MIDTERM 1 NOTES/ REVIEW

Experiment 1

Concepts:

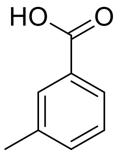
- How to isolate an organic compounds: react, extract, purify then TLC
- Extraction
- Sublimation
- Thin Layer Chromatography (TLC)

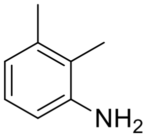
Extraction

- Used to remove large amounts of side products/impurities/salts as a first step
- Involves an aqueous phase and an organic phase
- Use acids and bases to move impurities (or your own product) into the aqueous phase
    - If you move your product into the aqueous phase you usually need to move it back into the organic phase unless you plan on precipitating out your product.
- After collecting all your product into the organic phase, use a brine wash to remove any traces of salt and water into the brine phase
- Phases must be immiscible
- Use Na_2SO_4 or $MgSO_4$ as a drying agent in the org. layer to remove any remaining traces of water!

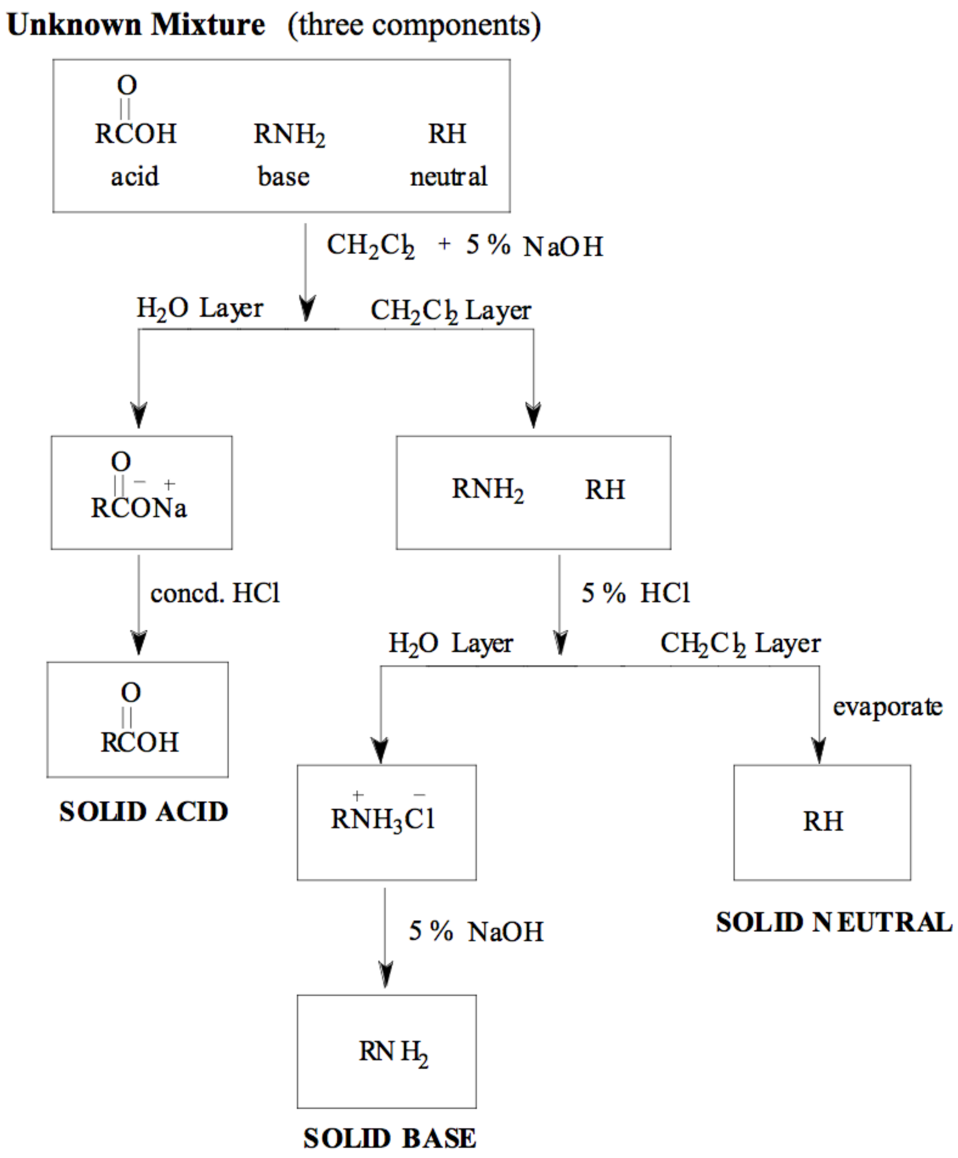
Test Questions

Provide a flow chart to isolate each of the compounds below which is presented to you as a powdered mixture:

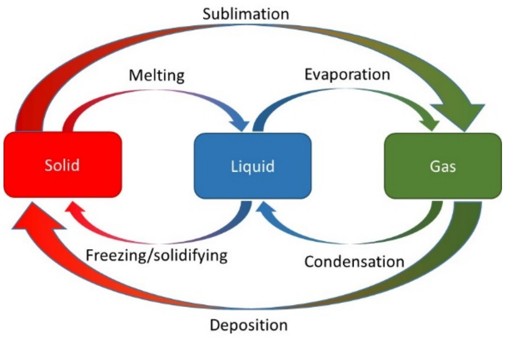




Acid/Base Extraction Separation Scheme



Sublimation



- Recall:
- You are either decreasing the pressure (via vacuum) or increasing the temperature such that your crude product sublimates.
- The cold finger must be filled with ice or dry ice such that your purified product deposits onto the cold finger

- Works based on the fact your intended product can sublimate while your impurities do NOT sublimate at the given temperature.

Test Question

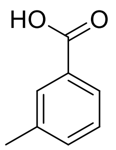
Explain why you must ensure no solvent is present in your crude mixture when performing sublimation purification.

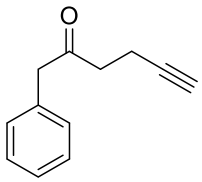
Thin Layer Chromatography

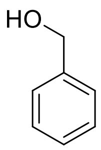
- Used to separate compounds on a silica plate to see what compounds are in your mixture, identify compounds using a standard or assessing purity
- Only aromatics, carbonyls, and unsaturated compounds show up under UV.
- Silica plates are polar compounds and so they hold onto polar compounds tightly (this is called the stationary phase)
- The mobile phase competes with the bonds between the compounds and the stationary phase and push the compounds up
    - More polar mobile phases are stronger and so can pull more polar compounds up the TLC plate
- The less polar the compound is the farther it moves up the plate
    - Since non-polar compounds do not "stick" to the polar stationary phase and so they move up easier
    - Polar compounds stick to the stationary phase and so they require polar solvents to push them up.
- R_f = distance from start / distance of solvent line
- Reverse chromatography uses NON-POLAR stationary phases and so polar compounds move farther up than non-polar compounds

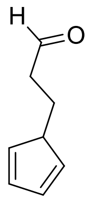
Test Question

1. Predict the TLC plate if you were to TLC a mixture of the following compounds using an appropriate eluent system to ensure optimal separation:

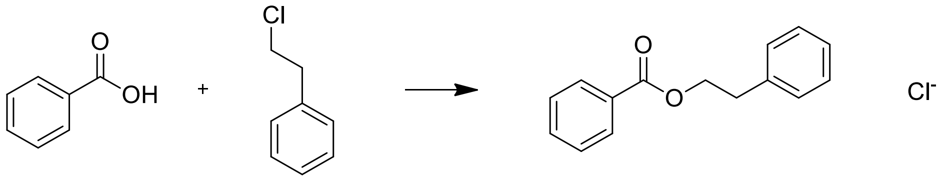




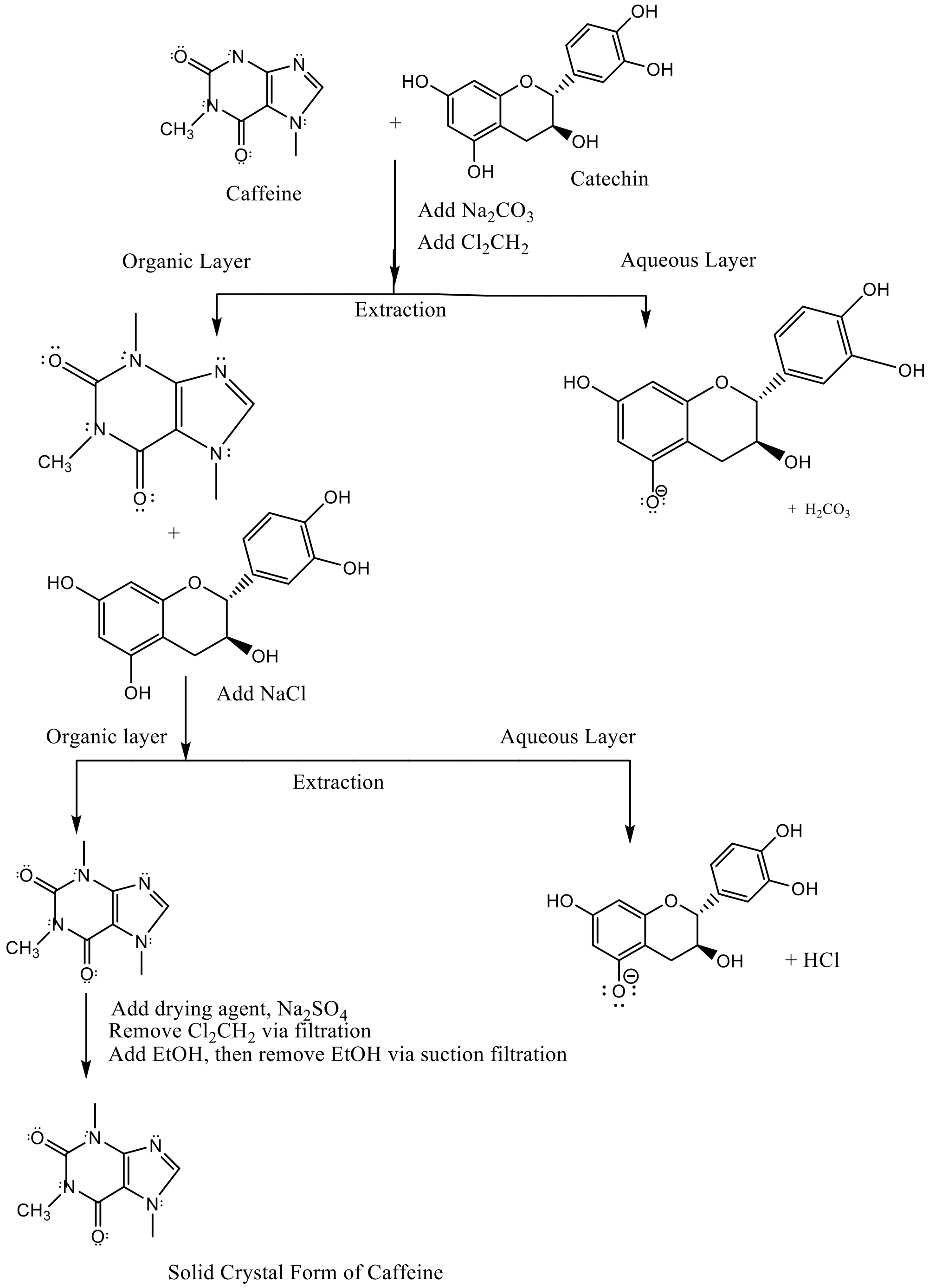




2. Predict the TLC plate of the following reaction at:
    a. The start of the reaction
    b. The middle of the reaction
    c. The end of the reaction
    Using an appropriate eluent system to ensure optimal separation.



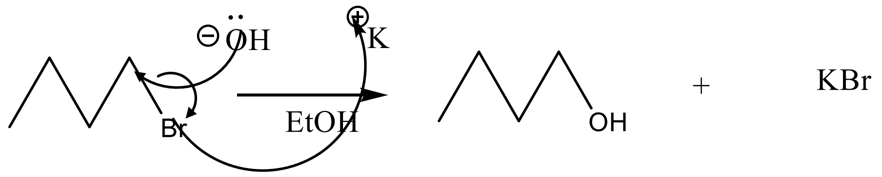
Flow Chart


Caffeine
+
Catechin
Add Na_2CO_3
Add Cl_2CH_2
Organic Layer
Aqueous Layer
Extraction
+ H_2CO_3
+
Add NaCl
Organic layer
Aqueous Layer
Extraction
+ HCl
Add drying agent, Na_2SO_4
Remove Cl_2CH_2 via filtration
Add EtOH, then remove EtOH via suction filtration
Solid Crystal Form of Caffeine

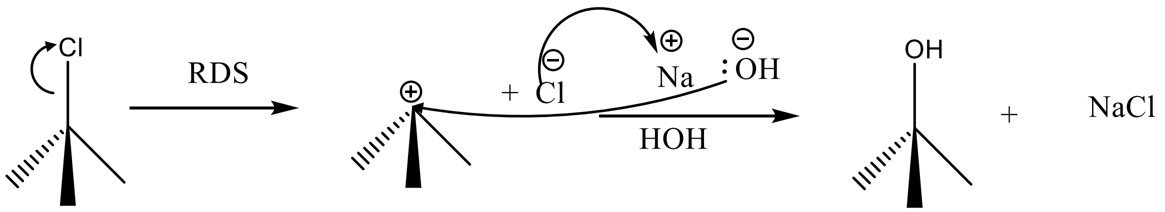
Experiment 2

Mechanism:

Part A: Sn2 reaction



Part B: Sn1 reaction



Sample Calculations

Part A

All Data used is from the sample taken at the 15 minute mark.

Mol HCl titrated = CΔV

=0.1M x 0.008L

=0.0008mol HCl

Mol KOH neutralized

= 1:1 mol KOH : mol HCl

=0.0008mol KOH

[KOH] $= \frac{mol\ KOH\ neutralized}{Volume\ of\ aliquot}$

$= \frac{0.008}{0.0051}$

=0.1969M

ln[KOH] = ln (0.1969) = -1.8562

1/[KOH] = 1/0.1969 = 6.373

$\therefore \mathit{The\ concentration\ of\ KOH\ is\ } 0.1969M \mathit{\ for\ Order\ } 0, -1.8562M \mathit{\ for\ Order\ } 1,$ $\mathit{and\ } 6.373M \mathit{\ for\ Order\ } 2$

Part B

All data used is from the 20% conversion

[tBuCl] that wasn't converted:

$c_1v_1 = c_2v_2$

$(0.1)(0.003) = (c_2)(0.02)$

$C_2 = 0.015M$

C_2 (% of tBuCl that was not converted) = [tBuCl] that was not converted

(0.015)(0.80) = 0.012M

$\therefore \mathit{the\ concentration\ of\ tBuCl\ left\ over\ in\ the\ solution\ with\ } 20\% \mathit{\ conversion\ for}$ $\mathit{Order\ } 0 \mathit{\ is\ } 0.012M$

$$\boldsymbol{ln}([\boldsymbol{tBuCl}]) = ln(0.012M) = -4.42\ M$$

$$\frac{\mathbf{1}}{[\boldsymbol{tBuCl}]} = \frac{1}{0.012M} = 83.2\ M$$

$$\therefore The\ first\ order\ concentration\ tBuCl\ is\ -4.42M and\ the\ second\ order\ concentration\ of\ tBuCl\ is\ 83.2\ M$$

Concepts:

Reaction kinetics and how to change kinetics of an S_N2 reaction based on the leaving group and how to change the kinetics of an S_N1 reaction based on the solvent.

Reaction Kinetics

The rate is determined by:

$$R = k\ [A]^x [B]^y$$

For the given equation:

$$A + B \rightarrow C + D$$

- k is the rate constants and only changes when the conditions of the reaction changes. It does not depend on the concentrations of products and reactants
- x and y are the orders of the reaction → these MUST be determined experimentally
- 0 order reactions: plot [reactant] vs. time where slope = -k
  - These reactions are where the formation of product does not depend on the consumption of reactant
  - Rare and usually we say a reactant is zero order with respect to another product
  - Enzyme-catalyzed reactions tend to be zero order
- 1st order reactions: plot ln [A] vs. time where slope = -k
  - This is determined from the change in [A] over the change in time t (derivative)
- 2nd order reactions: plots 1/[A] vs. time where slope = k
  - This is only valid when reactant concentrations are equal ([A] = [B])
- You should know the units and rate equations for each order for good measure

Nucleophilic Substitution

- There are 2 kinds of nucleophilic substitutions: S_N2 and S_N1
- S_N2 is bimolecular → the nucleophile attacks the electrophile WHILE the leaving group is leaving
  - Product formation depends on both electrophile and nucleophile → therefore second order reaction → therefore $d[A]/dt = -k[A][B]$
  - You get inversion of stereochemistry because nucleophile attacks from the back
  - This substitution is favoured by primary carbons

- S_N1 is unimolecular → nucleophile attacks the electrophile AFTER the leaving group leaves
    - Product formation only depends on electrophile concentration → therefore first order reaction → therefore $d[A]/dt = -k[A]$
    - You get a mix of stereochemistry since the carbocation intermediate becomes sp^2 which is flat so the nucleophile can attack from either side of the carbon (this is usually a 50/50 mix)
    - This substitution is favoured by tertiary carbons

Effect of Leaving Group on Substitution

- What you should have seen in the experiment was that the rate of the bromobutane was much quicker than the rate of the chlorobutane reaction
- This is because bromine has a larger valence shell and is essentially farther from the carbon, this means it is very willing to leave.
- The chlorine on the other hand is closer to the carbon and is less likely to leave.
- Based on this, will you have a faster or slower rate with iodine? How about with fluorine?
- What about the nucleophile? Does the rate increase with a strong nucleophile such as NaH? What about a weak nucleophile such as H_2O?
- You should be able to judge the rate of a reaction (fast or slow) based on the leaving group, and the nucleophile
- For good measure you should know what solvents favour S_N2 and what solvents favour S_N1 (and by favour I mean increase the rate of)
- You should also recognize when something will be S_N2 and when it will be S_N1

Effect of solvent on the S_N1 reaction

- You should have noticed that when the reaction was run in a solvent containing more acetone, the reaction rate decreased
- This is because the leaving group is a chloride ION, which is stabilized by water molecules surrounding it
- In a solvent containing more acetone, there is less water to stabilize the chloride ion and so the chloride is less likely to leave, slowing down the substitution reaction.
- You should be able to consider how the solvent affects the rate of reaction by considering whether the solvent is polar or non polar and protic or aprotic

Experiment 3

Formulas

$$P_{gas} = P_{atm} - P_{water} - P^*$$

$$n_{KBr} = n_{gas} + n_{butanol} = n_{E2} + n_{Sn2}$$

Sample Calculations:

all calculations are of 1-bromobutane at reflux
Pgas:

$$P^* = \frac{22.6\, mm\ of\ H_2O}{13.6\, mm\ of\ H_2O} = 1.662\ mmHg$$

$$\begin{aligned} Pgas &= Patm - Pwater - P^* \\ &= 756mmHg - 15.8mmHg - 1.662mmHg \\ &= 738.538mmHg \times 0.00131578947atm \\ &= 0.972\ atm \end{aligned}$$

$\therefore$ *the pressure of the gas was* $0.972\ atm$

Moles of Butene:

$$\begin{aligned} n = \frac{PV}{RT} &= \frac{(738.538\ mmHg \times 0.001333\ bar)(27\ mL \times 10^{-3} L)}{(0.08314\ L\ bar\ K^{-1} mol^{-1})(18.4℃ + 273.15\ K)} \\ &= 0.001096589\ mol \times 10^3 mmol \\ &= 1.097\ mmol \end{aligned}$$

$\therefore$ *the moles of butene are* $1.097\ mmol$
Moles of Butanol:
nKBr = ngas + nbutanol
nKBr – ngas = nbutanol
16.55mmol – 1.097mmol = 15.453 mmol
$\therefore$ *the moles of butanol are* $15.453\ mmol$

Yield:
C_4H_9Br (l) + KOH (s) → $C_4H_{10}O$ (l) + KBr (s)

$$1.5 g_{1-bromobutane} \times \frac{1 mol_{1-bromobutane}}{137.034\ g_{1-bromobutane}} \times \frac{1 mol\ KBr}{1\ mol_{1-bromobutane}} \times \frac{119\ g\ KBr}{1\ mol\ KBr}$$

$$= 1.30\ g\ KBr$$

$$\%yeild = \frac{theoretical\ mass\ of\ KBr}{actual\ mass\ of\ KBr} \times 100\%$$

$$= \frac{1.30\ g}{1.97 g} \times 100\%$$

$$= 66.0\%$$

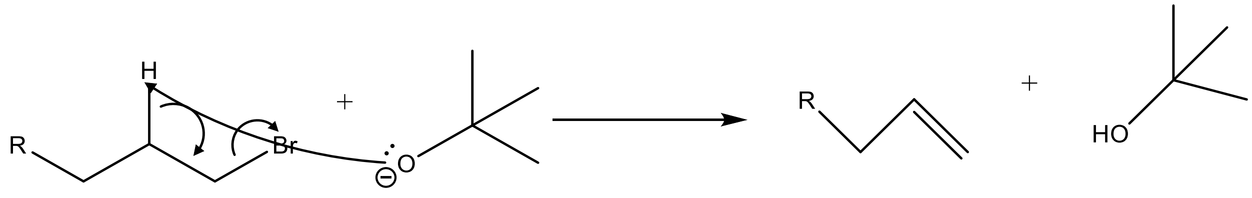
$$\therefore the\ percent\ yeild\ of\ KBr\ in\ the\ reaction\ of\ 1 - bromobutane\ and\ KOH\ is\ 66.0\ \%$$

Sn2:E2 ratio:

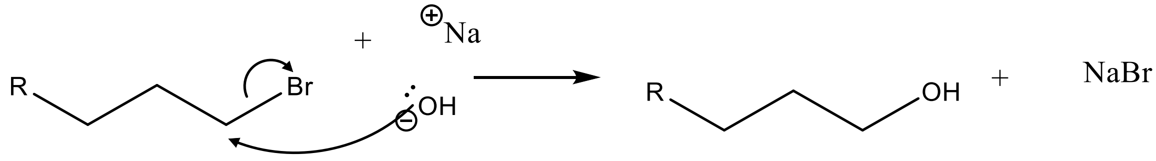
$$\frac{nSn2}{nE2} = \frac{nbutanol}{ngas} = \frac{15.5\ mmol}{1.097 mmol} = 14.13 \quad \therefore the\ Sn2{:}\, E2\ ratio$$

Mechanisms

Scheme 1: E2 reaction



Scheme 2: Sn2 reaction



Concepts:

How to favour S_N2 or E2 product by changing the reaction conditions and the electrophile.

Tip 1: Memorize the table in the introduction

1-bromobutane + KOH at reflux vs 1-bromobutane + KOH at 55 °C

- From the S_N2:E2 ratios, you should have seen that both were dominated by the S_N2 reaction
- HOWEVER, at reflux, more E2 product was formed than at 55 °C (which produced A LOT more S_N2 product in comparison)
- This shows that primary α-carbons undergo the substitution reaction, but introducing heat does cause the elimination product to form

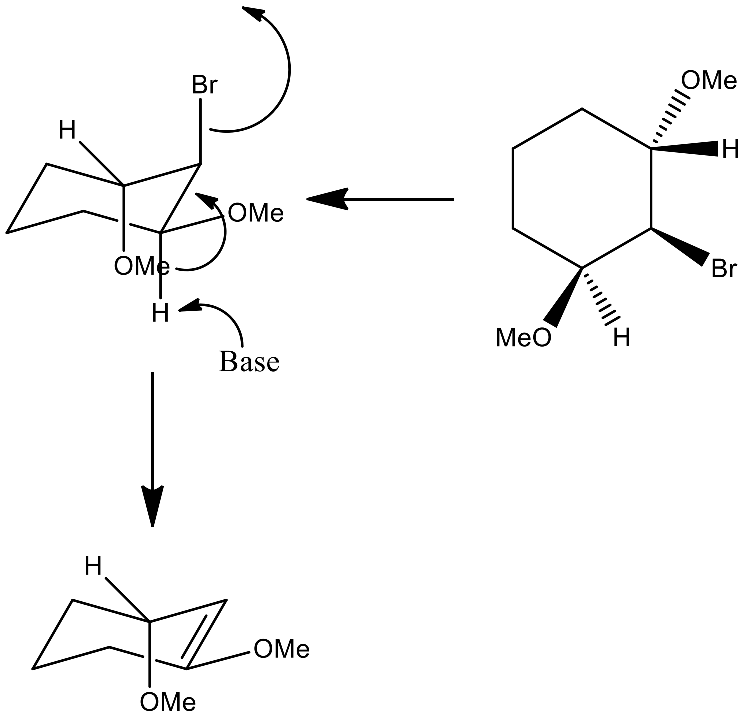
- This means that if it's a primary α-carbon and I wanted elimination, I would need to introduce A LOT of heat or use a very bulky base or a whole new electrophile
    - Using a different solvent with a higher boiling point lets me raise the heat above the ~80 °C which EtOH refluxes at

1-bromobutane + KOH at reflux vs 2-bromobutane + KOH at reflux

- From the S_N2:E2 ratios you should have noticed that 2-bromobutane produced almost exclusively the E2 product, since from the table you see that Strong base + secondary α-carbon = E2 product

Eliminations: Antiperiplanar

- One very important aspect of eliminations is the antiperiplanar requirement.
- We tend to miss this aspect with alkyl chains because the ends of alkyl chains are twistable
- The main importance antiperiplanar-ism comes into play is with cycloalkanes, especially cyclohexanes (which can be in the chair or boat conformation if you recall)
- You should be comfortable drawing chair/boat conformations and knowing syn/anti, up/down drawings for these conformations
- In regards to E2, an E2 reaction will only occur if the leaving group is "antiperiplanar" to the hydrogen, resulting in a "cascade" like elimination reaction.



- You have to consider antiperiplanar-ism since if it isn't satisfied, you probably won't get elimination but instead the substitution

Zaitsev vs. Hoffman Eliminations

- Zaitsev is the elimination in which the most substituted (and most stable) alkene is obtained
- Hoffman elimination yields the least substituted alkene (and the less stable alkene)
- This lets us select what kind of alkene or where the double bond is formed
- **<u>Generally</u>**, Zaitsev conditions require a small base and the typical conditions we use is: NaOMe (base), in MeOH (solvent) under higher temp.
- Generally, Hoffman reactions require a large bulky base and the typical conditions we use is: KO^tBu (base), ^tBuOH (solvent), under cold temp (~ 0 °C)

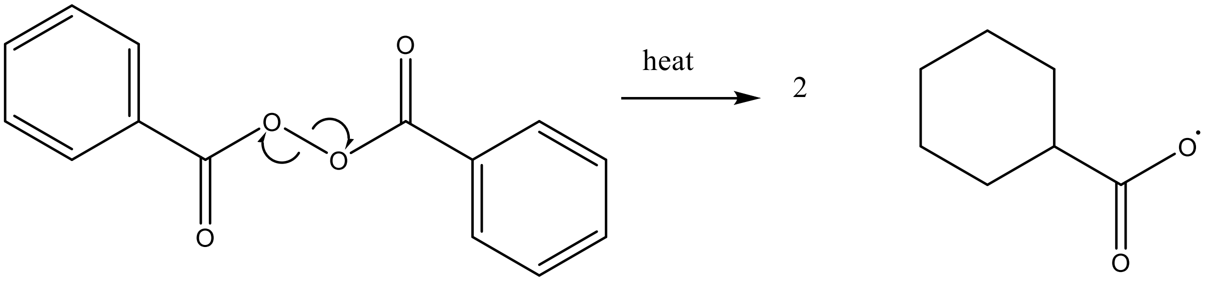
There isn't much "tricky" stuff in this lab, but the main concept I think is that if I ask for a certain substituted product or alkene product then you should know the conditions and reagents (including the electrophile if it's not given) necessary to make said product.

One tricky thing I can think of is CYCLIZATION. If there is a nucleophile and an electrophile on the same compound they will always react first because INTRAmolecular (within the molecule) reactions are A LOT faster than INTERmolecular reactions (between molecules).

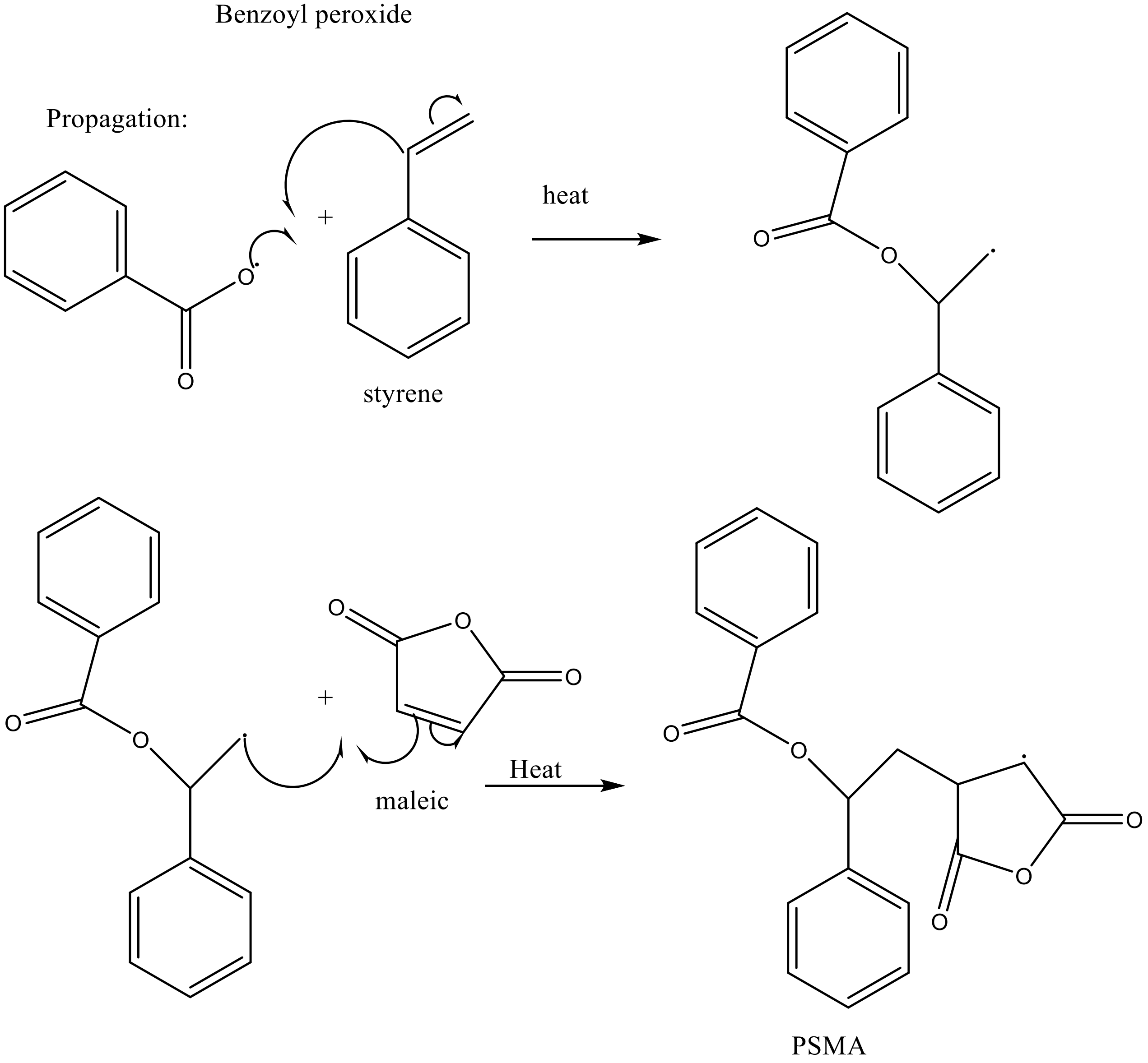
Experiment 4

MECHANISM OF CHAIN-GROWTH OF PSMA:

Initiation:



Propagation:



Concepts:

Learning the mechanisms of polymerization by applying nucleophile-electrophile interactions that occur over and over again.
Knowing how functional groups affect the physical properties of a material especially when these functional groups are repeated (building blocks of the universe!)

Chain Growth Polymers

- Involve alkene monomers
- Relies on the formation of a radical, anion or cation to reaction with another alkene and link together

Mechanism

- The first step of a chain growth polymer is always INITIATION
  - Here the first monomer is activated through some sort of initiator (e.g.: radical, acid, base)
- The next step is always PROPOGATION
  - Here the activated monomer reacts with another monomer to start forming the chain
- The last step can be called "Propogation" still or just "Last step" (I know… anticlimactic)
  - Here the chain ends, either with 2 radicals reacting together (Rather than radical + neutral), or with a cation reacting with an anion, or electrophile reacting with a nucleophile

Homopolymer

- 1 alkene monomer is repeated (they are all the same)
- **Polyacrylamide** is a homopolymer

Alternating Co-polymers

- 2 alkene monomers (A and B) alternate (ABABABABAB)
- **Polystyrene-maleic anhydride** is an alternating Co-polymer (1:1 mixture of polystyrene and maleic anhydride)

Random Co-polymers

- Alkene monomers in a random order (ABBABABABBBABABABAAAABABA)

Step-Growth Polymers

- Step-growth polymers are polymers formed from the DISPLACEMENT of a molecule (if water is displaced, they are called condensation polymers)
- The simple difference between step-growth polymers and chain growth polymers is whether or not something is displaced!

Polymer Stereochemistry

- Similar to homopolymer, alternating copolymers and random co-polymers, polymer stereochemistry follows the same pattern

- All the same stereochemistry = Isotactic polymer
- Alternating stereochemistry = syndiotactic polymer
- Random stereochemistry = atactic polymer

Cross-linking

- Cross-linking the reaction linking ALREADY MADE polymers to each other
    - Slime is the linking of polyvinyl alcohol chains together using sodium borate or sodium silicate
    - The borate and silicate link the chains together and the additional capacity to hydrogen bonds make the slime… slimey
    - DNA is also a "cross-linking" as hydrogen bonds between cytosine and guanine, or thymine and adenosine nucleosides "cross" link the chains together

Part A: Co-polymer Polystyrene-maleic anhydride

- To calculate the theoretical yield the following steps must be taken:
    - Find the limiting reagent:
        - n styrene = (V*ρ)/MW = (2.5 mL * 0.909 g/mL)/104.15g/mol = 21.8 mmol
        - n maleic anhydride = m / MW = 1.5 g / 98.06 g/mol = 15.3 mmol
    - Assume 1:1 mixture and find total moles
        - n total = n maleic anhydride + n styrene = n maleic anhydride * 2 = 43.6 mmol
- To calculate how much you have in terms of moles (assuming you have 3.0 g)
    - Assume 1:1 mixture and you can just do total mass/(MW of styrene + MW of maleic anhydride) = n maleic anhyhdride since that is 1 repeating unit
    - For those of you who don't believe me, here's the proof

$$n_T = n_S + n_M = 2n_M$$

$$\frac{m_S}{M_S} + \frac{m_M}{M_M} = 2\left(\frac{m_M}{M_M}\right)$$

$$\frac{m_S}{M_S} = \frac{m_M}{M_M}$$

$$\frac{m_S}{} = \frac{M_S}{M_M} m_M$$

$$m_T = m_M + m_S$$

$$m_T = m_M + \frac{M_S}{M_M} m_M$$

$$m_T = m_M\left(1 + \frac{M_S}{M_M}\right)$$

$$m_M = \frac{m_T}{\left(1 + \frac{M_S}{M_M}\right)}$$

$$\frac{m_M}{M_M} = \frac{m_T}{\left(1 + \frac{M_S}{M_M}\right) M_M}$$
$$\frac{m_M}{M_M} = \frac{m_T}{\left(M_M + \frac{M_S}{M_M} M_M\right)}$$
$$\frac{m_M}{M_M} = \frac{m_T}{(M_M + M_S)}$$

Since it's a 1:1 mixture $n_M = n_S = m_T/(M_M + M_S)$

A more chemical explanation is that 1 repeating unit consists of 1 styrene and 1 maleic anhydride unit and so the molecular weight is the 2 added together

- So from 3 g, we have 2xn maleic anhydride = 2x the above equation = 29.7 mmol
- 29.7 mmol / 43.6 mmol = 68%

Part B: Nylon

- As before, to calculate the yield you would just determine the molecular weight of 1 repeating unit (here you have to be careful as Nylon is not simply reactant A + reactant B, as water is loss and an amide bond is formed)
  - As opposed to polystyrene maleic anhydride which is literally polystyrene + maleic anhydride nothing gained or loss (look up the formula for each monomer and look up 1 repeating unit of polystyrene maleic anhydride and see for yourself!)
- 1 repeating unit of nylon 6,6 = $C_{12}H_{22}N_2O_2$
- MW = ~226 g/mol
- Find limiting reagent:
  - 20 mL 2% adipoyl chloride = 0.4 mL adipoyl chloride (Density = 1.25 g/mL, MW = 183.03 g/mol) → 2.73 mmol
  - 10 mL 2% hexamethylenediamine = 0.2 mL hexamethylenediamine (Density = 0.840 g/mL, MW = 116.21 g/mol) → 1.45 mmol
  - Again we do 1:1 mix so 1.45x2 = 2.89 mmol theoretical yield
- Lets say we have 0.3 g
  - In terms of moles we have 0.3/ 226 g/mol (MW of 1 repeating unit) = 1.33 mmol
  - So 46% yield
- **The base is to deprotonate the hexamethylenediamine, making it a nucleophile to attack the adipoyl chloride, which is an acyl chloride**

Part C:

Although you don't have to calculate yield for this section, you should know the structure of how borate cross links polyvinylchloride chains (it is the same with silicate, except rather than B it's Si)

Ending Notes

- Not quite sure what they'll test for this section

- I suggest knowing the mechanism for how polystyrene maleic anhydride is formed
- Know the mechanism to form nylon 6,6 and the formation of other nylon derivatives if I gave you OTHER acyl chlorides and OTHER diamines
- Know how borate cross-links polyvinyl alcohol chains and the structure of broate-linked polyvinyl alcohol chains and how it would look like if it was silicate instead.
- Know the answers to all the questions