Chemistry 4322/8322	**Final Examination**	May 14, 2019
	1:30 – 4:30 PM	
Advanced Organic Chemistry		T. R. Hoye

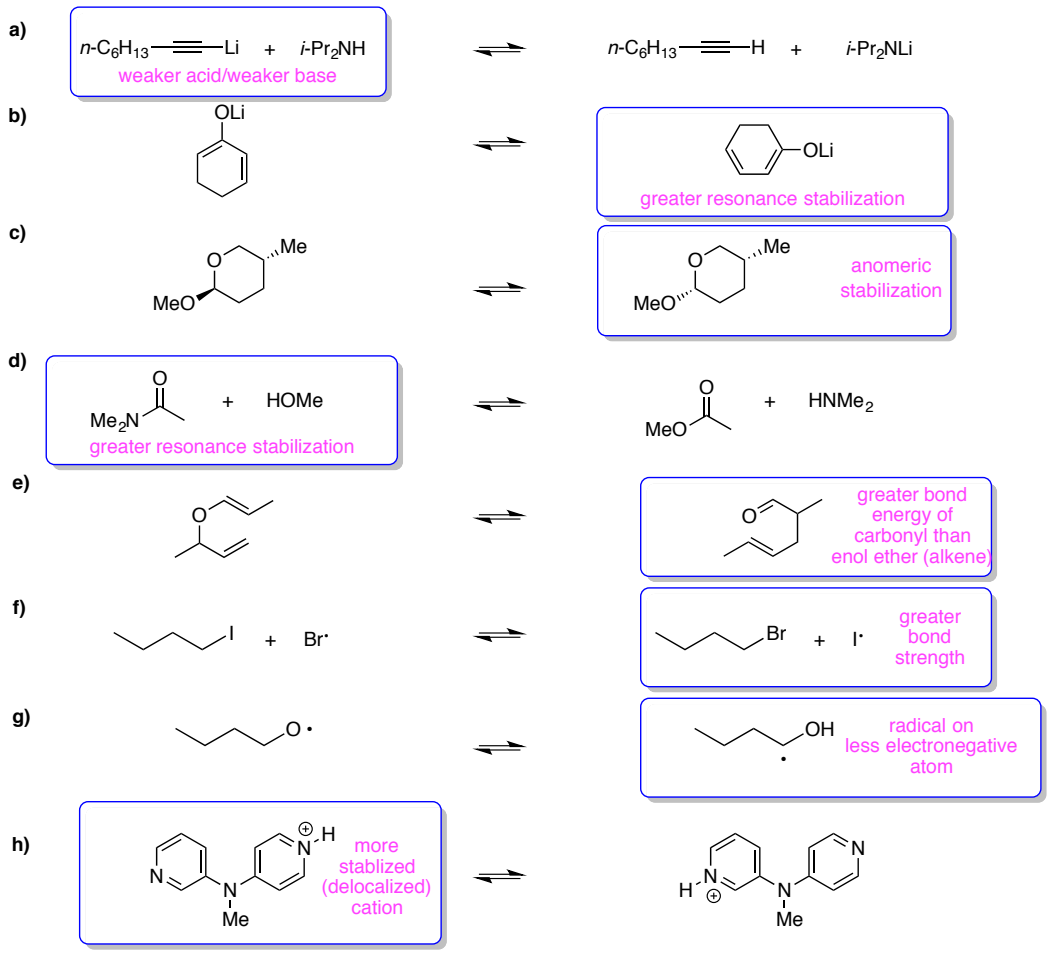
Name _____**ANSWERS**_____

There are 162 points on the exam.

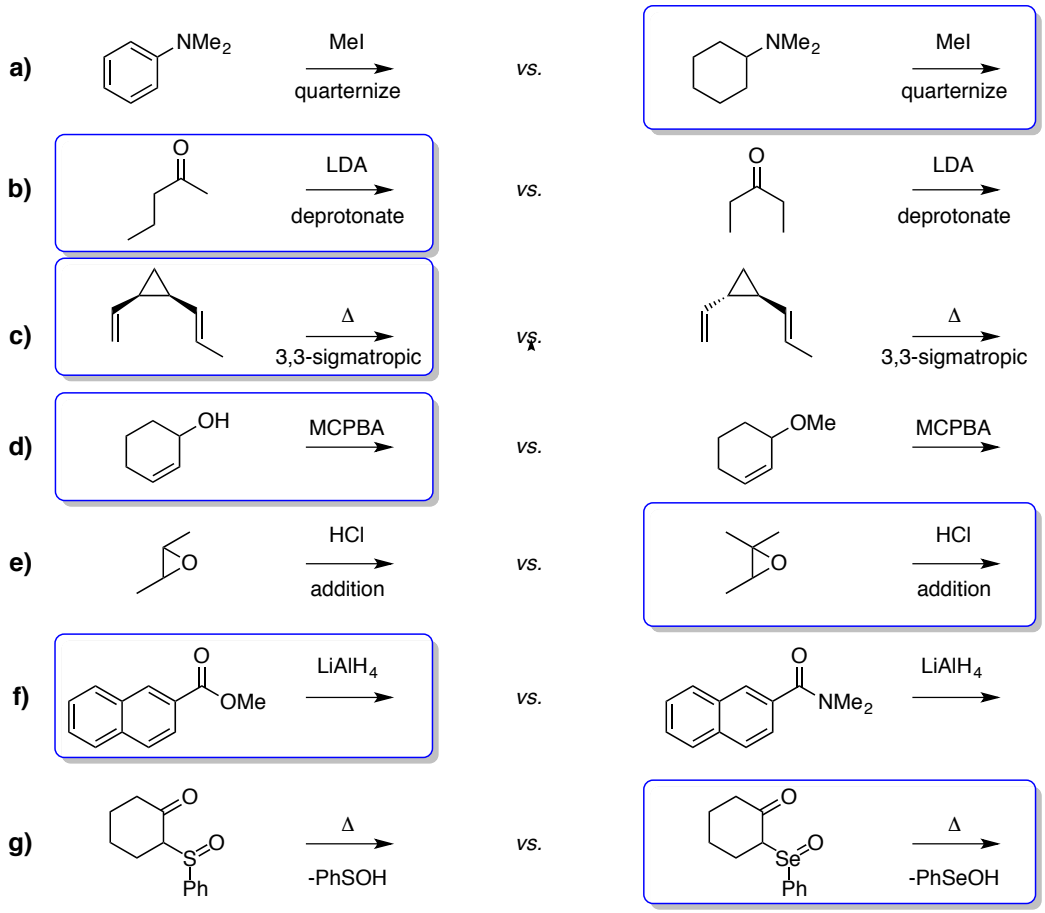
Answer all questions directly in the space provided on the eight exam pages. You may not use books, notes, models, etc.

Part I	**16 / 16**
Part II	**14 / 14**
Part III	**14 / 14**
Part IV	**12 / 12**
Part V	**08 / 08**
Part VI	**08 / 08**
Part VII	**48 / 48**
Part VIII	**42 / 42**
Total	**162 /162**

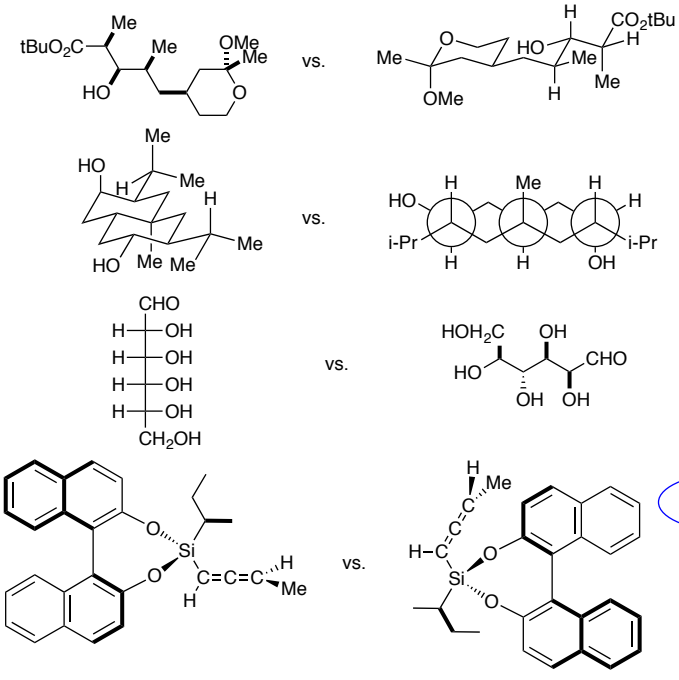
I. **(16 points)** Indicate whether each of the following equilibria lies predominantly to the left or to the right by circling the side corresponding to the more stable species.



II. **(14 points)** Within each of the following seven pairs of reactions, circle the one that proceeds at the faster rate under the same reaction conditions.

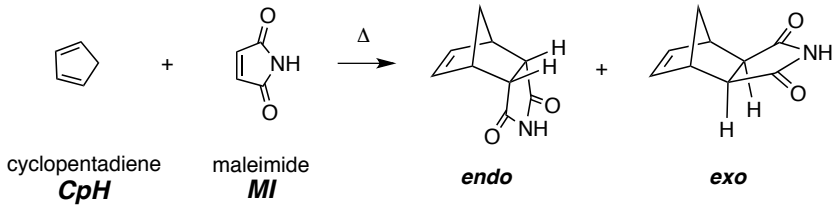


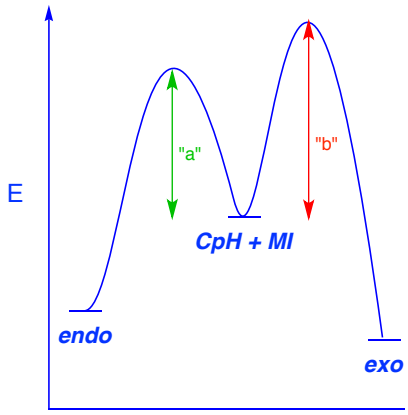
III. (14 points) Indicate (circle the word) whether the two stereoisomers for the following pairs of structures are the *same*, a pair of *enantiomers*, or a pair of *diastereomers*. *If* they are diastereomers, indicate the number of stereogenic centers that are different in the two structures. Ignore differences in conformation.



IV. **(12 points)** Discuss the concept of kinetic vs. thermodynamic control as it applies to the energetics of the following Diels-Alder reaction. When maleimide (**MI**) is allowed to react with cyclopentadiene (**CpH**) at room temperature, the ratio of the ***endo*** and ***exo*** products is 19 : 1. When the reaction is performed at 90 °C (or if the solution of the initial 19 : 1 mixture is subsequently heated to 90 °C), the ratio of ***endo*** to ***exo*** is (or becomes) 1 : 6.

Limit your answer to the space inside the box below. Use an energy diagram. Three–five sentences should suffice for your answer. There is no need to explain the origin of the selectivity (i.e., the secondary orbital interactions in the transition states or steric features of the products). I am looking for a qualitative description, not one that converts ratios into energy differences quantitatively.





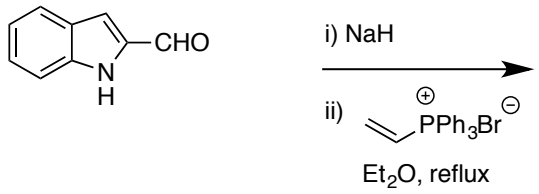
This is an example of a reaction that can lead to two products where the less stable of the two (the ***endo*** isomer) is formed more rapidly than the more stable counterpart (the ***exo*** isomer). As shown in the simple potential energy diagram above, the activation barrier for formation of **endo** from **CpH** + **MI** is lower than the barrier leading to ***exo***, even though G° of ***exo*** is below that of ***endo***. Under conditions where the reverse reaction of ***endo*** back to **CpH** + **MI** is sufficiently slow, the product ratio will reflect the relative heights of the two activation barriers (*i.e.*, **endo** will predominate). At higher temperature and/or longer times, the system will approach its equilibrium state, and the product ratio will reflect the relative free energies of the two products (*i.e.*, ***exo*** will predominate to the extent dictated by $\Delta G°_{endo/exo}$).

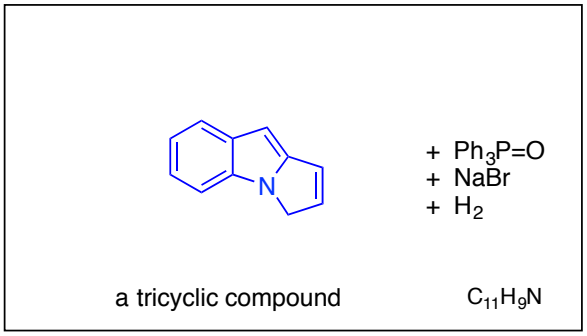
Alternative language for an explanation:

The energy of activation for the cycloaddition of **CpH** with maleimide (**MI**) to give the ***endo*** ("a"), is lower than that to give ***exo*** ("b"). Therefore, ***endo*** is the kinetically favored product. The ***exo*** is more stable than ***endo***. Given enough time and energy, the system will equilibrate to give a preponderance of ***endo***. The overall rate limiting step for the equilibration is cycloreversion of ***endo*** back to **CpH** and **MI**.

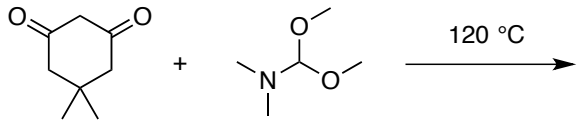
V. (**8 points**) Provide the structure of the major product in each of the reactions **a**)-**b**).

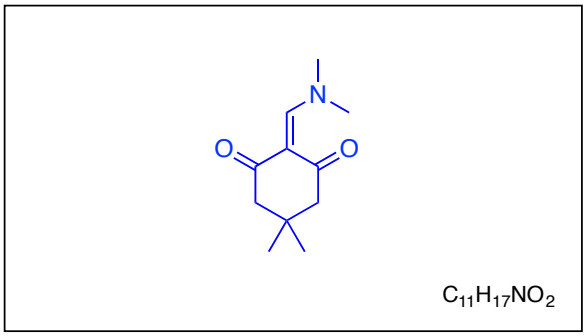
a)



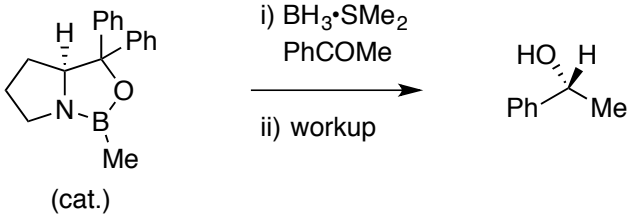


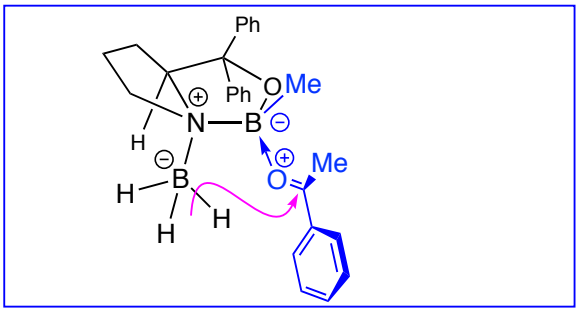
b)





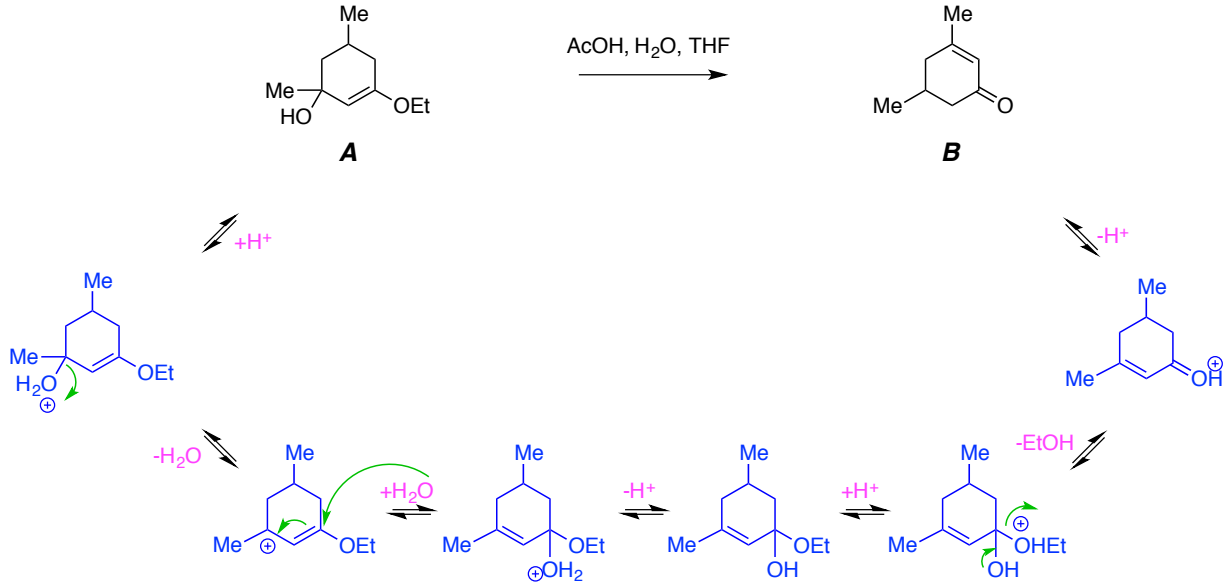
VI. (**8 points**) In the box, provide a detailed drawing that allows for rationalization of the sense of enantioselectivity of the following CBS reduction. Do not use any words in answering this question; use the template in the box as the starting point for orienting your drawing.



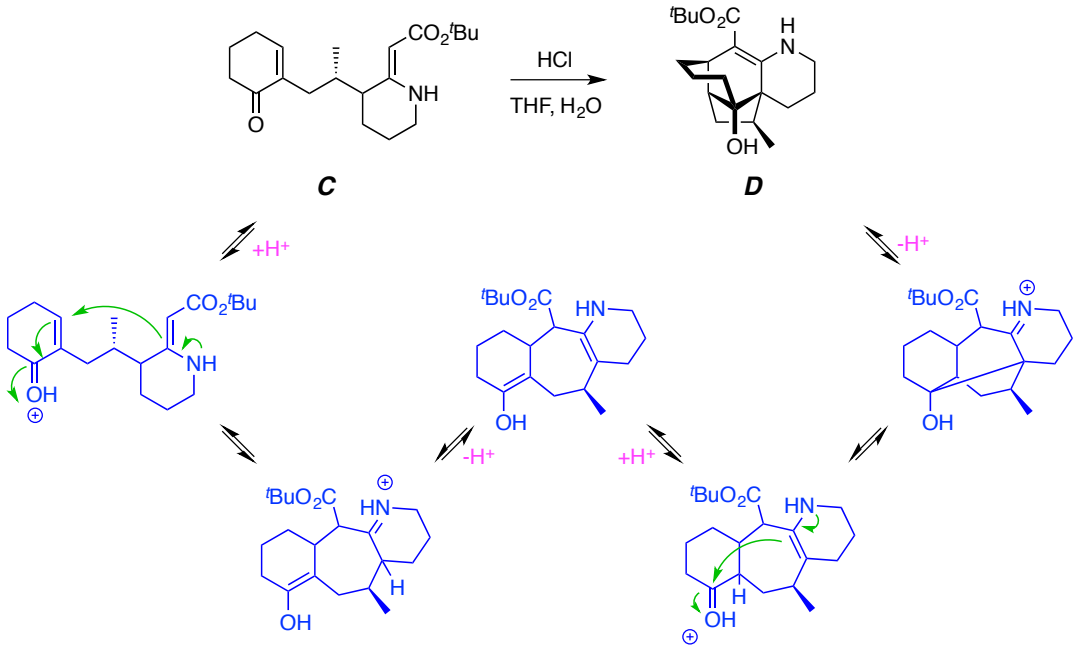


VII. (48 pts) Provide a detailed mechanism to account for each of the following four reactions. Show *ALL* intermediates, equilibria, and bond-making and -breaking steps.

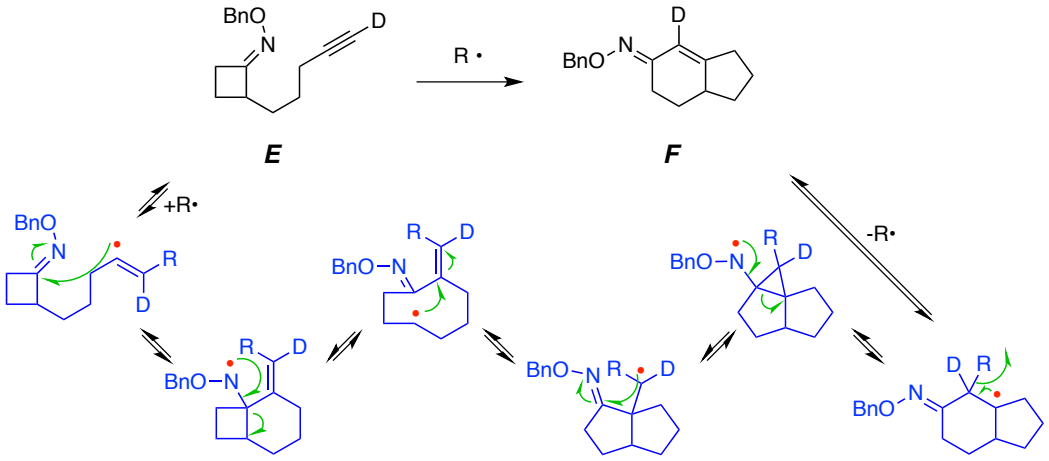
a) (12) The acid-catalyzed hydrolysis of the enol ether **A** to the enone **B**.



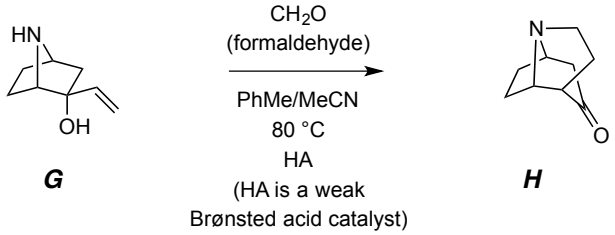
b) (10) The acid-catalyzed conversion of the vinylogous carbamate **C** to the polycyclic, tertiary alcohol **D**.



c) **(12 pts)** For the purpose of this mechanism, all you need to know about "R•" is that it is a free radical capable of undergoing reversible addition to and elimination from carbon-centers. The specifics of what it is (which we have not discussed or encountered) is otherwise not important. Account for how "R•" promotes the isomerization of **E** to **F**. Hints: note that "R" does not appear in the product, two consecutive ring expansion events are involved, and "R" is covalently present in every intermediate.



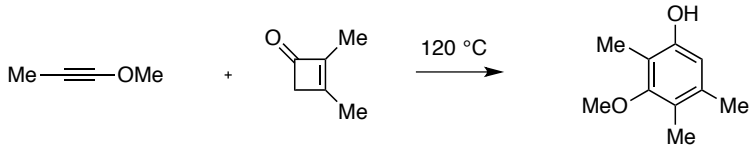
d) **(14 pts)** Production of the tricyclic aminoketone **H** by the aza-Cope-Mannich reaction of aminoalcohol **G**.



VIII. (42 pts, 7 each) Each of the following known transformations involves a series of consecutive reactions. In each case four possible sequences for the individual reaction types (or steps in the overall cascade) is suggested. Circle the one answer corresponding to the correct sequence.

Note: **"electrocyclization" here refers to *either* a ring-opening or a ring-closing event.** For example, a "4π-electrocyclization" can refer to *either* the ring closure of 1,3-butadiene to cyclobutene or the ring opening of cyclobutene to 1,3-butadiene.

a) Generation of the phenol **3** from alkyne **1** and enone **2**.



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

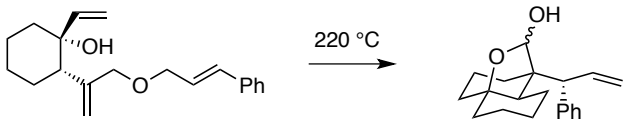
i) tautomerization, [4+2] cycloaddition, 4π-electrocyclization

ii) 4π-electrocyclization, tautomerization, [4+2] cycloaddition

iii) 4π-electrocyclization, [2+2] cycloaddition, 4π-electrocyclization, 6π-electrocyclization, tautomerization

iv) [2+2] cycloaddition, 4π-electrocyclization, tautomerization

b) Conversion of the triene **4** to the decalin derivative **5**. [Note: not every step (i.e., tautomerization and hemiacetal formation) in the overall transformation is included in the list of sequences.]



4 ***5***

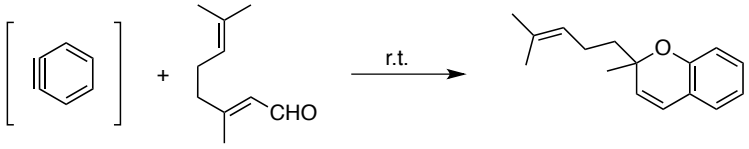
i) carbonyl-ene reaction, Cope rearrangement, Claisen rearrangement

ii) Cope rearrangement, Claisen rearrangement, carbonyl-ene reaction

iii) Claisen rearrangement, carbonyl-ene reaction, Cope rearrangement

iv) **Cope rearrangement, carbonyl-ene reaction, Claisen rearrangement**

c) *o*-Benzyne (**6**) plus the enal **7** to the benzopyran derivative **8**.



6 ***7*** ***8***

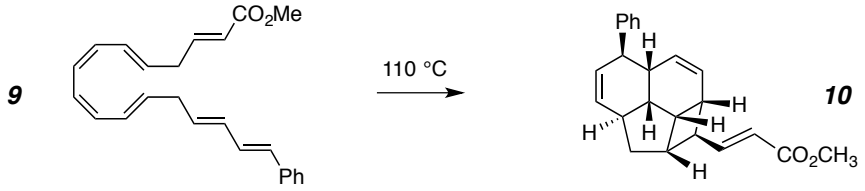
i) [2+2]-cycloaddition, 6π-electrocyclization, 4π-electrocyclization

ii) [4+2]-cycloaddition

iii) [2+2]-cycloaddition, 4π-electrocyclization, 6π-electrocyclization

iv) [4+2]-cycloaddition, 6π-electrocyclization, 4π-electrocyclization

d) Conversion of the heptaene **9** to the tetracyclic triene **10**.



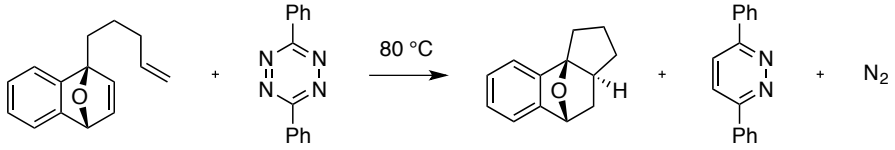
i) Diels-Alder reaction, 6π-electrocyclization, 6π-electrocyclization

ii) 8π-electrocyclization, Diels-Alder reaction, 4π-electrocyclization

iii) 8π-electrocyclization, 6π-electrocyclization, Diels-Alder reaction

iv) 6π-electrocyclization, 8π-electrocyclization, Diels-Alder reaction

e) Reaction of the tricyclic diene **11** with 3,6-diphenyl-1,2,4,5-tetrazine (**12**) to produce the tetracycle **13**, 3,6-diphenylpyridazine (**14**), and molecular nitrogen. (Hint: in the absence of **12**, **11** is stable indefinitely at 80 °C.)



11 (single enantiomer) ***12*** ***13*** (racemic) ***14***

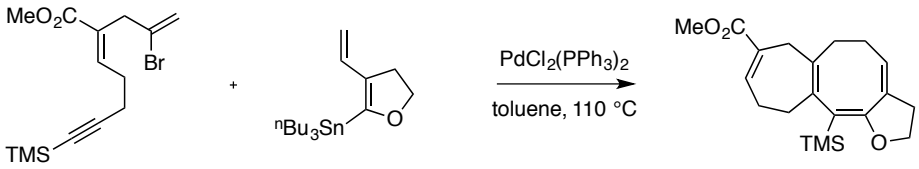
i) Diels-Alder, retro-Diels-Alder, retro-Diels-Alder, Diels-Alder

ii) retro-Diels-Alder, Diels-Alder, retro-Diels-Alder, Diels-Alder

iii) retro-Diels-Alder, Diels-Alder, Diels-Alder, retro-Diels-Alder

iv) Diels-Alder, retro-Diels-Alder, Diels-Alder, retro-Diels-Alder

f) Union of the dienyne **15** with the dienylstannane **16** to produce the tricyclic tetraene **17**.



15 ***16*** ***17***

i) oxidative addition, transmetallation, carbopalladation, reductive elimination, 8π-electrocyclization

ii) oxidative addition, carbopalladation, transmetallation, reductive elimination, 8π-electrocyclization

iii) oxidative addition, transmetallation, 8π-electrocyclization, reductive elimination

iv) ligand exchange, 6π-electrocyclization, oxidative addition, reductive elimination

• • • end of exam • • •

You may pick up your graded exam from Dan Lee (413 Smith) after noon on Thursday, May 16.

* * * Have a very productive summer of research. * * *