Chem 112 B: Midterm 2, Tuesday April 5, 2011

Name: KEY

*UID:*_____ *GSI:*_____

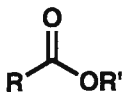
*There are a total of **8 pages** on this exam including this one.*

Question 1	_____(12 pts)
Question 2	_____(28 pts)
Question 3	_____(35 pts)
Question 4	_____(35 pts)
Question 5	_____(25 pts)
Question 6	_____(40 pts)
Total	**_____(175 points)**

Question 1

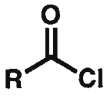
Name the functional groups of the following carboxylic acid derivatives and rank them according to their relative rates of reactivity in a hydrolysis reaction. (Most reactive = 1; least reactive = 6). (12 pts)

1 pts each



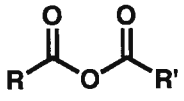
ESTER

(4)



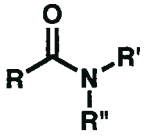
ACID CHLORIDE

(1)



ACID ANHYDRIDE

(2)

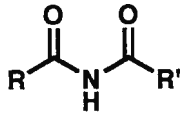


AMIDE

(5)

NITRILE

(6)



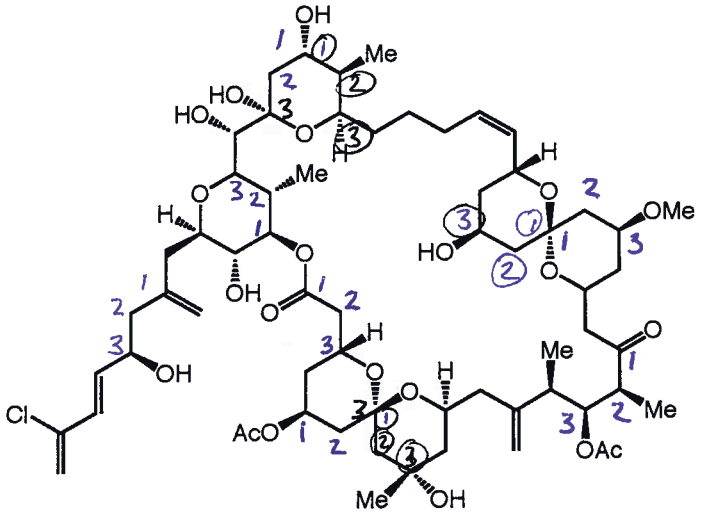
IMIDE

(3)

Question 2

Spongistatin (**A**) is an inhibitor of tumor cell growth and is under study in clinical trials as an anticancer drug candidate.

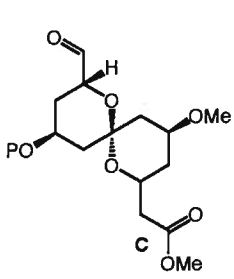
1 pt for each

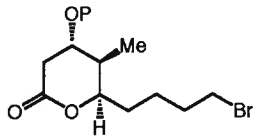


Spongistatin 1 (**A**)

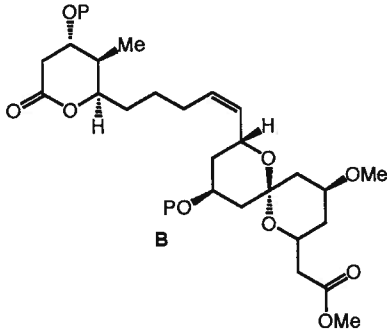
(a) Identify **ten** *potential* aldol disconnections using consecutive numbering (i.e., 1,2 and 3) for each aldol motif in the structure above that may be applied to the synthesis of **A**. (10 pts)

(b) Provide reagents and the steps associated with the formation of a portion of spongistatin, **B**, from **C** and **D**. (P is a protecting group) (15 pts for steps).

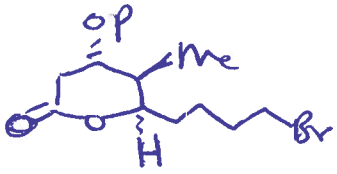




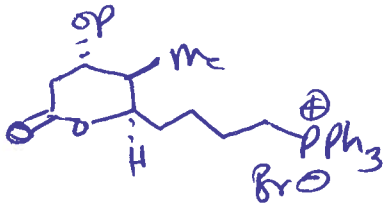
D



B

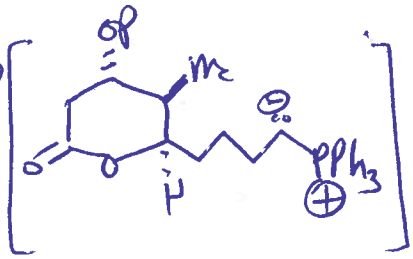


PPh_3 → ~~+5~~



NaH, then C → B

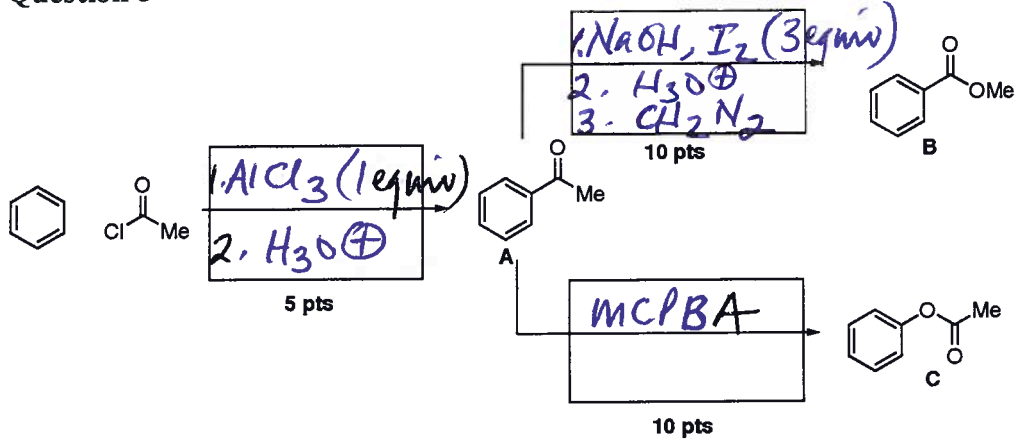
NaH → ~~+5~~



then C → ~~+5~~

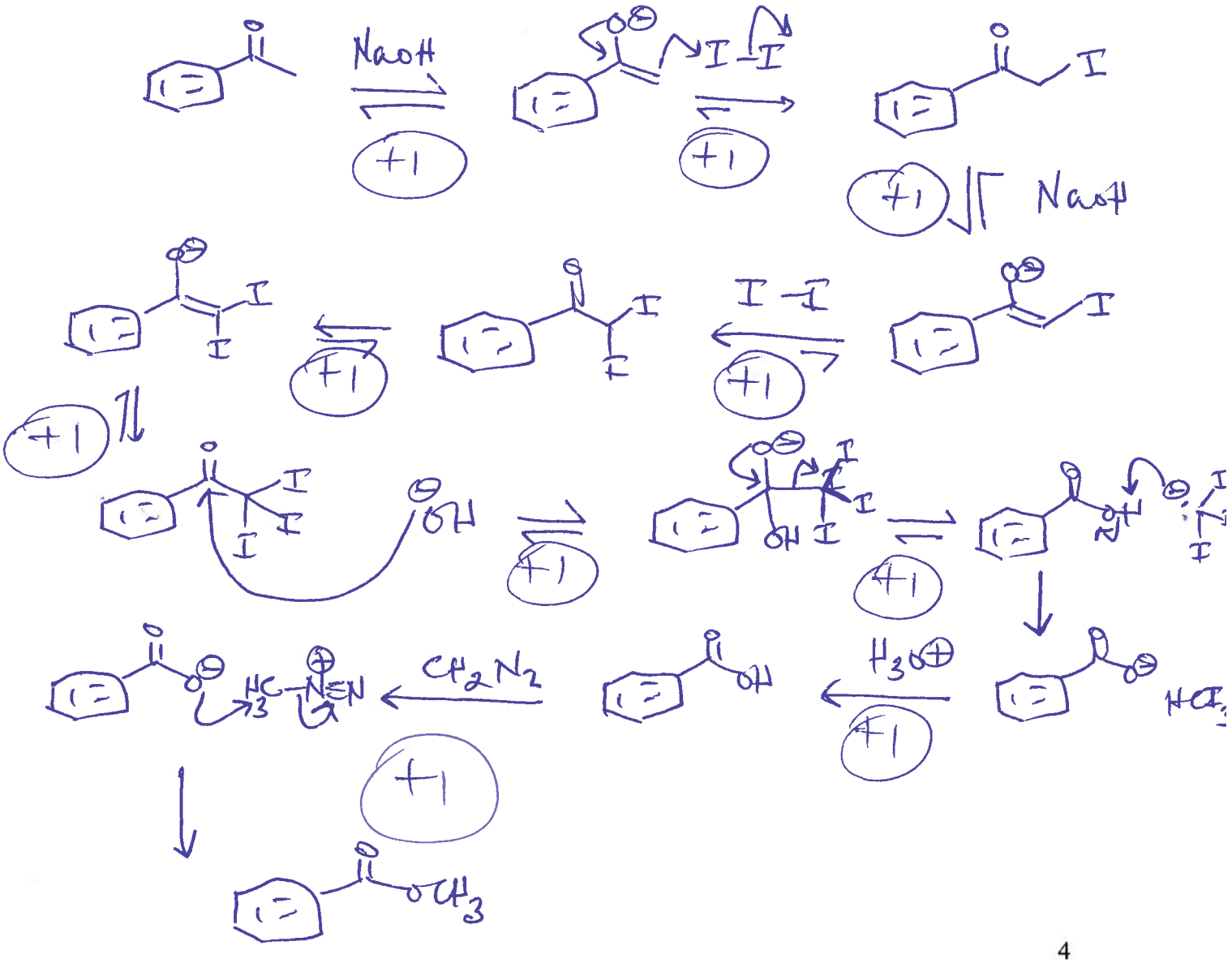
(c) What is the key reaction in (b)? Wittig (3 pts)

Question 3



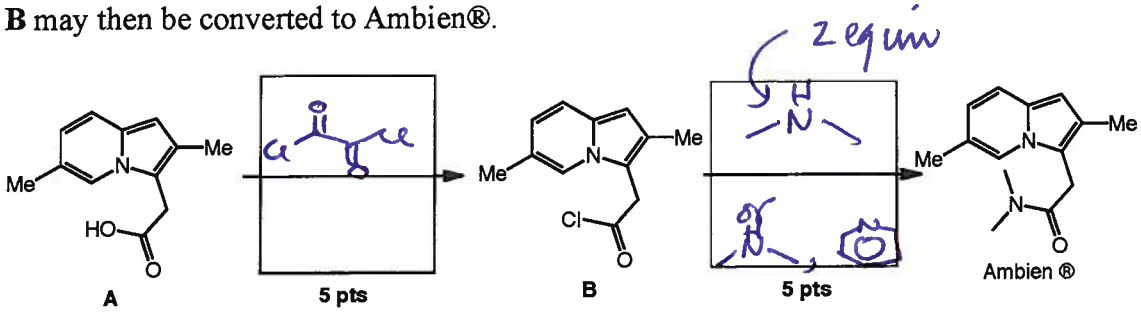
(a) Provide reagents associated with the formation of **A**, **B** and **C** per the scheme shown above. (Hint: this could be a multistep process) (25 pts).

(b) Provide a mechanism for the conversion of **A** to **B**. (10 pts).



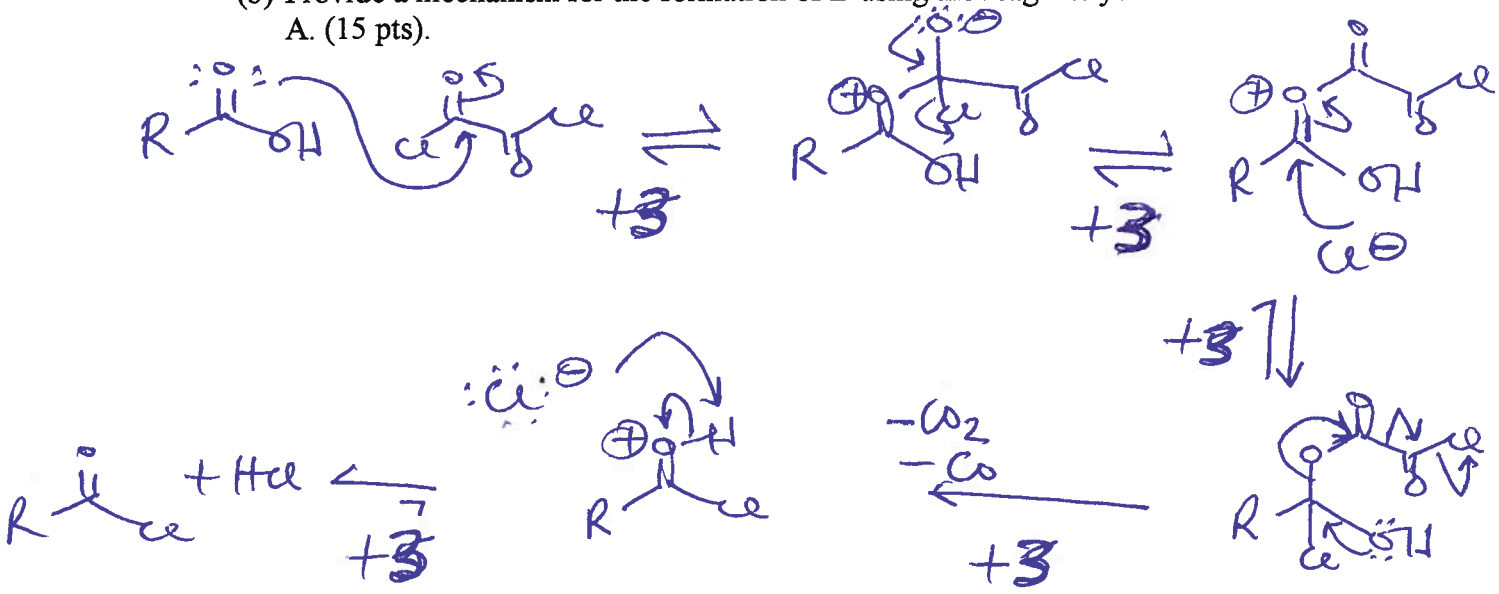
Question 4

The synthesis of the sleep aid Ambien® may involve the formation of **B** from **A**. **B** may then be converted to Ambien®.



(a) Provide reagents in the boxes above for the conversion of **A** to **B** and for **B** to Ambien®. (10 pts)

(b) Provide a mechanism for the formation of **B** using the reagents you listed in Part A. (15 pts).

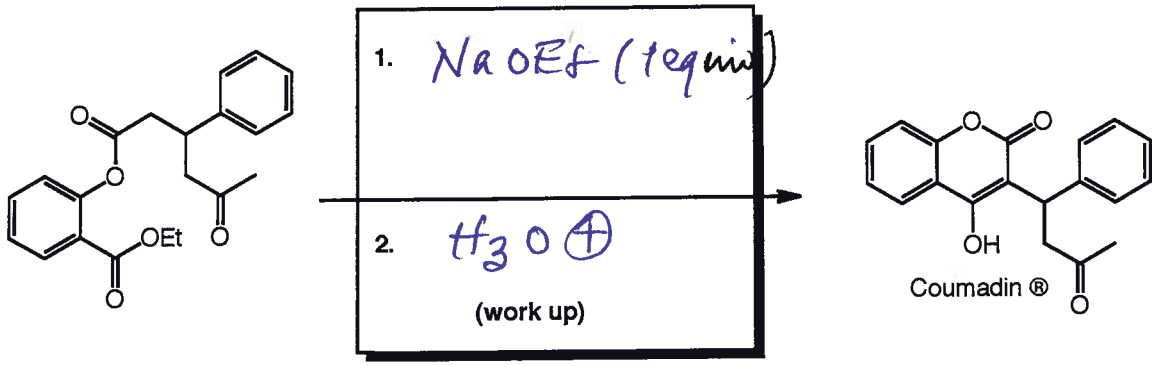


(c) Provide reagents for conditions that may be used to convert **A** to Ambien® *in one pot* using an *active ester*. (10 pts)

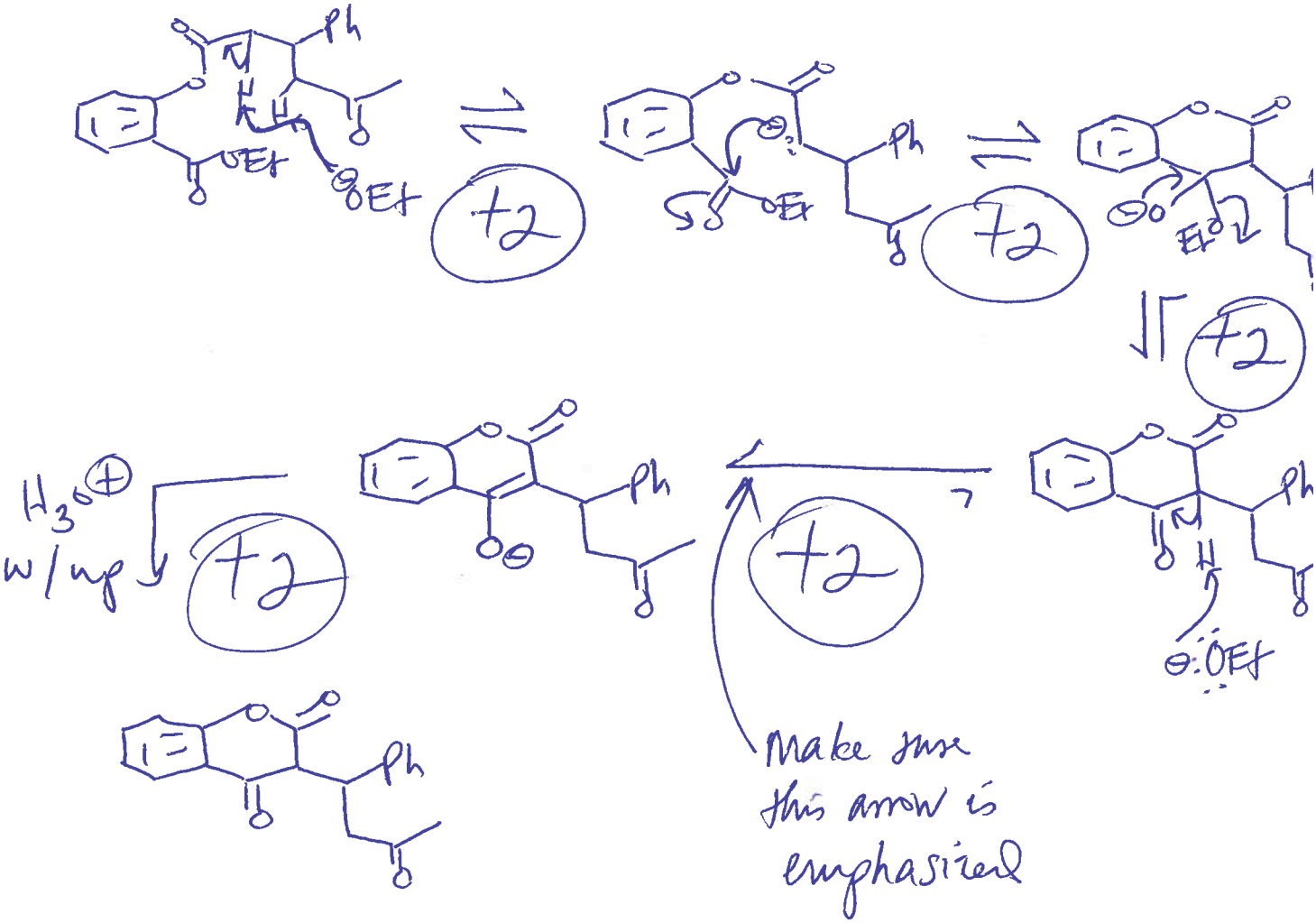
Question 5

The Claisen reaction, also known as the Claisen condensation and its intramolecular version, provides a direct way to access the 1,3-dicarbonyl motif.

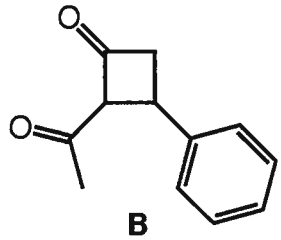
A) Provide *reagents* for the transformation shown below for the synthesis of the anticoagulant coumadin®. Be specific about the number of equivalents of reagents (if necessary) and work up conditions. (5 points)



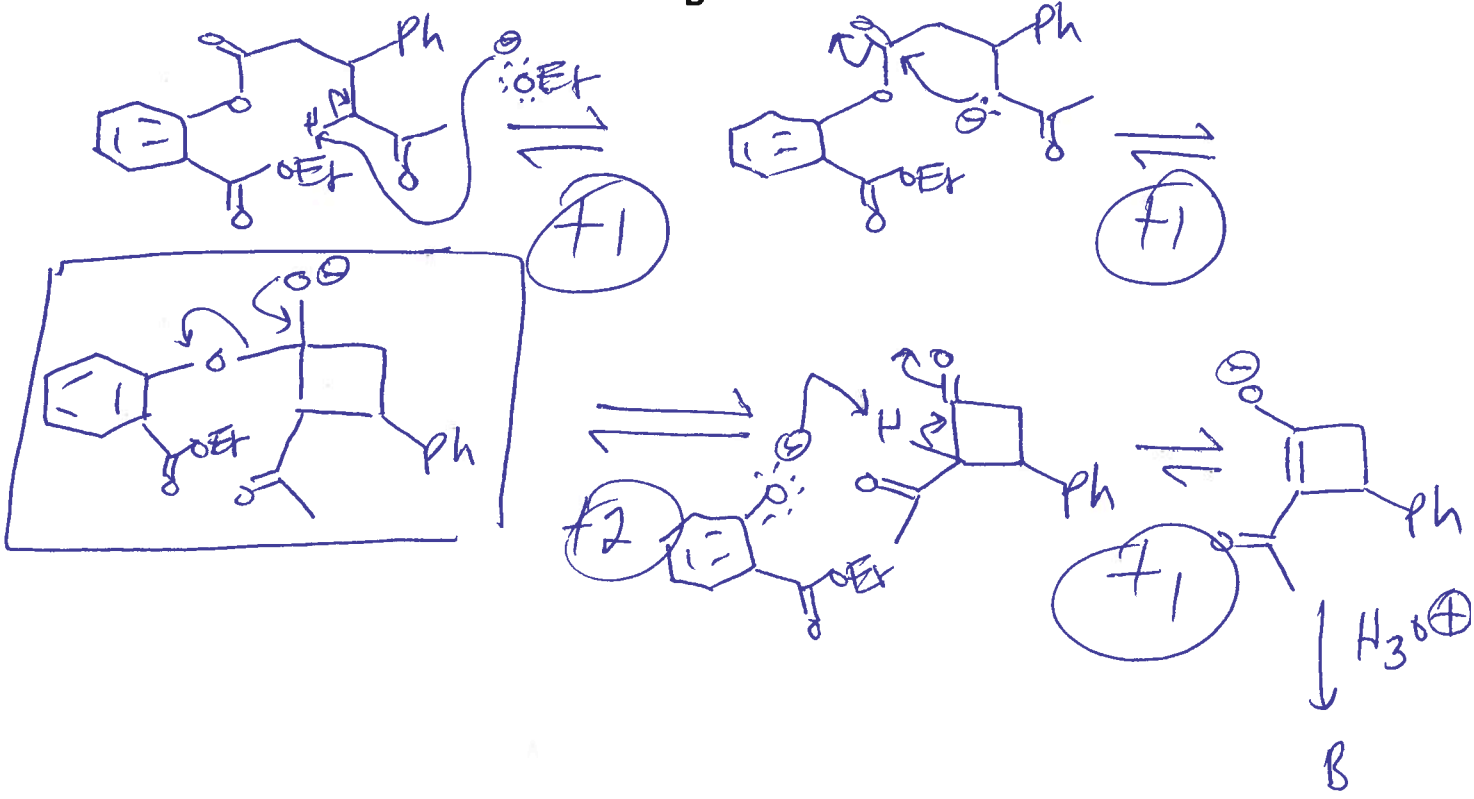
B) Provide a mechanism for the transformation shown in part A. (10 points)



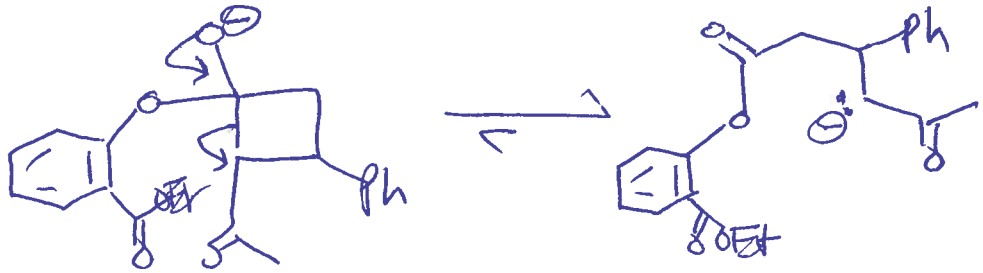
C) Provide a mechanism for the formation of the side product, **B** (5 pts).



B



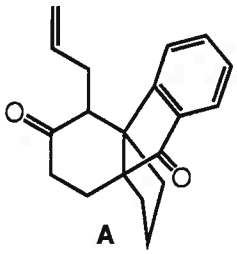
D) Why is **B** not formed in an appreciable quantity? (5 points)



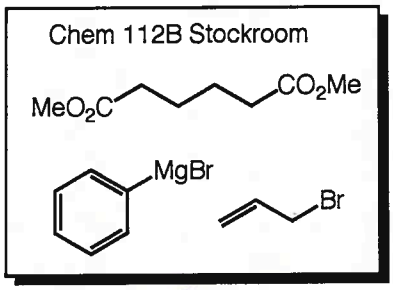
This is reversible because of strain release

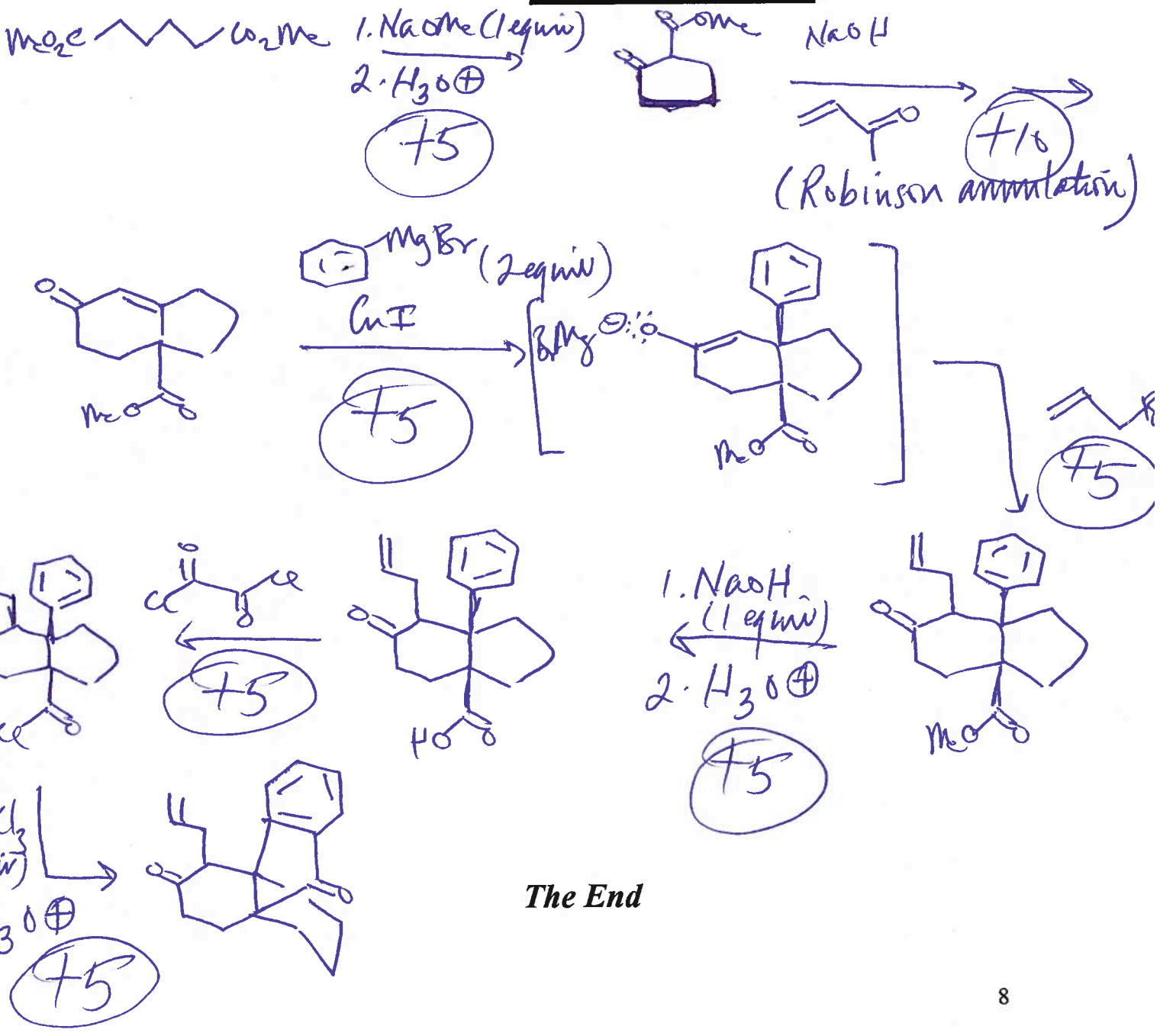
Question 6

(a) Provide a *forward* synthesis of **A** from the Chem 112B stockroom compounds shown in the box below and any other reagents of your choosing 4 carbons or less. (40 pts) (Hint: Consider a Dieckmann condensation, aldol condensation, conjugate addition, saponification and Friedel-Crafts acylation in that order). PLEASE SHOW ALL REAGENTS.



A





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