Winter 2024

Chemistry 4000 Midterm #1

____/50 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 0/50 on this exam.

Signature: _____ Date: _____

First name (please write as legibly as possible within the boxes)

Last name

Student ID number

1) Please read the test carefully before starting. It has 6 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.

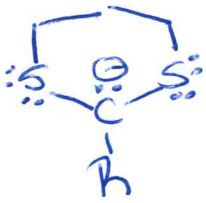
Question Breakdown

Q1	Q2	Q3	Q4	Q5	Q6	Q7								Total
/ 3	/ 3	/ 8	/ 6	/ 8	/ 12	/ 10								/ 50

1. **[3 marks]**

(a) Give an example of a reagent that would correspond to a d^1 synthon. *[1 mark]*





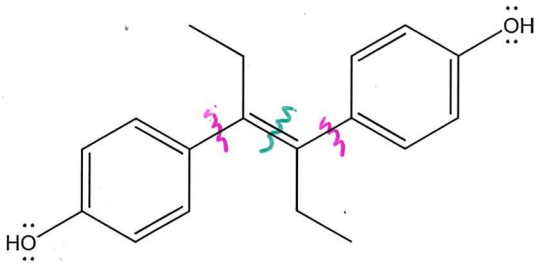
(b) Give an example of a reagent that would correspond to an a^2 synthon. *[1 mark]*



(c) What do d^1 and a^2 synthons have in common? *[1 mark]*

They are both umpoled (non-natural reactivity).

2. The molecule below is stilboestrol, a compound with strong oestrogenic activity. **[3 marks]**



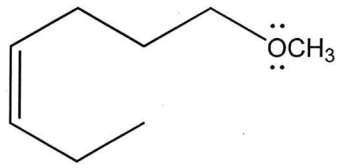
If you had to propose a synthesis of stilboestrol, what disconnection(s) would you propose? You can draw it/them on the picture above. Give at least two reasons for your choice(s).

Many answers are viable. Two options are shown. Lists of reasons are not exhaustive.

A (two pink disconnections)
- splits the target into three roughly equally sized pieces (two of which are the same)
- disconnections are immediately next to branches and/or rings so required synthons are simple in structure

B (one green disconnection)
- splits the target into two equally sized pieces (symmetry!)
- disconnection is between branches so synthons are simple in structure

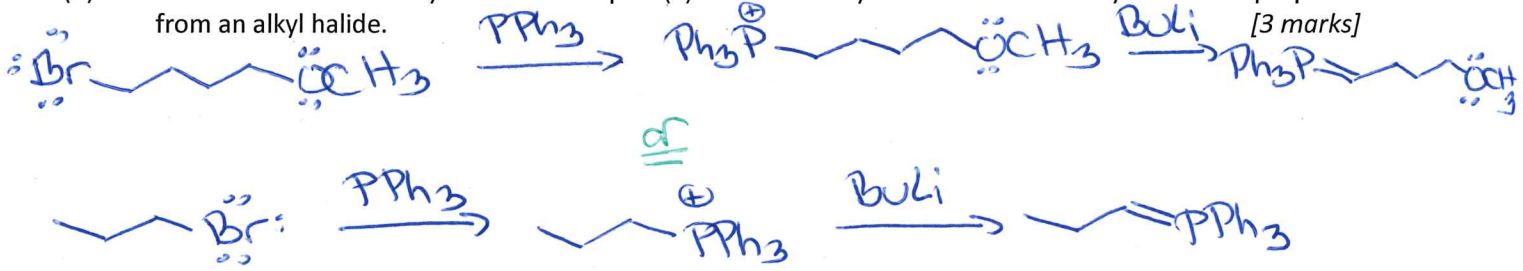
3. The following molecule can be prepared using a Wittig reaction: **[8 marks]**



(a) Draw a pair of organic reactants that can be used to perform this Wittig reaction. *[2 marks]*

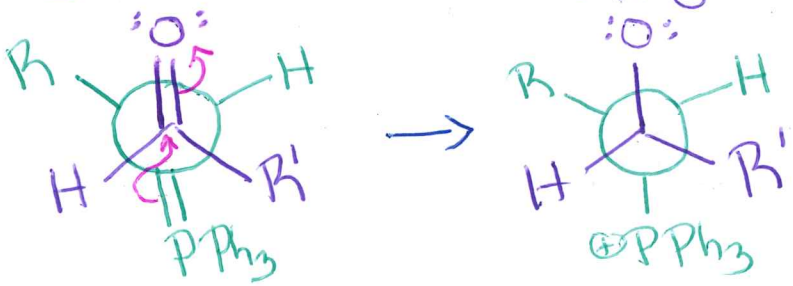


(b) One of the reactants in your answer to part (a) should be an ylide. Show how that ylide can be prepared from an alkyl halide. *[3 marks]*

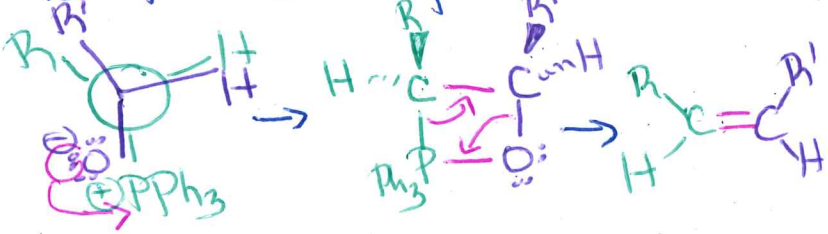


(c) Why is a *cis* double bond obtained in this reaction? *[3 marks]*

The ylide attacks the carbonyl such that the two R groups are as far away from each other as possible:

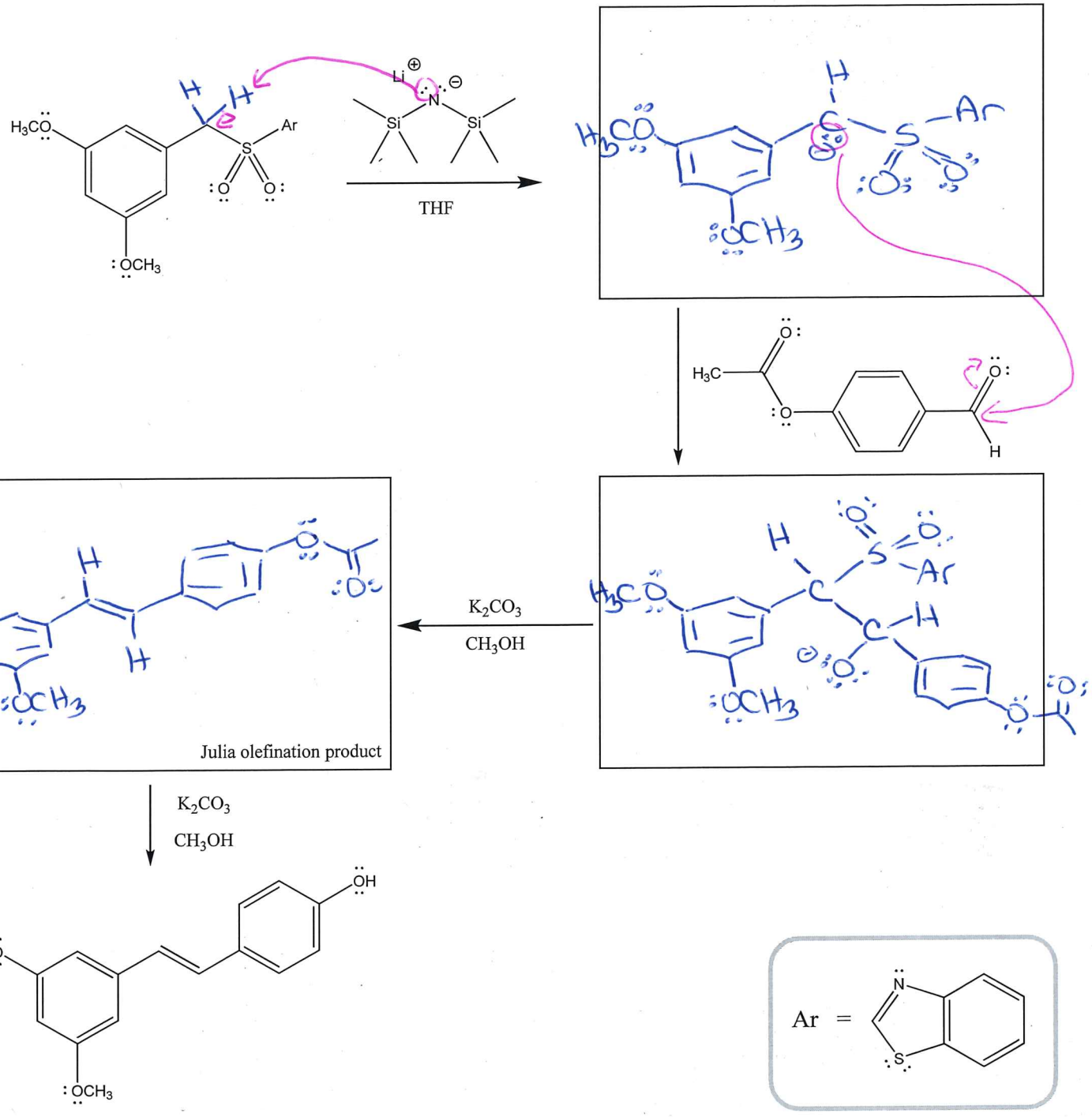


For the betaine to be converted into the oxaphosphetane, the new C-C bond must rotate to bring $O^{\ominus}$ next to $P^{\oplus}$ which puts both R next to each other:



4. Pterostilbene can be prepared by a version of the Julia olefination in which a different aromatic ring is used instead of benzene, allowing for milder reagents in the last step. As such, adding K_2CO_3 in methanol both finishes the Julia olefination and does another reaction. Assume that the Julia olefination is completed first, and draw that product in the box provided. K_2CO_3 in methanol then converts the Julia olefination product into the final product drawn.

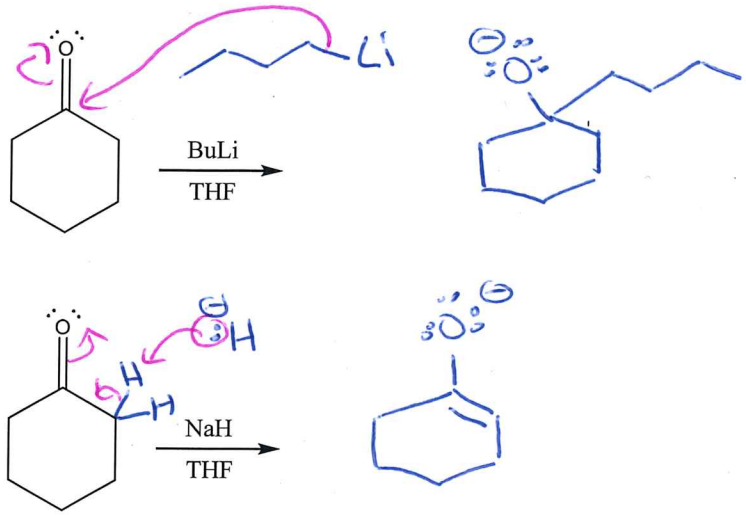
Fill in the blanks in the reaction sequence below: **[6 marks]**



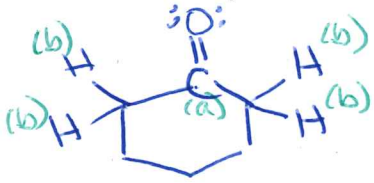
5. **[8 marks]**

(a) Draw the product of each reaction. Do NOT assume any work-up that is not shown. *[4 marks]*

Hint: Only one of these two strong bases is nucleophilic.



(b) Use an argument based on Hard Soft Acid Base theory to explain why these two reactions have different products. For full marks, your answer must address both species reacting in each reaction. *[4 marks]*

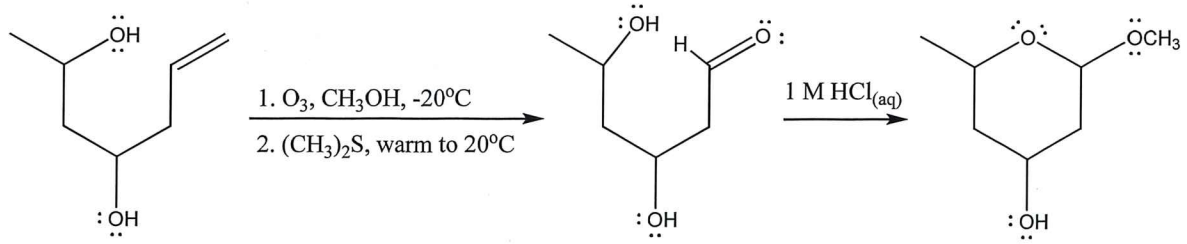


Cyclohexanone can accept electrons at any of five atoms:
- four equivalent hydrogen atoms (all labeled (b))
- the carbonyl carbon (labeled (a))

Hydrogen atoms are much smaller than carbon atoms so can be viewed as "harder" electron pair acceptors than the carbonyl carbon. $H:^{\ominus}$ is significantly smaller than the nucleophilic C in . $H:^{\ominus}$ has a much greater charge density ∴ is harder than $C^{\delta-}$. The harder electron pair donor attacks the harder electron pair acceptor, and the softer electron pair donor attacks the softer electron pair acceptor.

6. The following ozonolysis with acidic work-up is an early step in a synthesis of Swinholide A, a (very large) compound with antifungal and possible anticancer activity that has been extracted from marine sponges:

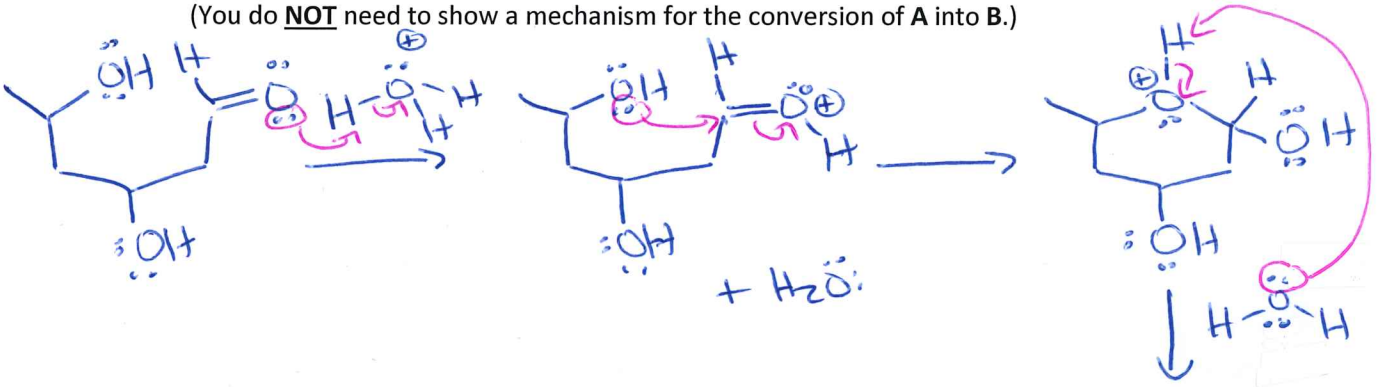
[12 marks]

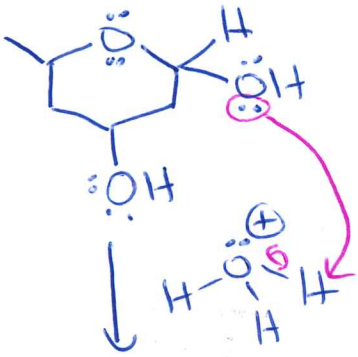


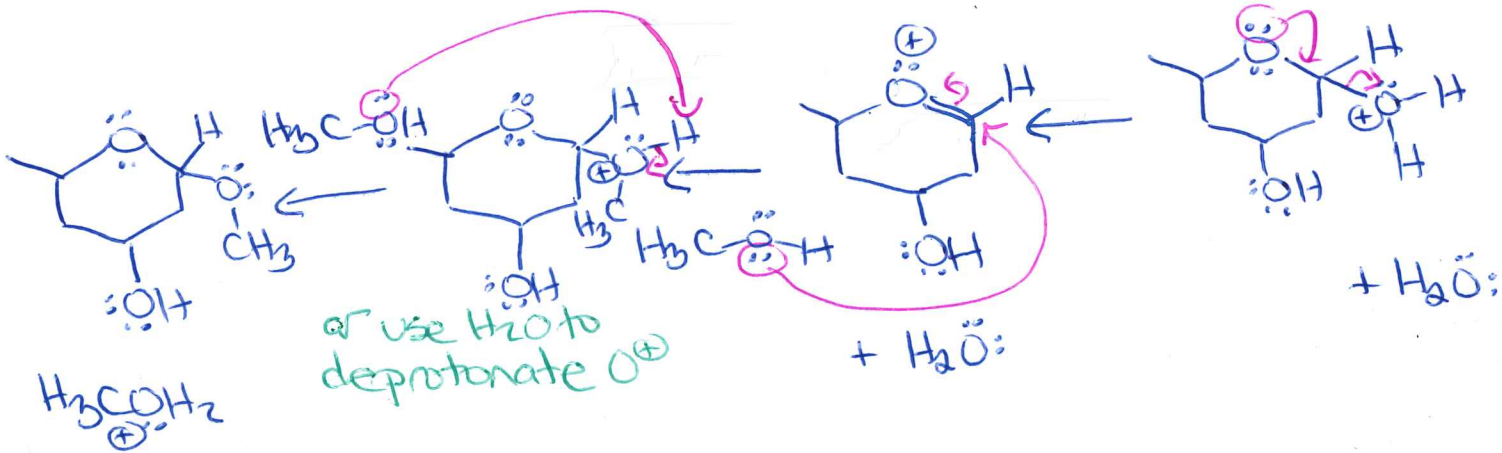
A **B** **C**

Propose a reasonable mechanism for the conversion of **B** into **C**. Because this is the work-up step, the solvent is still methanol.

(You do **NOT** need to show a mechanism for the conversion of **A** into **B**.)





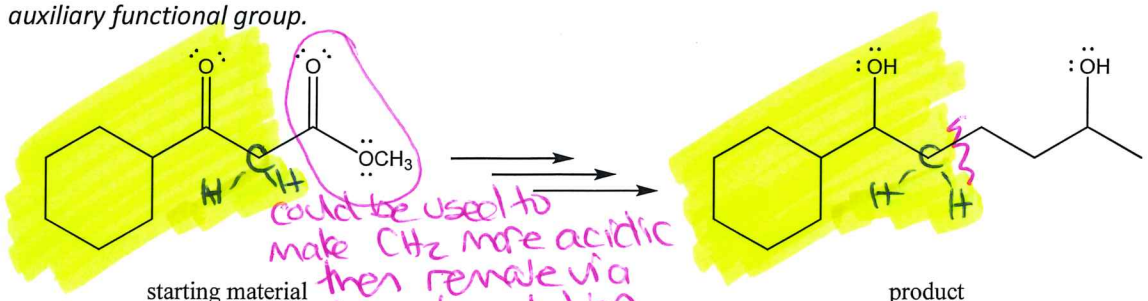


7. How would you make the molecule below? **[10 marks]**

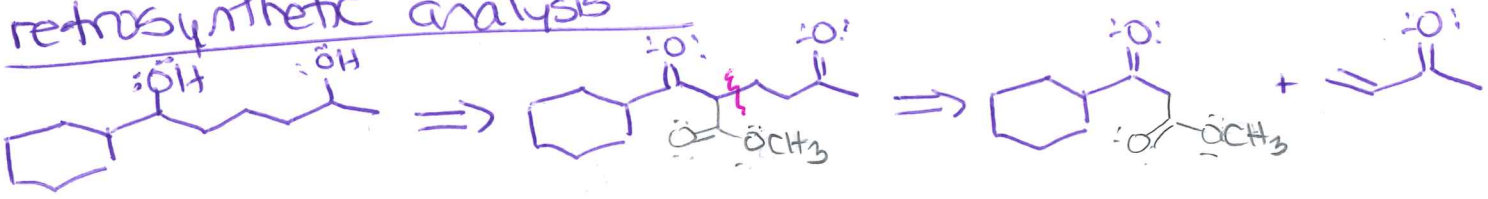
Your answer should take the form of a retrosynthetic analysis followed by chemical equations for the reactions in the synthesis itself. Write an equation for each reaction. Show all required reagents, and number steps within a reaction if order of addition is important.

*In addition to the starting material shown below, you may use any reactants that you could reasonably expect to be commercially available and that **contribute no more than 6 carbon atoms to the final product**. (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.)*

Hint: The most straightforward approach to this question will treat part of the starting material provided as an auxiliary functional group.



retrosynthetic analysis



proposed synthesis

