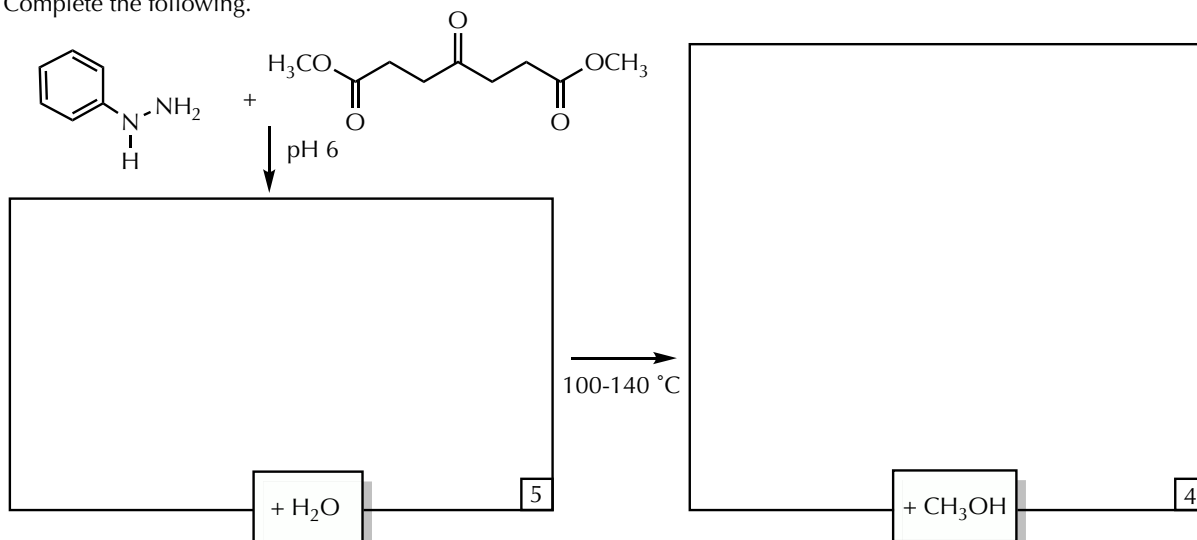


Question 1 (24 points)

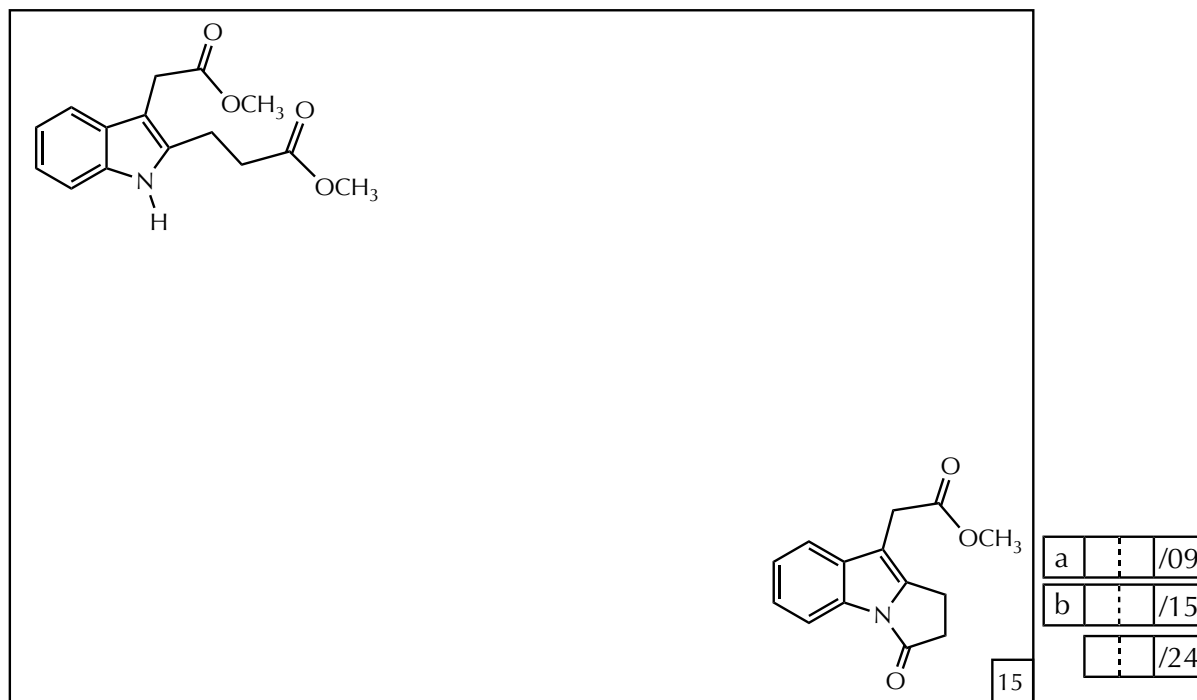
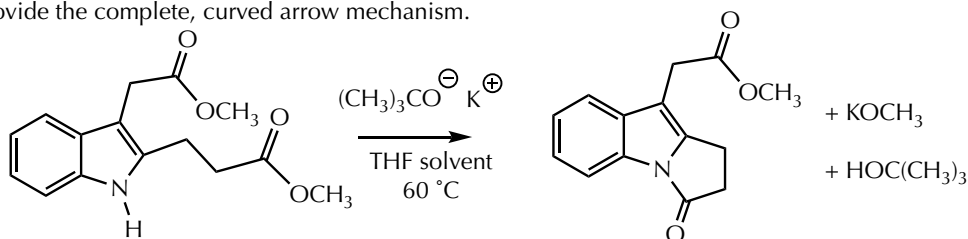
Name: _____

A biologically active compound known as MK-1029 blocks a receptor that is involved in stimulating an allergic reaction associated with respiratory diseases (*Org. Process Res. Dev.* **2022**, 26, 648). A few steps from a reported synthesis are included in this question.

(a) Complete the following.



(b) Later in the synthesis, the following reaction is carried out. The starting material, called an indole, has a pK_a value of about 16. Provide the complete, curved arrow mechanism.

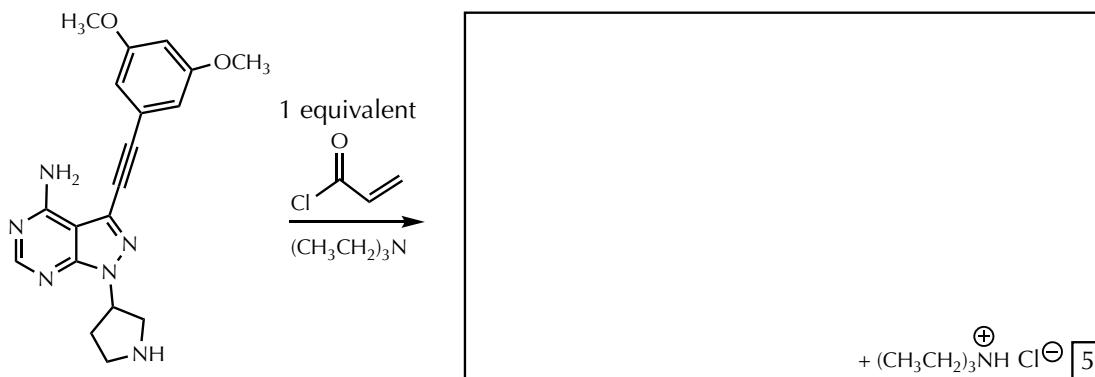


Question II (28 points)

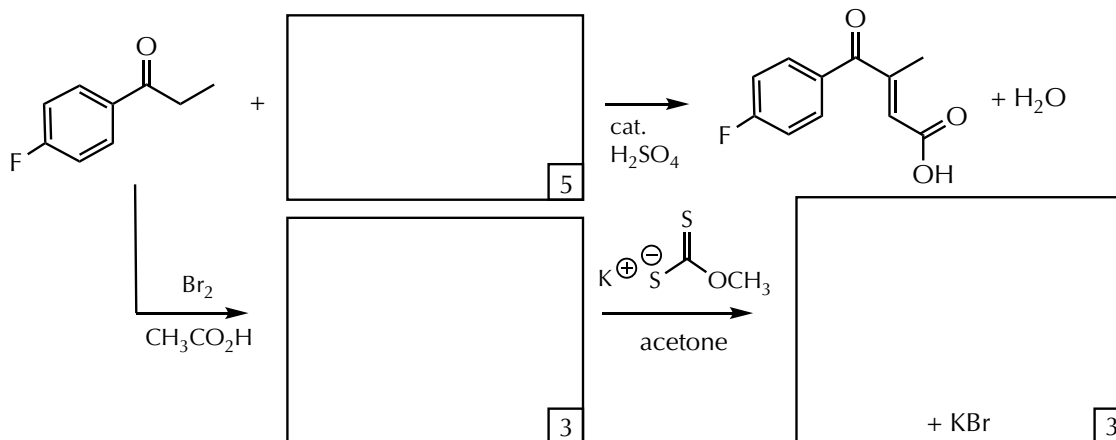
Name: _____

Complete the following reaction schemes. Be sure to number different experimental steps if needed.

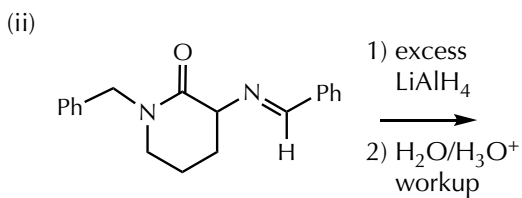
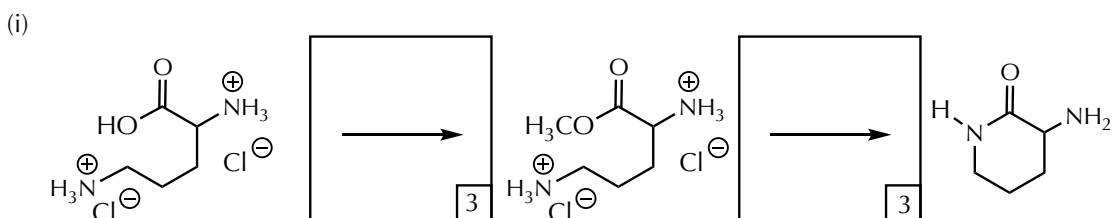
(a) synthesis of futibatinib, a fibroblast growth factor inhibitor (*Org. Process Res. Dev.* **2022**, 26, 43)



(b) synthesis of 6-fluoromenadione, an intermediate in the synthesis of biologically active agents (*Org. Process Res. Dev.* **2022**, 26, 1152)



(c) from the preparation of pharmacophores, molecular units that are integrated into the synthesis of prospective drug targets (*Org. Process Res. Dev.* doi.org/10.1021/acs.oprd.2c00152)



note: two functional groups are reduced to give a product with only uncharged atoms

a	...	/05
b	...	/11
c	...	/12
	...	/28

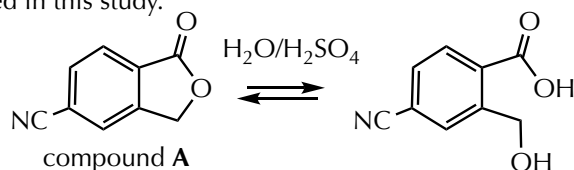
6

Question III (28 points)

Name: _____

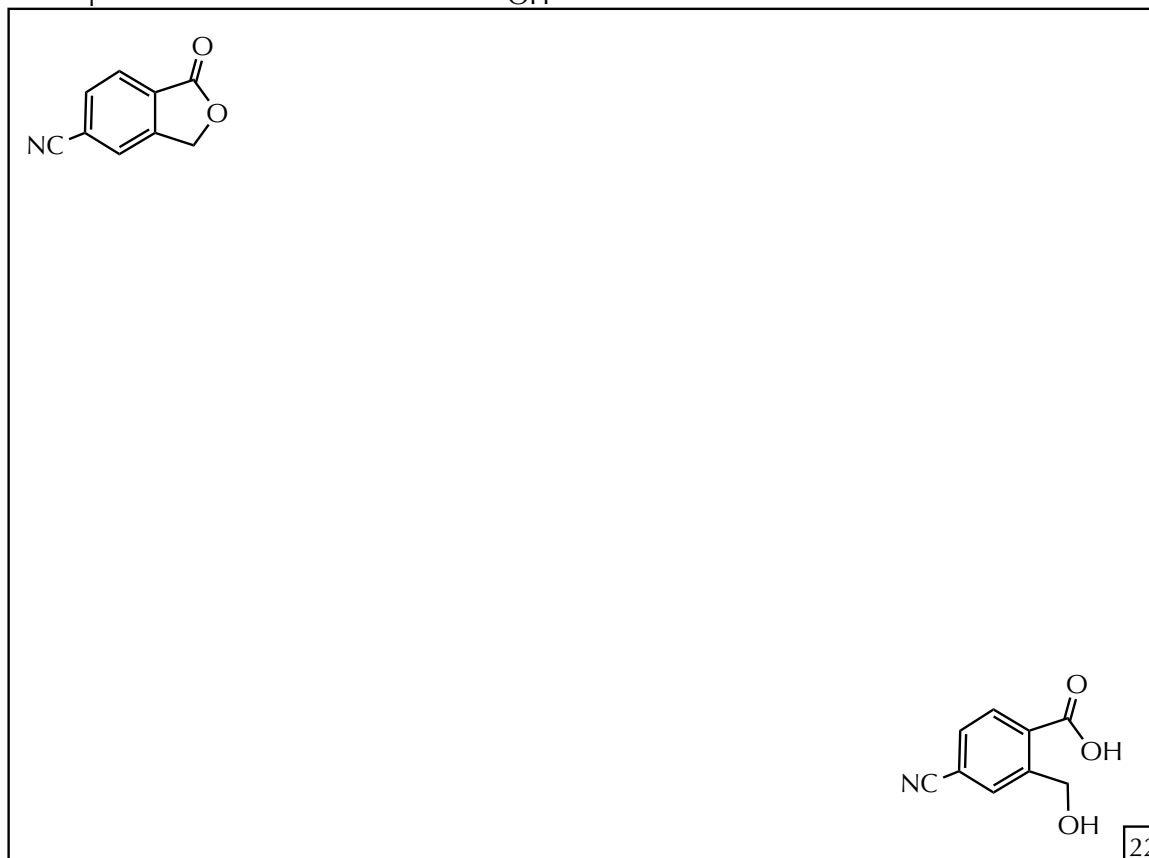
The acid and base catalyzed hydrolysis reaction of lactones was germane to a study on developing new therapeutics for a rare form of leukemia (*Org. Process Res. Dev.* **2022**, 26, 2739).

(a) Provide the complete, stepwise mechanism for the acid catalyzed hydrolysis of the lactone (compound **A**) used in this study.



Use H-B as your general Brønsted acid and B^\ominus as a general Brønsted base.

Draw intermediates as their significant (closed shell) resonance contributors.



(b) Because of the net entropic disadvantage, the K_{EQ} for the hydrolysis reaction, under the conditions shown above, was less than 10^{-2} . Only one of the three other reaction conditions (shown below) gave a ring-opened product as the major outcome. Which set of conditions resulted in a ring-opened product? Draw the outcome.

(i) Which conditions (mark one) resulted in a ring-opened product as the outcome?

<input type="checkbox"/>	KOH in H_2O
<input type="checkbox"/>	CH_3OK in CH_3OH
<input type="checkbox"/>	CH_3OH with catalytic H_2SO_4

3

(ii) Draw the outcome. No credit if the incorrect conditions were selected.



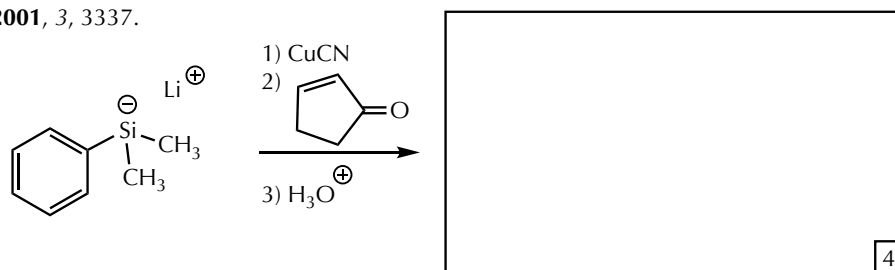
a				/22
b				/06
				/28

Question IV (20 points)

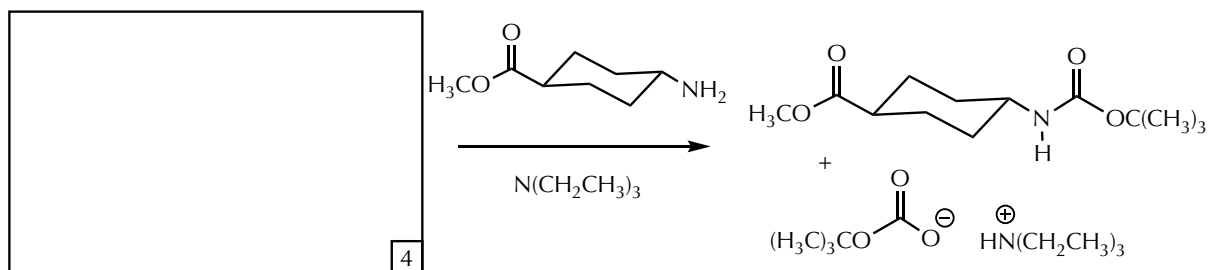
Name: _____

Complete the following as required.

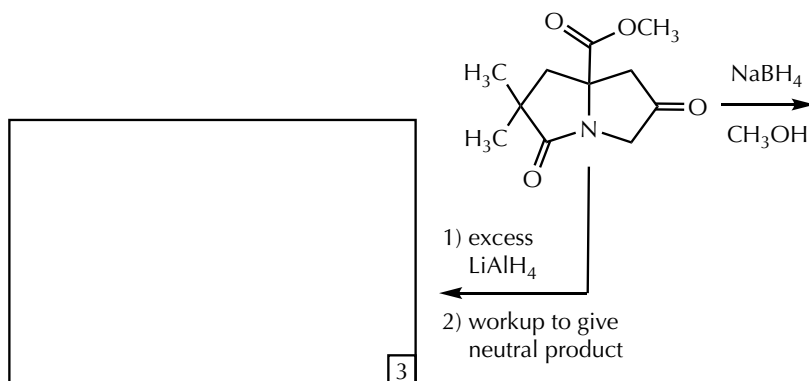
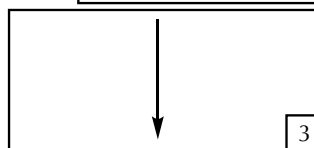
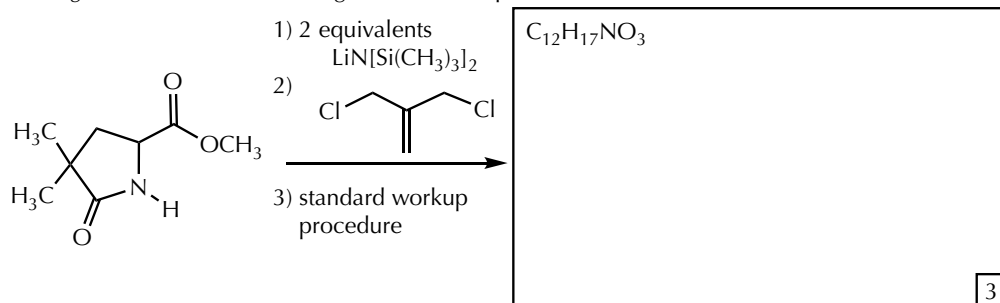
(a) *Org. Lett.* **2001**, 3, 3337.



(b) *Org. Process Res. Dev.* **2022**, 26, 2483.



(c) *Org. Process Res. Dev.* doi.org/10.1021/acs.oprd.2c00200.



connectivity only

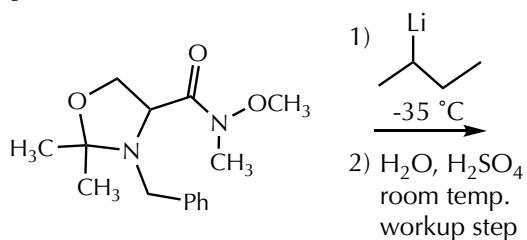
a	:	/04
b	:	/04
c	:	/12
	:	/20

Question V (20 points)

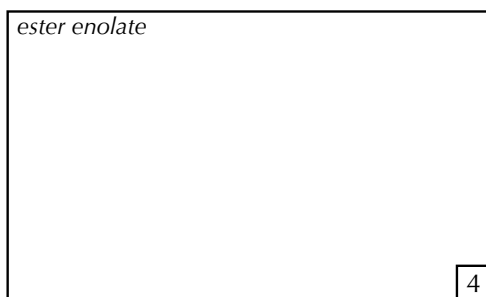
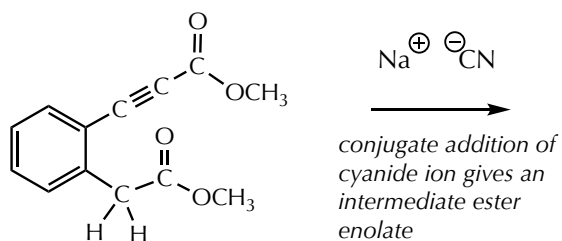
Name: _____

Complete the following as needed.

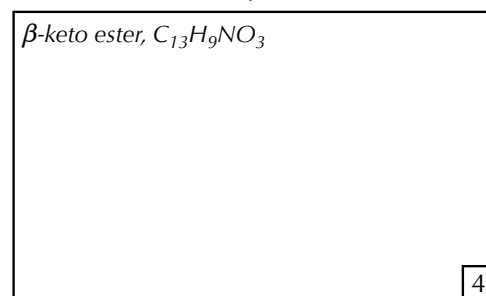
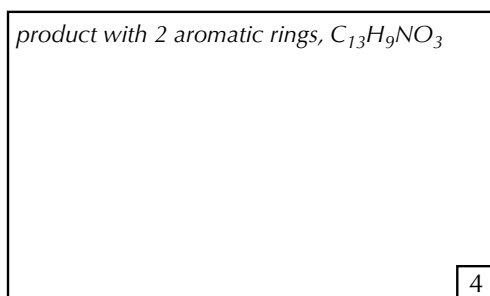
(a) *J. Org. Chem.* **2004**, 69, 3233.



(b) *Org. Lett.* **2002**, 4, 1403.

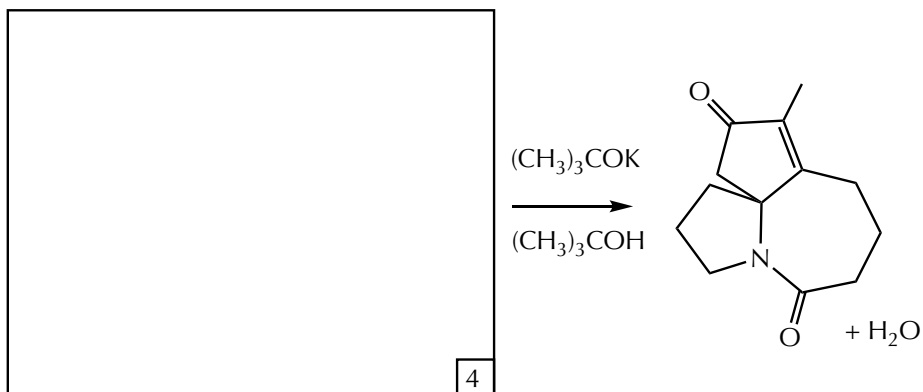


Dieckmann condensation
(intramolecular acylation
of the ester enolate) gives
a β -keto ester



keto-enol
tautomerization

(c) *Org. Lett.* **2010**, 10, 1763: an intramolecular aldol condensation



a	...	/04
b	...	/12
c	...	/04
	...	/20