

Name: \_\_\_\_\_

Date: \_\_\_\_\_

Exam start time: \_\_\_\_\_

Exam end time: \_\_\_\_\_

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

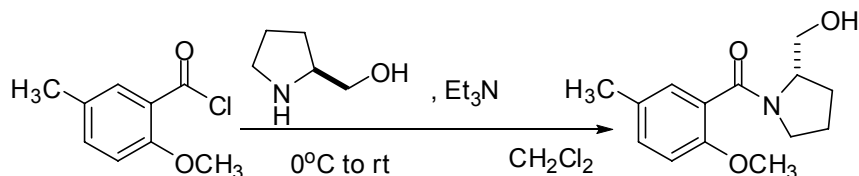
Prof. Malachowski

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 missing boxes 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.)



<i>Specs/Compd</i>	5-Me-o-anisic acid chloride	L-prolinol	triethylamine	dichloromethane	Hydroxy-amide
fw (g/mol)	184.66	101.15	101.19	--	249.30
d (g/mL)	--	--	0.726	--	--
mp (°C)	--	--	-115	-97	--
bp (°C)	--	--	89	40	--
<i>Scale</i>					
mmol				--	
eq	1.0	1.0	2.5	--	1.0
g				--	
ml	--	--			--

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

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.)

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.)

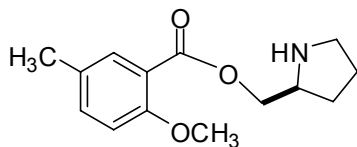
5) Label the nucleophile in your mechanism with an 'Nu'. (5 pts.)

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

7) What role does the Et<sub>3</sub>N play? (5 pts.)

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:*



The isolation procedure for this reaction involves washing the reaction solution with 2 N H<sub>2</sub>SO<sub>4</sub>, 5% NaHCO<sub>3</sub> and brine.

9) What, if anything, is removed by washing with 2 N  $\text{H}_2\text{SO}_4$ ? (4 pts.)

10) What, if anything, is removed by washing with 5%  $\text{NaHCO}_3$ ? (4 pts.)

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

After the isolation procedure, a TLC on a silica gel plate showed the following results.

*lane 1*: L-prolinol

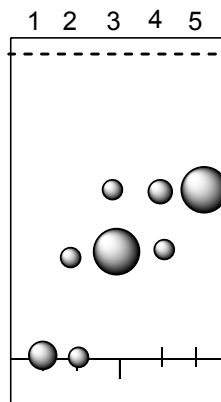
*lane 2*: co-spot of L-prolinol and crude rxn. product

*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.)

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

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.)

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.)