CHEM 347 – Organic Chemistry II (for Majors)

Instructor: Paul J. Bracher

Quiz #5

Due in Monsanto Hall 103 by:

Monday, April 28th, 2014, 5:00 p.m.

Student Name (Printed)	Solutions
Student Signature	N/A

Instructions & Scoring

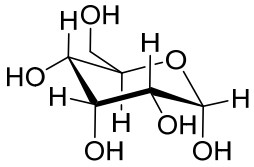
- This quiz must be turned in by the due date listed above.
- You are allowed access to any materials you wish and may discuss the questions with other students.
- Place your answers on the official answer sheet. If you print your own, please print it back-to-back on a single sheet of paper.
- Your quiz may be photocopied.

Problem	Points Earned	Points Available
I		28
II		17
III		21
IV		16
V		18
TOTAL		100

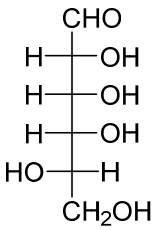
Original Problems, Required Answers, Supplemental Information

Problem I. Multiple choice (28 points total; +4 points for a correct answer, +1 points for an answer intentionally left blank, and 0 points for an incorrect answer.) For each question, select the best answer of the choices given. Write the answer, legibly, in the space provided on the answer sheet.

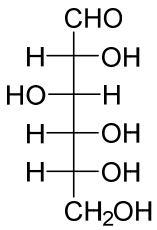
(1) C The pyranose **A** is equivalent to the aldohexose represented by which of the Fischer projections below?



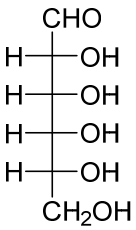
A



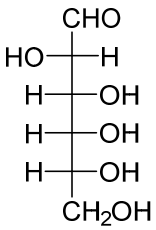
(a)



(b)



(c)



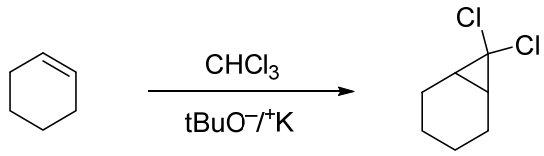
(d)

none of the above

(e)

- There a couple of ways to solve this problem. The first is to assign *R* and *S* designations to the stereocenters in the Lewis structure then to do the same to those in the Fischer projections. To save time, you can stop assigning them to a Fischer projection once you notice a difference with those in the pyranose, because if even one stereocenter is different, they are different molecules. A faster way to work this problem would be to remember the Fischer projection for D-glucose (in which only the hydroxyl group on the third carbon points left) and the fact that the pyranose structure for D-glucose has all of the substituents on the chair ring in equatorial positions. You can then look at the structure for **A**, see which groups are flipped to axial positions (relative to D-glucose), then flip those stereocenters in the Fischer projection of D-glucose.

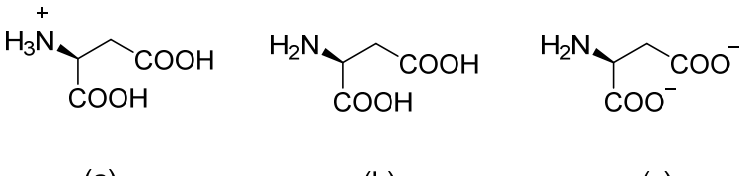
(2) D Which of the following statements best describes the following reaction?



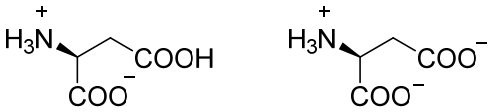
(a) the *tert*-butoxide serves as a catalyst
(b) the mechanism involves a carbanion intermediate
(c) an intermediate possesses a neutral carbon atom that lacks a full octet
(d) statements (b) and (c) are both correct
(e) statements (a), (b), and (c) are all correct

- The mechanism for this reaction involves deprotonation of chloroform by the alkoxide base. The base is never regenerated, so it is not a catalyst. A chloride anion then leaves from the carbanion intermediate to generate dichlorocarbene. The carbon atom in this intermediate has an sp^2 orbital with an electron pair and a vacant unhybridized p orbital. With two bonding pairs and one lone pair, the carbon atom lacks a full octet.

(3) E What structure represents the predominant form of the amino acid Asp when it is dissolved in an aqueous medium buffered at pH 7? You'll want to know Asp's pK_{a1} = 2.10, pK_{a2} = 3.86, and pK_{a3} = 9.82.



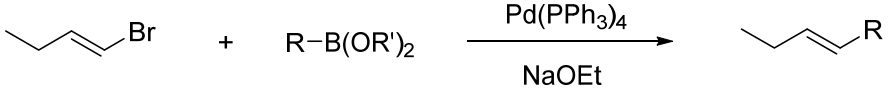
(a) (b) (c)



(d) (e)

- The equation for determining the extent to which an acid (with a given pK_a) is protonated at a given pH is pH = pK_a – log([HA]/[A^-]). When the pH equals the pK_a of an acid, the acid will be 50% protonated, 50% deprotonated. At any higher pH (more basic), the acid will be predominantly deprotonated. Here, the pH is higher than the pK_a of the two carboxylic acids, so they will be deprotonated. But since the pH is lower than the pK_a of the protonated amine, it will remain predominately protonated.

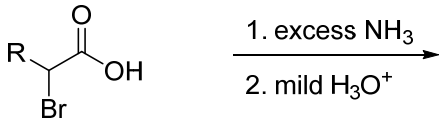
(4) D Which of the following is not a correct statement about the reaction shown below?



(a) the mechanism involves an oxidative addition to the palladium atom
(b) the mechanism involves a reductive elimination to form the product
(c) the presence of base accelerates the reaction
(d) the Pd complex is present in higher concentration than the vinyl halide
(e) the reaction works better for aryl boronic esters than alkyl boronic esters

- This is a Suzuki coupling. The mechanism involves oxidative addition of the alkyl halide to the palladium metal, transmetallation of the bromide ligand with the R group on the boronic ester, followed by reductive elimination of the organic ligands to generate the product. Base speeds the transmetallation step. The palladium(0) complex is a catalyst that is regenerated at the end of each cycle, so it is used in significantly lower concentration than the vinyl halide.

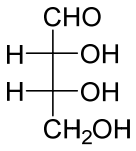
(5) A Rank the following amino acids in order of increasing simplicity/ease of preparation by the reaction shown below. The hardest amino acid to prepare by this method should be listed first in your answer. Assume the R group is the natural side chain of the amino acid without any modification.



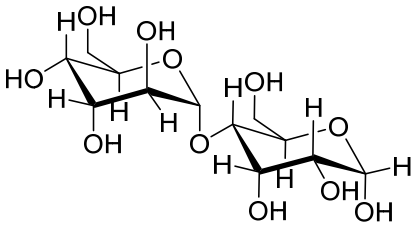
(a) proline < cysteine < phenylalanine
(b) phenylalanine < proline < cysteine
(c) phenylalanine < cysteine < proline
(d) cysteine < proline < phenylalanine
(e) proline < phenylalanine < cysteine

- This method for the synthesis of individual amino acids proceeds by an S_N2 reaction of ammonia (NH_3) on the alkyl halide. Proline is the only amino acid with a secondary amine, so it cannot be made by this reaction. Cysteine has a free thiol on its side chain that could interfere with the reaction by displacing the Br^- by an intramolecular reaction. There is no such competing reaction for phenylalanine.

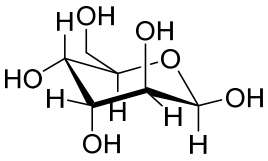
(6) D How many of the carbohydrates below will be oxidized by Tollens' reagent to produce a silver mirror on the side of the reaction vessel?



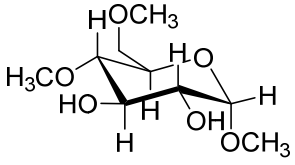
B



C



D

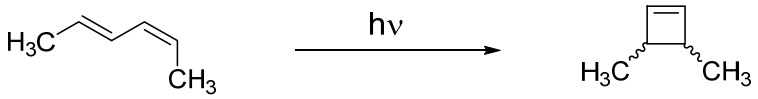


E

(a) zero
(b) one
(c) two
(d) three
(e) four

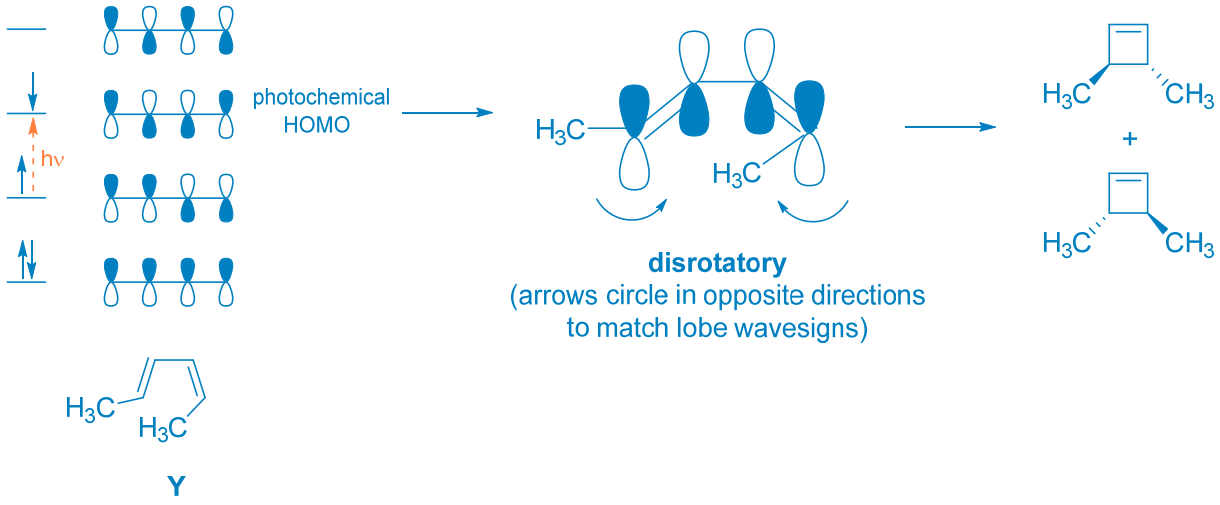
- A reducing sugar is one that has an aldehyde group capable of being oxidized. The aldehyde need only be in equilibrium with a hemiacetal, because the oxidation is irreversible and will eventually convert all of the aldehyde. Unlike hemiacetals, full acetals require acid to generate the aldehyde form, and thus, are not reducing sugars (unless acid is present). Given these constraints, **B** is reducing (it has an aldehyde), **C** is reducing (it has a hemiacetal), **D** is reducing (it has a hemiacetal), and **E** is not reducing (it has a full acetal but no hemiacetals or aldehydes).

(7) D Which of the following statements best describes the photochemical electrocyclic ring closure of (*2E*,*4Z*)-2,4-hexadiene?



(a) the reaction produces two different products
(b) the reaction produces the same product with light as with heat
(c) the reaction proceeds with a disrotatory mechanism
(d) statements (a) and (c) are both correct
(e) statements (a), (b), and (c) are all correct

- This is an electrocyclic ring closure. To predict the stereochemistry of the product(s), you need to: (i) construct a molecular orbital diagram, (ii) fill electrons into the orbitals and populate the appropriate HOMO, and (iii) twist the terminal atoms to match wavesigns of the p orbital lobes:



- Heat would produce the cyclobutene with both methyl groups in a *cis* orientation. This product is a meso compound, and thus, has no enantiomer.

Problem II. Structural determination of a carbohydrate (17 points). On your way to take an IR spectrum of a pure sample of D-glyceraldehyde, you are abducted by an overweight alien with bad breath and sandals. When you arrive on his home planet, the alien assigns you the task of determining the structure of a compound their species calls Q-billibop. You are given access to a laboratory and you discover the following:

1. Q-billibop is an aldopentose.

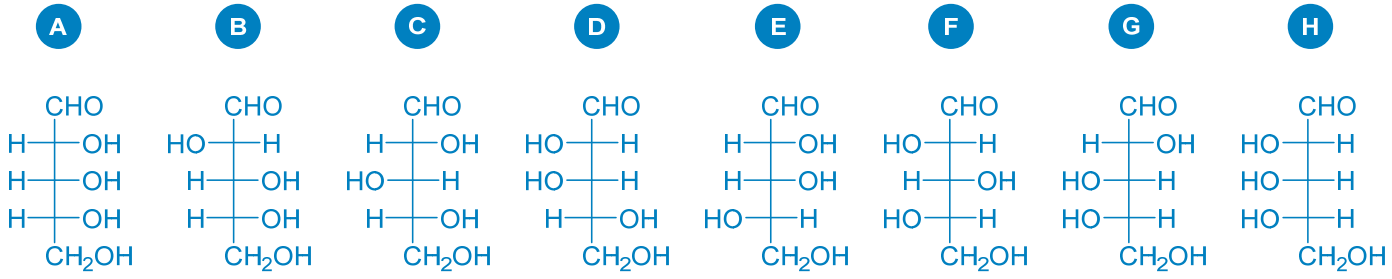
2. Treatment of Q-billibop with HNO_3 produces a compound that is optically active.

3. Subjecting Q-billibop to the Kiliani-Fischer Synthesis (1. NaCN, 2. H_2, Pd-$BaSO_4$, 3. mild H_3O^+) produces two new compounds that can be separated and purified. Both compounds are optically active, but one of these compounds loses its optical activity when treated with HNO_3.

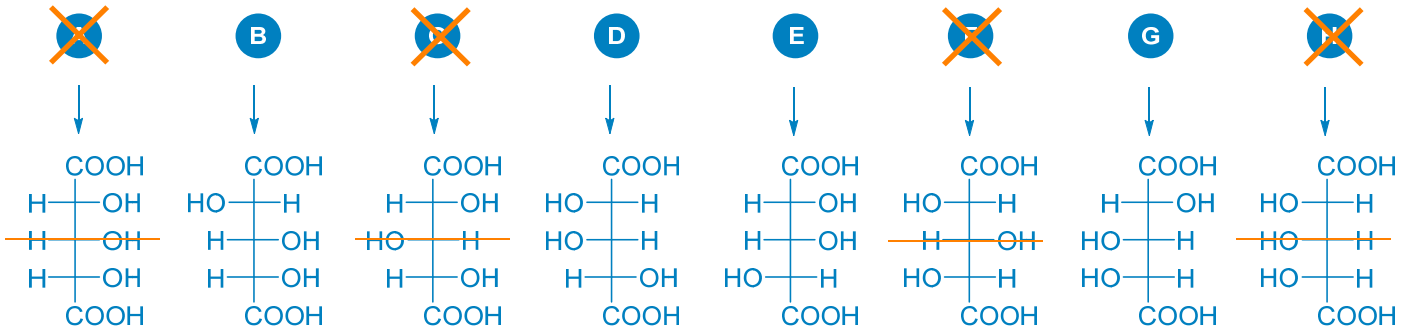
4. Subjecting Q-billibop to two rounds of Wohl degradation produces an aldotriose that melts at the same temperature as your sample of D-glyceraldehyde, but rotates plane-polarized light in the opposite direction.

Draw a Fischer projection of Q-billibop and show your work for how you determined the stereochemistry of its chiral carbons.

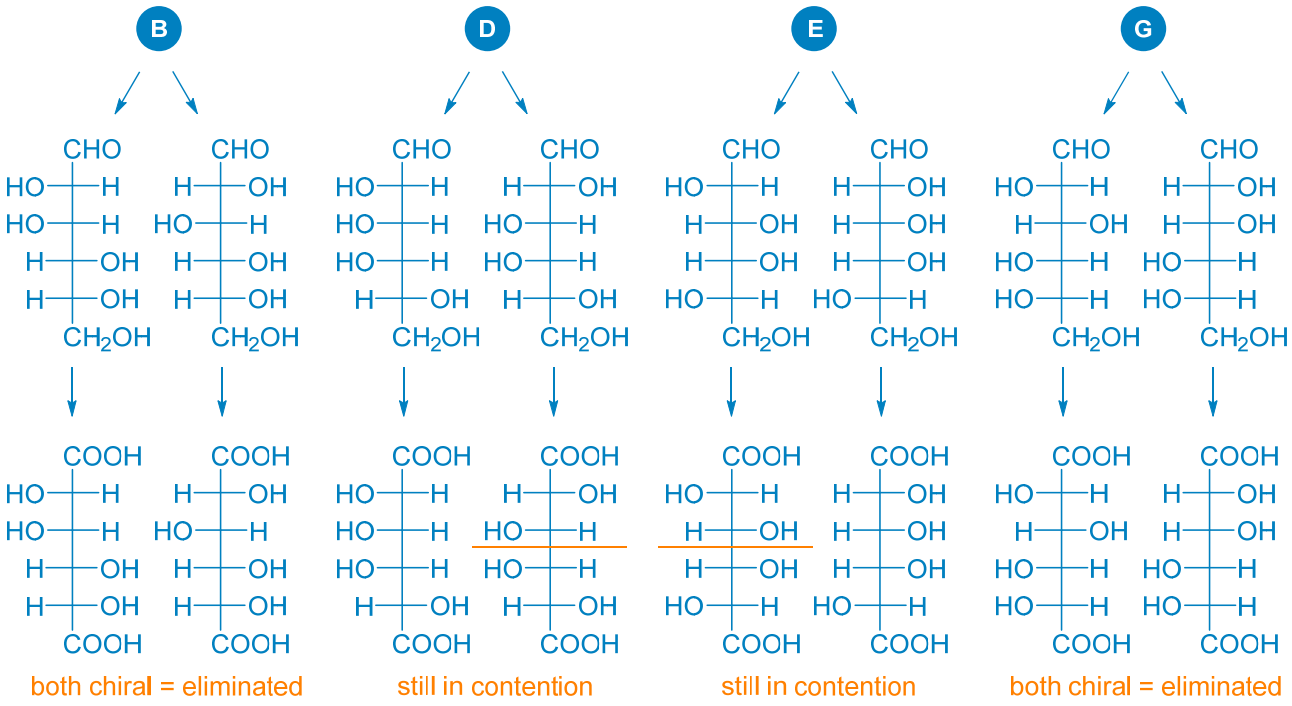
The best way to work this problem is to draw out all of the possibilities and then use the data to eliminate sugars one by one. Here, we are told that Q-bilibop is an aldopentose. Aldopentoses have three stereocenters, and thus, there are $2^3 = 8$ possibilities:



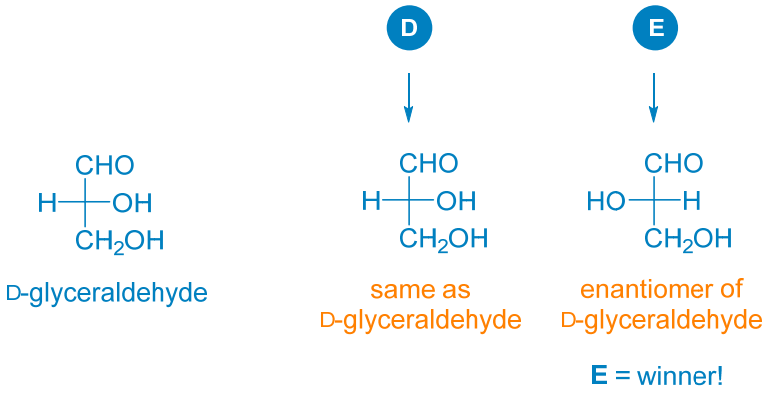
Now that we have all the possibilities, labeled **A** through **H**, let's start ruling them out with the data. You are told that treatment of Q-billibop with HNO_3—which will oxidize the termini of the sugars to carboxylic acids—yields a compound that is optically active. While this oxidation will not affect the stereochemical designations of the individual secondary alcohols, it could still produce optically inactive products that have internal planes of symmetry. Since we know Q-billibop produces an optically active diacid, we can rule out the possibilities that would produce meso compounds with the internal planes of symmetry shown below (in orange). Specifically, we rule out **A**, **C**, **F**, and **H**:



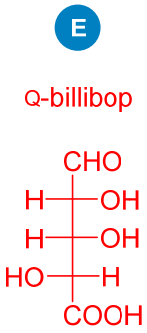
Next, you perform a Kiliani-Fischer extension of the aldopentose into an aldohexose. Let's see what that would produce for the sugars than are still in contention (**B**, **D**, **E**, and **G**):



Aldopentoses **B** and **G** produce aldohexoses that are both chiral, so **B** and **G** can be eliminated. Aldopentoses **D** and **E** yield aldohexoses that match the observations in point #3, so these are the two remaining sugars in contention to be the structure of Q-billibop. Now, we must examine the final piece of data: what happens following two rounds of Wohl degradation:

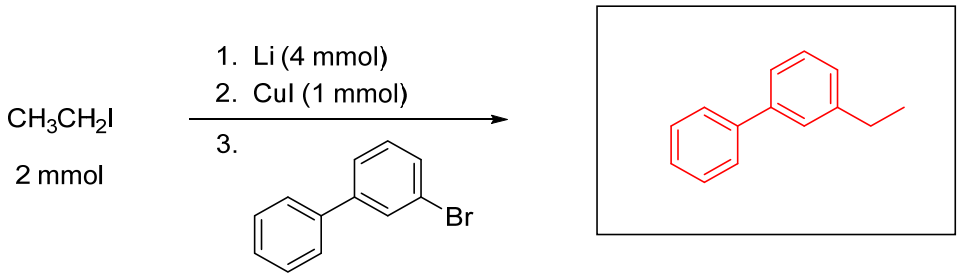


The data suggest that the product of two rounds of Wohl degradation is the enantiomer of D-glyceraldehyde (since it rotates light in the opposite direction but has the same melting point). Aldopentose **E** yields this result, but not **D**. Therefore, **E** must be the structure of Q-billibop:



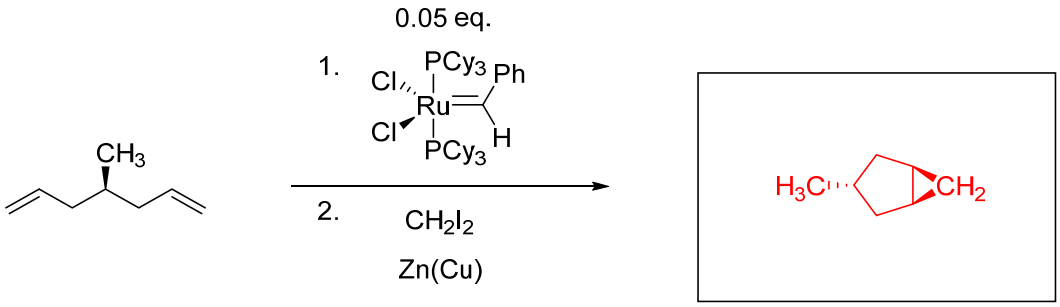
Problem III. Reactions (21 points). The following chemical reactions are missing their starting materials, products, or reagents. Write the missing compounds into the empty boxes below, as appropriate. For missing products, draw the single organic product that you expect to be produced in the highest yield among all of the possibilities. In some cases, there will be more than one correct answer that will merit full credit.

(1) (7 points)



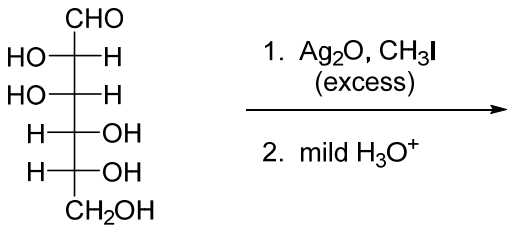
- The first step converts the ethyl iodide into ethyllithium. The next step prepares the organocuprate (Gilman) reagent Et_2CuLi. The final step is coupling of an alkyl group on the orgocuprate reagent to the aryl bromide (the Corey–House reaction).

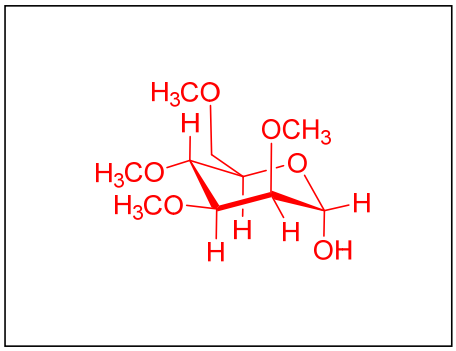
(2) (7 points)



- The ruthenium complex is Grubbs' catalyst. The first reaction is a ring-closing metathesis reaction to generate a cyclopentene compound. The second reaction is a Simmons–Smith cyclopropanation. The carbene will add to the less sterically hindered side of the cyclopentene ring, so the cyclopropane ring and methyl group will have a *trans* relationship.

(3) (7 points)

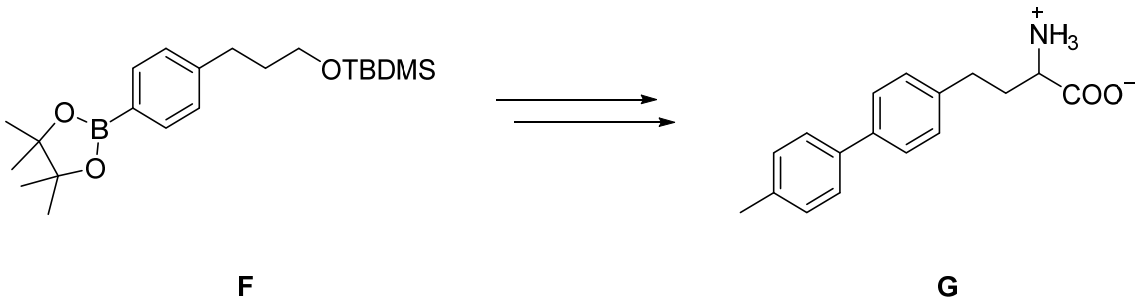




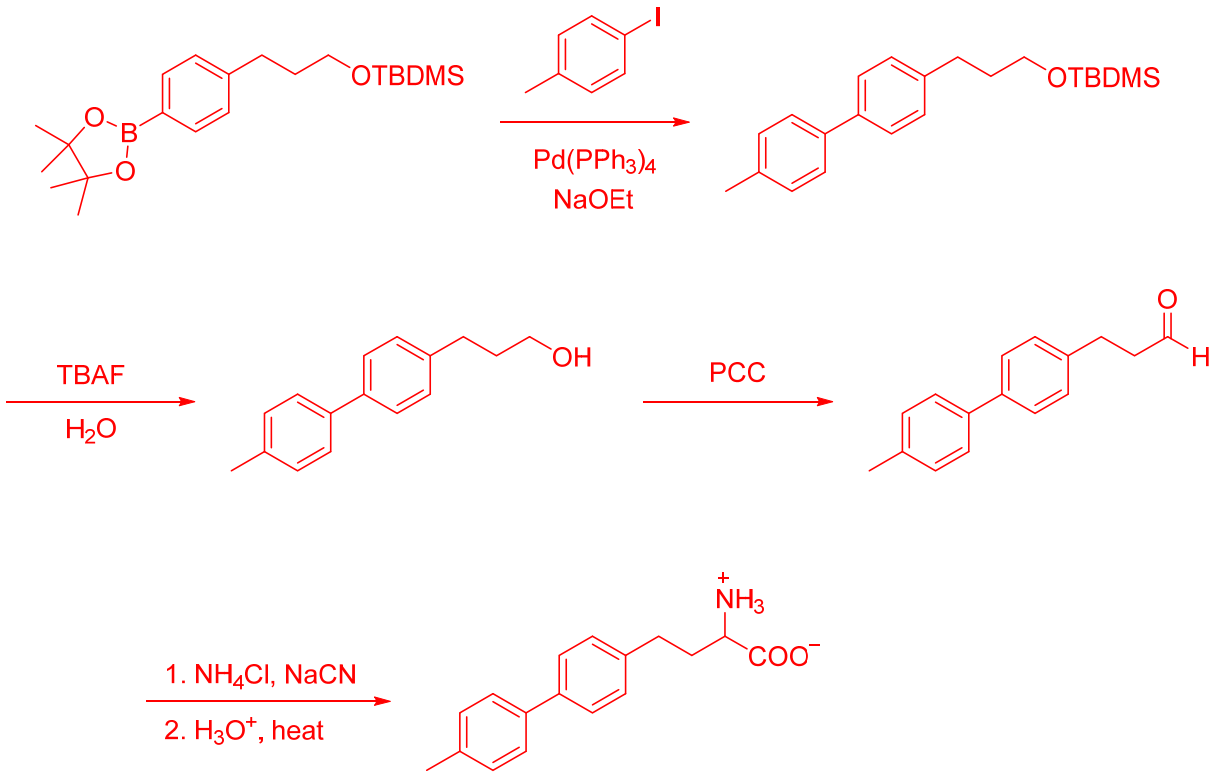
(fill in the rest of this pyranose structure)

- The starting material is D-mannose, which translates to the pyranose substitution pattern depicted above. The first reaction methylates all of the hydroxyl groups in the pyranose to OCH_3 groups. In the second reaction, the mild acid can hydrolyze the acetal at carbon-1 to a hemiacetal, but the conditions are not strong enough to hydrolyze the methyl ethers.

Problem IV. Synthesis (16 points). Design an efficient synthesis of compound **G** from compound **F** and any other materials your wish. Do not worry about stereoselectivity—you can produce a racemic mixture of the final product.

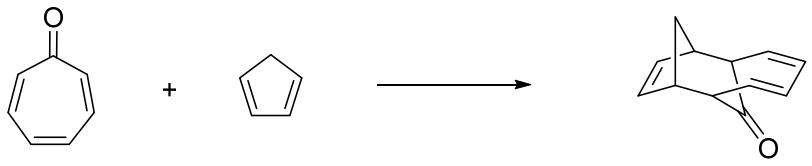


F **G**



The boronic ester in the starting material screams "Suzuki coupling", and since the other side of the molecule is already protected, it makes sense to perform the Suzuki coupling first. The amino acid portion can be intalled with a Strecker reaction should we convert the protected alcohol into an aldehyde. The deprotection is achieved with TBAF and the oxidation with PCC.

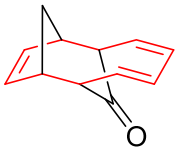
Problem V. Pericyclic Reactions (18 points). Consider the cycloaddition reaction depicted below:



J **K** **L**

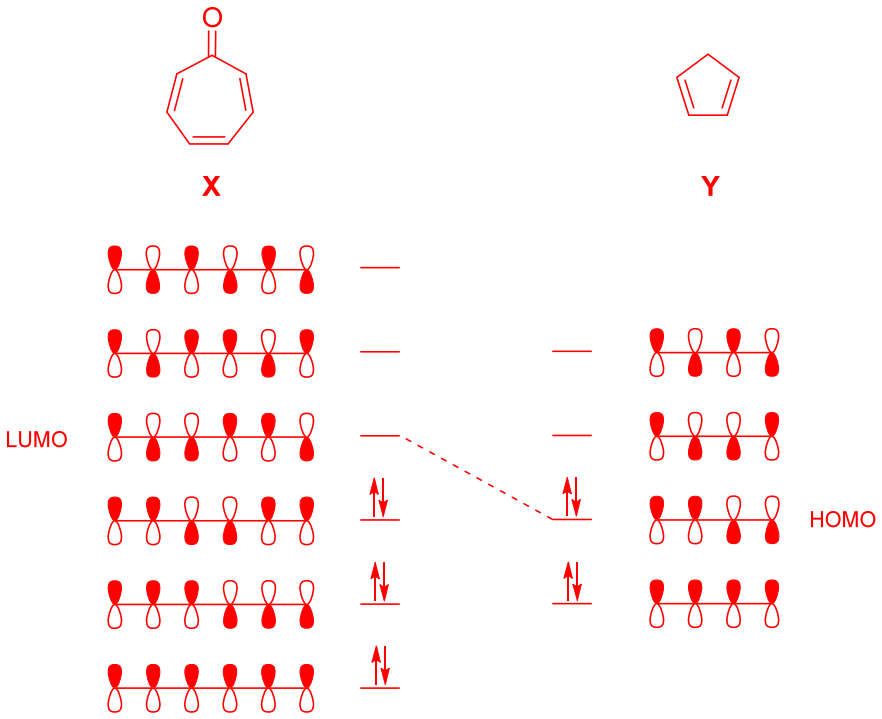
(a) Classify the reaction as an [m+n] cycloaddition. Draw all of the molecular orbitals for the two π systems that react to form the new ten-atom ring. Construct these molecular orbitals by showing permutations of atomic p orbitals interacting constructively or destructively. Use different colors or shading to indicate the wavesigns of the orbital lobes. (For an example, see slide 8 of the lecture 34 slides.)

This reaction is a [6+4] cycloaddition. The 6-atom and 4-atom π systems react to form a new 10-atom ring in the product (highlighted below). Note that two of the π bonds are lost (to form two new σ bonds), while the remaining 3 π bonds are in the ten-membered ring.



L

We construct the molecular orbitals of the two π systems as follows. Note that each higher MO has an extra node (destructive interaction between the wavesigns of the p orbitals) relative to the MO below it.



(b) Would you expect this reaction to proceed thermally (with heat), photochemically (with light), or both ways? Explain why in one or two sentences.

This reaction only proceeds under thermal conditions, where the two terminal orbitals of each π system match in symmetry. If one of the π systems is excited by a photon, a different HOMO—with opposite symmetry—will be populated such that the wavesigns of the termini of the π systems will not match.