Preparation of Derivatives from Unknown Carboxylic Acid

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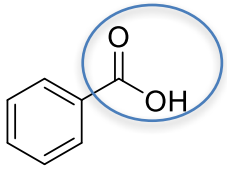
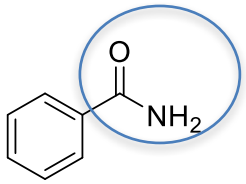
CH 361

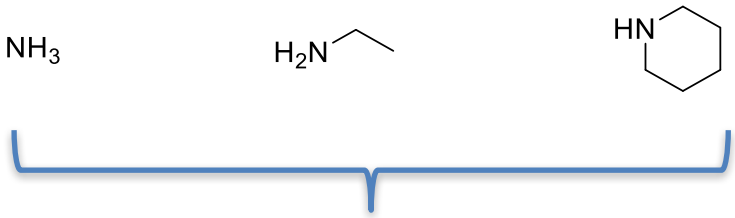
Functional Groups



Carboxylic acid

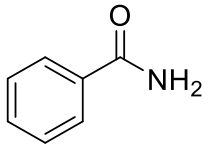


amide

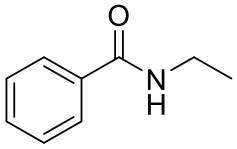


amines

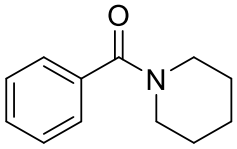
Types of Amides



amide

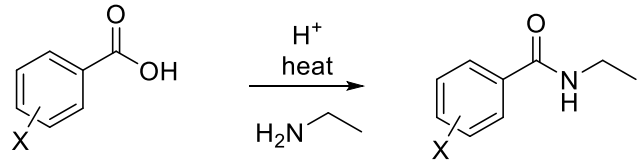


secondary amide



tertiary amide

Acid

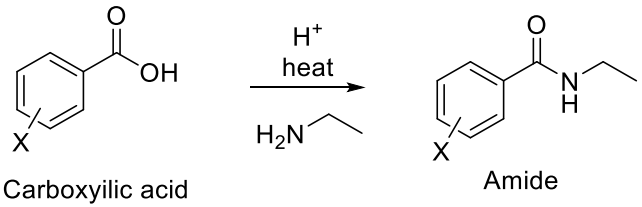


Carboxyilic acid

Amide

Amide Bonds

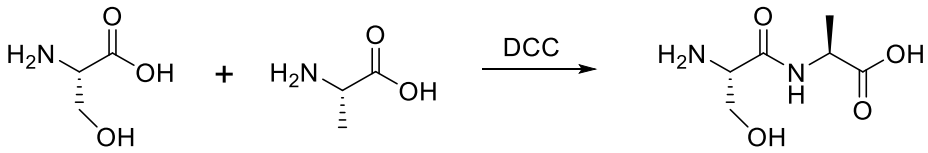
Acid



Carboxyilic acid

Amide

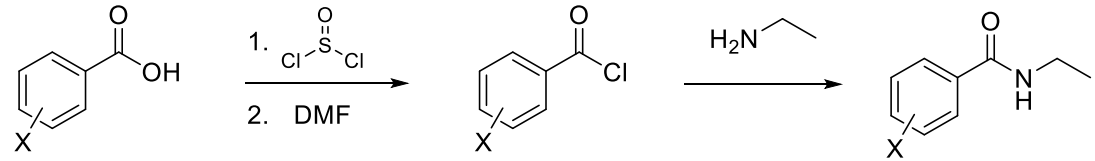
Coupling Reagent



Amino acids

Peptides

Thionyl chloride



Carboxyilic acid

Carboxyilic acid chloride

Amide

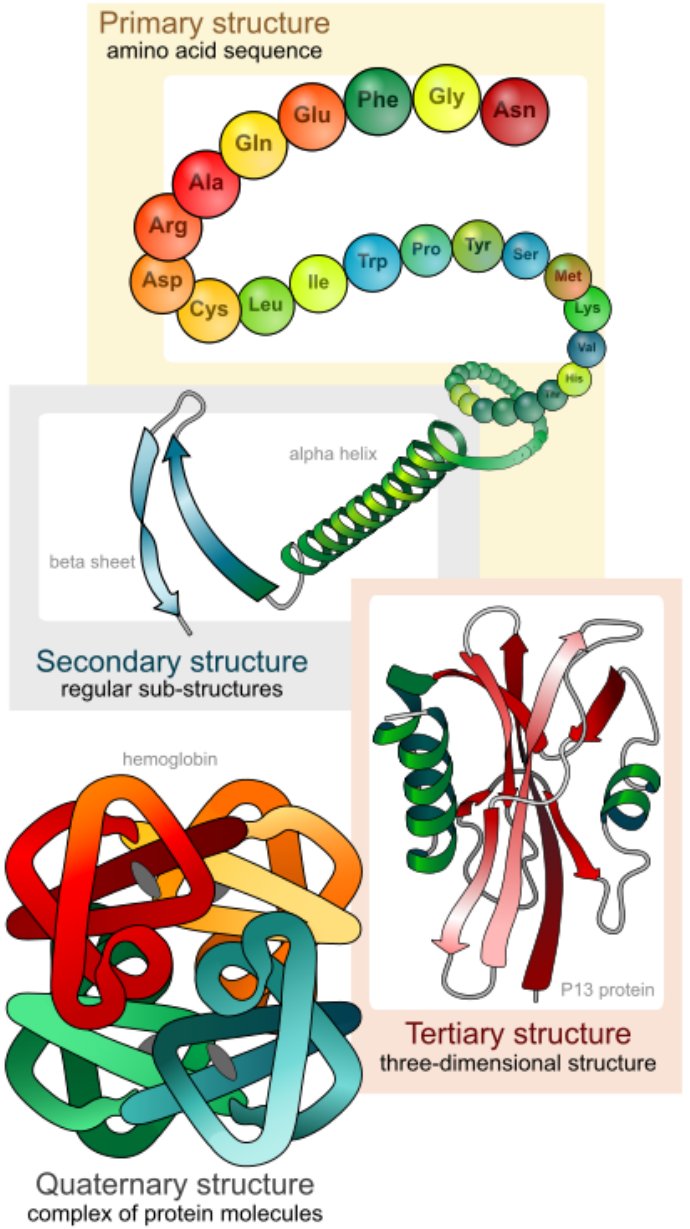


Image: https://en.wikipedia.org/wiki/Protein_structure#/media/File:Main_protein_structure_levels_en.svg

Preparation of Derivatives

Why prepare a derivative from of unknown acid?

- Confirm the identification of unknown organic compound
- Cannot confirm unknown acid/organic compound solely from melting point & pKa
- Liquid substance provides relatively unreliable boiling point
  - Prepare a solid derivative to obtain a melting point

General Outline

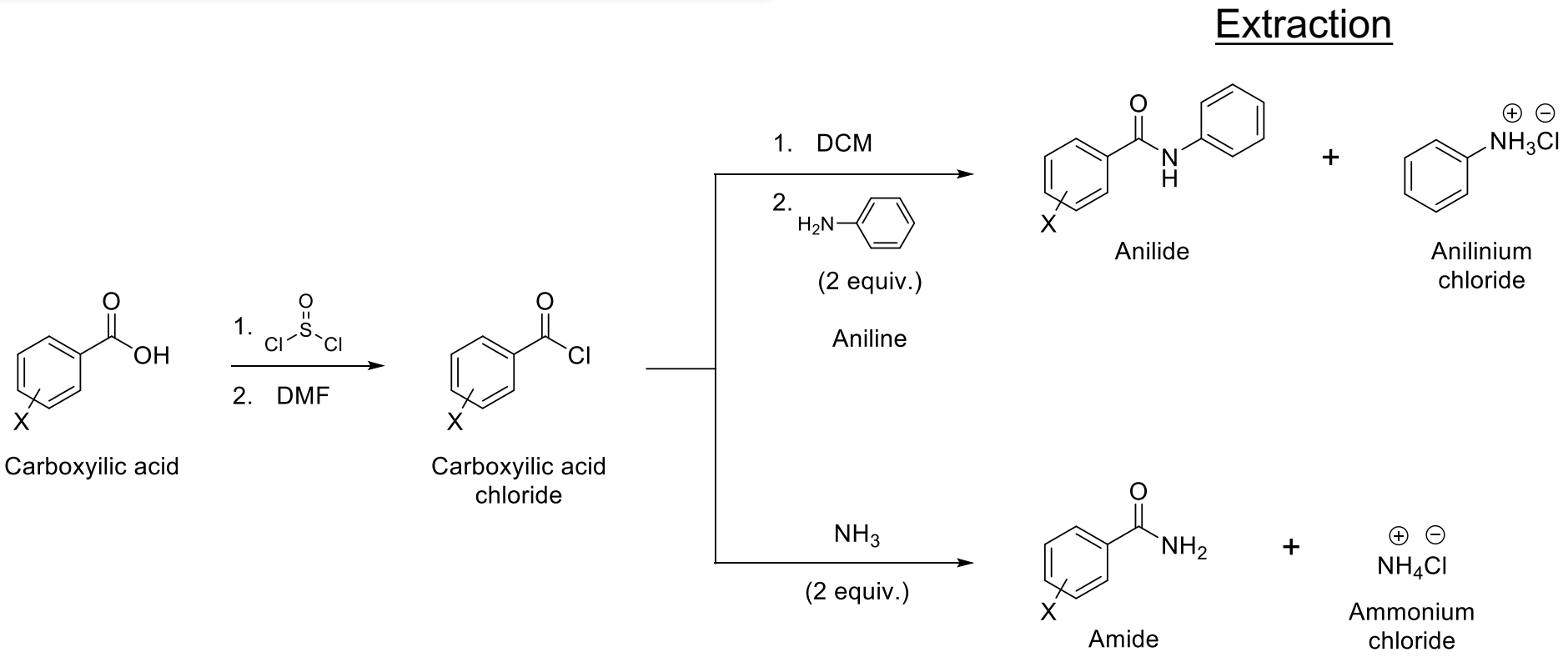
1. Reaction
   - ❑ Glassware setup/Drying tube

2. Purification Techniques
   - ❑ Extraction (separatory funnel)
   - ❑ Drying agent (magnesium sulfate)
   - ❑ Recrystallization (if necessary)

3. Calculations
   - ❑ Percent yield

4. Confirmation of derivatives & unknown acid
   - ❑ Melting point

Synthetic Schemes

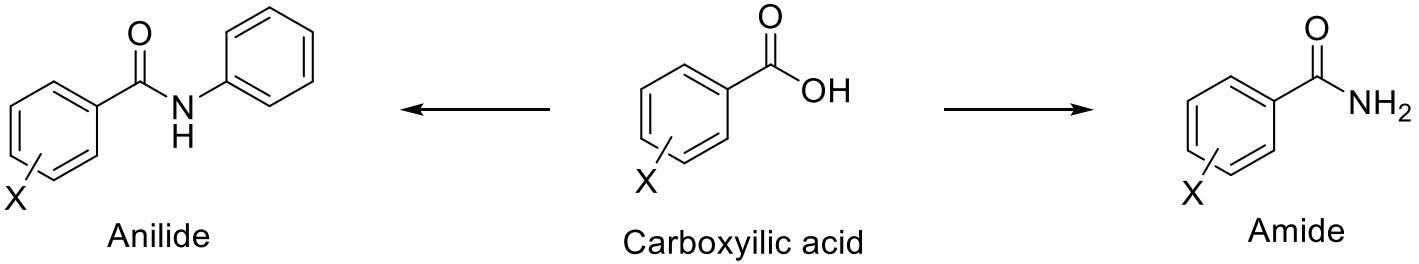


Common Abbreviations

DMF = dimethylforamide

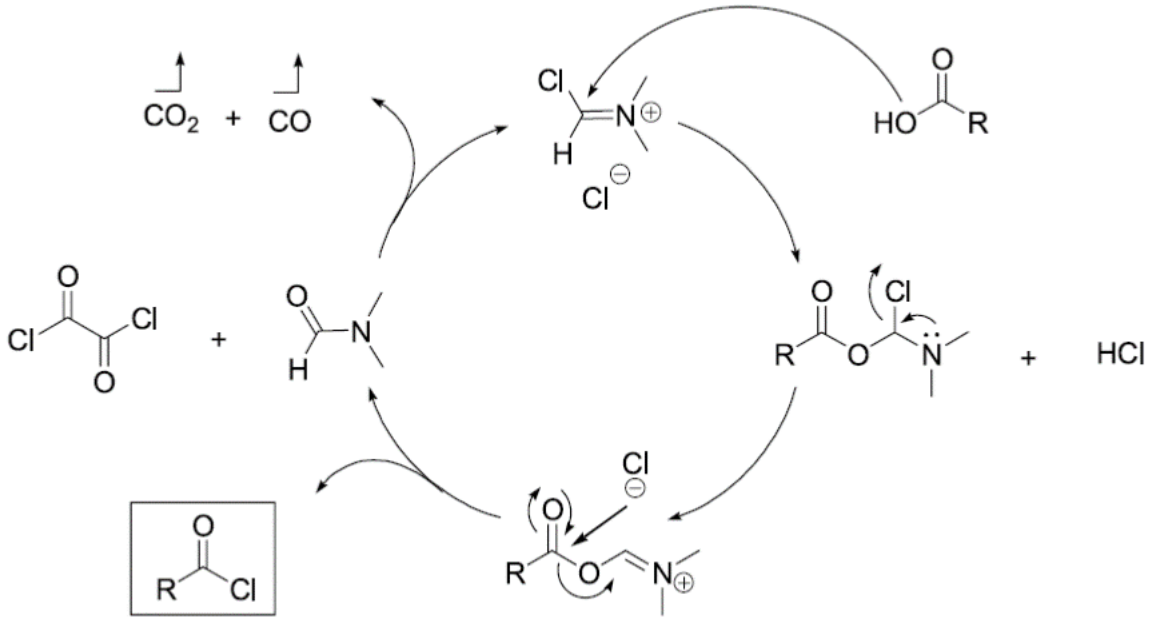
DCM = dichloromethane (methylene chloride)

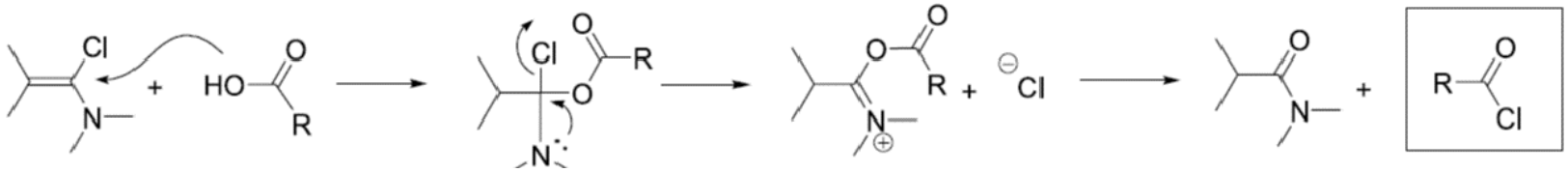
Anilide or Amide?



Name	Formula	MW	MP	pKa	Anilide	Amide
2-phenylbenzoic	$C_{13}H_{10}O_2$	198.22	113	3.46	109-110	177
2-chlorobenzoic	$C_7H_5O_4Cl$	156.57	140	2.92	114	142
3-nitrobenzoic	$C_7H_5NO_4$	167.12	140-142	3.48	153-156	142
1-naphthoic	$C_{11}H_8O_2$	172.18	161	3.7	162	202

Mechanism





C.A. G. N. Montalbetti, V Falque. Tetrahderon 61 (2005) 10827-10852

Reaction Setup

- Dry all glassware in the oven for 30-60 minutes
- Prepare drying tube with cotton & drying agent ($CaCl_2$)
  - Prevents moisture from entering the reaction vessel
  - *Water will hydrolyze the acid chloride*
- Heat reaction to 50-60^oC via water bath
- Formation of HCl & SO_2 (bubbling)
- Transfer to amine nucleophile
  - Ammonia is gaseous

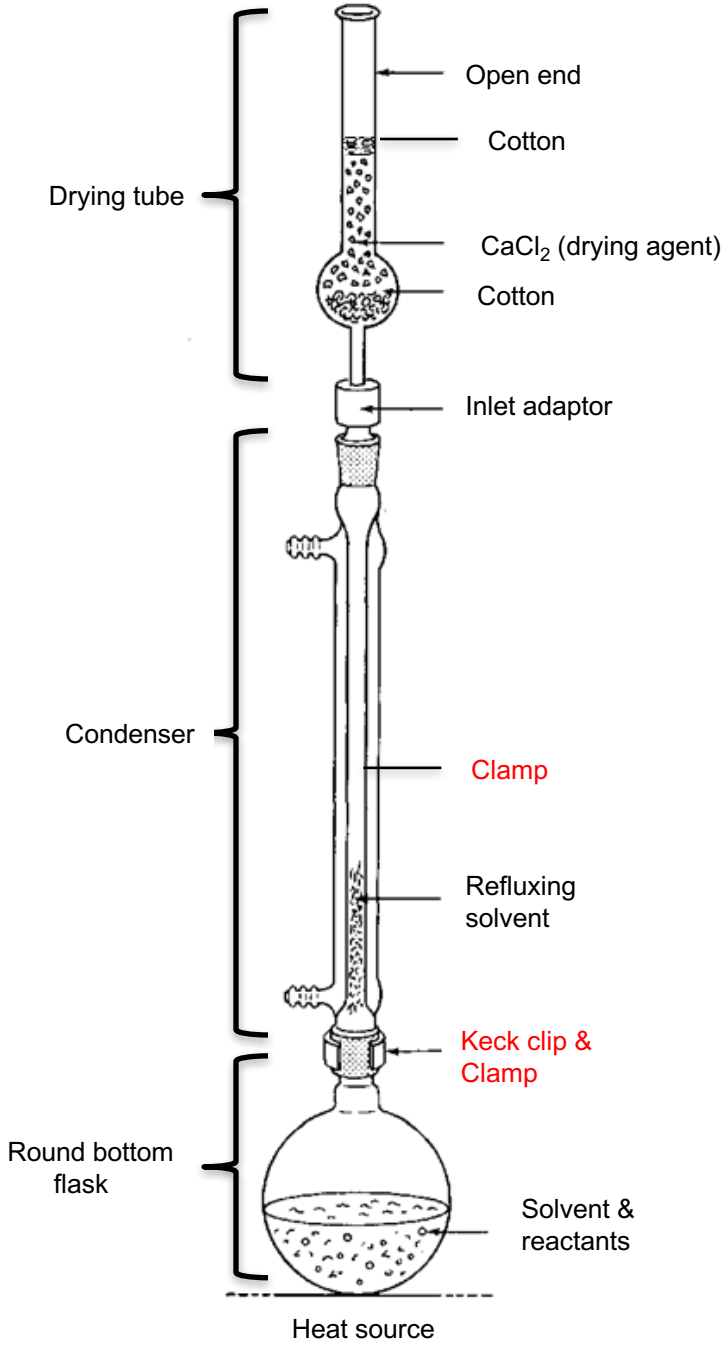
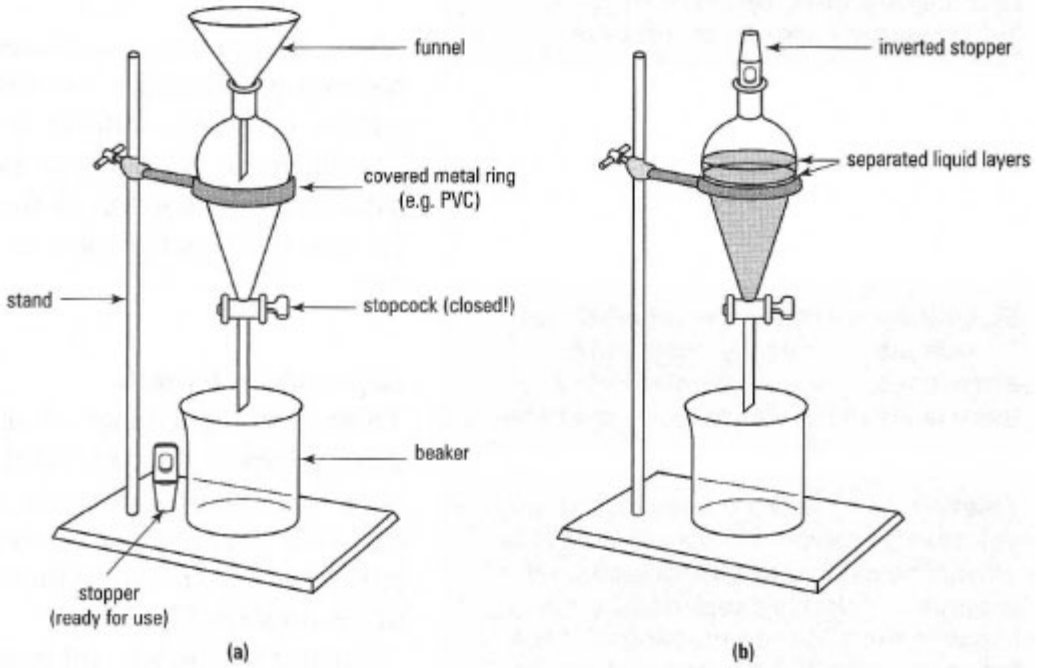


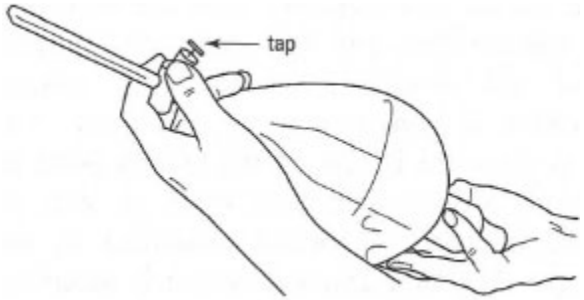
Image: http://what-when-how.com/organic-chemistry-laboratory-survival-manual/reflux-laboratory-manual/

How to use a separatory funnel

https://www.youtube.com/watch?v=1tmqUVSVPo4

Extraction via Separatory Funnel





**Always hold the separatory funnel at the neck and stoppered end when shaking

***Periodically invert & open the stopcock to release the built up pressure

*Make sure to close the stopcock before adding in solvent

Images: http://www.eplantscience.com/index/dean/liquidliquid_extraction.php

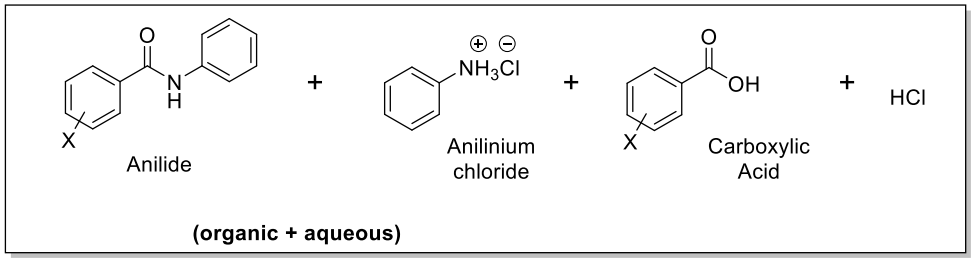
Aqueous Washes

- “Like dissolves like.”
  - Polar solvents are miscible with polar solvents vice versa for nonpolar solvents.
  - Polar and nonpolar solvents are not miscible with each other.

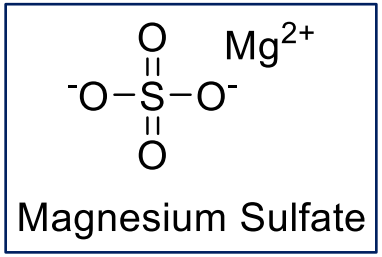
Questions:

- Are DCM and water miscible?
- Which layer will be on top?
- Which layer will be on bottom?
- Which layer contains your product?

Separation Tree (Anilide)



Drying Agent



Magnesium Sulfate

Dry dissolved derivative over anhydrous magnesium sulfate.

- The drying agent is hydroscopic and readily absorbs water.
- $MgSO_4$ is ionic and will not dissolve in organic solvent.
- Clumps = organic solvent is “wet” (add more drying agent)
- Fine powder = solvent is dry (snow globe)

*Make sure to swirl the flask well.

Images: http://quiz2.chem.arizona.edu/vip/extraction/

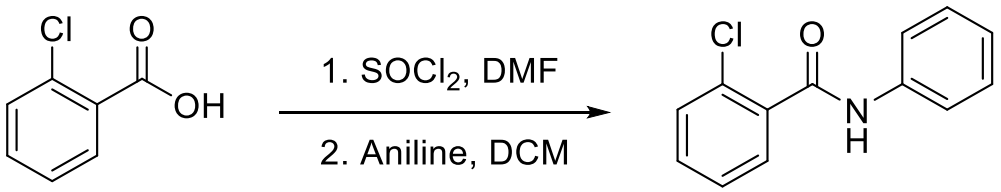
Recrystallization

- If necessary, recrystallize from ethanol or ethanol-water
  - Separate the recrystalizallized derivative on a Hirsch funnel

- Dry on a clay plate or in drying oven before determining melting point

Percent Yield

$$\% \text{ yield} = \frac{\text{actual yield}}{\text{theroetical yield}} \times 100\%$$

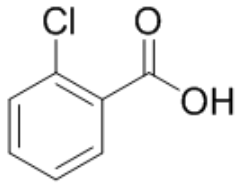
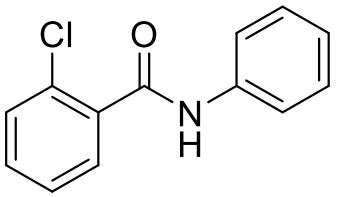
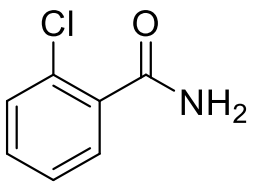


Compound	Boiling Point (°C)	Molecular Weight (g/mol)	Density (g/mL)	Mass (g)	Volume (ml)	mmol	equivalence
Carboxylic acid	-	156.57	-	0.5071	-	3.239	1.000
$SOCl_2$	166.3	118.97	1.638	-	3.55	5.73	1.77
Aniline	184.1	93.13	1.0217	-	2.05	22.5	6.95
Anilide	-	231.68	-	0.5413	-	2.336	0.7212

= weighed out

= calculated

Confirmation of Unknown Acid + Derivatives

Structure			
Compound Name	2-chlorobenzoic acid	2-chloro-N-phenylbenzamide	2-chlorobenzamide
Reported Melting Point	138 –140^{o}C	114^{o}C	142 –144^{o}C
Observed Melting Point	137 – 139^{o}C	112 – 114^{o}C	140 – 143^{o}C
Reported pKa	2.89	-	-
Observed pKa	2.85	-	-