

Amine Unknowns

Overview:

You will receive an amine as an unknown. Your job will be to both identify your compound and prepare a derivative. Several pieces of information will be useful:

- Water solubility tests (big or small? Aromatic or not?)
- Solubility in acid-water. (Many basic amines ionize and dissolve in acid-water.)
- Boiling point or melting point of starting material.
- The melting point of the derivative.
- H-NMR information on the starting material.

Classifying Tests

1. Water Solubility Test (Helpful, but not always decisive or clear-cut.)

- Add 15 drops of water to a small test tube, and then add 2 drops or a spatula tip of sample. Stir vigorously. Is it homogeneous or heterogeneous? If heterogeneous, do the droplets float or sink?

- Interpretation:

- a. **Small:** Amines with <6 carbons always dissolve.
- b. **Big:** Amines with >10 carbons have $\leq 5\%$ solubility (never dissolve)
- c. **Borderline:** Amines with 6-9 C's may or may not dissolve.
 - a. Amines are more soluble than alcohols; no 7-carbon alcohols would dissolve.
 - b. Water solubility depends on basicity. Amines in which the nitrogen lone pair is sp^3 hybridized tend to dissolve much better than if the lone-pair is p.
 - c. For basic sp^3 -hybridized amines, the solution may take on a cloudy look when they dissolve. This is due to the basicity and the formation of ammonium hydroxide.

2. HCl/Water Solubility Test

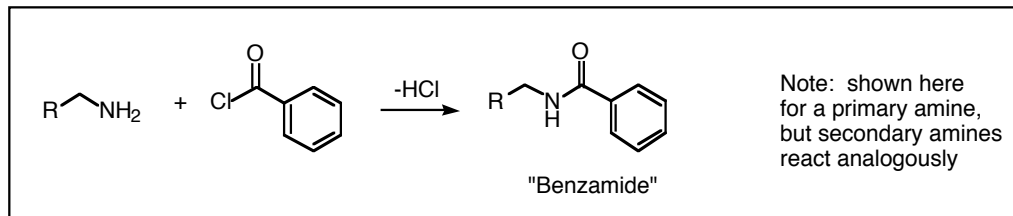
- Same procedure as above, except use a large test tube, use acid-water (HCl-solution in dispensing hood), add a stir-bar, and use 25 drops of acid-water instead of 15. Use magnetic stirring.
- Interpretation: Most amines with normal basicity will be protonated and become soluble. If you had a sample that didn't dissolve in water, but does dissolve easily in acid-water, it is likely to be an amine. Caution: solid amines sometimes take a while to ionize and dissolve, and amines in which the nitrogen is conjugated and has the nitrogen lone-pair in a p orbital may be relatively nonbasic and may not dissolve.

3. Amines Smell Variably Rancid. Liquids with sp^3 lone pairs smell worse than solids (less volatile).

4. Many Amines are Solids

5. NMR:

- Splitting: The N-H hydrogens in an amine experience hydrogen bonding. So like alcohol hydrogens, they tend to be a little broad and normally don't participate in splitting.
- NH or NH₂ signals can integrate for 1H or 2H, and typically show in the 1-3 ppm range.
- Chemical shift: hydrogens on a nitrogen-bearing carbon are not moved as far as when the carbon is oxygenated, but more than when it's allylic. Typically the additivity factor is about 1.5 ppm, and for a typical CH₂ group connected to an amine nitrogen, the CH₂ group would show up around 2.7 ppm.
- On an aniline (ArNH₂), the hydrogens ortho to the nitrogen are typically pushed upfield, into the 6 ppm window. This is because an amino group is a strong electron donor, so it makes the ortho carbons more electron rich and "shields" the ortho hydrogen, pushing them upfield.

Derivatives: Benzamide Derivatives

1. Place a small stir-bar and 2 mL of aqueous sodium hydroxide solution into a large test tube.
 - a. ~1M is good. ($\geq 3M$ NaOH/H₂O may weaken the filter paper).
2. Add the amine, about 15 drops if it's a liquid, about 0.20 g if it's a solid.
3. Stir the solution vigorously, and add about 15 drops of benzoyl chloride.
4. Stir vigorously for 5 minutes.
5. Then acidify with aqueous HCl (this helps the amide to crystallize), while continuing to stir vigorously. (Use pH paper to confirm that the pH is lower than 7. This can be done by touching a boiling stick into the mixture, then touching it onto a strip of pH-paper. An acidic solution should turn the paper red.) There is no risk in making it too acidic.
6. Cool on ice for one minute.
7. Filter the lumpy product through a Buchner funnel, using vacuum. **Pulverize/crush any chunks.**
 - If material is chunky, transfer to a small weighing boat. Place a second empty boat on top, and then grind down on the top boat to crush/grind/pulverize the solid material between the two boats. Then return the material to your Buchner funnel.
 - Chunks/blocks are a problem because contaminants (either amine or benzoyl chloride derivatives) may be entrapped and may not have any exposure/contact with the subsequent acid-water or base-water rinses that are intended to ionize and extract those impurities.
8. Wash repeatedly: with 2 x 10 mL of cold water, then 2 x 10 mL of HCl/water (to wash off unreacted amine).
9. **Recrystallize**, perhaps adding ethanol or water as necessary. A suggested starting point is 3mL of ethanol and 10 drops of water. But the solubilities will vary greatly from unknown to unknown, so you need to make whatever adjustments are appropriate for your particular sample. You shouldn't need these anymore, but several recrystallization reminders (read):
 - Use a small Erlenmeyer (25 or 50-mL), not a beaker, to reduce solvent evaporation.
 - Make all your adjustment decisions while the solution is boiling hot.
 - Heating your Erlenmeyer in a hot-water beaker (150-mL) is convenient, to provide more even heating and to avoid overheating on the hot-plate surface.
 - You and your hood partner should also warm up some ethanol in case you need to add some
 - Other than when you're just starting, don't add cold solvents.
 - During cooling, cover flask to avoid evaporation of the hot solvent.
 - If no crystals form even after slowly cooling and then icing, try adding ice chip(s).
 - If after chilling you seem to have no solvent, add some cold ethanol. You need solvent for the impurities to have a place to swim!
 - Your rinse solvent should be similar to what you think your actual solvent blend is. But avoid water if possible so that your crystals will dry better.

Micro-Boiling Points in the Melting Point Apparatus (if you have a liquid unknown)

A microscale boiling point can be taken in a melting point tube that has an inverted "bell" in it. Add about 7 μ L of liquid via syringe and tapping. Pre-boiling bubbling will often occur as the air inside the bell heats and expands and gets displaced by sample evaporation. When the boiling point is reached, the liquid level should begin to drop (slowly at first, more rapidly the more "above" the boiling point you are.) Sometimes more rapid bubbling often takes place, but not always. Keep heating somewhat beyond the point

where you think boiling has occurred, because you may not be experienced enough to distinguish “pre-boiling” bubbles from real boiling bubbles. And in some cases, you’ll never see bubbles. Even so, at or somewhat beyond the boiling point, vaporization should accelerate such that the liquid level will drop. Watch for this.

These boiling points will not be very accurate, especially for an inexperienced user. Don't trust them to be accurate better than to about 10 degrees. While the observed boiling points are imprecise, they still greatly shorten the list of candidates.

Amine Candidates

Bp of Starting Amines (Liquids)	Unknown	mp of Benzamide Derivative
48	Propylamine	84
55	Diethylamine	42
78	Butylamine	42
159	Dibutylamine (Bu ₂ NH)	oil
182-185	Benzylamine (PhCH ₂ NH ₂)	105
184	Aniline	163
185	PhCH(CH ₃)NH ₂	120
196	N-Methylaniline (PhNHCH ₃)	63
200	2-Methylaniline	144
204	3-Methylaniline	125
208	2-Chloroaniline	99
210	2-Ethylaniline	147
216	2,6-Dimethylaniline	168
218	2,4-Dimethylaniline	192
218	2,5-Dimethylaniline	140
225	2-Methoxyaniline	60
230	3-Chloroaniline	120

Mp of Starting Amines (Solids)	Unknown	mp of Benzamide Derivative
35-38	PhCH ₂ NHPh	107
41-48	4-methylaniline	158
49-51	2,5-dichloroaniline	120
52-55	Diphenylamine (Ph ₂ NH)	180
57-60	4-methoxyaniline	158
57-60	2-aminopyridine	165
58-66	4-bromoaniline	204
71-73	2-Nitroaniline	110
112-114	3-nitroaniline	157
115-116	4-methyl-2-nitroaniline	148
138-140	2-methoxy-4-Nitroaniline	149
148-149	4-Nitroaniline	199

Note: amines are hydrophilic, and tend to absorb some water from the air. Some of the starting amines may also have trace isomeric impurities. The result of moisture and/or impurities means that some of the starting materials may have melting points that are a little bit depressed.

Unknown No. _____ Name _____

1. Physical Examination of Starting Material

a) Physical State _____ b) Color _____ c) Odor _____

2. Solubility Tests on Starting Material

Solubility in Water: _____ If Insoluble, Does it Float or Sink?

Solubility in HCl/Water: _____

3. Boiling point or melting point for starting material:

“Literature” value:
(list, previous page)

4. Recrystallized Derivative

observed mp

literature mp

5. H-NMR (attach, with assignments/interpretation.)

- **On the proton spectrum, create a standard 4-column summary table of your H-NMR data, detailing chemical shifts, integrations, and splittings, and “source” hydrogens.**
- Draw the structure of your molecule, with identifiers by each carbon (a, b, c...).
- Then on your standard summary table include a column in which you explain which “source” hydrogens (a, b, or c, etc...) are responsible for which signals. Note: if the sample is too concentrated, the splitting may in some cases get broadened and become problematic.
- **Aromatic H's:** Do analyze aromatic H's for solid samples. For liquid samples with aromatics, the aromatic H's will have overlapping so won't be useful to detail.

6. What is My Actual Unknown? (Letter, Structure and Drawing of structure)

7. Comments, difficulties, complaints, etc..