Name: _____ Student Number: _____

Chemistry 2600 Final Exam (Version A)
April 19th, 2008

INSTRUCTIONS

1) Read the exam carefully before beginning. There are 9 questions on pages 2 to 10 followed by a periodic table and a blank page for rough work. You are also provided with an NMR Data Sheet (as posted on the class website). **Please ensure that you have a complete exam. If not, let an invigilator know immediately**. All pages must be submitted.
2) You are allowed to bring one index card (maximum size 3"x5") into the exam with you as a "cheat sheet". This card must be submitted with your exam.
3) You are allowed to bring a ruler and a molecular model kit.
4) No electronic devices of any kind (including calculators) are permitted.
5) If your work is not legible, it will be given a mark of zero.
6) Marks will be deducted for incorrect information added to an otherwise correct answer.
7) When drawing molecules, clearly show any relevant stereochemistry. If a mixture of diastereomers is produced, draw both/all of them.
8) If you think that you see another student cheating, write a note on your exam paper and raise your hand to show an invigilator so that we can investigate the situation.
9) **DO NOT OPEN THE EXAM UNTIL YOU ARE TOLD TO BEGIN.**
   Beginning prematurely will result in removal of your exam paper and a mark of 0.
10) You have **3 hours** to complete this exam. Nobody may leave the exam room during the first hour or the last 15 minutes of the exam.

Confidentiality Agreement:
I agree not to discuss (or in any other way divulge) the contents of this exam with or in the presence of any CHEM 2600 student who has not yet written their final exam. *(The last official timeslot ends at 5pm on Monday, April 21st, 2008.)*

Signature: _____ Date: _____
Course: CHEM 2600 (Organic Chemistry II)
Semester: Spring 2008
The University of Lethbridge

Q	Mark
1	/ 8
2	/ 4
3	/ 4
4	/ 3
5	/ 15

Q	Mark
6	/ 15
7	/ 10
8	/ 20
9	/ 1

Total	/ 80

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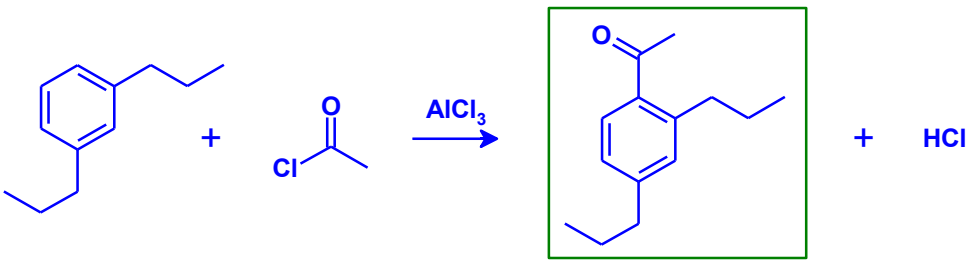
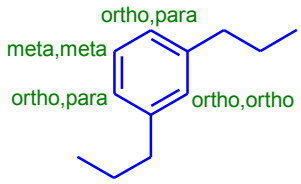
1. **[8 marks]**

(a) Draw the major organic product of the reaction between 1,3-dipropylbenzene and acetyl chloride (CH_3COCl) in the presence of aluminum chloride.



(b) With reference to the reaction mechanism, explain the regioselectivity of this reaction.

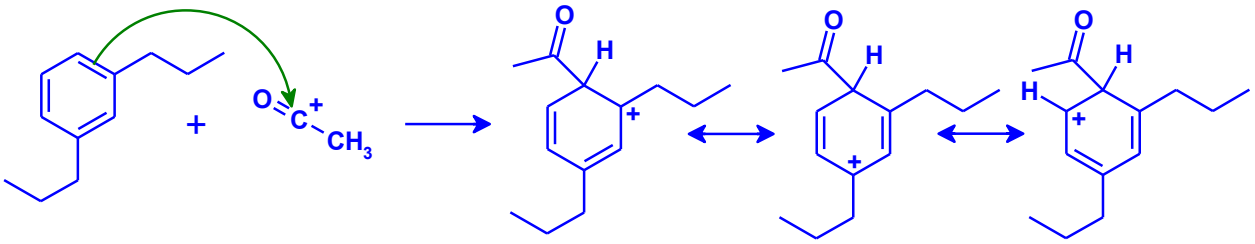
There are three sets of potential sites at which to add the acetyl (CH_3CO) group:



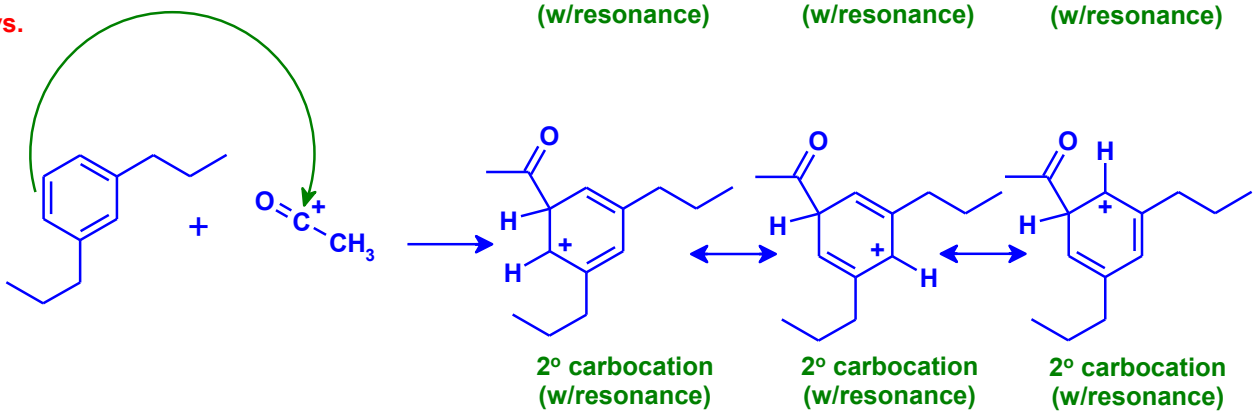
The two propyl groups are ortho/para directors because they stabilize the intermediate carbocation (for those products) inductively:

FIRST:

THEN:



vs.



Thus, the meta,meta product is not the major product.

The ortho,para product is favoured over the ortho,ortho product due to steric effects. (Electronically, the two are favoured equally.)

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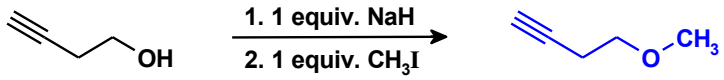
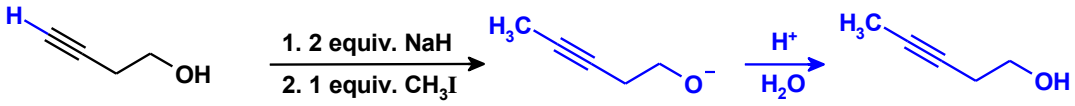
2. Draw the product of each reaction. **[4 marks]**

(a)



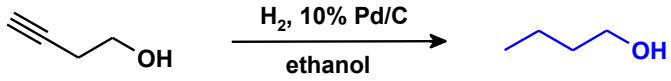
The first equivalent of base deprotonates the most acidic H (i.e. the alcohol), making a good nucleophile which attacks the electrophilic CH_3I.

(b)



The first equivalent of base deprotonates the most acidic H. The second equivalent of base deprotonates the second most acidic H (i.e. the terminal alkyne). NaH is a strong enough base to deprotonate a terminal alkyne (pK_a of 35 for H_2 vs. pK_a of 25 for ethyne). The strongest nucleophile then attacks CH_3I. C^- is a stronger nucleophile than O^-.

(c)



Catalyst not poisoned, so alkyne hydrogenated to alkane.

(d)

Markovnikov addition twice.

3. Explain how you could use spectroscopy to differentiate between this pair of isomers. Your answer should make reference to at least <u>two</u> types of spectroscopy (IR, ^{1}H NMR or ^{13}C NMR). *Note that you are <u>not</u> being asked to completely describe each spectrum. You are being asked to point out key differences between spectra of the two isomers. Be specific.* **[4 marks]**

Pick two:

^{1}H NMR:	quartet (3H), triplet (2H), broad singlet (2H)	three singlets (one broad)
^{13}C NMR:	amide = 160 – 180 ppm	ketone = 180 – 220 ppm (usually >200ppm)
IR:	amide = 1630 – 1670 cm^{-1}	ketone = 1705 – 1725 cm^{-1} (when not conjugated)

Other answers were accepted; however, I was not looking for answers any longer than the above.

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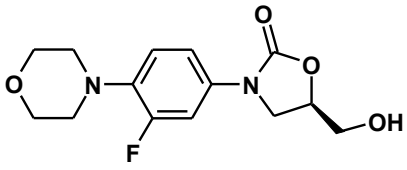
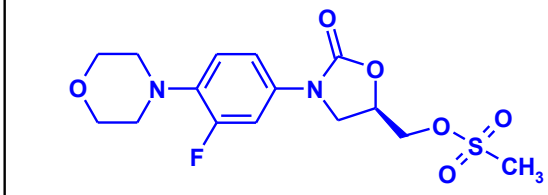
4. Linezolid is an antibacterial drug marketed by Pharmacia as Zyvox®. Fill in the blanks in the last few steps of the synthesis of linezolid (shown below). **[3 marks]**

Some reaction conditions have been simplified for clarity.



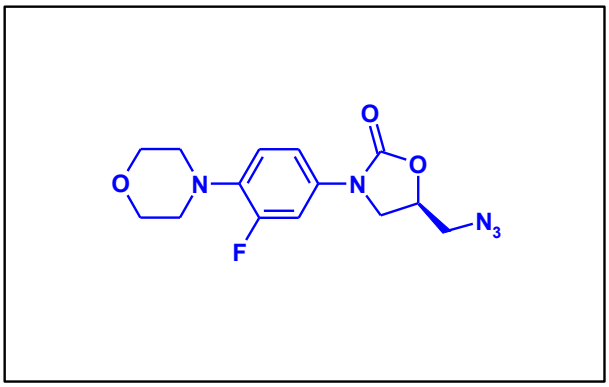
CH_3SO_2Cl

Et_3N, CH_2Cl_2

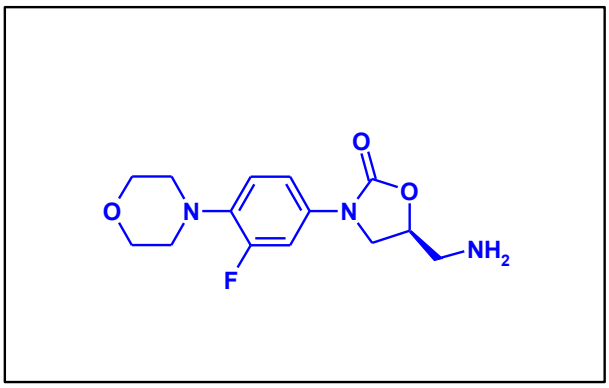


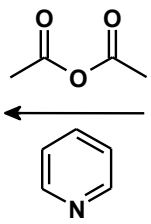
Note that CH_3SO_2Cl = MsCl

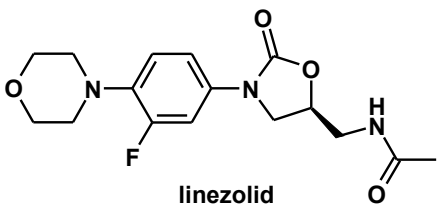
NaN_3
polar solvent
heat



H_2
10% Pd/C
solvent







linezolid

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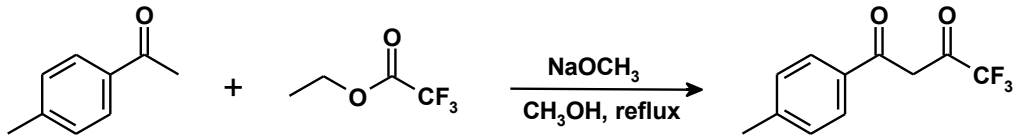
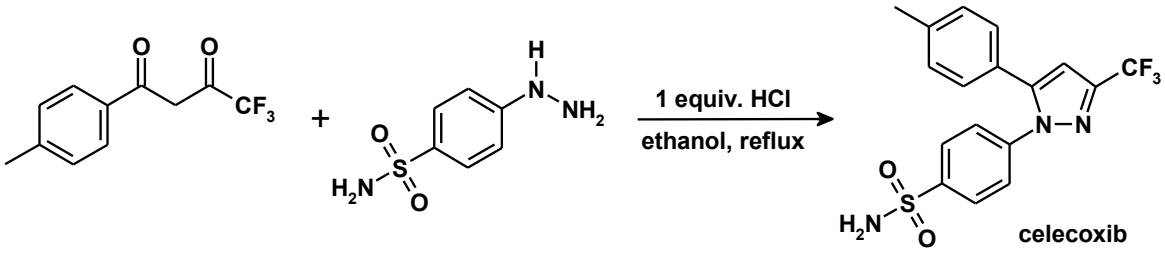
5. One synthesis of celecoxib (an anti-inflammatory marketed by Pfizer as Celebrex®) is shown below. **[15 marks]**

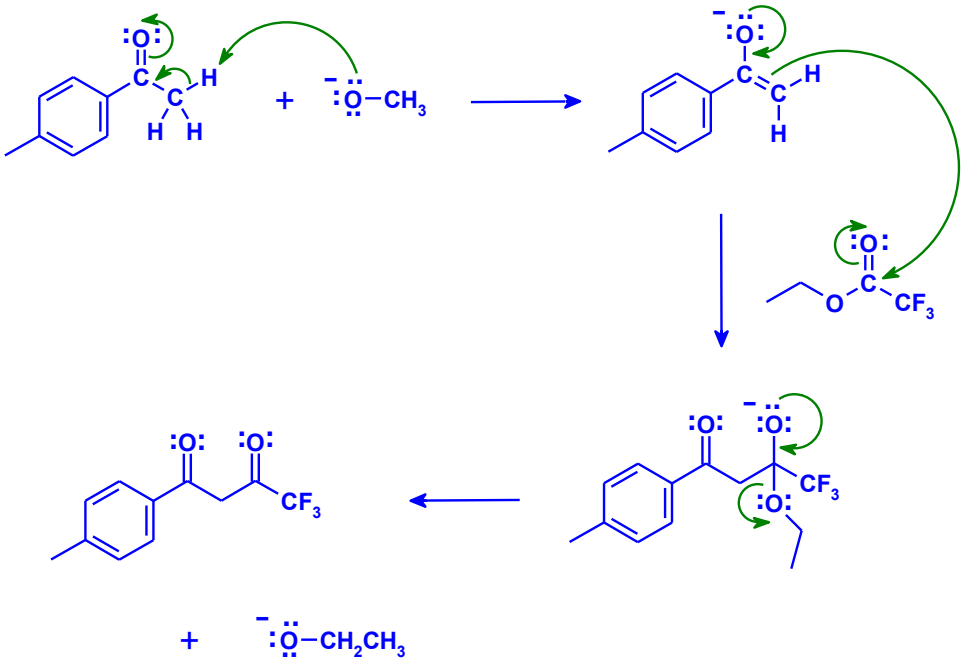
Step 1:



Step 2:



(a) Draw the mechanism for Step 1 of this synthesis. *4 marks*



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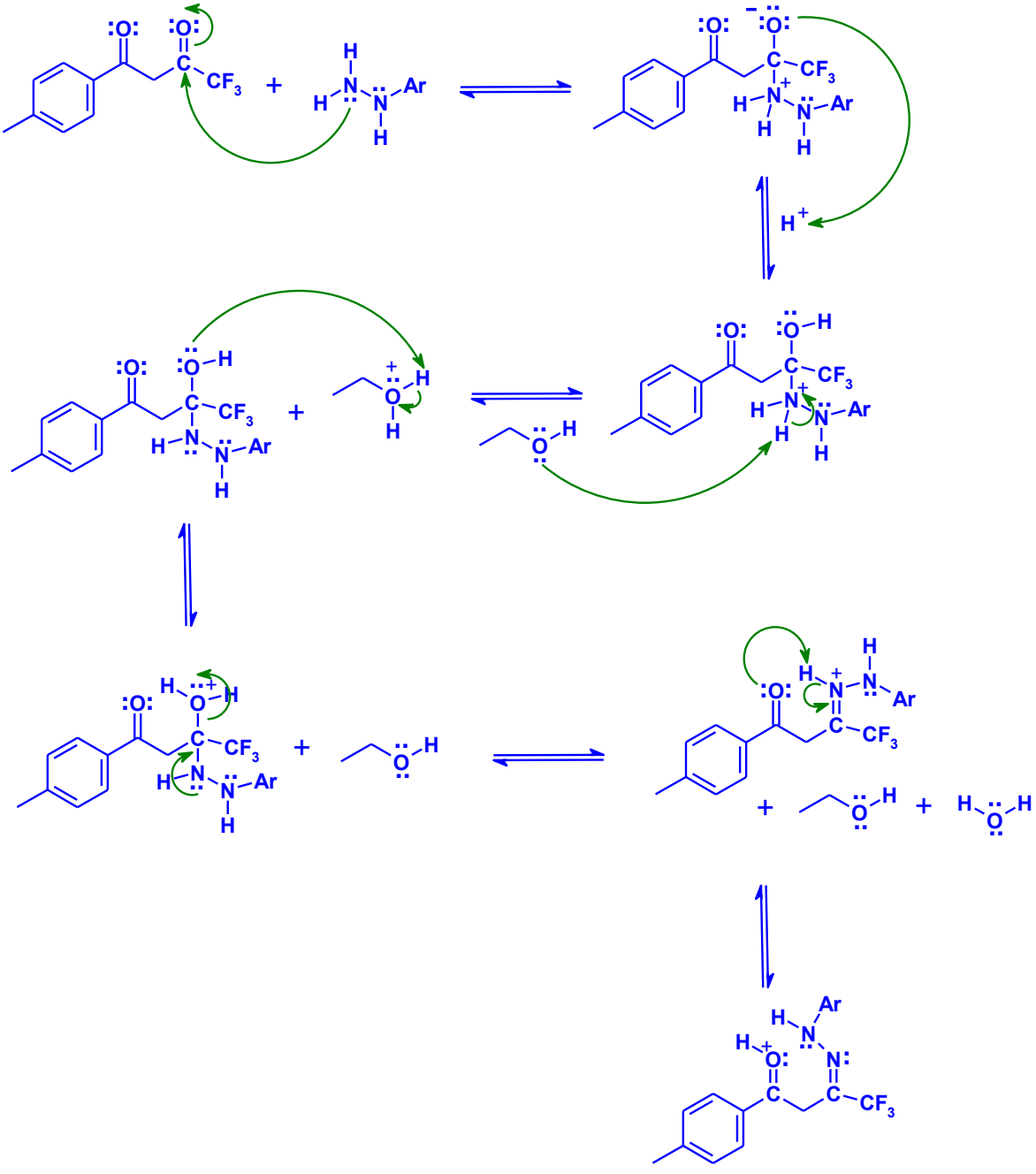
5. *continued*

(b) Draw the mechanism for Step 2 of this synthesis. *Please abbreviate $C_6H_4SO_2NH_2$ as Ar.*

11 marks



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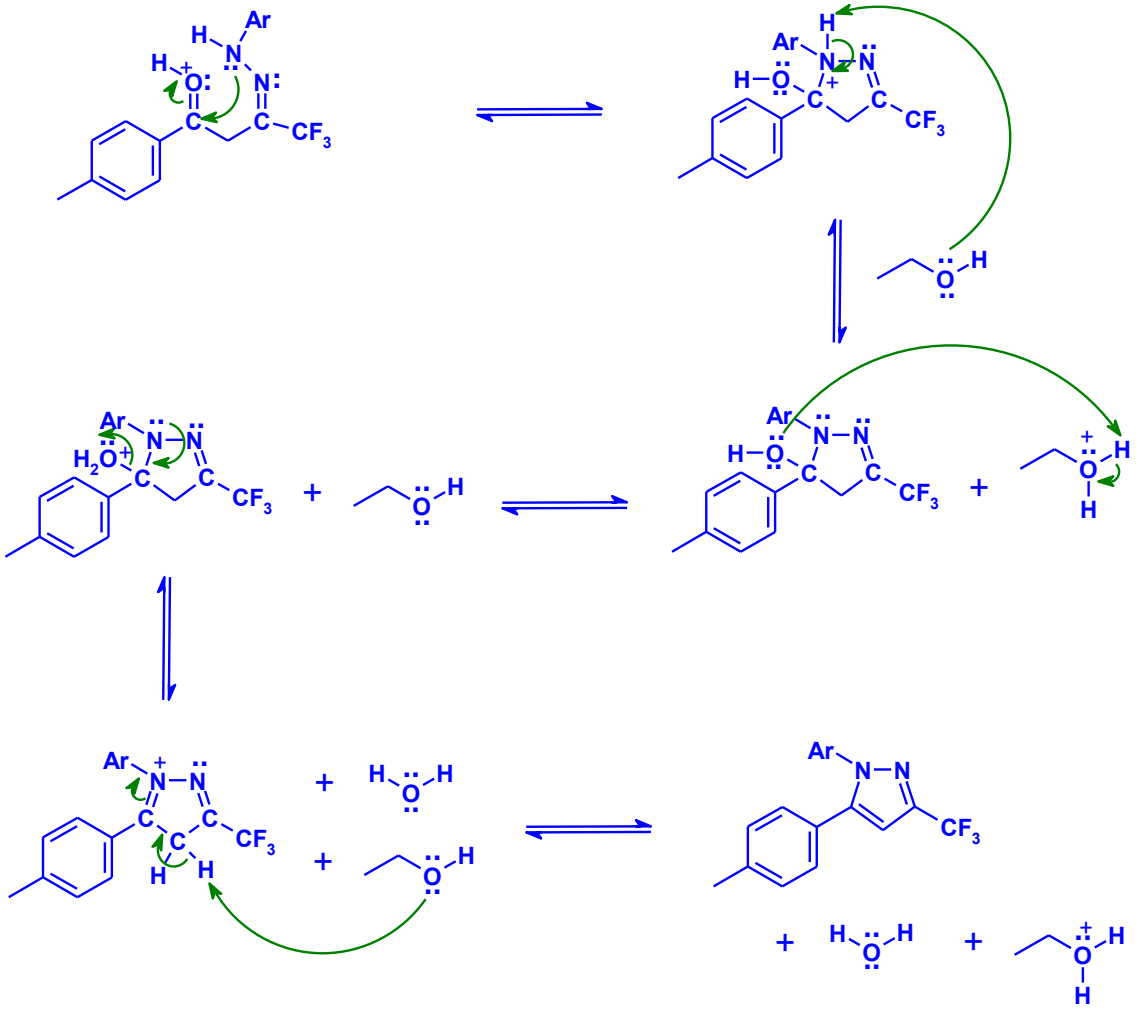

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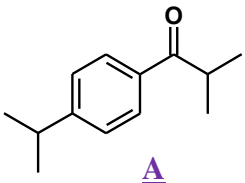
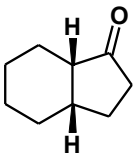
6. Choose any **three** of the molecules below and propose a synthesis of each. **[15 marks]**

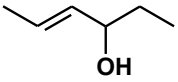
- Your organic reactants must be stable compounds that contain no more than five carbon atoms. They may be hydrocarbons, alkyl halides or alcohols and may contain C=C or C≡C bonds. You are also allowed to use benzene, bromobenzene or phenol.
- If you wish to use an organic reactant (including Grignard reagent) that does not meet these requirements, you must show how to make it from starting materials that do.
- You may use any inorganic reagents, acids, bases, catalysts, etc.
- Acids, bases, catalysts, etc. do not need to meet the "organic reactant" requirements if the organic part will not be present in the final product.
- Clearly indicate stereochemistry of reaction products where appropriate. Assume that all stereochemistry shown is relative and that you are to make racemic product.
- You are not required to show mechanisms for this question.
- If you work out syntheses for more than three of the molecules, clearly indicate which three you want marked by circling those compounds. Otherwise, I will mark the first three syntheses given.
- If you run out of space on this page, continue your work on the next page.



A



B

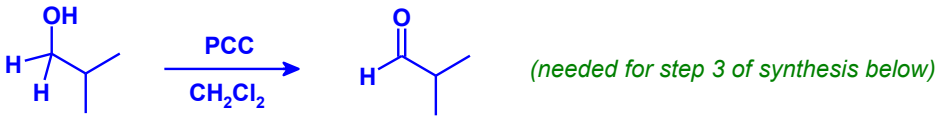


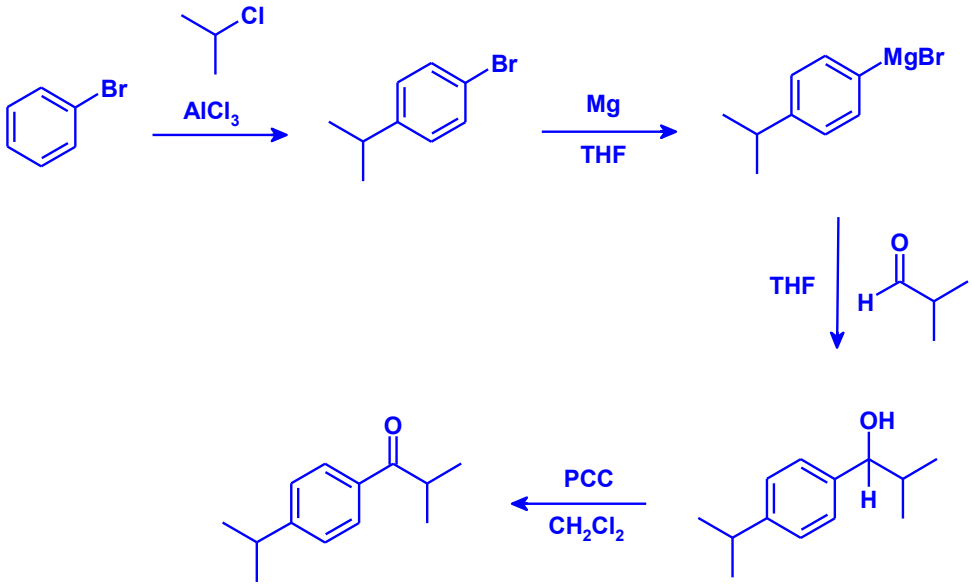
C

D

There were several acceptable approaches to each molecule; the answers here are representative. Each synthesis was worth 5 marks.

A





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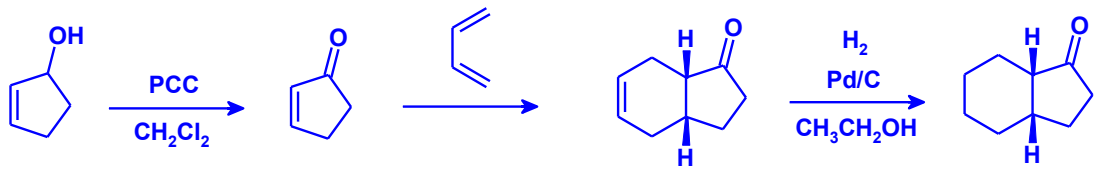
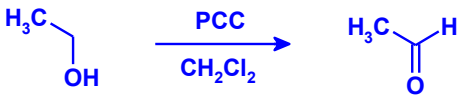
6. *continued*

B

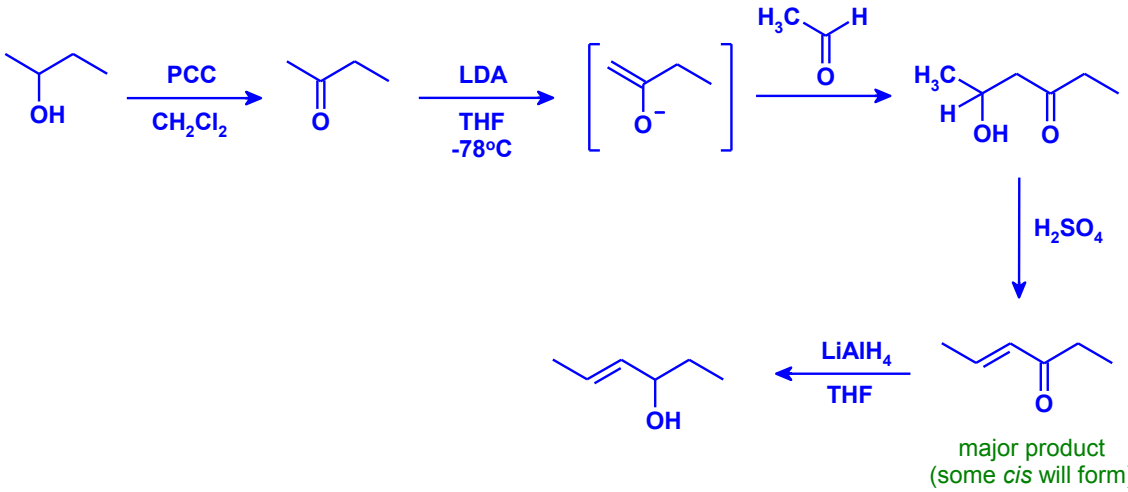


Diels-Alder reaction gives only cis-fused rings

C

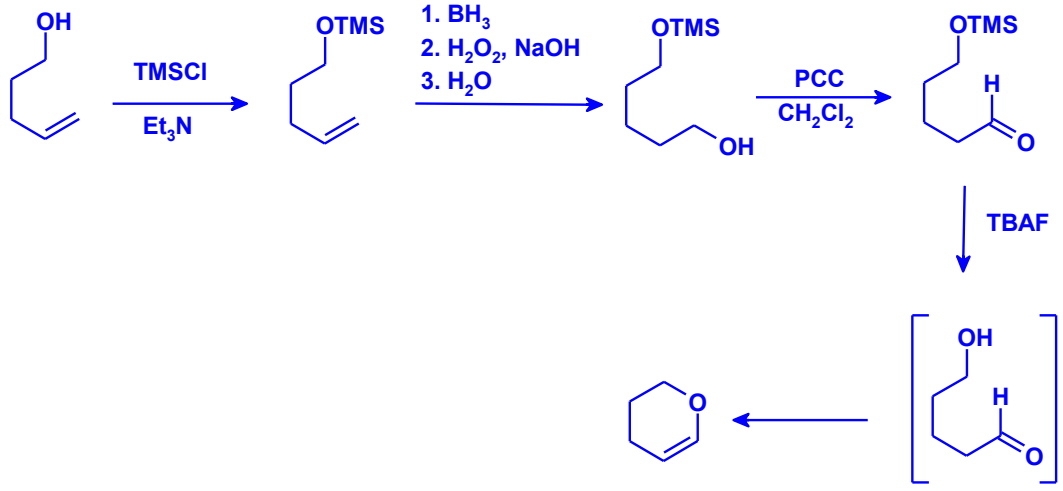


(needed for step 3 of synthesis below)



major product
(some *cis* will form)

D



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7. Compound **"A"** has the molecular formula C_5H_6 and has a ^{13}C NMR with three signals. It dimerizes readily. When treated with a strong base, anion **"A⁻"** is generated which gives only one signal on its ^{13}C NMR. **[10 marks]**

(a) Draw compound **"A"**.

Logic: A = C_5H_6

Deprotonation will make $A^- = C_5H_5^-$

In order for all five C in A^- to be equivalent, they must each be bonded to the same number of H. Therefore, each C in A^- must be bonded to one H. The only way to do this is to have A^- be cyclic as shown below.

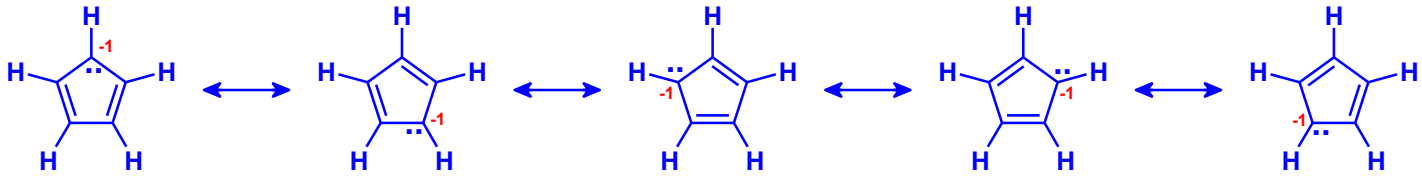
Once we know what A^- is, the structure of A can be found by protonating A^-.

Confirmation: Cyclopentadiene has a plane of symmetry so it only has 3 types of C.

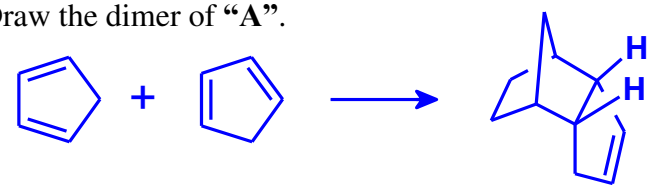
We've seen in class that cyclopentadiene reacts with itself in a Diels-Alder reaction, giving dicyclopentadiene (i.e. the dimer), whose structure is shown in the answer to part (c).

(b) Draw anion **"A⁻"** and explain why it only gives one signal on the NMR.

The cyclopentadienyl anion ($C_5H_5^-$) has 6 π electrons in a flat cyclic pi system; therefore, it is aromatic. It can be shown through resonance that all five carbon atoms are equivalent, bearing an average charge of -0.2:



(c) Draw the dimer of **"A"**.

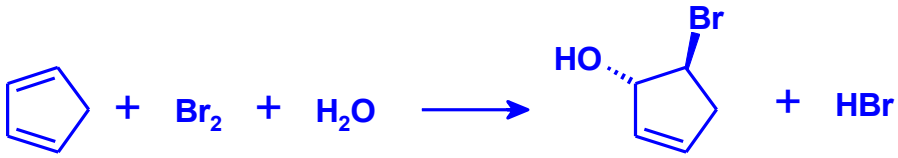


(d) Draw the product(s) formed when **"A"** reacts with 1 equivalent of HCl.

Markovnikov addition (make the resonance-stabilized carbocation).

1,2- and 1,4-addition give the same racemic product.

(e) Draw the product(s) formed when **"A"** reacts with 1 equivalent of Br_2 in water.



Markovnikov addition; -OH and –Br are trans.

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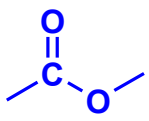
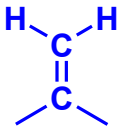
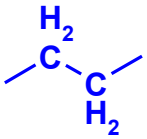
8.

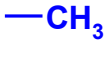
	Evidence	Conclusion
	$C_6H_{10}O_3$	DU = 2
IR:	Strong broad peak at ~3450 cm^{-1}	O–H (since no N)
	Strong peak at ~1720 cm^{-1}	C=O
	Medium peak at ~1640 cm^{-1}	C=C (since no N)
^{13}C NMR:	Six peaks	all C different
	~168 ppm	C=O (ester or $–CO_2H$; could have been amide, but no N)
	Two peaks at 120-140 ppm	C=C
	Two peaks at 60-70 ppm	two more C (likely attached to heteroatom(s))
	One peak below 20 ppm	likely CH_3
^1H NMR:	Integrations are 1 : 1 : 2 : 2 : 1 : 3	
	Singlet (3H) at ~2 ppm	CH_3 next to C=X or C≡X (but if have C=O and C=C, can't also have C≡X since 2 DU already accounted for)
	Broad singlet (1H) at ~3 ppm	exchangeable H; likely OH (see IR)
	Pair of triplets at 3.85 and 4.25 ppm (2 H each); no other coupling on NMR	$-CH_2-CH_2-$ (each C bonded to heteroatom; O is only option)
	Singlet (1H) at ~5.6 ppm	-CH of alkene (no H *cis* or *trans*)
	Singlet (1H) at ~6.2 ppm	-CH of alkene (no H *cis* or *trans*)

Pieces:









Notes:

No peaks on ^1H NMR above 7ppm, so definitely no aldehyde or carboxylic acid!
$–CH_3$ cannot be next to $–CH_2CH_2–$ because it would no longer be a singlet.
–OH cannot be next to $–CO_2–$ because we have no evidence for a peracid.
Both C of $–CH_2CH_2–$ should be next to an O due to their shifts on the ^1H NMR. So, put that piece between –OH and $–CO_2–$. That puts the alkene on the other side of the ester and the methyl group next to the alkene: