Final Examination for **Chem 313**

7:00 p.m. December 6, 2013; **Time: 2.5 hours**

This examination consists of **13** pages, including this cover page and three pages of scrap paper. It is out of 100 points. You may remove the pages of scrap paper.

Last Name answer Key First Name _____

Signature _____ Student Number _____

Student Conduct during Examinations

Each examination candidate must be prepared to produce, upon the request of the invigilator or examiner, his or her UBCcard for identification.

Examination candidates are not permitted to ask questions of the examiners or invigilators, except in cases of supposed errors or ambiguities in examination questions, illegible or missing material, or the like.

No examination candidate shall be permitted to enter the examination room after the expiration of one-half hour from the scheduled starting time, or to leave during the first half hour of the examination. Should the examination run forty-five (45) minutes or less, no examination candidate shall be permitted to enter the examination room once the examination has begun.

Examination candidates must conduct themselves honestly and in accordance with established rules for a given examination, which will be articulated by the examiner or invigilator prior to the examination commencing. Should dishonest behaviour be observed by the examiner(s) or invigilator(s), pleas of accident or forgetfulness shall not be received.

Examination candidates suspected of any of the following, or any other similar practices, may be immediately dismissed from the examination by the examiner/invigilator, and may be subject to disciplinary action: i. speaking or communicating with other examination candidates, unless otherwise authorized; ii.purposely exposing written papers to the view of other examination candidates or imaging devices; iii. purposely viewing the written papers of other examination candidates; iv. using or having visible at the place of writing any books, papers or other memory aid devices other than those authorized by the examiner(s); and, v. using or operating electronic devices including but not limited to telephones, calculators, computers, or similar devices other than those authorized by the examiner(s)—(electronic devices other than those authorized by the examiner(s) must be completely powered down if present at the place of writing).Examination candidates must not destroy or damage any examination material, must hand in all examination papers, and must not take any examination material from the examination room without permission of the examiner or invigilator.

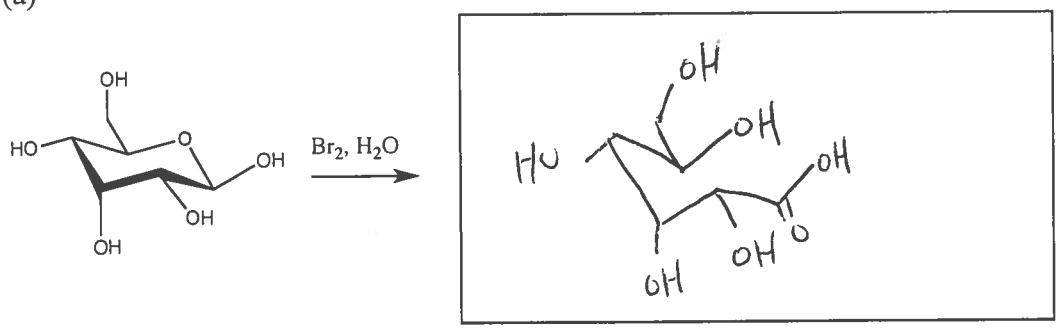
Notwithstanding the above, for any mode of examination that does not fall into the traditional, paper-based method, examination candidates shall adhere to any special rules for conduct as established and articulated by the examiner.

Examination candidates must follow any additional examination rules or directions communicated by the examiner(s) or invigilator(s).

1. [27]	_____
2. [1]	_____
3. [2]	_____
4. [5]	_____
5. [4]	_____
6. [8]	_____
7. [7]	_____
8. [10]	_____
9. [6]	_____
10. [10]	_____
11. [8]	_____
12. [4]	_____
13. [8]	_____
Total [100]	_____

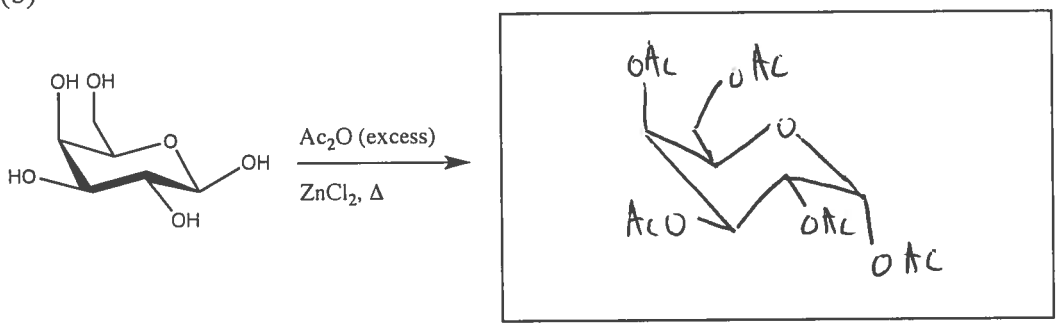
1. [27 points] Predict the products of the reactions below. Show stereochemistry where appropriate. You only need to draw the key product, not the by-product.

(a)



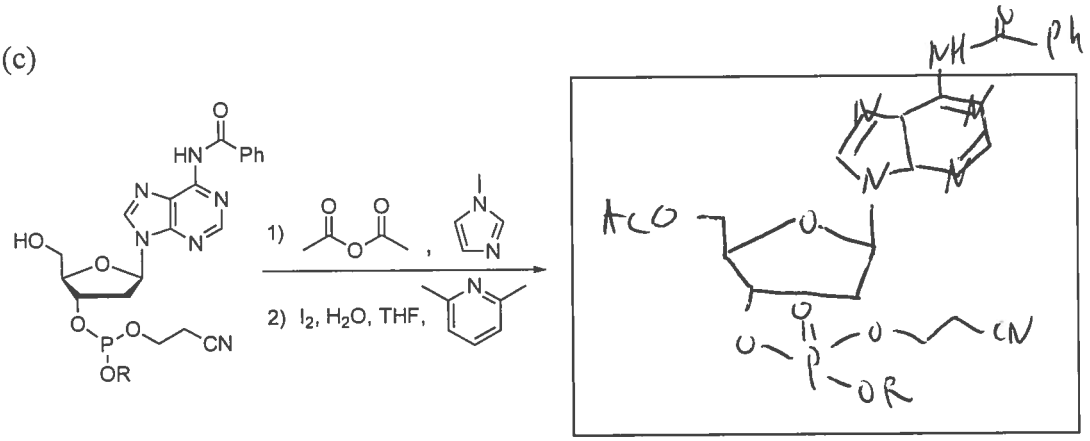
Any form of the main product is OK.

(b)

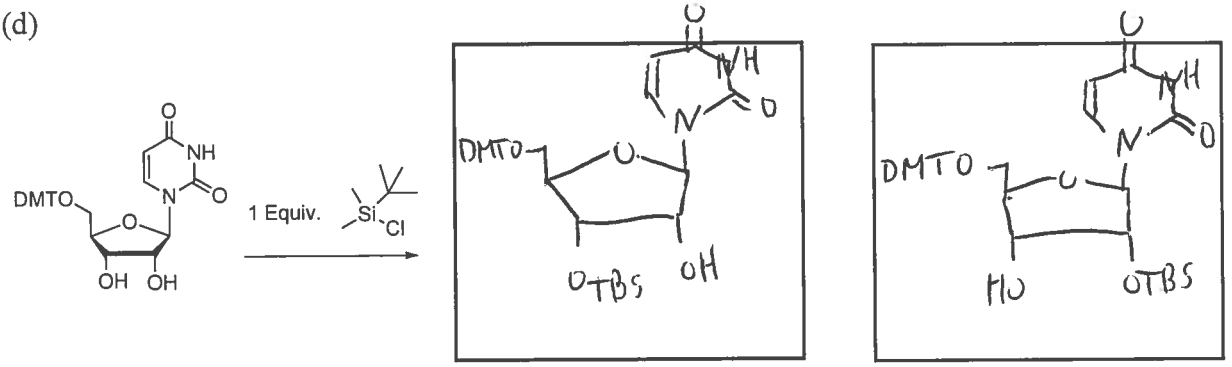


Main Product Only

(c)



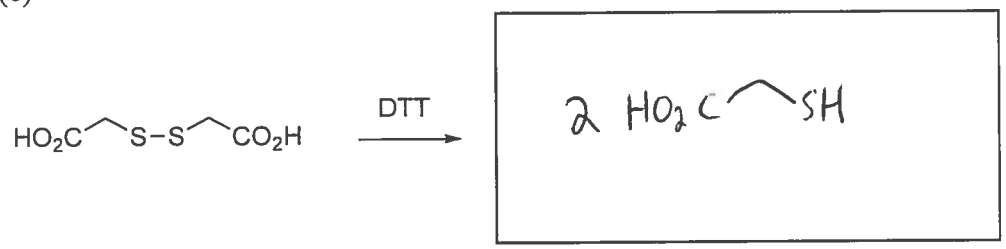
(d)



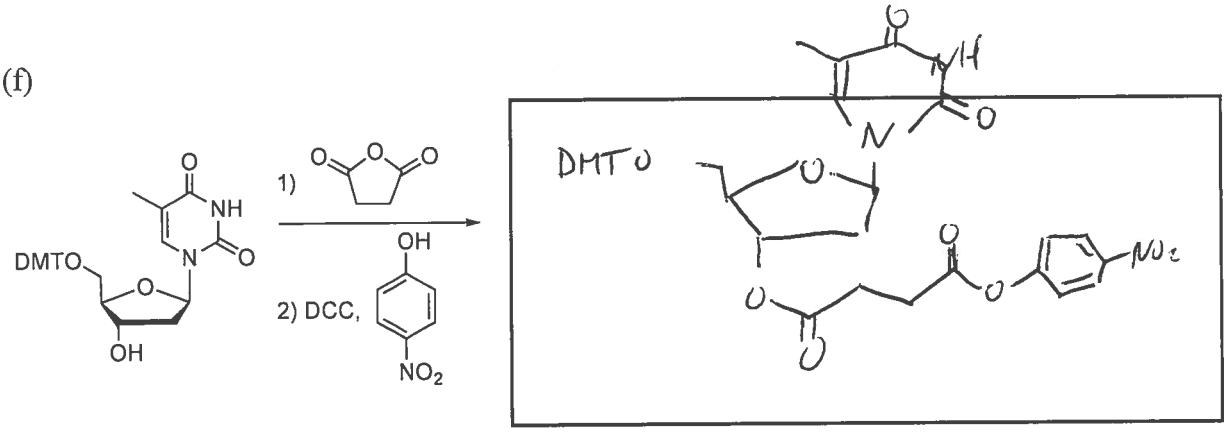
Two Major Products Only

1. Continued

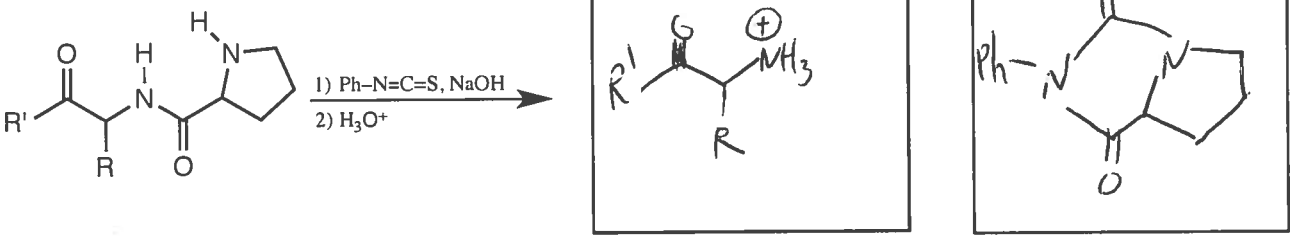
(e)



(f)



(g)



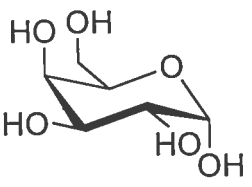
2 Major Products

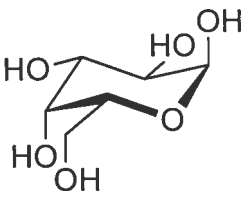
2. [1 point] The two compounds below are (circle the best answer):

(a) Enantiomers (b) Diastereomers

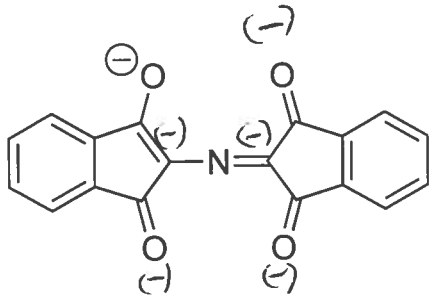
(c) Identical (d) Conformers

(e) Constitutional Isomers (f) Resonance Structures

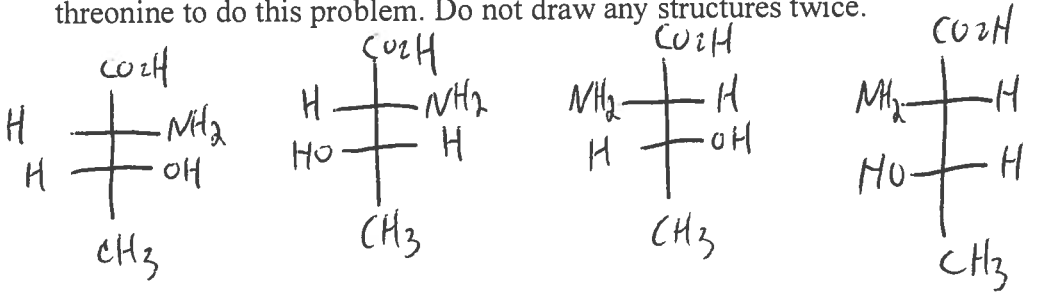




3. [2 points] Place a (–) next to each atom on the structure below that can carry a charge in a resonance structure. It is not necessary to draw other resonance structures.



4. [5 points] Draw all the isomers of the α-amino acid threonine obtained via the Gabriel synthesis using acetaldehyde (CH_3CHO) as the key electrophile. Draw stereochemistry clearly where appropriate; suggestion: use Fischer Projections. Note: you do not need to know the structure of threonine to do this problem. Do not draw any structures twice.



5. [4 points] A natural protein, **N**, contains four cysteines (R = CH_2SH). **Propose experiments** that would address the following questions. Be clear about conditions you propose (e.g., solvent, pH, reagents needed). Assume you have a way to test for the activity of protein **N**, and that only the natural form of **N** will have any activity. You have no spectrometers. (a) In its native form (i.e., the natural form that has activity), does **N** contain any disulfide bonds? (More than one correct answer is possible.) add DTT, pH 9, test for activity:

If there is activity, N does not contain disulfi

If there is no activity, N does contain disulfi

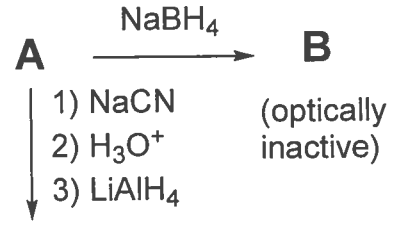
(b) If **N** does contain disulfides, is the natural form of **N** the thermodynamically most stable form?

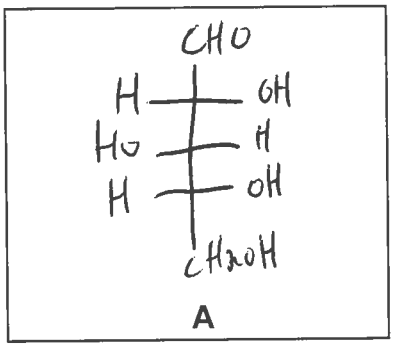
add to GluOx/GluRed buffer pH 9, test for activity

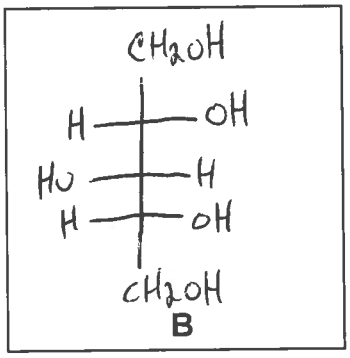
If active, the answer is yes.

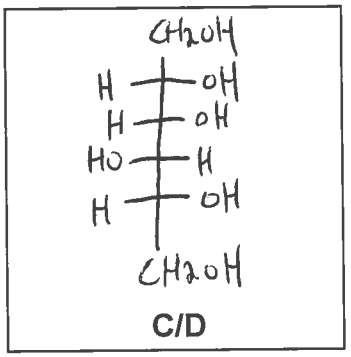
If inactive, the answer is no.

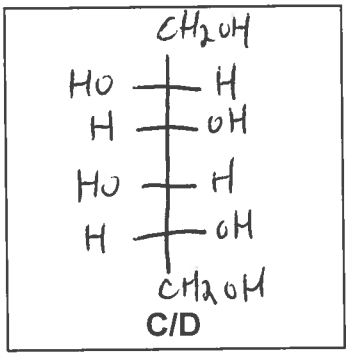
6. [8 points] **A** is a pure sugar that yields **B** as the only product after treatment with $NaBH_4$. **A** yields **C** and **D** after the treatments shown. Propose structures for **A-D**. (You don't need to show your work.)



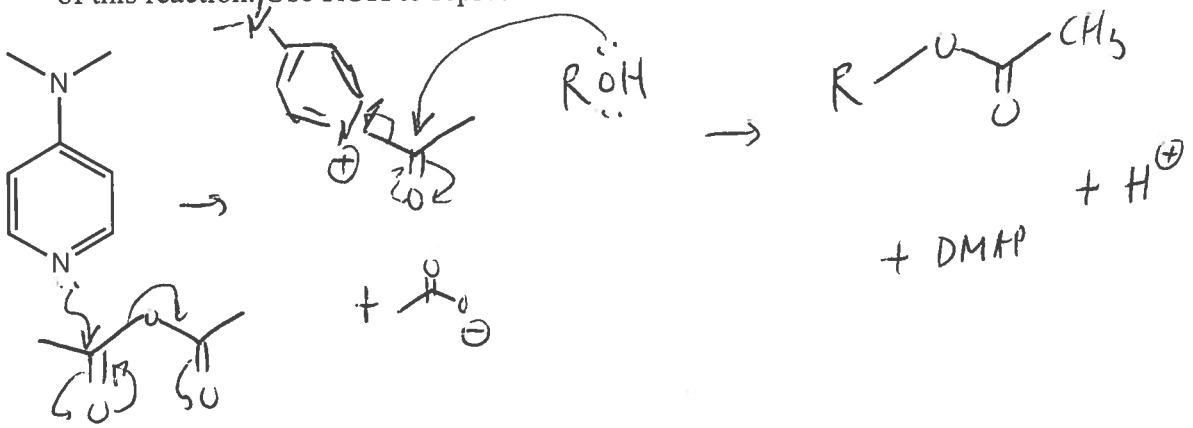






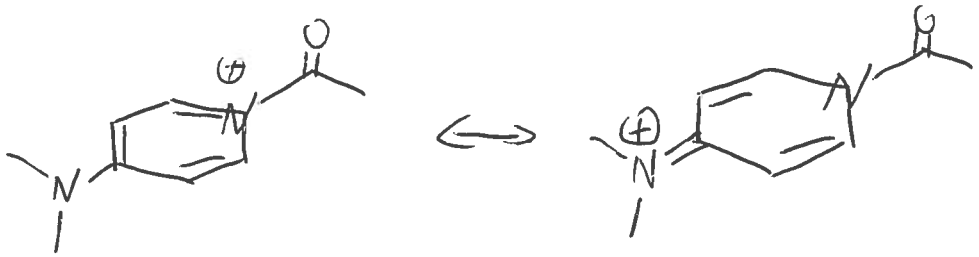


7. [7 points] (a) DMAP, 4-dimethylaminopyridine, below, is often used as a nucleophilic catalyst in capping (using Ac_2O) the 5' OH of a growing oligo during DNA synthesis. Show the mechanism of this reaction. Use ROH to represent the 5' OH.



(b) What is an advantage of DMAP over pyridine as a nucleophilic catalyst? Explain using structures.

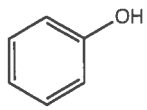
The NMe_2 group enhances the nucleophilicity of the pyridyl N:



CB = conjugate base

8. [10 points] Explain the relative acidities of the pairs below:

(a)



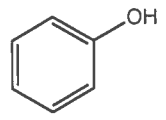
CH_3CH_2OH

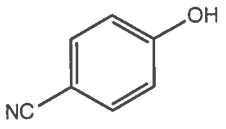
pK_a: 10.0 17

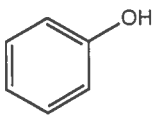
$CH_3CH_2O^{\ominus}$: the charge is localized

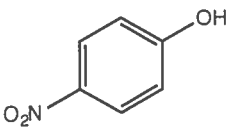
: the charge is delocalized around the ring.

(b) Provide a simple explanation that covers both pairs:

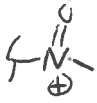




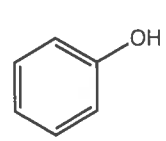


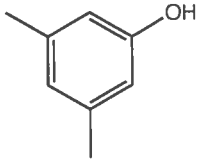


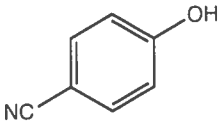
pK_a: 10.0 8.0 10.0 7.2

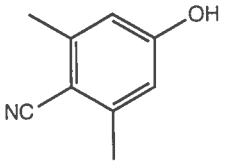
↳ C≡N and  are ewg's ; they stabilize the CB's.

(c) Provide a simple explanation that covers both pairs:





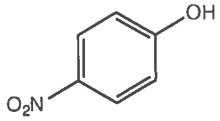


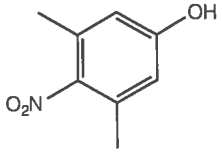


pK_a: 10.0 10.2 8.0 8.2

The Me groups are weakly edg's via hyperconjugation.

(d) Provide an explanation for the pK_a differential below. Note that the magnitude is different from that in part (c): you need to provide a somewhat different explanation to that you gave for part (c).





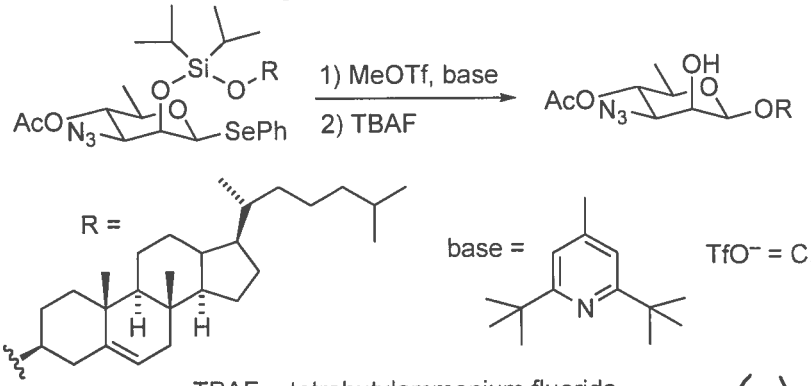
pK_a: 7.2 8.2

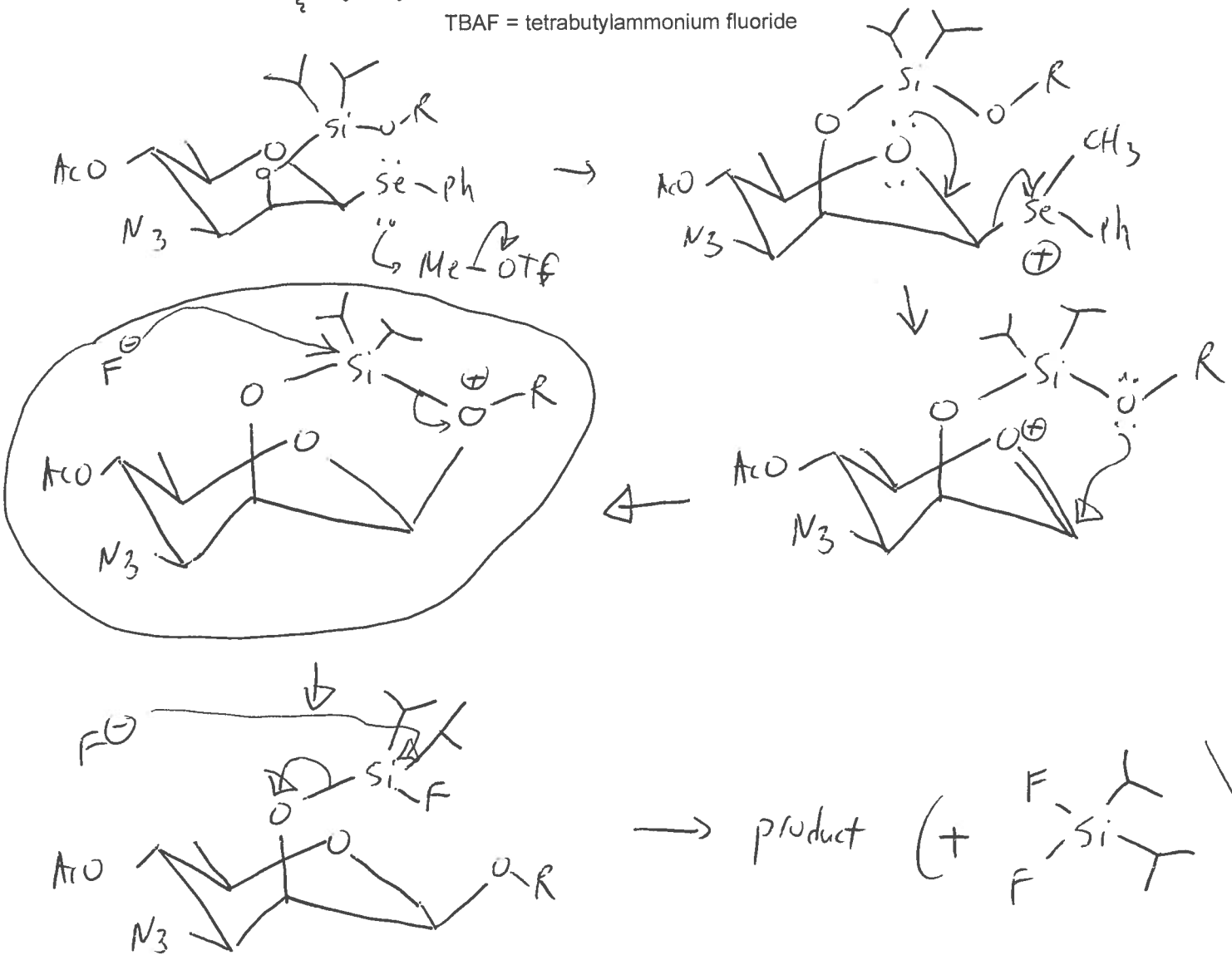
The Me groups sterically push the nitro group out of conjugation with the ring, thus the nitro group loses some of its ewg effect.

(e) What two electronic factors can be separated out, at least in part, from the data in part (d) and that the pK_a of phenol is 10.0? Explain.

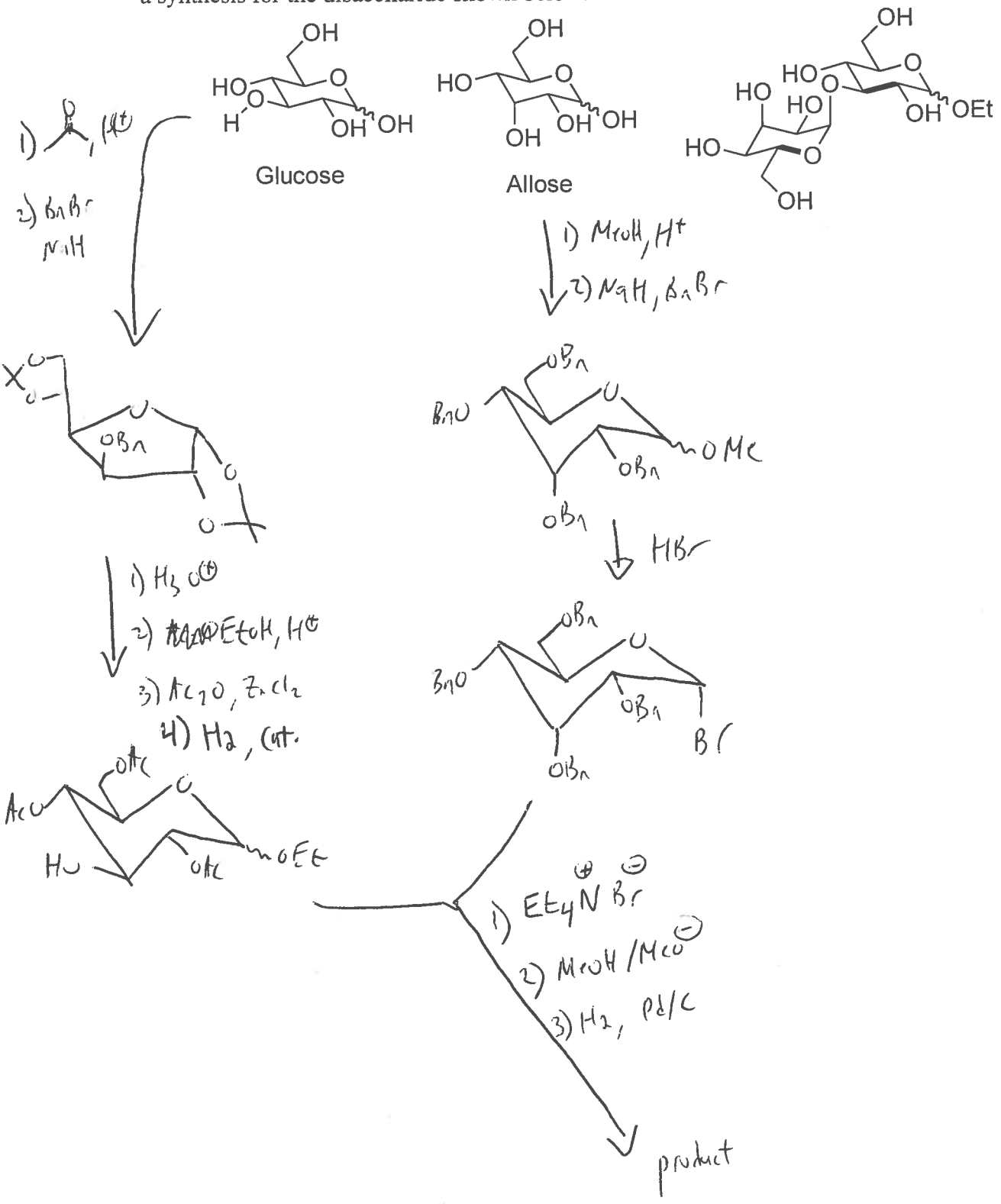
Resonance and induction. Resonance is disrupted, at least in part, while induction remains intact.

9. [6 points] In order to achieve high 1,2-cis selectivity, researchers linked cholesterol (ROH) to a sugar using the procedure below. Propose a mechanism for both steps. **Circle** the intermediate formed after the first step. Hint: The intermediate is charged. Notes: TfO^- is a good leaving group; the selenium of R–Se–R can be nucleophilic (Se is just under S on the Periodic Table). Assume water is present in the final workup of the product. (Org. Bioorg. Chem. **2010** 3596)

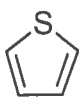




10. [10 points] With glucose and allose as your only sugars, and any other reagents you want, propose a synthesis for the disaccharide shown below.



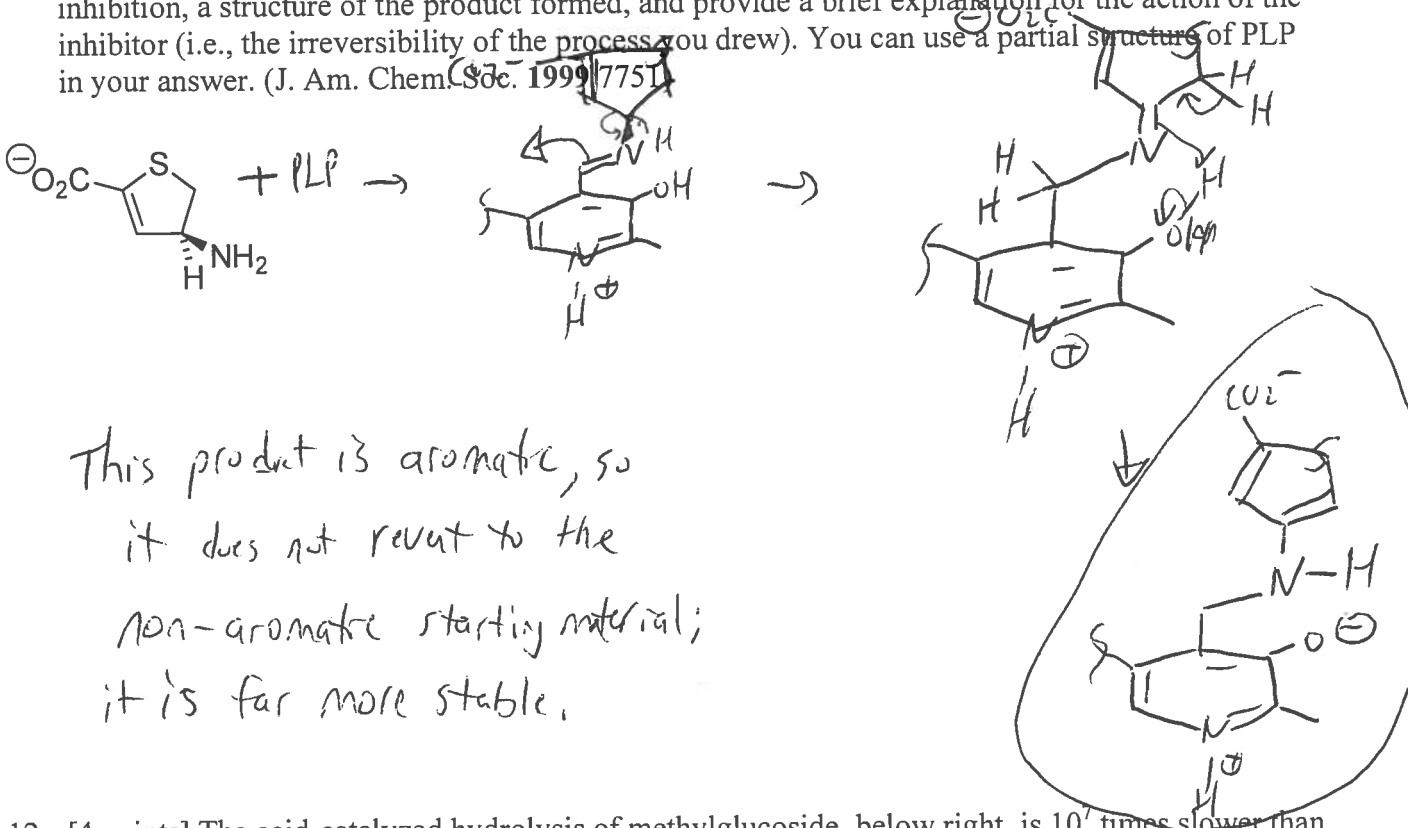
11. [8 points] (a) Thiophene is aromatic. Provide a brief explanation.



Thiophene

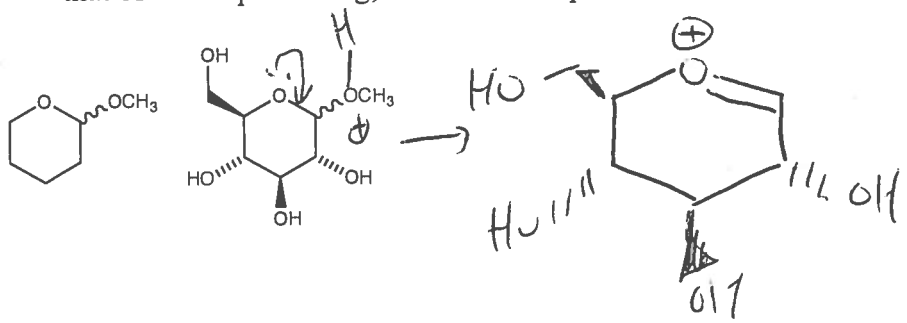
It has 6 π e⁻ in a closed loop of sp^2-hybridized atoms.

(b) Inhibition of γ-aminobutyric acid amino transferase (a PLP enzyme) has been achieved using (*S*)-4-amino-4,5-dihydro-2-thiophenecarboxylic acid (below). This work shows that knocking out the enzyme itself is not necessary as the inhibitor acts only on PLP. Propose a mechanism for this inhibition, a structure of the product formed, and provide a brief explanation for the action of the inhibitor (i.e., the irreversibility of the process you drew). You can use a partial structure of PLP in your answer. (J. Am. Chem. Soc. **1999**, 7751)



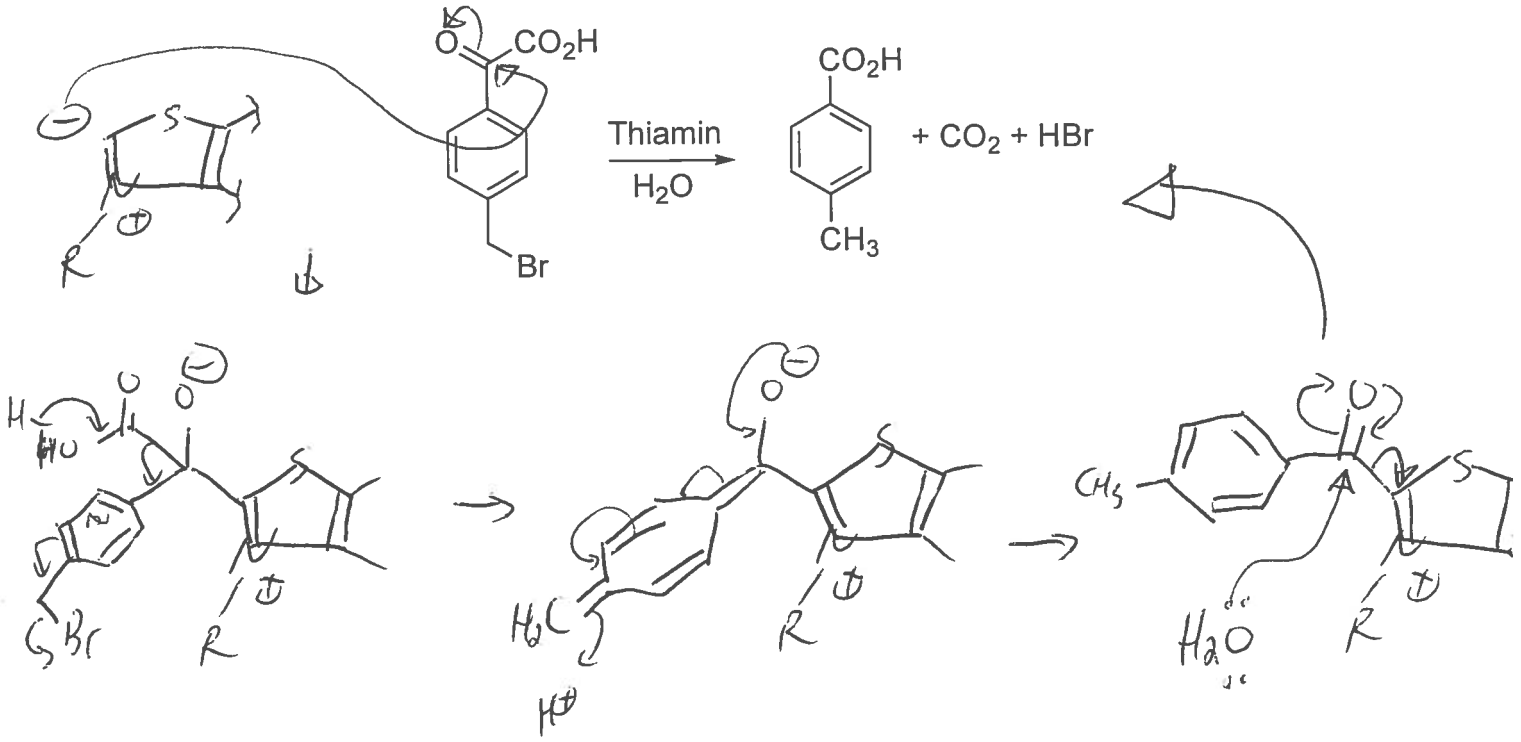
This product is aromatic, so it does not revert to the non-aromatic starting material; it is far more stable.

12. [4 points] The acid-catalyzed hydrolysis of methylglucoside, below right, is 10^7 times slower than that of its simple analog, below left. Explain.



This oxocarbenium is inductively destabilized by the 2-OH, compared to the simple analog, which lacks a 2-OH.

13. [8 points] (a) Propose a mechanism for the thiamin-catalyzed reaction shown below.



(b) Based on the above reaction, which is faster, loss of Br^- or protonation at C2α? Explain your answer.

Loss of $Br^{\ominus}$. Protonation at C2α would not give the product

Prot. @ C2α would yield: