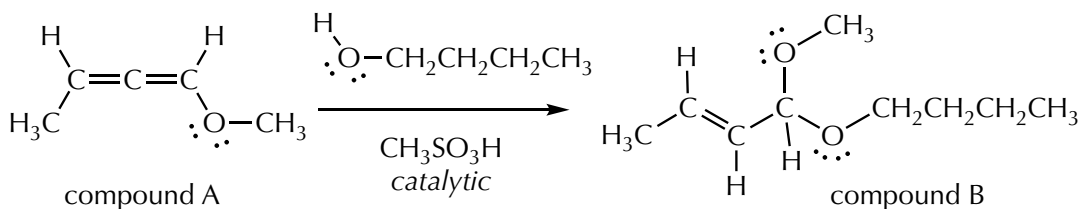


Question 1 (20 points)

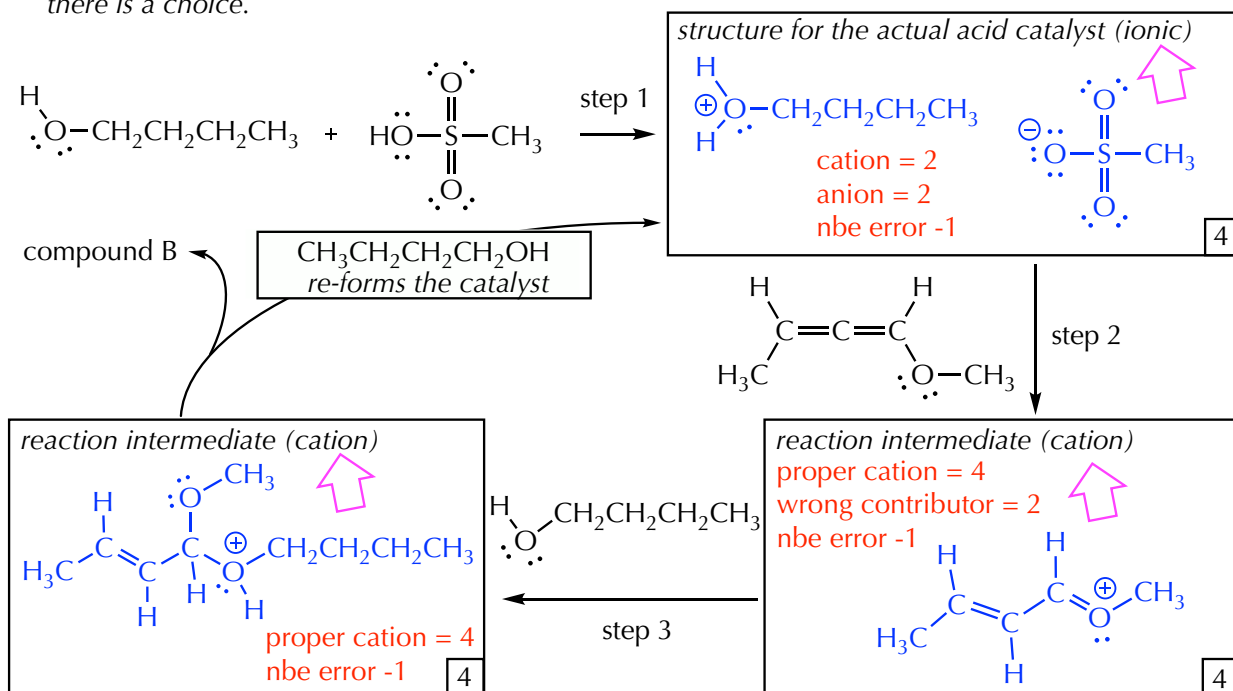
NAME _____

The reaction between compound A and 1-butanol ($\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}$), using a catalytic amount of methanesulfonic acid ($\text{CH}_3\text{SO}_3\text{H}$, $\text{p}K_a \sim -2$) gives compound B (*J Org Chem*, **1987**, 52, 7820).



- (a) Complete the mechanism for this reaction by providing the intermediates (no curved arrows are being called for, only the structures). Clearly indicate molecular geometry as needed.

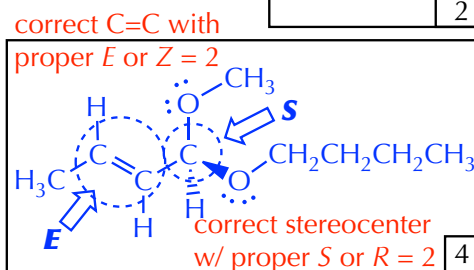
Take care to show nbe pairs and charges, and use the most significant resonance contributor when there is a choice.



- (b) How many stereoisomers exist for the connectivity represented by compound B?
- (c) How many of the stereoisomers for the connectivity represented by compound B are chiral?

4	no partial	2	<p>bad geometry cannot assign R/S to it!</p>
4	no partial	2	

- (d) Draw one of the stereoisomers for compound B. Double check that you have the right connectivity and the geometry is clear! Circle and give the stereochemical label(s) for the part(s) of the structure that are sources of stereoisomerism.



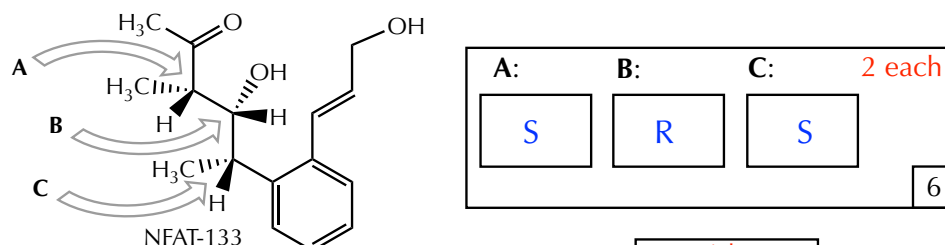
a	/12
b	/02
c	/02
d	/04
	/20

Question II (28 points)

NAME _____

"The soil bacterium *Streptomyces pactum* ATCC 27456 produces a number of polyketide natural products. Among them is NFAT-133, an inhibitor of the nuclear factor of activated T cells (NFAT) that suppresses interleukin-2 (IL-2) expression and T cell proliferation" (*J Nat Prod*, **2021**, *84*, 2411).

(a) Assign the stereochemical labels to the indicated stereocenters in NFAT-133.



(b) How many enantiomers does NFAT-133 have?

no partial
1 2

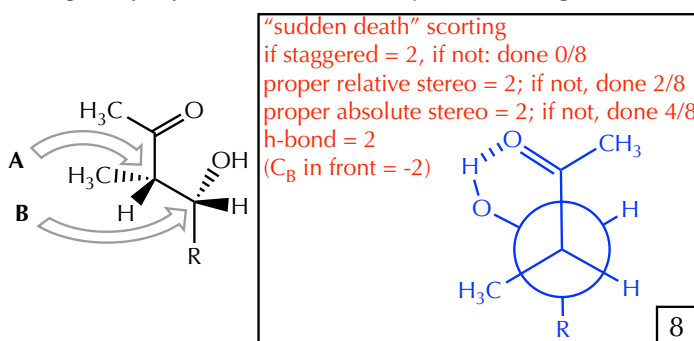
(c) How many chiral diastereomers does NFAT-133 have?

no partial
14 2

(d) How many achiral diastereomers does NFAT-133 have?

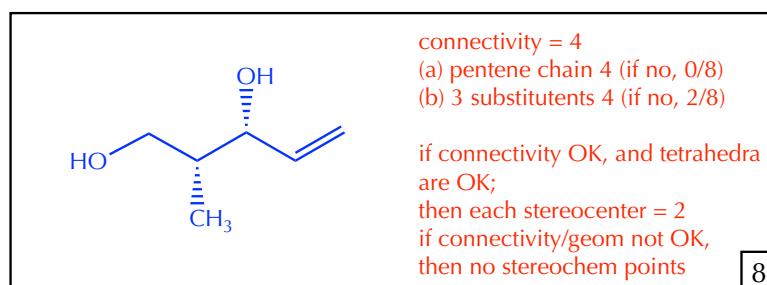
no partial
0 2

(e) Using the following abbreviation for the NFAT-133 structure, provide the Newman projection for the conformation of the C_A-C_B bond, as shown, using C_A as the front atom. Pay careful attention to using the proper stereoisomer in your drawing.



This conformation is stabilized by a single significant intramolecular interaction. Draw a representation of this stabilizing interaction on your answer.

(f) A laboratory synthesis of NFAT-133 can be designed from (2*R*,3*R*)-2-methyl-4-pentene-1,3-diol. Draw the structure of this compound, including the clear representation for the stereochemistry.



note: poorly represented tetrahedra cannot be read as *R* or *S*, so this is automatically incorrect



a	/	06
b	/	02
c	/	02
d	/	02
e	/	08
f	/	08
	/	28

Question III (24 points)

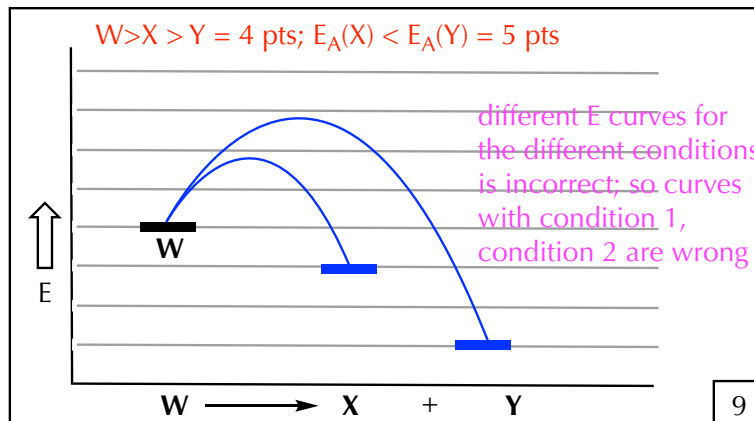
NAME _____

A reaction with the following characteristics was reported in 2007 (*Org Lett*, **2007**, 4809).



Reaction condition 1:
room temp., 15 minutes
Result: X:Y = 20:1 ratio

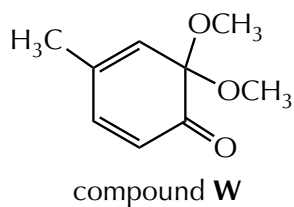
Reaction condition 2:
85 °C, 3 hours
Result: X:Y = 0:100 ratio



- (a) The two implied reactions are proposed to each take place in one step with no intermediate. Draw an energy diagram that is consistent with these data. Exact energy differences are not provided, but the relative energy levels and curves that you draw need to be consistent with the results given above.
- (b) Which of the following reaction parameters could be used to maximize the concentration of X that forms relative to the concentration of Y? Check all that apply.

<input type="checkbox"/>	increase the temperature	<input checked="" type="checkbox"/>	decrease the reaction time	2 pt each correct; -2 incorrect (missing or wrong X) (to 0)	4
<input checked="" type="checkbox"/>	decrease the temperature	<input type="checkbox"/>	increase the reaction time		

- (c) The structure for compound W is shown below. How many ¹³C-NMR signals would it have? How many ¹H-NMR signals, and what would their ratio be?

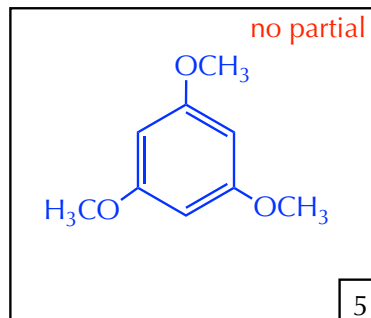


Number of ¹³ C-NMR signals?	8	no partial	6
Number of ¹ H-NMR signals?	5	no partial	
Ratio of ¹ H-NMR signals?	6:3:1:1:1	no partial	

- (d) There is a structural isomer of compound W (C₉H₁₂O₃) with the following characteristics:

- contains a benzene ring
- no OH group in its infrared spectrum
- has no acidic protons with pK_a < 40
- has 3 ¹³C-NMR signals
- has 2 ¹H-NMR signals (3:1 ratio)

What is the structure of this compound?

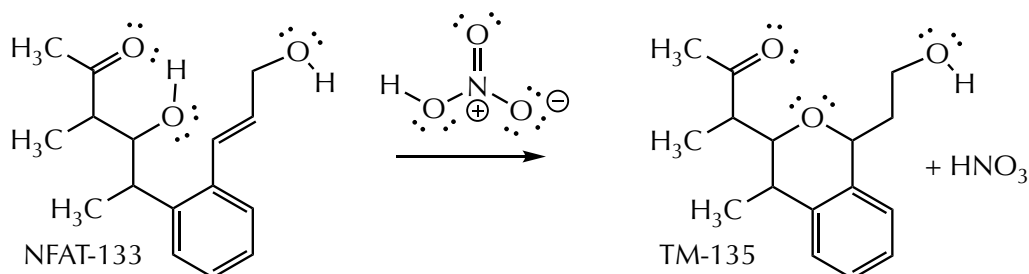


a	:	:	/09
b	:	:	/04
c	:	:	/06
d	:	:	/05
:	:	:	/24

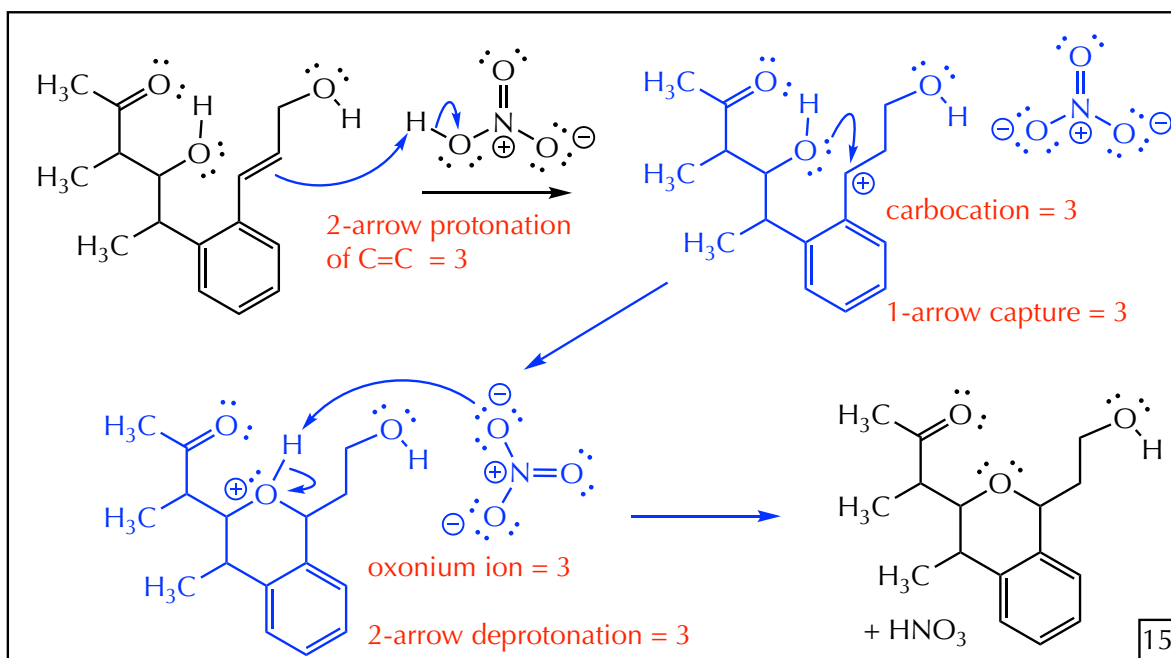
Question IV (20 points)

NAME _____

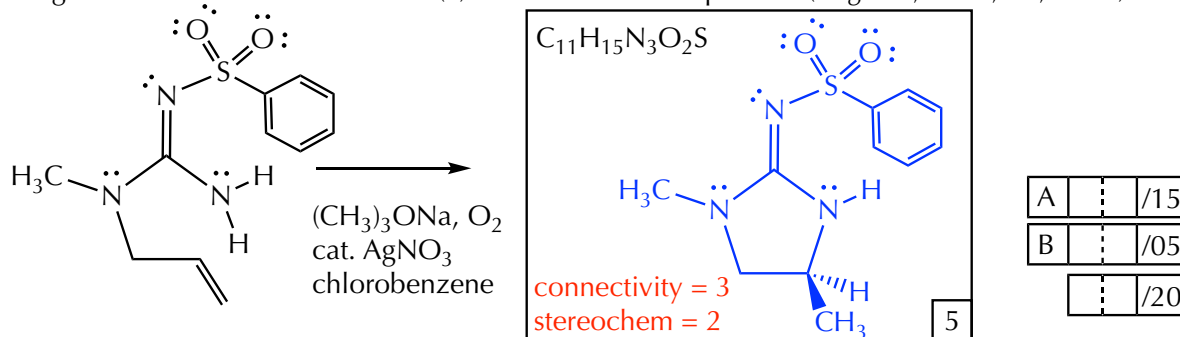
- A. When NFAT-133 was placed in solution and treated with a drop of nitric acid, the formation of TM-135 was observed (*J Nat Prod*, **2021**, *84*, 2411).



The reaction mechanism is proposed to be the direct reaction between NFAT-133 and nitric acid to give a high energy intermediate, followed by its intramolecular capture and subsequent reaction to re-form the nitric acid. Draw the curved arrow mechanism consistent with these data.



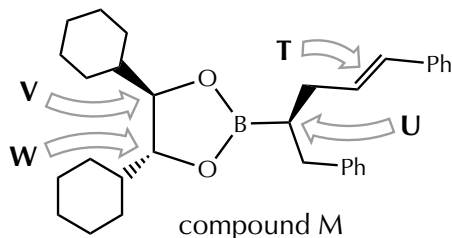
- B. The following reaction conditions lead to the intramolecular addition of the weak Brønsted acid to the alkene, resulting in a cyclic product, isomeric with the starting material and with a single new stereocenter. Draw the (*S*)-enantiomer of this product (*Org Lett*, **2016**, *18*, 2331).



Question V (28 points)

NAME _____

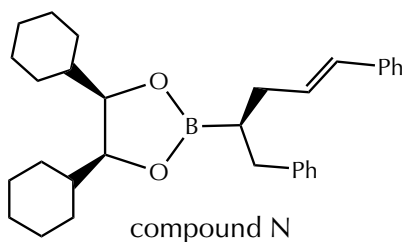
- A. Compound M is a useful reagent used for preparing other chiral organic compounds.
 (a) Assign the stereochemical configurations to the indicated sites.



V	R	T	E	2 pts each
W	R	U	S	
				8

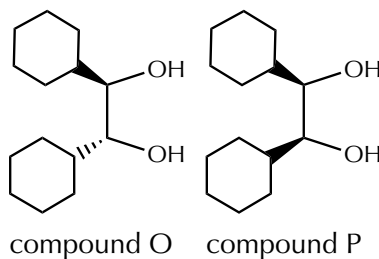
2 pts each X
 -2 for blank
 where there is an
 X or X where
 there is a blank

- (b) Mark which of the following statements are true about compound N.



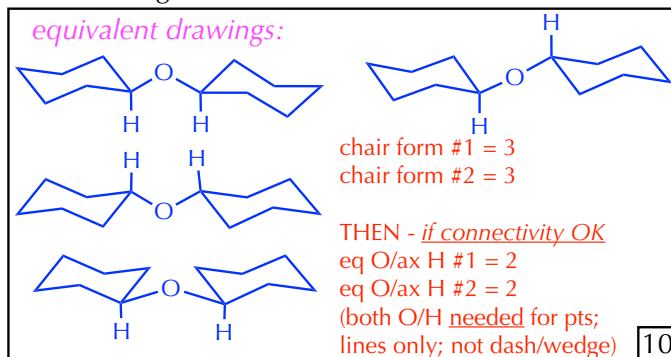
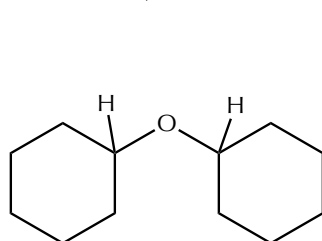
<input type="checkbox"/>	compound N is the enantiomer of compound M
<input checked="" type="checkbox"/>	compound N is chiral
<input type="checkbox"/>	compound N is a conformation of compound M
<input checked="" type="checkbox"/>	compound N is a chiral diastereomer of compound M
<input type="checkbox"/>	compound N is <i>meso</i>
<input checked="" type="checkbox"/>	compound N and compound M are stereoisomeric
<input type="checkbox"/>	compound N and compound M are structural isomers
6	

- (c) Compounds M and N are prepared from compounds O and P, respectively.



<input type="checkbox"/>	compound P is the enantiomer of compound O
<input type="checkbox"/>	compound P is chiral
<input type="checkbox"/>	compound P is a conformation of compound O
<input type="checkbox"/>	compound P is a chiral diastereomer of compound O
<input checked="" type="checkbox"/>	compound P is <i>meso</i>
<input checked="" type="checkbox"/>	compound P and compound O are stereoisomeric
<input type="checkbox"/>	compound P and compound O are structural isomers
4	

- B. Draw the most stable conformation for the following compound. *Think about it for a minute.* The conformational analysis for the following compound results in a structure where both rings are in chair forms and both occupy the most stable position with respect to one another. Start with how you might draw the most favored chair conformation for something simple, such as cyclohexanol, as your starting point. Include only the H atoms shown here in your drawing. Take care to provide completely unambiguous directions for the orientation of your bonds. For full credit, clear and consistent drawing matters.



Aa	:	/08
Ab	:	/06
Ac	:	/04
B	:	/10
	:	/28