Concepts for the final exam (CHEM 321)

Mechanisms

Electronegativity
Bronsted acidity-basicity; Lewis acid, Lewis base
Electrophiles and nucleophiles
Electron movement and stabilization
Hybridization, atomic orbitals, molecular orbitals; quant. mech. basis of octet rule
Steric repulsion, repulsion of electron clouds
Energetics (kinetics versus thermodynamics), energy diagrams, transition state E
Stabilization of charged and high E intermediates, transition states
Resonance structures
Chirality and stereochemistry (absolute and relative); regiochemistry of reactions
Conformational analysis (acyclic and cyclic compounds); torsional and angle strain
Aromaticity and conjugation, allylic and benzylic positions
Carbocations, carbanions, free radicals (conditions and stabilization)
Intramolecular and intermolecular reactions
Competition reactions (relative rates (kinetic) or product stability (thermodynamic))

Methods of adding functionality

Alkene addition by acids (form ethers, alcohols, halides)
Hydroboration
Halogenation (alkenes, alkynes, aromatics)
Epoxidation, opening with acid or base
Dihydroxylation
SN2 reactions (nucleophiles, electrophiles); SN1, E2, E1
Catalytic hydrogenation
Ozonolysis
Reduction and reactions of alkynes
Free radical reactions
Functional group manipulation (ROH -> ROTs -> RNu)

Methods of C-C bond formation

Diels-Alder
SN2 with –CN, alkyne carbanions
Carbenes/diazomethane

Applications of organic chemistry/drug discovery/pharmaceutical development

Biological effects

New concepts and reactions in CHEM 322

Mechanisms

Electrophilic aromatic substitution
Electron donating groups, electron withdrawing groups, directing effects
Anatomy of a carbonyl: bonding, resonance, electrophilicity and nucleophilicity
Acid/base reactions; acidity of carbonyls and carbonyl derivatives, amines
Carbonyls under acidic and basic conditions; nucleophiles and electrophiles
Effect of electron-withdrawing and -donating groups on reactivity
Nucleophilicity of alcohols, thiols, amines (and deprotonated forms)
Kinetic versus thermodynamic control

Analytical chemistry

1H and 13C NMR; chemical shift; coupling, coupling constants, tree diagrams
Homotopic, enantiotopic, diastereotopic, equivalent H/C
Mass spectrometry (mass/charge ratio); elemental analysis, degrees of unsaturation
Infrared spectroscopy

Methods to add functionality

Aromatic nitration, halogenation; Birch reduction, benzylic reactions
Friedel-Crafts acylation, alkylation
Heck reaction, cross-coupling reactions
Interconversions of functional groups on aromatic rings
Oxidation and reduction to interconvert alcohols/acids/aldehydes/ketones/aldehydes/acid chlorides/amides/amines/etc.
Hydrates, hemiacetals, and acetals; cyclic acetals
Protecting aldehydes and ketones as acetals
Imines, enamines, iminiums
Hydride addition (reduction) to carbonyl derivatives
Alcohols from alkenes; oxidation of alcohols
Ester formation and hydrolysis
Halogenation of C-alpha to make electrophilic
Acid chlorides and anhydrides as strong electrophiles
Conversion of alcohol to leaving group or halide (electrophile or nucleophile, as Grignard)
Amines by SN2, reduction (of nitro, imine, nitrile, amide)
Synthesis of amides from amines and acid chlorides or carboxylic acids; peptide synthesis

Methods of C-C bond formation

Cross-coupling reactions, Heck reaction
Cyanide addition (cyanohydrin formation, SN2)
Aldol reaction
Michael reaction
Organometallic/Grignard reagent reaction with carbonyls, epoxides
Enolates and enols as nucleophiles (i.e. SN2)
Wittig reaction (carbonyl -> alkene)
Claisen condensations
Malonic ester synthesis
Mannich, Strecker reactions

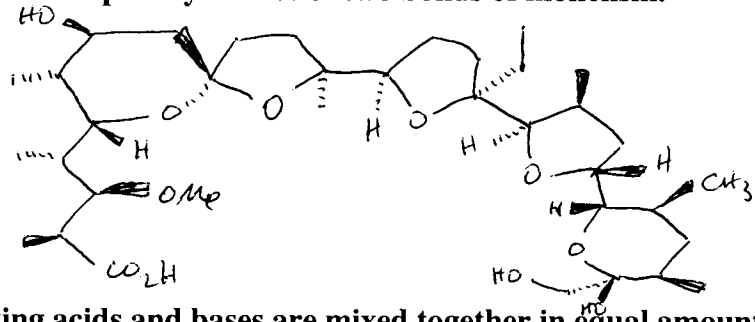
Applications of organic chemistry

Examples given in class

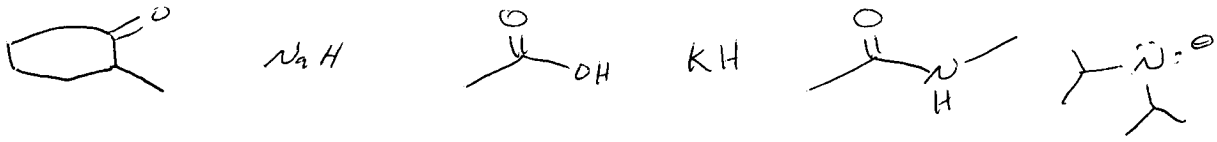
Practice Problems for the final exam (NOT a practice exam)

↳ Actual final exam will contain a much higher % of questions on carbonyl chemistry!

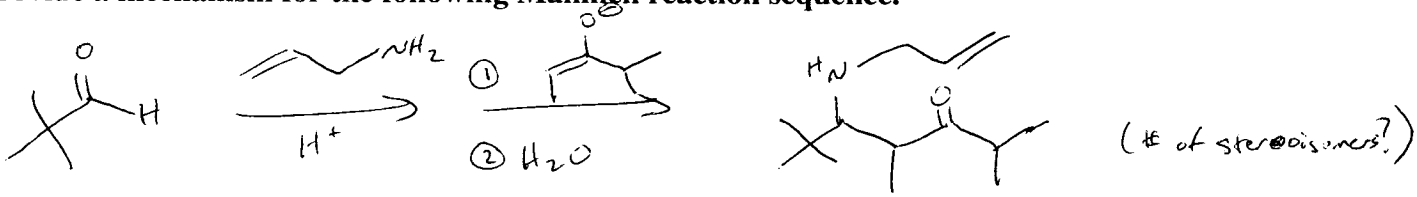
1. Identify the functional groups in monensin, an ionophore (compound which helps cations cross membranes) antibiotic used as an additive in poultry and cattle feeds. Circle and label the functional groups. How many stereocenters does monensin have? Have many stereoisomers of monensin exist? Propose syntheses of two bonds of monensin.



2. The following acids and bases are mixed together in equal amounts (1 mole each). Which species are observed at equilibrium?

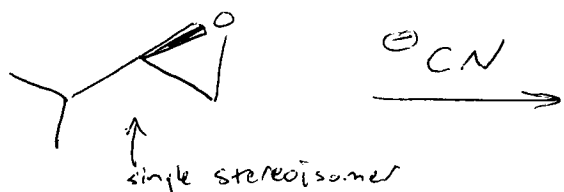


3. Provide a mechanism for the following Mannich reaction sequence.



(# of stereoisomers?)

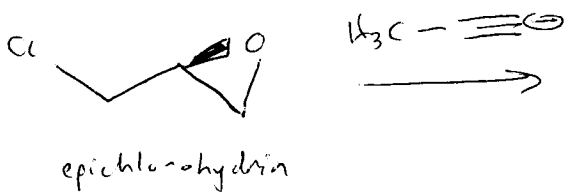
4. The reaction below could produce two regioisomers, via nucleophilic attack on either carbon of the epoxide. NMR can be used to determine which product is actually formed. Draw both products and predict the NMR spectrum of the products. How would the NMR change if ^{-13}CN was used? (Recall that carbon NMR detects ^{13}C in natural abundance (1%); in this case only the ^{13}C isomer is used.) Provide a mechanistic prediction of which product is formed in this reaction.



single stereoisomer

Pay close attention to stereochemistry

5. The reaction below could produce three products (via attack on any of the three carbons of epichlorohydrin). Explain how you could use various techniques in analytical chemistry to differentiate the products.

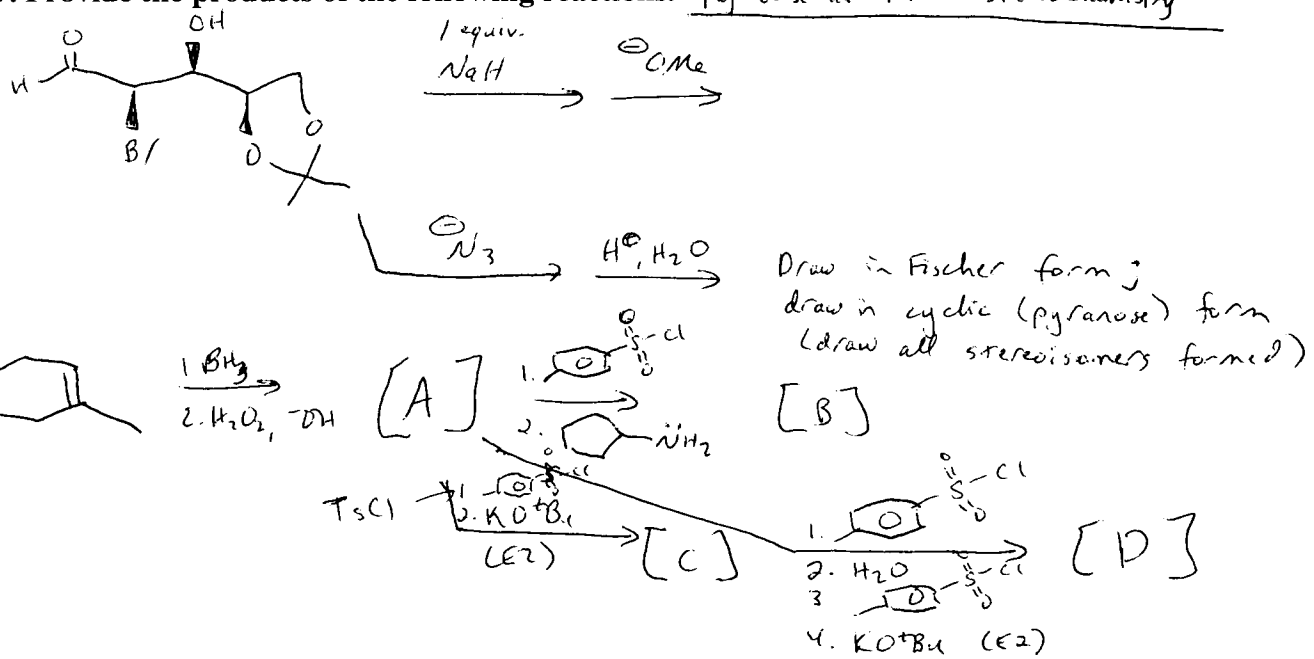


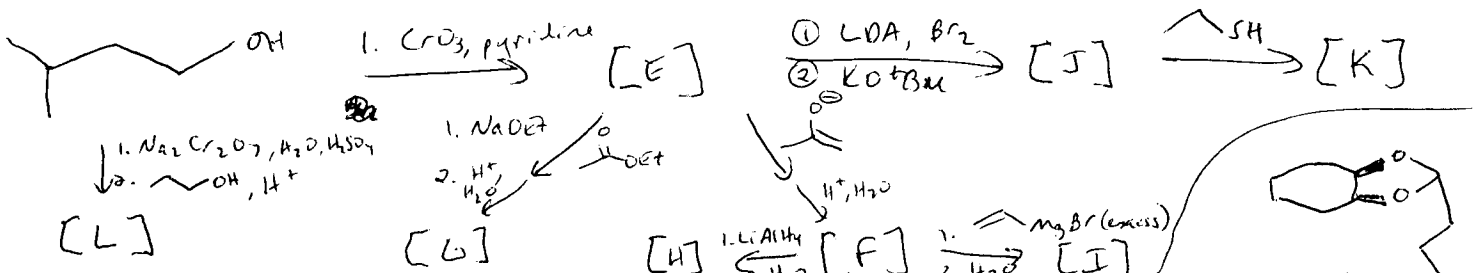
epichlorohydrin

↗ Fischer projection

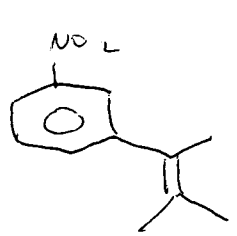
6. Draw the structures of the two D-aldotetroses. Mixture with $NaBH_4$, followed by aqueous workup, allows easy characterization of each. Explain.

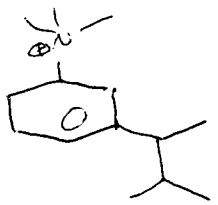
7. Provide the products of the following reactions. Pay close attention to stereochemistry



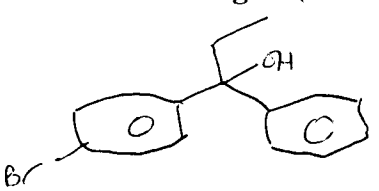


8. Propose syntheses of the following compounds using the indicated reagents.



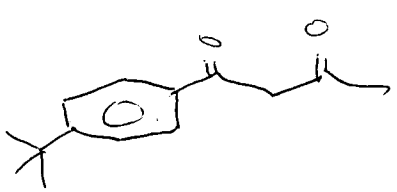


from nitrobenzene ← from (or nitrobenzene)

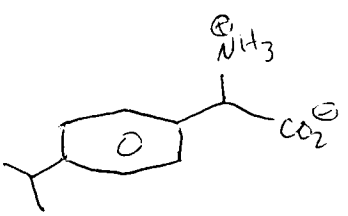


using bromobenzene as the only source of aromatic C's

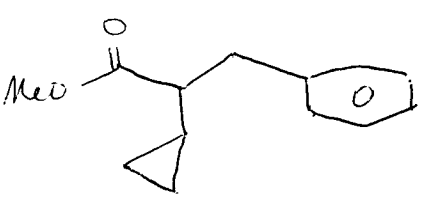
using cyclohexene as the sole C source



from benzene



from benzene (via Strecker)



from malonic ester (and any other cmpds)