Recrystallization and Crystallization

Introduction:

Although the knee-jerk reaction of most current chemists is to purify products by use of column chromatography, frequently the much more effective methods of crystallization and recrystallization are overlooked. These methods will often achieve purity that column chromatography can not.

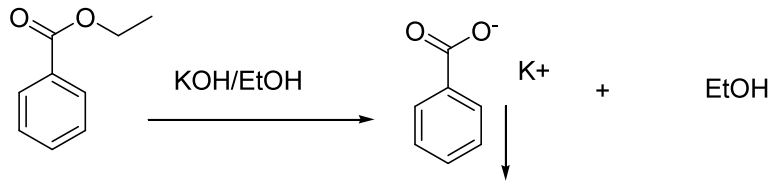
Definitions:

Crystallization is an isolation technique. Conditions are created where the material is no longer soluble. You obtain crude material from a reaction this way, but it can also be used to purify.

Recrystallization is a purification technique, involving taking a solid into solution, and then changing conditions so as to allow crystals to re-form.

Gedank Experiment:

A solution of KOH and ethyl benzoate in absolute ethanol is heated, then cooled:



The potassium benzoate formed is insoluble in ethanol, and precipitates. This is crystallization. Because of the way it is formed, it may trap ethyl benzoate or KOH in the solid.

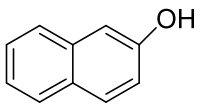
Let's filter out the potassium benzoate, and put it into water. If we warm it, it will go into solution. If we now slowly adjust the pH by adding dilute HCl, benzoic acid will be formed, which will be increasingly insoluble as the pH lowers. The benzoic acid will crystallize. If we now filter it out, we will have purified benzoic acid, but have we recrystallized? No. We have performed a second crystallization, since we have in effect done a reaction by changing the pH.

If we now take the benzoic acid thus obtained, and put it into benzene, heating it to dissolve it. Now we cool, and crystals form. We isolate them by filtration. They will now be purer and we have accomplished recrystallization. Note that recrystallization involves no chemical change of the material to be purified.

Both crystallization and recrystallization require understanding the conditions under which the desired material will be insoluble.

Is crystallization/recrystallization an option?

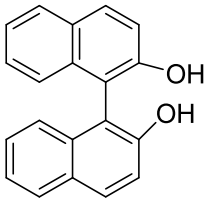
Look for rigidity, basic amines that can be converted to an acid salt, carboxylic acids, hydrogen bonds, and planarity, especially resulting from an aromatic system. Heterocycles generally crystallize well. Melting points are a general guide (higher is more likely a candidate), but can be deceiving: they reflect the lattice energy of formed, regular crystals, not necessarily how easy it is to get the crystals to form. The more degrees of freedom, the more difficult to purify by recrystallization. Methyl esters will often crystallize, where the higher esters will not. Examples:



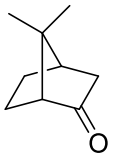
easy

Tartrate

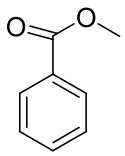
moderate



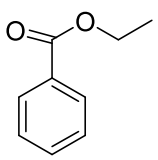
racemic: very easy
As tartrate diester: very easy resolution



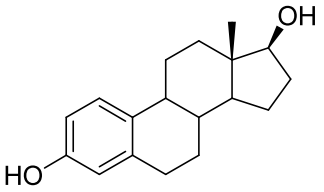
Very easy



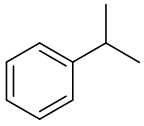
Easy
Mp = 91 C



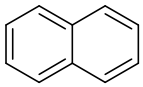
Liquid



Very easy



liquid



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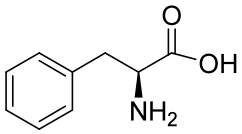

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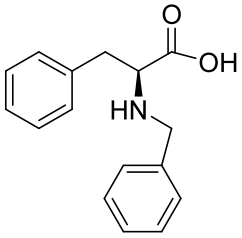
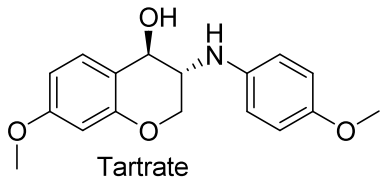


Difficult

For resolutions by recrystallization, they will only be successful if the optical center in one enantiomer is not buried, and if it has an effect of changing the nature of the unit cell:



Tartrate

Very difficult resolution