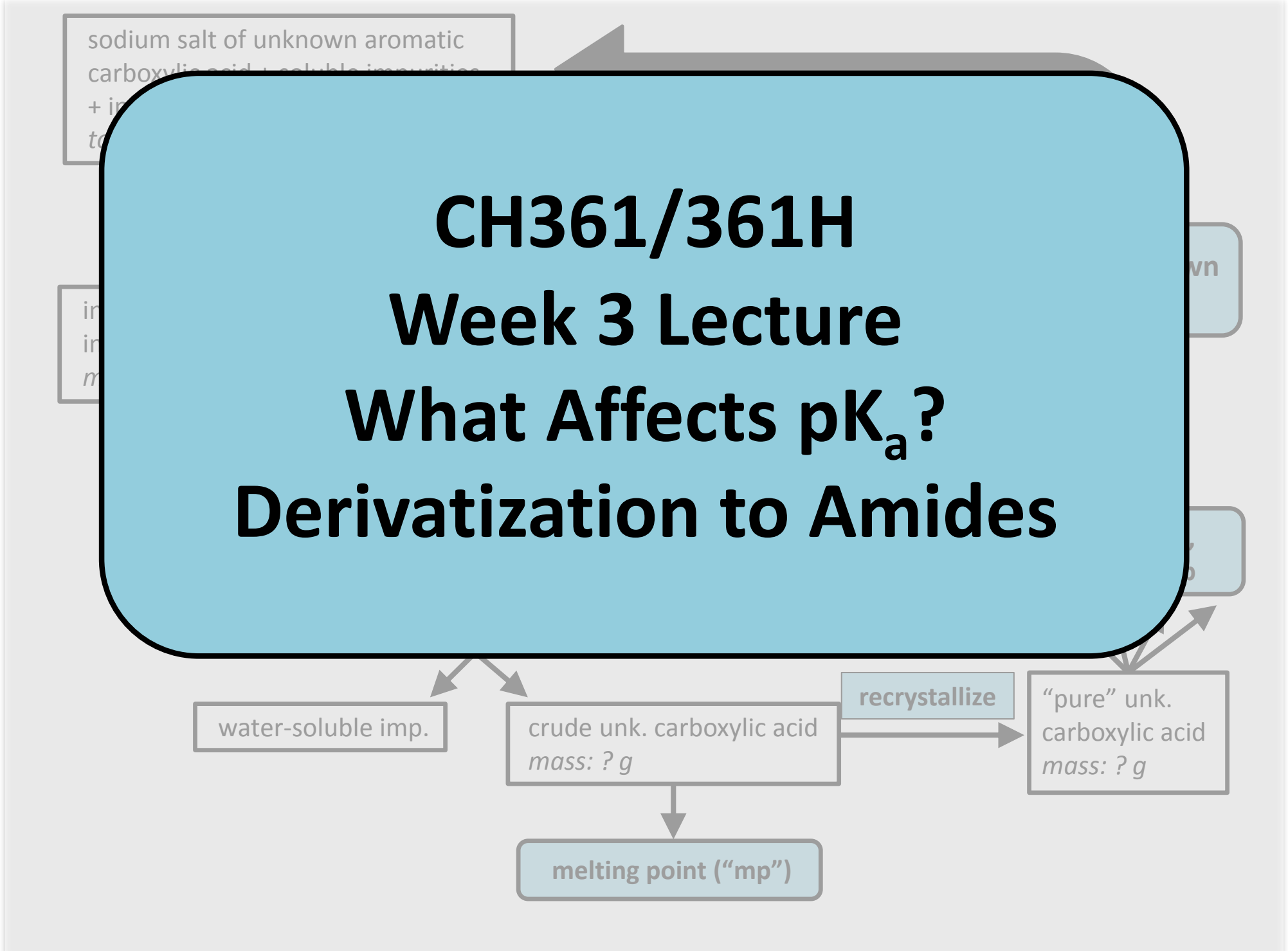
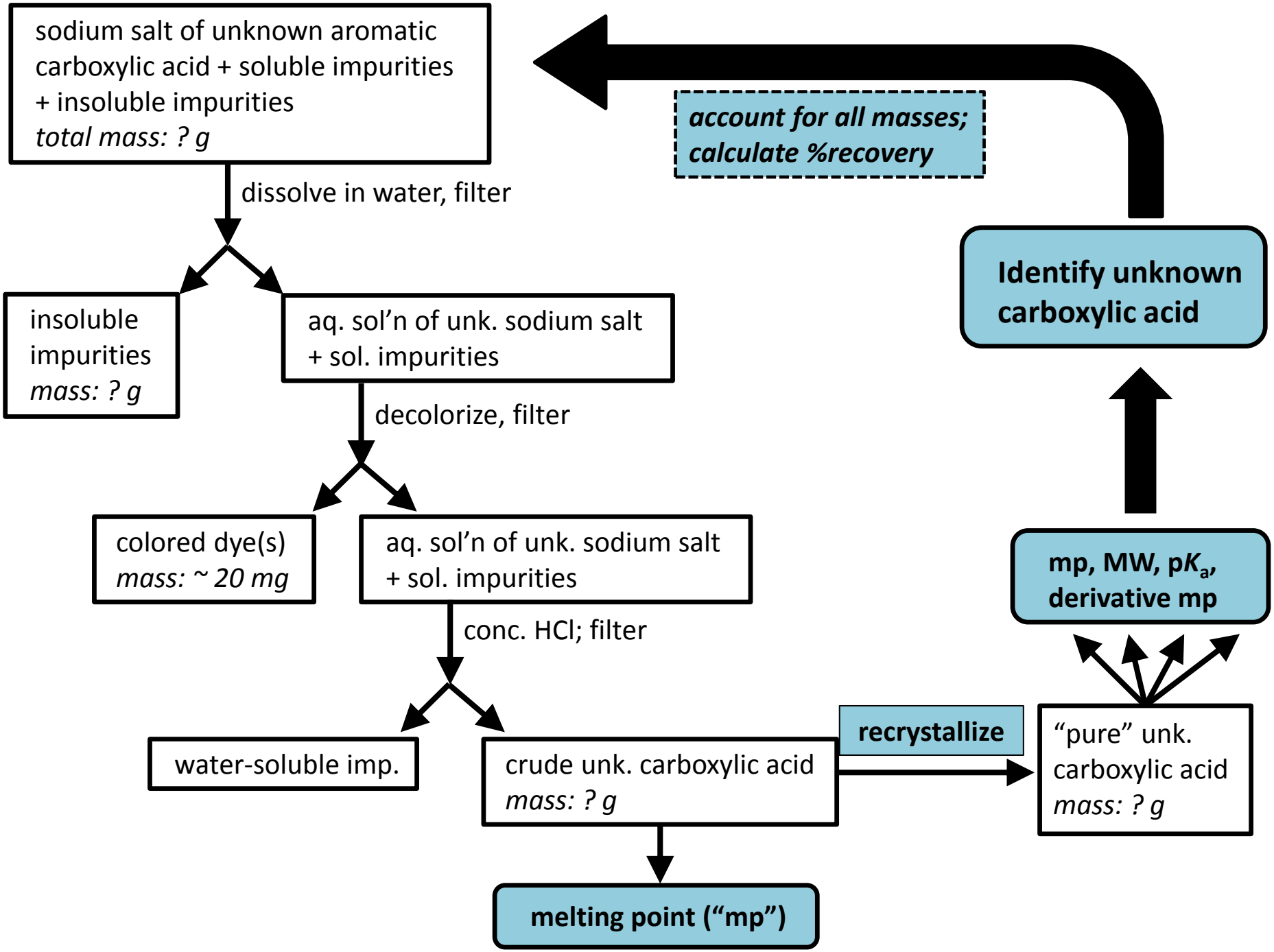
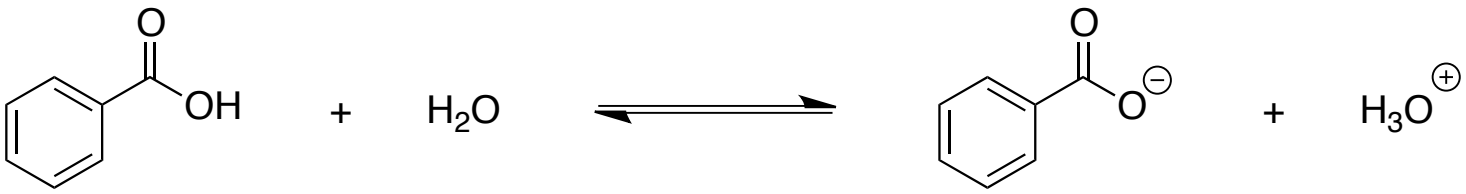


CH361/361H
Week 3 Lecture
What Affects pK_a?
Derivatization to Amides


sodium salt of unknown aromatic carboxylic acid + soluble impurities + insoluble impurities
total mass: ? g
dissolve in water, filter
insoluble impurities
mass: ? g
aq. sol'n of unk. sodium salt + sol. impurities
decolorize, filter
colored dye(s)
mass: ~ 20 mg
aq. sol'n of unk. sodium salt + sol. impurities
conc. HCl; filter
water-soluble imp.
crude unk. carboxylic acid
mass: ? g
recrystallize
"pure" unk. carboxylic acid
mass: ? g
melting point ("mp")
mp, MW, pKa, derivative mp
Identify unknown carboxylic acid
account for all masses; calculate %recovery

Affect of solvent and temperature on pK_a



benzoic acid

pK_a = 4.19

$$K_a = \frac{\left[PhCO_2^- \right] \left[H_3O^+ \right]}{\left[PhCO_2H \right]} \qquad pK_a = -\log_{10} K_a$$

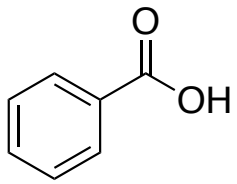
- carboxylic acid must be fully dissolved to determine pKa, but, many have low to modest solubility in pure water; ***how could acid be fully dissolved?***

- raising temperature helps to dissolve acid, but pKa is defined at standard state, different temperature will change pKa value; **solution must be at rt when conducting potentiometric titration**

- addition of ethanol raises pKa; need to approximately correct for likely effect of any added EtOH (see p. 16 of lab manual for correction data)

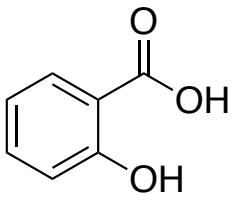
(**note:** adding ethanol will **not** affect outcome of end-point titration)

Affect of substituents on pK_a



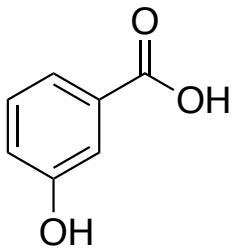
benzoic acid

pK_a **4.19**



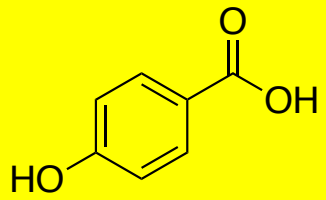
2-hydroxybenzoic acid

2.97



3-hydroxybenzoic acid

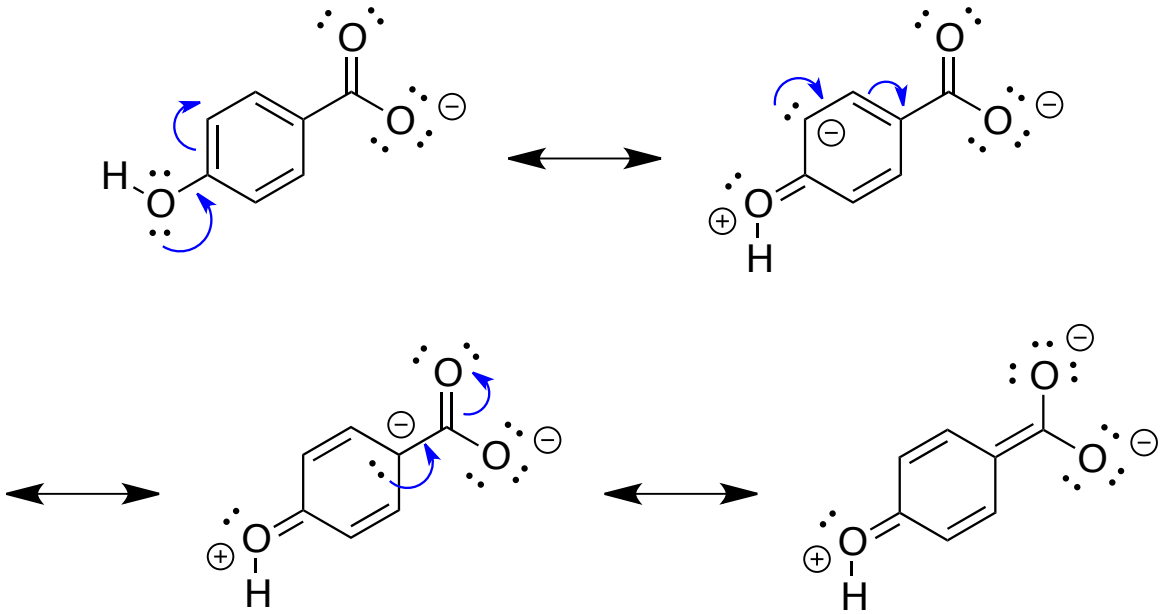
4.08



4-hydroxybenzoic acid

4.61

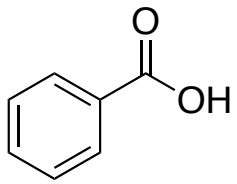
- OH group in *para* position:



- due to *resonance*, electron density from O-atom lone-pair is *delocalized* over aromatic ring leading to *increased* negative charge character near carboxylate anion

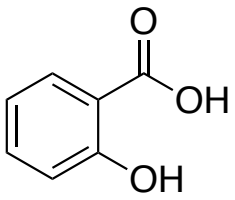
- results in *destabilization* of conjugate base (lowers acidity; raises pKa)

Affect of substituents on pK_a



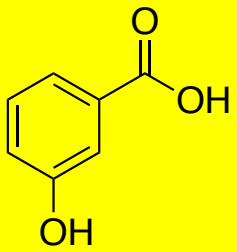
benzoic acid

pK_a **4.19**



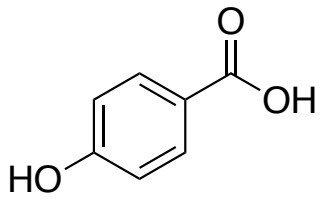
2-hydroxybenzoic acid

2.97



3-hydroxybenzoic acid

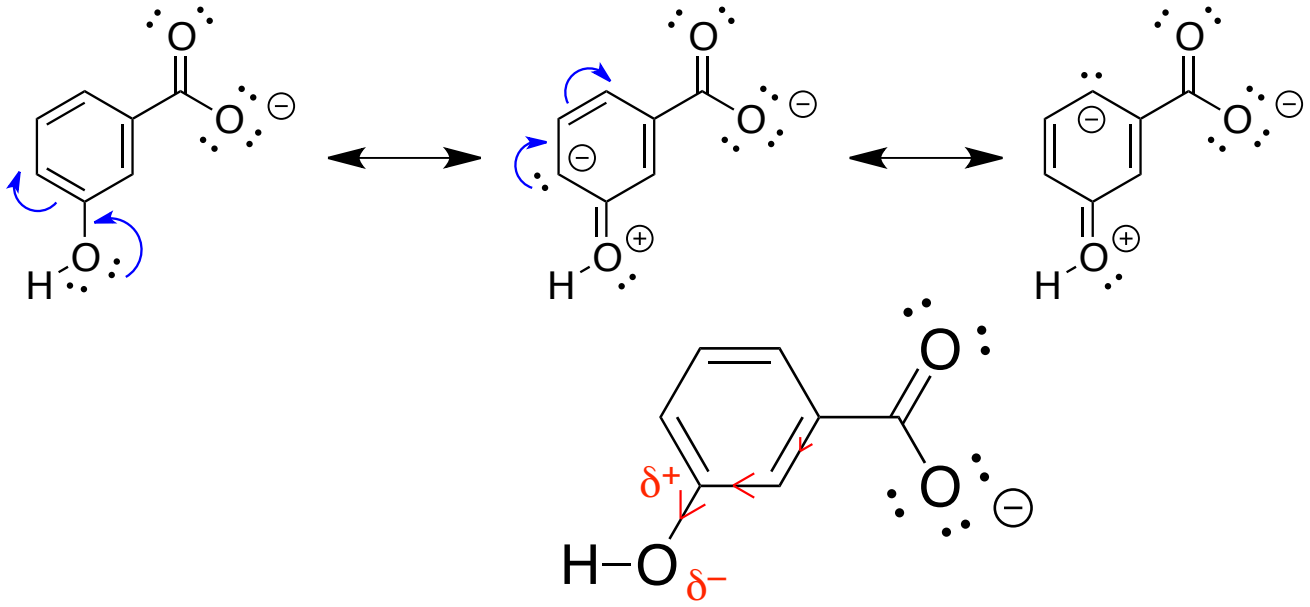
4.08



4-hydroxybenzoic acid

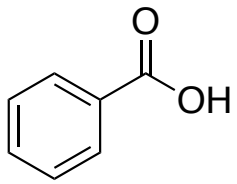
4.61

- OH group in *meta* position:



- resonance does not push significant charge density to site of carboxylate anion
- but, electronegative character of O-atom leads to C–O sigma-bond polarization
- carboxylate anion stabilized by *inductive effect* (a localized effect)

Affect of substituents on pK_a

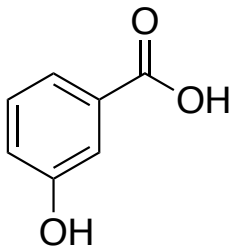


benzoic acid

pK_a **4.19**

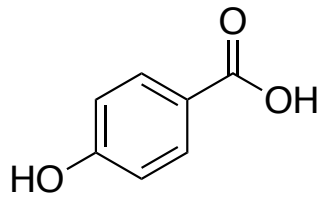
2-hydroxybenzoic acid

2.97



3-hydroxybenzoic acid

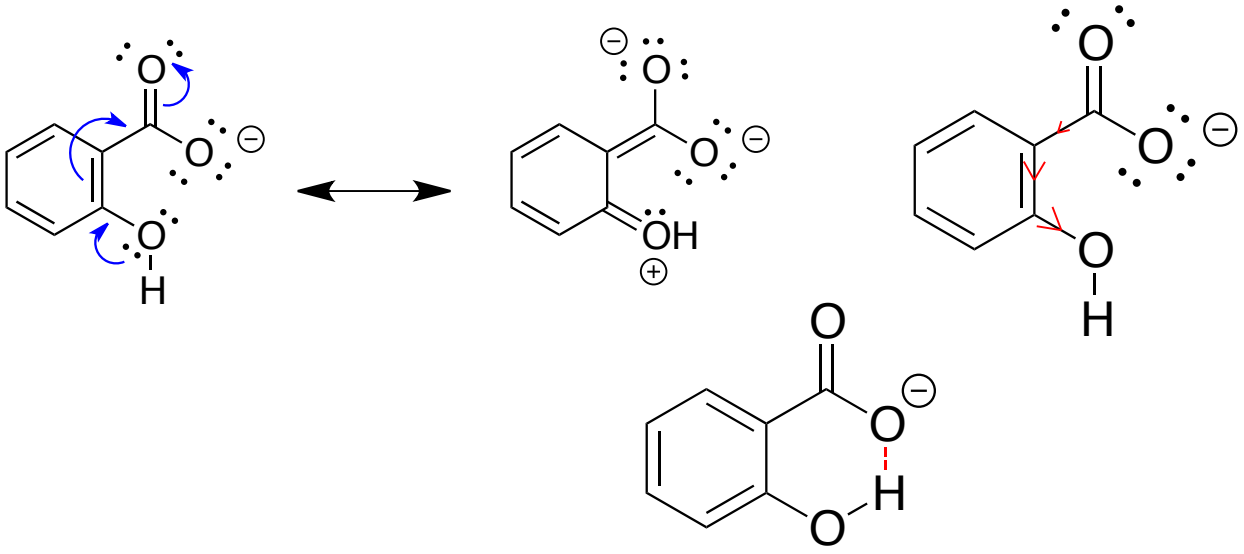
4.08



4-hydroxybenzoic acid

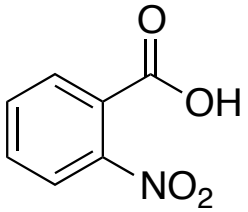
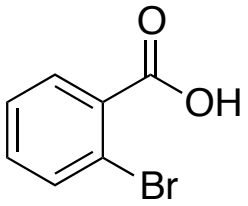
4.61

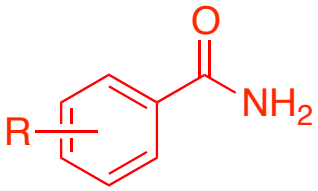
- OH group in *ortho* position:



- as in *para* case, resonance again pushes significant charge density to site of carboxylate anion
- inductive effect is also maximized (close proximity)
- intramolecular hydrogen-bond provides additional stabilization to carboxylate anion

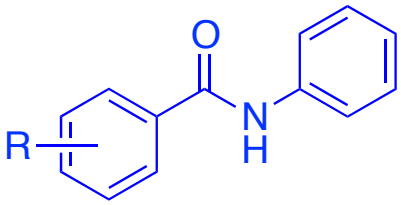
Synthesis of a derivative to aid identification of unknown aromatic carboxylic acid

	mpt	mol. wt.	pK_a	'amide' mpt	'anilide' mpt
	146 °C	167.12	2.22	176 °C	155 °C
	148 °C	201.02	2.85	155 °C	141 °C

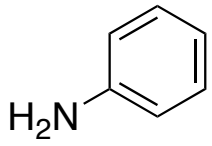


'amide'
a 1° amide

ammonia

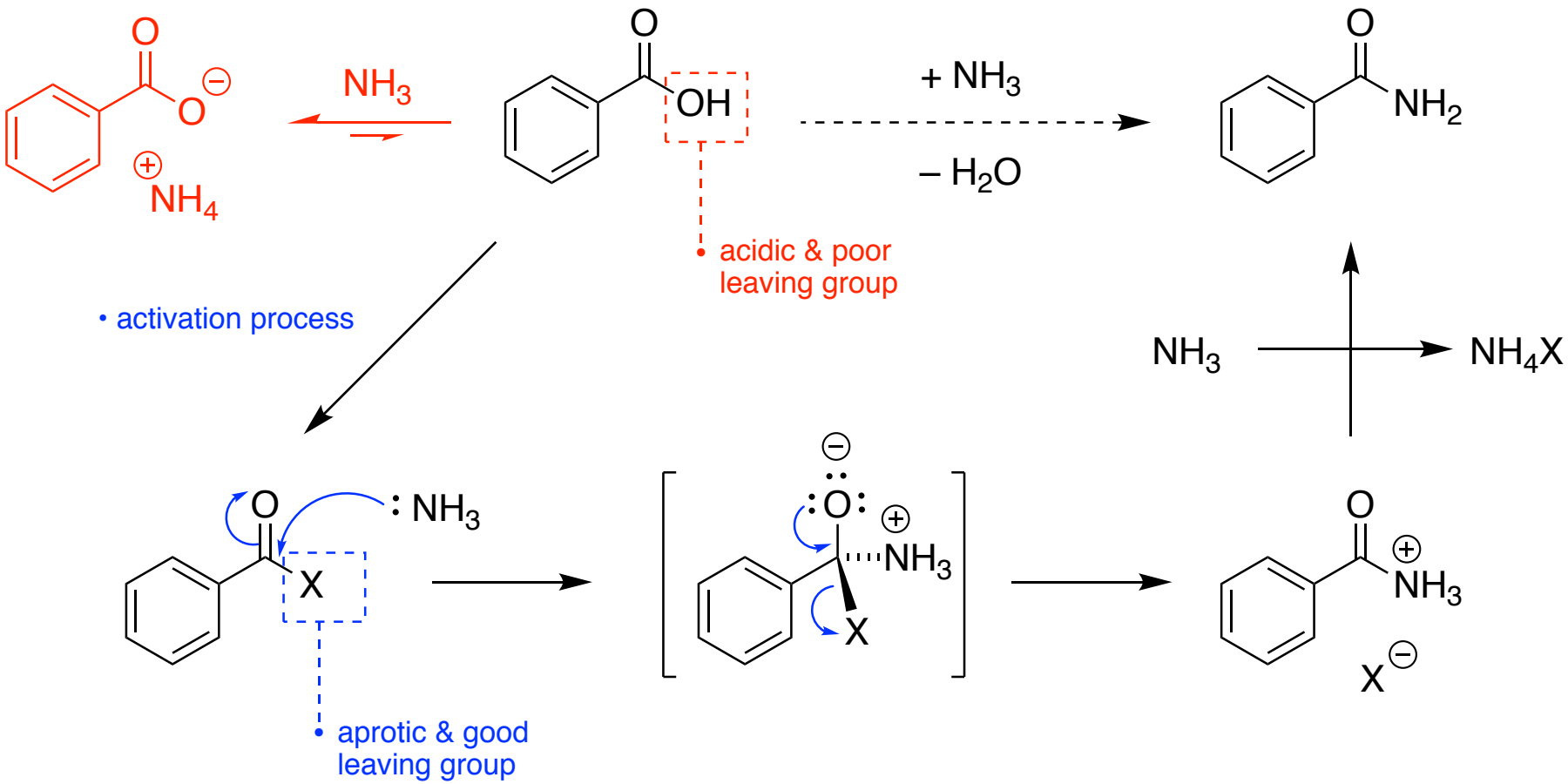


'anilide'
a 2° amide of aniline

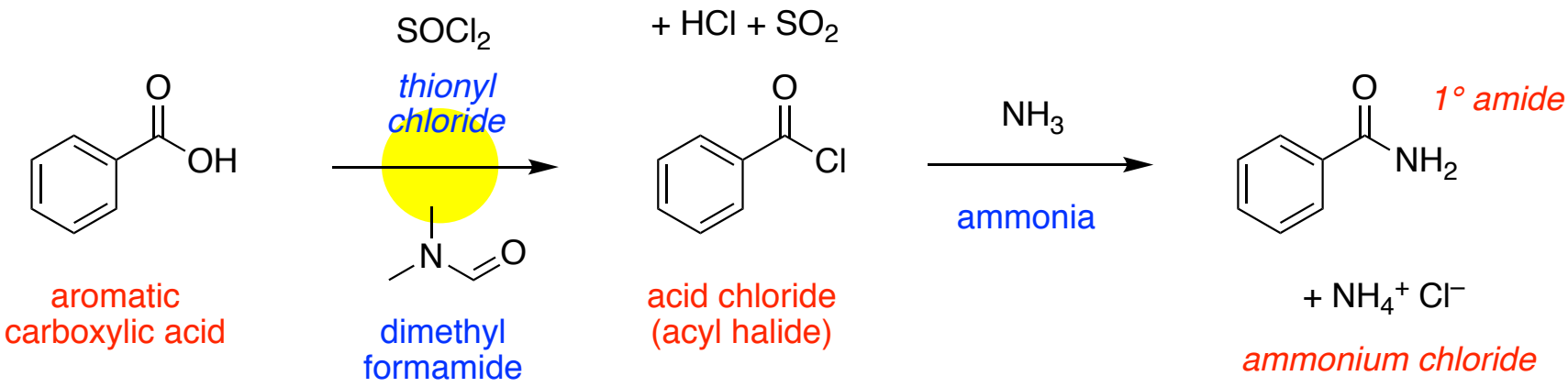


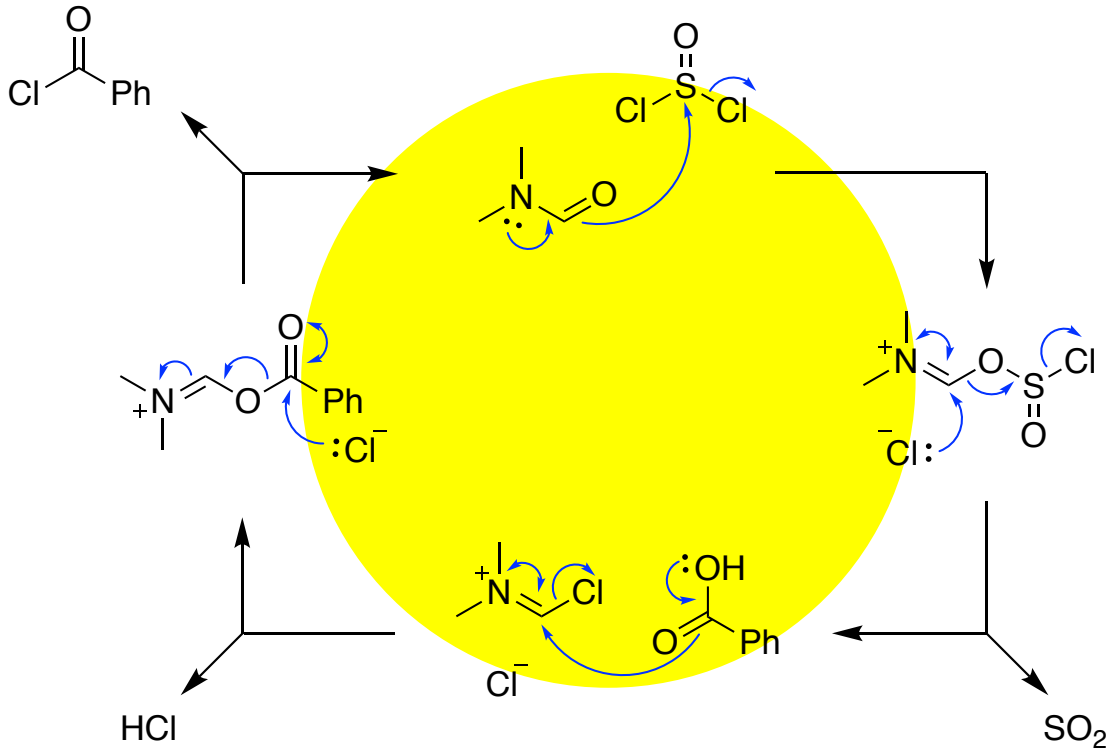
aniline
(aminobenzene)

Amide Formation Strategy: Interconversion of Carboxylic Acid Derivatives



Conversion of a Carboxylic Acid to an Acyl Chloride and Further to Amide

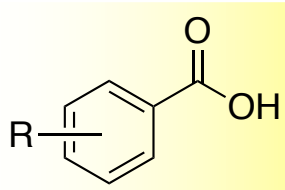




- dimethyl formamide (DMF) *catalyzes* the formation of the acyl chloride
- DMF is not consumed in the reaction, but it accelerates the rate of the transformation

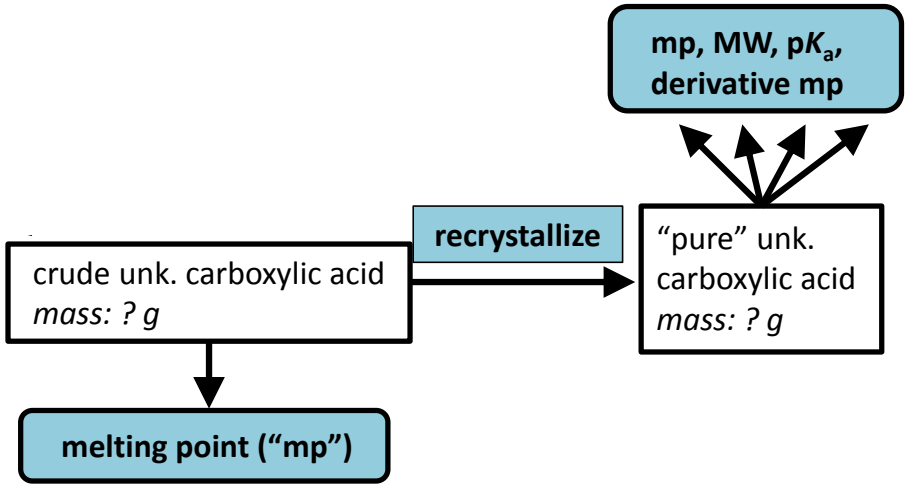
Tasks for Week 3: Finish Large Batch Recrystallization, End-point Titration

- *polar non-ionic compound*
- *sparing solubility in H_2O*



+ related impurities

precipitate (solid)



Wednesday	• finish large batch recrystallization, dry solid, calculate %recovery, obtain accurate mp; TIME ALLOWING, begin end-point titration
Friday	• (finish large batch recrystallization), end-point titration
(Friday)	• TIME ALLOWING – begin potentiometric titration