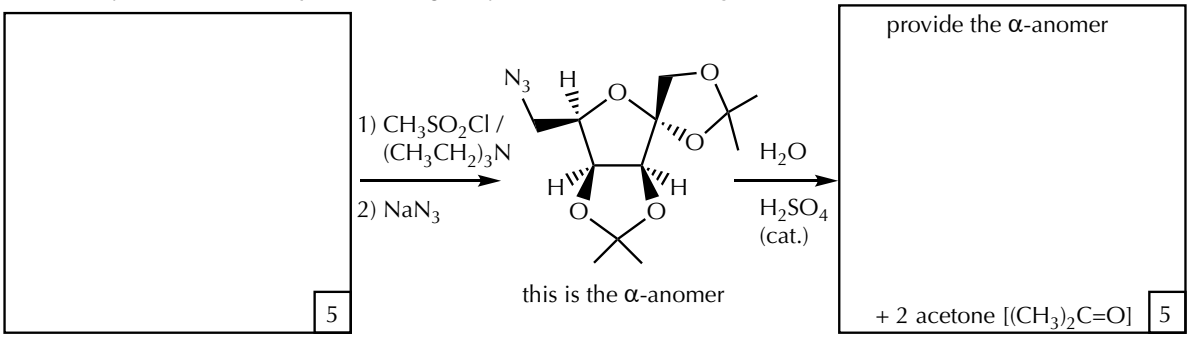
CHEM 215
WN 2022
Final exam

Cover page and pKa table removed; 120 minutes

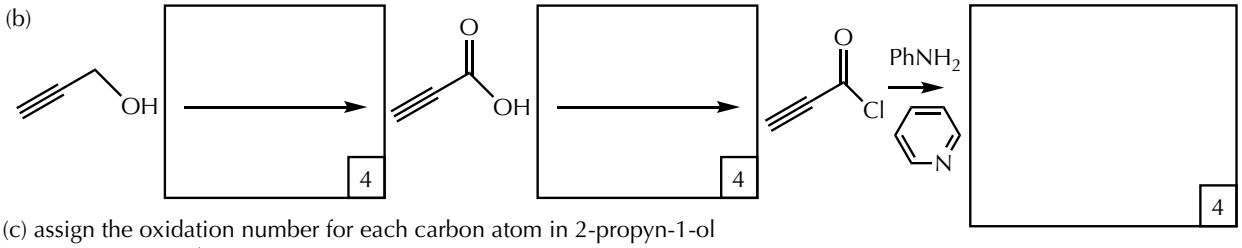
Question 1 (50 points) **Name** _____

Provide the missing product(s), starting material(s), or reaction conditions for the following transformations. Include stereochemistry when it is known, and otherwise follow the directions.

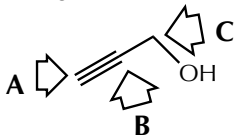
(a) from the synthesis of DGJ, a potential drug for lysosomal disorders (*Org Lett*, **2011**, *13*, 4064)



(b)



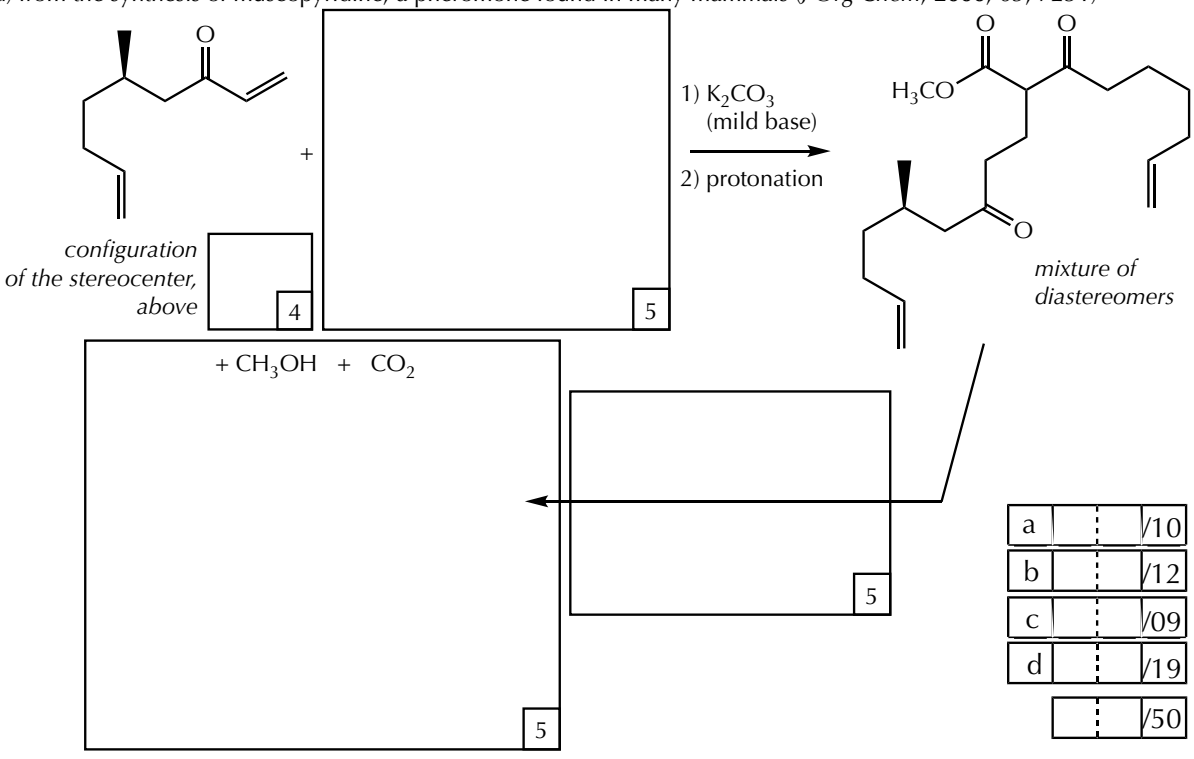
(c) assign the oxidation number for each carbon atom in 2-propyn-1-ol



A 3 **B** 3 **C** 3

be sure to include the mathematical sign + or -

(d) from the synthesis of muscopyridine, a pheromone found in many mammals (*J Org Chem*, **2000**, *65*, 7231)



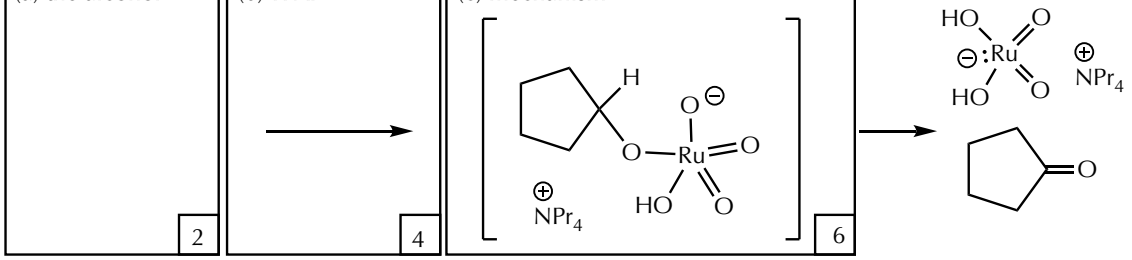
a		/10
b		/12
c		/09
d		/19
		/50

Question II (40 points) **Name** _____

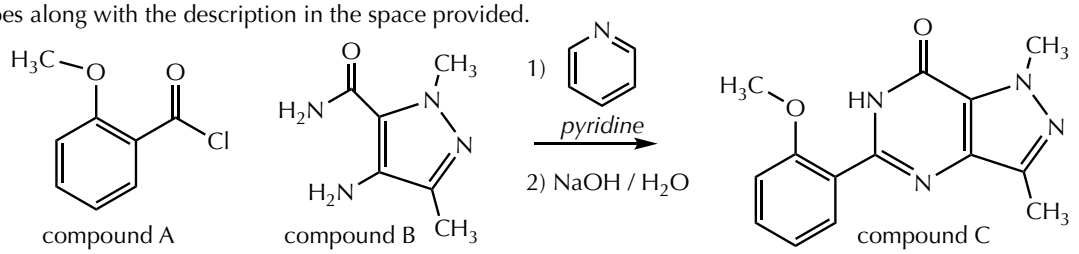
A. Tetrapropylammonium perruthenate (TPAP) is an oxidizing agent. In its mechanism of action, an Ru=O undergoes an addition reaction by an alcohol to give the intermediate shown in the brackets. The intermediate then undergoes an intramolecular reaction that results in the products shown on the far right. Draw three things: (a) the structure of the alcohol, (b) the structure of TPAP (an ionic compound), and (c) the curved arrow mechanism for the intramolecular reaction.

Pr = propyl $-CH_2CH_2CH_3$

(a) the alcohol 2 | (b) TPAP 4 | (c) mechanism 6



B. The main steps in the mechanism for the following transformation are provided as descriptions. Draw the result that goes along with the description in the space provided.



(a) Step 1. Compound A reacts with pyridine to give an acylpyridinium intermediate. Draw this intermediate, which is an ionic compound. 6

(b) Step 2. Draw the 2° amide that results when the acylpyridinium intermediate undergoes an acylation reaction with the 1° amine in compound B. 6

(c) Step 3. The 1° amide in the product of part (b) is deprotonated by NaOH to give its conjugate base. Draw the most significant resonance form of the conjugate base (an ionic compound) 6

(d) Step 4. Draw the uncharged tetrahedral intermediate when the anion from Step 3 undergoes an intramolecular addition to the 2° amide, followed by protonation. 6

(e) To form the observed product, the mechanism is proposed to be (i) assisted ionization of a hydroxyl group to give a stabilized carbocation followed by (ii) deprotonation. What label best describes this mechanism (select one)? 4

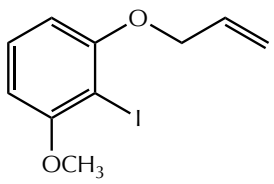
☐ E2 ☐ S_N1 ☐ E1cb
☐ S_N2 ☐ E1 ☐ A_N

A	/12
B	/28
	/40

Question III (50 points) **Name** _____

Complete the following reactions.

(a)



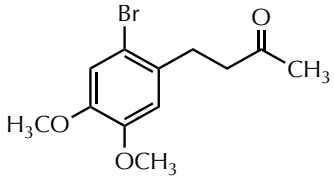
$HSnBu_3$

$[(CH_3)_3CO]_2$, Δ

+ I-$SnBu_3$ 7

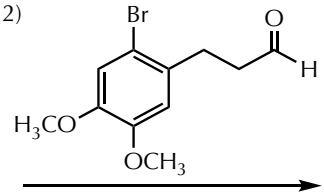
a racemic mixture results, draw one of the enantiomers

(b) *Org Lett*, **2022**, *24*, 1491.



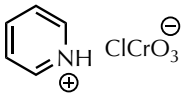
1) $[(CH_3)_2CH]_2NLi$ (LDA)

2)



3) protonation

4)



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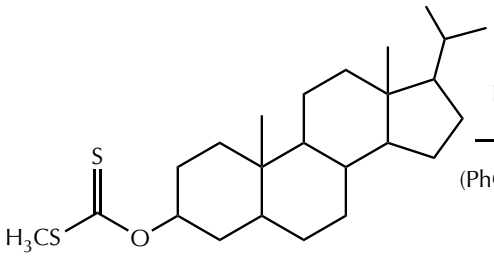
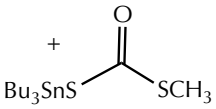
(c) *J Org Chem*, **2002**, *67*, 1192.



$HSnBu_3$

$(PhCO_2)_2$, Δ

\+



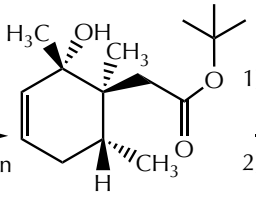
6

(d) *Org Lett*, **2022**, *24*, 921.

8

1) 1 equiv. CH_3Li low temp.

2) protonation



1) excess $LiAlH_4$

2) protonation

7

1) $(COCl)_2$ $(CH_3)_2SO$

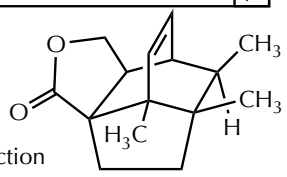
2) $(CH_3CH_2)_3N$

7

many steps

8

intramolecular Diels-Alder reaction



result from normal *endo* transition state model

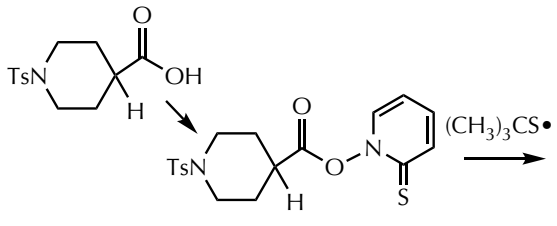
a		/07
b		/07
c		/06
d		/30
		/50

Question IV (26 points) **Name** _____

A. There is a radical reduction of carboxylic acids called the Barton decarboxylation. The mechanism is analogous to the reduction reaction of alcohols via the xanthate ester derivative. Compound D, which is derived from the corresponding carboxylic acid, is heated with *tert*-butylthiol, $(CH_3)_3CSH$ and AIBN. The resulting *tert*-butylthio radical, $(CH_3)_3CS\bullet$, reacts with compound D to give a radical intermediate. The intermediate then fragments into the three-part mixture shown below, on the far right. Draw two things:

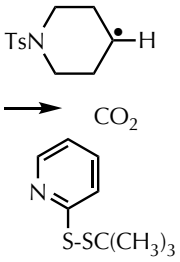
(a) a resonance contributor of the intermediate derived from compound D plus the *tert*-butylthio radical

(b) the radical (fish-hook arrow) mechanism for its fragmentation reaction into the three-part mixture

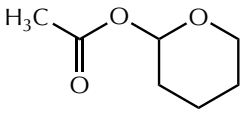


draw intermediate & the mechanism

10



B. The mechanism of the following isomerization reaction is described below. Provide the structures corresponding to these descriptions.



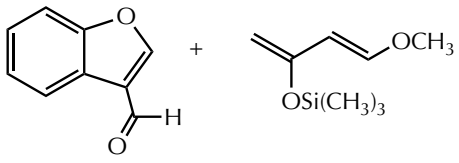
Under acid-catalyzed conditions, protonation of the carbonyl group is followed by assisted ionization to give a carboxylic acid and a resonance-stabilized carbocation. Draw them (most significant contributors).

10

The enol tautomer of the carboxylic acid recombines with the carbocation and it is deprotonated to give a structural isomer of the original starting material as the observed product. Draw it.

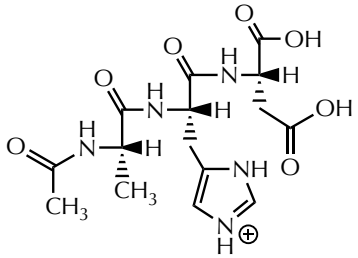
6

C. Provide one of the enantiomers of the product from this highly regio- and diastereoselective (*endo* transition state) Diels-Alder reaction (*J Org Chem*, **2009**, *74*, 1237).



15

D. The N-acetyltripeptide shown here is in its low pH (~ pH 1) form. To second decimal place accuracy (i.e., 9.35), estimate the value of its isoelectric point.

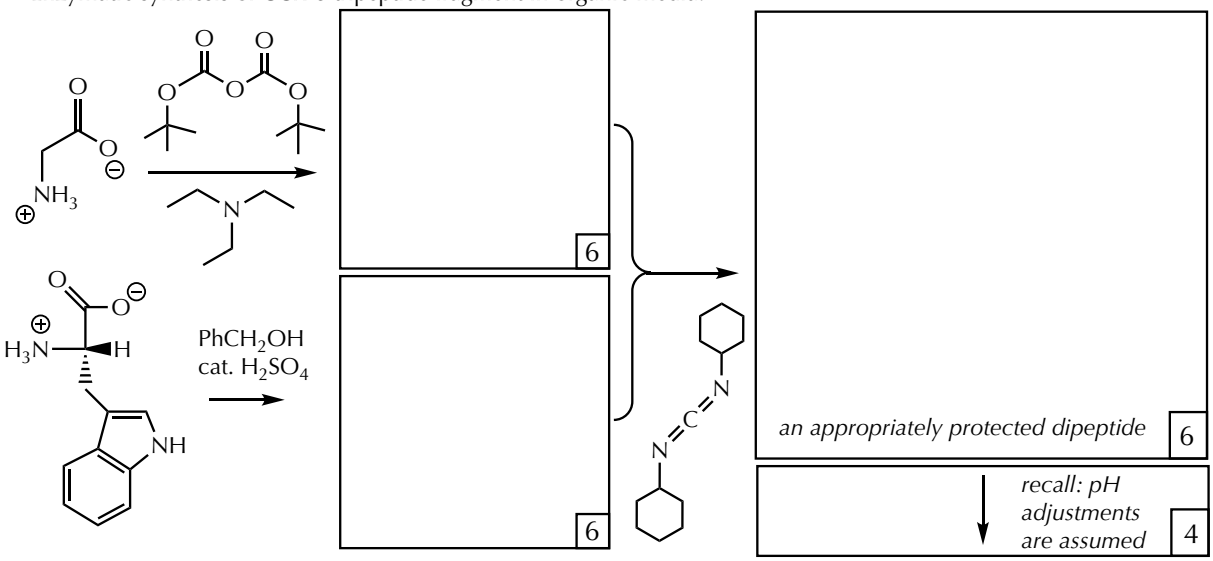


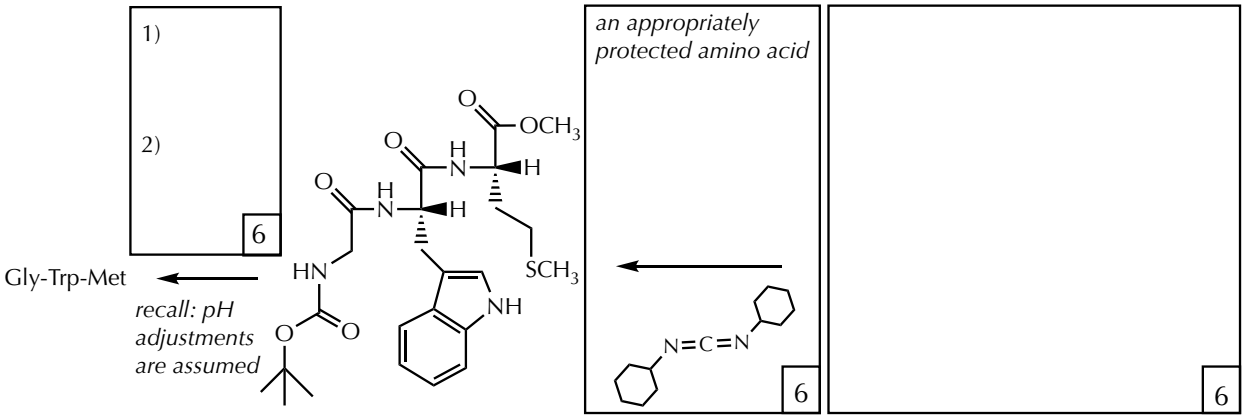
4

A		/10
B		/16
C		/15
D		/04
		/45

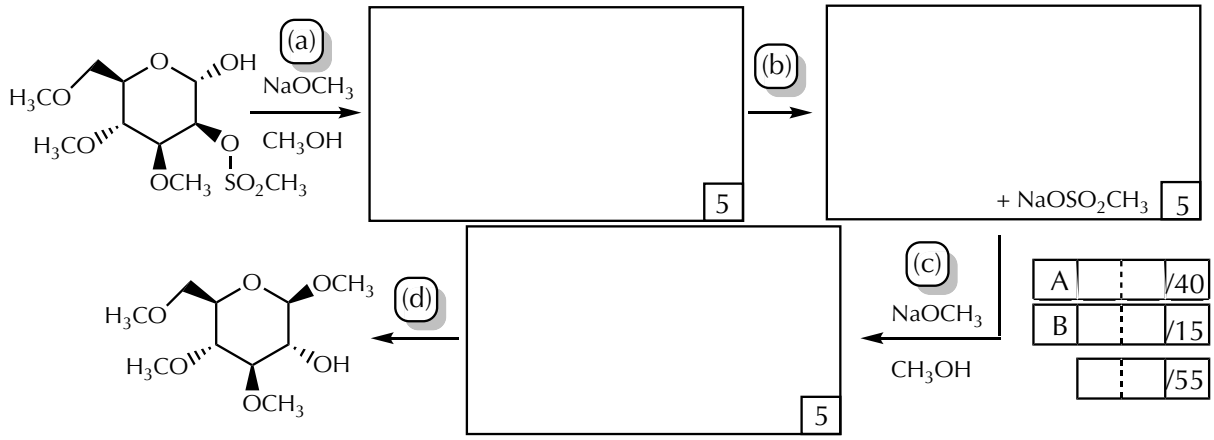
Question V (55 points) **Name** _____

A. Provide the missing structures in the following tripeptide synthesis. <u>*Assume that there are pH adjustments that result in forming the uncharged structure (when structures are called for).*</u> Note that a zwitterionic structure is uncharged, so pay attention to the relative pK_a values for the groups. From: Capellas, *et al.*, *Biotech and Bioeng*, **1996**, "Enzymatic synthesis of CCK-8 tripeptide fragment in organic media."





B. When the following carbohydrate derivative is treated with sodium methoxide, a four-step transformation takes place in which the carbohydrate is (a) deprotonated, (b) undergoes an intramoleular reaction, (c) undergoes an intermolecular reaction with sodium methoxide, and (d) is reprotonated to give the final product shown on the lower left. What are the structures of the intermediates? Draw carefully the stereochemical features. Balance equations.



A		/40
B		/15
		/55