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Exam start time: 8:00 PM Exam end time: 9:30 PM

Research Methods (CHEM 251)
Synthetic Organic Chemistry Part
Final Examination

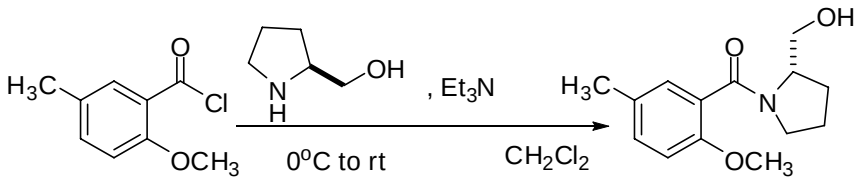
Prof. Malachowski

Due: October 25, 2007, 5 PM

Honor Code: You may take this examination while consulting your course lecture notes, lab notebook and handouts. You are not to consult any other electronic or written material during the exam. You have 1.5 consecutive hours to complete the exam. You should not discuss the exam with anyone until all students have handed in their exam. There are a total of four questions. The point values for each question are written with the question.

You are a brand new graduate student in the lab of a famous Nobel Prize winner and you are given this as your first amide synthesis reaction. Your research director tells you to run this reaction with 5.00 g of the acid chloride starting material. Fortunately, the reaction has been performed previously in the literature and you know how many equivalents of each reagent you should use. Unfortunately, it was performed by a chump named Malachowski, so it's dicey at best that you can reproduce the results.

1) Fill in the boxes that are missing and make sure all the quantities shown are correct. According to the article the authors used 20 mL of dichloromethane per gram of acid chloride. (20 pts.)



Specs/Compd	5-Me-o-anisic acid chloride	L-prolinol	triethyl amine	dichloro-methane	Hydroxy-amide
fw (g/mol)	184.66	101.15	101.19	--	249.30
d (g/mL)	--	--	0.726	--	--
mp (^{o}C)	--	--	-115	-97	--
bp (^{o}C)	--	--	89	40	--
Scale					
mmol	27.1	27.1	67.8	--	27.1
eq	1.0	1.0	2.5	--	1.0
g	5.00	2.74	6.86	--	6.76
ml	--	--	9.44	100	--

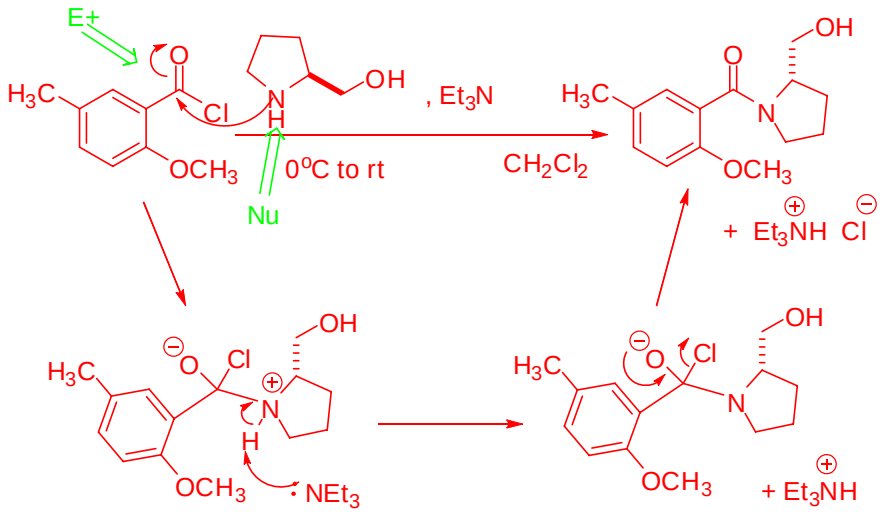
2) Which size round bottom flask should you use to perform the reaction? (5 pts.)

Since the total volume of reagents will be approximately 120 mL, a 250 mL flask should be used.

3) Sometimes when a reaction is proceeding slowly it is useful to heat it at reflux. If you heated this reaction at reflux temperature, what would that temperature be? (5 pts.)

40^{o}C, the boiling point of the solvent, CH_2Cl_2

4) Draw the mechanism of this reaction on the next page. You may abbreviate structures to simplify the process, but be sure the essential components of the mechanism are clear. (15 pts.)



5) Label the nucleophile in your mechanism with an 'Nu'. (5 pts.)

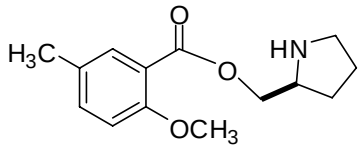
6) Label the electrophile in your mechanism with an 'E+'. (5 pts.)

7) What role does the Et_3N play? (5 pts.)

Triethylamine, Et_3N, is a base or proton scavenger.

8) This reaction is an example of chemoselectivity, the selective reaction of one functional group over another. For example, the nitrogen or amine of L-prolinol reacts to form the amide product instead of the oxygen or alcohol group reacting to form an ester (structure shown below). Why is this reaction chemoselective for the nitrogen over the oxygen? (5 pts.)

Ester product that might be formed if oxygen of L-prolinol reacted instead of the nitrogen:



Amines are much better nucleophiles than alcohols.

The isolation procedure for this reaction involves washing the reaction solution with 2 N H_2SO_4, 5% $NaHCO_3$ and brine.

9) What, if anything, is removed by washing with 2 N H_2SO_4? (4 pts.)

The acid wash removes basic components like Et_3N and unreacted L-prolinol from the organic layer.

10) What, if anything, is removed by washing with 5% $NaHCO_3$? (4 pts.)

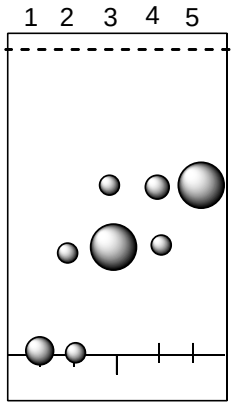
The base wash will remove acid components like carboxylic acids. Although there are no carboxylic acids, the acid chloride may be hydrolyzed to the acid or there may be some residual acid left over from the acid chloride reaction.

11) What, if anything, is removed by washing with brine? (4 pts.)

Brine washes remove water dissolved in the organic layer.

After the isolation procedure, a TLC on a silica gel plate showed the following results.
lane 1: L-prolinol
lane 2: co-spot of L-prolinol and crude rxn. product
lane 3: crude rxn. product
lane 4: co-spot of crude rxn. product and acid (!)
lane 5: acid precursor to acid chloride

mobile phase: EtOAc



12) How many chemical compounds appear to be in the crude reaction product? (5 pts.)

Based on TLC, two.

13) What is the approximate R_f value of the crude reaction product? (5 pts.)

Rougly 0.3-0.35.

14) If you wanted to adjust the R_f down to a lower value, how should you change the TLC? Be as precise as possible. (5 pts.)

Reduce the polarity of the mobile phase by adding a less polar solvent. For example a 7:3 mix of EtOAc/hexanes might work.

After a column purification, the following GC and MS were generated from the main material isolated.

The gas chromatogram has one peak at ~12.00 min.
The mass spectrum has peaks at 249 (~1), 231 (~5), 218 (~15) and 149 (100)

15) What conclusions can be drawn from the GC and MS? (8 pts.)

The product is pure based on the one peak in the GC and the ion at 249 in the mass spectrum matches the mass of the product. The base peak (149), the largest peak in the mass spectrum, can be understood as the result of fragmentation of the C(=O)---N bond and the loss of L-prolinol. The peak at 231 could occur from the loss of H_2O. The peak at 218 could be the loss of CH_2OH or OCH_3, both with a mass of 31. Therefore, this is probably the desired product. It is now time to party.