

**CHEM 330**

**Final Exam**  
December 5, 2014

**ANSWERS**

**Your name:** \_\_\_\_\_

This a closed-notes, closed-book exam

The use of molecular models is allowed

**This exam consists of 12 pages**

Time: 2h 30 min

1. \_\_\_\_\_ / 30

2. \_\_\_\_\_ / 30

3. \_\_\_\_\_ / 30

4. \_\_\_\_\_ / 40

5. \_\_\_\_\_ / 40

6. \_\_\_\_\_ / 40

7. \_\_\_\_\_ / 40

**TOTAL** \_\_\_\_\_ / 250 = \_\_\_\_\_ / 100

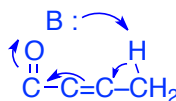
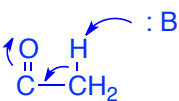
This exam counts for 50% of your CHEM 330 final grade

1. (30 pts.) Write a chemical equation and a brief sentence to illustrate each of the following mechanistic models:

a. Principle of vinylogy

**the interposition of a C=C unit between the components of a functional group generates a new functional entity, which retains the chemical characteristics of the original. For instance:**

an enolizable carbonyl compound: deprotonation is possible because of resonance delocalization of (-) charge on the electronegative O atom

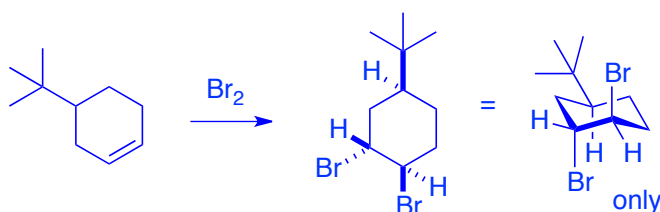


a vinylog of the original: resonance delocalization of (-) charge on the O atom still possible through the C=C bond: can undergo deprotonation

b. Fürst-Plattner rule

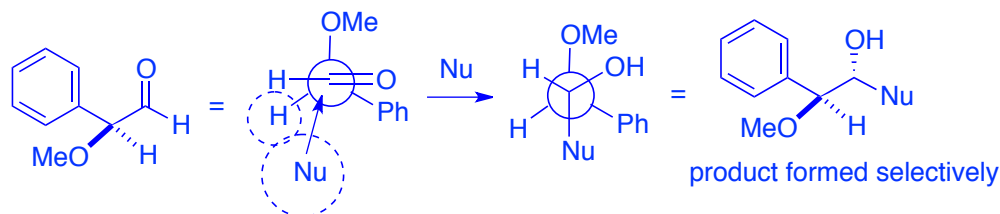
**electrophilic cyclohexene derivatives (epoxides, halonium ions, ...) react with nucleophiles to form *trans*-diaxial products selectively. Example:**

products selectively. Example:

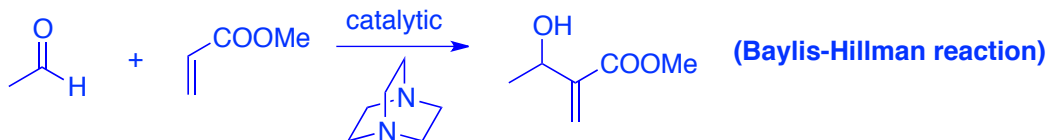
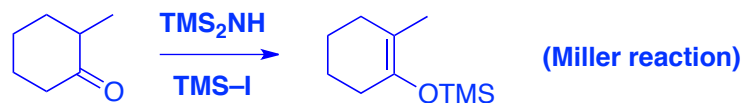
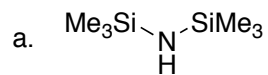


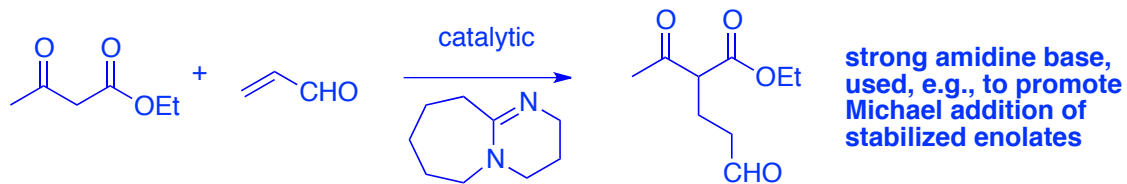
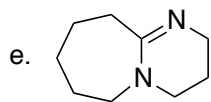
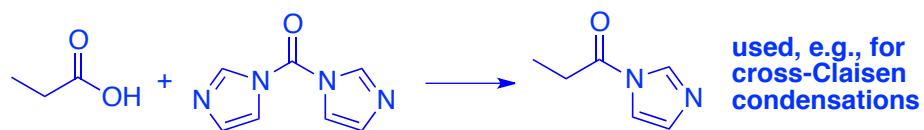
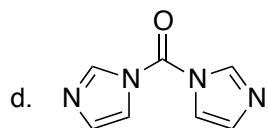
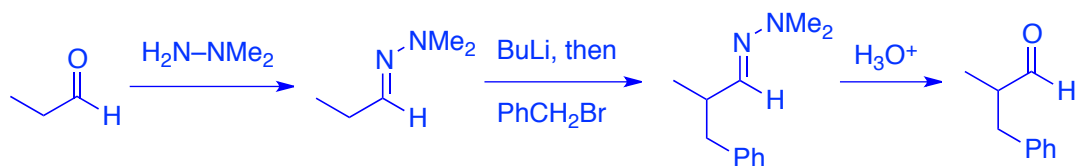
c. Felkin-Ahn model

**an  $\alpha$ -heterosubstituted aldehyde is most reactive toward nucleophilic addition when the C- $\alpha$ -heteroatom  $\sigma$  bond is approximately perpendicular to the plane of the C=O group. Nucleophilic attack then occurs preferentially from a conformation in which the incoming nucleophile can approach along a Dunitz-Bürgi angle from the side of the smaller  $\alpha$ -substituent. To illustrate:**



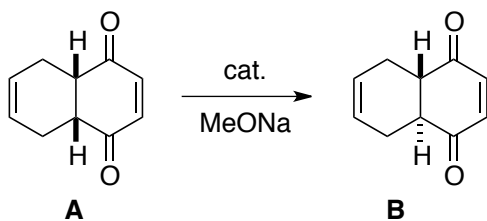
2. (30 pts.) Write a chemical equation to show an example of a reaction that involves the use of the following nitrogen-containing reactants (**do not** write mechanisms – just the reactions):



c.  $\text{H}_2\text{N}-\text{N}(\text{CH}_3)_2$ 

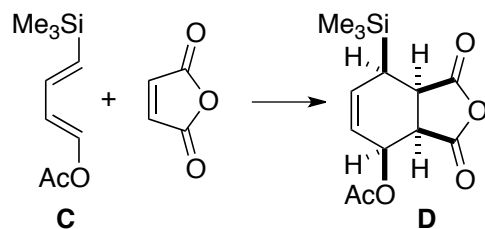
3. (30 pts.) Check the appropriate box to indicate whether the following statements are true or false:

a. Reaction of **A** with catalytic MeONa yields **B**:



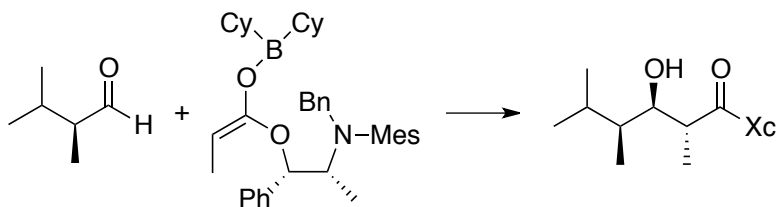
true false

b. Reaction of **C** with maleic anhydride yields **D**:



true false

c. The reactants shown below are stereochemically matched:



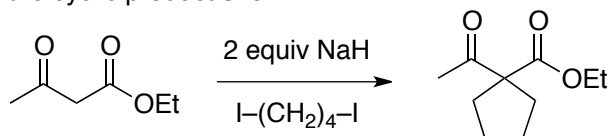
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d. The copper atom undergoes oxidative addition in the course of the following reaction:



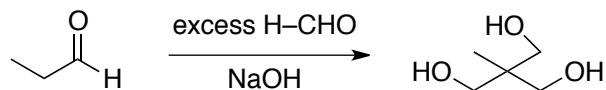
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e. The following procedure is satisfactory for the preparation of the cyclic product shown



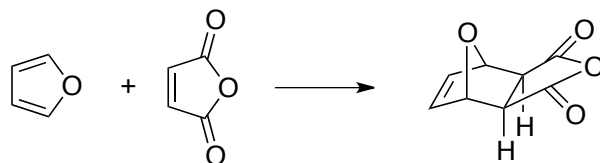
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- f. The following procedure is satisfactory for the synthesis of the triol shown



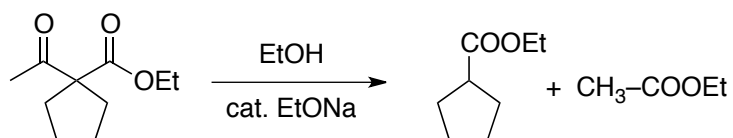
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- g. The Diels-Alder reaction of furan with maleic anhydride gives the exo-adduct due to a lack of secondary orbital interactions



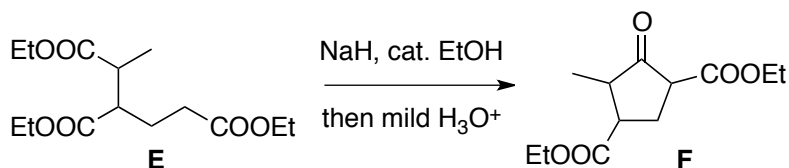
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- h. The process shown below is a reverse Claisen condensation:



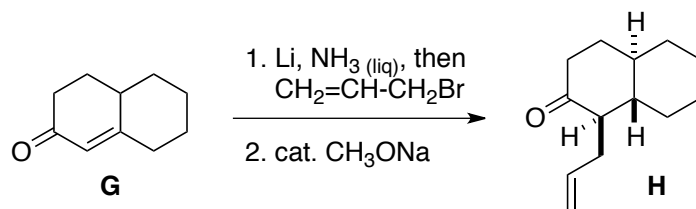
true  false

- i. Treatment of **E** with NaH / cat. EtOH, followed by mild H<sub>3</sub>O<sup>+</sup>, will produce **F**:



true  false

- j. Treatment of **G** with Li in liquid NH<sub>3</sub>, followed by allyl bromide and then catalytic MeONa, will produce **H**



true  false

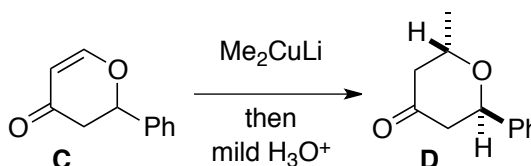
4. (40 pts.) Provide a succinct explanation for the following experimental observations:

- a. Deprotonation of ketone **A** with 0.95 equiv of LDA, followed by reaction with TMS-Cl, produces silyl enol ether **B**, **BECAUSE**:



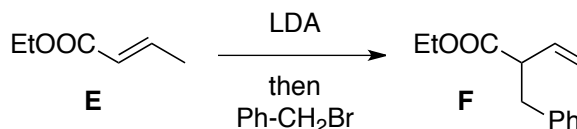
the remaining 0.05 equivalents of ketone **A** act a proton source ("shuttle") and induce equilibration of the initially formed kinetic enolate to the thermodynamic one

- b. Reaction of compound **C** with  $\text{Me}_2\text{CuLi}$ , followed by mild  $\text{H}_3\text{O}^+$ , selectively yields **D**, **BECAUSE**:



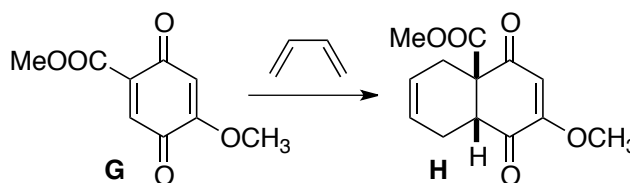
the cuprate tends to attack in an axial mode, in such a way that the 6-membered ring evolves toward a chair (or half-chair) conformer. This constitutes the more energetically favorable reaction pathway

- c. Treatment of compound **E** with LDA, followed by benzyl bromide, selectively yields **F**, **BECAUSE**:



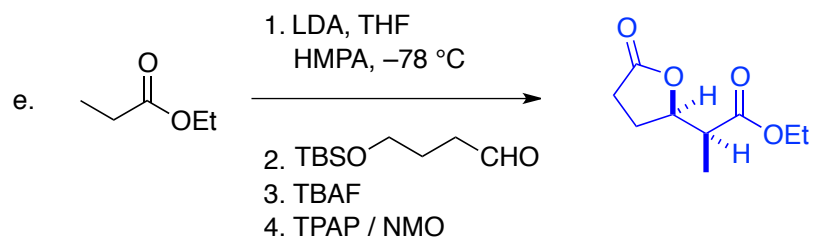
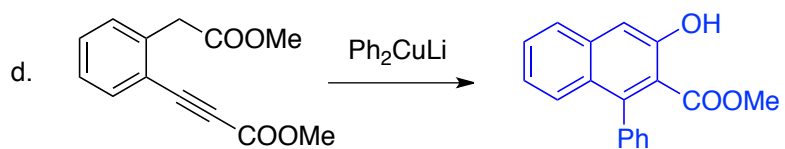
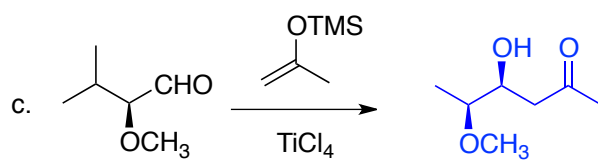
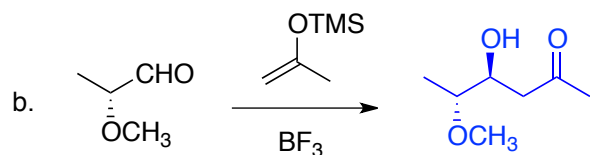
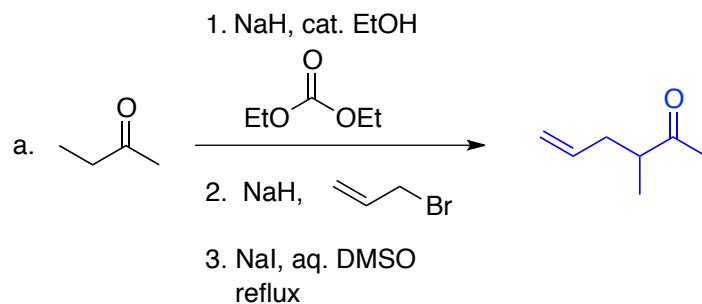
as expressed by the principle of least motion, atoms within a molecule tend to undergo the least possible extent of repositioning during a reaction. In the present case, compound **F** (the resultant of  $\alpha$ -alkylation of the dienolate of **E**) forms through a process that requires the repositioning 3 out of 5 non-H atoms of the substrate. The hypothetical  $\gamma$ -alkylation requires the repositioning of all 5 atoms. Therefore, compound **F** is formed preferentially

- d. Benzoquinone **G** undergoes Diels-Alder reaction selectively at the double bond bearing the COOMe group, **BECAUSE**:

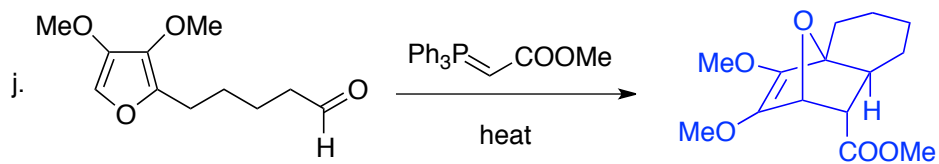
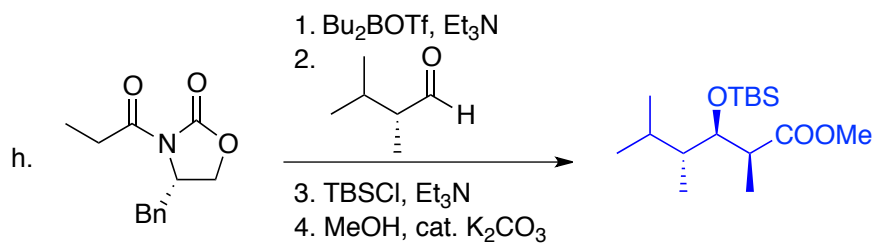
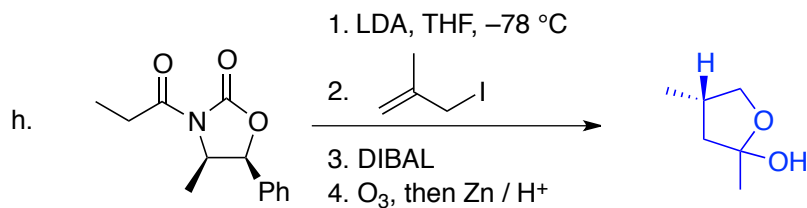
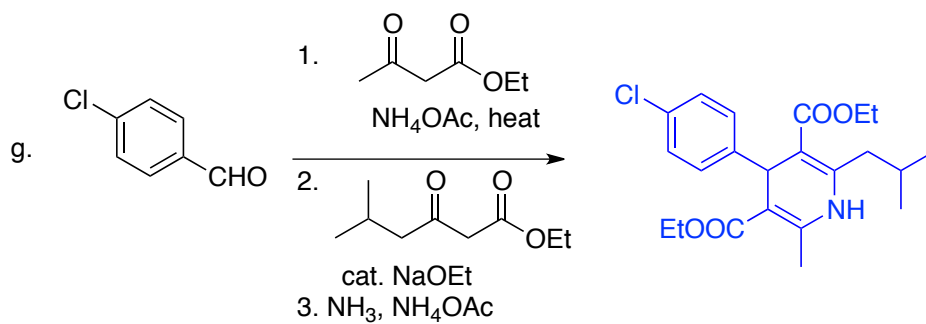
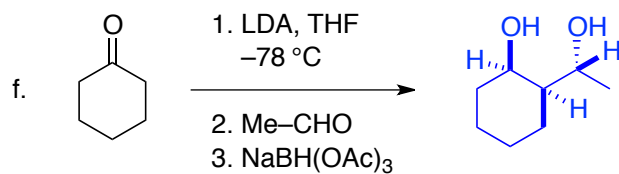


a COOMe group *lowers* the LUMO energy of a  $\pi$  bond, while a  $\text{CH}_3\text{O}$  group *increases* it. This is a regular-demand DA reaction, so the key FMO interaction is between the HOMO of the diene and the LUMO of the dienophile. The HOMO-LUMO energy gap for reaction at the COOMe-substituted  $\pi$  bond is smaller. Therefore reaction at the COOMe-substituted  $\pi$  bond is faster

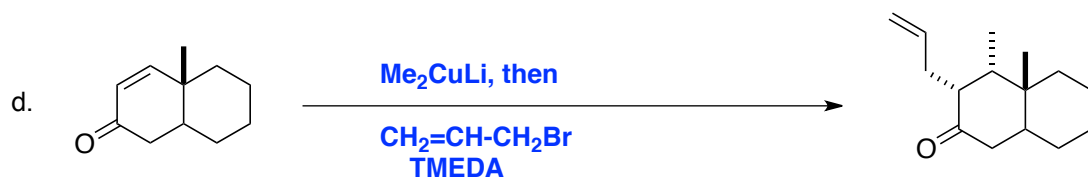
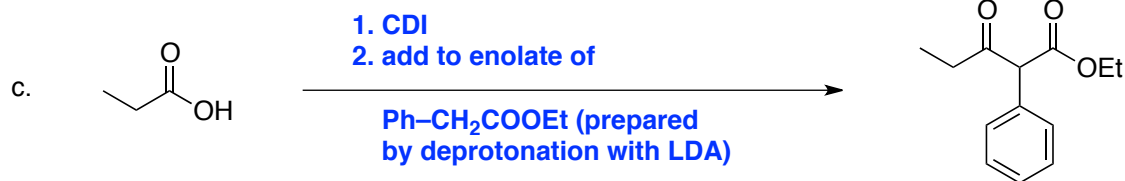
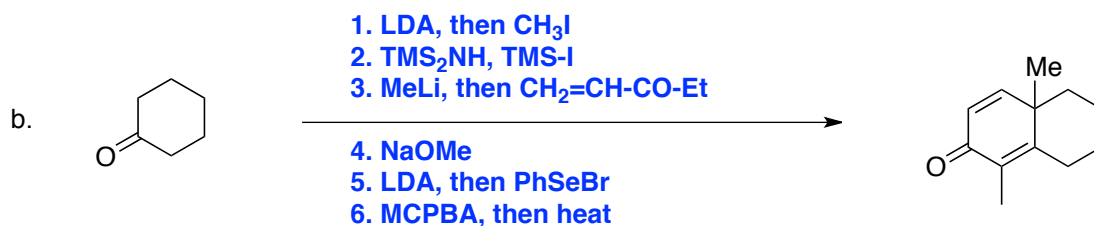
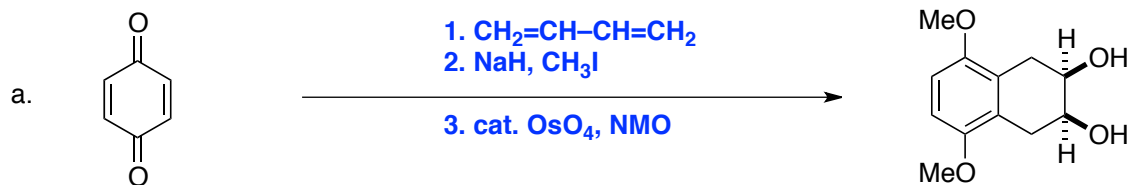
5. (40 pts.) Predict the structure of the major product expected from the following reactions. Notes: (i) it is not necessary to draw mechanisms; (ii) aqueous workups at appropriate stages are understood.







6. (40 pts.) Complete the following equations by indicating all the reagents that are necessary to effect the transformations shown. Provide your answers as a numbered list of reagents, in the correct order, written over/under the reaction arrows. **Note:** aqueous workups are understood and do not need to be included in your answers.



7. (40 pts.) Propose a method to achieve the enantioselective synthesis of the molecules shown below starting with the suggested compounds plus any additional building blocks that might be required (simple carbonyl compounds, alkyl halides,...). Be careful about protecting groups and configurations of stereocenters. Assume the availability of all needed reagents, auxiliaries, etc. Present your answer as a **clear** flowchart.

**It is not necessary to draw mechanisms or to indicate aqueous workups.**

