Chemistry 4321/8321	**Midterm Examination I**	October 10, 2012
	7:00 – 9:00 PM	
Organic Synthesis		T. R. Hoye

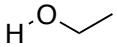
Name _____

Part I	**/ 10**
Part II	**/ 18**
Part III	**/ 24**
Part IV	**/ 20**
Part V	**/ 08**
Part VI	**/ 20**
Total	**/ 100**

There are 100 points on the exam.
Answer all six of questions **I-VI** directly in the space provided on the six exam pages. You may not use books, notes, models, etc.

I. (10 points) Within each set, **circle** the **strongest acid** and place a rectangle around the weakest acid.

a)

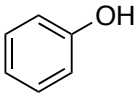


ethanol

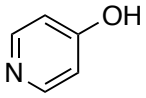
hydrogen chloride

hydrogen fluoride

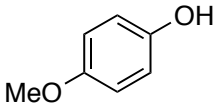
b)



phenol

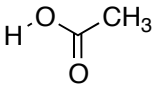


4-hydroxypyridine

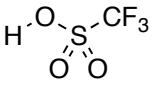


hydroquinone methyl ether

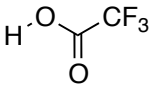
c)



acetic acid

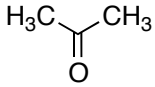


triflic acid

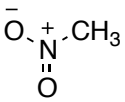


trifluoroacetic acid

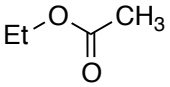
d)



acetone

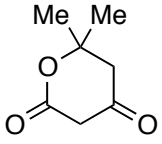


nitromethane

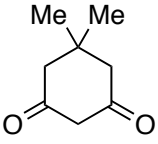


ethyl acetate

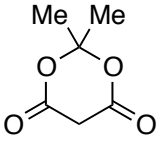
e)



6,6-dimethyl pyran-2,4-dione



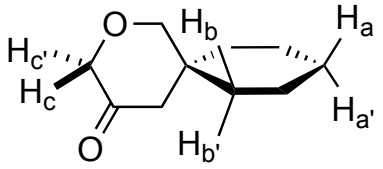
dimedone



Meldrum's acid

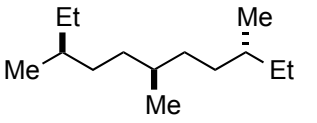
II. (18 points)

a) For each pair of similar hydrogen atoms or faces of the sp^2-hybridized carbon atom, circle the word that properly describes their topicity relative to one another.

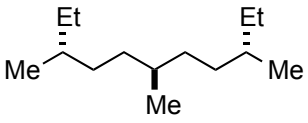


H_a / $H_{a'}$	homotopic	enantiotopic	diastereotopic
H_b / $H_{b'}$	homotopic	enantiotopic	diastereotopic
H_c / $H_{c'}$	homotopic	enantiotopic	diastereotopic
carbonyl carbon "front" face vs. "back" face	homotopic	enantiotopic	diastereotopic

b) Indicate the relationship (circle the proper word) between each of the following pairs of molecules. For any that are diastereomers, indicate the number of stereogenic centers at which the two have opposite configuration.

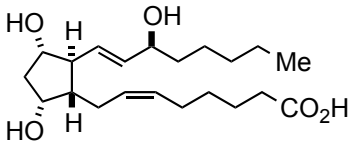


vs.

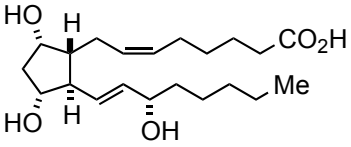


same enantiomeric diastereomeric

(if so, how many stereogenic centers are different?) ☐

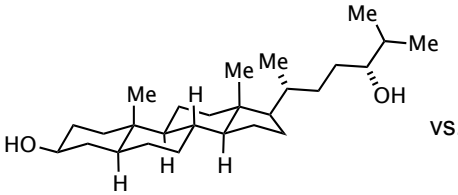


vs.

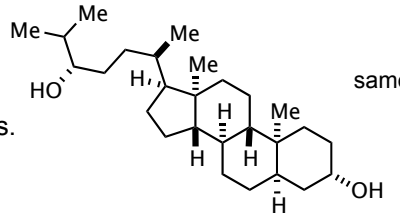


same enantiomeric diastereomeric

(if so, how many stereogenic centers are different?) ☐



vs.

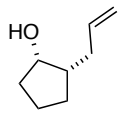


same enantiomeric diastereomeric

(if so, how many stereogenic centers are different?) ☐

III. (24 points) Provide the structure of the major product you expect for each of the following six transformations [**a)**–**f)**]. Clearly show the *relative configuration among all stereocenters* for the products of reactions **b)** and **e)**.

a)

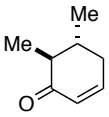


OsO_4, $NaIO_4$

dioxane, water

$C_7H_{12}O_2$

b)

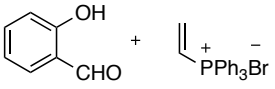


1) Me_2CuLi

2) H_3O^+ quench

$C_9H_{16}O$

c)

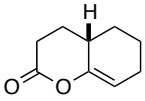


NaH, THF

$Ph_3P{=}O$ +

C_9H_8O

d)

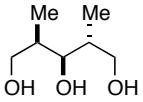


1) EtMgBr

2) aqueous NaOH

$C_{11}H_{16}O$

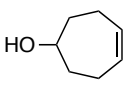
e)



H^+ (cat.)

$C_{14}H_{20}O_3$

f)

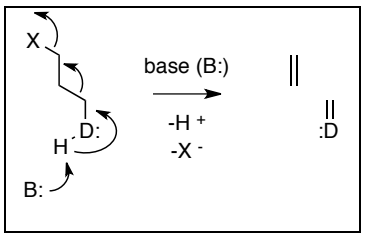


a) O_3, CH_2Cl_2

b) Ac_2O, Et_3N
DMAP

$C_7H_{10}O_3$

IV. (20 points) This problem is about a reaction known as the Grob fragmentation. The general form of this process is shown in the box to the right, where X is a leaving group and D is a heteroatomic, electron-donating atom (typically, O or N). There is a large stereoelectronic requirement for this fragmentation—the breaking C–C bond needs to be anti to the C–X bond.

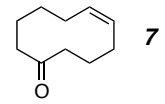


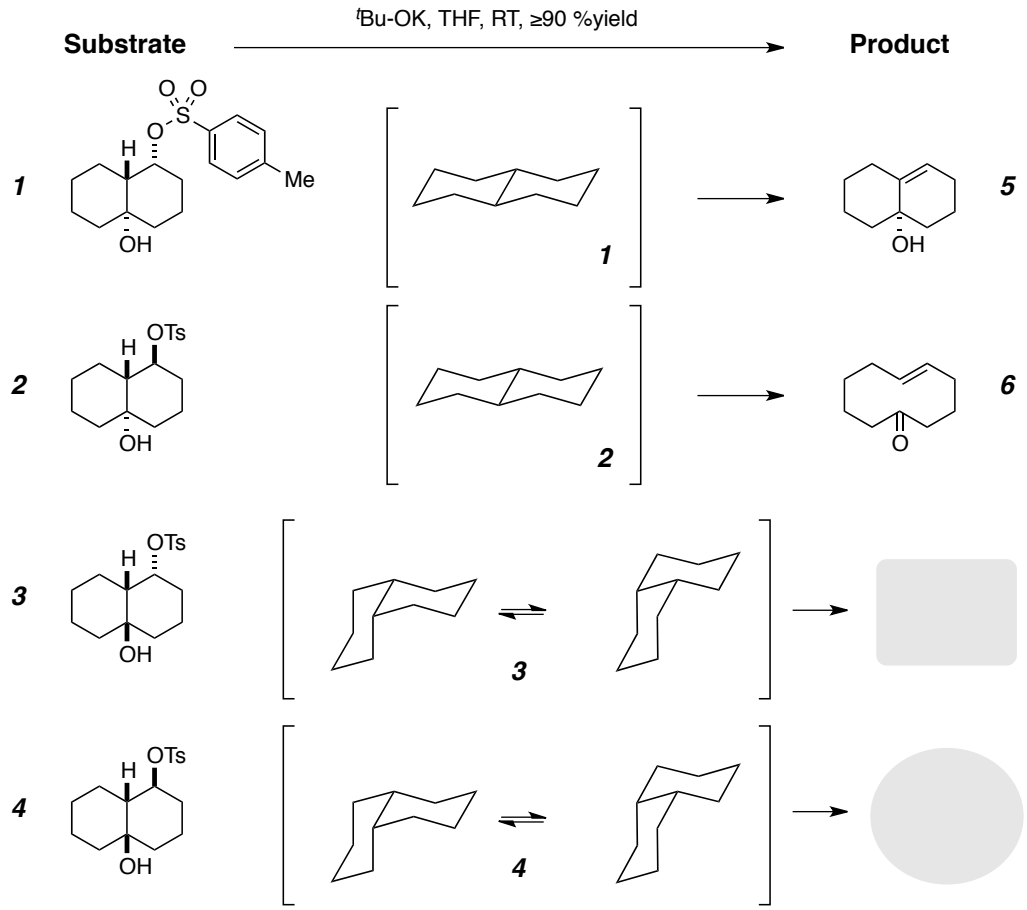
Each of the diastereomeric *p*-toluenesulfonate esters ($ROSO_2PhMe \equiv ROTs$) **1**-**4** gives one predominant product (in over 90% yield) when treated with the base, potassium *tert*-butoxide.

a) Isomer **1** does *not* undergo Grob fragmentation; instead, it gives alkene **5** by a simple E2 elimination process. Add the bridgehead H and OH and the OTs groups in structure **1** to the *trans*-decalin version of that diastereomer [brackets]. Use curly arrows to account for the formation of **5**.

b) Isomer **2** gives (*E*)-cyclodec-5-enone (**6**), the product of Grob fragmentation. Add the bridgehead H and OH and the OTs groups in structure **2** to the *trans*-decalin version of that diastereomer in [brackets]. Use curly arrows to account for the formation of **6**.

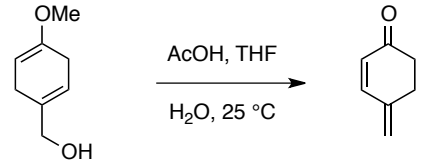
c) Each of isomers **3** and **4** gives *either* **5**, **6**, or (*Z*)-cyclodec-5-enone (**7**) as the product. Add the bridgehead H and OH and the OTs groups in structures **3** and **4** to the *cis*-decalin version of each diastereomer [brackets]. For each of the *cis*-decalin equilibria, **circle the more stable conformer**. Show the curly arrows for the base-promoted reaction within each of these more stable conformers. Inside the gray box (from **3**) or gray oval (from **4**) write the structure number of the product (*i.e.*, **5**, **6**, or **7**) that is predicted by each of these analyses.



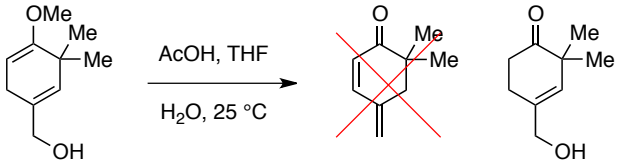


V. **(8 pts)** Provide a detailed mechanism to account for the conversion of **8** to **9**. Show *ALL* intermediates, equilibria, and bond-making and -breaking steps. There is more than one reasonable pathway that can be envisioned for this acid-catalyzed process; these differ by the order of the fundamental processes involved.

*** For a **5-point bonus**, make sure that the mechanism you provide is consistent with the following two facts: (1) This reaction occurs under mildly acidic (pK_a AcOH = 5) conditions. (2) The *gem*-dimethylated analog **10** does *not* give an appreciable amount of the analogous product **11** under the same conditions but, instead, the ketone **12**.

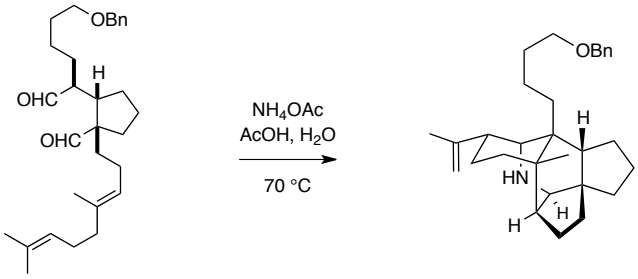


8 ***9***



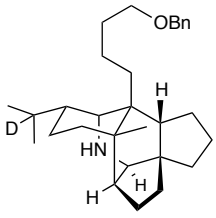
10 ***11*** ***12***

VI. **(20 pts)** Based on elegant work from the early 1990s reported from the laboratories of Professor Clayton H. Heathcock, it can be confidently expected that if dialdehyde **13** were treated with ammonium acetate in warm aqueous acetic acid, the polycyclic amine **14** would be formed efficiently. Provide a detailed mechanism to account for this transformation. Show *ALL* intermediates, equilibria, and bond-making and -breaking steps.



13 ***14***

If deuterated benzylammonium acetate ($PhCD_2NH_3^+AcO^-$) were to be used instead of ammonium acetate, it can be expected that a deuterated *and reduced* analog of **14**, namely **15**, would be formed instead. Provide a mechanistic rationale (1-2 sentences and 1-2 structures) for this different outcome. [Hint: the deuterated benzaldehyde (PhCDO) is the benzyl amine-derived byproduct.]



15

end of exam