

CHEM 332 - STUDY GUIDE

/Techniques/

Recrystallization - A method to purify solids

* Dissolve a solid in a solvent at elevated temperature, allowing crystals to form as the solution cools.

* This works because of the trend that solids tend to be more soluble in a hot solution than a cold one

* So if you are trying to recrystallize A from B, choose a solvent with the following properties:

- B is highly soluble in the solvent
- A is highly soluble in hot solvent but sparingly soluble in cold solvent

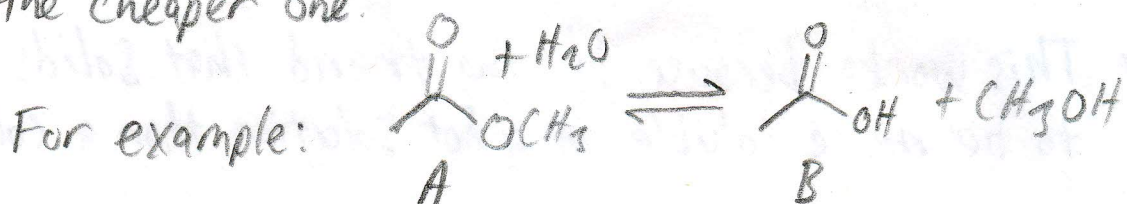
- Therefore, as the solvent cools, A will crystallize while B remains dissolved

* Sometimes hot filtration is necessary before crystallization to remove colored impurities.

Reaction Equilibrium

* If a reaction is reversible, it is said to be in equilibrium. Often one desires that the reaction favor a particular product over others. There are a couple methods to make this happen.

1. Use an excess of a particular starting material, usually the cheaper one.



- To drive the reaction towards products, one can add water. That way, when the carbonyl carbon gets attacked, there will be a statistical bias against molecule A because there is so much H_2O available to consume.

2. Distill one of the products. As the product is distilled, it is removed from the reaction mixture. Therefore, more product is made to compensate for the lack of product.

Note: The same scenario holds true if you can get your product to precipitate out of solution. More product will be formed to compensate for the missing precipitate product.

3. If you can drive your reaction forward by removing water, a drying agent can be used.

Simple Distillation

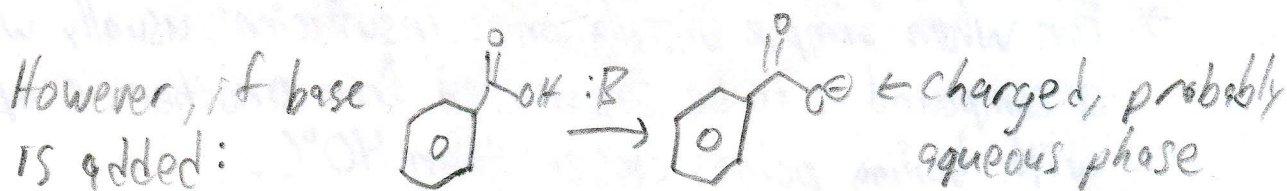
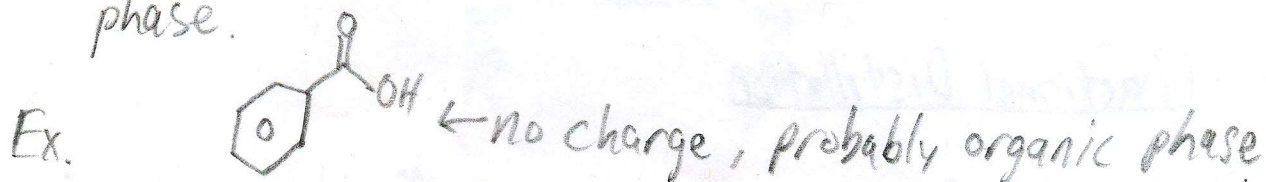
- * Apparatus used to separate pure substances from a mixture if the boiling point separation between each substance is greater than 40°C . So, the desired compound is usually the one with the lower boiling point.

Fractional Distillation

- * For when Simple Distillation is insufficient, usually when a compound is to be separated from another compound with boiling points closer than 40°C .
- * The column is packed with material on which several microdistillations occur, where the product becomes increasingly more pure with each one.
- * Azeotropic mixtures have a boiling point minimum as a specific component mixture. Therefore, distillation will not produce a pure compound, but rather a mixture of azeotropic composition.

Extraction

- * The separation of compounds based on solubility in one of (usually) two immiscible phases.
- * In most cases there will be an organic and an aqueous phase.



- * Another important consideration is density. Density determines which phase will be on top/bottom. As a general rule, alkyl halides are more dense than water, so an organic layer containing alkyl halides will be on the bottom. Otherwise, the organic layer tends to be on top.
- * If unsure, one can take a drop of the top layer and put it in water. If the drop is miscible in water, the top layer is aqueous. Otherwise, it is organic.

Thin-Layer Chromatography (TLC)

- * A method for identifying compounds on the basis of polarity
- * A mixture is dissolved in solution and blotted via capillary tube onto a TLC plate. This plate is put into a chamber containing a solvent and is allowed to develop. As the solvent creeps up the plate, the pure components from the original mixture also creep up the plate, but each at its own characteristic rate depending on its affinity for the solvent.
- * The retention factor (R_f) for each component is calculated as follows:

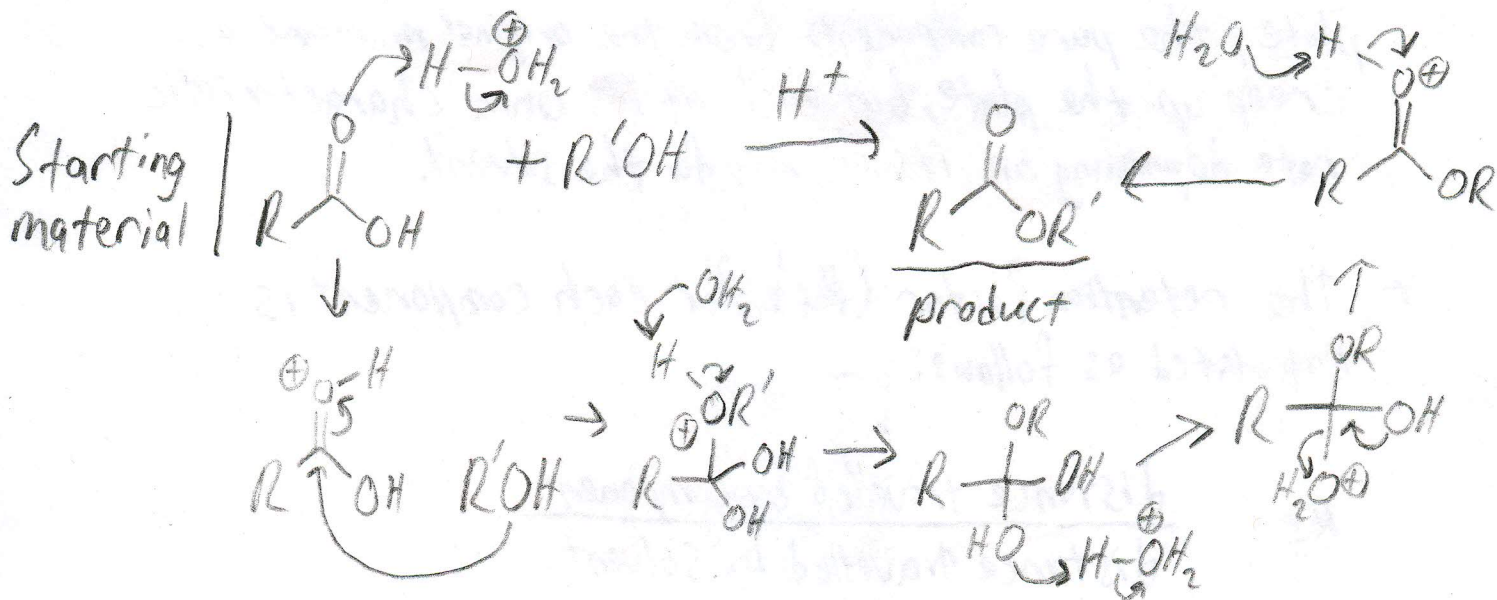
$$R_f = \frac{\text{distance travelled by component}}{\text{distance travelled by solvent}}$$

- * The presence of these components can be determined using ultraviolet (UV) light and/or chemical stains.

/Reactions/

Fischer Esterification

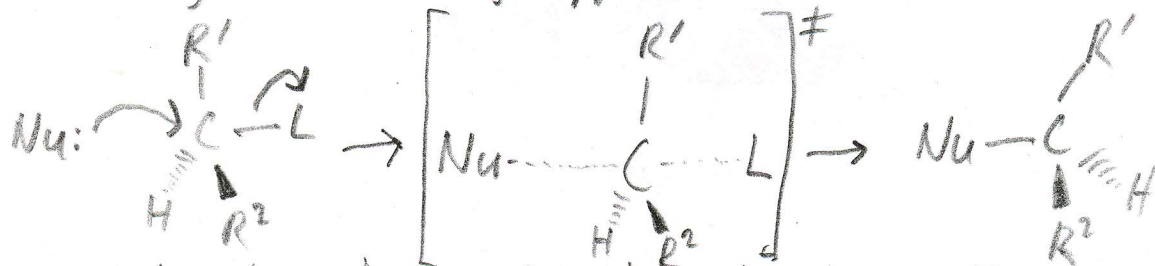
- * Used to make an ester from a carboxylic acid, anhydride, or acyl chloride, using an alcohol. Under favorable conditions, this reaction can also be used to synthesize carboxylic acids from esters, in the reverse reaction.



- * This reaction can also be base-catalyzed

S_N2 - Nucleophilic bimolecular substitution

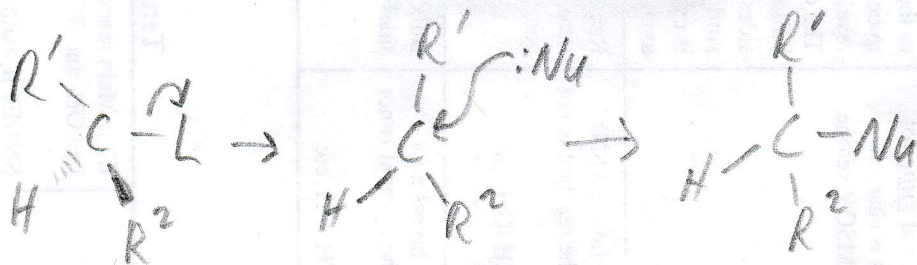
- * This is carried out in a concerted mechanism; all the bond making and breaking happens at the same time.



- * Note that the product has the reverse stereochemistry because the nucleophile attacked from behind.

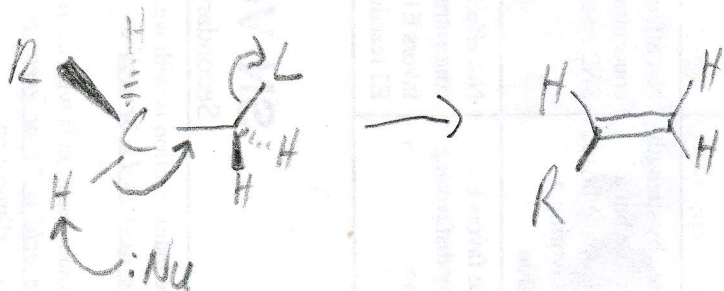
S_N1 - Nucleophilic unimolecular substitution

* In this case, the leaving group, L, leaves first, giving a trigonal planar intermediate. From there the nucleophile can attack from either side, thus producing two products, enantiomers



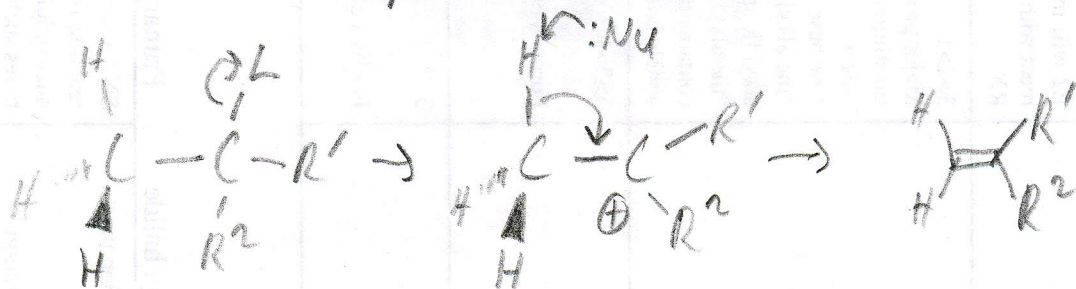
E2 - Elimination, bimolecular

* This is a concerted reaction that tends to compete w/ S_N2



E1 - Elimination, unimolecular

* This reaction competes with S_N1



* See attached for a comparison of S_N1, S_N2, E1, E2

Substitution and Elimination Reactions Comparative Chart

Reaction	Structure of RX	Reactivity of Nu:	Conc. Of Nu:	Solvent	Stereochemistry
SN2	1>2>3 Only this reaction and E2 will most likely react with a primary RX	Strong nucleophile favors reaction	High concentration of nucleophile favors reaction	Aprotic polar solvent favors a SN2 reaction if <i>either</i> of the reactants is charged ex: DMF DMSO Acetone	inversion of configuration
E2	3>2>1 Major product is more substituted alkene unless *the base is large *the alkyl halide is an alkyl fluoride *the alkyl halide contains one or more double bonds	Strong Base favors reaction	High concentration of base favors reaction	Aprotic polar solvent favors a E2 reaction if <i>either</i> of the reactants is charged ex: DMF DMSO Acetone	If the reactant has 2 H bonded to the carbon from which a H is to be removed, both E and Z result. The conformers that has the bulkiest groups on opposite sides will be the major product. Anti and syn elimination— if it is cyclohexane, it has to be axial (anti)
SN1	3>2>1 Forms a carbocation	Not effected by strength of nucleophile but a weak nucleophile favors it by not favoring a SN2 reaction	Not effected but low concentration disfavors a SN2 reaction	Protic polar favors a SN1 reaction if the reactant is not charged. Ex: H2O, CH3OH, etc.	Racemization (with some inversion because of ion pairing)
E1	3>2>1 Forms a carbocation	Weak base favors E1 reaction by disfavoring E2 reaction	Not effected but a low concentration of base favors E1 by disfavoring a E2 reaction	Protic polar favors a E1 reaction if the reactant is not charged. Ex: H2O, CH3OH, etc.	Bulkiest groups on opposite sides

SN Versus E

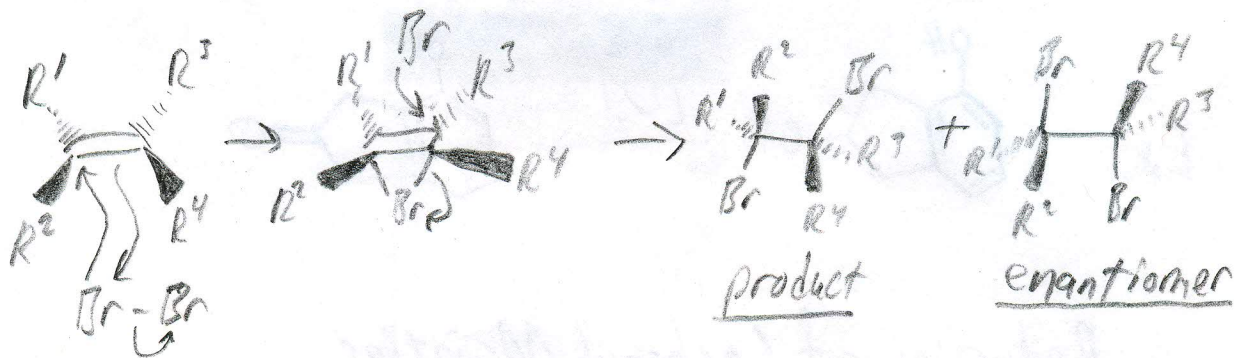
Methyl halide	Primary halide	Secondary halide	Tertiary halide
SN2 reaction most favored	SN2 when the main reaction is with good nucleophiles/weak bases such as I- and CH3CO2-	SN2 if the main reaction is with weak base or Nu: where Pka of <i>conjugate acid is 11 or less</i> ex: I- or CH3CO2-	E2 if Main reaction is with strong bases like OH- and RO-
No Elimination reactions!	E2 if you use strong bulky bases such as t-butoxide steric effects	E2 if the main reaction is with a strong base or Nu: where Pka of <i>conjugate acid is 11 or greater</i> -, high temperatures and bulky bases increas elimination SN1/E1 are common in reactions with weak Nu: in polar protic solvents like water, high temps favor E1	SN1/E1 if main reaction is with a poor Nu: High temperatures favor E1 out of the two.

Courtesy

Wake Forest University

Bromination of Alkenes

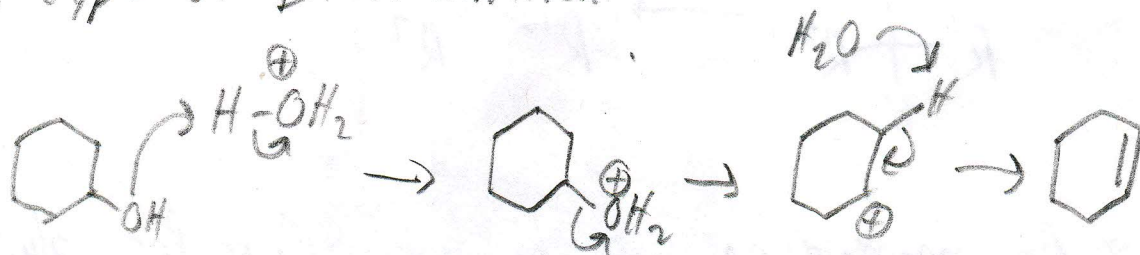
* This reaction involves a cyclopropyl intermediate and ends with anti attack by Br^- .



* Two products can be formed, as shown. This reaction does not work with other halides, such as Cl_2 .

Dehydration

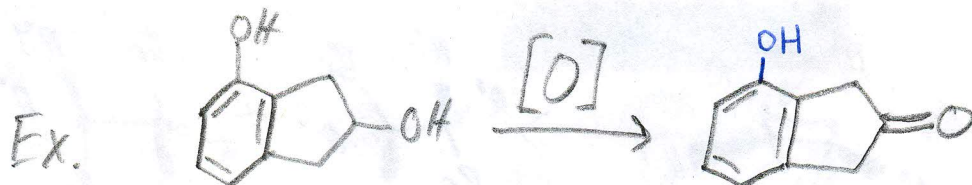
* A type of E1 elimination



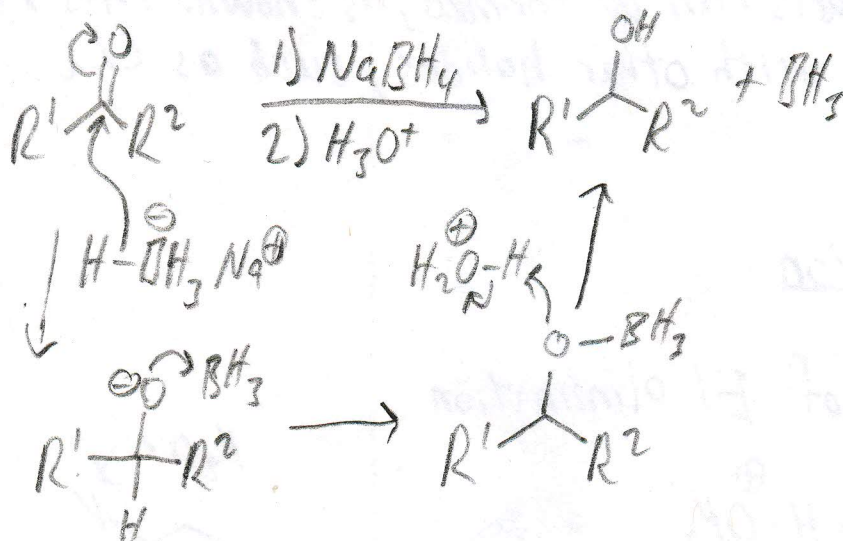
* Acid is required to catalyze this reaction because while $-\text{OH}$ is not a very good leaving group, $-\text{OH}_2^+$ is.

Oxidation of Alcohols

* Three reagents are commonly used to perform oxidation of alcohols: H_2CrO_4 , HOX , and KMnO_4

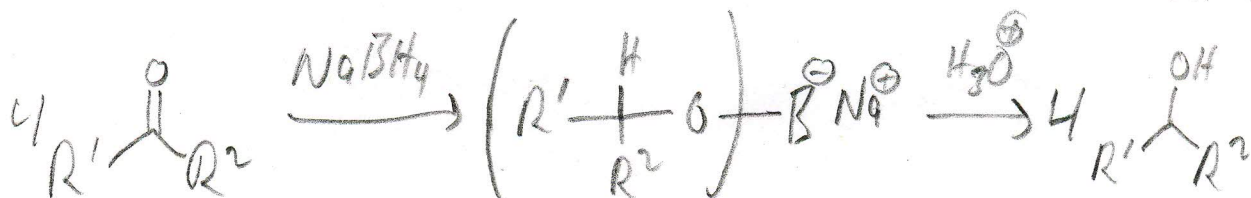


Reduction of Carbonyl Moieties



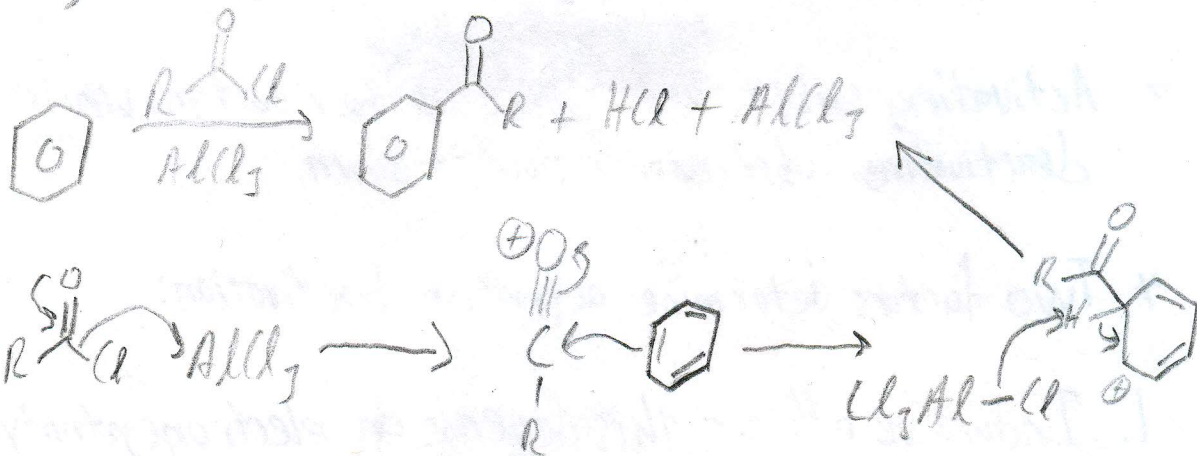
* An important point is that boron (B) is less electronegative than both carbon and hydrogen, which is why the hydrogen takes its shared electrons when it leaves in the first step.

* Note also that 1 mole of NaBH_4 can react w/ 4 moles of starting material.

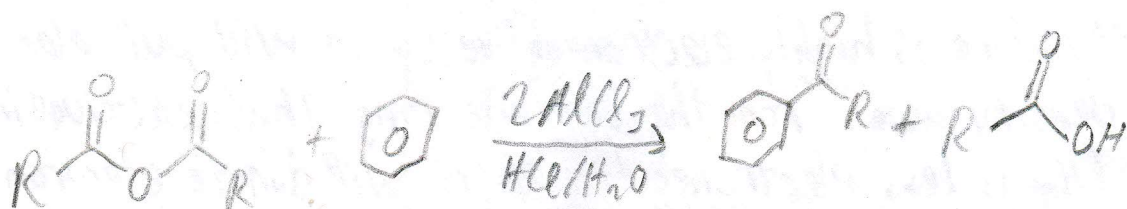


Friedel-Crafts Acylation

* This reaction places an acyl group on a phenyl ring using an acyl chloride.



* Anhydrides will also add an acyl group to a phenyl ring too, but they require 2 equivalents of AlCl₃



Bromination of a Benzene Ring

* This is classified as an electrophilic aromatic substitution.



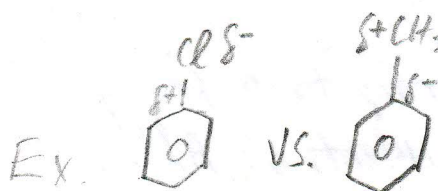
Reactivity of a Benzene Derivative

* If there is already a substituent on a benzene ring, it will affect reactivity and regiochemistry of an additional reaction.

* Activating substituents speed up the reaction, while deactivating substituents slow it down.

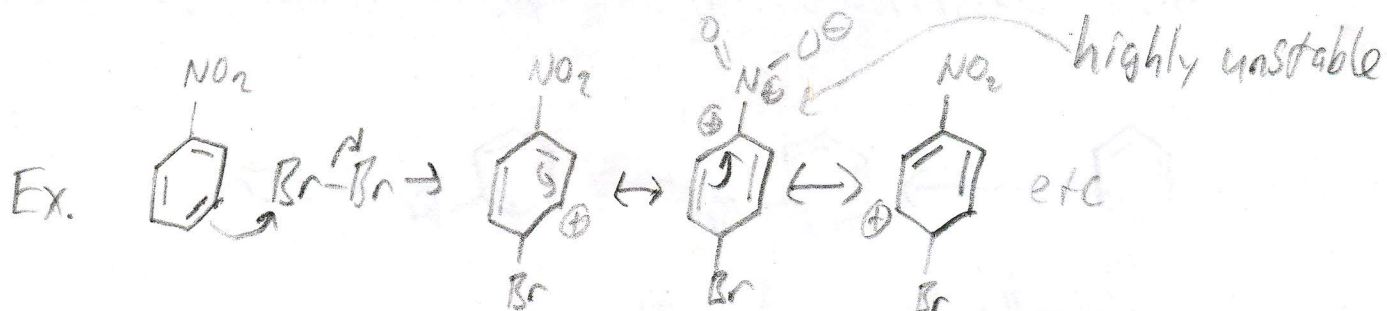
* Two factors determine activation/deactivation:

1. Inductive effect - this depends on electronegativity of the substituent.



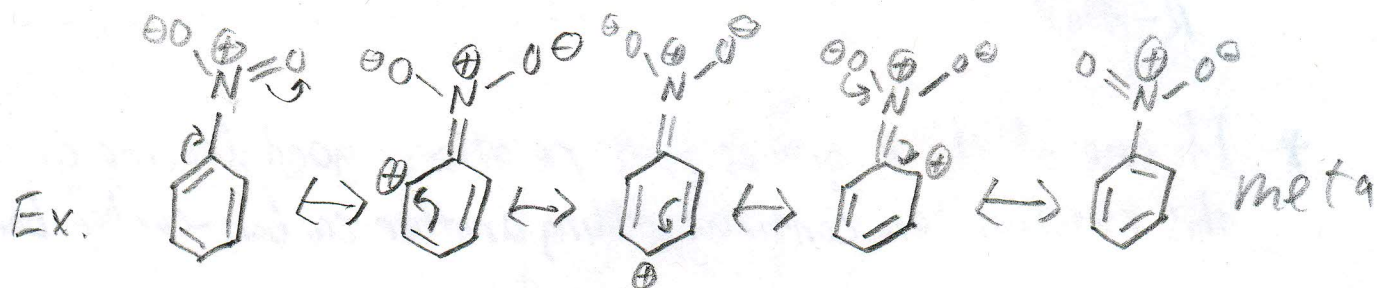
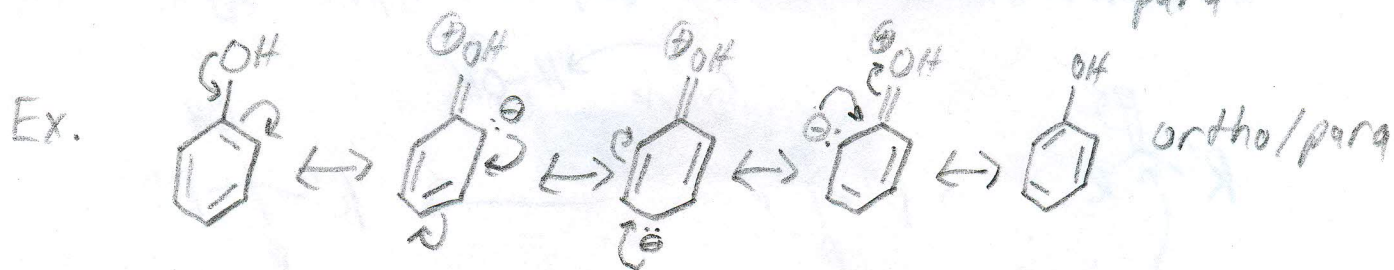
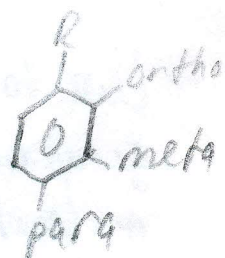
- Chlorine is highly electronegative so it will pull electron density away from the benzene ring, thus deactivating it. CH_3 is less electronegative so it will donate electron density into the benzene ring, thus activating it.

2. Resonance effect - Electron density can enter or leave a ring by resonance, thus activating/deactivating the ring.



* Two positive charges next to one another makes this unstable.

* Substituents also make the ring ortho/para- or meta-directing.



* So, the electron-rich positions will be directed to.

* Note the the NO_2 does not direct towards the meta position; rather, it directs away from the ortho/para positions by making them more positive.

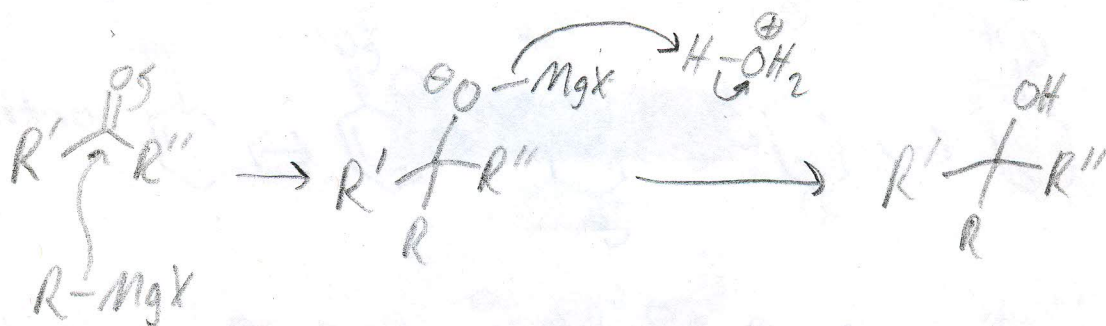
Grignard Reagents

* These reagents are used to form carbon-carbon bonds at the carbonyl carbon.

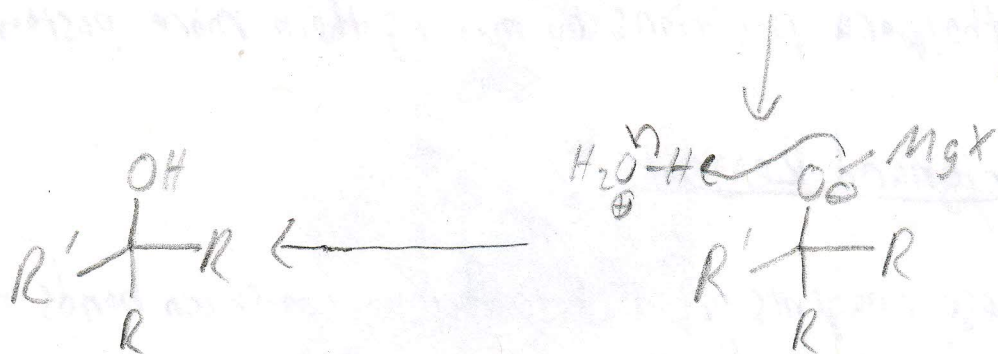
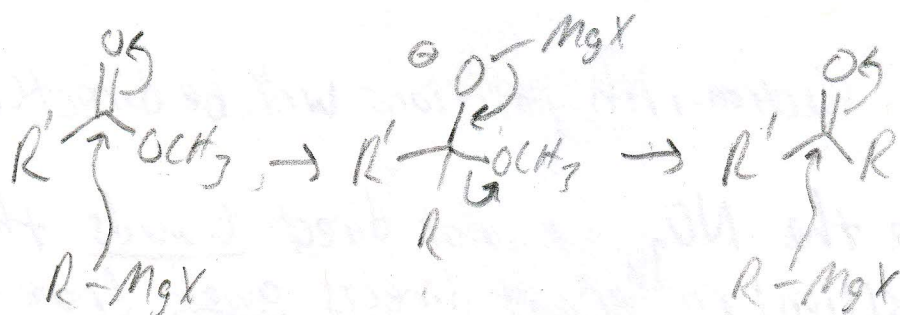
* The Grignard reagent is made by mixing an alkyl halide with magnesium in an aprotic solvent.



* Due to the relative electronegativities of the alkyl group and the Mg, the alkyl group will act as a nucleophile and adds to the carbonyl carbon, producing an alcohol.

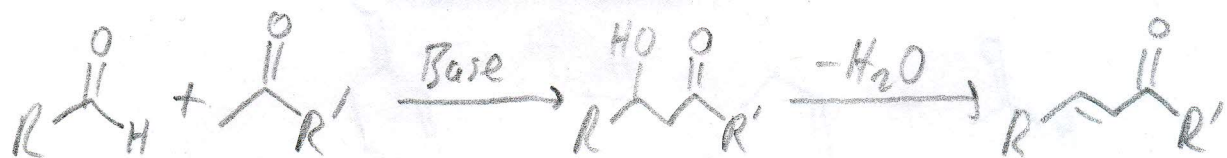


* If one of the R groups is a relatively good leaving group, this reaction can continue, adding another carbon-carbon bond:

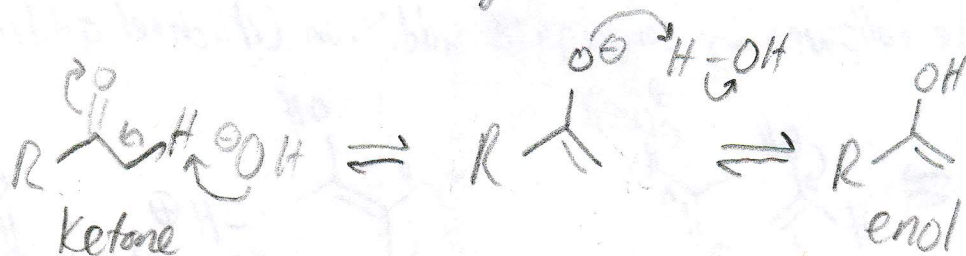


Alcol Condensation

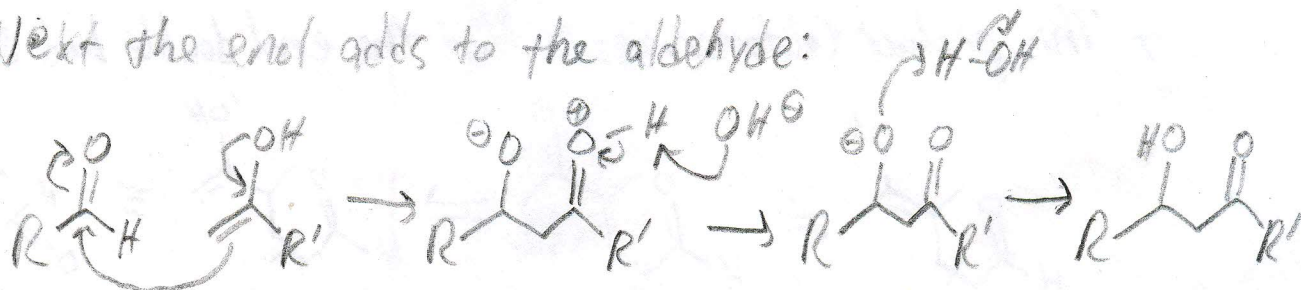
* This reaction is actually two reactions in one. First there is an addition of an enolate to a carbonyl group, and there is a condensation.



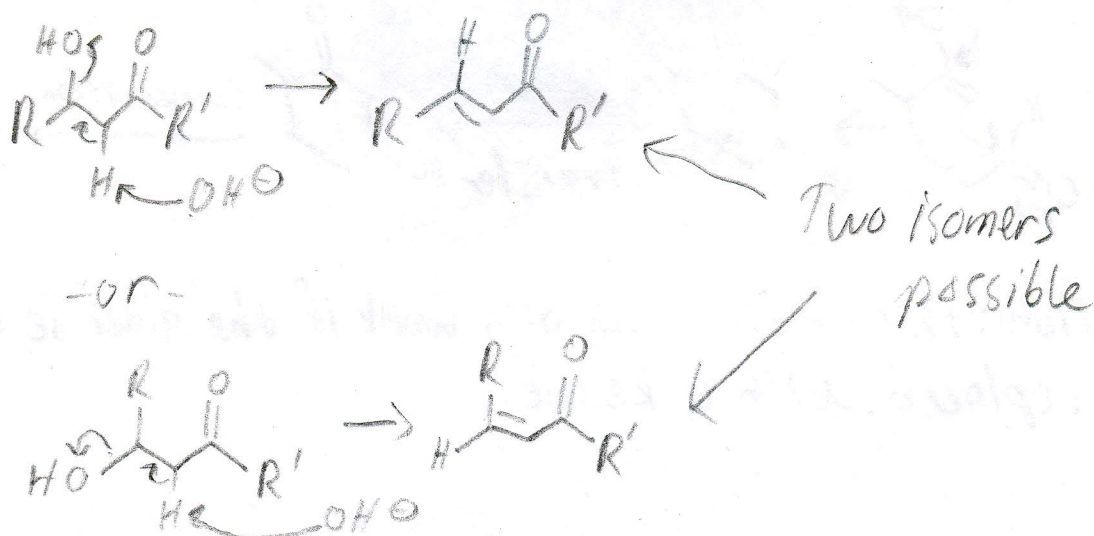
* First the ketone undergoes tautomerization to an enol:



* Next the enol adds to the aldehyde:

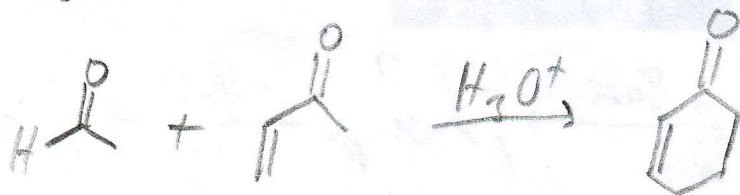


* Finally, the molecule is condensed (or dehydrated):

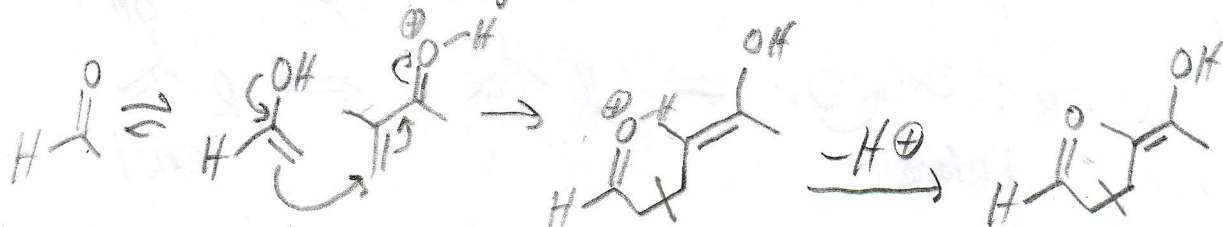


Robinson Annulation

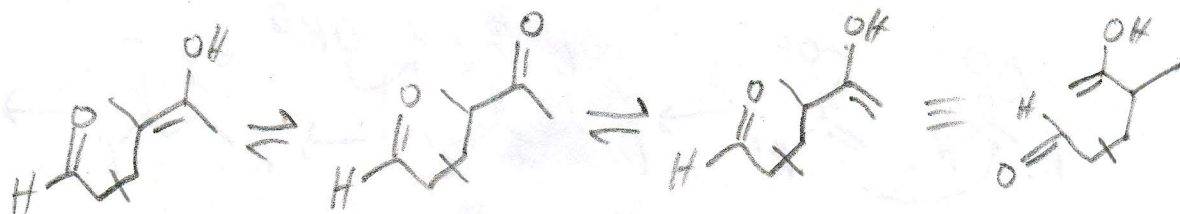
- * This reaction consists of a Michael addition followed by an intramolecular Aldol condensation to form a six membered ring bearing a ketone



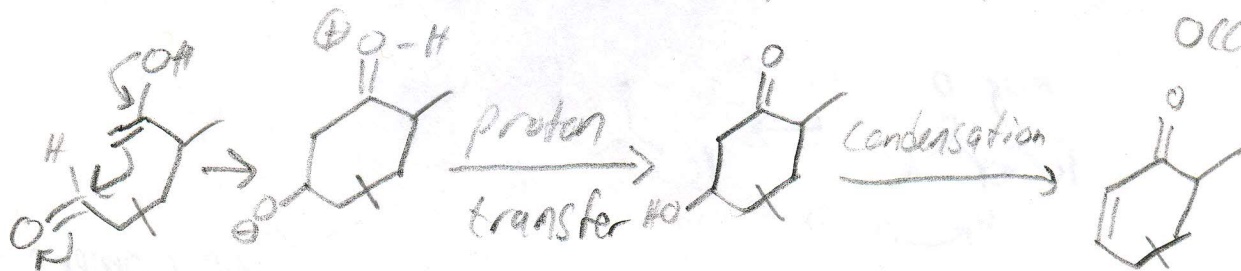
- * The reaction begins with tautomerization of the aldehyde followed by conjugate addition (Michael addition):



- * This product tautomerizes so that the enol double bond shifts



- * Then an intramolecular Aldol addition, followed by condensation, occurs.

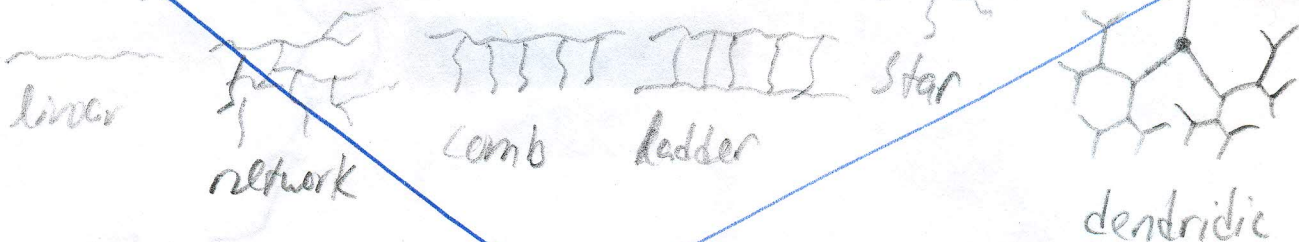


- * Note: this reaction will also work if the aldehyde is replaced with a ketone.

/Polymers/

* A polymer is a repeated chain or network of single units (monomers)

* Some types include the following:

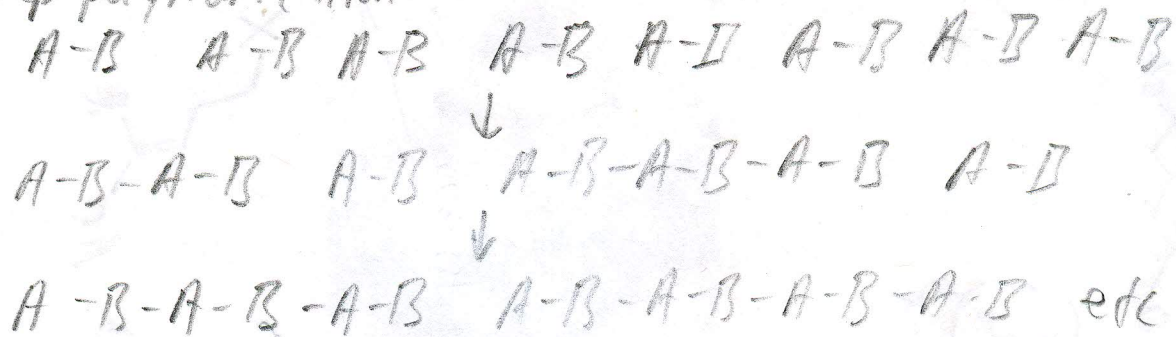


* Polymers can also come in distinct sequences:

- homopolymer: A-A-A-A-A-A-A
- copolymers:
- random - A-A-B-A-B-B-B-A-B-B
 - alternating - A-B-A-B-A-B-A-B
 - block - A-A-A-A-A-B-B-B-B-B
 - graft - A-A-A-A-A-A-A-A-A-A
 B-B-B-B-B-B

* Polymers commonly form by two methods:

1. Step polymerization:



2. Chain polymerization: Initiator = I_n

