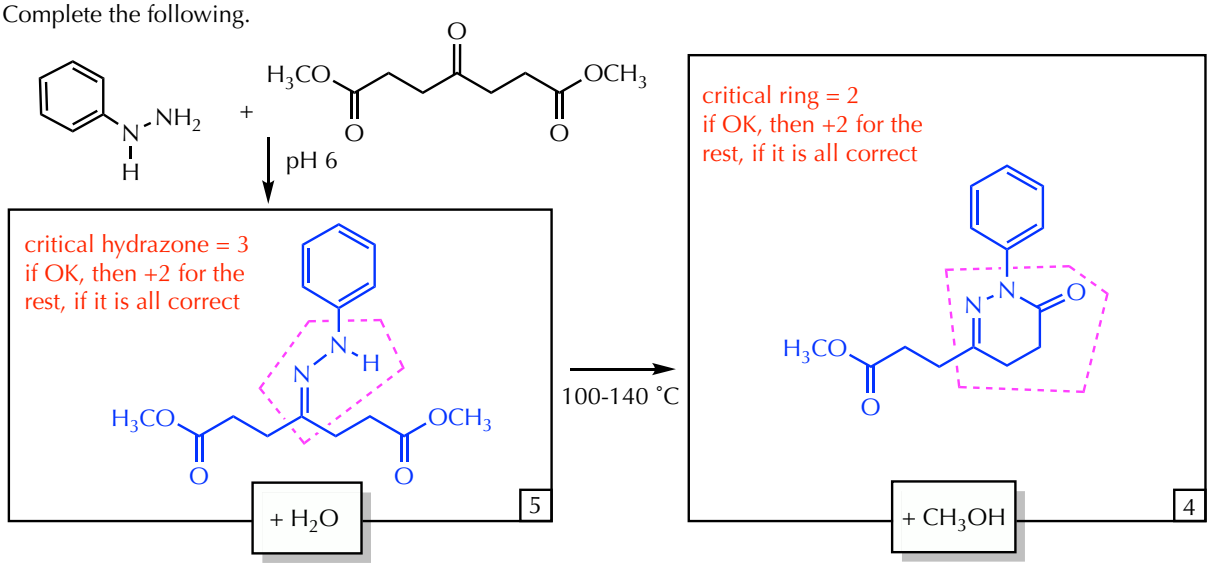
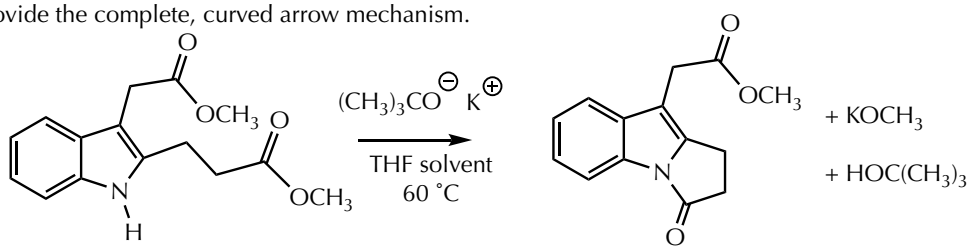
Question I (24 points) Name: _____

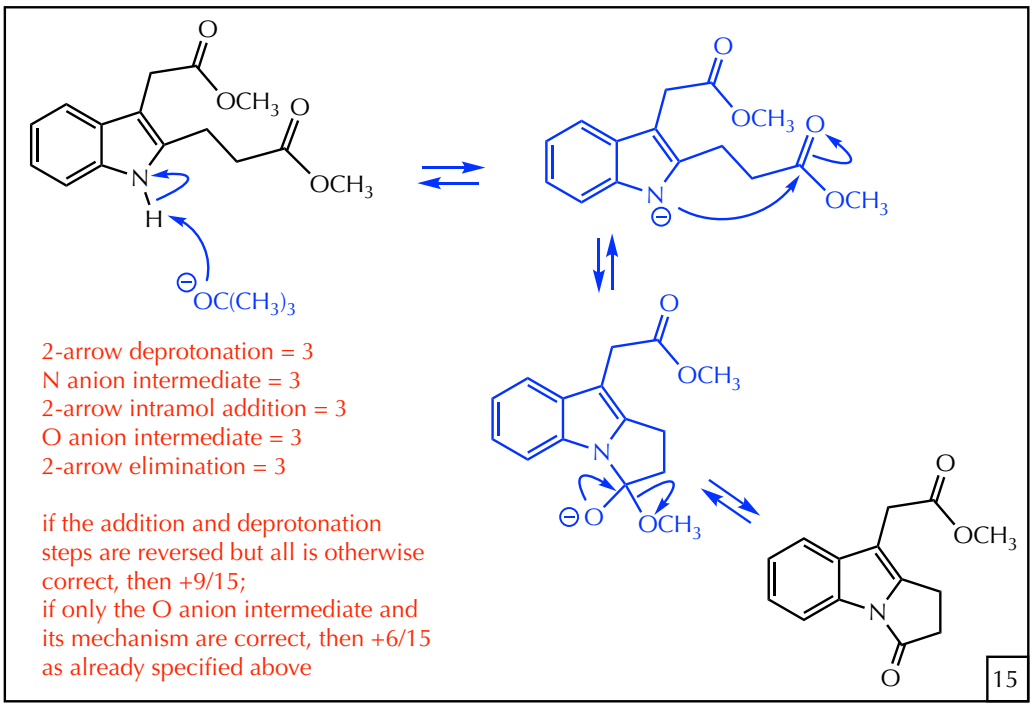
A biologically active compound known as MK-1029 blocks a receptor that is involved in stimulating an allergic reaction associated with respiratory diseases (*Org. Process Res. Dev.* **2022**, *26*, 648). A few steps from a reported synthesis are included in this question.

(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.



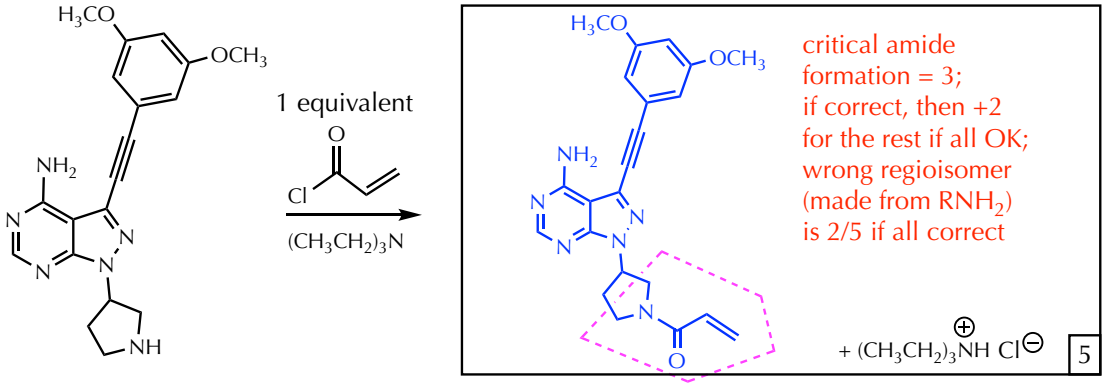


a		/09
b		/15
		/24

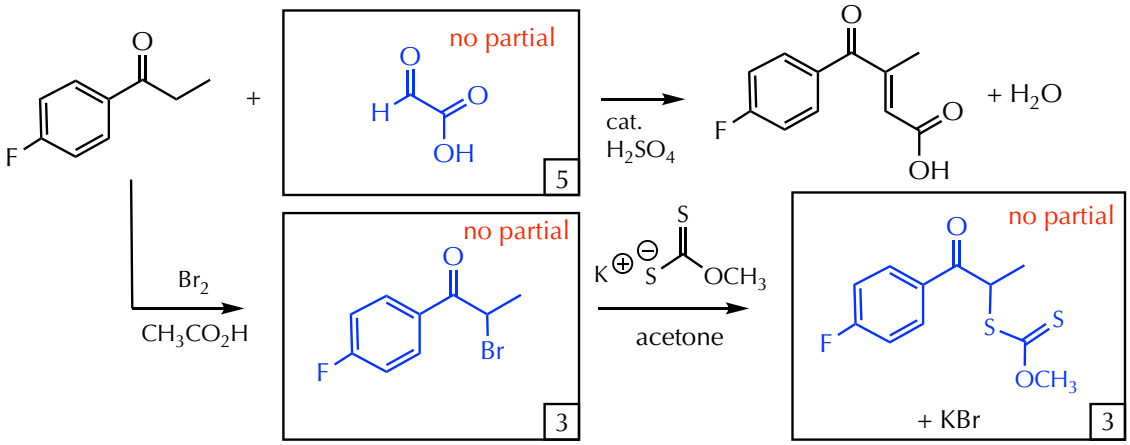
Question II (28 points) Name: _____

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)

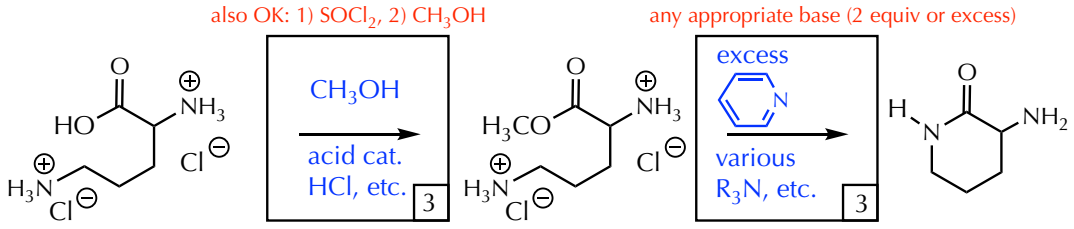


(b) synthesis of 6-fluoromenadione, an intermediate in the synthesis of biologically active agents (*Org. Process Res. Dev.* **2022**, *26*, 1152)

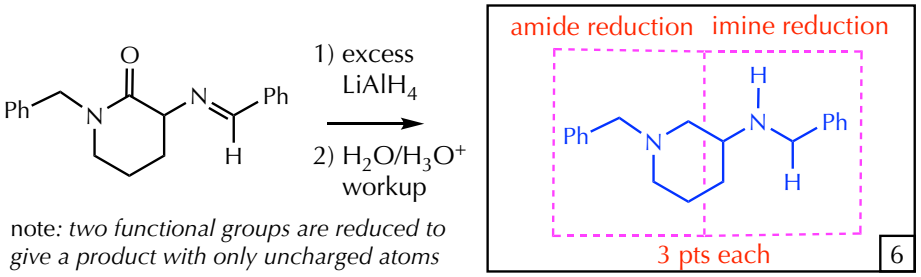


(c) from the preparation of pharmacophores, molecular units that are integrated into the synthesis of prospective drug targets (*Org. Process Res. Dev.* doi.org/10.1021/acs.oprd.2c00152)

(i)



(ii)



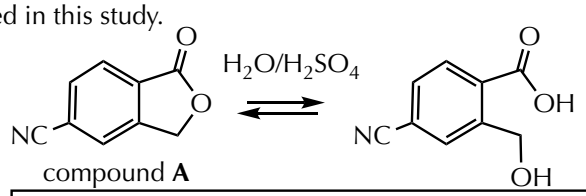
note: *two functional groups are reduced to give a product with only uncharged atoms*

a		/05
b		/11
c		/12
		/28

Question III (28 points) Name: _____

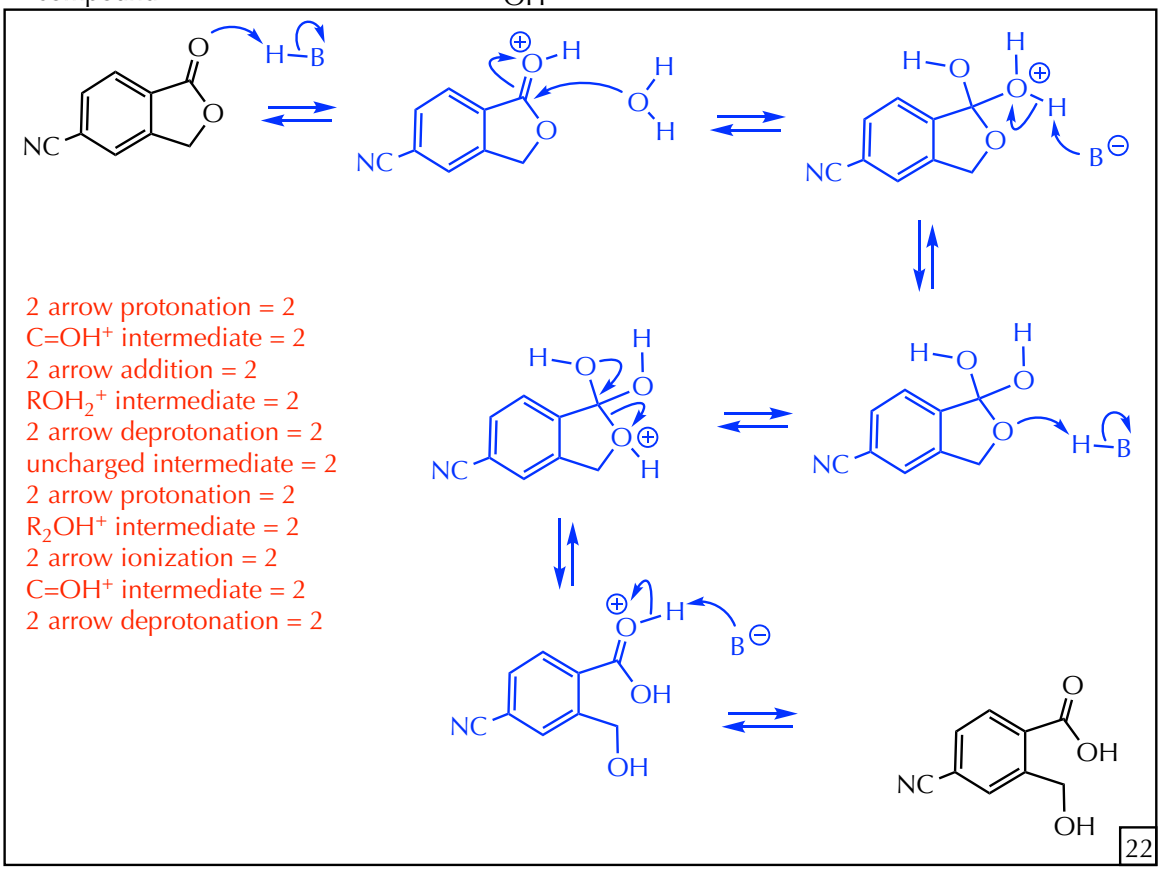
The acid and base catalyzed hydrolysis reaction of lactones was germane to a study on developing new therapuetics for a rare form of leukemia (*Org. Process Res. Dev.* **2022**, *26*, 2739).

(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.

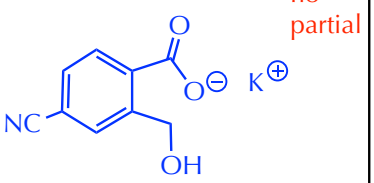


(b) Because of the net entropic disadvantage, the K_{EQ} for the hydrolysis reaction, under the conditions shown above, was less than 10^{-2}. Only one of the three other reaction conditions (shown below) gave a ring-opened product as the major outcome. Which set of conditions resulted in a ring-opened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

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

X	KOH in H_2O	no partial
	CH_3OK in CH_3OH	
	CH_3OH with catalytic H_2SO_4	3

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



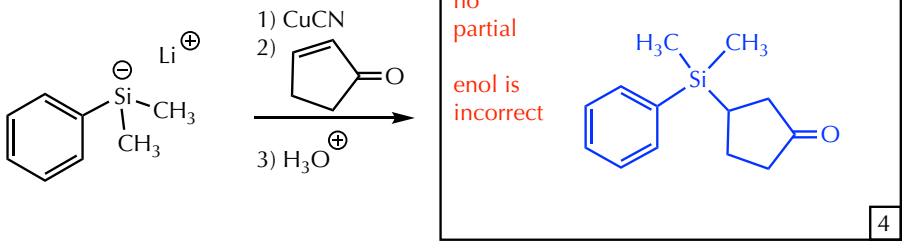
a		/22
b		/06
		/28

Question IV (20 points)

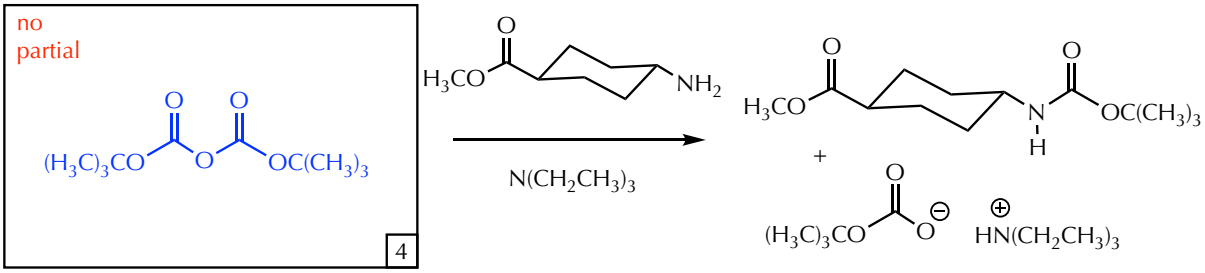
Name: _____

Complete the following as required.

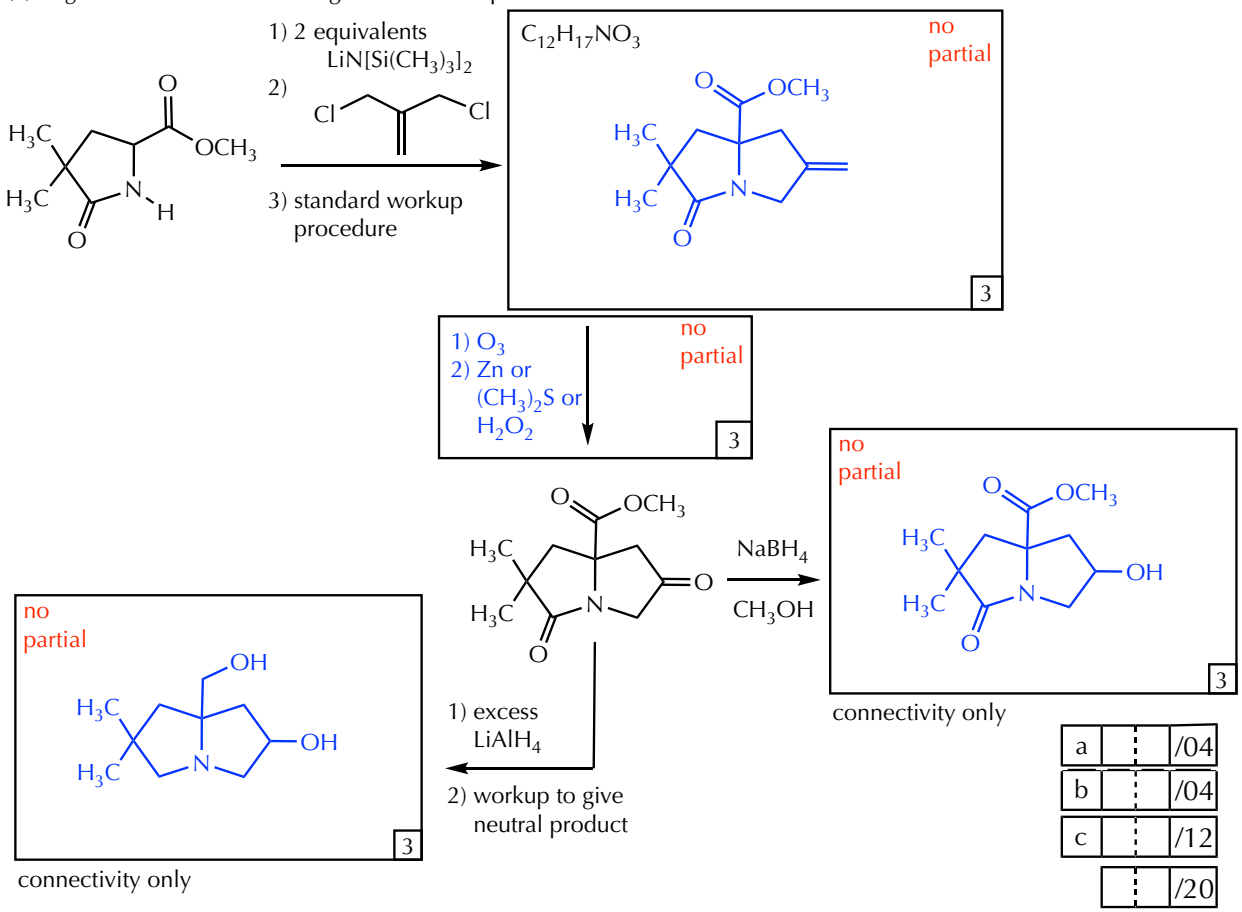
(a) *Org. Lett.* **2001**, *3*, 3337.



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



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



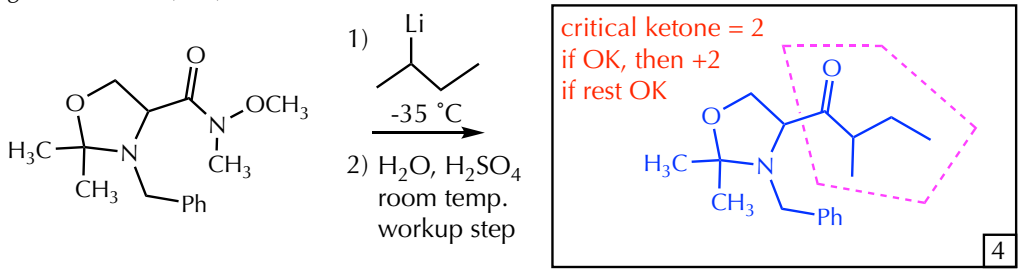
a		/04
b		/04
c		/12
		/20

Question V (20 points)

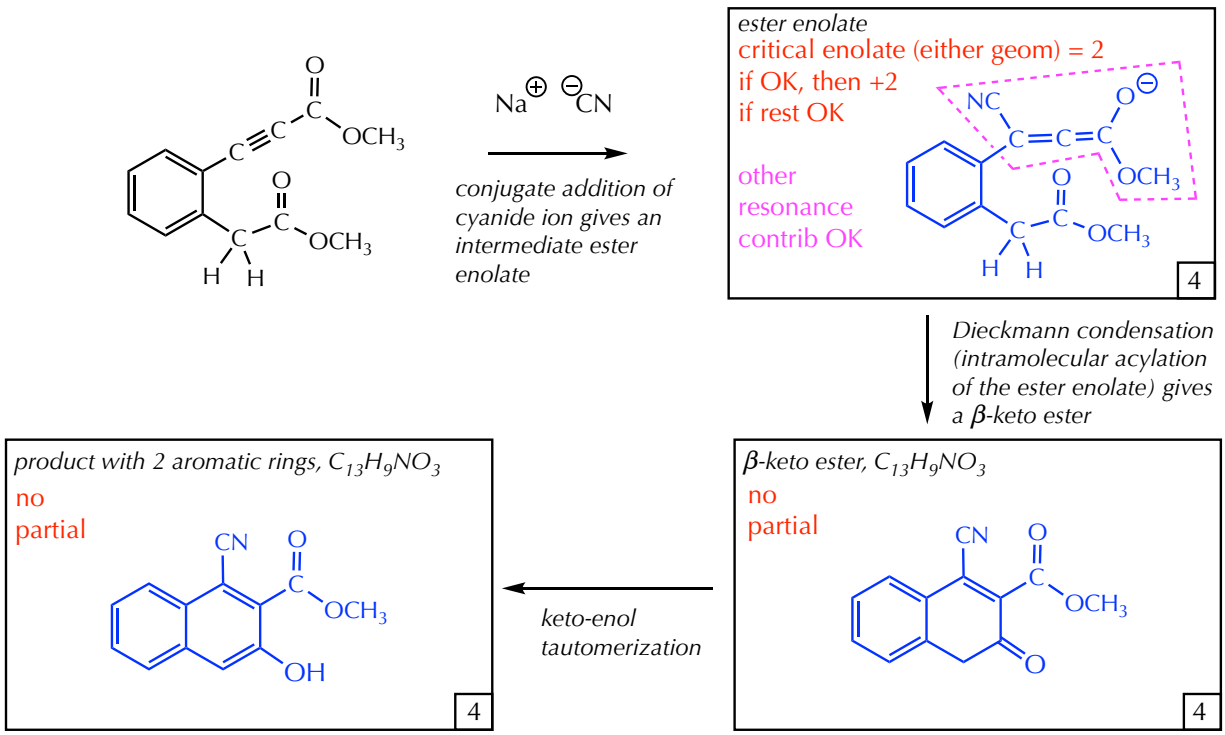
Name: _____

Complete the following as needed.

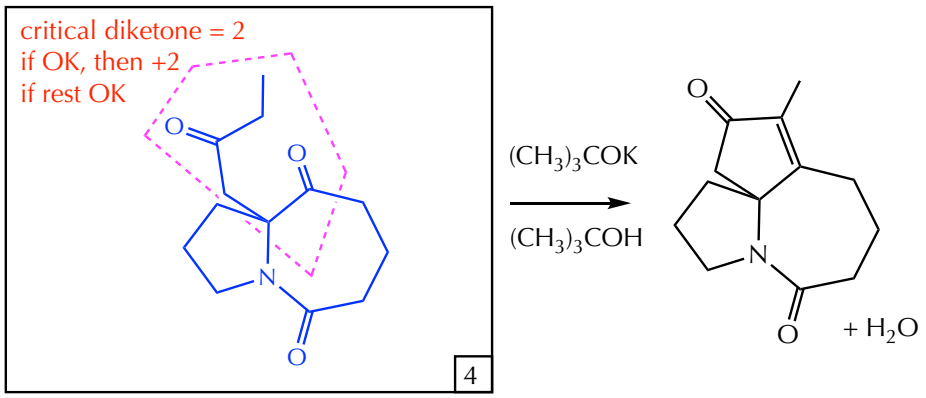
(a) *J. Org. Chem.* **2004**, *69*, 3233.



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



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



a		/04
b		/12
c		/04
		/20