CHEM 330

Exam 1
October 17, 2014

Your name: _____

This exam contains 6 pages

This a closed-notes, closed-book exam

You may use your set of molecular models

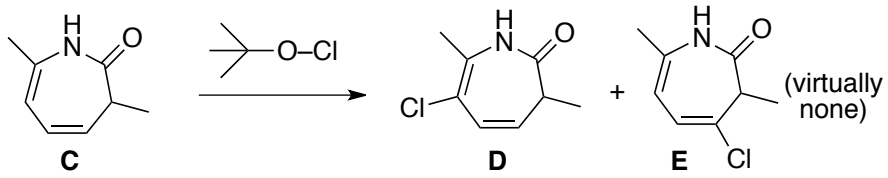
Time: 1.5 h

1. _____ / 15
2. _____ / 20
3. _____ / 20
4. _____ / 20
5. _____ / 25

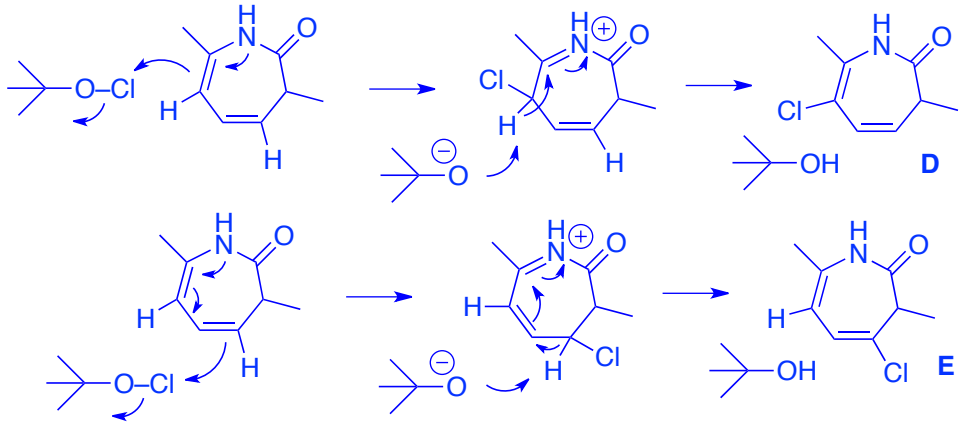
TOTAL _____ / 100

This exam counts for 25% of your CHEM 330 final grade

1. (15 pts.) Illustrate how one may invoke the principle of least motion to account for the fact that the reaction of compound **C** below with *tert*-BuO–Cl (a source of Cl^+) yields **D**, accompanied by little – if any – **E** (obviously, it is essential to draw clear mechanisms for the formation of **D** and **E**):

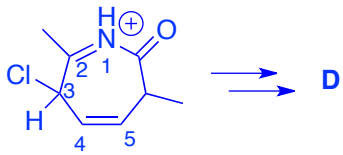


The mechanism for the formation of **D** and **E** must be:



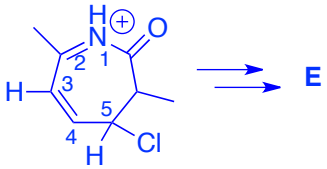
The reaction clearly occurs under conditions of kinetic control, because it is not possible for the ionic intermediates shown above to revert to the starting materials (upon connecting to a carbon atom, the chlorine atom acquires a favorable oxidation state of –1 and it becomes the negative end of the C–Cl bond dipole, barring its departure as Cl^+).

Relative to **C**, the reactive intermediates that lead to **D** and **E** are such that:



- atoms 1 and 2 move closer
- atoms 2 and 3 move farther
- atoms 3 and 4 do not move
- atoms 4 and 5 do not move

lesser extent of internal motion: favored based on the principle of least motion

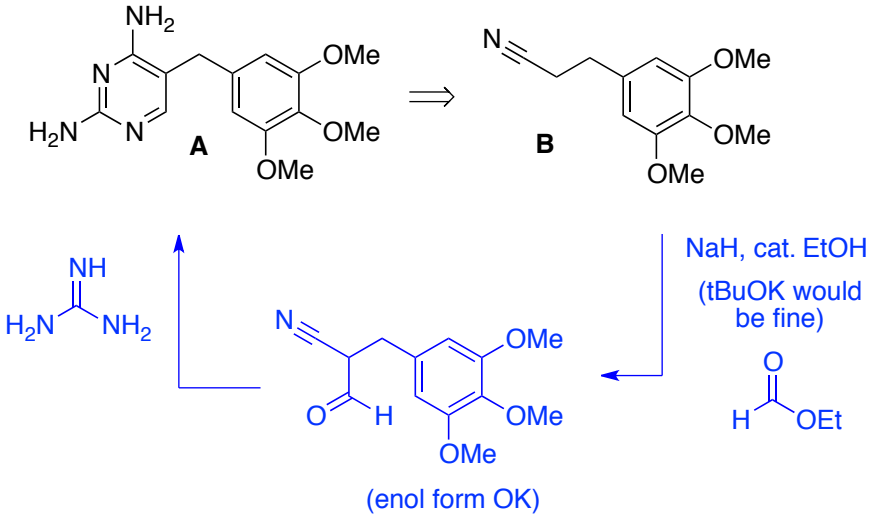


- atoms 1 and 2 move closer
- atoms 2 and 3 move farther
- atoms 3 and 4 move closer
- atoms 4 and 5 move farther

greater extent of internal motion: disfavored based on the principle of least motion

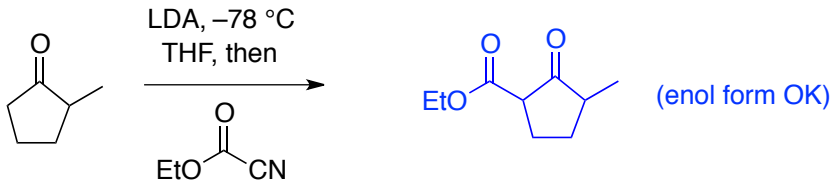
Therefore, the principle of least motion would predict the kinetically faster formation of the reactive intermediate that leads to **D**, i.e., the preferential formation of **D** under conditions of kinetic control.

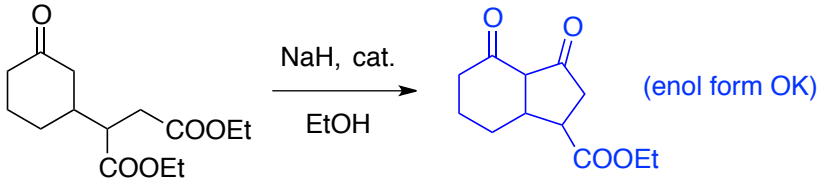
2. (20 pts.) Trimethoprim, **A**, is a bacteriostatic drug that is prepared starting with compound **B**. Draw a reaction flowchart to show how **B** may be converted into **A**. Assume the availability of all needed reagents (acids, bases, alkyl halides, esters, etc.) **Note**: it is not necessary to draw mechanisms. Also, aqueous workups after each reaction are understood and need not be specified.

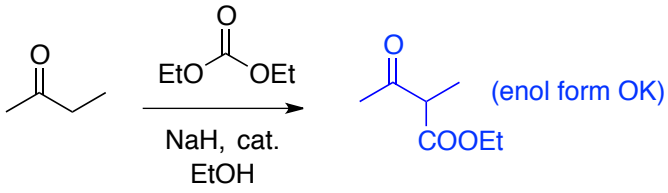


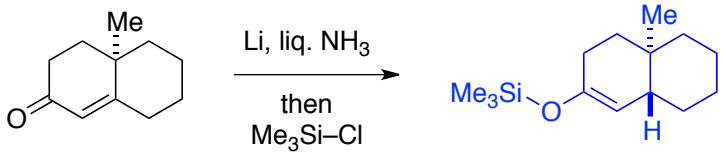
alternative reagents may be OK

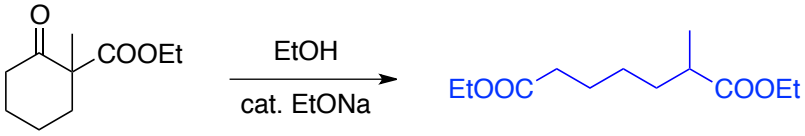
3. (20 pts.) Draw the structure of the major product expected from the reactions shown below. If no reaction is expected, answer "NO REACTION." **Note**: it is understood that each reaction is subject to a final aqueous workup.

a. 

b. 

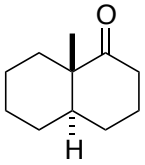
c. 

d. 

e. 

4. (20 pts.) Propose a method to achieve the transformations shown below. In each case, a multistep sequence (= not just one reaction, but several) may be required. Indicate all requisite reagents, in the correct order, as a numbered list above/below the reaction arrow. **Aqueous workups after each step are understood and there is no need to specify them.**

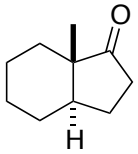
a.



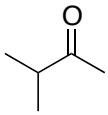
1. LDA, then TMS-Cl (TMSOTf / iPr$_2$NEt OK)
2. O_3, then H_2O_2 / H^+
3. EtOH, H_2SO_4

(other simple alcohols + strong acids OK)

4. NaH, cat. EtOH
5. Aq. HCl, reflux (Krapcho OK)



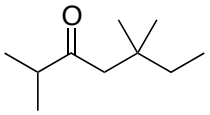
b.



1. LDA, then TMS-Cl (TMSOTf / iPr$_2$NEt OK)

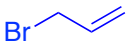
2. 

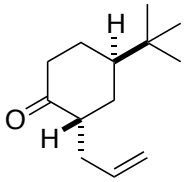
, $TiCl_4$



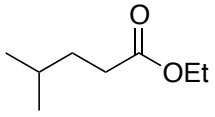
c.

MeLi, then



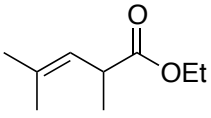


d.

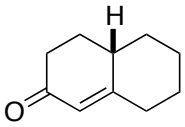


1. LDA, then PhSeBr
2. MCPBA

3. heat
1. LDA, then Me–I

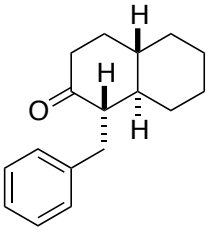


e.



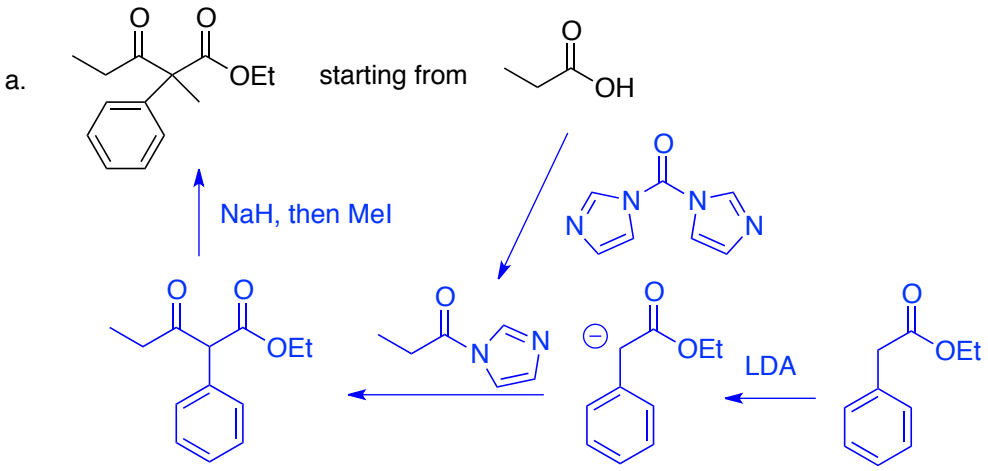
1. Li, liq. NH_3, tBuOH, then $PhCH_2Br$

2. NaOMe (e.g.)



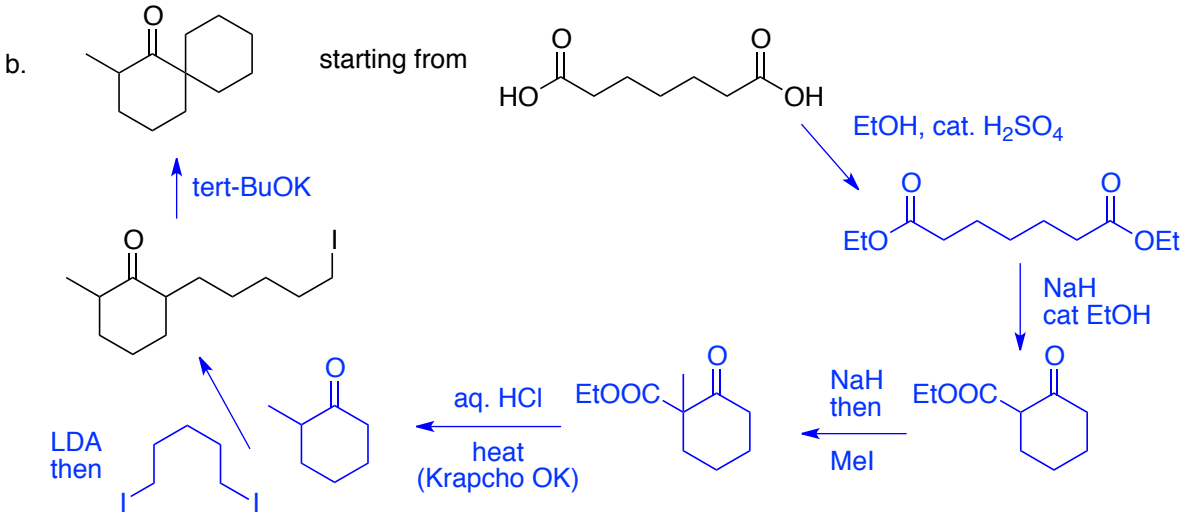
5. (25 pts.) Propose a method to synthesize the substances shown below starting from the indicated materials. Assume the availability of all reagents needed to convert the starting compound into the product (e.g, acids, bases, alkyl halides, etc.). Present your answer as a flowchart. **It is not necessary to draw mechanisms**. **Also, aqueous workups after each step are understood and do not need to be indicated.**

a.



other answers may be OK

b.



other answers may be OK