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**Research Methods (CHEM 251)
Synthetic Organic Chemistry Part
Final Examination**

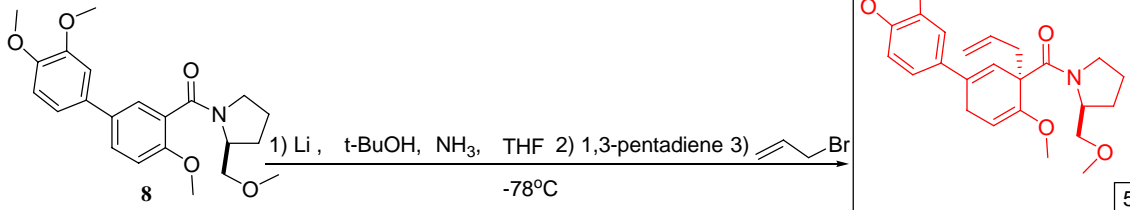
Prof. Malachowski

Due: December 16, 2005, 5 PM

Honor Code: You may take this examination while consulting your course lecture notes, lab notebook and handouts. You are not to consult any other electronic or written material during the exam. You have 1.5 consecutive hours to complete the exam. You should not discuss the exam with anyone until all students have handed in their exam. There are a total of four questions. The point values for each question are written with the question.

1. Preliminary experimentation has succeeded in the Birch-Cope sequence. It is time to increase the scale of the reaction to push intermediates ahead in an effort to make the final (+)-mesembrine product. Using your familiarity with the Birch reduction-allylation reaction and the experimental section of the class project manuscript, answer the following questions. Beware of significant figures!

a) To begin, we will need to calculate the necessary reagents and determine the appropriate glassware. Complete the reaction table below by filling in the appropriate numbers in the boxes. (0.5 pts. each) Beware of significant figures!



m.w. (g/mol)	385.5	6.94	74.1	17	72.1	68.1	121	427.5
d (g/mL)	—	—	0.775	—	0.889	0.683	1.398	—
b.p. (°C)	—	—	83	-33	65-7	42	70-1	—
m.p. (°C)	—	180	23-6	-78	-108	-87	-119	—

Scale:

mmol	2.59	6.48	2.59	—	—	—	6.48	2.59
equiv.	1.00	2.50	1.00	—	—	—	2.50	1.00
g	1.00	0.045	0.192	—	—	—	0.783	1.11
ml	—	—	0.248	330	24	—	0.560	—

b) What size and type of round bottom flask should you select? (4 pts.)

With a reaction volume close to 400 mL, a 1L three neck round bottom flask should be used.

c) If the reaction temperature is lowered to -110°C, what problems might occur? (4 pts.)

The solvents, NH₃ and THF, might both freeze, thereby making mixing in the reaction difficult.

d) Some Birch reduction reactions are conducted under an ammonia reflux. What would be the temperature of the reaction under these conditions? (4 pts.)

-33°C

e) What will be the approximate concentration of **8** in the reaction? (4 pts.)

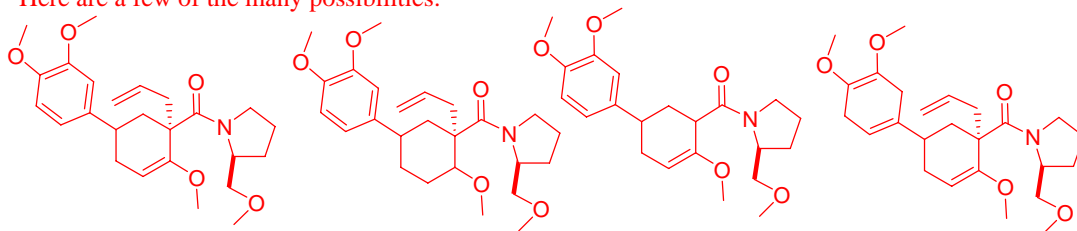
2.59 mmol/~360 mL volume= 0.0072 M

f) We have found that the stereoselectivity of the reaction can be increased if the reaction is run under more dilute conditions. What would have to be done to run the reaction under more dilute conditions? (4 pts.)

Add more NH_3 and THF.

g) One common problem in the Birch reductions run in our class was over-reduction of the aromatic system. Draw one possible product of over-reduction of **8**. (4 pts.)

Here are a few of the many possibilities:



h) What analytical tools could be used to confirm over-reduced products and what would you look for with these tools? (6 pts.)

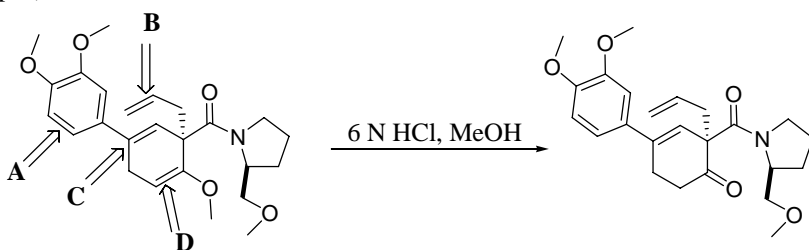
^1H NMR: more alkane proton signals and fewer alkene proton signals.

^{13}C NMR: more alkane signals and fewer alkene signals.

MS: molecular weight for over-reduced products would increase by 1 for each additional proton in the over-reduced system.

An over-reduced system that was not allylated would lack the alkene and alkane peaks of the allyl group in the NMR and the extra 41 mass units in the MS.

2. In the following hydrolysis reaction, only alkene **D** reacts. Describe why alkenes **A-C** do not react. (15 pts.)



a) Why doesn't **A** react?

A is part of an aromatic system and therefore too stable.

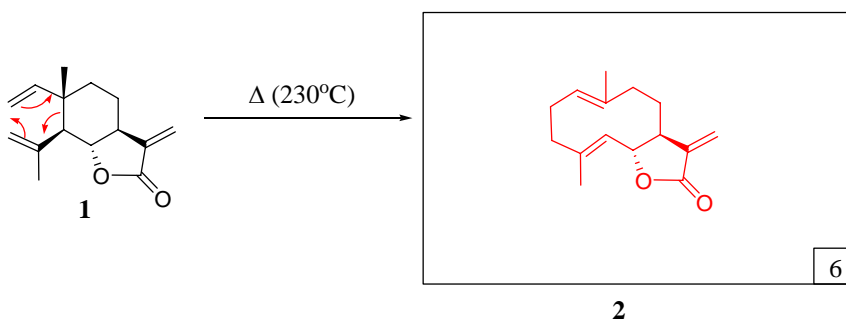
b) Why doesn't **B** react?

B is a monosubstituted alkene, therefore it is less electron rich than **D** and since this is an electrophilic addition reaction, the better nucleophile reacts first.

c) Why doesn't **C** react?

C is trisubstituted like **D**, but it does not have an ether substituent (-OCH₃). Therefore, like **B**, it is less electron rich (a poorer nucleophile) than **D**.

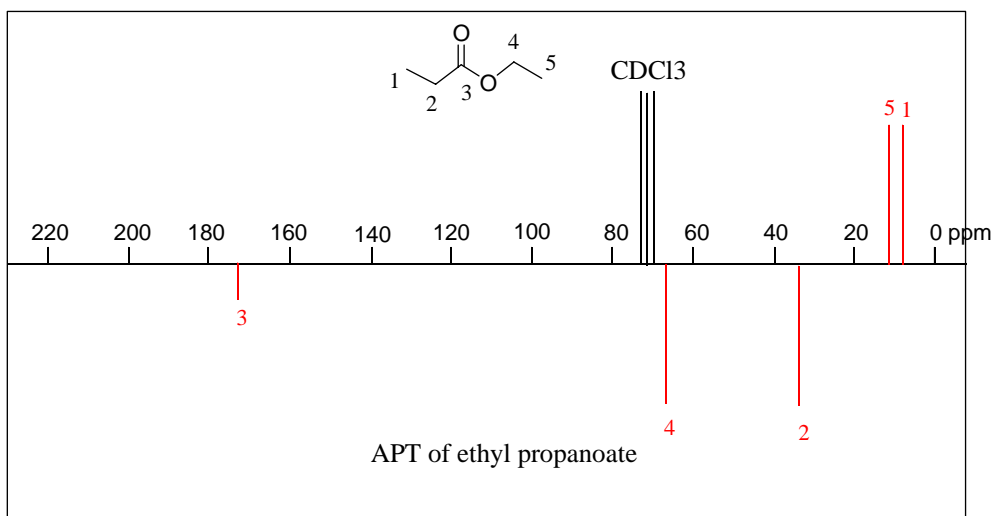
3. a) Show the mechanism (curved electron flow arrows) and product of the Cope rearrangement of **1**.



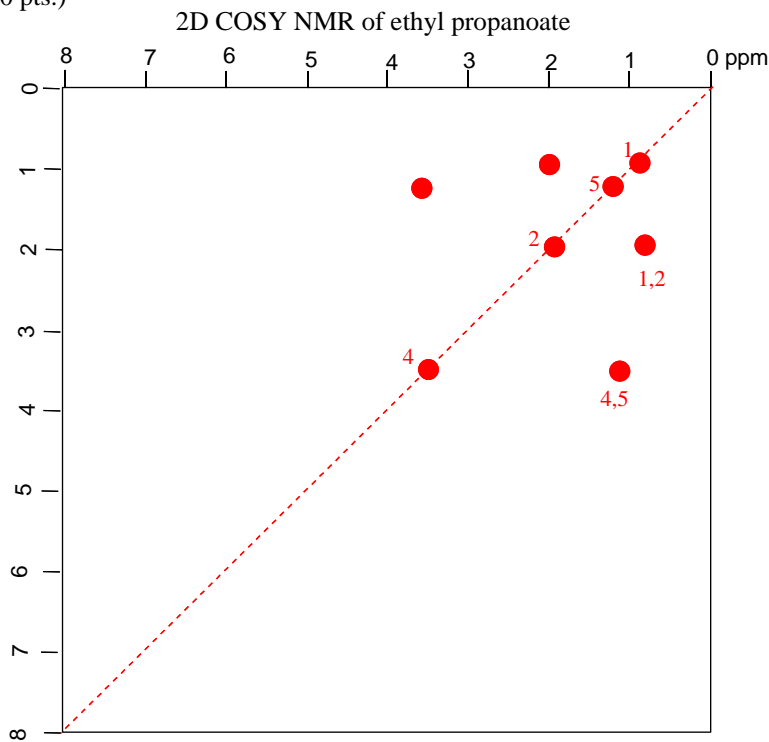
b) As reported in the scientific literature, this reaction affords only 33% of **2** along with 67% of **1**. Explain why this might be happening. (6 pts.)

The Cope rearrangement is an equilibrium under thermodynamic control, therefore **1** must be more stable than **2**. This is probably because the cyclohexane ring of **1** is more thermodynamically stable than the cyclodecadiene ring formed in **2**.

4. a) Draw the expected APT spectrum for ethyl propanoate. Label the ^{13}C signals on the spectrum with the numbering scheme in the structure below. There are chemical shift tables on page 7 of the exam that may help in answering the NMR questions. (10 pts.)



b) Draw the expected COSY spectrum for ethyl propanoate. You should place dots on the 2D spectrum in the locations where there would be signals. Label the dots on the spectrum with the numbering scheme in the structure above. You only need to label one of the two crosspeaks. You do not need to show the spectrum projections on the axes nor do you need to worry about showing peak splitting information. (10 pts.)



c) Draw the expected HMQC spectrum for ethyl propanoate. You should place dots on the 2D spectrum in the locations where there would be signals. Label the dots on the spectrum with the numbering scheme in the structure on page 5. You do not need to show the spectrum projections on the axes nor do you need to worry about showing peak splitting information. (10 pts.)

