

NAME: \_\_\_\_\_ Section: A Student Number: \_\_\_\_\_

Spring 2015

**Chemistry 4000 Final**

\_\_\_\_\_/ 70 marks

- INSTRUCTIONS:
- 1) Please read over the test carefully before beginning. You should have 10 pages of questions and a periodic table.
  - 2) Unless otherwise stated in the question, explain all of your answers fully. Use diagrams where appropriate. When invoking any argument based on resonance, you must draw all relevant resonance structures.
  - 3) ALL structures must be drawn showing lone pairs, non-zero formal charges and reasonable bond angles – regardless of whether they are expanded, condensed or line-bond. Marks will be deducted for poorly drawn structures.
  - 4) Marks will be deducted for incorrect information added to an otherwise correct answer.
  - 5) If your work is not legible, it will be given a mark of zero.
  - 6) Calculators are not allowed. You are not permitted to have any electronic devices with you during the exam unless authorized by the instructor.
  - 7) You may use a molecular model kit.
  - 8) You have 3 hours to complete this test.

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**Confidentiality Agreement:**

I agree not to discuss (or in any other way divulge) the contents of this exam until after 1:00 pm Mountain Time on Wednesday, April 29<sup>th</sup>, 2015. I understand that breaking this agreement would constitute academic misconduct, a serious offense with serious consequences. The minimum punishment would be a mark of 0/70 on this exam; the maximum punishment would include expulsion from this university.

Signature: \_\_\_\_\_

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

Course: CHEM 4000A (Medicinal Chemistry)

Semester: Spring 2015

The University of Lethbridge

**Question Breakdown**

<b>Q1</b>	/ 4
<b>Q2</b>	/ 3
<b>Q3</b>	/ 4
<b>Q4</b>	/ 3
<b>Q5</b>	/ 10
<b>Q6</b>	/ 4
<b>Q7</b>	/ 2
<b>Q8</b>	/ 5
<b>Q9</b>	/ 5
<b>Q10</b>	/ 4
<b>Q11</b>	/ 6
<b>Q12</b>	/ 20

<b>Total</b>	/ 70
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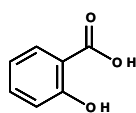
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1. Explain why an  $a^3$  synthon is a natural synthon. Your explanation should include an example. [4 marks]

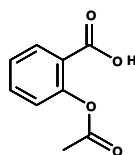
2. Choose one of the following two questions to answer. Clearly indicate which option you chose. If you answer both, only the first answer will be marked. [3 marks]

**Option A**

Aspirin is made from salicylic acid, which can be extracted from willow bark.



salicylic acid



aspirin

When I mentioned we were looking at ‘green chemistry’, my husband suggested that maybe someone could suggest a method for making aspirin that didn’t require cutting down so many willow trees. Evaluate his suggestion using the principles of green chemistry.

**Option B**

I recently read an article about development of “ball milling” techniques in chemistry. Essentially, the reactants would be put into a reaction vessel with small steel balls and the whole thing would be rotated. The motion of the balls (and associated friction) would create ‘hot spots’ of localized high temperature and pressure where reactions would occur. Evaluate this technique using the principles of green chemistry.

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3. Certain elements have another element with which they form particularly strong bonds. These pairs of elements are said to have a strong affinity for each other. We saw several such pairs of elements over the course of the semester. **[4 marks]**

(a) Identify one pair of elements that have this type of strong affinity for each other. *[1 mark]*

(b) Explain how this affinity is useful in synthesis. Include a sample reaction equation in your answer (but also explain why the reaction is useful in the “big picture”). *[3 marks]*

4. List three major factors you must consider when choosing a protecting group. Explain why each factor is important. **[3 marks]**

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5. Give an example of each of the following reactions. Your example should take the form of a chemical equation including structures of all organic reactants and products. Other necessary reagents should be listed over the arrow. **[10 marks]**

(a) Birch reduction

(b) Michael addition (aka conjugate addition)

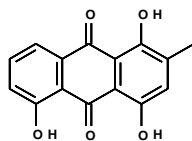
(c) Wittig reaction

(d) Suzuki coupling

(e) Robinson annelation

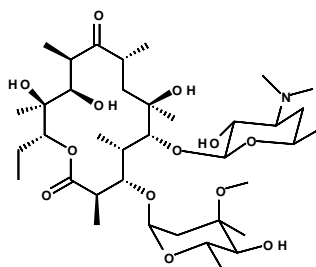
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6. The molecule shown below is islandicin.



When beginning a retrosynthetic analysis of this molecule, which would be the best bond(s) at which to propose disconnection(s)? Why? Give three reasons for your choice(s). **[4 marks]**

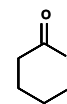
7. The molecule shown below is erythromycin A. What would you consider to be the two greatest synthetic challenges in developing a synthesis for this molecule? **[2 marks]**



You do **not** have to suggest how to overcome these challenges!!!

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8. When I was working on my PhD, the first step in my synthesis involved making a double Grignard reagent by reacting 1,4-dibromobutane with excess magnesium then adding  $\delta$ -valerolactone (*shown at right*). Finally, the reaction was worked up by adding water.



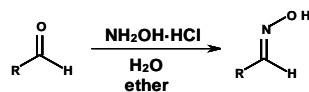
$\delta$ -valerolactone

Propose a mechanism for this reaction and identify the final organic product.

**[5 marks]**

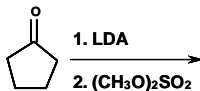
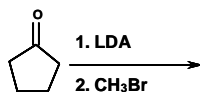
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9. Later on in this synthesis, I reacted an aldehyde with hydroxylamine hydrochloride to make the oxime (*see reaction equation below*). Propose a mechanism for that reaction. **[5 marks]**



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10. Explain why different products are obtained for the two reactions shown below.



As part of your answer, you must also identify the organic product of each reaction. **[4 marks]**

11. Some sizes of rings are easier to make than others. **[6 marks]**
- (a) Comment on the relative difficulty in making 3-membered rings vs. 4-membered rings. Which is easier to make and why? **[2 marks]**
- (b) Give an example of a reaction making a 3-membered ring by forming two bonds at once. *Naming the reaction is not a sufficient answer! Show how it is done.* **[2 marks]**
- (c) Give an example of a reaction making a 4-membered ring by forming two bonds at once. *Naming the reaction is not a sufficient answer! Show how it is done.* **[2 marks]**



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

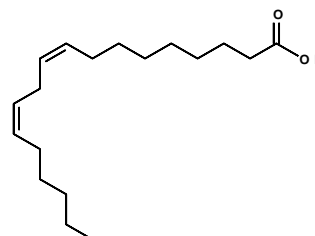
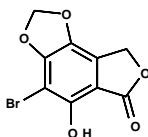
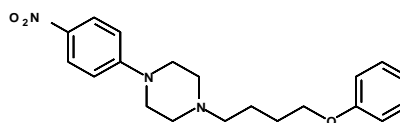
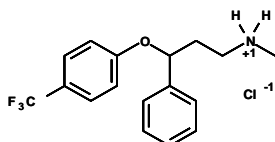
Your answers should take the form of a retrosynthetic analysis followed by chemical equations for the reactions in the synthesis itself. Show all required reagents, and number steps within a reaction if order of addition is important.

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**



If you choose this synthetic target, you may **NOT** use starting materials containing *cis* double bonds.

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12. *continued...*

*[10 marks]*

**First Retrosynthesis and Synthetic Proposal**

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12. *continued...*

[10 marks]

**Second Retrosynthesis and Synthetic Proposal**

