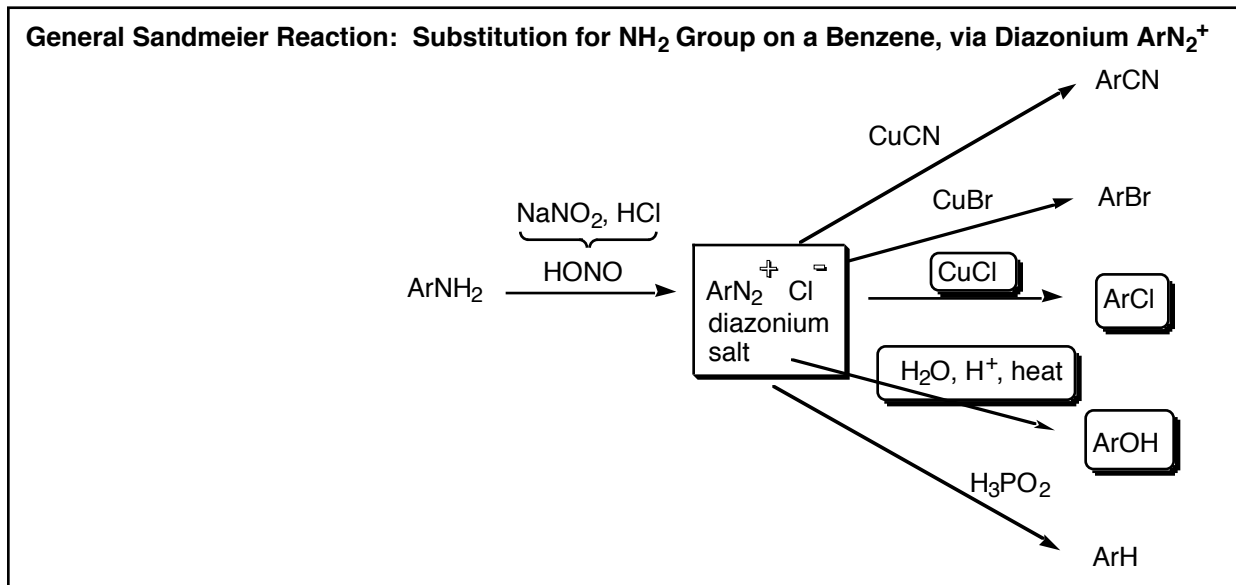
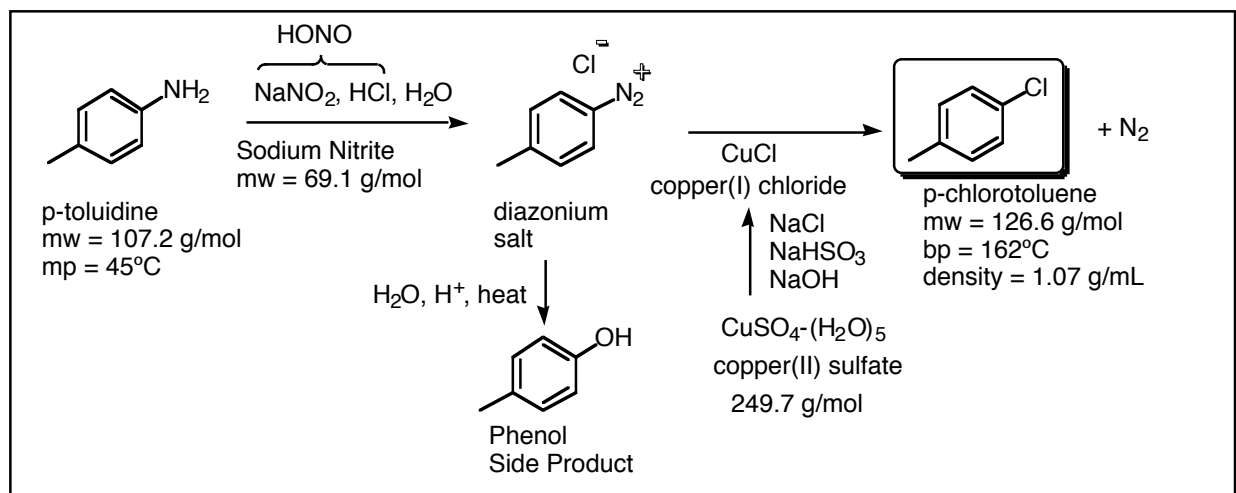


The Sandmeyer Reaction: Substitution for an NH₂ on an Aromatic Ring



Intro The “Sandmeyer Reaction” is a versatile method for replacing the amine group of a primary aromatic amine with a number of different substituents. The amine is treated with “nitrous acid” (HNO₂) under acidic conditions, which produces the diazonium ion. The diazonium can then undergo substitution reaction with various reactants, particularly copper(I) substrates. Although the substitution can be simplistically viewed as a direct ionic substitution reaction (anion as nucleophile, molecular N₂ as a premier leaving group), the actual mechanism is actually more complicated and involves radicals.



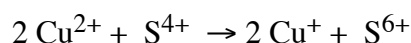
Today's Reaction: Synthesis of p-Chlorotoluene

In today's experiment, we will use copper(I) chloride (CuCl) as our “nucleophile”, to produce the chloride product. The diazonium ion has limited stability in water; it tends to react to give phenols (ArOH) upon standing or unnecessary warming. The principle organic side product will be the phenol resulting from competing reaction with water. This will be removed by aqueous extraction using NaOH/water in a separatory funnel. (The phenol anion is intensely red.)

Molecular nitrogen is produced as the final substitution reaction proceeds. This is evidenced by formation of bubbles.

The reaction is fairly complex because none of the actual reactants is stable. Three different reactants need to be made “*in situ*” (“in the site”, or “in the pot”), rather than being available straight from a stockroom shelf.

- Nitrous acid: The HNO_2 (HONO) required for converting the amine into the diazonium is not stable. It is made by mixing sodium nitrite (the weak base conjugate) with HCl. Under acidic conditions, the HONO gets protonated and loses water to give ^+NO cation, which reacts with the amine and is followed by a series of proton transfer-elimination steps to give the actual cationic diazonium species.
- The diazonium species: This too must be made *in situ*, from the amine and the *in situ*-generated nitrous acid.
- The copper (I) chloride: This is prepared *in situ* from cheap, stable copper(II) sulfate by a reduction/substitution reaction. Cu(II) gets reduced to Cu(I) by a reduced form of sulfur (S in the +4 oxidation state), which in turn gets oxidized to sulfate-type sulfur (S in the +6 oxidation state).

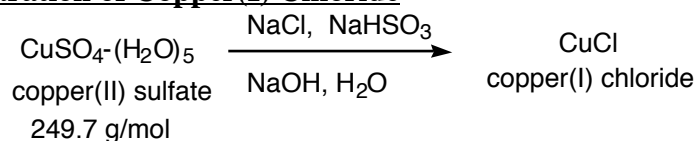


The reaction goes through many different steps, so will have many solubility and color changes. In addition, since both the diazonium ion and the CuCl need to be prepared prior to the final substitution reaction, it will be helpful to subdivide the experiment into three parts.

- Part 1: Preparation of the copper(I) chloride
- Part 2: Preparation of the diazonium ion
- Part 3: Reaction of the diazonium with the copper(I) chloride to produce the final product.

Reaction Procedure

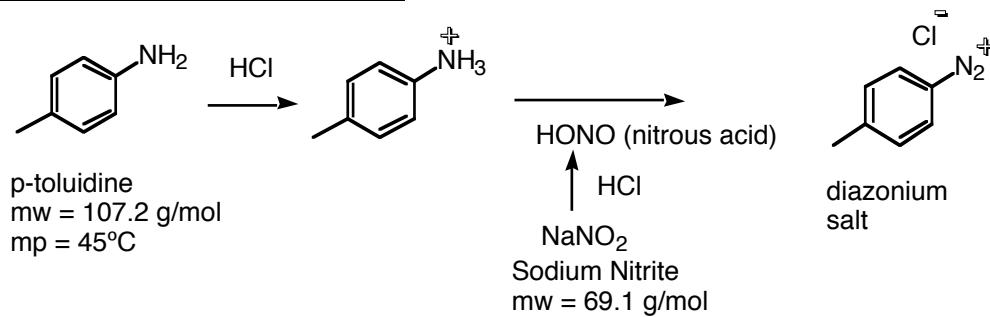
Part 1: Preparation of Copper(I) Chloride



1. Clamp a 250-mL round-bottomed flask to a vertical rod.
2. Weigh 15.0 g of copper(II) sulfate hydrate, and add to the flask.
3. Add 50-mL of warm tap water. (You are going to heat this to boiling, so if you run the tap so that it's already pretty warm to start with, it won't take as long to boil as if you start with cold water...)
4. Place a heating mantel underneath the flask, and heat the solution to boiling such that the copper sulfate dissolves completely. The pretty blue color is the color of Cu^{2+} with water molecules coordinated. (The sulfate is spectator.) You may as well set the power setting to “high” so that you can heat it to boiling as fast as possible.
5. Once the copper sulfate dissolves, turn the heat off.
6. Add 7.0 g of NaCl. (The solution can still be hot). The color change results from a change in the copper coordination sphere from copper-water bonds to some copper-chloride bonds.
7. Add 30-mL of the NaOH/NaHSO_3 /water pre-mixed solution. Add somewhat slowly, over 30-90 seconds. Shake the solution very well. The color change results from a change in copper's oxidation state from $\text{Cu}^{2+} \rightarrow \text{Cu}^+$.

8. After shaking well, let the solution cool, resting in an ice-bath, allowing the white CuCl to settle out.
9. Decant (pour off) most of the water layer.
10. Add an additional 50 mL of cold tap water, swirl again, and again let the CuCl settle, then decant most of the water again. Put it back in an ice-water bath.
 - Note: a little residual water is not a problem.
 - Note: Should I worry if a little bit of the CuCl gets poured out in the water? You can decide only if you know what's the limiting reactant! If the copper sulfate is limiting, then losing copper reagent will cost you in terms of yield. If copper sulfate is excess, then losing a little bit of CuCl shouldn't matter.
11. Dissolve the solid in 23 mL of concentrated hydrochloric acid. The solution is susceptible to air oxidation, so it shouldn't not be allowed to stand for longer than necessary. If the diazo compound produced in Part 2 isn't close to being ready, you may wish to wait before adding the concentrated HCl here. Keep the solution in an ice-water bath after everything is added.

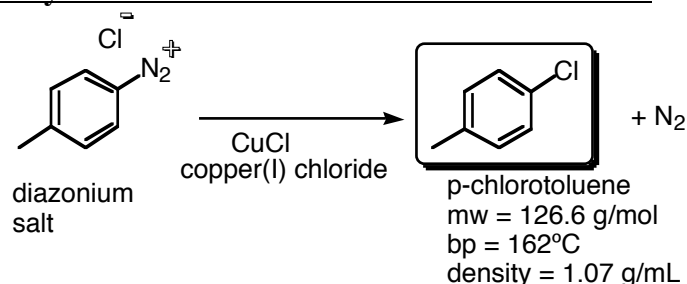
Part 2: Preparation of The Diazonium Salt



1. Weigh out 5.50 grams of p-toluidine and place it into a 125-mL Erlenmeyer flask with a stir bar.
 - Note: p-Toluidine is an amine and has a bad smell. It is also relatively non-volatile; if you spill some today, the putrid smell will linger for perhaps weeks before the material completely evaporates. So for the sake of yourself and all other students who will use this lab this semester, please be super careful that you don't spill any on the bench or balance or anywhere! And leftover stuff with specks on, wash/rinse in the hood.
2. Add 8 mL of water.
3. Set up a little vapor chimney by putting a tube on the narrow end of a funnel, hooking the other end of the tube to an aspirator, and dangling the big end of the funnel over your Erlenmeyer.
4. Measure out 12.5 mL of concentrated hydrochloric acid, and add 6 mL to the Erlenmeyer.
5. Stir the solution and heat it until the solid dissolves. (You have formed an ionic ammonium ion, which is soluble in hot water)
 - $\text{p-TolNH}_2 + \text{HCl} \rightarrow \text{p-TolNH}_3^+$
6. Take the solution off the hot plate, and add the remainder of the 12.5 mL of HCl.
7. Cool thoroughly in an ice-water bath. (Although p-TolNH_3^+ is soluble in hot water, it precipitates from cold water.)
8. In a separate beaker, make up a solution of 3.70 g of sodium nitrite in 10 mL of water.
9. Take a small beaker and weigh out about 5 grams of ice.

- Pour the ice into the Erlenmeyer flask with the ammonium ion. The function of the ice is to absorb heat released when the diazonium compound forms. Keeping the temperature cold helps to prevent formation of the undesired phenol side product.
- Then pour in the sodium nitrite solution, with vigorous stirring. Add it a little bit slowly, in portions over 2-3 minutes.
- Stir the solution in hopes that everything dissolves. If so, things are probably in good shape.
- If the solid doesn't dissolve within 10 minutes, you may wish to add another 0.50 g of sodium nitrite.
- After the solution seems dissolved, or about five minutes after completing your addition of sodium nitrite, test the solution for excess nitrous acid by doing the following test: Get a piece of starch paper, poke a glass rod into the solution, and then put the rod into a test tube. Add a few drops of water. Then take the wet glass rod and touch it onto a strip of starch-iodide paper. If it turns dark blue, that means you have excess nitrous acid, which is what you want. If it doesn't turn blue, then add another 0.3 g of sodium nitrite. (The sample is diluted because strong hydrochloric acid alone also produces the same color on starch-iodide paper, after a slight induction period.)
- Leave the solution in the ice bath until you are ready to use it.

Part 3: Sandmeyer Reaction. Formation of 4-Chlorotoluene



- Once both the copper(I) chloride (Part 1) and the diazonium salt (Part 2) are prepared, pour the diazonium ion solution through a funnel into the copper(I) chloride solution.
- Rinse the Erlenmeyer with an additional 10 mL of water.
- Swirl and shake the mixture for 5 minutes.
- Watch for all the changes that happen. Among them, watch for the initial separation of a complex of the two components and its subsequent decomposition that results in liberation of molecular nitrogen (bubbles!) and formation of a thin oil layer on top. (This layer will be the product, which as a neutral organic molecule is insoluble in the water solvent.)
- Set the system up for a simple distillation, using a heating mantel to heat. Collect the distillate in a 100-mL graduated cylinder, which means that you heating mantel and flask will need to be elevated considerably. Clamp a large iron ring onto the vertical rod as a support for the heating mantel.
- Don't start distilling until there is at least some visible oil layer. But if there is, you can go ahead with the simple distillation. Set the heating mantle power to high, so you distill as fast as possible.
- Note: The product has a formal boiling point of 162°C, way higher than water. But it turns out that by doing a fast, indiscriminate simple distillation, the vapor is a mixture of both product and water. Thus, you don't actually want to do a careful, slow, fractional distillation or you wouldn't be able to get the product over!
 - As you watch the distillate, the product should eventually "egg-yoke" to the bottom, because it is more dense than water. Notice that it floated in the round-bottomed flask, because the water there was filled with salts and was more dense than the

- product. But when pure water is distilled over, the product is more dense and thus sinks.
8. How long should you keep distilling? If you have calculated your theoretical yield, you can make an educated decision! If you know how many grams of product you are expecting, that will tell you approximately how many mL of product you should expect to collect! Alternatively, if you see that the organic layer isn't growing any further, then you can also stop distilling.
 9. Once you think you've distilled long enough, turn the heating mantel off. Make sure that your flask is very securely clamped to the vertical rod, then lower the heating mantel away. It will take a long time for your solution to cool off enough to clean up, and it will take even longer if you keep the heating mantel on it. So the sooner the heating source is removed, the sooner you'll be able to clean up and leave!

Workup: Purification/Isolation of 4-Chlorotoluene

Your crude distilled product will be not only wet, but will also be contaminated by variable amounts of p-TolOH, the phenol side product. Phenols are somewhat acidic, because the resulting phenoxide anion is stabilized by conjugation and is thus more stable than hydroxide. The purification will take advantage of this by ionizing the phenol such that it partitions into water, while the neutral organic product stays in ether.

1. Pour your distillate into a separatory funnel.
2. Rinse the graduated cylinder with 15 mL of ether.
3. Add 5 mL of 3-M sodium hydroxide solution.
 - Notice which layer the color goes into. The color change is because $\text{p-TolOH} + \text{HO}^- \rightarrow \text{p-TolO}^- + \text{H}_2\text{O}$, and phenoxide p-TolO^- is strongly colored.
4. Pour off the aqueous layer. If there is still a lot of color, wash with another 5 mL of 3-M sodium hydroxide.
5. Dry the ether layer over about 2.5 grams of sodium sulfate.
6. Filter through some glass wool into a pre-weighed 50-mL round-bottomed flask, and rinse adequately with ether.
7. Concentrate the solution by rotary evaporation to remove the ether.
8. Weigh your liquid product, and take an H-NMR.

Cleanup:

Pour the entire residue from your round-bottomed flask into the "copper waste" bottle. Rinse with water at first, and pour the rinse down the drain. Then rinse/wash/scrub with acetone to get the flask to clean up.

Questions: None assigned.

Lab Report: Standard synthesis style lab report. You may write a combined report with your partner, if you had one. Be sure to include detailed observations on many of the things that happened! For product, include yield, % yield, and H-NMR.

