Fall 2025 **Chemistry 4000 Midterm** ____/60 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 0/60 on this exam.

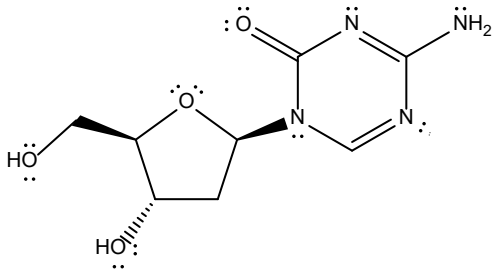
Signature: _____ Date: _____

1) Please read the test carefully before starting. It has six pages of questions.
2) You have also been given a page with a periodic table. It does not have a QR code, so nothing written on it will be graded. If you need scrap paper, use the back of any page of the test.
3) **DO NOT WRITE ON ANY QR CODE!!!** Work on pages without a QR code will not be graded.
4) You may use a molecular model kit. You may not have written materials in your model kit.
5) No electronic devices are allowed. This test does not require a calculator.
6) ALL structures must be drawn showing lone pairs, non-zero formal charges and reasonable bond angles – regardless of whether you are using line-bond notation. Marks will be deducted for poorly drawn structures.
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 2 hours to complete this test.

Question Breakdown

Q1	**Q2**	**Q3**	**Q4**	**Q5**	**Q6**									**Total**
/ 4	/ 7	/ 13	/ 16	/ 10	/ 10									/ 60

1. The compound below is decitabine (trade name Dacogen®), a drug used to treat myelodysplastic syndrome (MDS), a type of cancer. **[4 marks]**

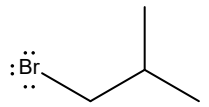


(a) Identify one feature in the structure of decitabine that would make it particularly challenging to synthesize. *[1 mark]*

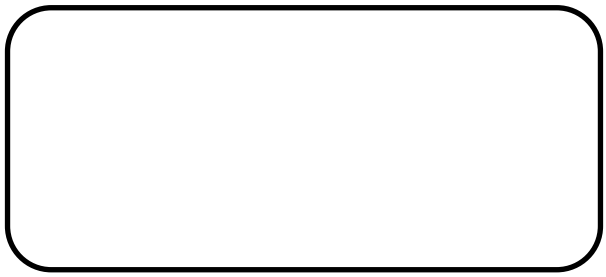
(b) If you had to develop a new synthesis for decitabine, what would be the first disconnection you would propose? Give two reasons for your choice. *[3 marks]*

2. A group of scientists were interested in comparing capsaicin (the main chemical responsible for the heat of chili peppers) to its geometric isomer. As part of their syntheses, they performed each of the two reaction sequences below. Fill in the blanks in each synthetic route. **[7 marks]**

(a)

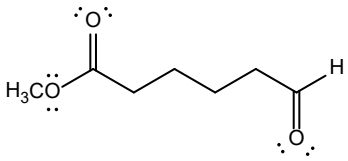


PPh_3



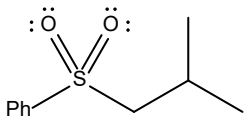
KOtBu



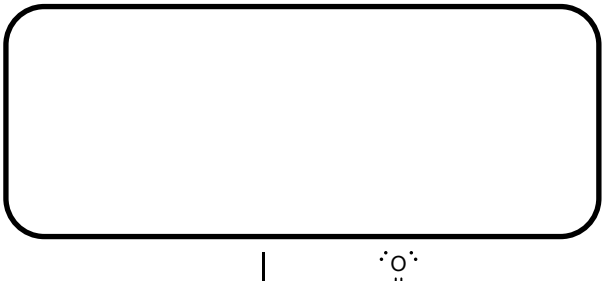


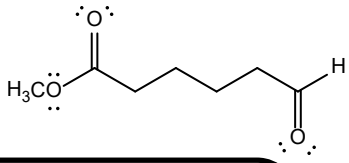


(b)

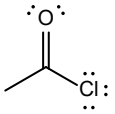


BuLi







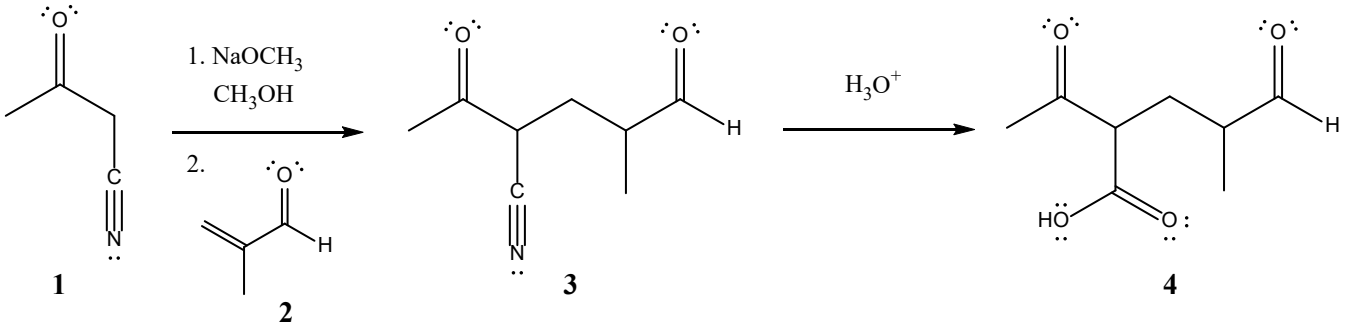




Na/Hg



3. Consider the reaction sequence below. **[13 marks]**



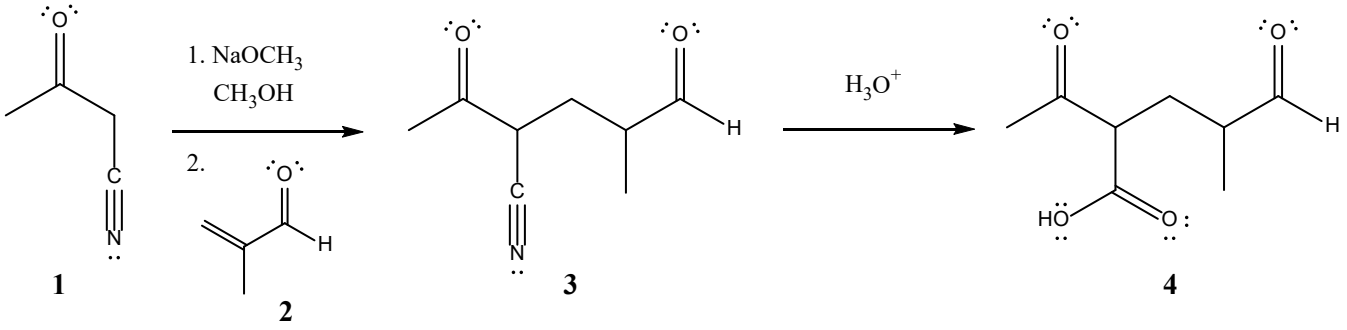
(a) In the first step, compound **3** is produced by treating compound **1** with sodium methoxide in methanol then adding compound **2**. Propose a reasonable mechanism for this reaction. *[5 marks]*

(b) In your answer to part (a), the nucleophile should have more than one nucleophilic site, and the electrophile should have more than one electrophilic site. Clearly identify each of those sites and explain why the reaction proceeds as shown above. In other words, why doesn't the reaction involve one (or more) of the other reactive sites? *[8 marks]*

4. We're not done with this reaction sequence yet! Propose a reasonable mechanism for the reaction of compound **3** with aqueous acid to give compound **4**. **[16 marks]**

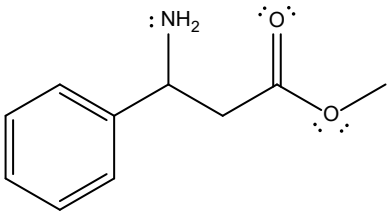
Assume that the solution contains as much H_3O^+ and water as you need.

You may abbreviate parts of the molecule not involved in the reaction as R. Please be careful not to draw multiple steps on the same molecule; if a process takes two steps, show the intermediate between them.



1 **2** **3** **4**

5. Consider the compound below. **[10 marks]**



There are four possible pairs of synthons corresponding to disconnections at carbon-carbon bonds between the two heteroatoms.

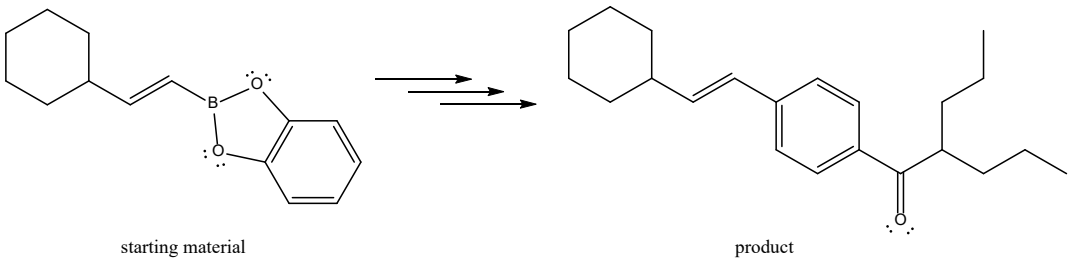
(a) Show the four possible pairs of synthons, labeling each synthon (as a^1, d^1, etc.) and identifying it as natural or umpoled. *[4 marks]*

(b) Choose one of your answers to part (a) and propose either a reaction or a short sequence of reactions that would make the target molecule according to that approach. *You may use any reagents or reactants that you could reasonably expect to be commercially available.* *[6 marks]*

6. How would you make the molecule below? **[10 marks]**

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

*In addition to the starting material shown below, you may use any other starting materials or reactants that you could reasonably expect to be commercially available <u>and</u> that **<u>contribute no more than 6 carbon atoms to the final product</u>**. (This means that you are allowed to use reagents like PPh_3 or mcpba – even though they contain more than 6 carbon atoms – because they do not add more than 6 carbon atoms to the final product. These examples should not be construed as a hint; just a clarification.)*



starting material product