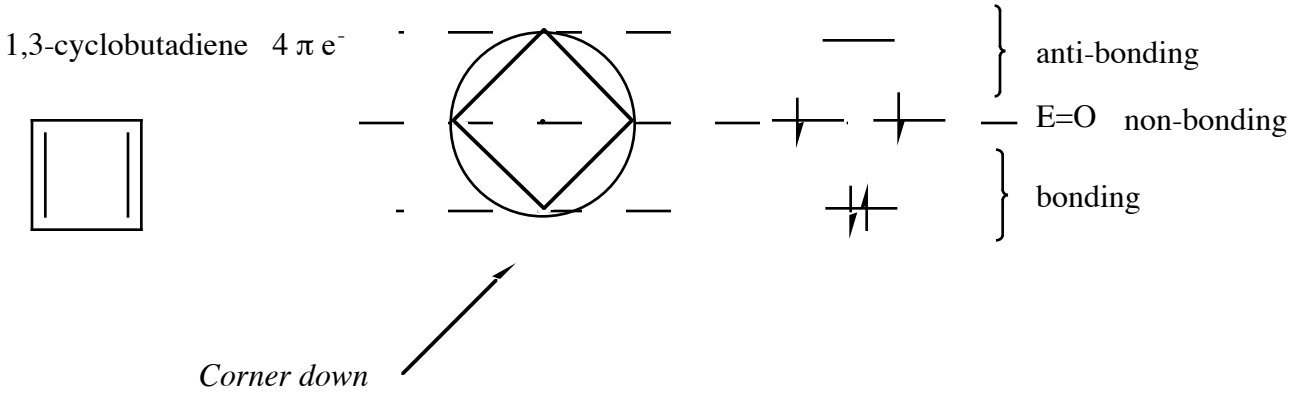
Relative stabilities of cyclohexene, 1,3-cyclohexadiene, 1,3,5-cyclohexatriene (hypothetical)), and benzene.

The Circle Trick

Aromatic Systems : 4n+2 e^-



Anti-aromatic Systems : 4n e^-



Try with cyclopropenyl and cyclopentadienyl cations.

Chapter 16 Lecture Outline

Chemistry of Benzene: Electrophilic Aromatic Substitution

Problems: 1, 4-7, **8**-**10**, 11, **13**, 14-16, 18, 23, 24, **25**, **27**, 28-31, 33-36,
40, **41**, 44-47, 49, 50, **51**, **54**, 55, 56, 59, 60, **62**, **65**, **70**, 73.

I. Electrophilic Aromatic Substitution

- A. Overview of reactions and mechanism of electrophilic substitution mechanism
  1. Halogenation
  2. Nitration
  3. Sulfonation
  4. Friedel-Crafts alkylation
  5. Friedel-Crafts acylation
- B. Substituent effect on electrophilic aromatic substitution
  1. Activating substituents
  2. Deactivating substituents
     a. *meta*-directing
     b. *ortho, para*-directing

II. Nucleophilic Aromatic Substitution

III. Benzyne

IV. Reactions at the side-chain of Alkyl and Alkenyl Benzenes

- A. Halogenation of alkyl benzenes
- B. Oxidation of alkyl and alkenyl benzenes

V. Reduction of Aromatic π Systems: High pressure hydrogenation

VI. Synthesis of Substituted Aromatics

The Aromatic Substitution Game

see *Journal of Chemical Education*, **1993**, *70*, 11

link: http://proquest.umi.com/pqdlink?Ver=1&Exp=01-16-2011&RQT=318&PMID=27231&clientId=622
accessible from Vanderbilt University

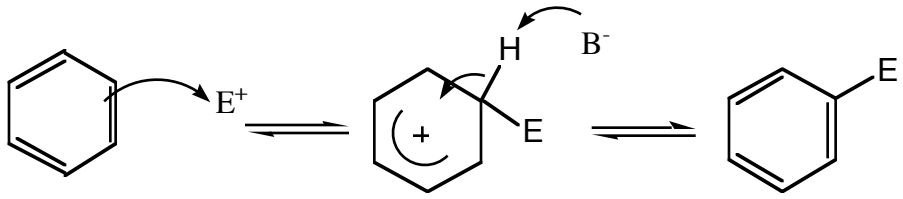
Important Concepts From Chapters 14-16

1. π-Conjugation is an array of mutually parallel *p* orbitals (empty or filled) on adjacent atoms (any atoms). The array can be:

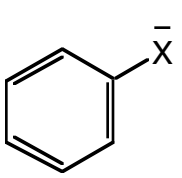
- linear ☞ polyenes
- cyclic ☞
  - aromatic if #of e^- in array =4n+2
  - anti-aromatic if #of e^- in array =4n
  - neither aromatic nor anti-aromatic if #of e^- in array =2n+1

2. Almost all bi-molecular chemical reactions proceed through interaction of HOMO of one reagent with LUMO of another one. Typically properties of a **nucleophile** are defined by its **HOMO** and properties of an **electrophile** are defined by its **LUMO**. In most cases these orbitals belong to the following group: σ, π, (n, π_n, p), π,* σ*, in order of increasing energy.

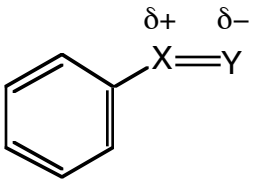
3. Aromatic molecules undergo electrophilic aromatic substitution reactions according to the following general scheme:



The rate of the reaction and the regiochemistry in the formation of di- and polysubstituted benzenes depends on π electron density in the aromatic compound and stability of the intermediate . These factors, in turn, are influenced by the elcectronic structure of the substituents present on the ring:



ortho, para directing



meta directing

Chapter 17 Lecture Outline

Alcohols &Phenolss

Problems: 1, 2, **4**, **6**, **7**, 8-10, 11, 12, **13**, **14**, 19, 21, **23**, 24-28, **30**, **31**, 33, 35-38, 40-42, 49, **52**, **57**, 60, 62, 64.

I. Nomenclature

II. General Properties
- A. Hydrogen bonding and Boiling points
- B. Acid-base reactions

III. Preparation of Alcohols
- A. Alkene hydration
  - 1. Oxymercuration-reduction ("Markovnikov" hydration)
  - 2. Hydroboration-oxidation ("anti-Markovnikov" hydration)
- B. Alkene di-hydroxylation (formation of 1,2-diols)
  - 1. *syn* di-hydroxylation with OsO_4
  - 2. *anti* di-hydroxylation *via* hydrolysis of epoxides
- C. Carbonyl group reduction (nucleophilic addition to the carbonyl)
  - 1. Hydride addition to aldehydes and ketones ($NaBH_4$ and $LiAlH_4$)
  - 2. Hydride addition to esters and carboxylic acids ($LiAlH_4$)
  - 3. Grignard reagent addition to aldehydes, ketones, esters and CO_2

IV. Reaction of Alcohols
- A. Deprotonation to form alkoxide anions
- B. Dehydration to form alkenes
- C. Conversion to alkyl halides
- D. Oxidation to carbonyl compounds
  - 1. Primary alcohols aldehydes
  - 2. Primary alcohols carboxylic acids
  - 3. Secondary alcohols ketones
- E. Alcohol functionality protection by silylation

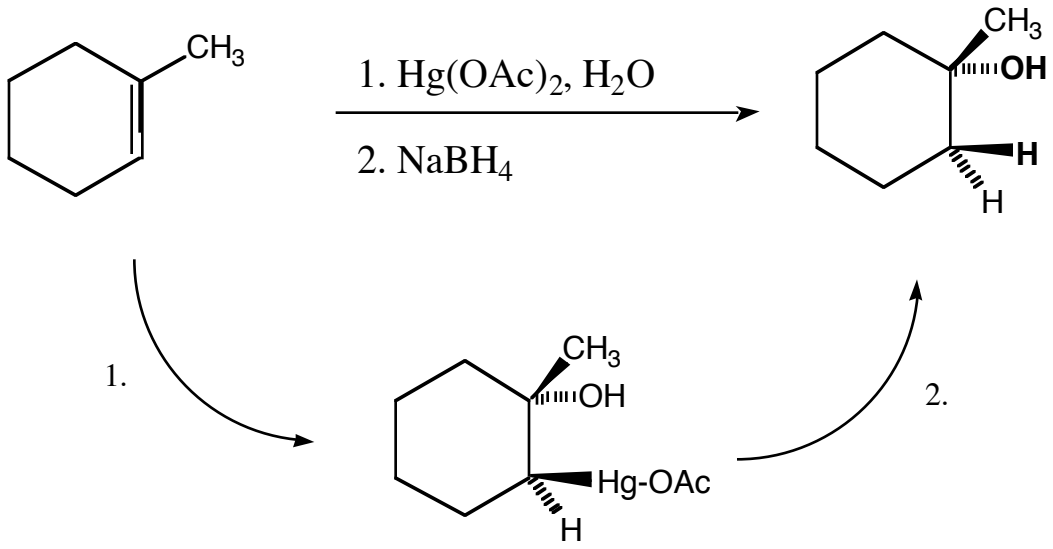
V. Preparation of Phenols
- A. The cumene method
- B. The sulfonic acid method

VI. Spectroscopy

Alkene Hydration (a review)

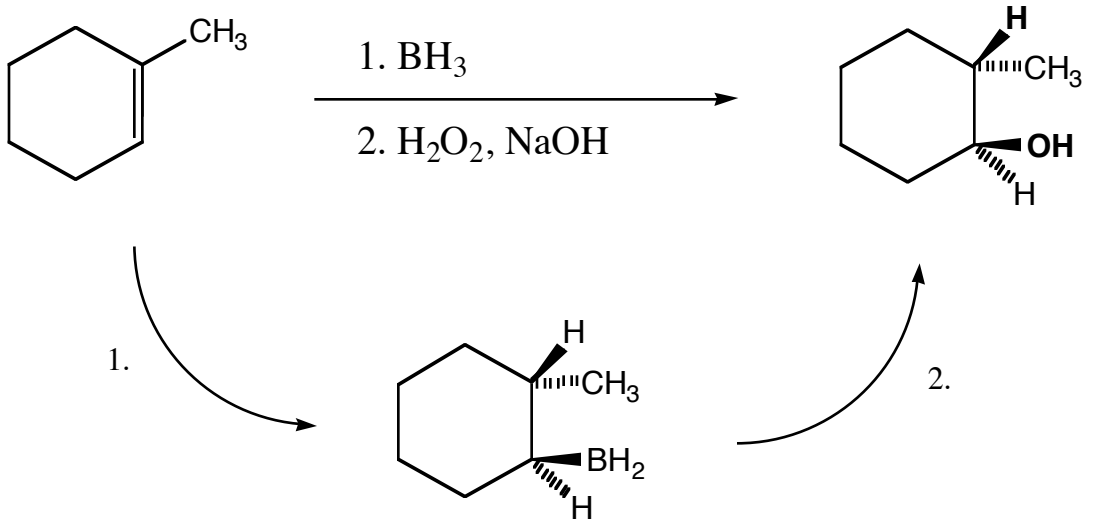
1. Oxymercuration-Reduction

Markovnikov orientation



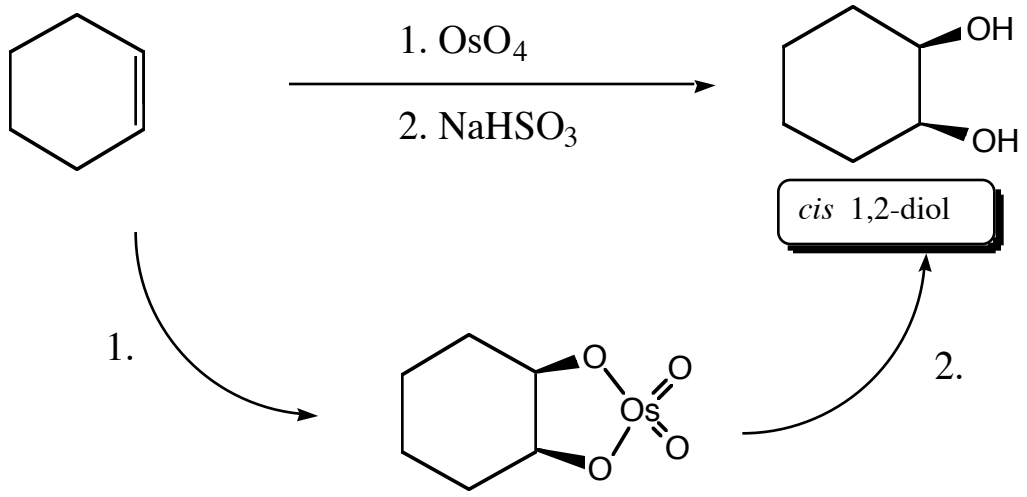
2. Hydroboration-Oxydation

anti-Markovnikov orientation

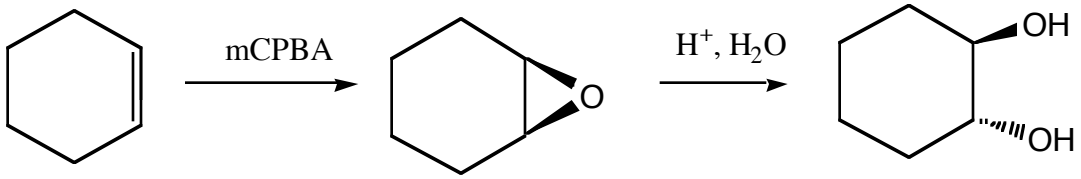


Alkene di-Hydroxylation to form 1,2-diols

1. *syn* di-hydroxylation with OsO_4

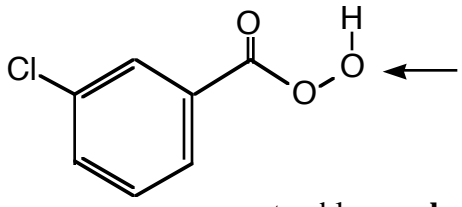


2. *anti* di-hydroxylation via epoxide formation and hydrolysis



an epoxide

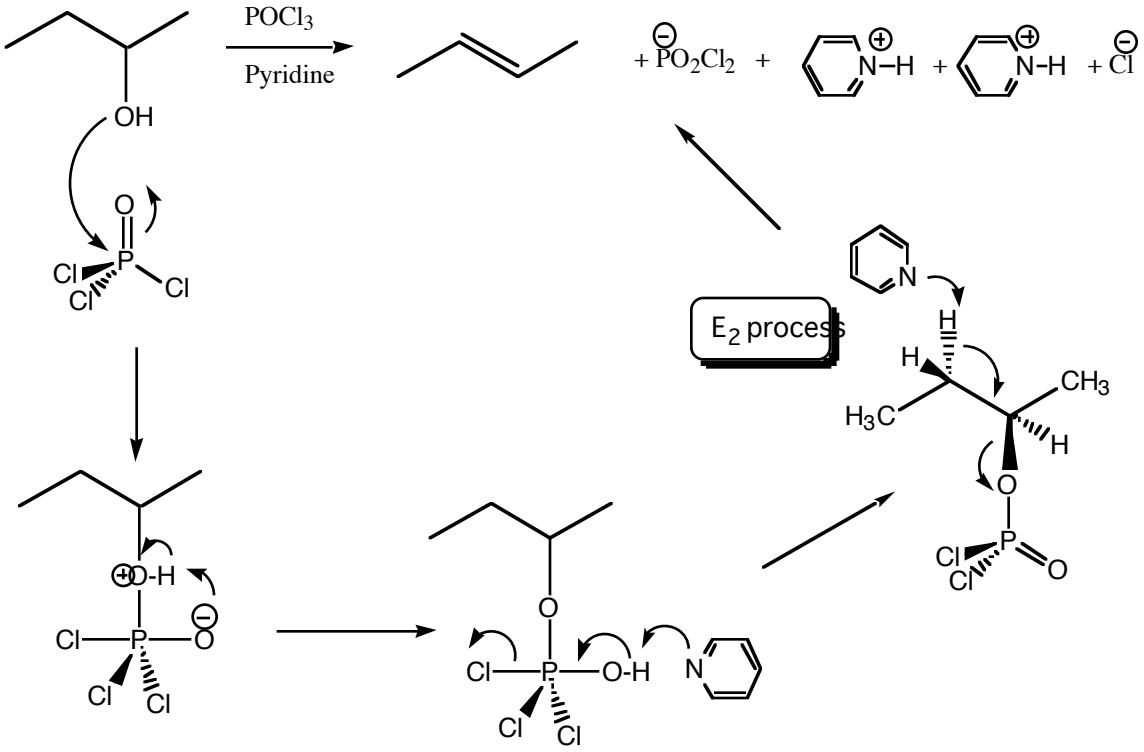
trans 1,2-diol



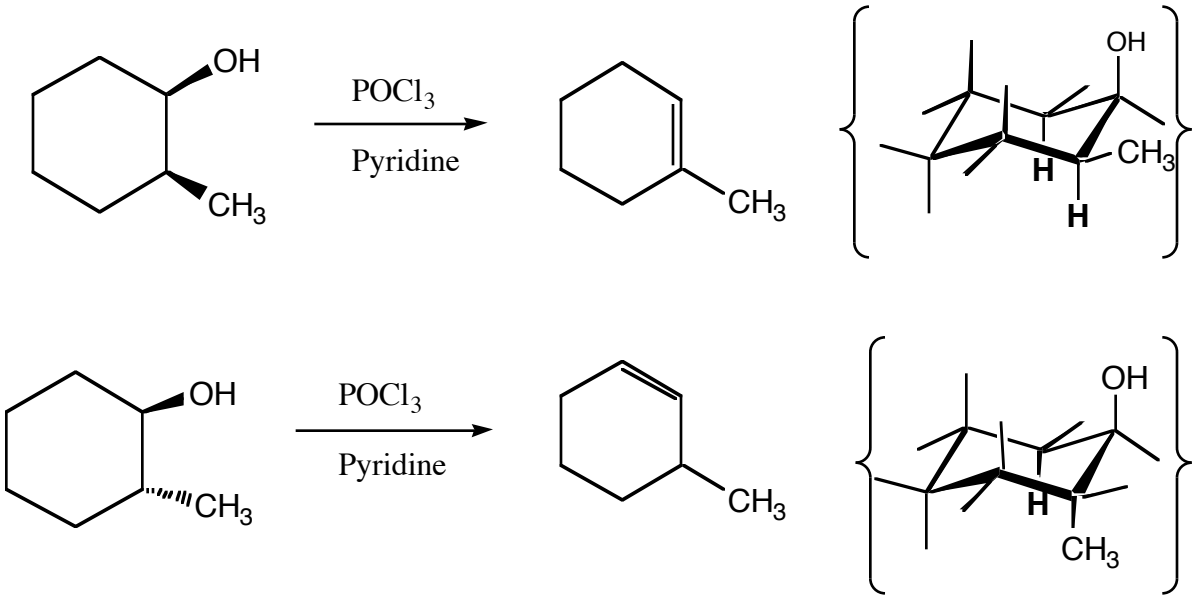
← this oxygen becomes epoxide oxygen

m*eta*-**c**hloro**per****b**enzoic **a**cid = mCPBA

Alcohol Dehydration to Form Alkene



Problem 13 (b & c)



Chapter 18 Lecture Outline

Ethers, Epoxides, Thiols & Sulfides

Problems: 1, **3**, 4-6, **7**, 8, 11-15, 17, 19, **21**-**22**, 24-30, 32-**34**, 40, **43**, **47**, 52, 54-55, 56c,d

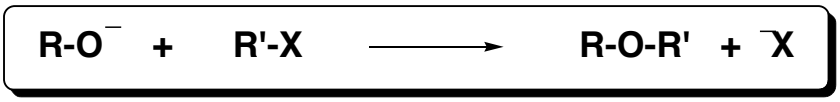
I. Nomenclature

II. Preparation of Ethers
- A. Williamson Ether Synthesis (S_N2 reaction)
- B. Alkoxymercuration-Demercuration of Alkenes
- C. Peracid Oxidation of Alkenes to form Epoxides

III. Reaction of Ethers
- A. Acidic Cleavage of Ethers
- B. Ring Opening of Epoxides
  1. Acid catalyzed ring opening
  2. Nucleophilic ring opening under neutral or basic conditions

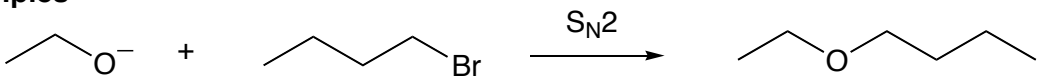
IV. Thiols, Sulfides, Sulfoxides, and Sulfones

Williamson Ether Synthesis

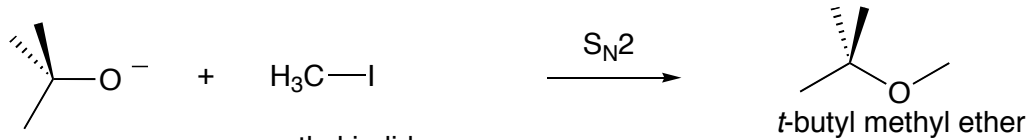


Alkyl halide R'-X must be primary for the Williamson Ether Synthesis

Examples

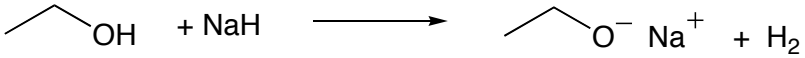


ethoxide butyl bromide butyl ethyl ether



t-butoxide methyl iodide *t*-butyl methyl ether

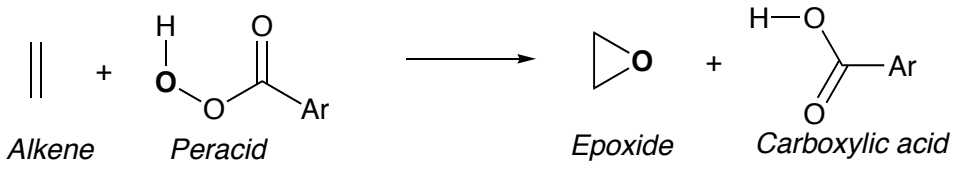
Alkoxides are made by deprotonation of alcohols



ethanol sodium ethoxide

Epoxidation of Alkenes by Peracids

Mechanism: a pericyclic reaction -cis addition of oxygen to C=C double bond

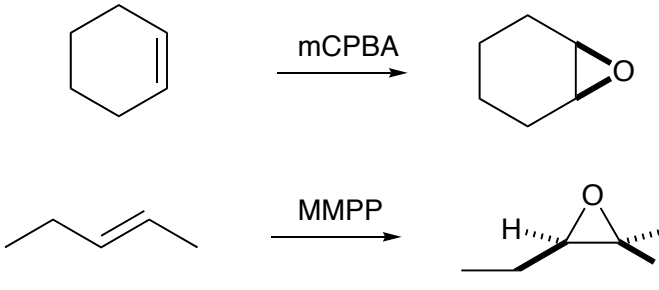


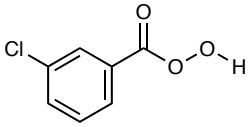
Typical Peracids

*** mCPBA Oxidation of Alkenes to Epoxides**

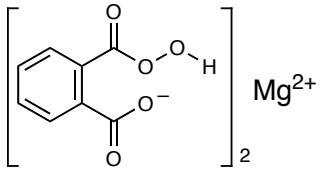
*** MMPP Oxidation of Alkenes to Epoxides**

Examples





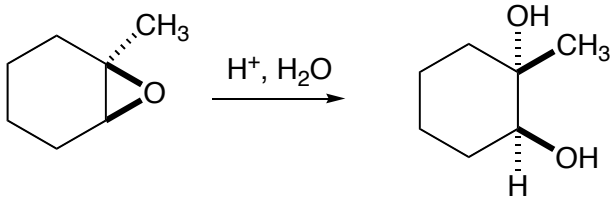
m-**c**hloro**per****b**enzoic **a**cid
m-CPBA



magnesium **m**ono**per****p**hthalate
MMPP

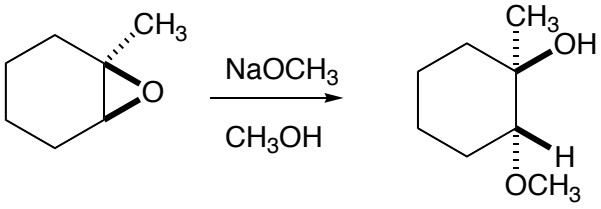
Epoxide Ring Opening

*** Acid Catalyzed**



protonation, S_N2 attack at most substituted site

*** Base Catalyzed or Nucleophilic Ring Opening**



"normal' S_N2 reaction

Chapter 19 Lecture Outline

Aldehydes & Ketones: Nucleophilic Addition to the Carbonyl

Problems: 1, 2, **3**, **4**, 5-9, 11-13, **16**, 18-21, 25, 27, 28, 32-**34**, 36-41, 43, 45, 46, 51, 55, 59ab, 61, 62, 65ab, 67bc.

I. The Carbonyl Group-General Comments

II. General Properties & Nomenclature

III. Preparation of Aldehydes
- A. Oxidation of primary alcohols
- B. Ozonolysis of alkenes
- C. Controlled reduction of esters

IV. Preparation of Ketones
- A. Oxidation of secondary alcohols
- B. Ozonolysis of alkenes
- C. Friedel-Crafts acylation of arenes
- D. Hydration of alkynes
- E. Cuprate addition to acid chlorides

V. Reaction of Aldehydes and Ketones
- A. Oxidation of aldehydes to carboxylic acids (via aldehyde hydrate)
- B. Nucleophilic addition reactions
  1. Hydration (addition of H_2O)
  2. Cyanohydrine formation (addition of HCN)
  3. Alcohol formation (addition of hydride or Grignard reagent)
  4. Imine formation (addition of R-NH_2)
     - a. oxime formation
     - b. semicarbazone formation
     - c. 2,4-dinitrophenylhydrazone formation
     - d. hydrazone
  5. Wolff-Kishner reduction (under basic condtitions)
  6. Clemmensen reduction (under acidic conditions)
  7. Enamine formation (addition of R_2NH)
  8. Acetal formation (double addition of ROH)
  9. Wittig reaction (addition of phosphorus ylides)
  10. Disproportionation of aldehydes: The Cannizzaro Reaction

VI. Nucleophilic addition to α,β-Unsaturated Aldehydes and Ketones
- A. Conjugate addition of primary and secondary amines
- B. Conjugate addition of "R^-" as organocuprates (R_2CuLi)

VII. Spectroscopy of Aldehydes and Ketones
- A. IR
- B. NMR (^1H and ^{13}C)
- C. MS

Chapter 20 Lecture Outline

Carboxylic Acids and Nitriles

Problems: 1a-d, 2, 3, **4**, **5**, 8-11, **12**, 13, 16, **20** -**26**, 28-29, 32-36, 38, **43**, 46-49, 53, 55.

I. Nomenclature

II. Acidity of Carboxylic Acids

III. Preparation of Carboxylic Acids
- A. $KMnO_4$ oxidation of alkenes and alkyl and alkenyl benzenes
- B. Jones oxidation of primary alcohols or aldehydes
- C. Hydrolysis of nitriles
- D. Carboxylation (rxn with CO_2) of Grignard reagents

IV. Reaction of Carboxylic Acids
- A. Deprotonation
- B. Reduction by $LiAlH_4$ (or BH_3)

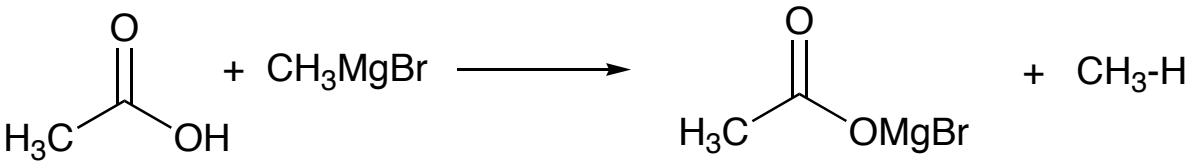
IV. Nitriles
- A. Preparation of nitriles
  1. from 1° R-X by S_N2 with CN^-
  2. from amides by dehydration using $SOCl_2$
- B. Conversion to *acids* by hydrolysis (acid or base catalyzed substitution by H_2O)
- C. Reduction to *amines* by $LiAlH_4$ or *aldehydes* by DIBAL-H
- D. Conversion to *ketones* by Grignard reagent (addition of R^- & imine hydrolysis)

V. Spectroscopy of carboxylic acids and nitriles

Reactions of Carboxylic Acids

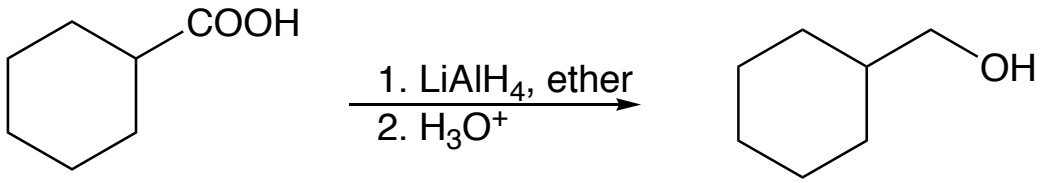
A. Deprotonation

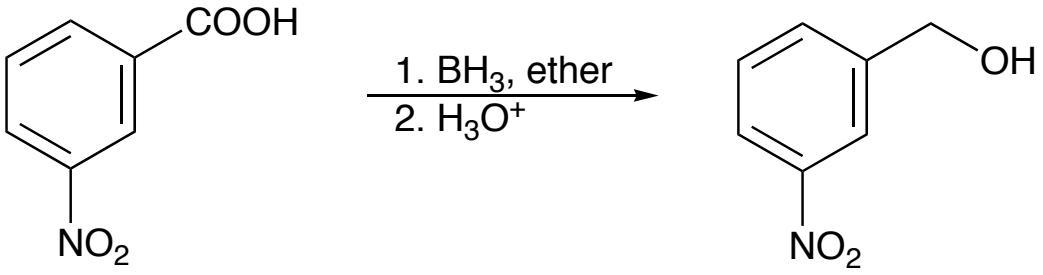
Example



D. Reduction by $LiAlH_4$ or BH_3

Examples





Chapter 21 Lecture Outline

Carboxylic acids derivatives and Nucleophilic Acyl substitution

Problems:
1a-g, 2, **3**, 4-13, 15-17, 19, 21, 23, 26, 32, 33, 36, 37, **41**-43, 45-47, 54, 57, **59**, 63-65.

I. Nomenclature of Carboxylic Acid Derivatives
- A. Acid chlorides
- B. Acid anhydrides
- C. Esters
- D. Amides
- E. Nitriles

II. Nucleophilic Acyl Substitution
- A. General mechanism
- B. Order of reactivity of carboxylic acid derivatives

III. Reactions of Carboxylic Acids
- A. Conversion to *acid chlorides* ($SOCl_2$)
- B. Conversion to *acid anhydrides* (dehydration)
- C. Conversion to *esters*
  1. carboxylate alkylation
  2. Fischer esterification (H^+, ROH)

IV. Reaction of Acid Chlorides
- A. Conversion to *acids* by hydrolysis (substitution by H_2O)
- B. Conversion to *esters* by alcoholysis (substitution by ROH)
- C. Conversion to *amides* by aminolysis (substitution by 1º or 2º amine)
- D. Conversion to *1º alcohols* by $LiAlH_4$ reduction (substitution and addition of H^-)
- E. Conversion to *ketones* by organocuprates (substitution by R^-)
- F. Conversion to *3º alcohols* by Grignard reagents (substitution and addition of R^-)

V. Acid Anhydrides
- A. Preparation of anhydrides
  1. dehydration of acids (especially good for formation of cyclic anhydrides)
  2. carboxylate reaction with acid chloride
- B. Conversion to *acids* by hydrolysis (substitution by H_2O)
- C. Conversion to *esters* by alcoholysis (substitution by ROH)
- D. Conversion to *amides* by aminolysis (substitution by 1º or 2º amine)
- E. Conversion to *1º alcohols* by $LiAlH_4$ reduction (substitution and addition of H^-)

VI. Esters
- A. Conversion to *acids* by hydrolysis (substitution by H_2O)
- B. Conversion to *amides* by aminolysis (substitution by 1º or 2º amine)
- C. Conversion to a*ldehydes* or *1º alcohols* by DIBAL-H or $LiAlH_4$ reduction
- D. Conversion to *3º alcohols* by Grignard reagents (substitution and addition of R^-)

VII. Amides

A. Preparation of amides

1. from acid chlorides (acyl substitution by 1° or 2° amine)
2. from esters (acyl substitution by NH_3, 1° or 2° amine)
3. directly from acids using DCC (acyl substitution by NH_3, 1° or 2° amine)

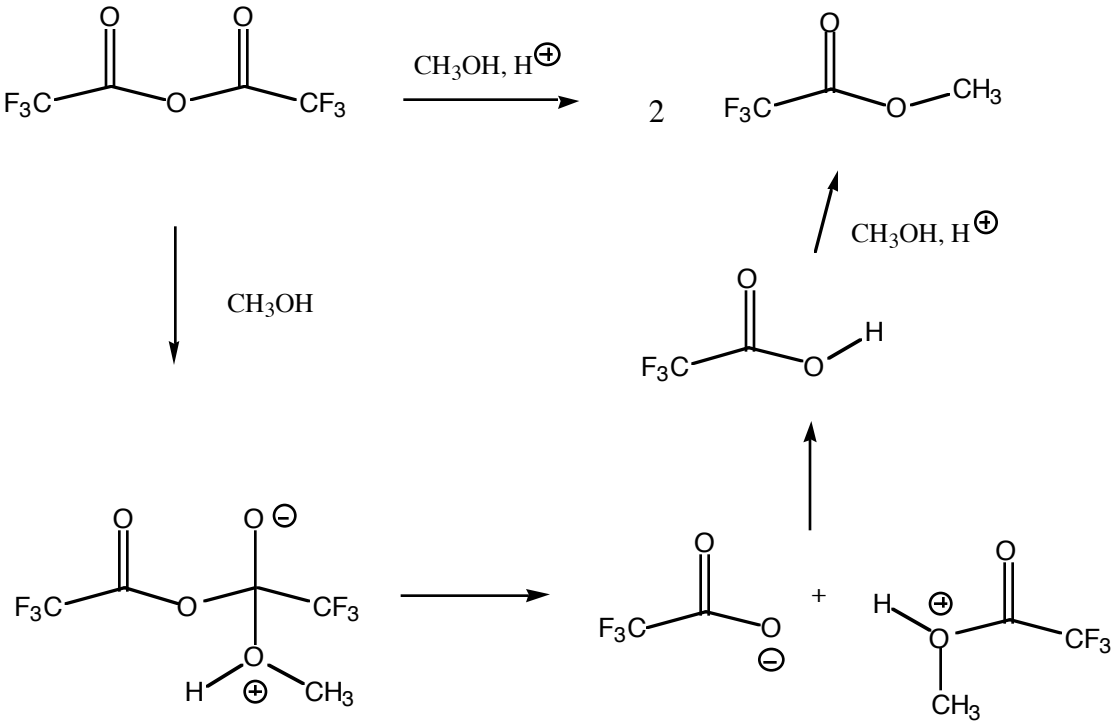
B. Conversion to *acids* by hydrolysis (acid or base catalyzed substitution by H_2O)

C. Reduction to *amines* by $LiAlH_4$

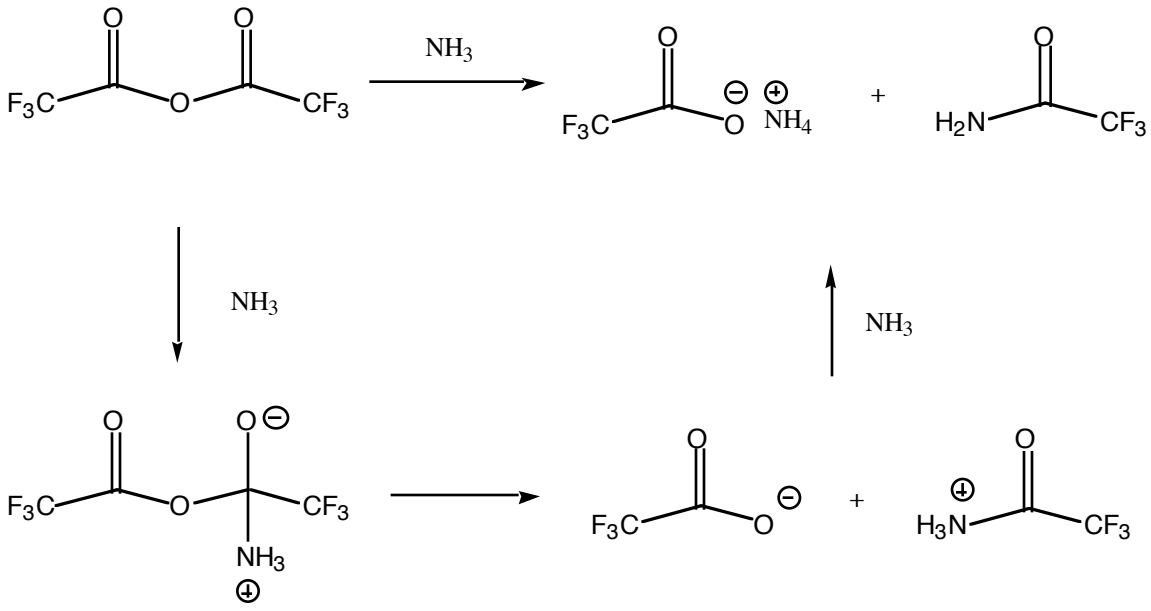
VIII. Polyesters and polyamides.

IX. Spectroscopy of Carboxylic Acid Derivatives (please read this section)

V.c. Conversion of anhydrides to esters by alcoholysis



V.d. Conversion of anhydrides to amides by reaction with NH_3, RNH_2, or R_2NH



Chapter 22 Lecture Outline

Carbonyl α-substitution reactions

Problems: 1, 2, **4**-**8**, 10, 11, 14, **16**-**24**, 26-30, 34, 35, 40, **44**, 45-49

I. Ketone-enole Tautomerization

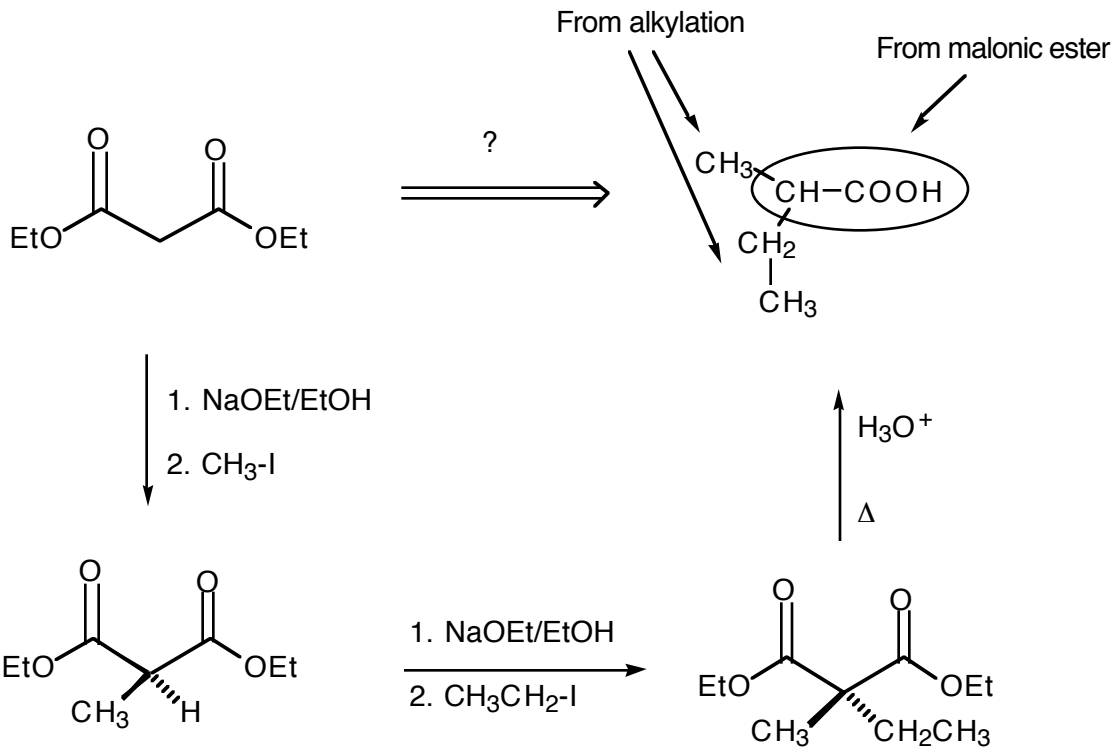
II. Enole Electrophilic α-Substitution Reactions
- A. α-Halogenation of ketones and aldehydes
- B. α-Halogenation of carboxylic acids

III. Enolate Anion Formation and Reactions of Enolates with Electrophiles
- A. α-Deprotonation of aldehydes, ketones, esters, and nitriles
- B. Halogenation of enolate anions and the haloform reaction
- C. Alkylation of enolate anions

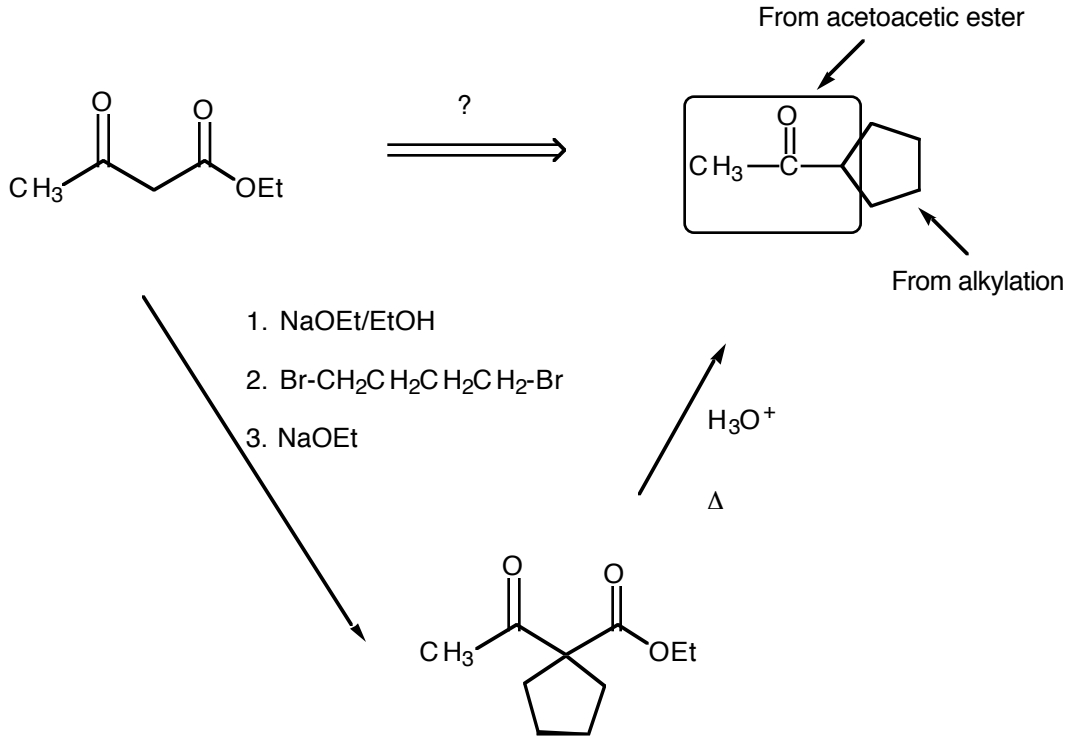
III. Malonic Acid Synthesis of α-Substituted Acetic Acids

IV. Acetoacetic Ester Synthesis of α-Substituted Acetones

Example of Malonic Ester Synthesis of Substituted Acetic Acids



Example of Acetoacetate Ester Synthesis of Substituted Acetones



Chapter 23 Lecture Outline

Carbonyl condensation reactions

Problems: 1, 3-5, **6, 7**, 8-10, **11**, **13**, 15, 16, **17**, 18, **21**-**25,** 26-30, **35**-46, 50, **51**, 54, 57-60.

I. Aldol Reactions, Aldol Condensations (of Ketones and Aldehydes)
- A. The Reaction
- B. The Mechanism
- C. Examples
- D. Mixed Aldol Reactions
- E. Intramolecular Aldol Reactions/Condensations

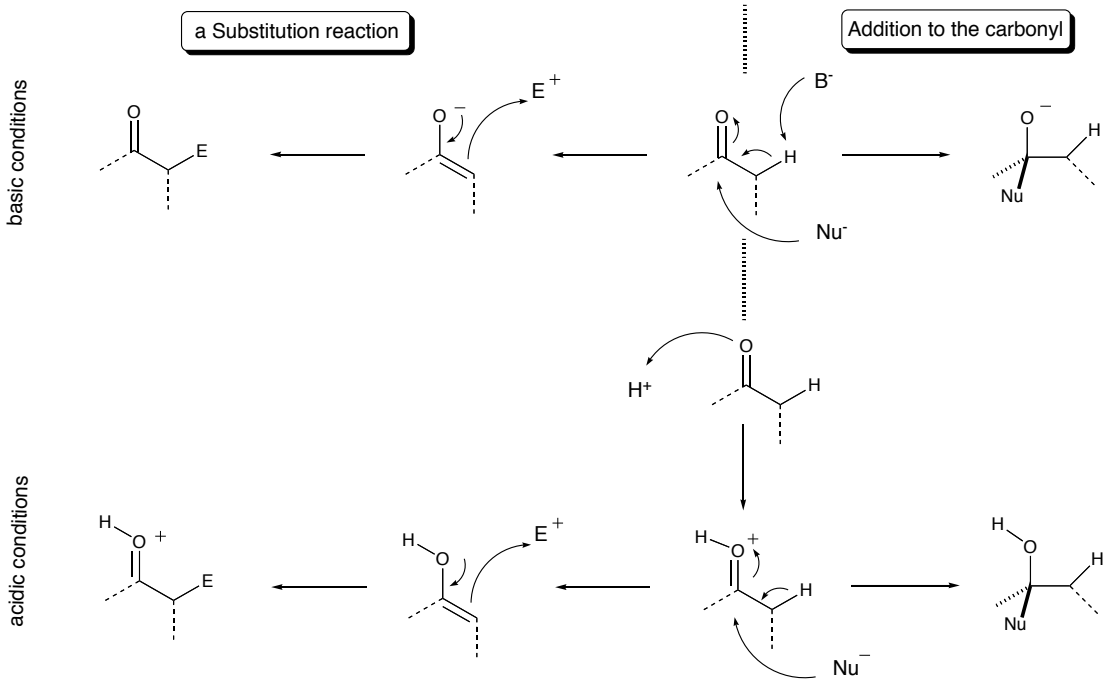
II. Claisen Condensations (of Esters)
- A. The Reaction
- B. The Mechanism
- C. Mixed Claisen Reactions
- D. Intramolecular Claisen Condensations-The Dieckmann Cyclization

III. Michael Reactions (of Enolates and α,β-Unsaturated Carbonyls)

IV. The Robinson Annulation Sequence (Michael+Intramolecular Aldol)

V. Stork Enamines as Enolate Equivalents in Michael Reaction

Reactivity of Carbonyl Compounds Having a Hydrogens (aldehydes, ketones, esters, nitriles, etc)



Chapter 24 Lecture Outline

Amines

Problems: 1-4, **6**-**8**, 10-14, **16**-**18**, **25**, 26, 29-40, **42**, 49, 53, 58-60, 64-68.

I. Nomenclature

A. Structure of common amines: piperidine, pyrrolidine, morpholine, pyridine, pyrrole, aniline, imidazole, pyrimidine, purine, indole, aziridine, and some naurally occurring amines

II. Physical Properties

A. Structure

B. Boiling points and water solubility (H-bonding)

C. ^1H NMR properties of N-**H** protons, exchange with **D** by D_2O

D. Basicity

1. aliphatic amines
2. aryl amines

III. Amine Synthesis

A. Alkylation and over-alkylation

1. Gabriel synthesis (or azide synthesis) of 1° amines
2. Reductive amination of aldehydes and ketones

B. Reduction of amides, nitriles, azides, and nitro compounds

C. Acyl nitrene rearrangements to 1° amines (conversion of carboxylic acid derivatives to amines

1. Hofmann rearrangement (R-$CONH_2$ + NaOH + Br_2 to R-NH_2)
2. Curtius rearrangement (R-COCl + N_3^- to R-NH_2)

IV. Amine Reactions

A. Acylation of amines

B. Hofmann elimination reactions

V. Amine reactions with nitrous acid, HONO, to form diazonium ions or nitrosoamines

1. 1° aliphatic amines and the formation of unstable alkyldiazonium ions, RN_2^+
2. 1° aryl amines and the formation of stable aryl diazonium ions, ArN_2^+

a. ArN_2^+ chlorination, bromination, cyanation (Sandmeyer reaction)

b. ArN_2^+ hydroxylation

c. ArN_2^+ deamination

d. ArN_2^+ coupling

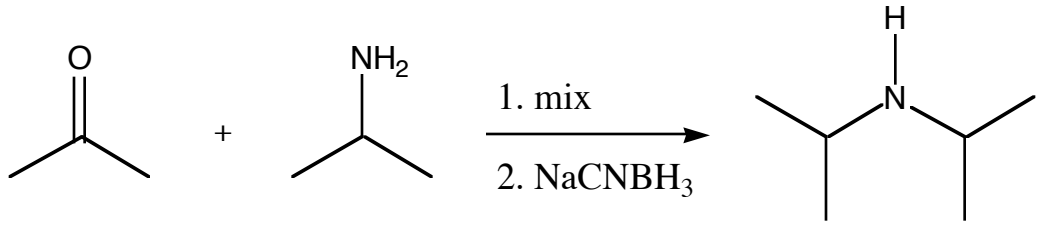
VI. Quaternary ammonium salts and Phase Transfer Catalysis

VII. Spectroscopy of Amines

III. Amine Synthesis

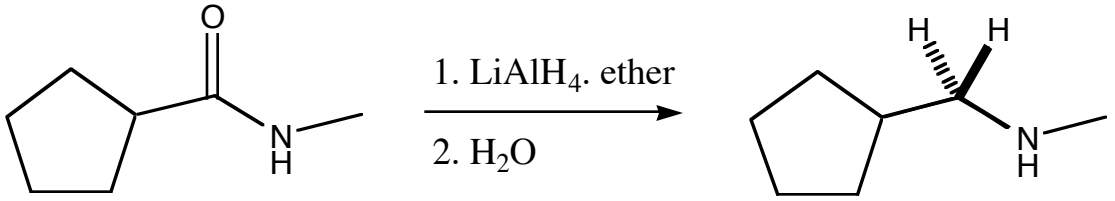
A2. Reductive Amination of Aldehydes and Ketones

Example

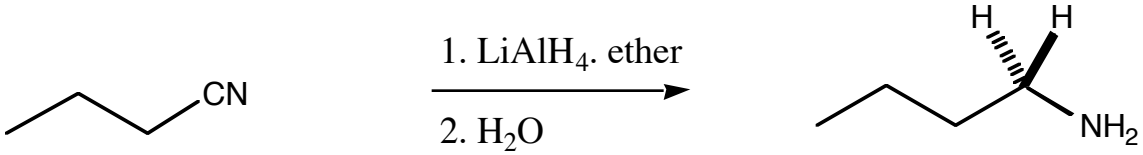


B. Reduction of Amides, Nitriles, and Nitrocompounds

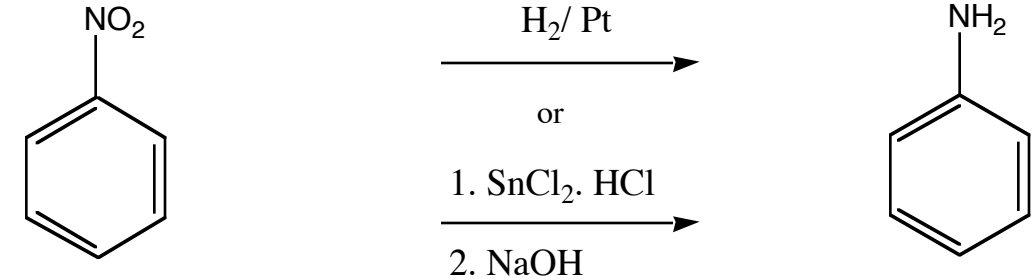
Examples



2^{o} Amide *2^{o} Amine*



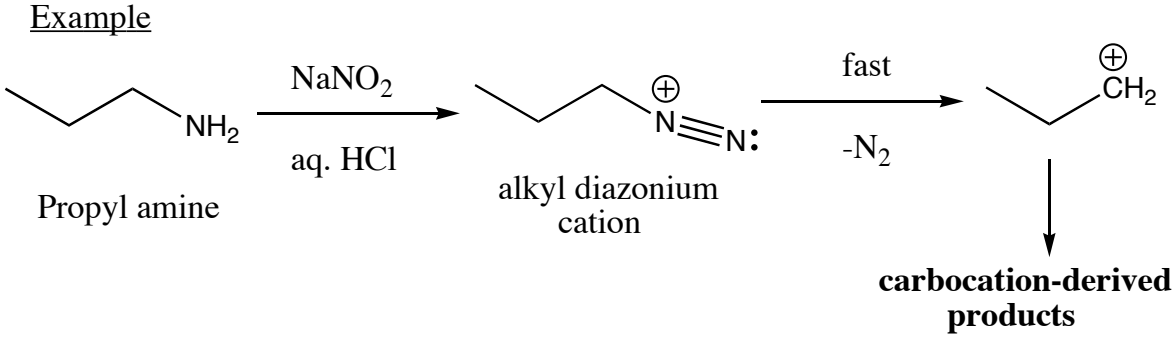
Nitrile *1^{o} Amine*



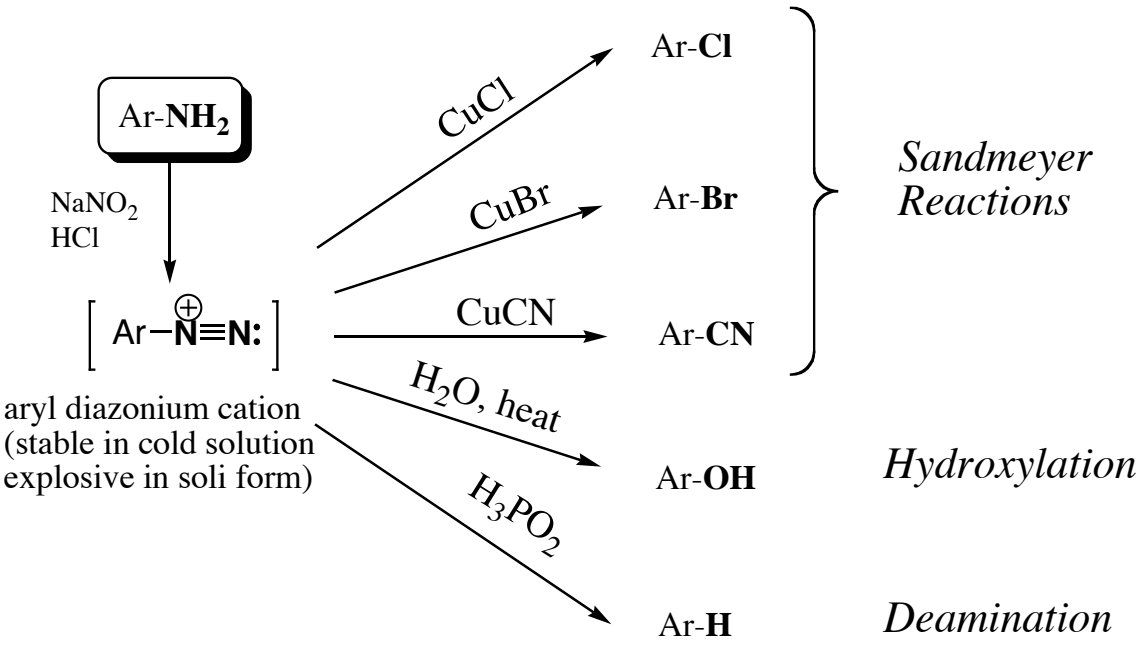
Nitrobenzene *Aniline*

V. Amine Reactions with HONO

1. 1º aliphatic amines form unstable alkyldiazonium cations



2. 1º aryl amines form stable alkyldiazonium cations



Chapter 25 Lecture Outline

Carbohydrates

Problems: **1**-4, 6, 7, 9, **10, 11**, 12, 13, **14**, 15-18, **20**, 22, 24, 25, **31-33**, 36, 37, 44, 48, 52, 54, 60

I. Introduction
- A. Definition of a Carbohydrate
- B. Nomenclature
  1. monosaccharides
  2. disaccharides
  3. polysaccharides

II. Monosaccharides
- A. Nomenclature: aldoses and ketoses (*known structures for glucose, fructose, and ribose*)
- B. Stereochemistry
  1. Fischer projections
  2. D, L nomenclature
  3. sugars to know: D-glyceraldehyde, D-ribose, D-glucose, D-fructose
- C. Cyclic forms: Pyranoses and Furanoses
  1. aldoses from cyclic hemiacetals
  2. ketoses from cyclic hemiketals
  3. ring stereochemistry
  4. configuration at the anomeric carbon and mutarotation

III. Reactions
- A. Alkylation or acylation of hydroxy groups to form ethers and esters
- B. Glycoside formation
- C. Borohydride reduction
- D. Oxidation of aldoses (chemical tests for "reducing" sugars)
- E. Kiliani-Fischer synthesis
- F. Wohl degradation

IV. Disaccharides
- A. Sucrose
- B. Maltose
- C. Cellobiose
- D. Lactose

V. Polysaccharides
- A. Starch
- B. Glycogen
- C. Cellulose

Chapter 26 Lecture Outline

Amino acids, Peptides, and Proteins

Problems: 1, 2, 5-8, **10**, **13**, 15, 16, 18, **20**, 22-25, 31, 34-36, **39**, 40, 41, 55

I. Nomenclature and Structure
- A. Stereochemistry
- B. Amino acids to know: L-alanine, glycine, L-cystine, L-valine, L-proline
- C. Isoelectric point

II. Synthesis
- A. Ammonolysis of α-bromocarboxylic acids
- B. Strecker synthesis (through amino nitriles)
- C. Reductive amination
- D. The amidomalonate synthesis

III. Peptides
- A. Structure and bonding
- B. Synthesis
  - 1. Solution synthesis and protective groups
  - 2. Merrifield synthesis (solid-phase synthesis)

IV. Proteins
- A. Classification and Structure of Proteins
- B. Enzymes

Chapter 27and 28 Lecture Outline

Lipids and Nucleic Acids

Problems: Chapter 27: 1-4, 6, 15, 21-25, 30, 44
Chapter 28: 8, 11, 12, 14, 21, 22,

I. Hydrolyzable lipids: Waxes, Fats, and Oils
- 1. Glycerols and Fatty Acids
- 2. Soaps
- 3. Phospholipids
- 4. Prostaglandins

II. Nonhydrolyzable lipids
- 1. Terpenes
- 2. Steroids

III. Nucleic Acids and Nucleotides
- 1. Amine Bases: Purines and Pyrimidines
- 2. Sugars: Ribose and Deoxyribose
- 3. Nucleosides and Nucleotides

IV. Structure of DNA

List of Reaction Mechanisms Covered in Chapters 14-26

Chapter 14
1. Diels-Alder reaction

Chapter 16
1. Electrophilic aromatic substitution
    a. bromination reaction
    b. nitration reaction
    c. sulfonation
    d. Friedel-Crafts alkylation
    e. Friedel-Crafts acylation
2. Nucleophilic Aromatic Substitution
    a. addition-elimination mechanism (ipso addition)
    b. elimination-addition (benzyne) mechanism
3. Benzylic Halogenation

Chapter 17
1. Alkene *cis* dihydroxylation with OsO_4
2. Alkene *trans* dihydroxylation *via* epoxidation-hydrolysis
3. $NaBH_4$ reduction of aldehydes and ketones
4. $LiAlH_4$ reduction of aldehydes and ketones and esters
5. Grignard reagent addition to aldehydes, ketones, esters, CO_2, ethylene oxide
6. Alcohol dehydration with $POCl_3$/pyridine
7. Alcohol conversion to alkyl bromide with PBr_3
8. Alcohol conversion to alkyl chloride with thionyl chloride
9. Alcohol oxidation with Cr^{+6} reagents:
    a. PCC in CH_2Cl_2
    b. Jones reagent
10. Silylation and desilylation of acohols

Chapter 18
1. Williamson ether synthesis
2. Alkene epoxidation by peracids
3. Acid cleavage of ethers
4. Epoxide ring opening
    a. acidic conditions
    b. basic or nucelophilic conditions

Chapter 19
1. Hydration of aldehydes and ketones
2. Cyanohydin formation from aldehydes and ketones
3. imine formation from aldehydes and ketones (oxime, semicarbazone, hydrazone formation)
4. Wolff-Kishner reduction of aldehydes and ketones
5. Enamine formation from aldehydes and ketones
6. Acetal formation from aldehydes and ketones
7. Wittig reaction of aldehydes and ketones
8. Cannizzaro reaction
9. Conjugate (1,4) addition of amines to α,β-unsaturated aldehydes and ketones

Chapter 20
1. Carboxylation of Grignard reagents
2. Reaction of 1° amides with $SOCl_2$ (formation of nitriles)
3. Hydrolysis of nitriles
4. Reduction of nitriles to amines or to aldehydes
5. Reaction of nitriles with Grignard reagents (formation of ketones)

Chapter 21
1. Reaction of carboxylic acids with $SOCl_2$ (formation of acid chlorides)
2. Formation of cyclic anhydrides by heating of diacids
3. Formation of esters from carboxylate salts and alkyl halides (S_N2)
4. Fischer esterification
5. Hydrolysis of acids chlorides (formation of acids)
6. Alcoholysis of acid chlorides (formation of esters)
7. Amonolysis and aminolysis of acid chlorides (formation of amides)
8. Reduction of acid chlorides to alcohols and aldehydes
9. Reaction of acid chlorides with organocuprates (formation of ketones)
10. Reaction of acid chlorides with Grignard reagents (formation of 3° alcohols)
11. Reaction of acid chlorides with carboxylate salts (formation of mixed acid anhydrides)
12. Hydrolysis of acid anhydrides (formation of acids)
13. Alcoholysis of acid anhydrides (formation of esters)
14. Amonolysis and aminolysis of acid anhydrides (fromation of amides)
15. Reduction of acid anhydrides to form alcohols
16. Basic hydrolysis of esters
17. Reduction of esters to form alcohols
18. Formation of amides from carboxylic acids and amines in the presence of DCC
19. Acidic hydrolysis of amides
20. Reduction of amides to form amines

Chapter 22
1. Enolization of ketones with strong bases (thermodynamic *vs* kinetic)
2. α-Bromination of ketones (acid catalyzed enolization)
3. α-Bromination of ketones and the haloform reaction (base catalyzed enolization)
4. Malonic ester synthesis of substituted acetic acids
5. Acetoacetic ester synthesis of substituted acetones

Chapter 23
1. Aldol reaction and aldol condensation reaction
2. Knoevenagel reaction
3. Intramolecular aldol reaction
4. Claisen reaction
5. Intramolecular Claisen reaction
6. Michael reaction
7. Robinson annulation reaction
8. Stork modification of Michael reaction (enamines)

Chapter 24
1. Gabriel synthesis

2. Reductive amination of aldehydes and ketones
3. Hofmann rearrangement
4. Curtius rearangement
5. Hofmann elimination
6. Formation of diazonium cations
7. Diazocoupling reaction

Chapter 25
1. Mutarotation
2. Formation of glycosides
3. Kiliani-Fischer synthesis

Chapter 26
1. Strecker synthesis
2. Amidomalonate ester synthesis of amino acids

Practice Exam #1

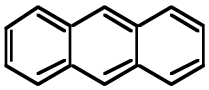
I. General Knowledge (28 pts)

1. (6 pts) π–Aromaticity is a fundamental concept in chemistry that involves some of the following terms (***circle* all that are necessary**):

circular array filled orbitals *p*-orbitals florist shop π-conjugation 4n+2 e^-

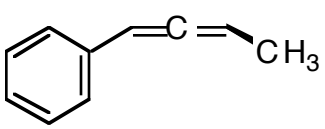
2. (8 pts) Give the structures of the molecules written below and provide the names of any structures shown.

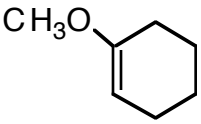
nitronium ion aniline benzyne any acylium ion (show 2 resonance structures)

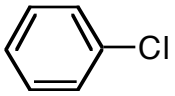


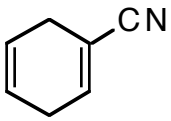
2-bromo-4-nitrophenol _____ pyridine 4-nitrotoluene

3. (4 pts) Circle the complete sets of any π conjugated atoms (of length ≥ 3 atoms) in the molecules below.



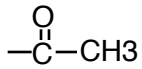






4. (4 pts) Attaching π electron donation groups to an aromatic ring (**circle one**) *activates* / *deactivates* the ring toward electrophilic aromatic substitution and directs the substitution reaction to (**circle all that apply**) the *ortho* / *meta* / *para* position(s).

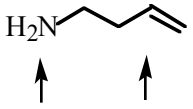
5. (6 pts) Circle **all** groups that deactivate benzene ring toward electrophilic aromatic substitution.



$-CF_3$ $-NH_2$ OCH_3 $-NO_2$ -NH-COCH3

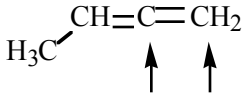
II. MO's, Aromaticity, and UV-vis Spectroscopy (30 pts)

1. (4 pts) Identify the hybridization level (i.e. sp^3 sp^2, sp) at the indicated atoms in the following molecules and give HOMO and LUMO orbital types for these molecules (σ, π, π^*, σ^*, or nonbonding):



LUMO ____

HOMO ____



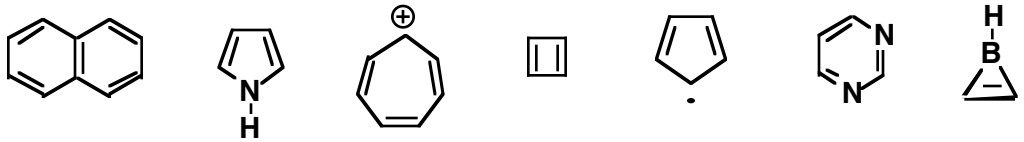
LUMO ____

HOMO ____

2. (6 pts) (a) Draw the π MO's for allyl cation showing their relative energies, labels, spatial properties, and electron population.

(b) The UV-vis absorption for allyl cation would involve a (fill in the blank) ___ to ___ transition.

3. (7 pts) Of the following, **circle** the aromatic molecules, **box-in** the anti-aromatic species, and do not disturb molecules which are neither aromatic nor anti-aromatic.



4. (6 pts) True or False (Circle **T** or **F**)

i. Nucleophilic properties of a molecule are controlled by its HOMO. **T** **F**

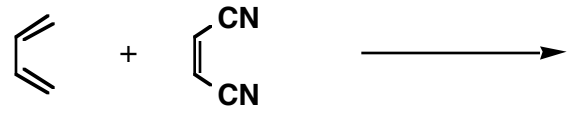
ii. Friedel-Crafts alkylation requires a Lewis acid as a catalyst. **T** **F**

iii. Aniline is less reactive toward electrophilic substitution than is benzene. **T** **F**

5. (7 pts) Using the "circle trick" construct the π MO energies of cyclopentadienyl anion. Is the molecule *aromatic, anti-aromatic* or *neither* (**circle one**)?

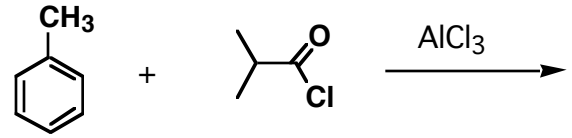
III. Reactions (17 pts; 3 pts each rxn, 1 pts each name) Draw structures of the expected organic products (some of these reactions may give you more than one product) formed under the following reaction conditions and provide the names of the reactions where requested.

1.



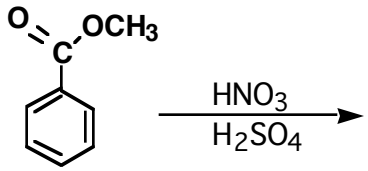
name:_____

2.



name:_____

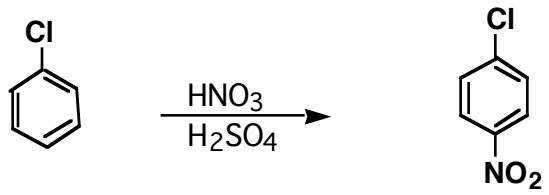
3.



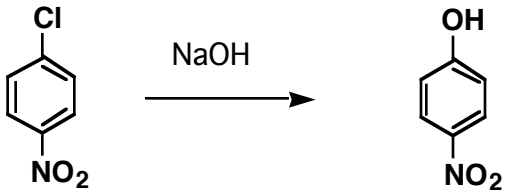
4, 5.

IV. Mechanism (20 pts) Provide detailed mechanisms for the transformations given below, showing each step in the process clearly. Show all resonance structures for the intermediates. I recommend that you use electron pushing arrows to show the flow of electrons.

(a) (10 pts)

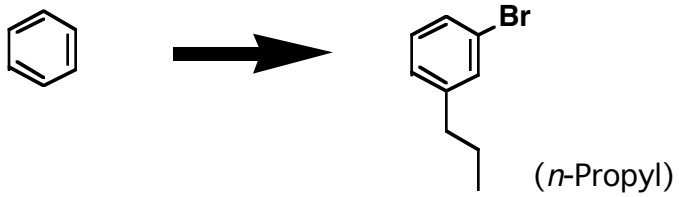


(b) (10 pts)

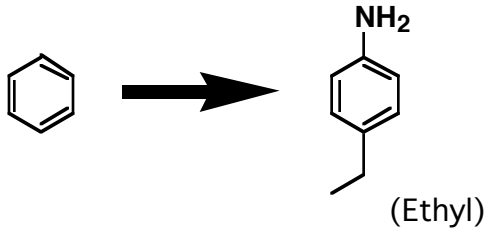


V. Synthesis (10 pts) Provide a reaction sequence to accomplish ***one of the two*** following conversions (left to right) using any reagents you need. Show reactants, products, and necessary reagents for each step in the sequence, but do not show mechanisms here. Partially correct answers will receive partial credit.

(1)



(2)



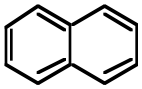
Practice Exam #2

I. General Knowledge & Exam 1 review (40 pts)

1. (12 pts) Give the structures of the molecules written below and provide the names of any structures shown.

trimethylsilyl ether of ethylene glycol

acetophenone



_____ the epoxide of propene

hydrazone of acetone

mCPBA

any thioacetal

osmate ester of cyclopentene

_____ thionyl chloride

2-methylcyclopentanone

2. (10 pts) Circle the π electron donating groups and <u>underline</u> the π electron withdrawing groups listed below.

$-OCH_3$ $-CH_3$ $-CO_2CH_3$ -F $-C(=O)CH_3$

-CHO $-CH_2$-CN $-NO_2$ $-NHCH_3$ -CN

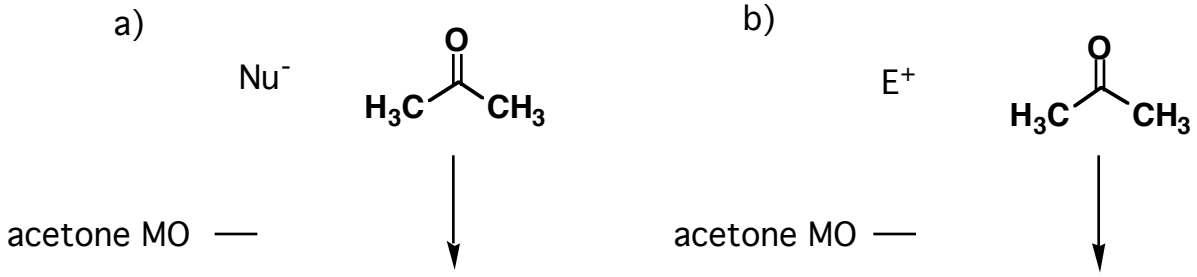
3. (6 pts) True or False. **Read the questions carefully**. (Circle **T** or **F**)

i. Alcohols are less acidic than water. **T** **F**

ii. $NaBH_4$ does reduce esters to alcohols. **T** **F**

iii. Ketones are more reactive than aldehydes toward nucleophiles. **T** **F**

4 (7 pts). A molecule of acetone reacts with a) a nuclephile and b) an electrophile.

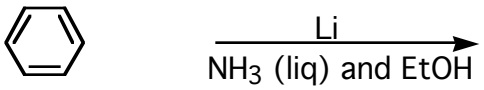


a) Using arrows, show the flow of electrons and draw products of each reaction.
b) Show resonance structures of the products where applicable.
c) Identify the MO's of acetone involved in each transformation (σ, π etc.) and describe them in terms of FMO's

5. (5 pts) Acid catalyzed formation of oxime of acetaldehyde is an example of nucleophilic addition to the carbonyl group. Please write this reaction below and show e- pushing arrows for the nucleophilic addition step and include the intermediate formed.

III. Reactions (35 pts) Draw structures (including stereochemistry) of the expected organic products formed under the following reaction conditions and provide the names of the reactions where requested.

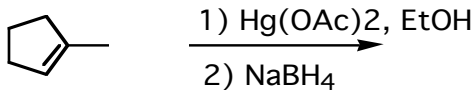
1.



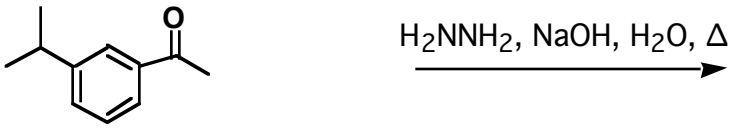
name:_____

2.

3.



4.

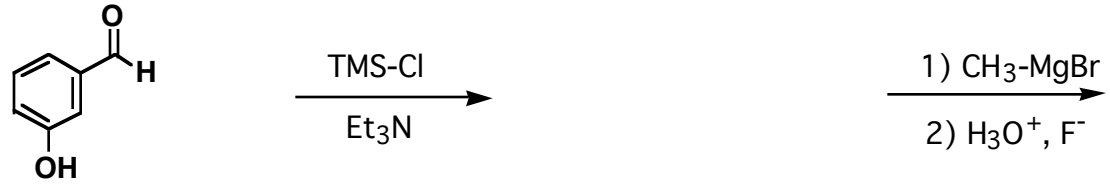


name:_____

5.

6.

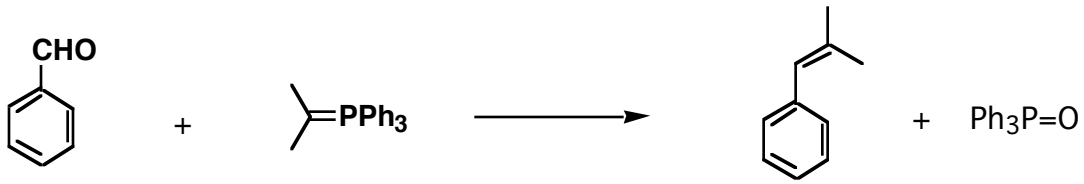
7.



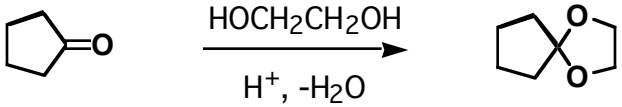
8.

IV. Mechanism (20 pts) Provide detailed mechanisms for the transformations given below, showing every step in the process clearly. Use electron pushing arrows whenever you wish (they are not required but may be helpful to you).

(a) (10 pts) Show also the formation of the ylide from the appropriate bromide.



(b) (10 pts)

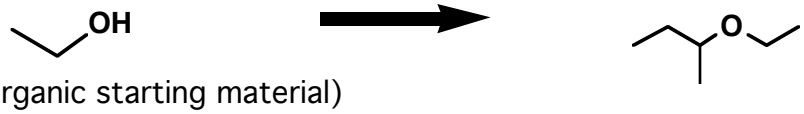


V. Synthesis (10 pts) Provide a reaction sequence to accomplish ***one of the two*** following conversions (left to right) using any reagents needed to convert the carbons of the starting material into the product structure. Show reactants, products, and necessary reagents for each step in the sequence, but do not show mechanisms here. Partially correct answers will receive partial credit.

(1)

(note: a hydrocarbon contains only carbon and hydrogen)

(2)



(Ethanol is the only organic starting material)

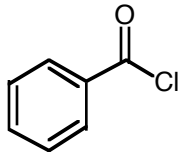
Practice Exam #3

I. General Knowledge (38 pts)

1. (9 pts) Give the structures of the molecules written below and provide the names of any structures shown.

hydrazone of acetone DIBAL-H benzamide

thionyl chloride ethylene glycol phthalic anhydride

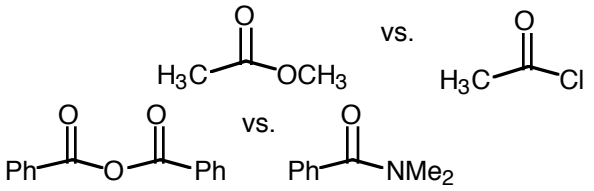


methyl formate _____ malonic acid

2. (6 pts) Circle the π electron donating groups and underline the π electron withdrawing groups listed below.

-Cl -NO_2 -NH_2 -CH_2CO_2H -$OC(O)CH_3$ -CF_3

3. (4 pts) For each pair of molecules, circle the structure which is most reactive toward *nucleophilic acyl substitution*. Box-in the leaving group in each of the four compounds.



4. (3 pts) Circle the strongest and box-in the weakest acid.

CH_3CH_2COOH FCH_2COOH CH_3COOH

5. (4 pts) True or False. **Read the questions carefully**. (Circle **T** or **F**)

i. Protonation of a carbonyl group increases its reactivity toward nucleophiles. **T F**

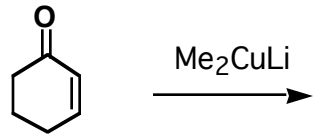
ii. $NaBH_4$ is a more potent reducing reagent than $LiAlH_4$. **T F**

6. (6 pts) One of the most common reactions of carboxylic acid derivatives is nucleophilic acyl substitution at the carbonyl group. Please write this reaction below for methoxide anion reaction with acetyl chloride and use e-pushing arrows for the nucleophilic addition step and the elimination step, showing also the intermediate formed.

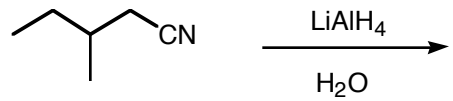
7. (6 pts) Reaction of an acid chloride (C_5H_9ClO) with lithium dimethylcuprate gives a product with the following spectroscopic properties: **IR** strong peak in 1710 - 1740 cm^{-1} range; **^{13}C NMR** (fully decoupled): δ (ppm) 206, 45, 29, 24; **^{1}H NMR**: δ (ppm) 2.1 (s, 3H), 1.1 (s, 9H) [s=singlet]
Write the structures of the acid chloride and the reaction product.

II. Reactions (32 pts total) Draw structures (including stereochemistry) of the expected organic products formed under the following reaction conditions and provide the names of the reactions where requested.

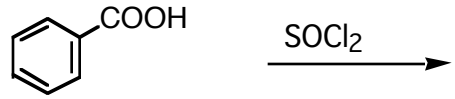
1.



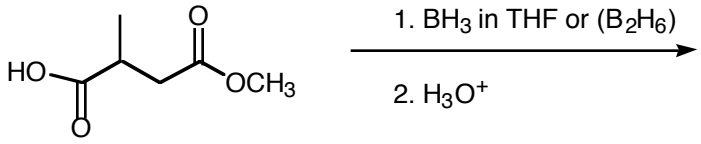
2.



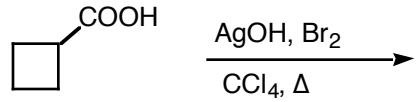
3.



4.



5.



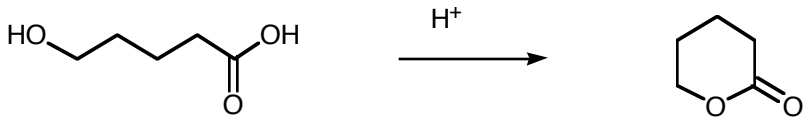
name:_____

6.

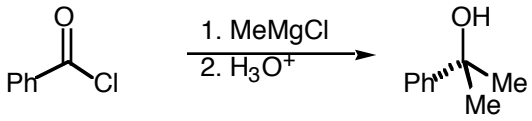
7.

III. Mechanism (20 pts) Provide detailed mechanisms for the transfrmations given below, showing every step in the process clearly. Use electron pushing arrows whenever you wish (they are not required but may be helpful to you).

(a) (10 pts)

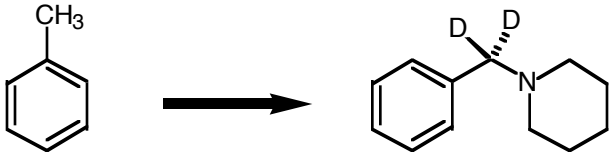


(b) (10 pts)



IV. Synthesis (15 pts) Provide a reaction sequence to accomplish ***one of the two*** following conversions (left to right) using any reagents needed to convert the carbons of the starting material into the product structure. Show reactants, products, and necessary reagents for each step in the sequence, but do not show mechanisms here. Partially correct answers will receive partial credit.

(1)



(2)

(you need only inorganic reagents)

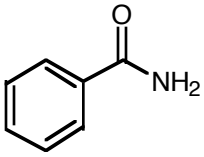
Practice Exam #4

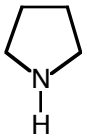
I. General Knowledge & Exam 3 review (38 pts)

1. (9 pts) Give the structures of the molecules indicated below and provide the names of any structures shown.

$CHBr_3$

_____ diethyl carbonate any enamine

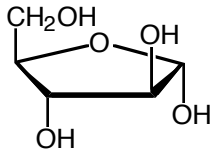




methyl formate _____ _____

the enolate anion of acetone any **L**-aldotetrose **D-**fructose (Fischer projection)

2. (8) A cyclic structure of **arabinose** is shown below. 1) Circle the anomeric carbon 2) Box-in the family carbon 3) Point an arrow at carbon atom(s) which differ in stereochemistry from that in rybose.

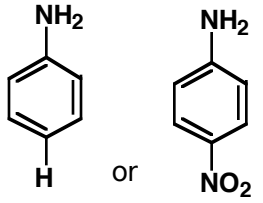


In each pair, circle what best describes the structure:

a) Fischer or Haworth projection
b) D or L family
c) α or β anomer
d) pyranose or furanose

Provide full name for this structure: _____

3. (4) Circle the more basic amine and explain why using resonance structures (show only the most importnat ones):



4. (6 pts) True or False. **Read the questions carefully**. (Circle **T** or **F**)

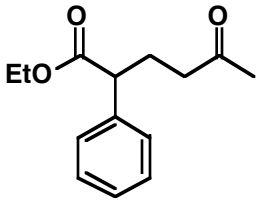
i. In unsymmetrical ketones, kinetic deprotonation occurs at the more substituted carbon atom. **T F**

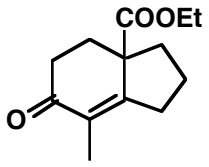
ii. It is easier to α-deprotonate ketones than esters. **T F**

iii. Enolate anions are isoelectronic with carboxylate anions. **T F**

5. (7 pts) Pyrolysis of acyl azides followed by hydrolysis of the resulting isocyanante is one of the most convenient ways to prepare amines from carboxylic acids. Please write this reaction below for the preparation of acyl azide from acetyl chloride and sodium azide and its subsequent pyrolysis to the corresponding isocyanate. Use e- pushing arrows for all steps, showing also the reactive intermediate formed.

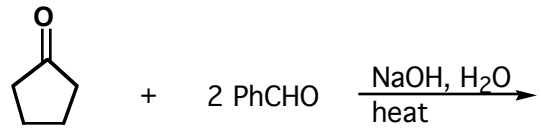
5. (4 pts) Write the organic reactant(s) needed to prepare the products below in one or two steps and provide the needed reagent(s) and/or conditions.





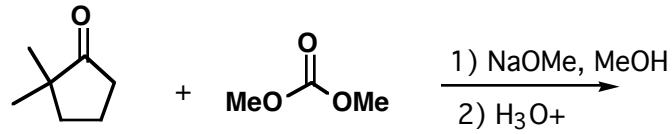
II. Reactions (32 pts) Draw structures (including stereochemistry) of the expected organic products formed under the following reaction conditions and provide the names of the reactions where requested.

1.

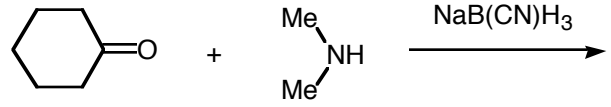


name:_____

2.



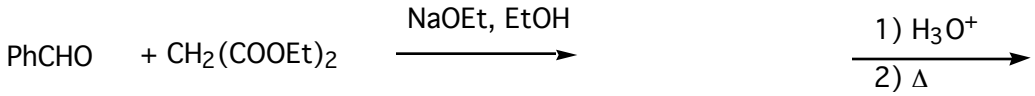
3.



4.

name:_____ product name: _____

5.



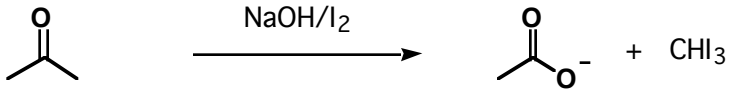
name:_____

6.

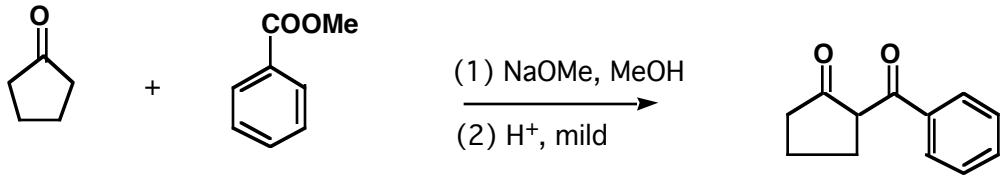
name:_____

III. Mechanism (20 pts) Provide detailed mechanisms for the transformations given below, showing every step in the process clearly. Use electron pushing arrows whenever you wish (they are not required but may be helpful to you).

(a) (10 pts)

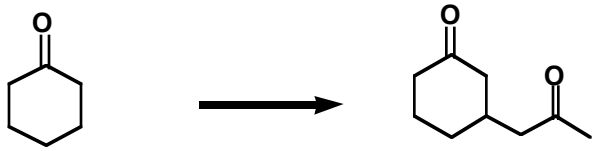


(b) (10 pts)

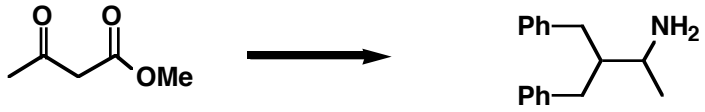


IV. Synthesis (15 pts) Provide a reaction sequence to accomplish ***one of the two*** following conversions (left to right) using any reagents needed to convert the carbons of the starting material into the product structure. Show reactants, products, and necessary reagents for each step in the sequence, but do not show mechanisms here.

(1)



(2)



Use benzyl bromide and any inorganic reagents