

Isolation and Purification of Organic Compounds

Extraction (Expt #2)

All techniques for isolation and purification of products use phase equilibria:

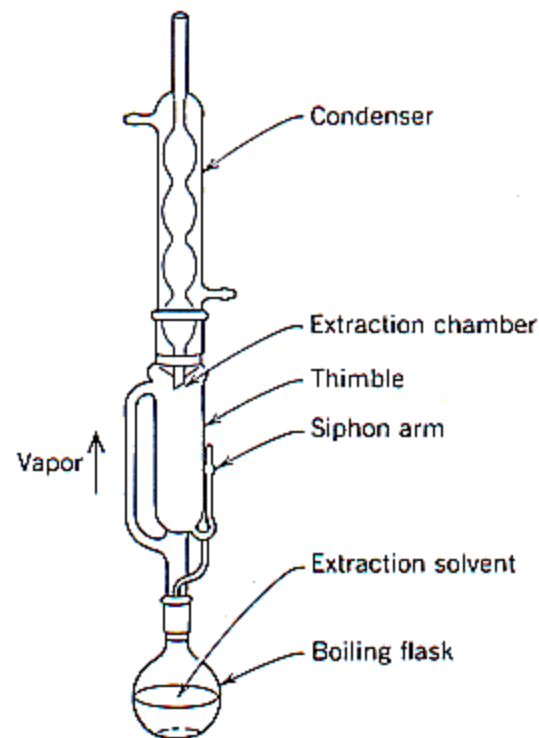
- isolate the desired product into one phase that is in equilibrium with another phase**
- The second phase ideally contains all other components of the mixture**
- equilibrium constants for distribution of materials between two phases are rarely either infinite or zero, so partial separation of the components usually occurs**
- phase equilibria used for purification may involve gas-liquid, gas-solid, liquid-liquid, or liquid-solid interfaces**
- Extraction procedures make use of phase equilibria at liquid-liquid and liquid-solid interfaces**

Extraction Procedures

Solid-liquid extraction

If the material to be extracted into the liquid is very soluble, simple stirring or shaking of a suspension of the solid in the liquid, followed by gravity filtration to remove insoluble impurities will suffice. You will do this operation in Expt #6.

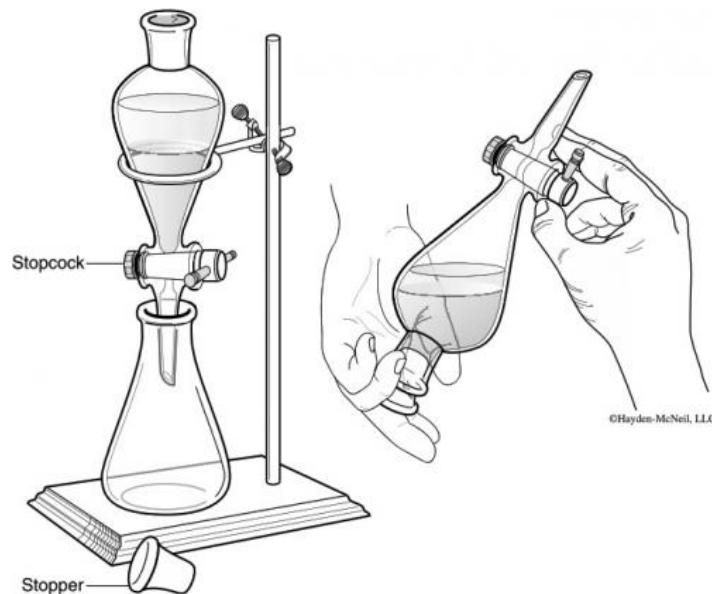
If the material to be extracted is less soluble, or is trapped in an insoluble matrix a continuous extraction device such as a Soxhlet extractor (right) is used. This device boils the extraction liquid, condenses it so that it can come into contact with the solid, and siphons the liquid back into the boiling flask. The extraction process occurs continuously until boiling is ceased. Over time the extraction solvent is enriched in the desired compound.



Extraction Procedures, Continued

Liquid-liquid extraction

Used to separate a component from one liquid phase into another. For most extractions one phase is an aqueous solution, and the other is an immiscible organic liquid. The two phases are shaken together gently in a separatory funnel (right), allowed to separate, and separated from each other by allowing the lower, more dense, phase to drain through the stopcock into an Erlenmeyer flask. The less dense phase is usually poured out through the top of the funnel to avoid contamination. Multiple extractions can be performed by returning/leaving the phase to be extracted in the funnel for additional extractions with the other solvent.



Common Extraction Solvents

Solvent	Density (g/mL)	Bp (°C)
CHCl_3	1.49	61
CH_2Cl_2	1.34	40
ethyl acetate	0.90	77
toluene	0.87	110
diethyl ether	0.71	36
hexanes	0.67	68-70
petroleum ether	0.64	35-60

The solvent must be immiscible with water, inexpensive, low boiling to allow easy removal from the desired product, and relatively non-toxic (all of these have some health and safety issues). Hexanes and petroleum ether are hydrocarbon mixtures composed mostly of hexane isomers and pentane isomers, respectively. All of these solvents except CH_2Cl_2 and CHCl_3 are flammable.

Extraction Equilibria

The equilibrium constant that governs the distribution of a solute, S, between two immiscible solvents is called the distribution coefficient or partition coefficient, K :

$$K = (\text{conc. of S in solvent A})/(\text{conc. of S in solvent B})$$

By convention, the concentration of S in the aqueous phase is placed in the denominator. For most moderately polar to non-polar organic compounds the distribution coefficient, K , will have a value between 0.5 to 10 for distribution between an organic solvent and water. This means that extraction is not infinitely efficient. Typically, multiple extractions are performed to isolate the desired compound. Your Manual shows by calculations that multiple extractions are more efficient than a single extraction with the same total volume of extraction solvent.

Solvents less dense than water will float on the aqueous solvent. Those more dense than water (CH_2Cl_2 and CHCl_3) will form the bottom layer.

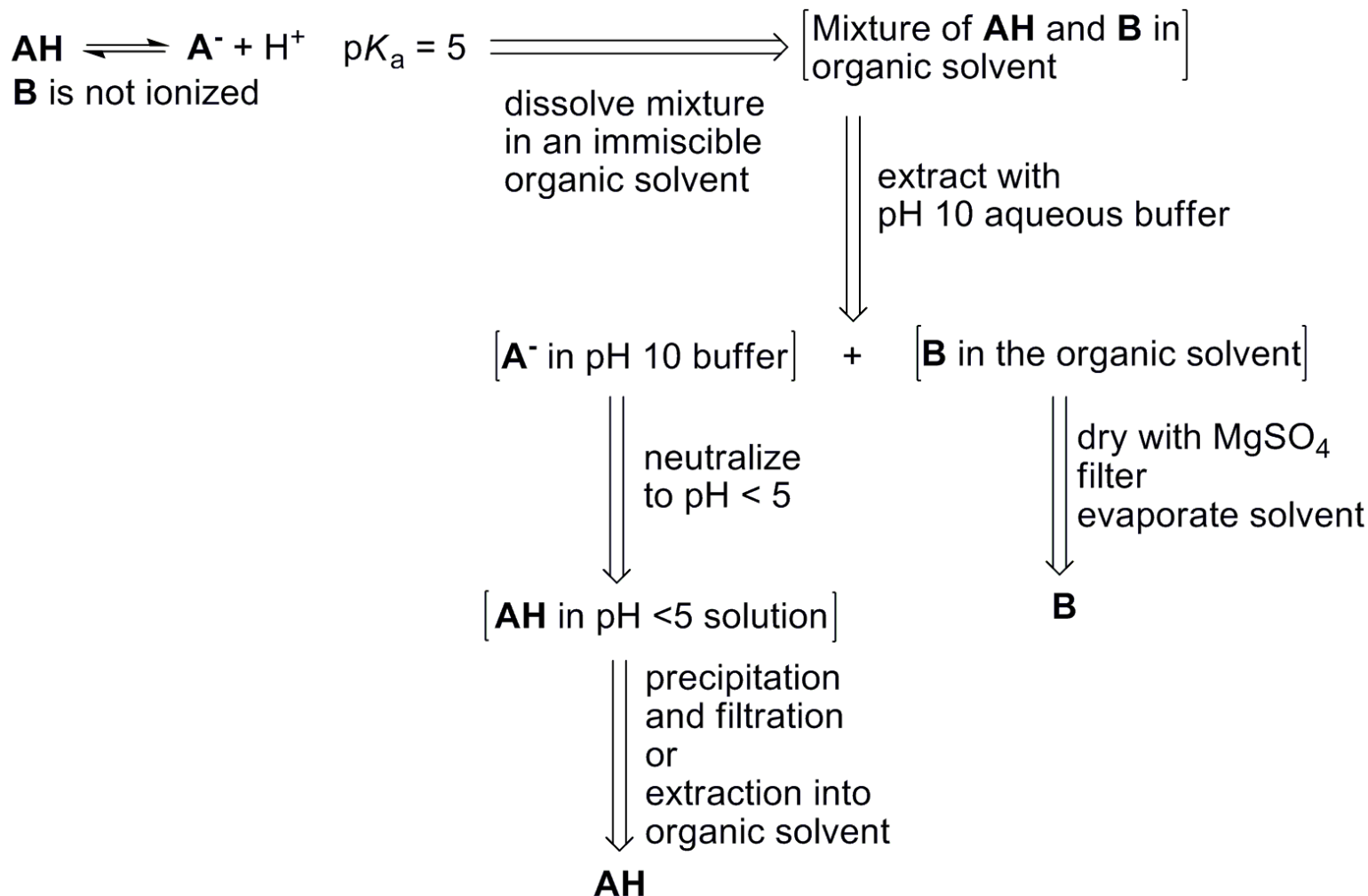
Extraction Efficiency and Purification

Because most neutral organic compounds will extract out of water into an organic solvent with a distribution coefficient equal to or greater than 1, simple extraction does not usually purify a mixture of organic materials. Extraction will separate neutral organic materials from inorganic ionic compounds or ionic organic materials that remain in water, but it would not be an efficient method to separate two neutral organic compounds from each other.

There is an important exception to this generalization. Weak organic acids or bases that can be ionized in water at pH 1 to 14 can be separated from neutral organics by extraction into an aqueous solution of the appropriate pH. This works because the weak organic acid or base is converted into a water soluble ion under these conditions, while a neutral organic material without acidic or basic properties will remain in the immiscible organic solvent.

An Example of an Acid-Base Extraction

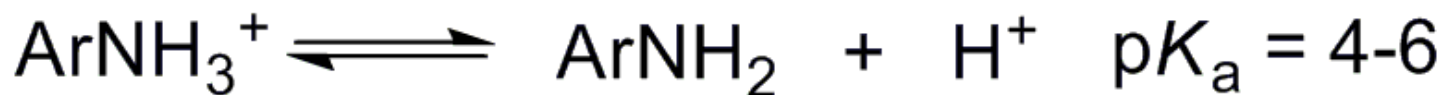
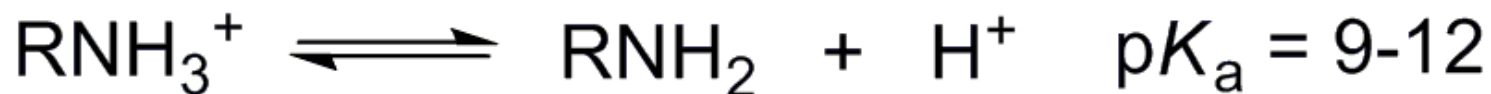
Example:
Separating AH and B



A weak organic acid will be extracted into a basic aqueous buffer as its conjugate base, a weak organic base would be extracted into an acidic aqueous buffer as its conjugate acid.

Extraction of weak bases

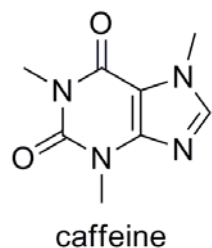
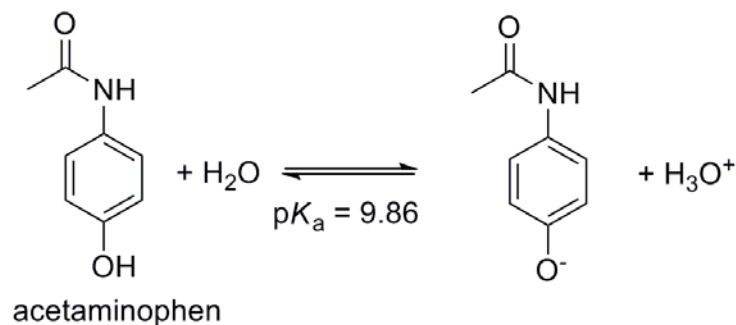
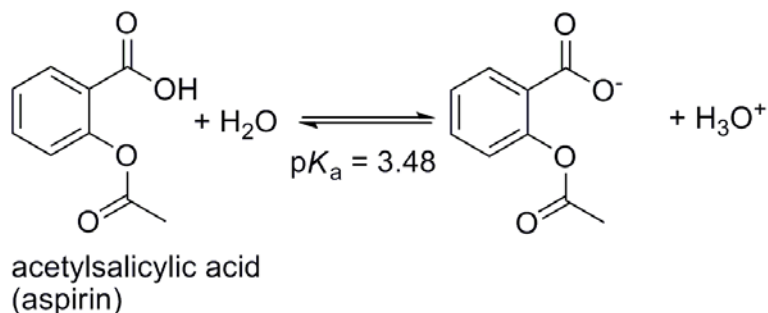
The most common organic weak bases are amines. Aliphatic amines have conjugate acids with pK_a s in the range of 9-12 depending on substituents on the alkyl group(s). Arylamines have conjugate acids with substituent dependent pK_a s of about 4-6



Both types of amines are converted into their cationic conjugate acids under acidic conditions, so they can be extracted from organic solvents into aqueous organic acids. Typically a 1 M HCl solution would be used unless it was necessary to separate weak bases of differing pK_a s. To obtain the neutral amine the acidic extract must be neutralized to a $\text{pH} > pK_a$ of the conjugate acid. The amine can then be collected by filtration or extraction from the aqueous solution into an organic solvent.

This Week's Experiment

You will make use of acid-base extraction procedures to separate a mixture of acetylsalicylic acid (aspirin), acetaminophen, and caffeine found in Extra Strength Excedrin[®].

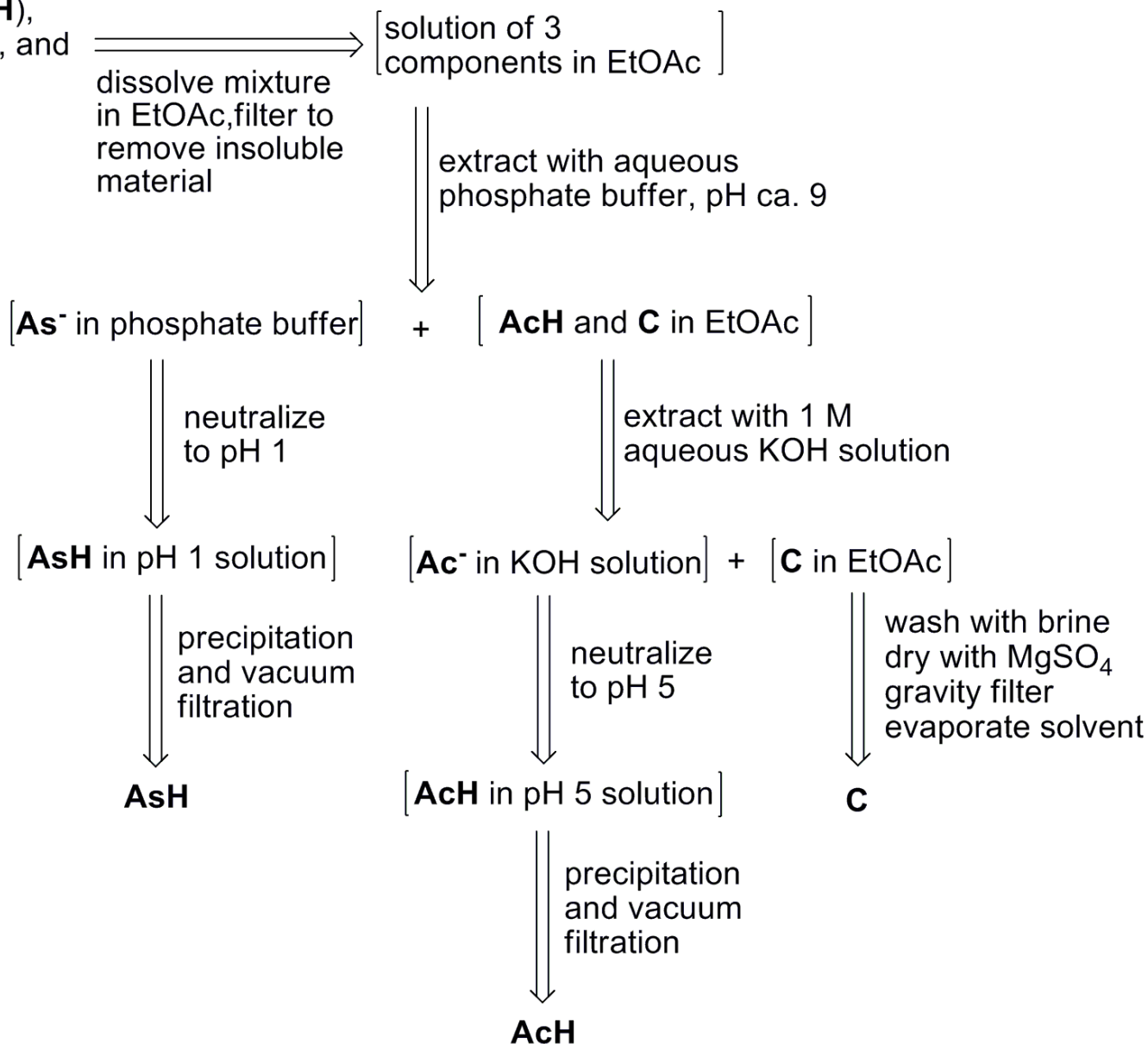


Aspirin and acetaminophen are both weak acids, but they have very different pK_a s that allow them to be separated from each other by using aqueous extraction solutions of different pH (< 10 to remove aspirin, > 10 to remove acetaminophen).

Caffeine is a neutral organic compound at pH > 1, so it will remain in the original organic solution of ethyl acetate (EtOAc) during the extractions.

Flow Chart

Mixture of aspirin (**AsH**),
acetaminophen (**AcH**), and
caffeine (**C**) in tablet



Experimental Hints

- 1. Grind the tablets to a fine powder to assist dissolution.**
- 2. Be patient when dissolving the tablets, use a low/moderate heat setting on the heater/stirrer. The organic components do not dissolve instantaneously.**
- 3. Make certain that the stopcock is closed when you filter the EtOAc solution into the separatory funnel.**
- 4. Release pressure periodically when gently shaking the solutions in the separatory funnel.**
- 5. Label all solutions carefully, you will have several solutions to keep track of.**
- 6. After extraction, make sure to adjust carefully to the indicated pH to maximize compound recovery.**
- 7. Both aspirin and acetaminophen are somewhat water soluble, make sure all solutions are cold, and that you use the minimum volume of water necessary to collect and wash the crystals.**
- 8. Make sure the EtOAc solution of caffeine is thoroughly dry before filtering and evaporating the solvent.**