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

crude unk. carboxylic acid mass: ? g

water-soluble imp.

recrystallize

“pure” unk. carboxylic acid mass: ? g

melting point ("mp")

Identify unknown carboxylic acid
account for all masses; calculate %recovery

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

melting point ("mp")

account for all masses; calculate %recovery

Identify unknown carboxylic acid

mp, MW, pK<sub>a</sub>, derivative mp

recrystallize

“pure” unk. carboxylic acid
mass: ? g

Identify unknown carboxylic acid

account for all masses; calculate %recovery
Affect of solvent and temperature on pK_a

\[ \text{benzoic acid} \]

\[ pK_a = 4.19 \]

\[ K_a = \frac{[\text{PhCO}_2^-][\text{H}_3\text{O}^+]}{[\text{PhCO}_2\text{H}]} \quad pK_a = -\log_{10} K_a \]

- 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 $pK_a$

- 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 $pK_a$)

<table>
<thead>
<tr>
<th>Substituent</th>
<th>$pK_a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzoic acid</td>
<td>4.19</td>
</tr>
<tr>
<td>2-Hydroxybenzoic acid</td>
<td>2.97</td>
</tr>
<tr>
<td>3-Hydroxybenzoic acid</td>
<td>4.08</td>
</tr>
<tr>
<td>4-Hydroxybenzoic acid</td>
<td>4.61</td>
</tr>
</tbody>
</table>
Affect of substituents on $pK_a$

- 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

\[
pK_a \quad 4.19
\]

2-hydroxybenzoic acid

\[
pK_a \quad 2.97
\]

3-hydroxybenzoic acid

\[
pK_a \quad 4.08
\]

4-hydroxybenzoic acid

\[
pK_a \quad 4.61
\]

• 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

<table>
<thead>
<tr>
<th>Compound</th>
<th>mpt (°C)</th>
<th>mol. wt.</th>
<th>pKₐ</th>
<th>'amide' mpt (°C)</th>
<th>'anilide' mpt (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>146</td>
<td>167.12</td>
<td>2.22</td>
<td>176</td>
<td>155</td>
</tr>
<tr>
<td>2</td>
<td>148</td>
<td>201.02</td>
<td>2.85</td>
<td>155</td>
<td>141</td>
</tr>
</tbody>
</table>

- **1° amide**
- **2° amide of aniline**
- **aniline** (aminobenzene)
Amide Formation Strategy: Interconversion of Carboxylic Acid Derivatives

- Activation process
  - Acidic & Poor Leaving Group
  - Aprotic & Good Leaving Group

\[
\text{NH}_3 + \text{R-COOH} \rightarrow \text{R-CO-NH}_2 + \text{H}_2\text{O}
\]

\[
\text{NH}_3 + \text{R-X} \rightarrow \text{R-CO-NH}_3^+ + \text{X}^-
\]
Conversion of a Carboxylic Acid to an Acyl Chloride and Further to Amide

aromatic carboxylic acid  $\xrightarrow{SOCl_2} \text{dimethyl formamide}$  acid chloride (acyl halide)  $\xrightarrow{NH_3} 1^\circ\text{amide}$

- 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 H₂O

\[ R \begin{array}{c} \text{O} \\ \text{O} \end{array} \text{OH} \]

precipitate (solid) + related impurities

\[ \text{crude unk. carboxylic acid mass: ? g} \]

recrystallize

“pure” unk. carboxylic acid mass: ? g

mp, MW, pKₐ, derivative mp

\[ \text{melting point ("mp"))} \]

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

\[ \text{OH} \]

\[ \text{O} \]

R

\[ + \text{related impurities} \]