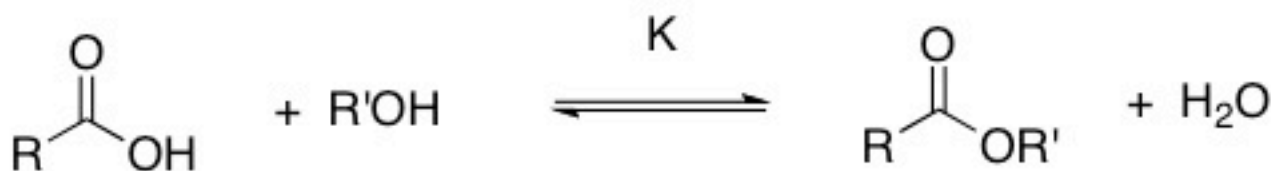
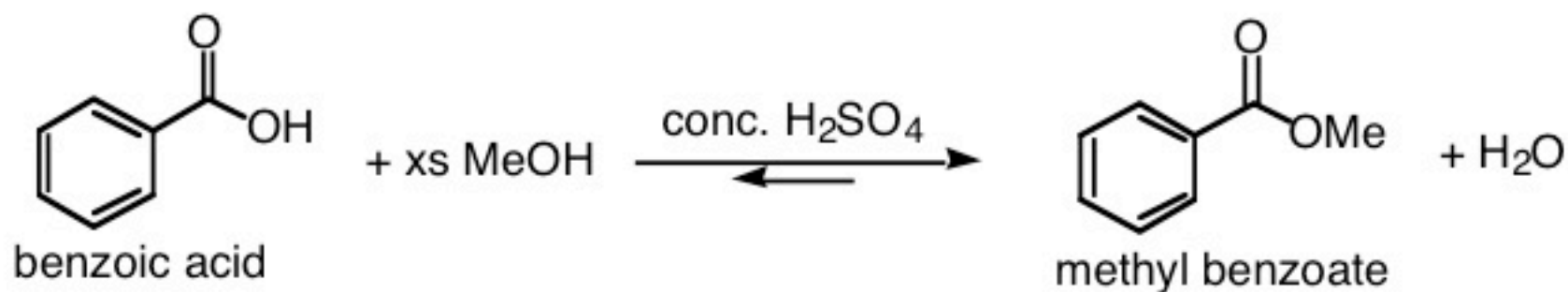
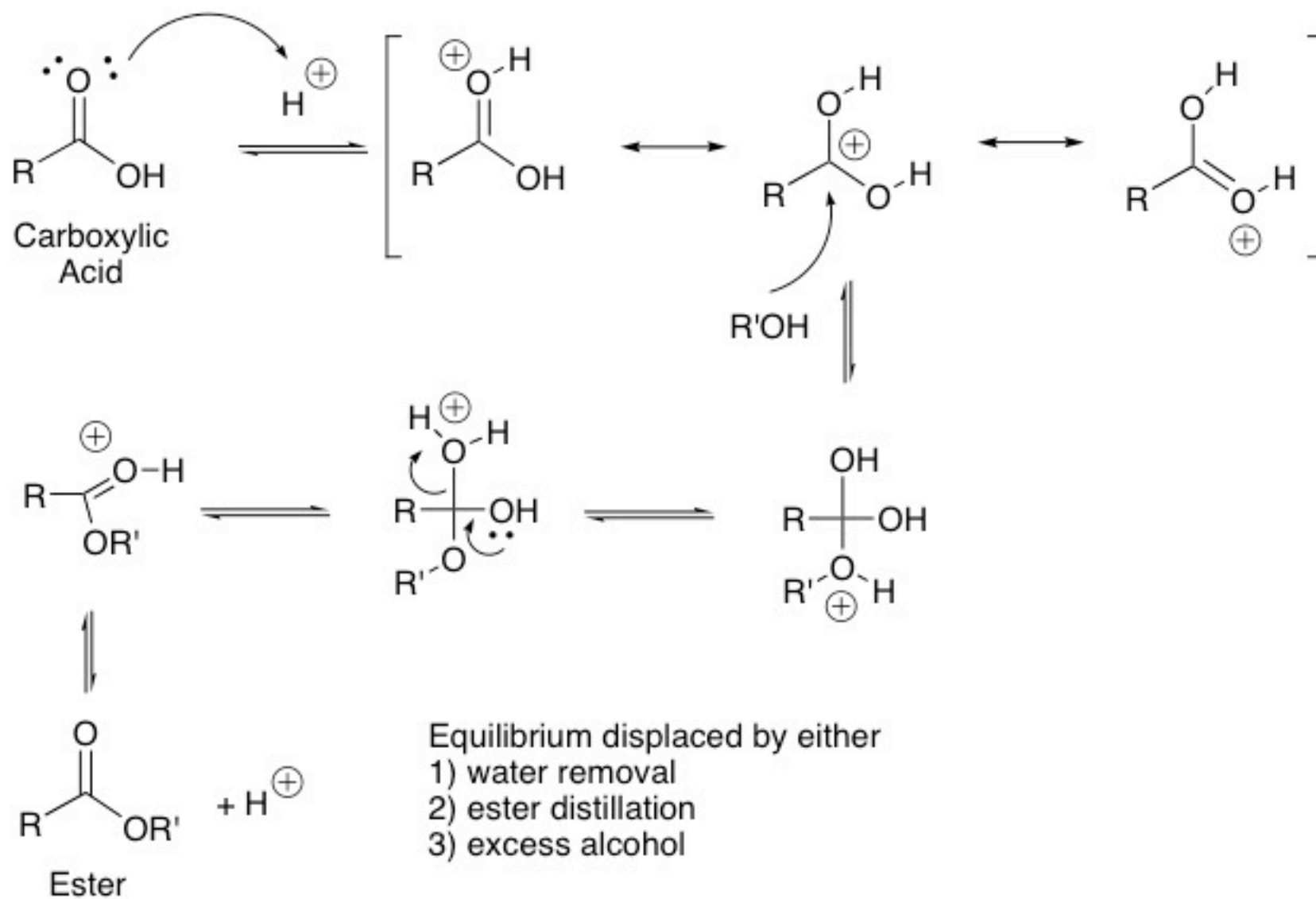


LAB 5 ESTERIFICATION

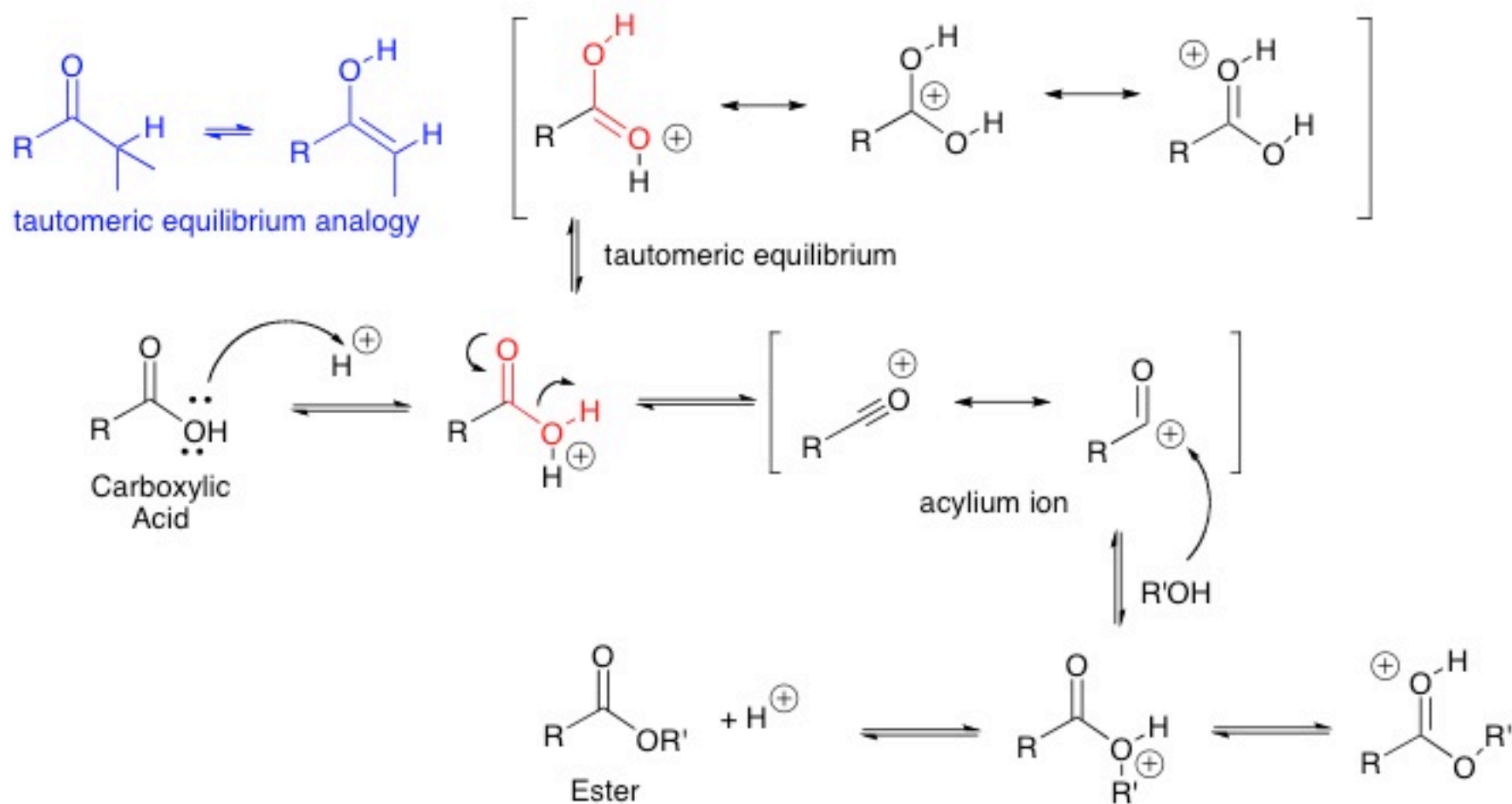
Fischer Esterification: METHYL BENZOATE

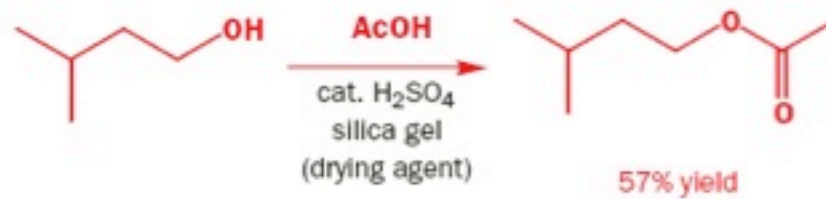
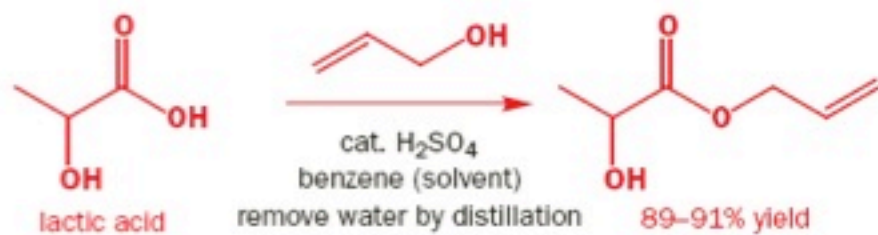
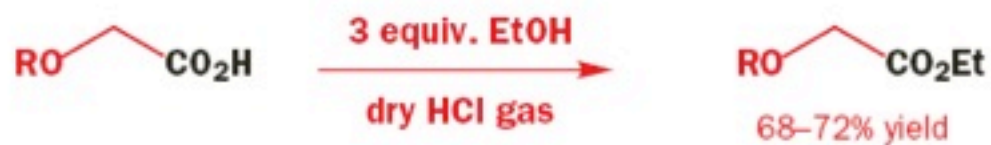


$$K = \frac{[\text{RCOOR}'] [\text{H}_2\text{O}]}{[\text{RCOOH}] [\text{R}'\text{OH}]}$$



Alternate mechanism: protonation at OH



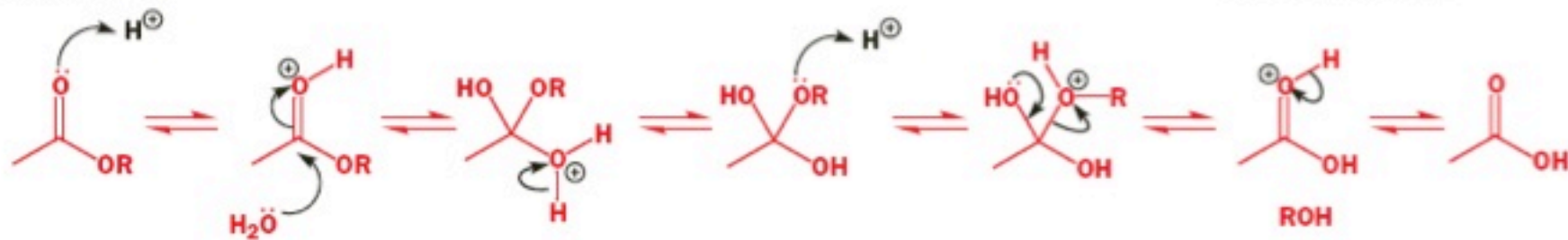


excess water forces reaction forward

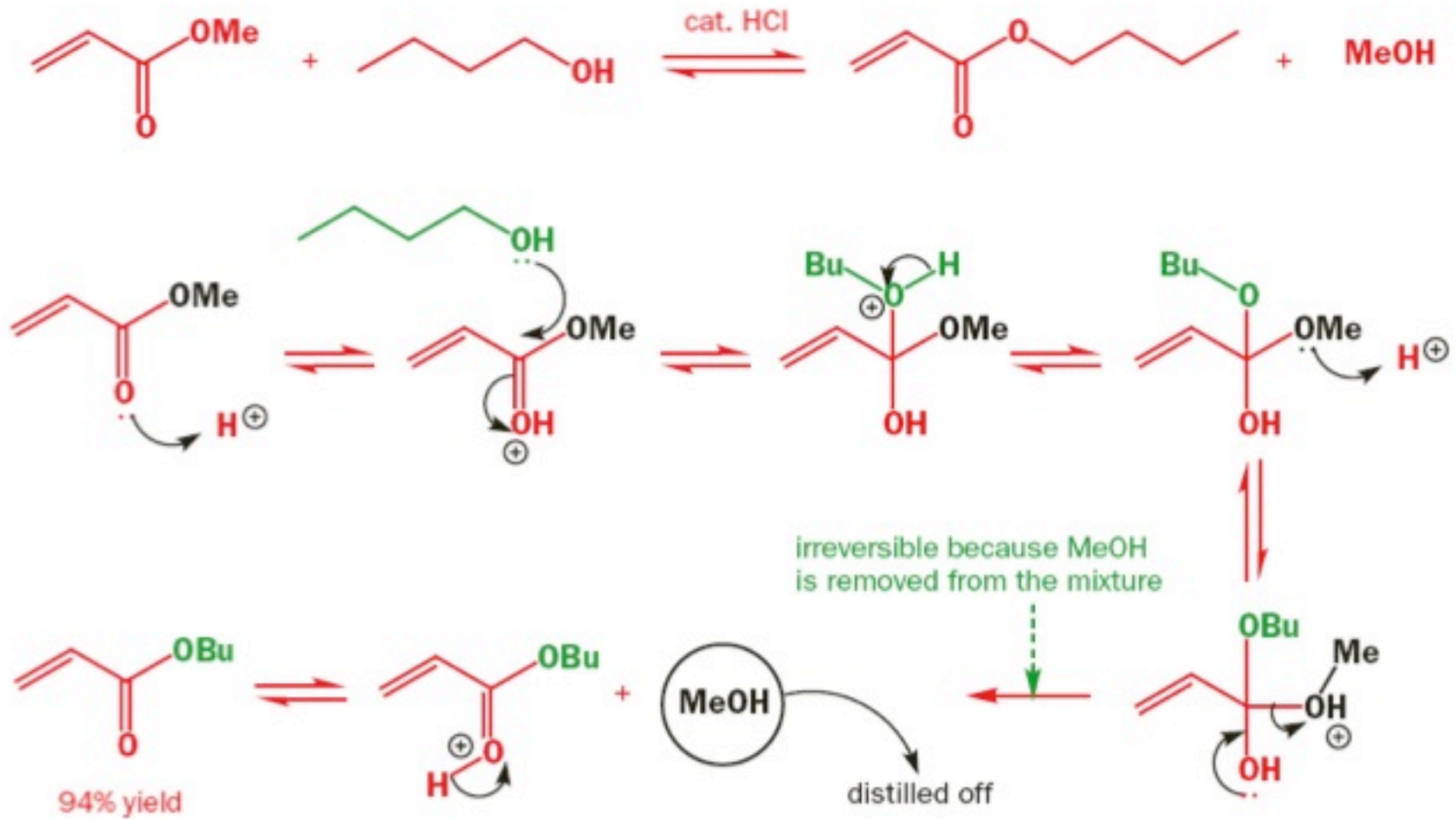
acid-catalysed ester hydrolysis

acid-catalysed ester formation

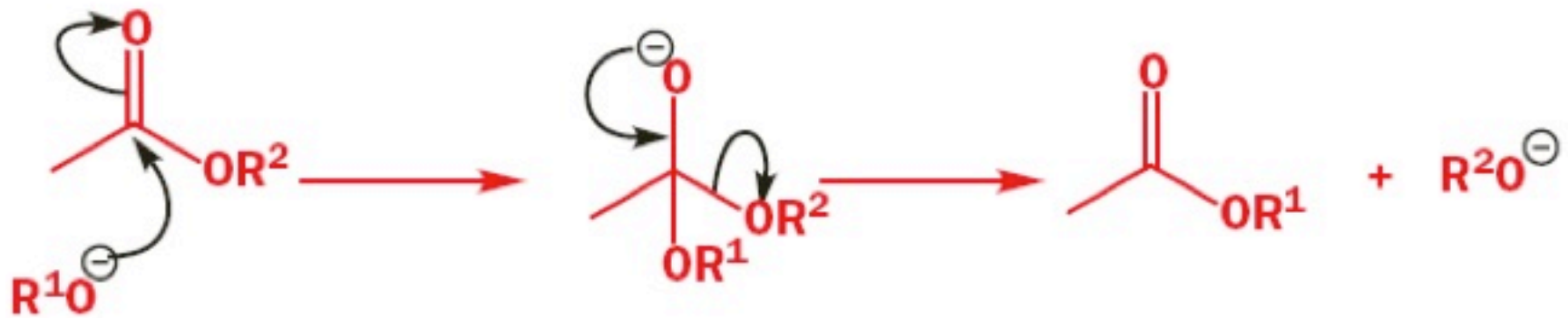
excess ester or removal of water forces the reaction backward



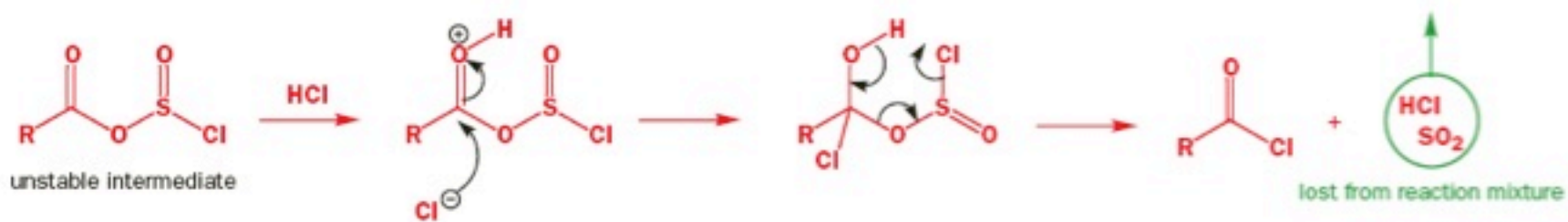
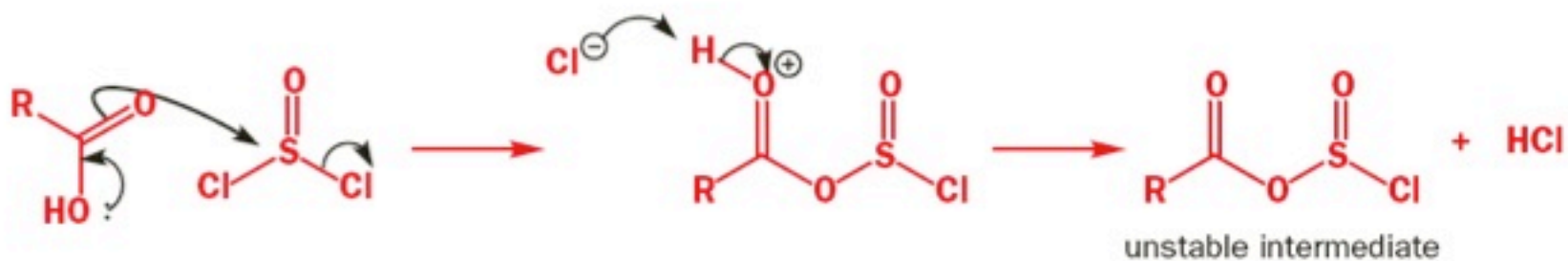
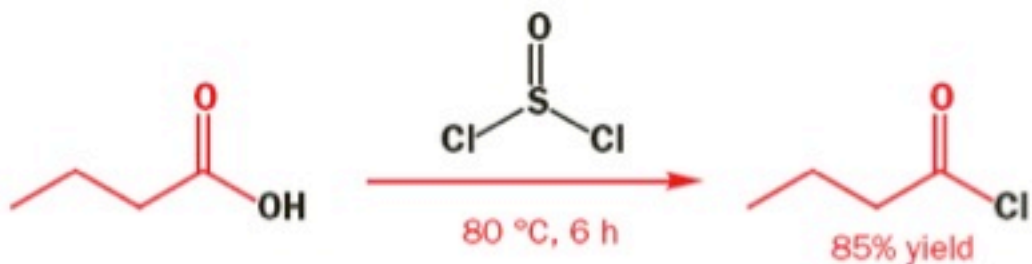
Transesterification under acidic catalysis



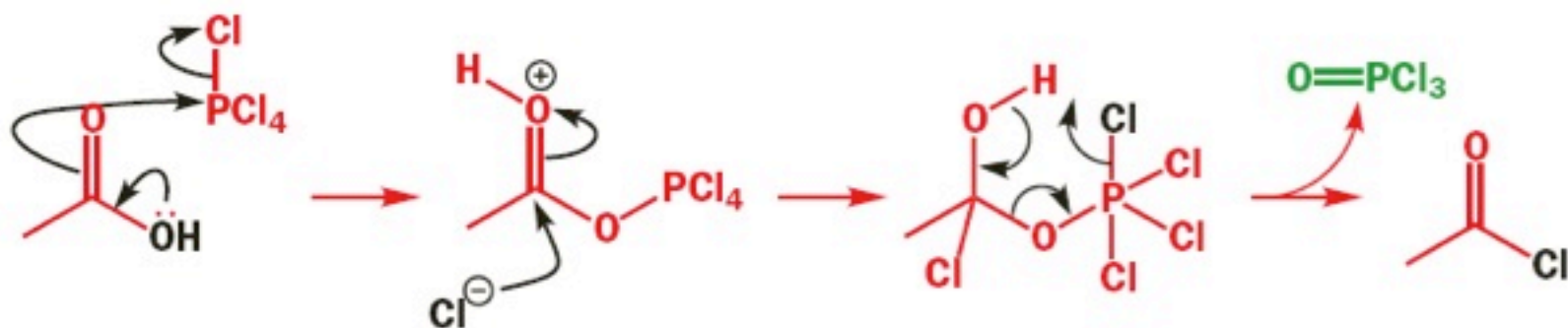
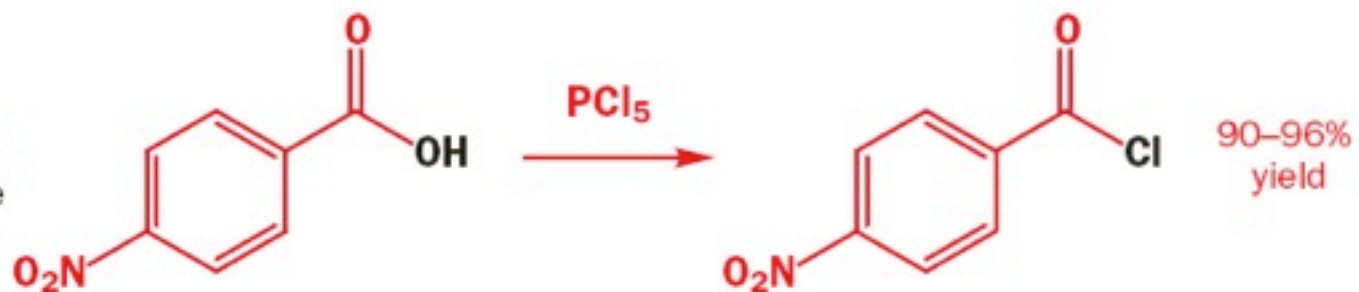
Transesterification under basic catalysis

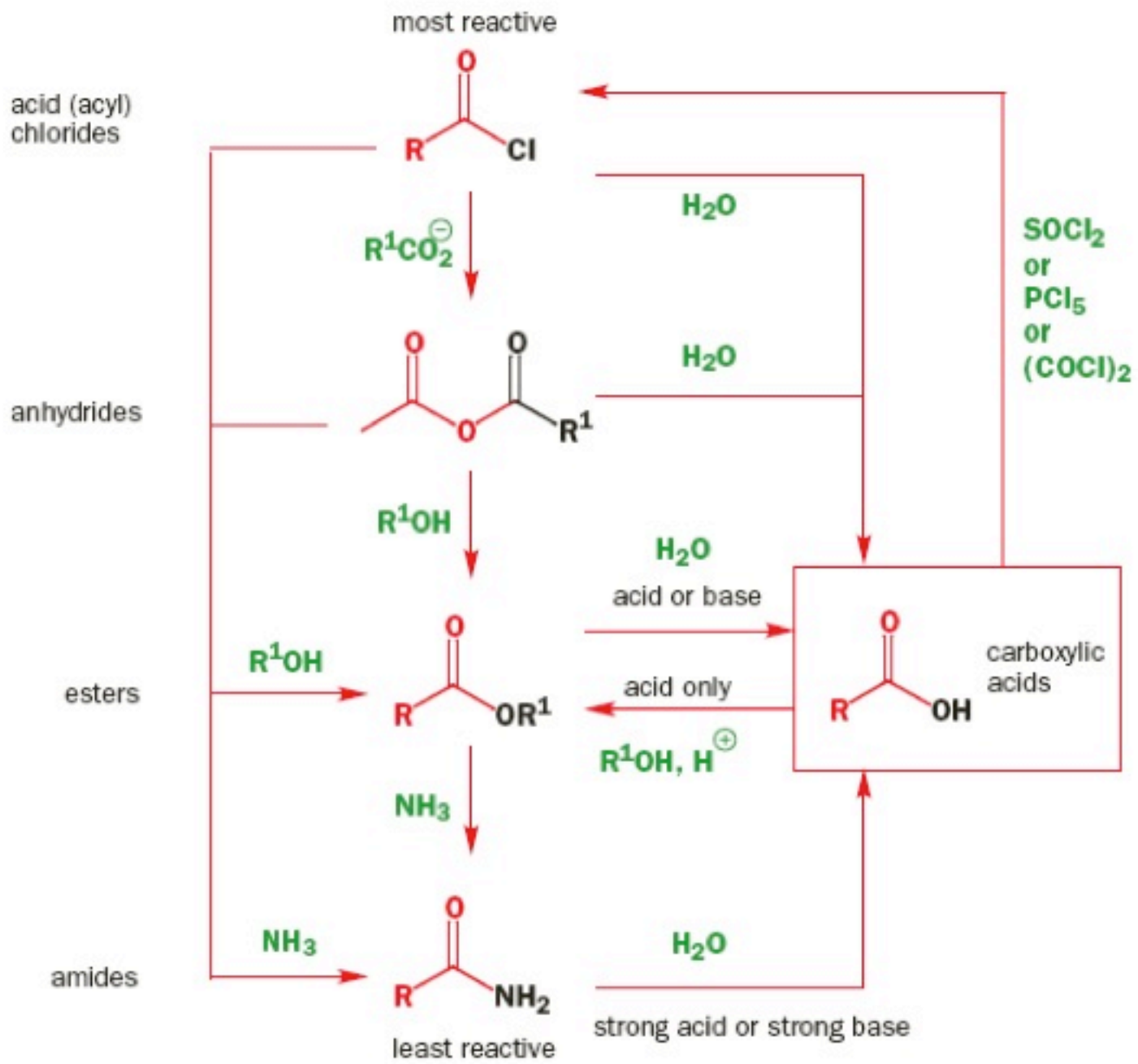


acid chlorides are made from carboxylic acids with thionyl chloride

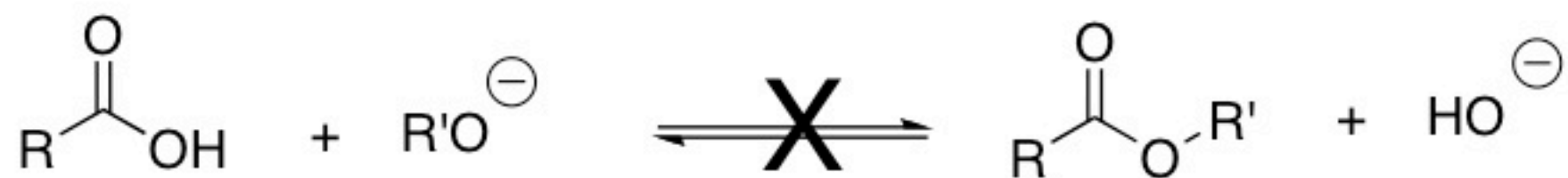


acid chlorides are made from carboxylic acids with phosphorus pentachloride





Carboxylic acids cannot be esterified
under basic conditions



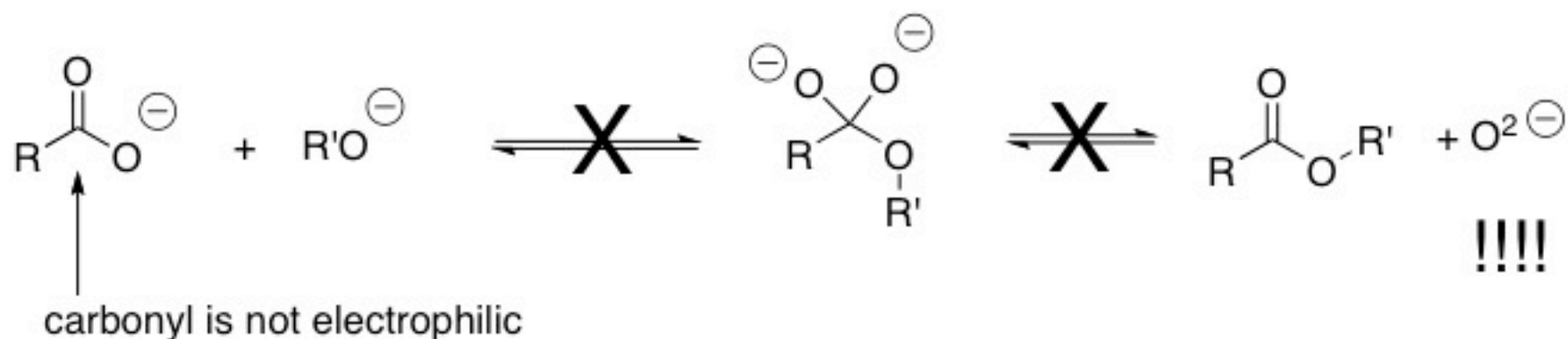


irreversible
due to pKa difference

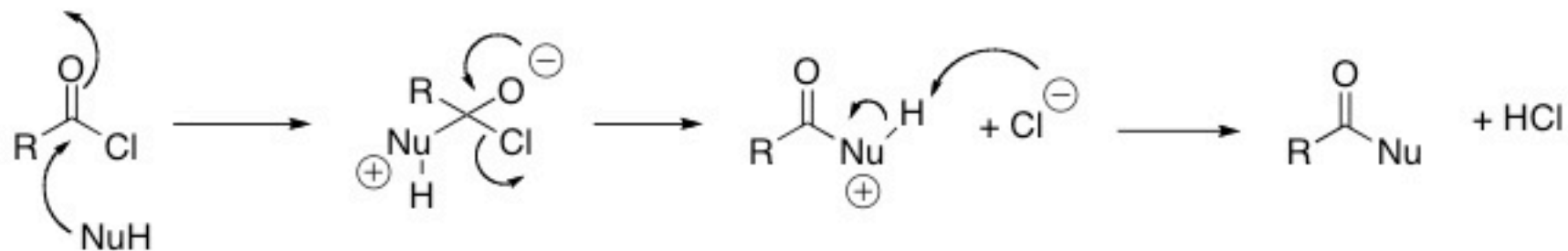
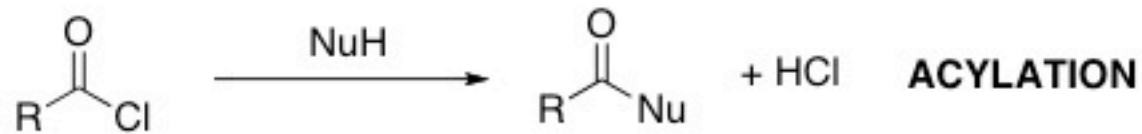
pKa carboxylic acid ~ 5

pKa RO^{\ominus} ~16-18

pKa difference >10

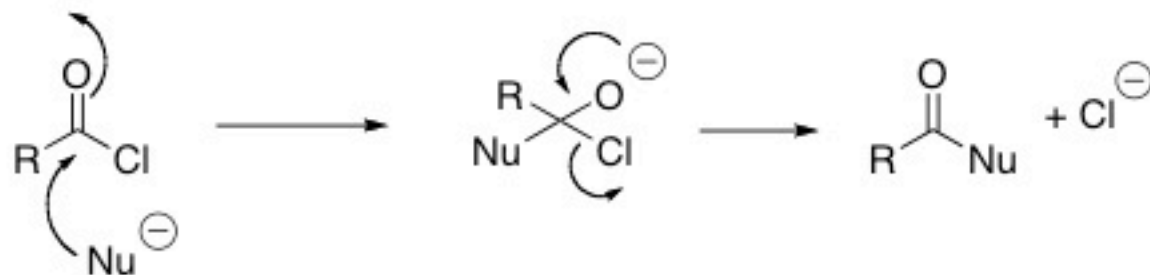


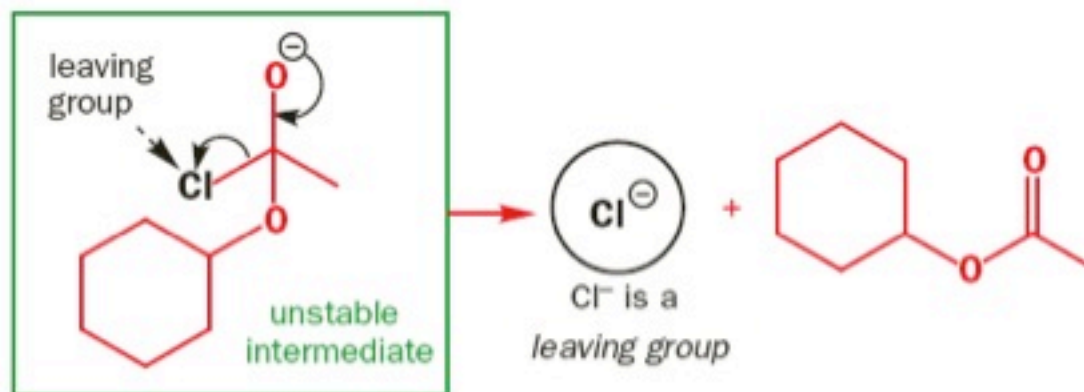
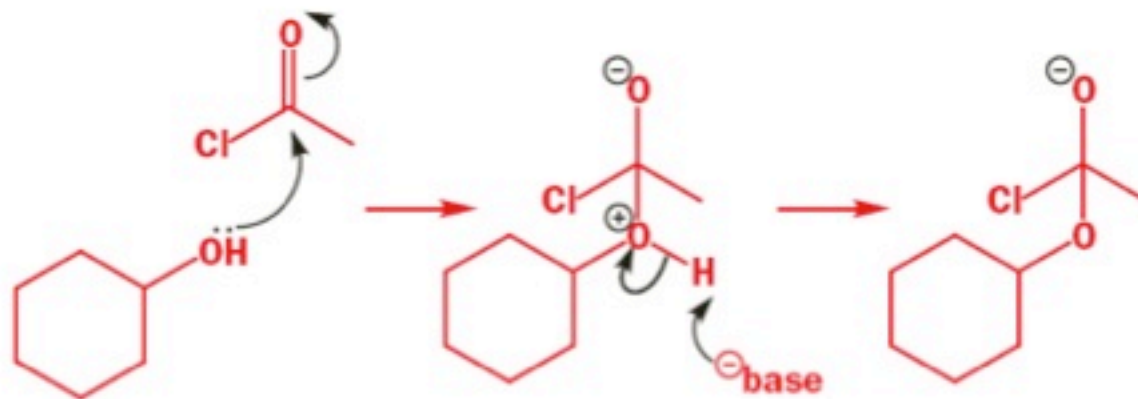
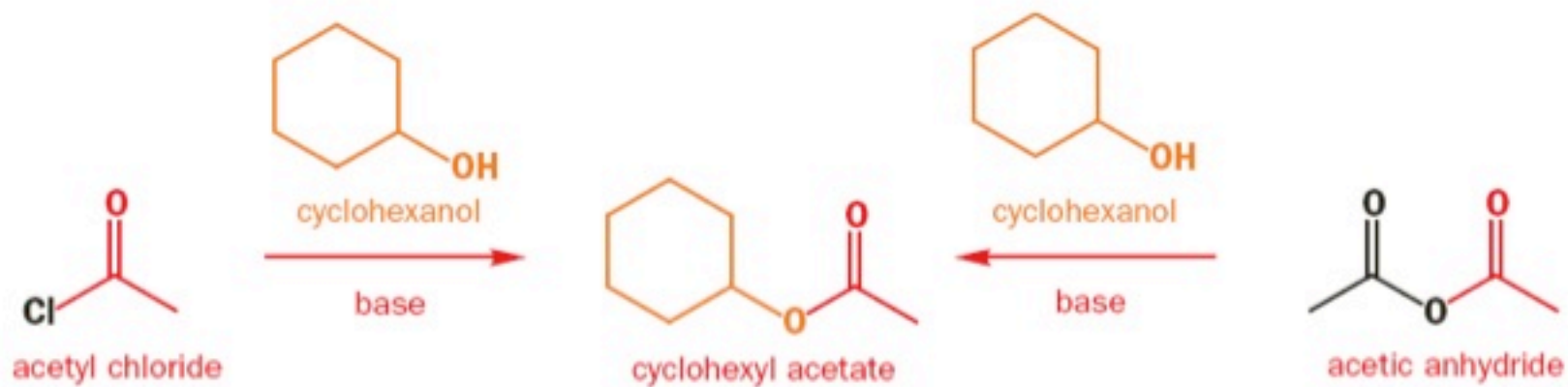
We will see in the Grignard reaction that carboxylate salts are very unreactive toward nucleophilic attack



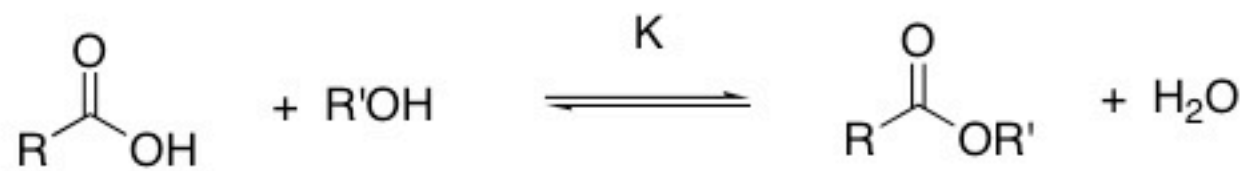
usually a base (pyridine, Et₃N...) is used to trap HCl

with Nu[⊖]
(ex: R₃ONa, RCOONa)





Leaving group	pK_{aH}
R^-	50
NH_2^-	35
RO^-	16
RCO_2^-	5
Cl^-	-7



$$K = \frac{[\text{RCOOR}'] [\text{H}_2\text{O}]}{[\text{RCOOH}] [\text{R}'\text{OH}]}$$



$$K = \frac{[\text{RCOOR}'] [\text{H}_2\text{O}]}{[\text{RCOOH}] [\text{R}'\text{OH}]}$$

The overall process of esterification is one involving an equilibrium among a variety of compounds, and for the reaction to give a high yield; the equilibrium must be shifted toward the products: the desired ester, and water. This can be accomplished either by removing one or more of the products from the reaction mixture as they are formed or by using a large excess of one of the starting reagents.

The effect of the latter approach is obvious from consideration of the mass law relating starting materials and products (equation). Increasing the amount of either the alcohol or the carboxylic acid will result in an increase in the amount of products formed since the equilibrium constant, K , for the reaction-must remain constant at a given temperature, no matter what quantity of either reagent is used.

$$K = \frac{[\text{RCOOR}'] [\text{H}_2\text{O}]}{[\text{RCOOH}] [\text{R}'\text{OH}]}$$

since K is a constant, then if $[\text{R}'\text{OH}] \uparrow$ (or $[\text{RCOOH}] \uparrow$)

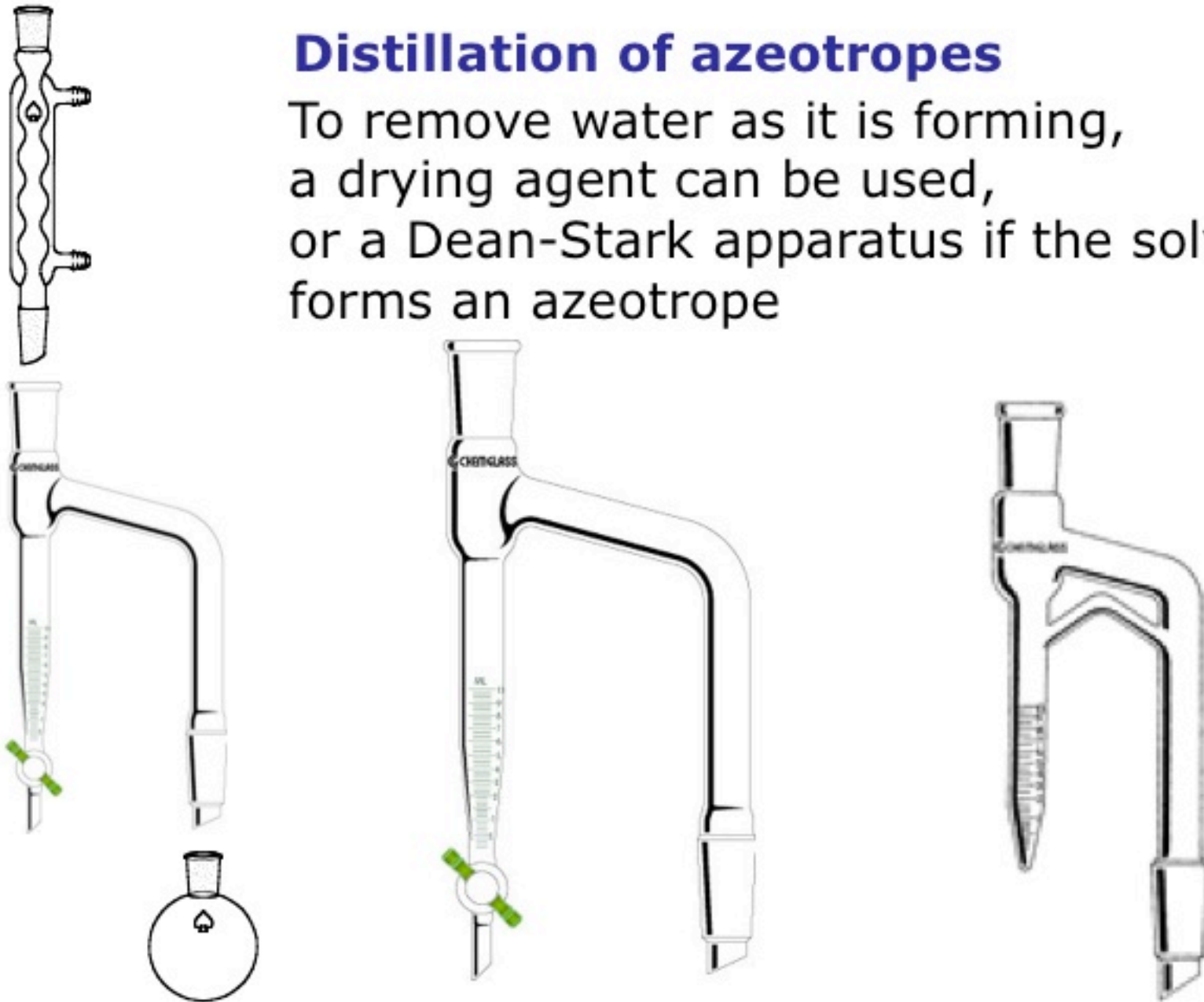
$[\text{RCOOR}']$ and $[\text{H}_2\text{O}]$ have to increase as well

if $[\text{H}_2\text{O}] \downarrow$ (or $[\text{RCOOH}] \downarrow$) as when either is being removed
then the system evolves with more product formation to keep K constant

To remove the ester from the reaction mixture it can sometimes be distilled as the reaction progresses (like we did for cyclohexene synthesis)

Distillation of azeotropes

To remove water as it is forming, a drying agent can be used, or a Dean-Stark apparatus if the solvent forms an azeotrope



Distilling receiver - Dean-Stark apparatus

$$K = \frac{[\text{RCOOR}'] [\text{H}_2\text{O}]}{[\text{RCOOH}] [\text{R}'\text{OH}]}$$

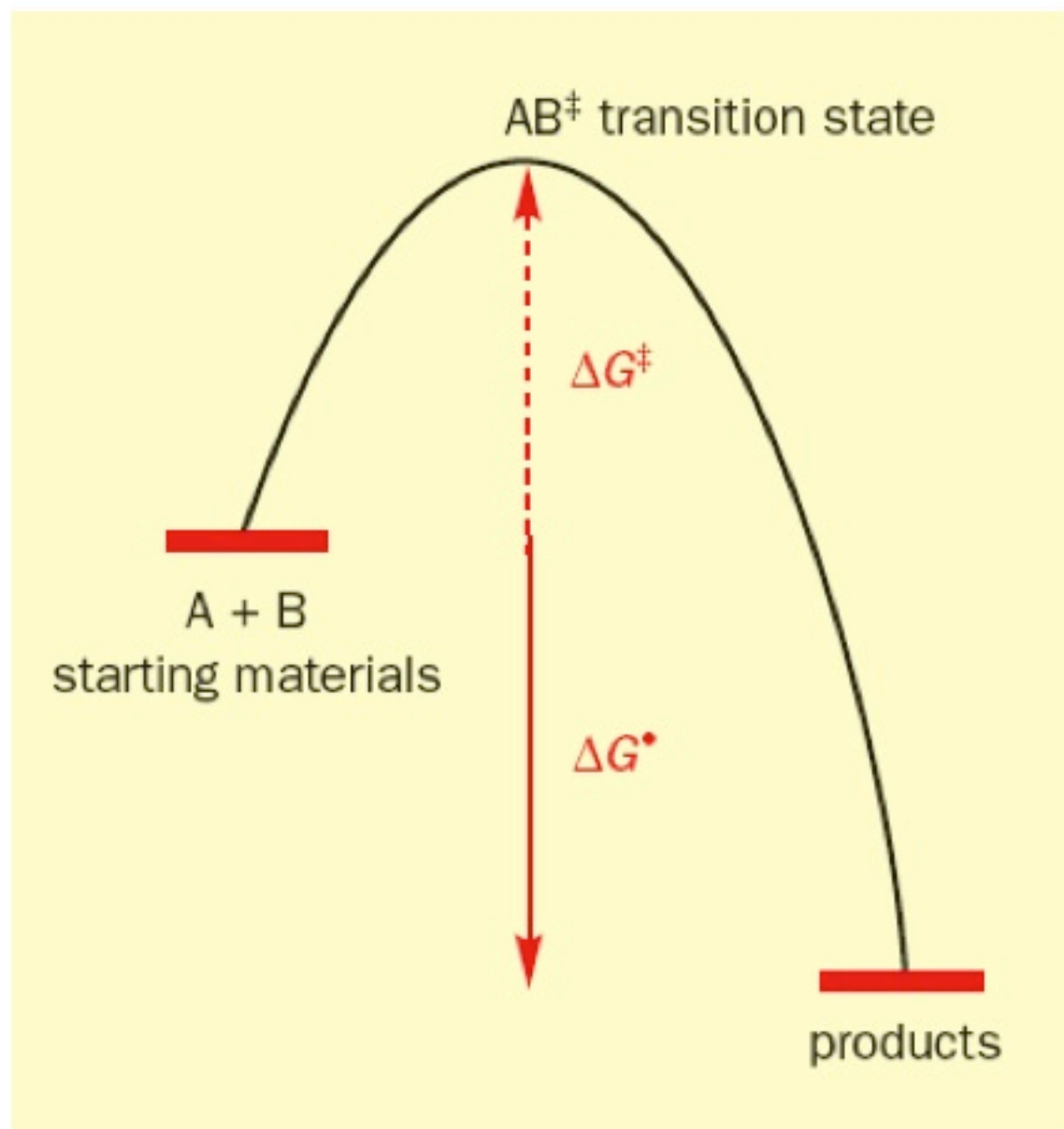
in this experiment we are using a large excess of methanol $[\text{MeOH}] \uparrow$

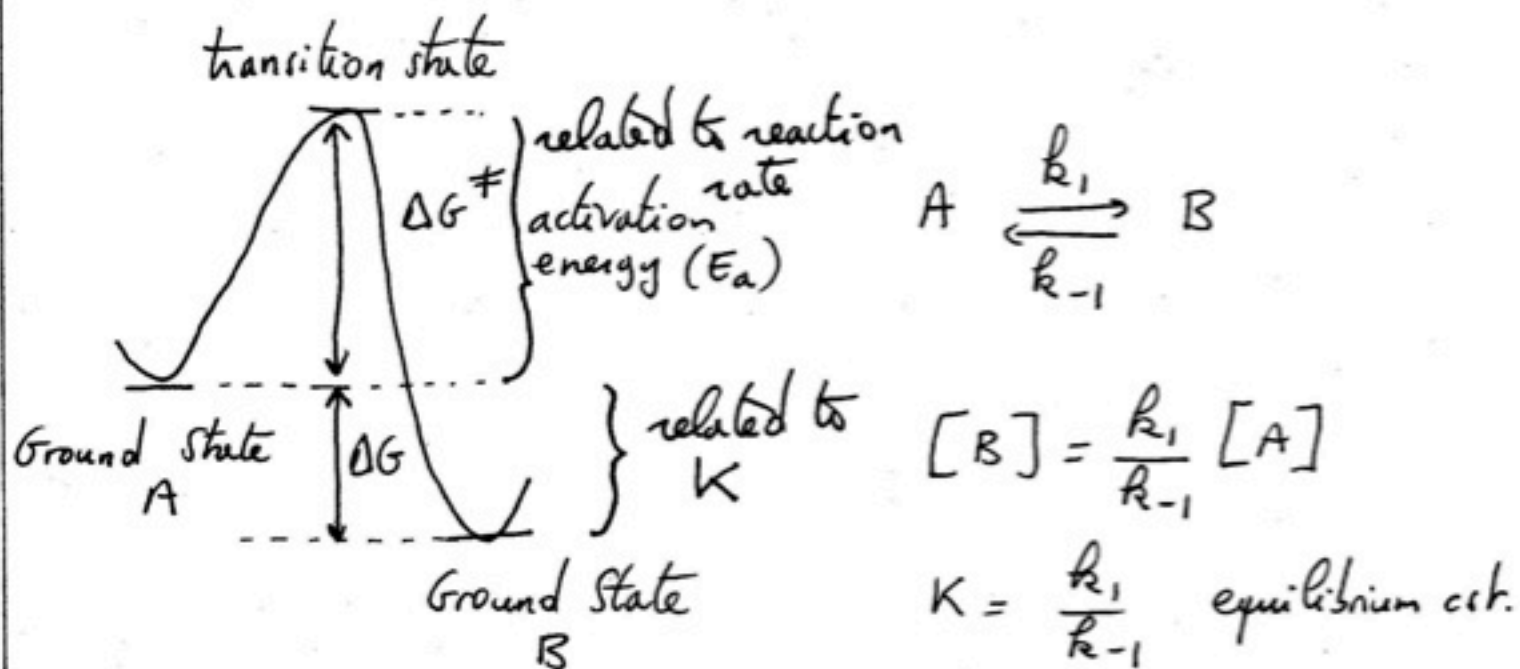
The problem which must be answered in your notebook should demonstrate the effect of doing this.

Since esterification under acidic conditions is an equilibrium, this implies that esters can be hydrolyzed also (reverse reaction)

In this situation, a large excess of water is usually employed

Note that ester hydrolysis is normally conducted under basic conditions, in which case it is not an equilibrium





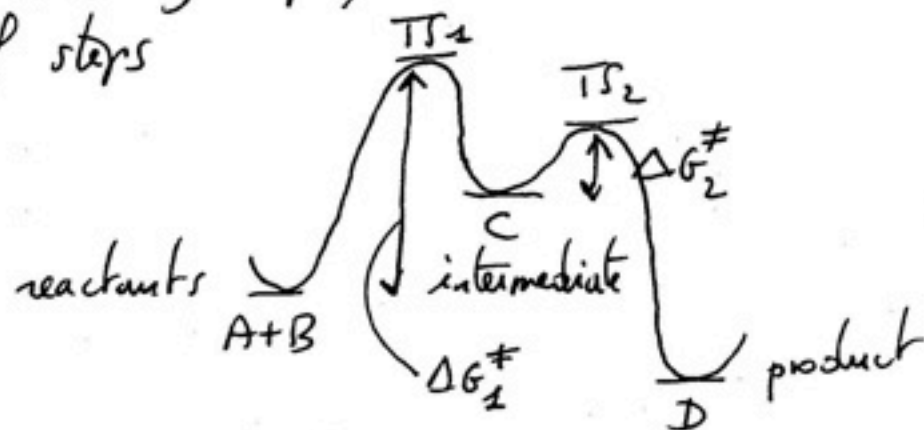
$$\Delta G = \Delta H - T\Delta S$$

free energy enthalpy entropy

$$\Delta G = -RT \ln K$$

THERMODYNAMIC QUANTITIES
are independent of reaction path
↳ DO NOT PROVIDE INSIGHT
INTO MECHANISM

RATE DETERMINING STEP (rds) is the most energetically demanding step, and is the slowest step in a sequence of steps



Reaction: $A+B \rightarrow D$
 Rate limiting step is
 $A+B \rightarrow C$ since
 $\Delta G_1^\ddagger \gg \Delta G_2^\ddagger$

HAMMOND POSTULATE (J. Am. Chem. Soc. 1955, 77, 334)

" If two states, as for example a transition-state and an unstable intermediate, occur consecutively during a reaction process and have nearly the same energy content, their interconversion will involve only a small reorganization of molecular structure "

If any endothermic process has a DETECTABLE rate, it cannot involve any large excess activation energy.

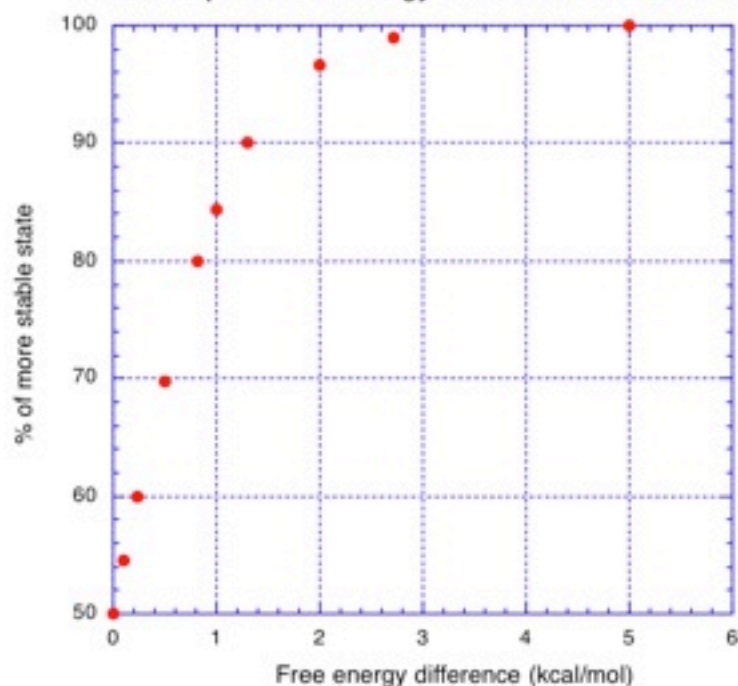
EQUILIBRIA, RATES, ENERGY DIAGRAMS, MECHANISMS

TABLE: Relationship between K_{eq} and ΔG°

ΔG° (kcal/mol)	K_{eq}	More stable state (%)
0	1	50
0.1	1.2	54.5
0.24	1.5	60
0.5	2.4	69.7
0.82	4.0	80
1	5.4	84.4
1.30	9	90
2	29.3	96.7
2.72	99	99
5	4631	99.98
10	2.1×10^7	99.999996

Note: at 25°C, the value of $2.3RT$ is about 1.4 kcal/mol

Relationship Between Energy Difference and Distribution



$$\Delta G^\circ = -RT \ln K$$

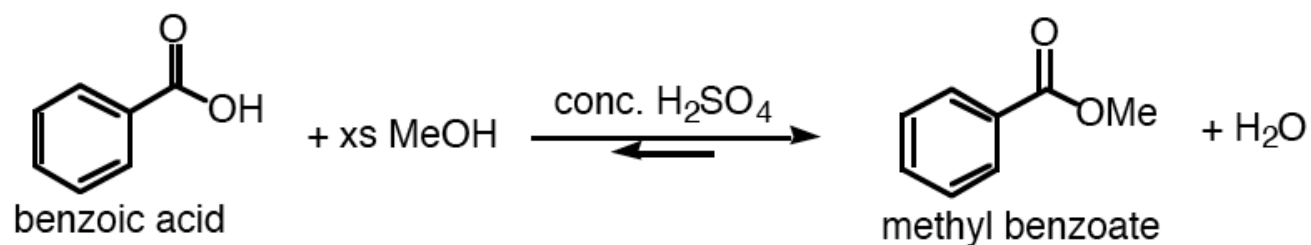
$$\Delta G^\circ = -2.3RT \log K$$

$$K = e^{-\Delta G^\circ/RT}$$

$$K = 10^{-\Delta G^\circ/2.3RT}$$

Le Chatelier's Principle: a system at equilibrium responds to a disturbance/stress so as to minimize the disturbance/stress

Lab5: Preparation of Methyl Benzoate



Reaction: Place 6.1 g of benzoic acid and 20 mL of methanol in a 100-mL round-bottomed flask, and carefully pour 2 mL of concentrated sulfuric acid down the side of the flask. Swirl the flask to mix the reagents, attach a reflux condenser, and gently heat the mixture at reflux for 1 hr. (Power controller setting ~ 6. Boiling chips can be used for the reaction.)

Work-up/Extraction: Cool the solution and transfer it to a separatory funnel containing 50 mL of water. Rinse the flask with 40 mL of dichloromethane, and add the rinsing to the separatory funnel. Shake the funnel to extract methyl benzoate and benzoic acid into the dichloromethane layer; **vent the funnel often**. Remove the organic and aqueous layers and wash the organic layer with a 25-mL portion of water. Remove the aqueous layer and wash the organic-layer with 25 mL of 0.6 M aqueous sodium bicarbonate. **CAUTION: foaming may occur**. Swirl the open funnel for a few seconds to assure that no vigorous reaction occurs; then shake the stoppered funnel **with frequent venting**. Separate the aqueous (bottom) layer. Test the aqueous layer to see that it is basic to litmus paper. If not, repeat the washing of the organic layer with an additional 25-mL portion of aqueous sodium bicarbonate. Combine this with the first bicarbonate washing and **SAVE THE SOLUTION**. Wash the dichloromethane layer with a 25-mL portion of saturated sodium chloride, then dry the ether solution with anhydrous magnesium sulfate.

Purification/Solvent removal: Remove the drying agent by gravity filtration into a 100-mL round-bottomed flask. Set up a simple distillation apparatus using the 100-mL flask, as the pot. (Since dichloromethane is very volatile, cool the receiving flask, and a power controller setting at, or below 3). Remove the dichloromethane by distillation and place the distillate in the waste dichloromethane recovery bottle.

Purification/Solvent removal: Remove the drying agent by gravity filtration into a 100-mL round-bottomed flask. Set up a simple distillation apparatus using the 100-mL flask, as the pot. (Since ether is very volatile, cool the receiving flask, and a power controller setting at, or below 3). Remove the ether by distillation and place the distillate in the waste ether recovery bottle.

Purification of the product by distillation: Transfer the crude methyl benzoate into a 50-mL round-bottomed flask, and attach the flask to an apparatus for simple distillation. Distill the ester using *an air-cooled condenser* rather than a water-cooled condenser (which can crack because of the high boiling point of the ester). [Power controller setting at 10] Collect the material boiling above 190° C in a weighed receiver, and turn in the product to your instructor.

Purification of the product by distillation: Transfer the crude methyl benzoate into a 50-mL round-bottomed flask, and setup an apparatus for simple distillation. Distill the ester using *an air-cooled condenser* rather than a water-cooled condenser (which can crack because of the high boiling point of the ester). [Power controller setting at 10. You can use aluminum foil and glass wool.] Collect the material boiling above 190° C in a weighed receiver, and turn in the product to your instructor.

Recovery of unreacted benzoic acid: Recover the unchanged benzoic acid from the aqueous sodium bicarbonate washing by carefully acidifying the basic solution with concentrated HCl. Cool the solution in ice and add the HCl dropwise since the reaction is exothermic and foaming occurs. Collect the precipitate of benzoic acid by vacuum filtration. Determine the weight of the dry benzoic acid and calculate the theoretical yield of methyl benzoate based on the weight of benzoic acid with which you started (6.1 g) less the weight of benzoic acid recovered. Turn in the product to your instructor.

TIPS: - During the extractions, make sure you know which layer you want. In doubt?? SAVE EVERYTHING!!

- Don't forget to answer the problem assignment (first page of the handout) in your notebook. It will be graded.

Problem Assignment

THIS PROBLEM MUST BE ANSWERED IN YOUR NOTEBOOK AND WILL BE GRADED.

Assuming the equilibrium constant for the esterification of benzoic with methanol is $K = 3$, calculate the theoretical yield of methyl benzoate expected using the molar amounts used in the experiment (Lab 5, above).

Concentrated sulfuric acid is added as a catalyst in the esterification procedure, even though another acid (benzoic acid) is one of the organic reagents used. Why is the sulfuric acid necessary?

