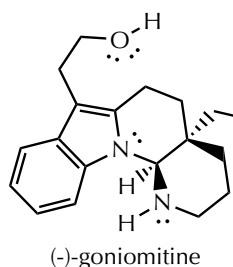


Question 1 (28 points)

Name: _____

(-)-Goniomitine (see below), isolated from a root bark in 1987, is currently being synthesized and investigated for its promising anticancer activity (*Angew. Chem., Int. Ed.* **2019**, *58*, 1174).

(a) Answer the following about this compound.



i. Stereochemical configuration of the center with the ethyl group?

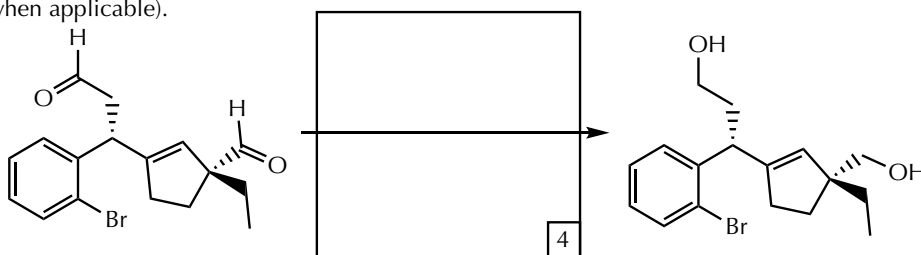
ii. Best value for the pK_a of its conjugate acid (using the table).

iii. Stereochemical configuration of the center with 2 nitrogen atoms?

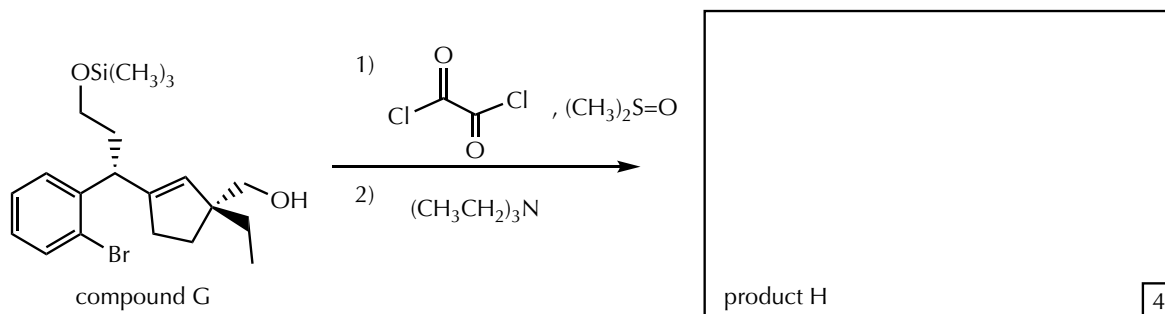
iv. How many aromatic rings in this compound?

v. Best value (using the table) for the lowest pK_a proton in this compound?

(b) Complete the following transformation from the synthesis of (-)-goniomitine (number different experimental steps when applicable).



(c) Complete the following transformation from the synthesis of (-)-goniomitine.



(d) Answer the following questions about the transformation in part (c).

i. The specific functional group transformation in the reaction of compound G to product H is from what to what? Include degree of substitution in the classification when possible.

 to

ii. In this reaction, is compound G behaving as a reducing agent or an oxidizing agent?

iii. One of the atoms in compound G undergoes a change in its oxidation state. What is its value:

in compound G?

in the product H?

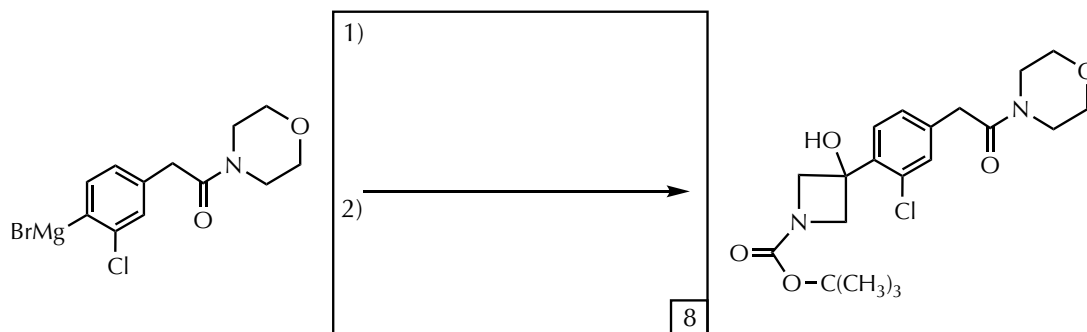
a	/	10
b	/	04
c	/	04
d	/	10
	/	28

Question II (26 points)

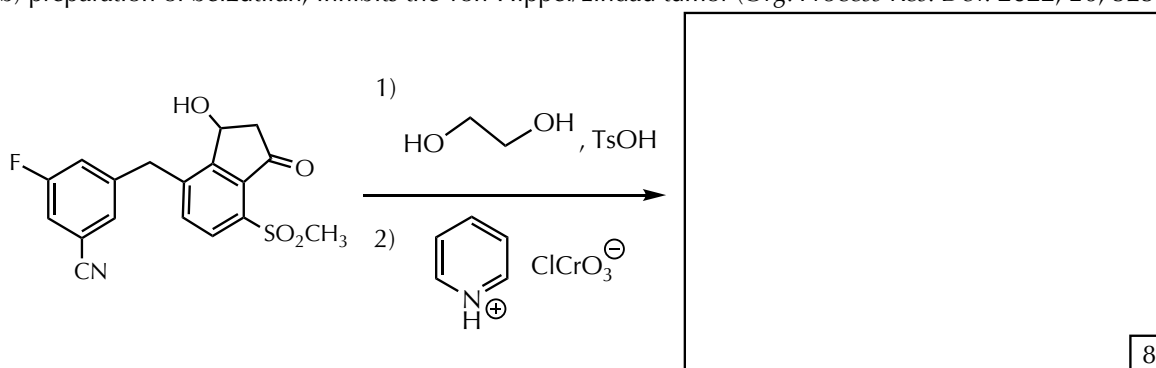
Name: _____

Complete the following reaction schemes.

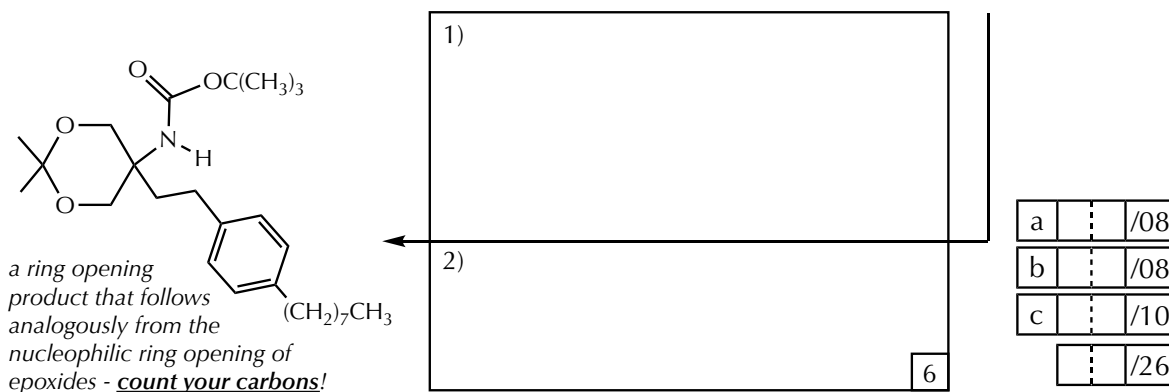
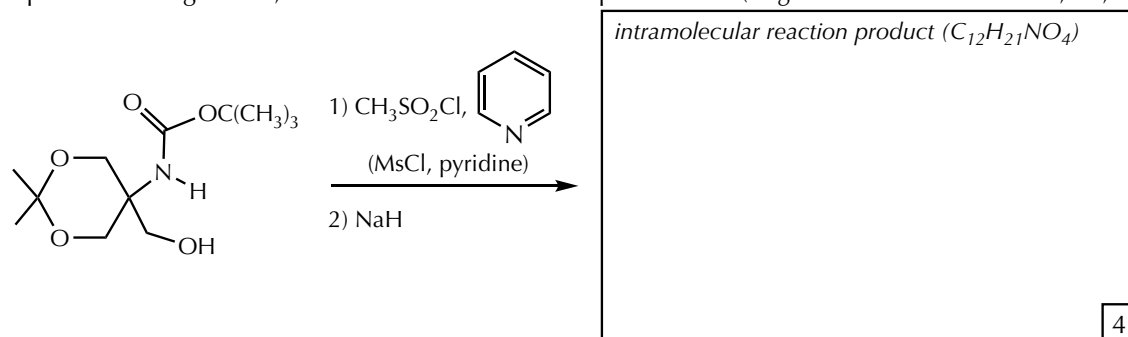
(a) an agonist for the treatment of non-alcoholic steatohepatitis (*Org. Process Res. Dev.* **2022**, 26, 745)



(b) preparation of belzutifan, inhibits the von-Hippel/Lindau tumor (*Org. Process Res. Dev.* **2022**, 26, 525).

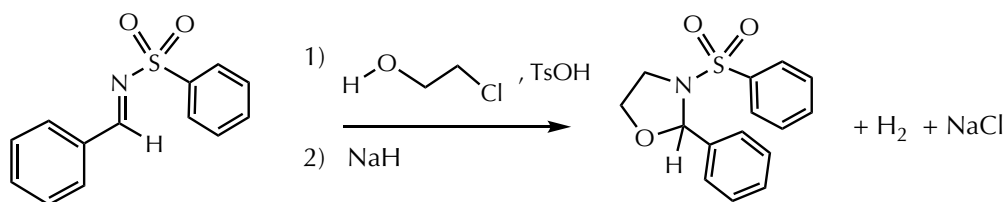


(c) preparation of fingolimod, immunomodulator for multiple sclerosis (*Org. Process Res. Dev.* **2022**, 26, 859).



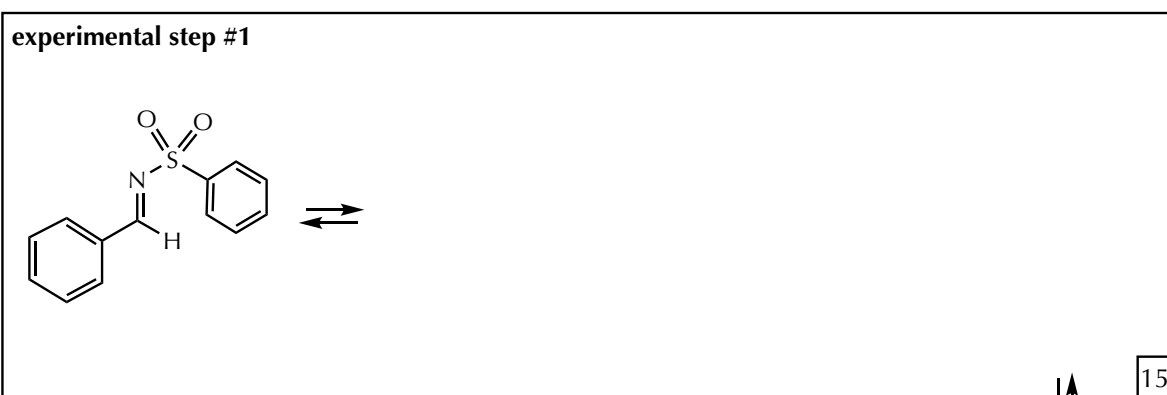
Question III (27 points)

Name: _____

The following transformation is analogous to one reported in *Org. Lett.* **2014**, 16, 4098.

Provide the complete, stepwise mechanism for the first experimental step according to this information:

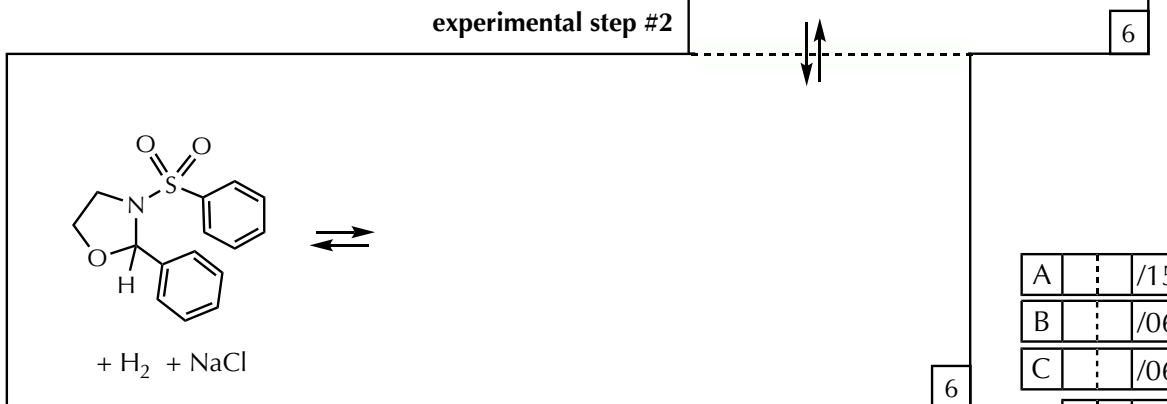
TsOH protonates the starting material to give a specific acid catalyzed addition reaction of the alcohol group of 2-chloroethanol to the CN bond; subsequent deprotonation (use the conjugate base of acid catalyst) gives an uncharged intermediate (A).



Draw the proposed uncharged intermediate (A), which is the addition reaction product.

Provide the complete, stepwise mechanism for the second experimental step according to this information:

the ionic base, sodium hydride, deprotonates the uncharged intermediate (A); the resulting anion undergoes an intramolecular reaction, forming the observed product.



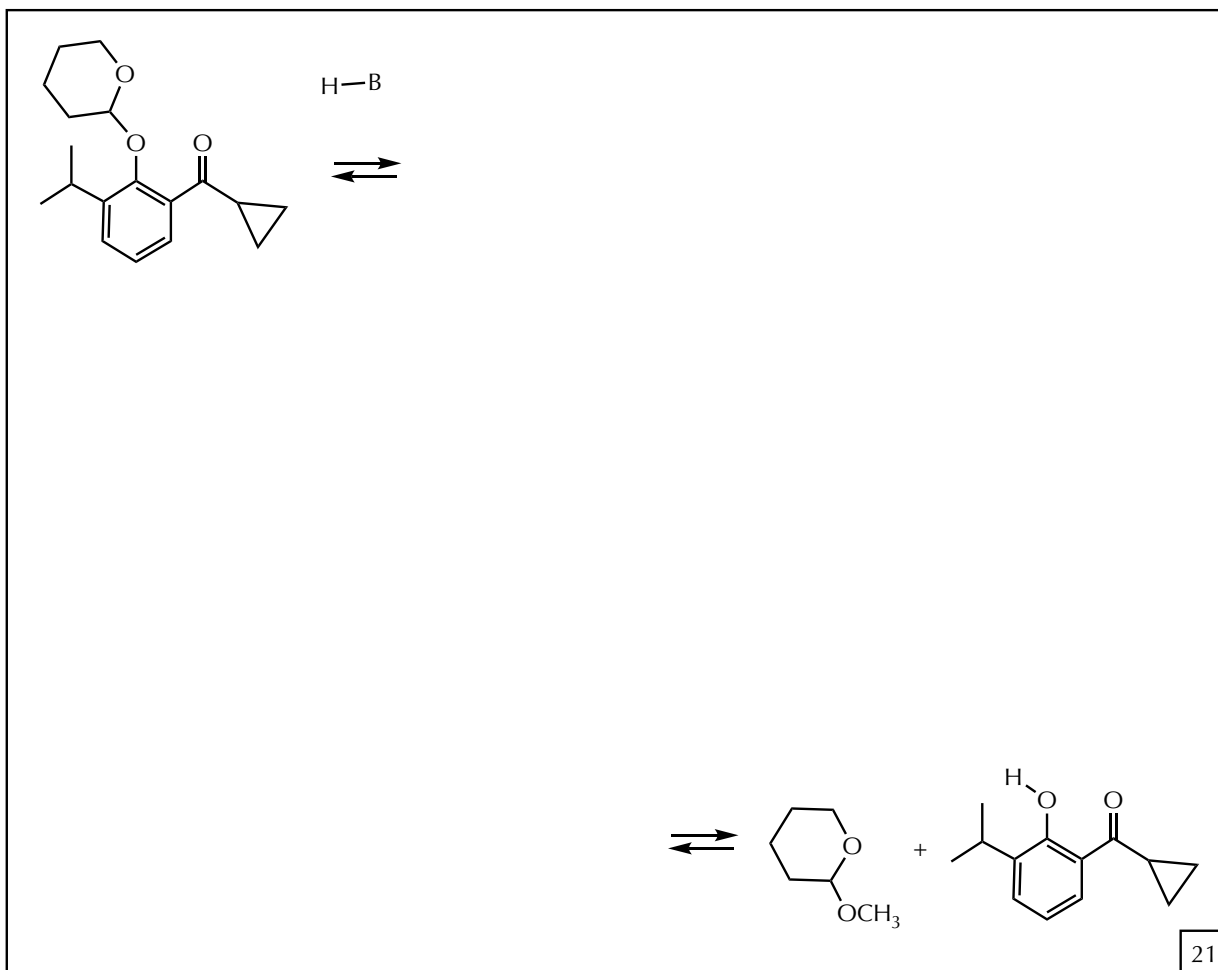
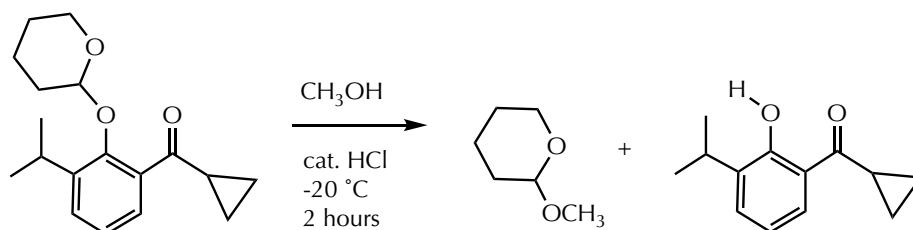
A	:	/15
B	:	/06
C	:	/06
	:	/27

Question IV (21 points)

Name: _____

From the abstract of *Org. Process Res. Dev.* **2022**, 26, 1054: "Propofol has been widely used as a clinical anesthetic for a few decades. Its derivative with a three-membered ring, Cipepofol, was found to be equally effective and with less side effects. Here, we report a process for the scale-up total synthesis of Cipepofol. It could be obtained in five steps from the commercially available 2-isopropylphenol... in a 14% overall yield, without column chromatographic purification."

The third step in the process is shown below. Analyze carefully the functional groups and decide on the overall transformation, then provide the complete, stepwise mechanism for the transformation. Use HB as any generally needed Brønsted acid and B:[⊖] as its conjugate base. All intermediates should be shown as closed shell resonance contributors.



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