

Name: Chase Utley Date: Oct. 23, 2008

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

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

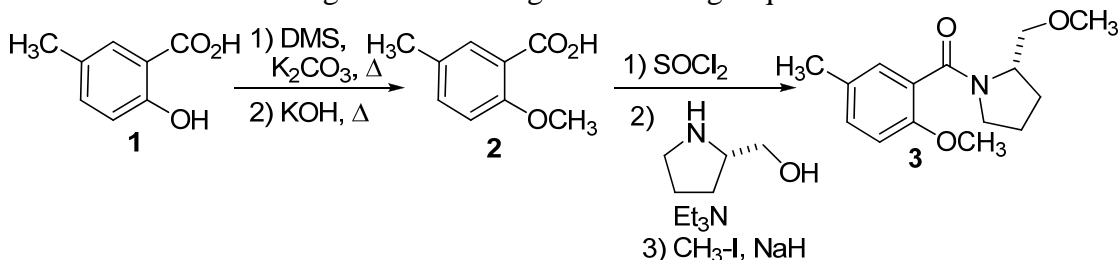
Prof. Malachowski

Due: October 24, 2008, 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 eight questions worth fifty points. The point values for each question are written with the question.

You are a brand new research director at DuNot Chemical Company. You feel considerable pressure to impress your supervisor Dr. Simpson who hired you. Dr. Simpson, Homer to his closest friends, has brought his daughter Lisa into the lab for the summer and has asked you to supervise her research activities.

Lisa's first task is to bring materials along the following sequence:



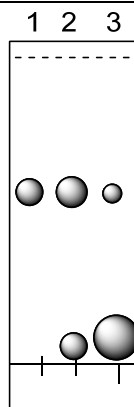
Her first question comes when she is running the saponification or hydrolysis reaction. Lisa shows you the following TLC of the reaction after 1 day at room temperature.

TLC analysis of crude saponification reaction after 1 day

lane 1: methyl 2-methoxy-5-methylbenzoic acid (starting material)  
 lane 2: co-spot of starting material and crude rxn. product  
 lane 3: crude rxn. product

mobile phase: 1:1 EtOAc/Hexanes

○ =UV and  $I_2$  positive



Homer, her Dad, looks at the plate and says it reminds him of cute, cuddly dancing donut holes and so he runs to his office for his mid-morning snack. Lisa turns to you for help and asks if the reaction is done yet.

1) So what do you tell her? Is the reaction done? What should she do next? (7 pts.)

The reaction is definitely not done since there is clearly starting material in the crude reaction lane. She should probably heat the reaction to make the saponification reaction go faster.

Lisa finishes the saponification reaction, but she comes to you with bad results after her extraction. Her theoretical yield is 3.0 g, but she only recovered 0.30 g from her extractions. You ask her to sample the pH of her first aqueous layer that she acidified at the end of the saponification reaction. She does so and returns to tell you it is pH~9.

2) What has gone wrong? Where is the rest of her product? Your explanation should include chemical structures to help Lisa understand the problem. (8 pts.)

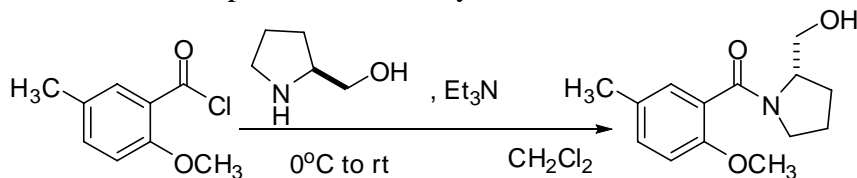
Lisa did not add enough acid to the saponification reaction to protonate the acid product. Consequently the acid product is still in the aqueous layer.



potassium carboxylate salt, an ionic compound that dissolves in aqueous solutions

carboxylic acid, not charged therefore dissolves in organic solvent

Lisa is a hard worker and is highly motivated, clearly a trait that she inherits from her Mom. She has advanced her products to the key amide reaction shown below.



Lisa comes to you with the following TLC analysis of her crude reaction after it stirred overnight.

TLC analysis of crude reaction before extractive work-up procedure

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 (!)

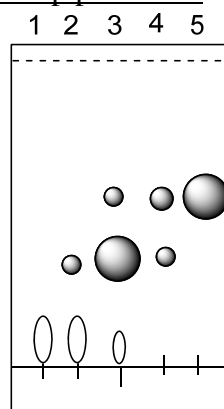
lane 5: acid precursor to acid chloride

mobile phase: 7:3 EtOAc/Hexanes

Note:

○ = I<sub>2</sub> positive, UV negative

● = UV and I<sub>2</sub> positive



You need to interpret Lisa's result:

3) How many chemical compounds appear to be in Lisa's crude reaction product? (4 pts.)

Based on TLC, three.

After an extractive work-up (add  $\text{CH}_2\text{Cl}_2$ ; wash with 2N  $\text{H}_2\text{SO}_4$ , 5%  $\text{NaHCO}_3$  and brine; dry with  $\text{Na}_2\text{SO}_4$ ), Lisa came to you with a second TLC:

TLC analysis of crude reaction after extractive work-up procedure

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 (!)

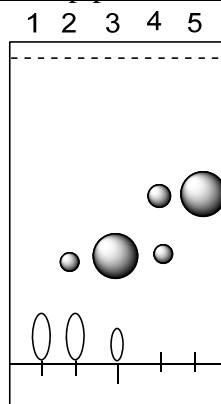
lane 5: acid precursor to acid chloride

mobile phase: 7:3 EtOAc/Hexanes

Note:

○ =  $\text{I}_2$  positive, UV negative

● = UV and  $\text{I}_2$  positive



Lisa says she can't remember if she did all the extractions because while she was performing the work-up, her father came by and insisted on showing her how he uses donuts to hold his round bottom flasks on the lab bench. Homer demonstrated how they could be custom made to fit any flask and any position with minor edible adjustments.

4) You recognize that Lisa did indeed fail to perform one of her extractive steps or washes. Which one did she omit? (7 pts.)

Yes, it looks like Lisa did not perform the 2N  $\text{H}_2\text{SO}_4$  wash to remove the L-prolinol.

5) What is the approximate  $R_f$  value of the impurity in the crude reaction product? (3 pts.)

Roughly 0.10-0.05.

6) Describe one additional analytical experiment that Lisa could perform to confirm this problem in the extractive work-up. Be sure to explain in detail the specific data in the experiment that will confirm the problem. (10 pts.)

If Lisa performed a GC-MS, then she would see a second peak at an earlier time (lower boiling, more volatile) for L-prolinol. This peak should have a molecular ion,  $M^+$ , of 101.

If Lisa performed an NMR, then she would see L-prolinol proton signals added to the L-prolinol peaks in the product. These would arise at 4.30-4.20 (m, 1H), 3.90-3.60(m, 2H), 3.30-3.10 (m, 2H), 2.20-1.50 (m, 4H) and would increase the integration signal at these positions relative to the proton signals for the product.

Lisa has finally gotten to the end of the synthesis. She runs a column with 1:1 EtOAc/hexanes, pools her fractions containing product and performs an NMR analysis. She comes to you with an NMR that has a singlet peak that she can't understand at 5.30; furthermore the product has a weight of 1.45 g which is 105% of the theoretical yield. She said that she also ran a GC-MS and the product looks pure. A TLC does not show any impurity either.

7) Explain to Lisa what impurity is responsible for the singlet peak at 5.30 in the NMR. Be sure to explain why it can't be seen in the GC-MS and on TLC. Suggest to her a way that she can remove this impurity. (8 pts.)

The peak at 5.30 is the solvent  $\text{CH}_2\text{Cl}_2$ . It would not show up in the GC-MS or TLC because it is a relatively volatile solvent that would be removed during the solvent delay on the GC and would evaporate from the TLC plate before detection. It can be removed by further concentration on the rotary evaporator or on the high vacuum pump.

Lisa is concerned about her father eating in the lab. In fact Homer now believes that the metal lab rack bars in his hood are actually meant to be donut holders. And just the other day, Lisa went to borrow glassware from his bench and she found he was using beakers to store donut holes.

8) Explain to Homer why this could present a problem. (3 pts.)

Food in the lab is always a problem because eating in the lab can allow dangerous chemicals to be introduced into your body through your mouth.

*Bonus question:* Do you have any other advice for Lisa in dealing with her father?