Chemistry 112B
Spring, 2005

Instructor: Matthew B. Francis

Second In-Class Exam
April 7th, 2005

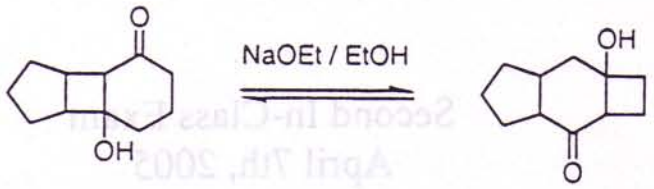
SID#: Key
(Do NOT put your name on the exam.)

(1)	_____	(6 points)
(2)	_____	(5 points)
(3)	_____	(5 points)
(4)	_____	(21 points)
(5)	_____	(6 points)
(6a)	_____	(6 points)
(6b)	_____	(39 points)
(6c)	_____	(6 points)
(6d	_____	(6 points)
TOTAL	_____	(100 points)

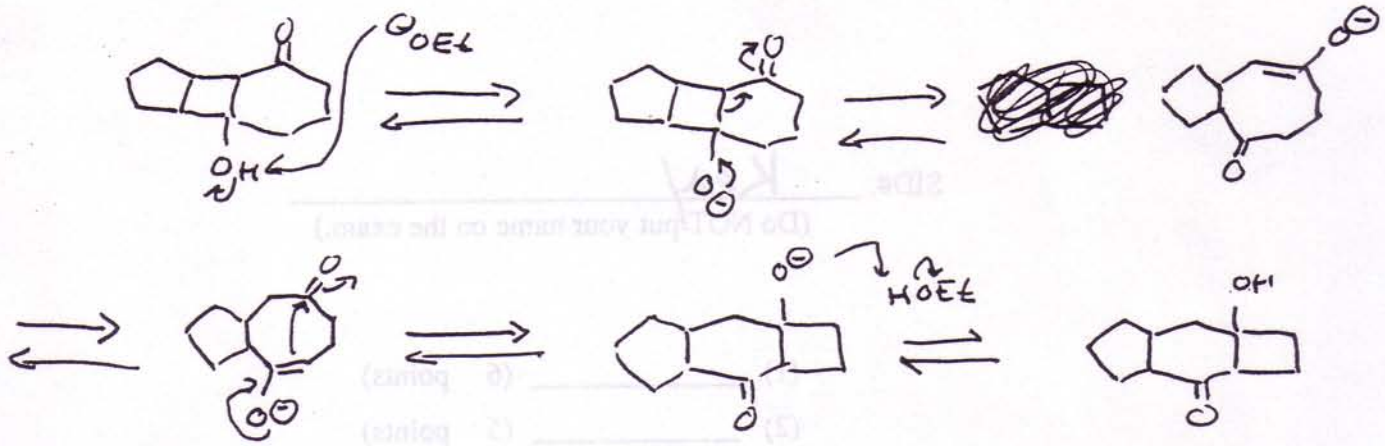
THERE SHOULD BE 9 PAGES IN THIS BOOKLET. NO CALCULATORS ARE ALLOWED DURING THE EXAM, BUT YOU MAY USE ANY MODEL KITS THAT YOU BRING WITH YOU. SCRATCH PAPER IS AVAILABLE FOR YOUR USE; HOWEVER, BE SURE TO WRITE ALL ANSWERS THAT YOU WANT US TO GRADE IN THE EXAM BOOKLET. YOU HAVE UNTIL 9:30 TO COMPLETE THE EXAM.

GOOD LUCK!

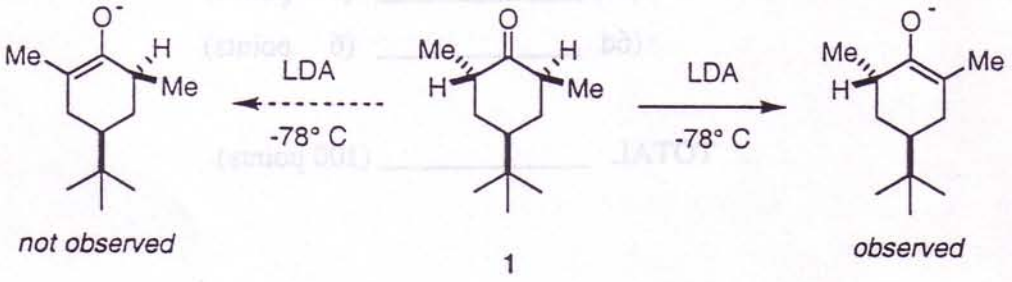
1. The two ketones in the following equation interconvert rapidly when placed under basic conditions:



Provide a mechanism for this interconversion (6 points).



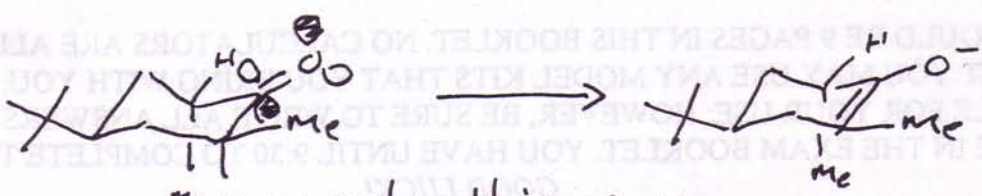
2. When compound **1** is treated with LDA at low temperature, only one of the two possible enolates is observed:



not observed **1** *observed*

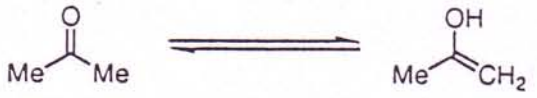
Provide a rationale for this behavior (5 points).

Draw as a chair:



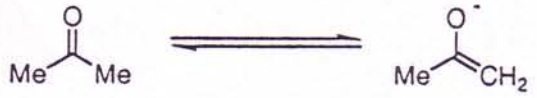
only this C-H bond has an overlap with the C=O π^* orbital

3. In class, we discussed the equilibrium of a ketone with its enol tautomer:



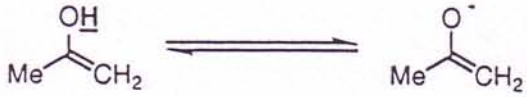
$K_{eq} = 10^{-8}$ (in water)

We also described the acidity of the alpha proton, which can be removed with base to form an enolate anion:

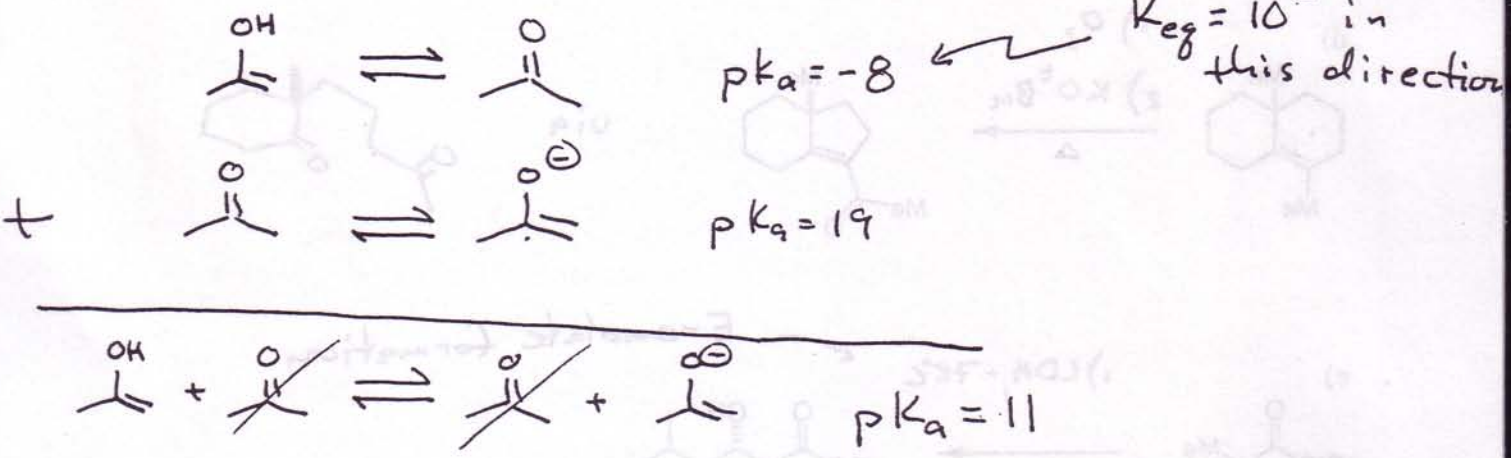


$pK_a = 19$ (in water)

Use these data and any additional information that you might need to estimate the pK_a of an enol proton (5 points).

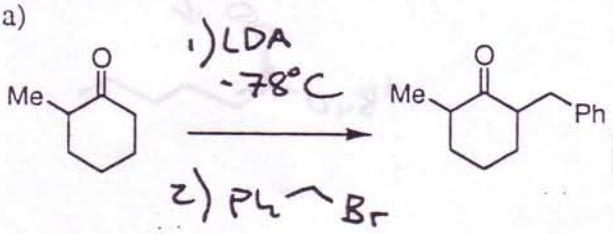


pKa = ???

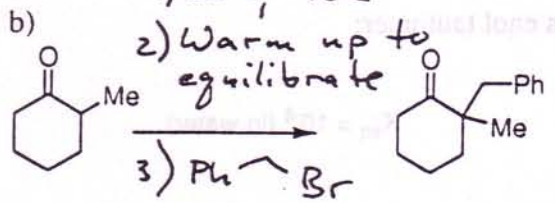


4. Provide all of the reagents required to carry out the following synthetic transformations. Where enolates are involved, be sure to supply specific reaction conditions as appropriate. Note that some of these conversions require more than one step (3 points each, 21 points total).

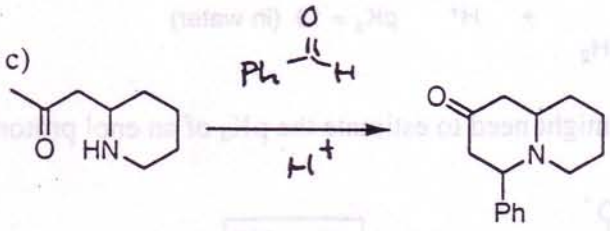
a)



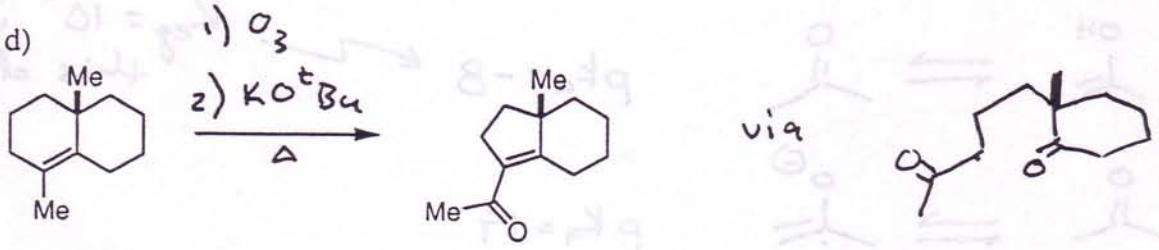
b)



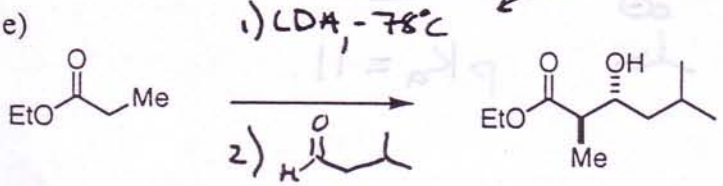
c)



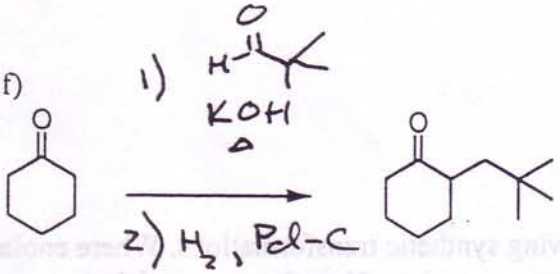
d)



e)

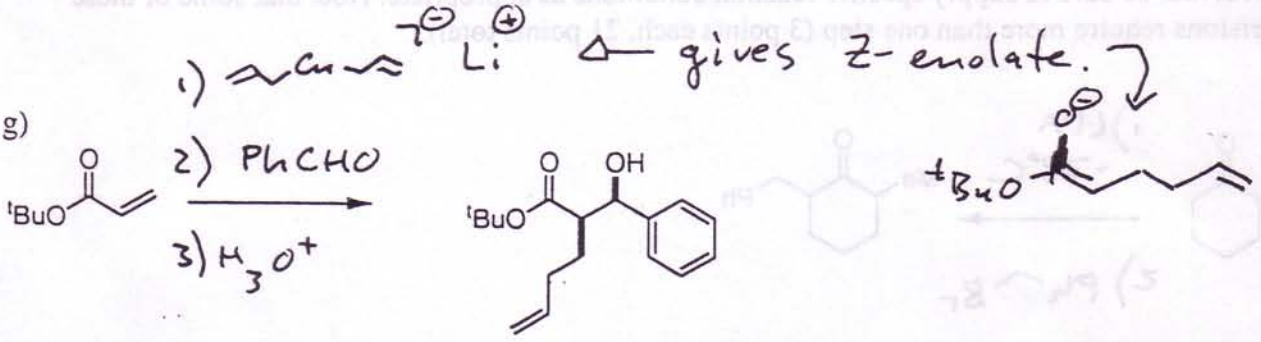


f)

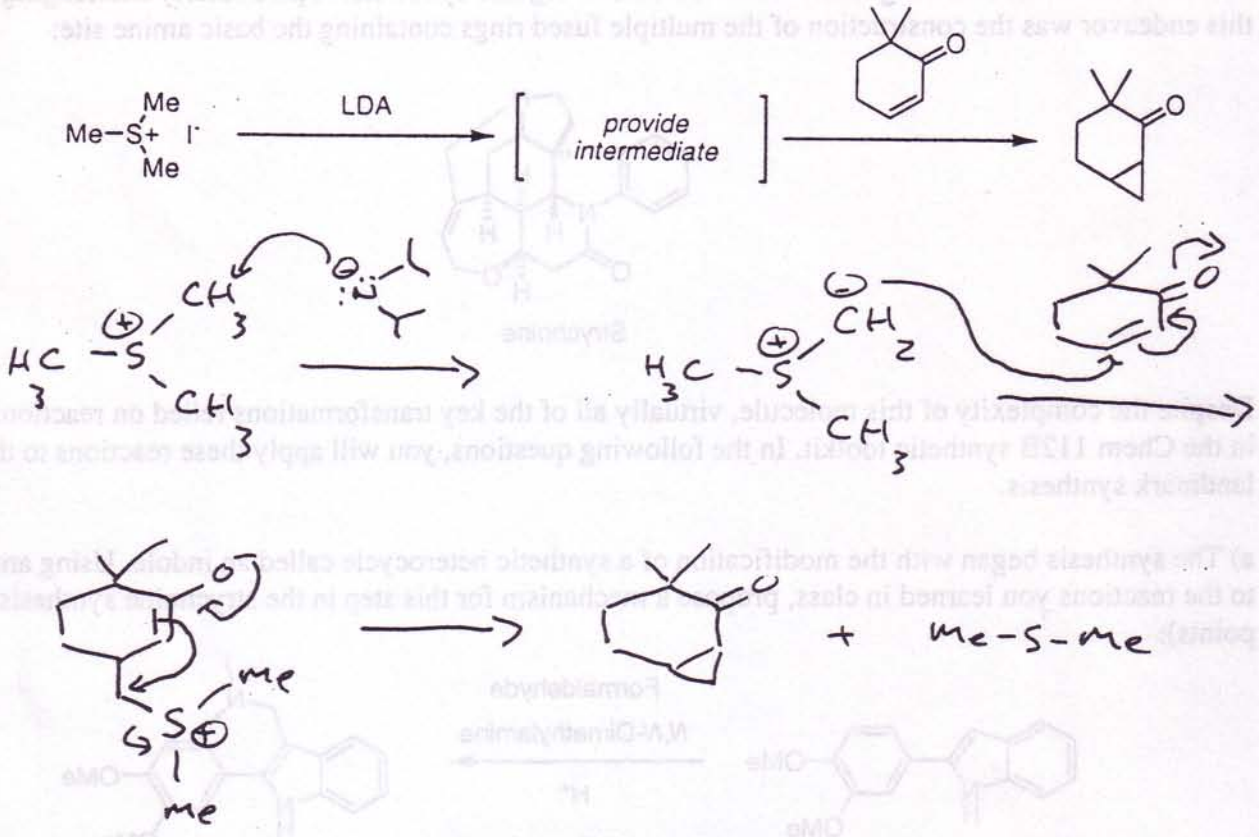


Hint: remember that S_N2 reactions do not occur at centers adjacent to *t*-butyl groups.

g)



5. Using analogies to reactions you have learned in class, provide a mechanism for the following cyclopropanation method (6 points):

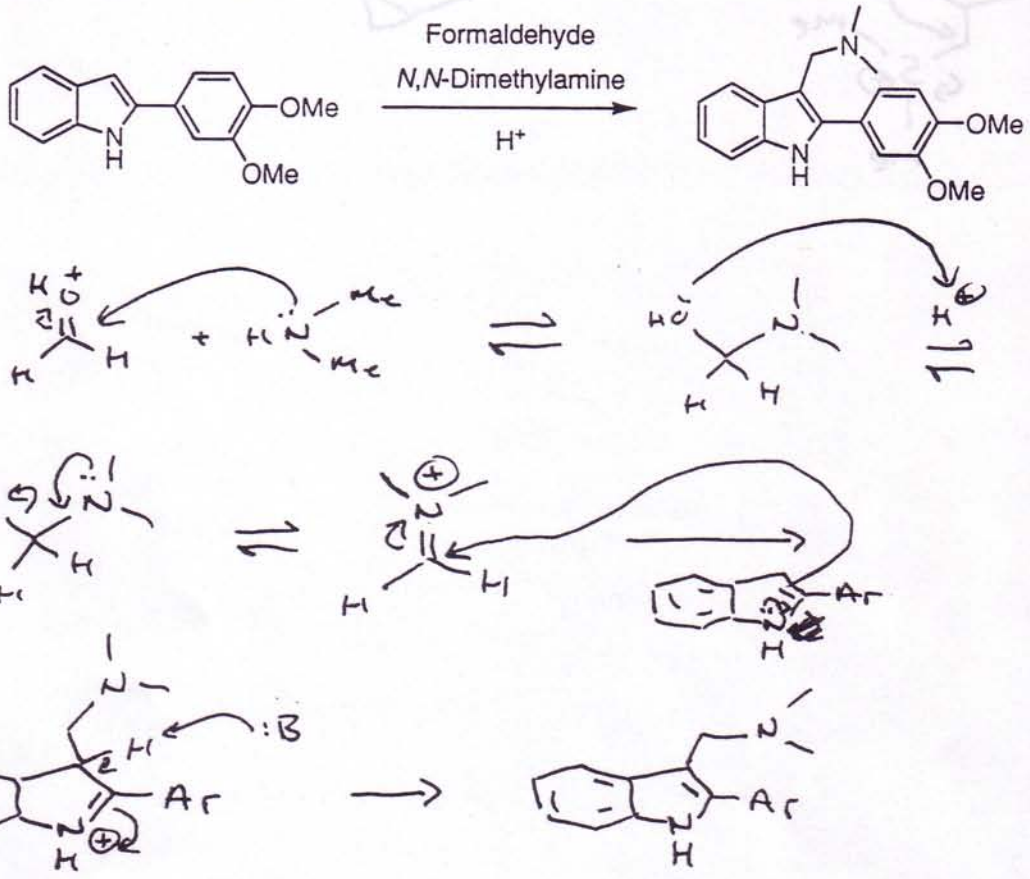


6. In 1954, Prof. R. B. Woodward reported the first total synthesis of strychnine, a work that is still considered to be one of the greatest achievements in organic synthesis. A particularly challenging aspect of this endeavor was the construction of the multiple fused rings containing the basic amine site:

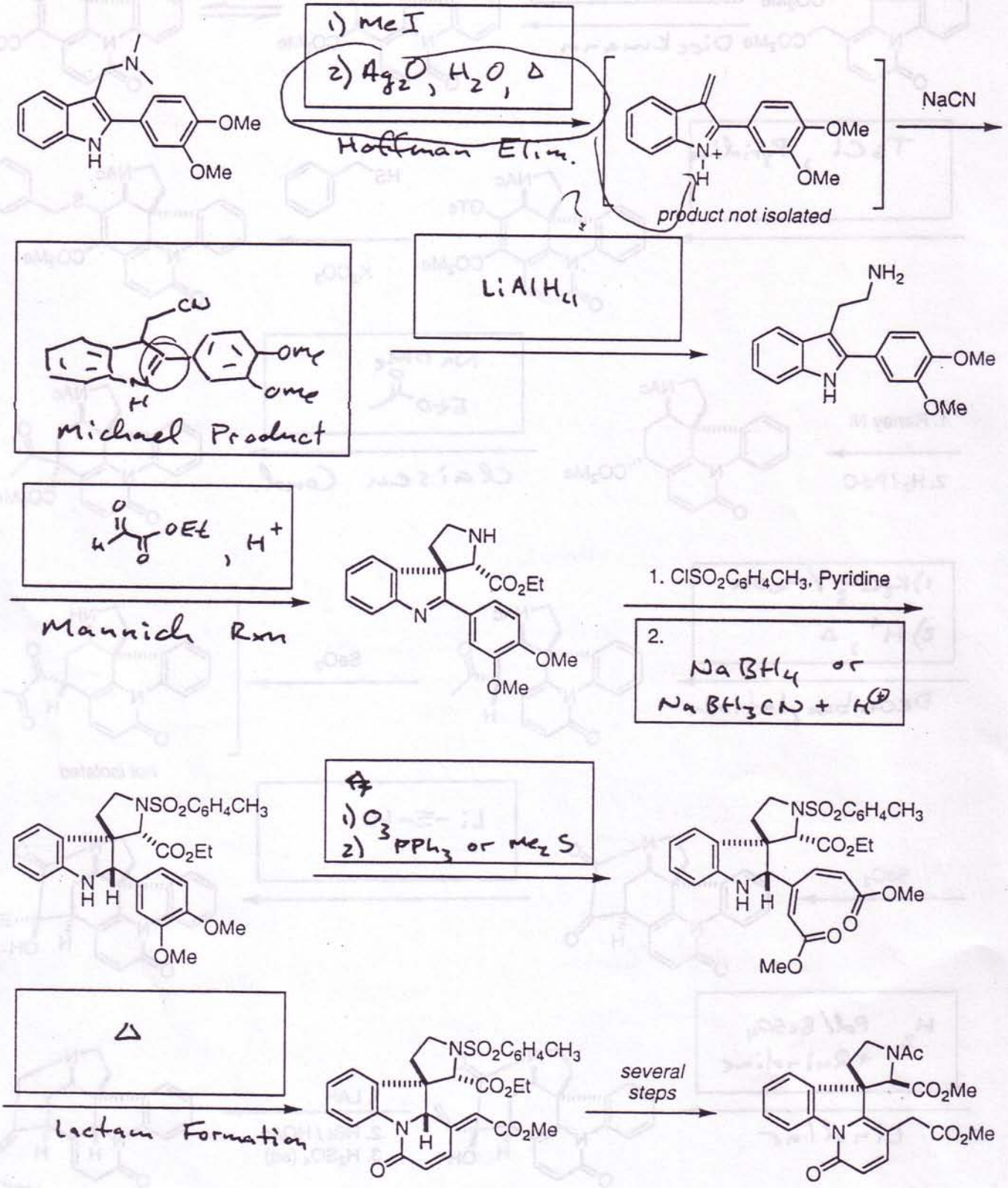
Strychnine

Despite the complexity of this molecule, virtually all of the key transformations relied on reactions that are in the Chem 112B synthetic toolkit. In the following questions, you will apply these reactions to this landmark synthesis.

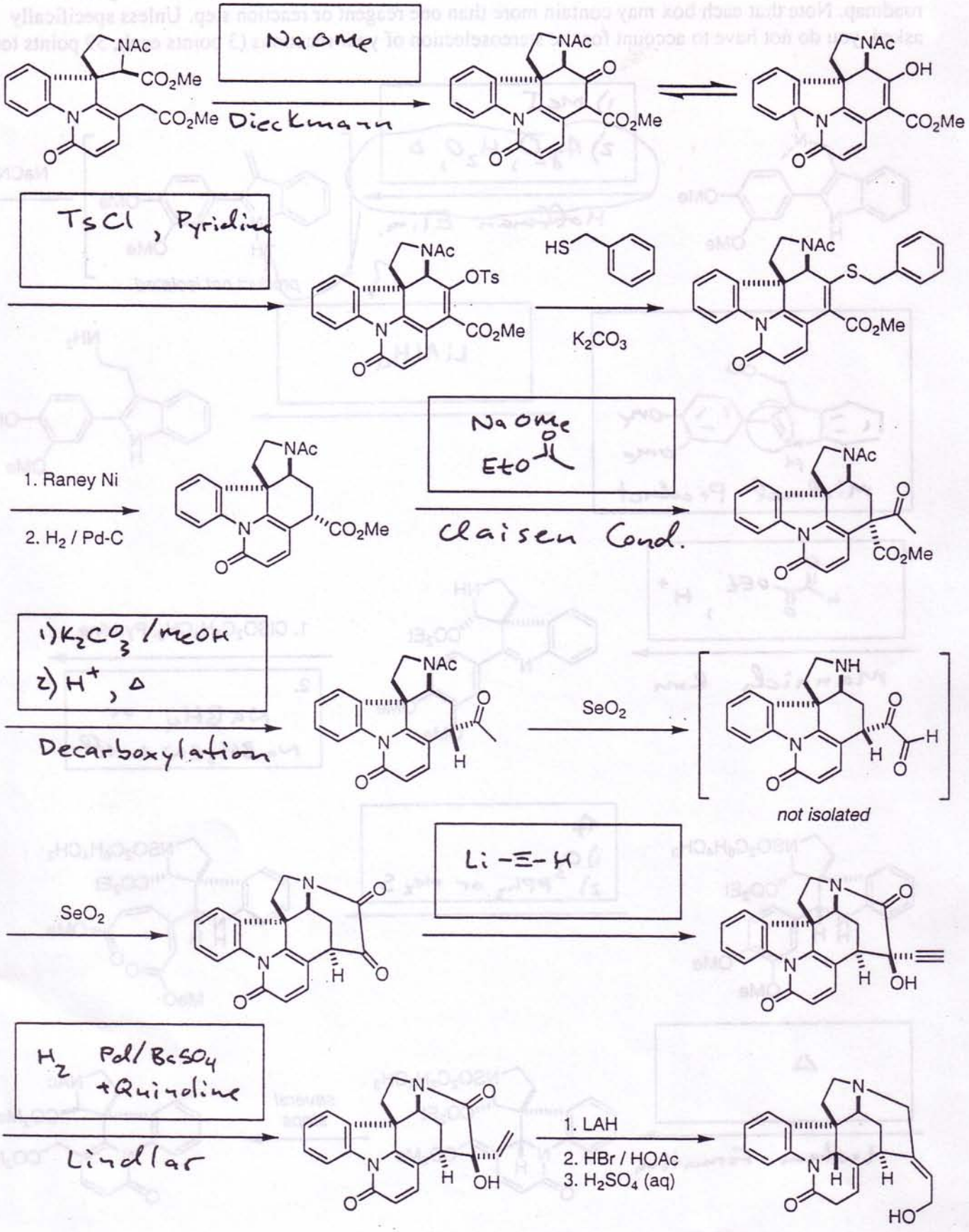
a) The synthesis began with the modification of a synthetic heterocycle called an indole. Using analogies to the reactions you learned in class, propose a mechanism for this step in the strychnine synthesis (6 points):



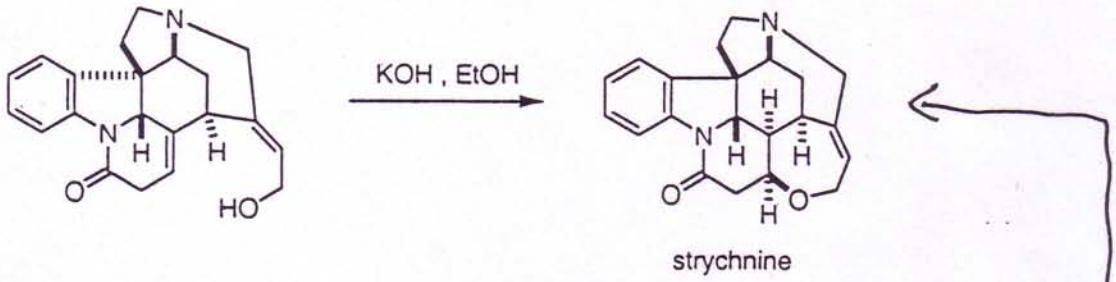
b) Continue the synthesis by filling in the missing reagents and structures in the following reaction roadmap. Note that each box may contain more than one reagent or reaction step. Unless specifically asked, you do not have to account for the stereoselection of your reactions (3 points each, 39 points total).



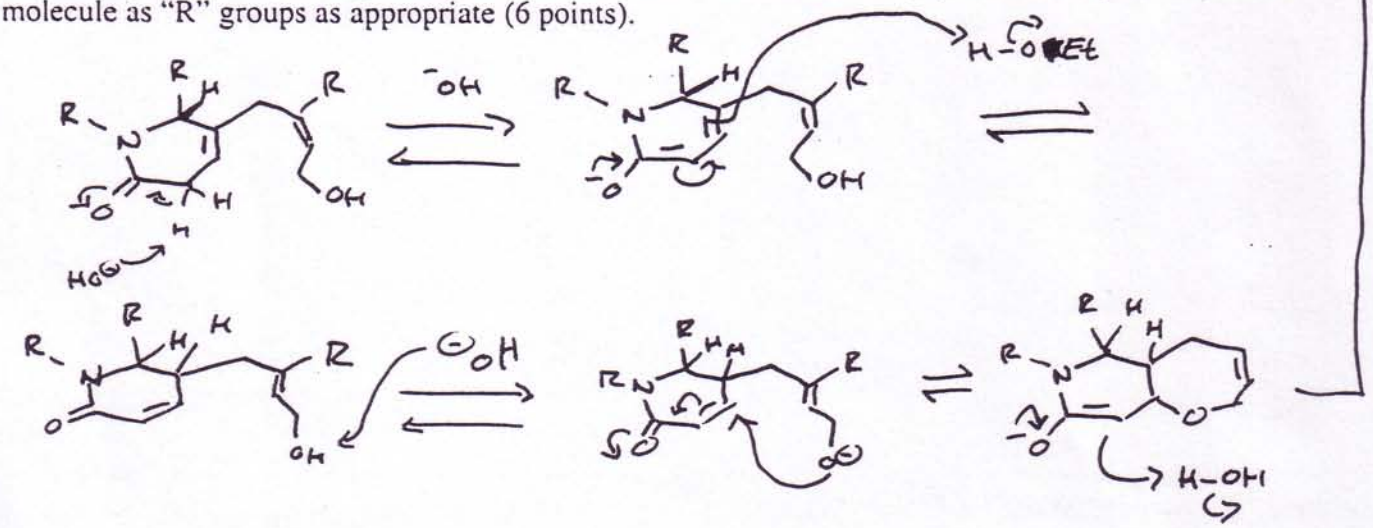
b) *Continued.*


NaOMe
Dieckmann
TsCl, Pyridine
HS
K_2CO_3
1. Raney Ni
2. H_2 / Pd-C
NaOMe
EtO
Claisen Cond.
1) K_2CO_3 / MeOH
2) H^+, Δ
Decarboxylation
SeO_2
not isolated
SeO_2
Li −≡− H
H_2 Pd/BaSO4 +Quinoline
Lindlar
1. LAH
2. HBr / HOAc
3. H_2SO_4 (aq)

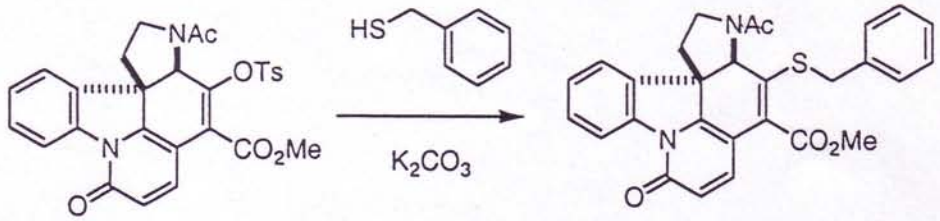
c) The final step of the synthesis involved the following ring closure reaction:



Provide a full arrow-pushing mechanism for this transformation. You may abbreviate portions of the molecule as "R" groups as appropriate (6 points).



d) A key transformation in this sequence is the conversion of a vinyl tosylate to a vinyl sulfide:



Propose a mechanism for this transformation. You may abbreviate portions of the molecule as "R" groups as appropriate (6 points).