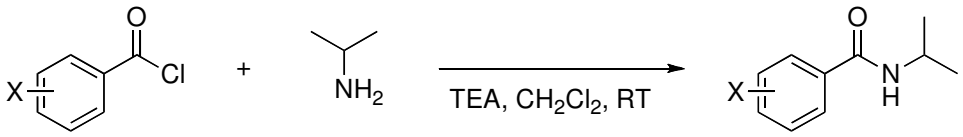
CHEM352L, Spring 2012
Solution Phase Amide Synthesis

This week you will prepare an amide by reaction of an acid chloride with an amine:



You will be using one of five possible acid chlorides, which are benzoyl chloride, 4-methoxybenzoyl chloride, 4-chlorobenzoyl chloride, 4-methylbenzoyl chloride, and 3-methylbenzoyl chloride; your TA will tell you which one you will be using when you come to the laboratory, so include all five in your data table. Triethylamine (TEA) is present as a base to react with the HCl that is generated in the reaction.

Background reading on the reactions of acid chlorides is posted on the course Blackboard site.

Pre-lab questions:

1. Prepare a flow chart, such as the one on page 142 of your lab manual, outlining the reactive acid base extraction for this experiment. It should indicate which compounds end up in each layer of your separatory funnel in each step of your extraction, showing all compounds in the correct protonation state.

Post-lab questions:

1. ^{1}H NMR spectra for all five possible amide products plus the amide that would be obtained using 4-nitrobenzoyl chloride and isopropylamine are posted on Blackboard. Identify each (*i.e.* spectrum A corresponds to 3-methylbenzamide). Briefly explain your reasoning in each case, and assign all NMR signals.
2. Primary amides show two strong bands in the region between 1700 and 1600 cm^{-1}. Why two, and to what process does each correspond at the molecular level (*e.g.* CO bending)?

Procedure:

1. To a 25 mL RBF containing a stir bar add 5 mL of 1 M acid chloride in dichloromethane and 0.8 mL triethylamine from the buret. Attach a condenser, turn on water for the condenser, and start stirring. You will not heat the solution, but the reaction is exothermic and dichloromethane has a low boiling point. ***Be sure the stir plate is NOT heating your solution!***
2. Dilute 0.5 mL (use graduated pipet) of isopropylamine in 5 mL of dichloromethane in a graduated cylinder.
3. Using a disposable glass pipet, mix the solution gently. Slowly add this solution in 1 mL portions, dropwise over 15 minutes through the condenser to the RBF using the same glass pipet.

4. After addition is complete, allow the reaction mixture to stir an additional 60 minutes at room temperature.
5. Transfer the reaction mixture using a pastuer pipet to a separatory funnel containing 5 mL of dichloromethane. Rinse the reaction vessel with an additional 5 mL of dichloromethane and transfer this rinse to the separatory funnel using a pastuer pipet.
6. Wash the dichloromenthane twice with 10 mL of 1 M HCl, being sure to remove the aqueous (top) layer.
7. Wash the dichloromethane twice with 10 mL of saturated sodium bicarbonate. ***Be careful! Residual HCl in the organic layer will bubble when it comes into contact with the sodium bicarbonate solution!***
8. Wash the dichloromethane twice with 10 mL of saturated sodium chloride (brine) solution.
9. Dry the organic layer with $CaCl_2$ and then gravity filter into a tared 50 mL Erlenmeyer flask.
10. Add a boiling stick and gently heat on a hot plate to remove most of the dichloromethane. Once the volume is about 2-4 mL, remove the flask from the heat - crystals should form rapidly. ***Be cautious not to evaporate to dryness!***
11. When crystallization is complete, remove the mother liquor by placing a pastuer pipet flush with the bottom of the Erlenmeyer flask. ***Crystals should remain in the hood during this time!!!***
12. Once all the mother liquor is removed, obtain a dry mass of the crystals. Perform a fast melting point determination and then a slow melting point determination. Report your slow melting point and your percent yield in the Results and Conclusions section of your notebook for the experiment.