Winter 2024 **Chemistry 4000 Final Exam** ____/66 marks

Confidentiality Agreement:
I agree not to discuss (or in any other way divulge) the contents of this exam with (or in the presence of) any CHEM 4000 student who has yet to write it. I understand that breaking this agreement would constitute academic misconduct. The minimum penalty would be a mark of 0/66 on this exam.

Signature: _____ Date: _____

1) Please read the test carefully before starting. It has 11 pages of questions.
2) You have been given a data sheet with a periodic table. This page does not have a QR code, so nothing written on this sheet of paper will be graded. If you wish to do rough work that you might want a grader to be able to see, use the back of any page of the test.
3) You are allowed to bring one index card (maximum size 3"x5") into the exam with you as a "cheat sheet". This card must be submitted with your exam.
4) You **may** use a molecular model kit. You may not have written materials in your model kit.
5) You may **not** use a calculator or any other electronic device.
6) **DO NOT WRITE ON ANY QR CODE!!!** Work on pages without a QR code will not be graded.
7) If your work is not legible, it will be given a mark of zero. For full credit, explanations must be complete. In many cases, complete explanations include drawing relevant structures. If delocalization of electrons is invoked, the relevant resonance structures must be drawn.
8) Marks will be deducted for incorrect information added to an otherwise correct answer.
9) You have 3 hours to complete this test.

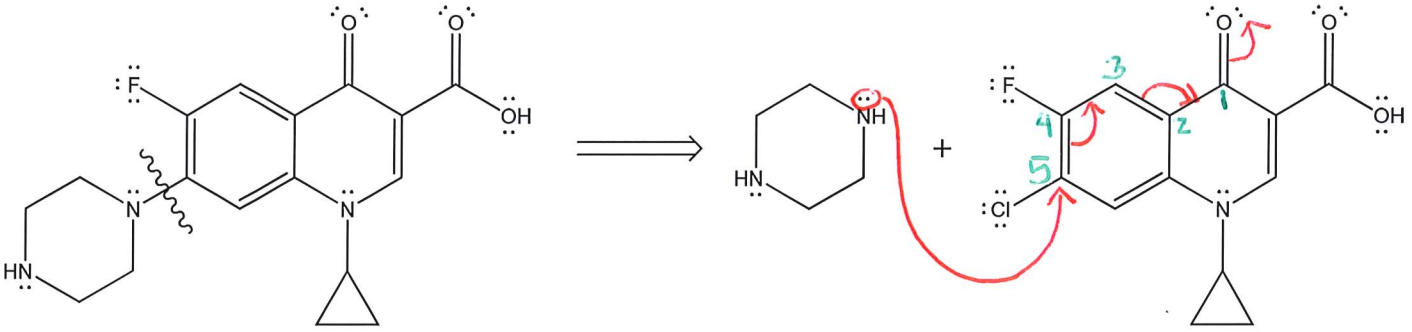
Question Breakdown

Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10						Total
/ 3	/ 3	/ 4	/ 4	/ 10	/ 9	/ 7	/ 5	/ 20	/ 1						/ 66

1. One of the molecules for which we worked through the synthesis was Ciprofloxacin. The corresponding retrosynthesis would begin with the following disconnection: **[3 marks]**

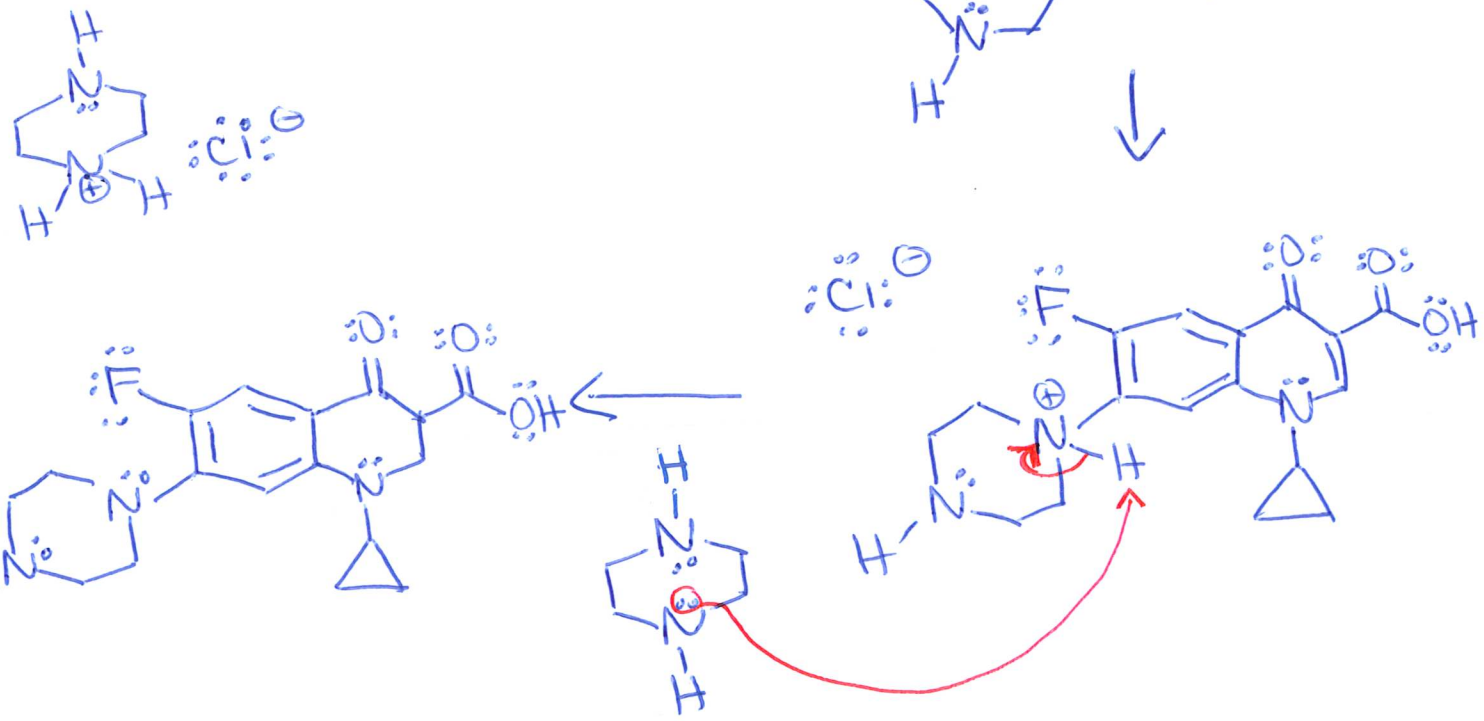
   Classify the synthon on the right (as a^1, d^1, etc.), and justify your answer by using curved arrows to show electron movement in the first step of the mechanism for the forward reaction corresponding to this disconnection.

   You may draw directly on the diagram.



a^5

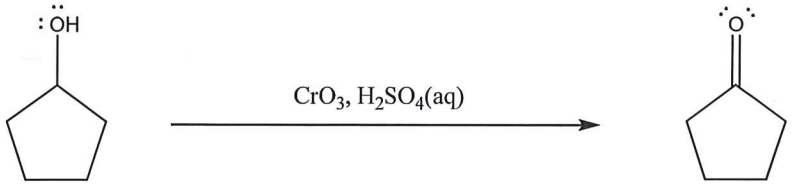
(acceptor synthon
5 atoms from heteroatom
accepting electron density)



2. Development of greener oxidation reactions is a topic of particular interest since many classical oxidation reactions are decidedly less-than-green.

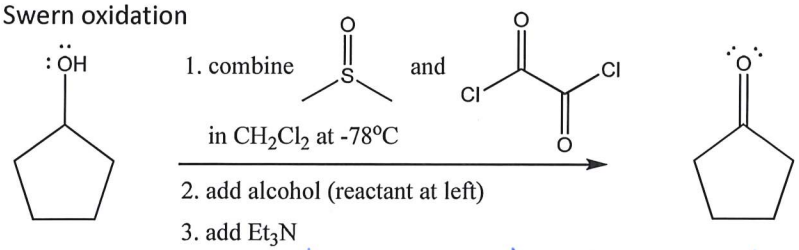
For each of the following oxidation reactions, identify one way in which it violates the principles of green chemistry. For each oxidation reaction, you are expected to identify a violation of a **different** principle of green chemistry (so that your overall answer to the question demonstrates that you know at least three of the principles of green chemistry). Sample answers provided **[3 marks]**

(a) Jones oxidation



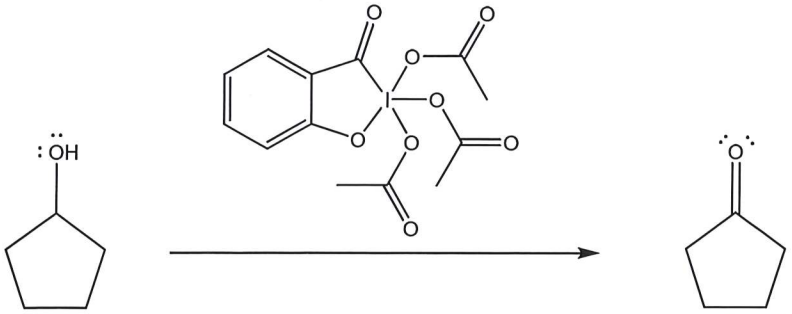
- CrO_3 is highly toxic
- H_2SO_4 is corrosive

(b) Swern oxidation



- very low temperature requires high energy input

(c) Oxidation with Dess-Martin periodinane



- atom economy is awful!
(this is a very large reagent to remove two H)

3. Identify two sizes of carbocycle* for which a two-bond disconnection strategy is effective. For each ring size, write an equation showing a forward reaction corresponding to a two-bond disconnection. **[4 marks]**

*A carbocycle is a ring containing only carbon atoms. It is fine if heteroatoms are attached to the ring.

(a) Sample answers

3-atom ring



4-atom ring

(b)

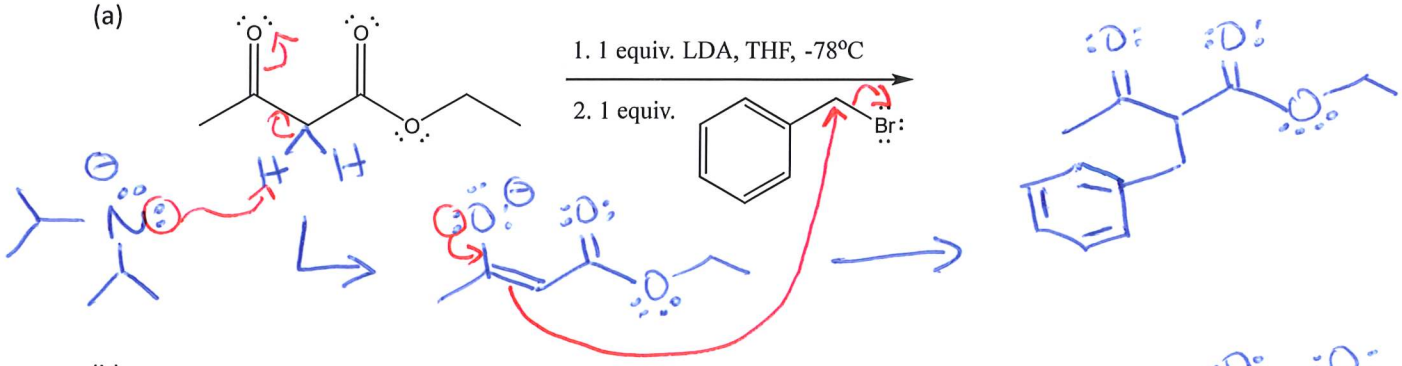


6-atom ring

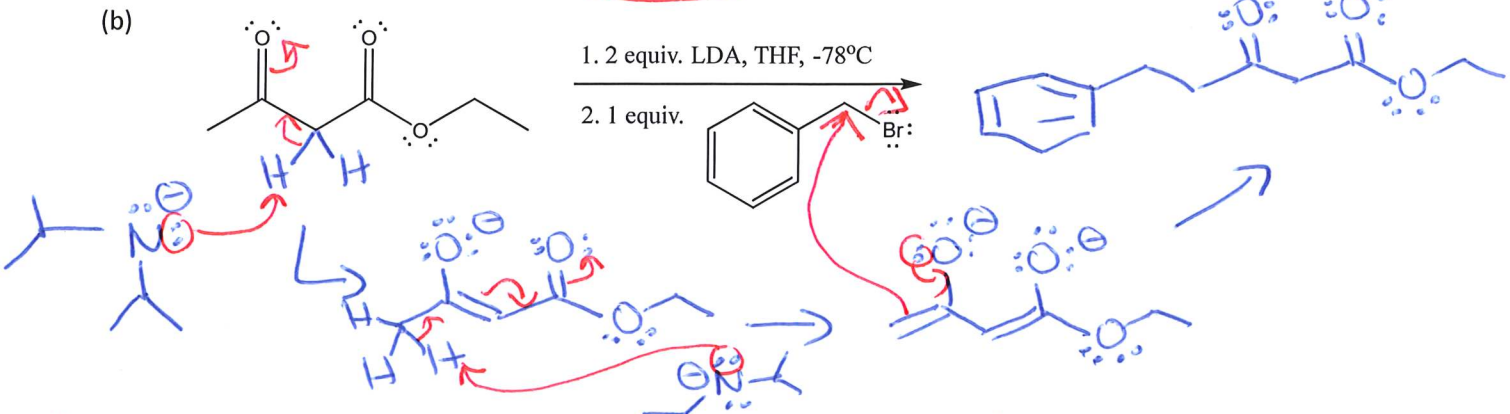


4. Draw the organic product for each of the following reactions (after aqueous work-up). **[4 marks]**

(a)



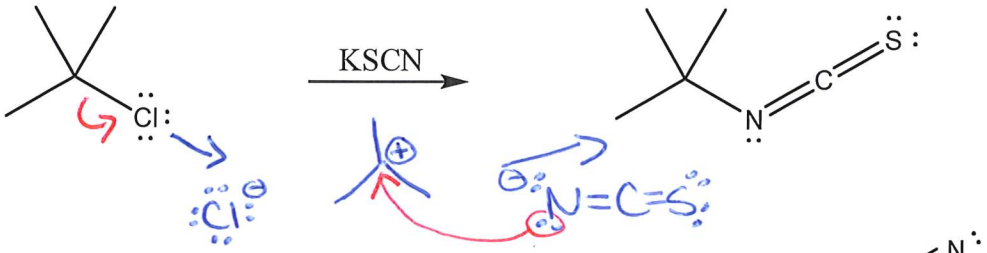
(b)



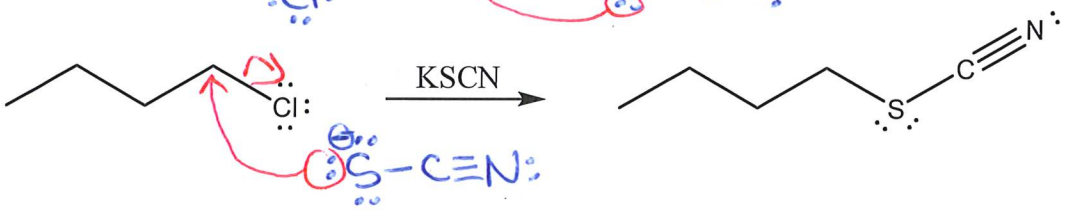
mechanisms were not required for full marks

5. Kornblum's rule was proposed before the development of Hard Soft Acid Base theory. It states that if an anion has two nucleophilic sites, the more electronegative atom will tend to attack in reactions that proceed via S_N1 mechanisms while the less electronegative atom will tend to attack in reactions that proceed via S_N2 mechanisms. This behaviour is demonstrated by the pair of reactions below:

3° ∴ S_N1



1° ∴ S_N2



Use Hard Soft Acid Base theory to explain why Kornblum's rule works for this pair of reactions. **[10 marks]**

For full marks, your answer must include the mechanism for each reaction.

As seen in the two resonance structures above, $SCN^{\ominus}$ has two nucleophilic sites:

$$:\ddot{S}-C\equiv N: \longleftrightarrow :S=C=\ddot{N}:^{\ominus}$$

The less electronegative atom (S) is also larger. It therefore has lower charge density and is the softer nucleophilic site.

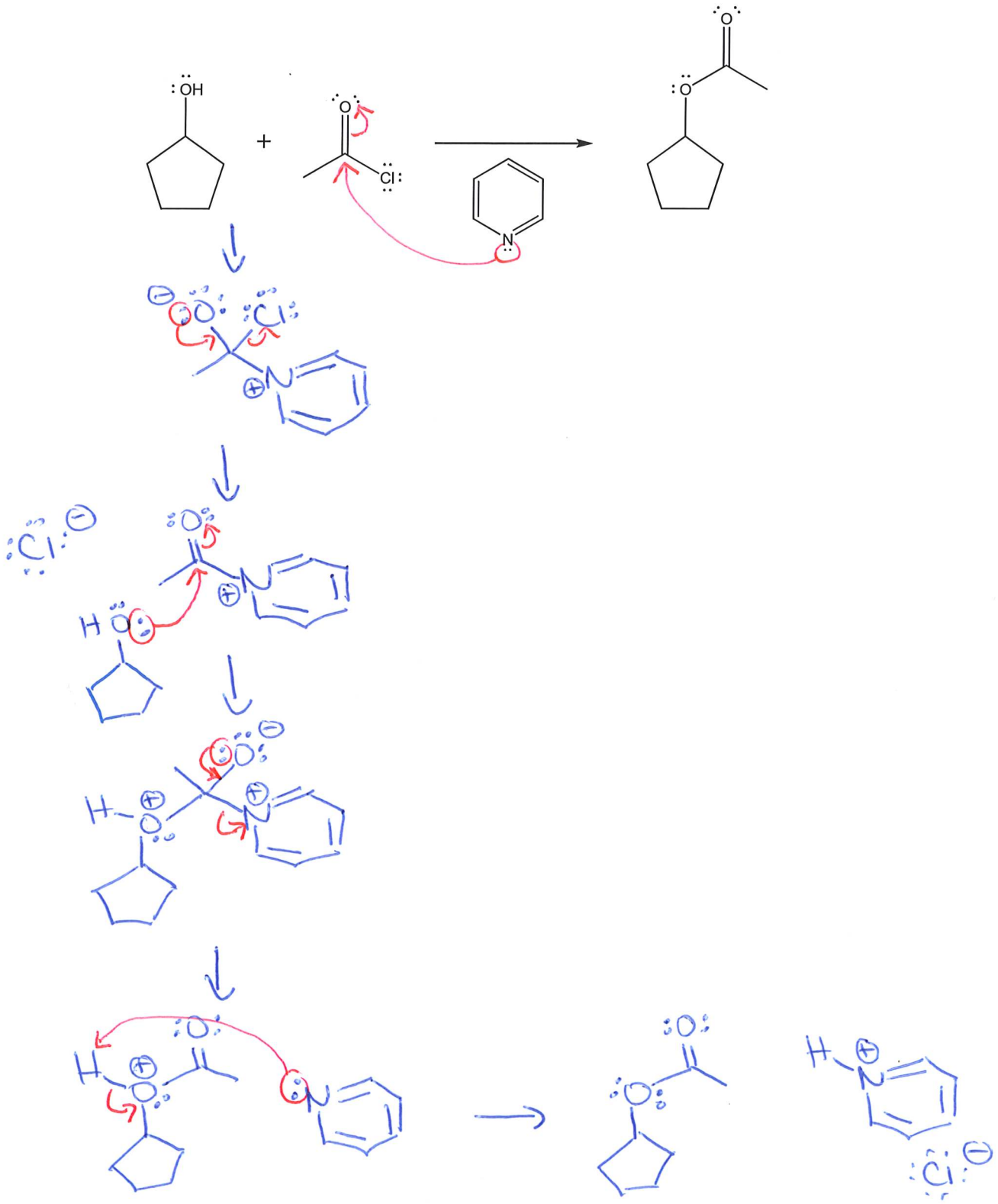
The more electronegative atom (N) is also smaller. It therefore has higher charge density and is the harder nucleophilic site.

The S_N1 mechanism involves a much harder electrophilic site (carbocation in the intermediate) than the S_N2 mechanism (whose electrophilic site is a slightly positive C still bonded to the halogen leaving group).

Since harder nucleophilic sites tend to attack harder electrophilic sites, $N^{\ominus}$ attacks $C^{\oplus}$ in the S_N1 reaction.

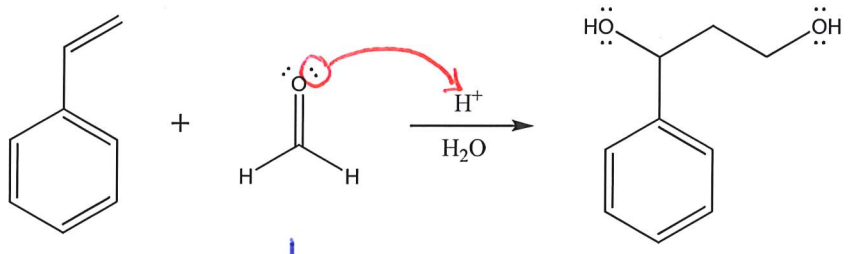
Since softer nucleophilic sites tend to attack softer electrophilic sites, $S^{\ominus}$ attacks C in the S_N2 reaction.

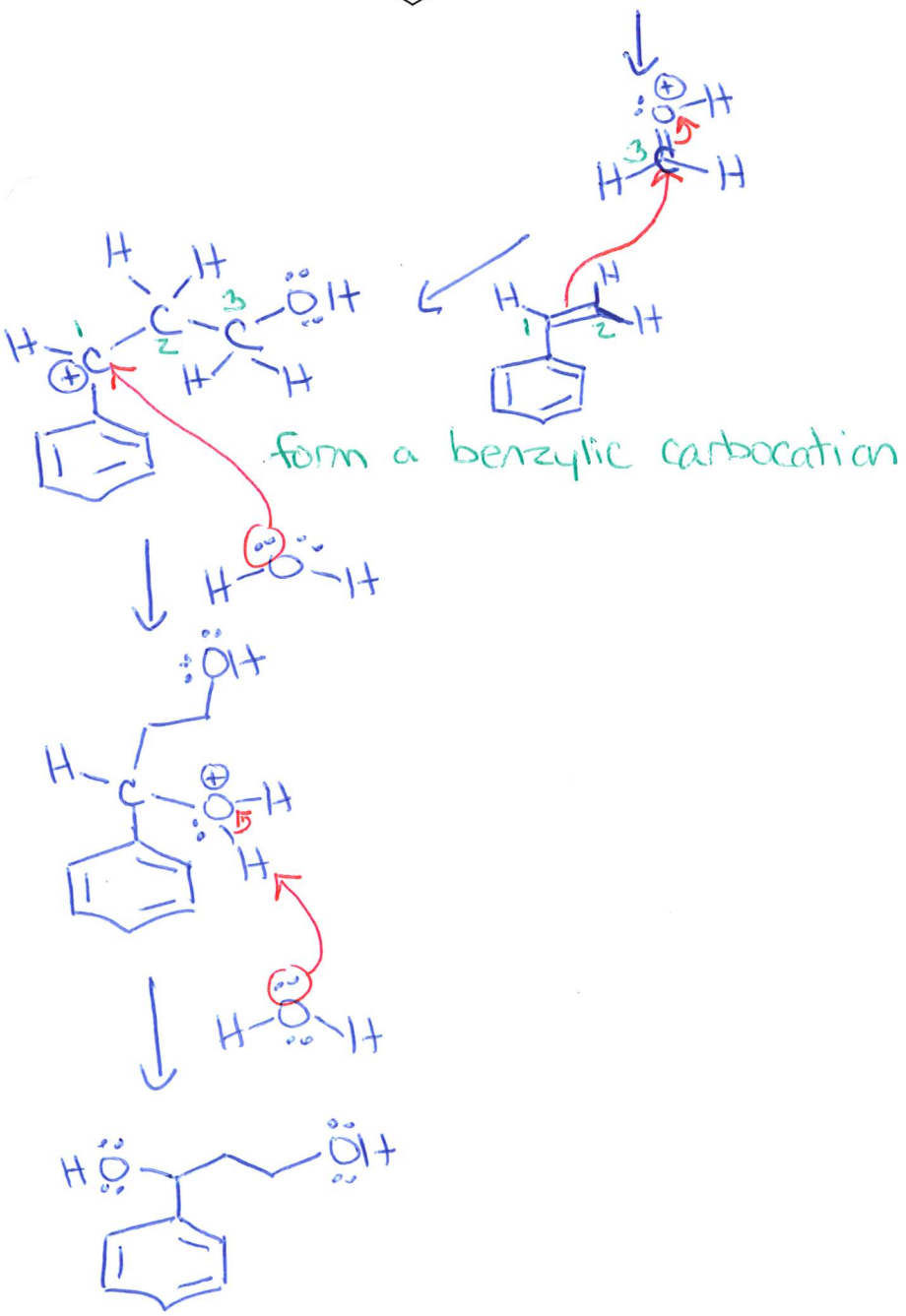
6. Nucleophilic catalysis is a strategy commonly employed when reaction of a weaker nucleophile with an acid chloride (or similar electrophile) is desired. Typically, an amine such as pyridine or triethylamine is added to the reaction and serves as both catalyst and base. Demonstrate both roles of the amine by showing the complete mechanism for the following reaction. **[9 marks]**



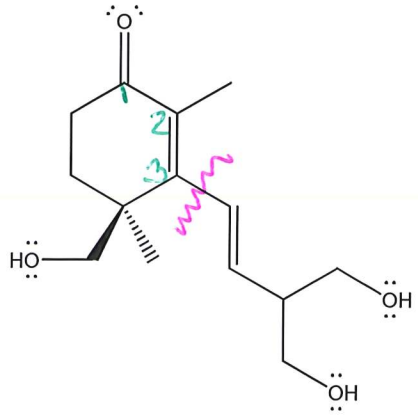
7. The reaction shown below is called a Prins reaction. Propose a reasonable mechanism for this reaction.

[7 marks]





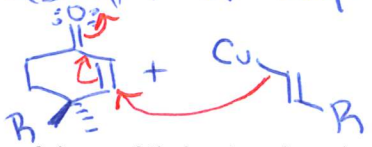
8. The molecule below is called cassiol: **[5 marks]**



(a) If you were going to develop a retrosynthesis for cassiol, what would be the first disconnection you would propose? Provide at least two reasons for your choice. *[3 marks]*

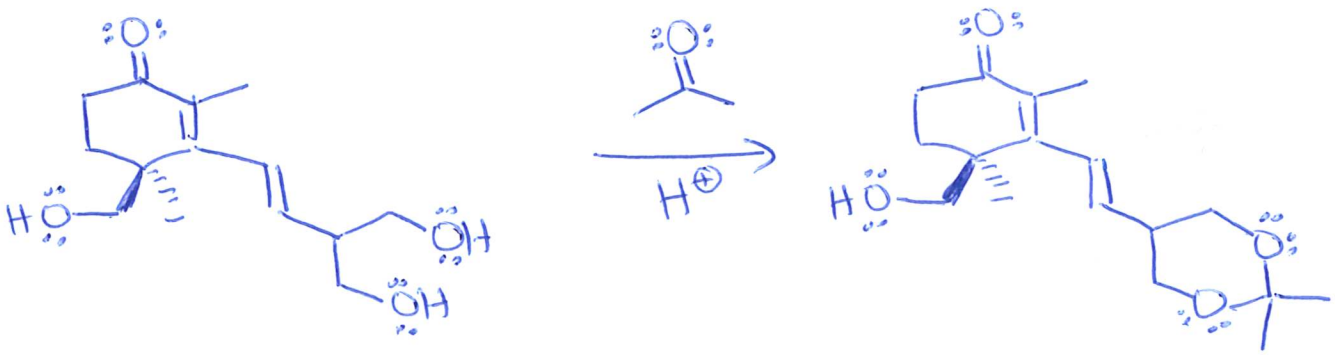
You do <u>NOT</u> need to propose a whole synthesis of cassiol!!!

Sample disconnection drawn on structure above
- disconnection is next to a ring ∴ simplifies skeleton
- the two synthons are similar in size and complexity
- the ring can act as an a^3 synthon (which is natural) ∴



or similar.

(b) Cassiol has three OH groups. If you wanted to protect two of them while leaving the other free to react, how could you do that? Identify any necessary reactants and/or reaction conditions. You do **<u>NOT</u>** need to show the mechanism of reaction (but it should be clear which two OH groups are being protected and how). *[2 marks]*



9. Choose **two** of the molecules below and propose a synthetic route to make each. **[20 marks]**

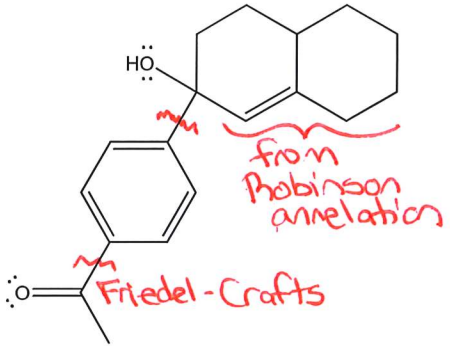
Your answers should take the form of a retrosynthetic analysis followed by chemical equations for the reactions in the synthesis itself. Show all required reagents, and number steps within a reaction if order of addition is important.

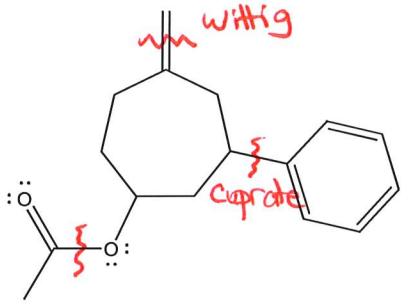
You may use any reagents that you could reasonably expect to be commercially available and that contribute no more than 7 carbon atoms to the final product.

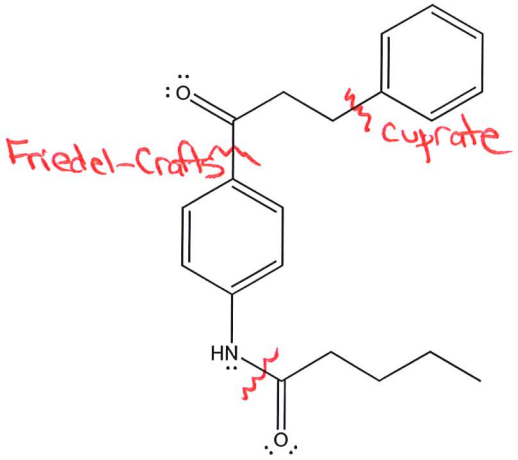
If you are suggesting a multi-step synthesis, write an equation for each step.

There are two pages after this. Use one of those pages for each synthesis and clearly identify the synthetic target at the top of the page. This page is scrap paper.

Options



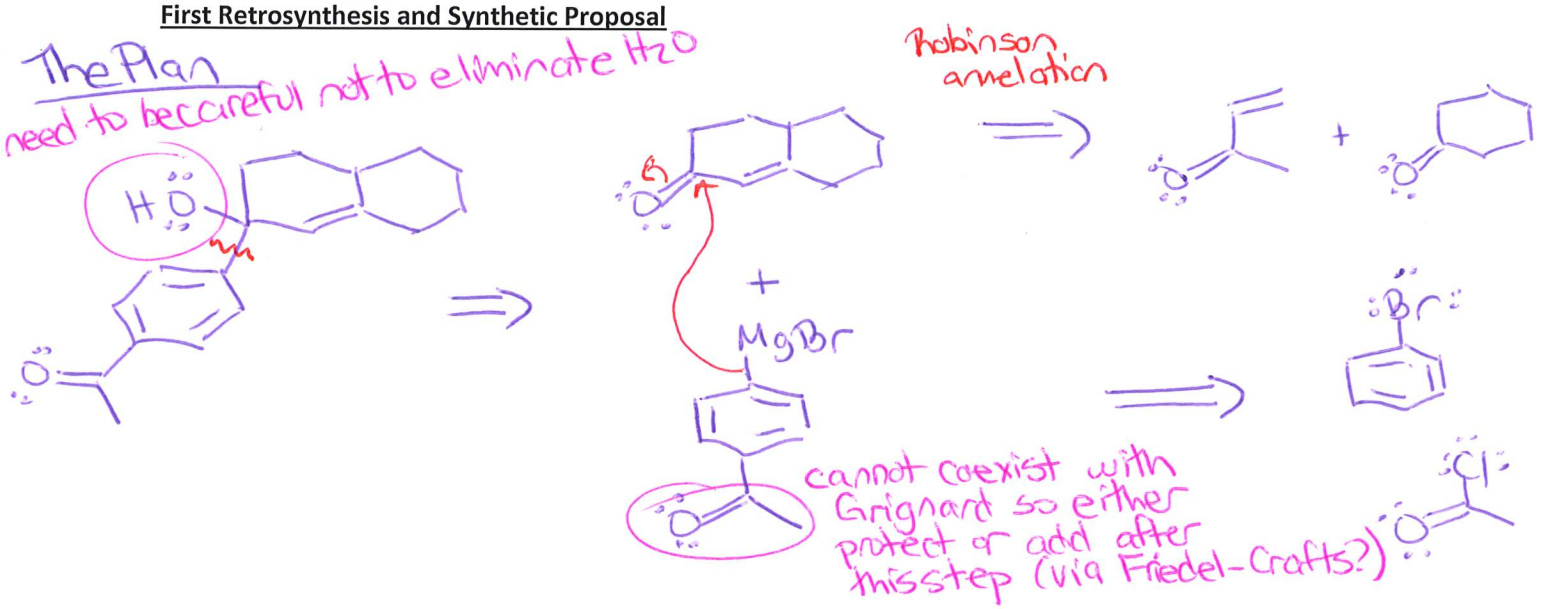


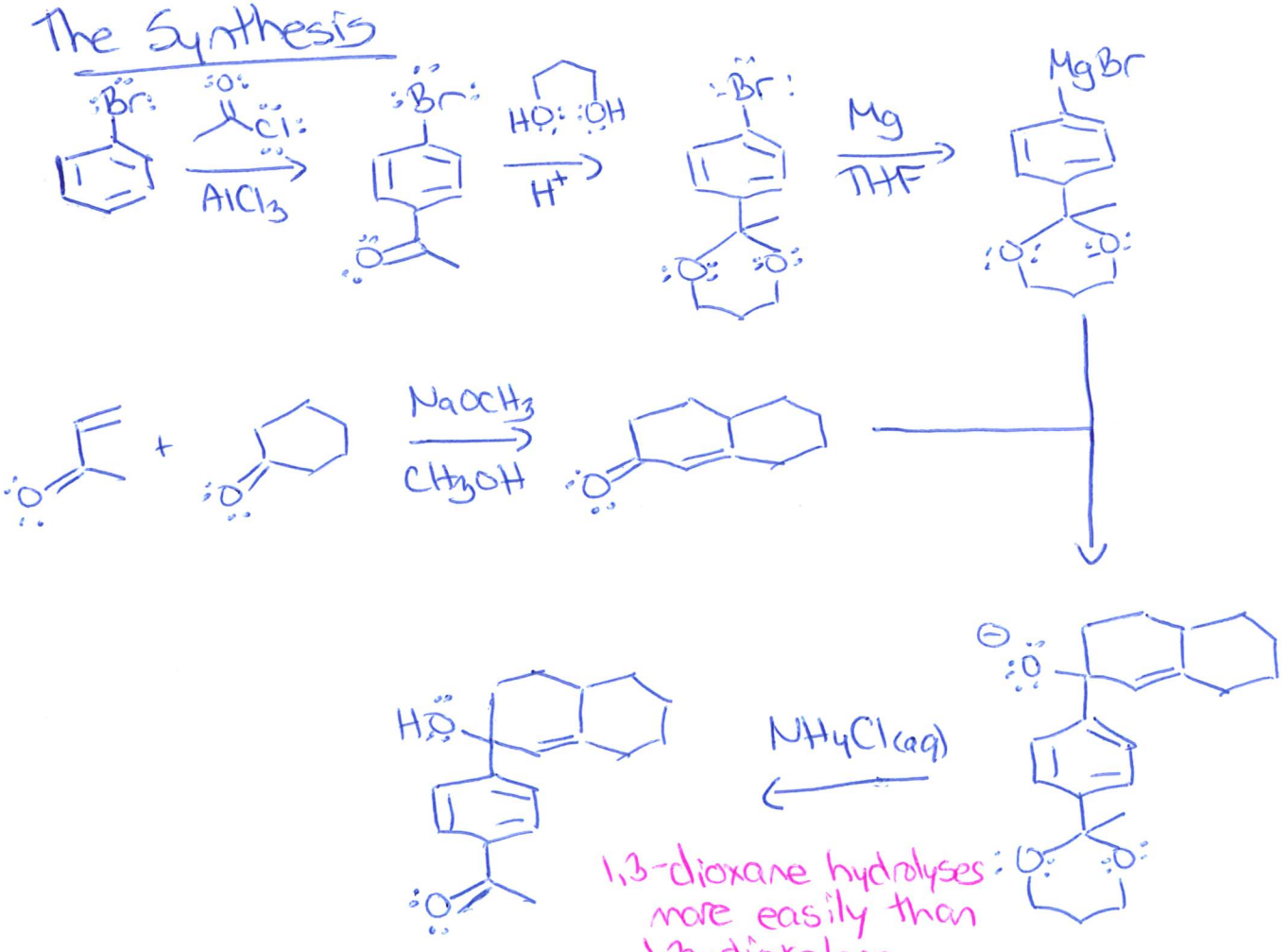


Many valid answers are possible. One is shown for each molecule.

9. *continued...* *[10 marks]*

First Retrosynthesis and Synthetic Proposal

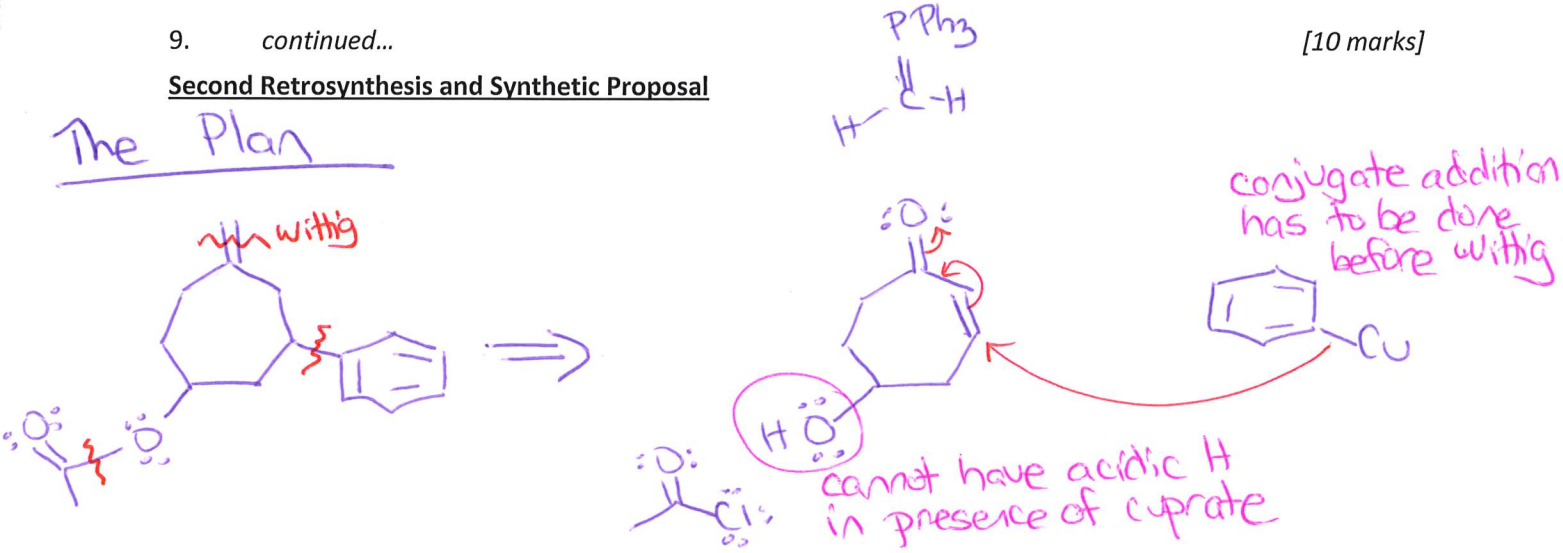




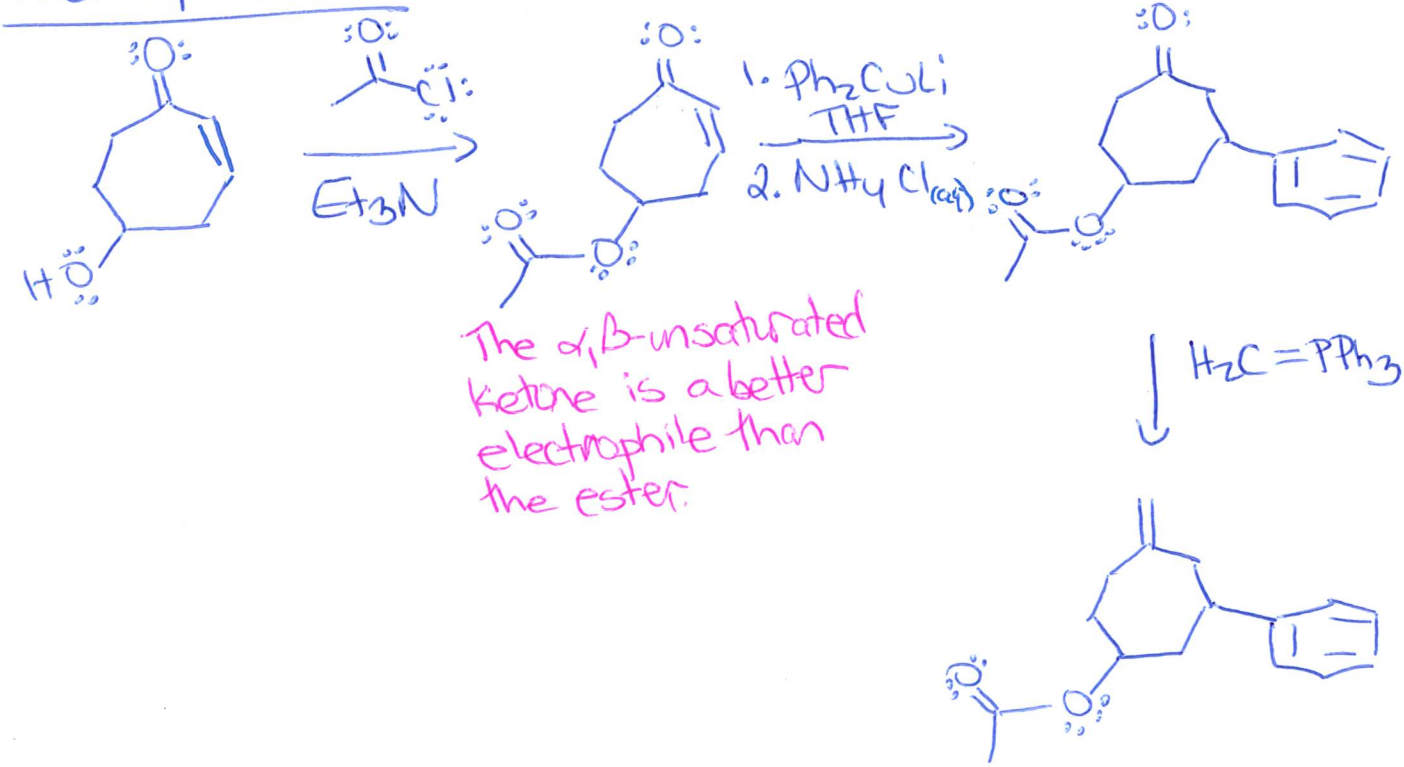
9. *continued...* *[10 marks]*

Second Retrosynthesis and Synthetic Proposal

The Plan



The Synthesis

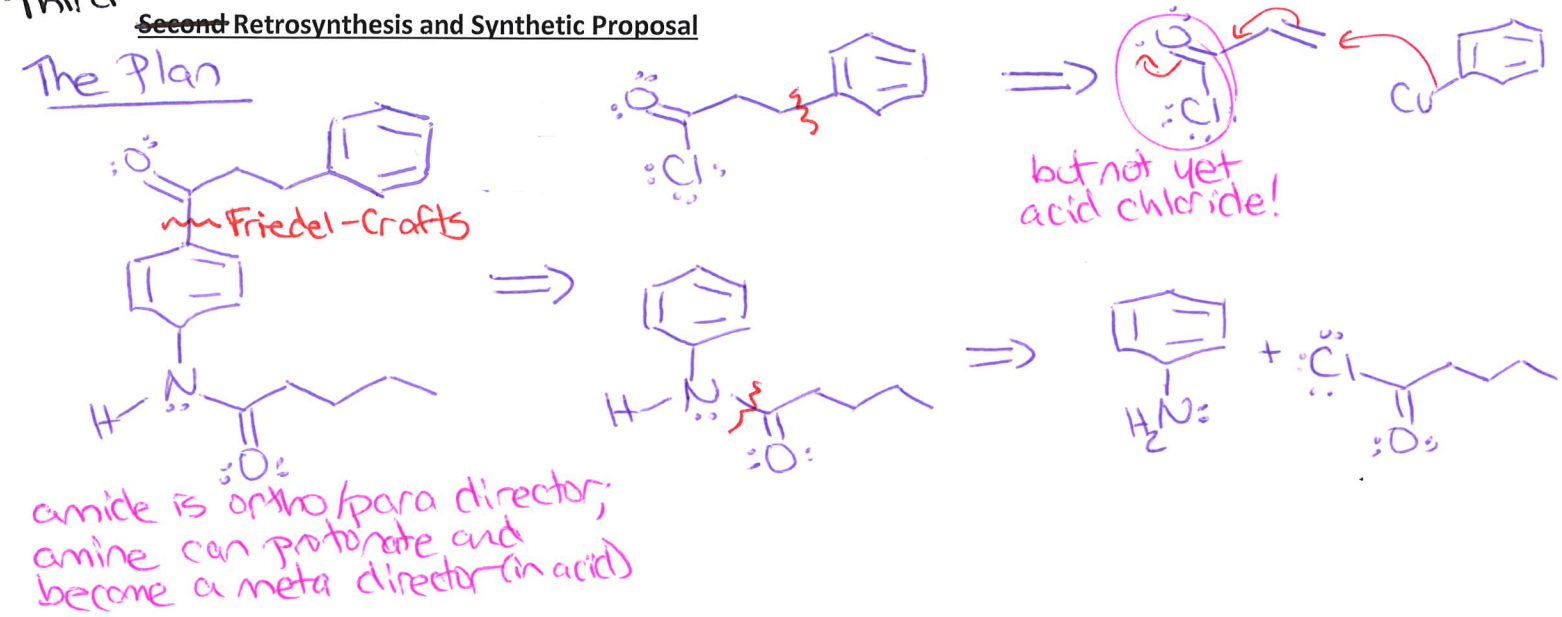


Third

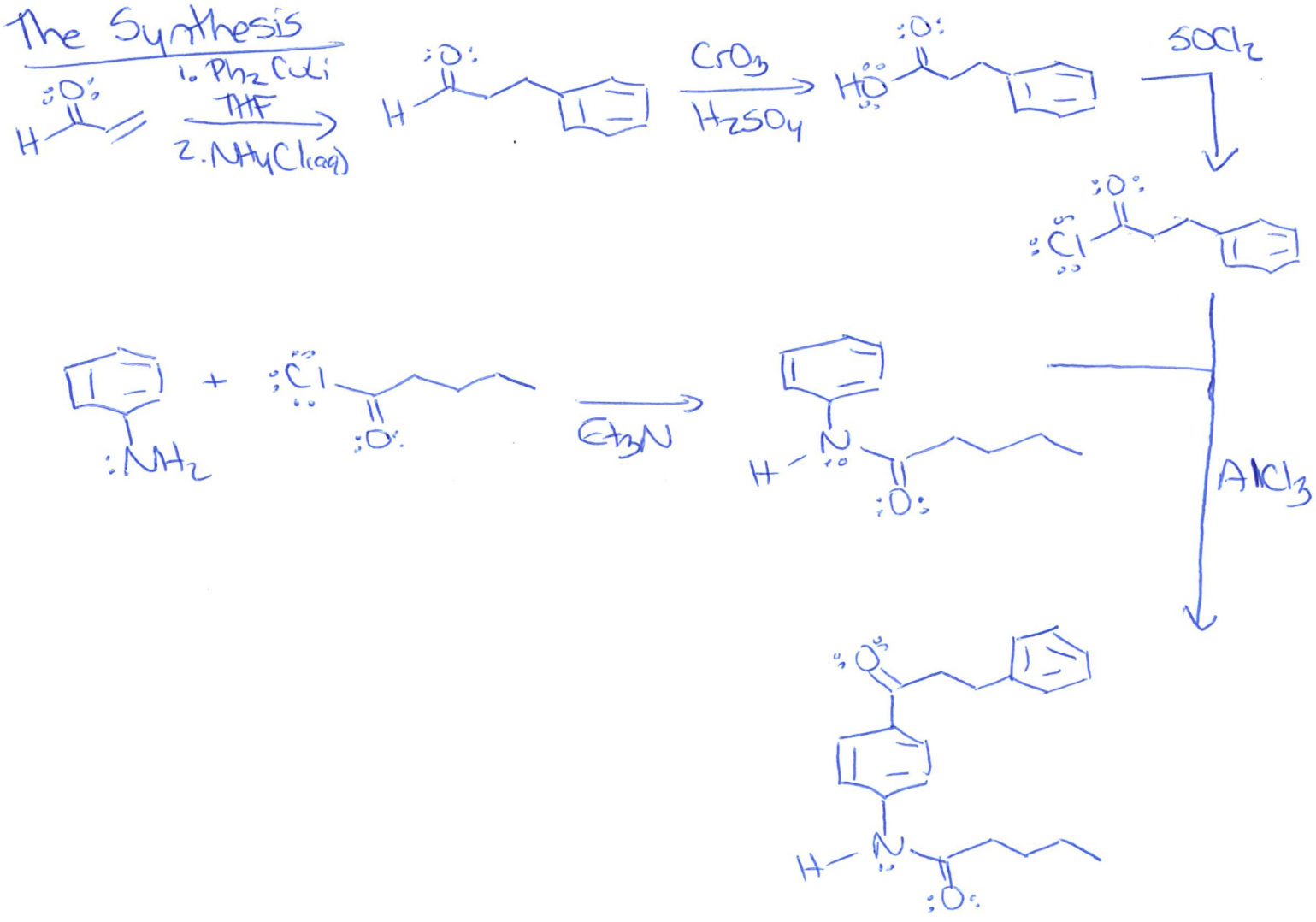
9. *continued...* *[10 marks]*

~~Second~~ **Retrosynthesis and Synthetic Proposal**

The Plan



The Synthesis



10. What was the most useful and/or interesting thing you learned in CHEM 4000? **[1 mark]**

...AND THAT'S ALL FOR CHEM 4000.

HAVE A GREAT SUMMER!