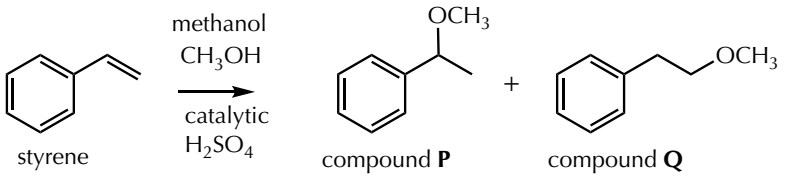
Question I (24 points)

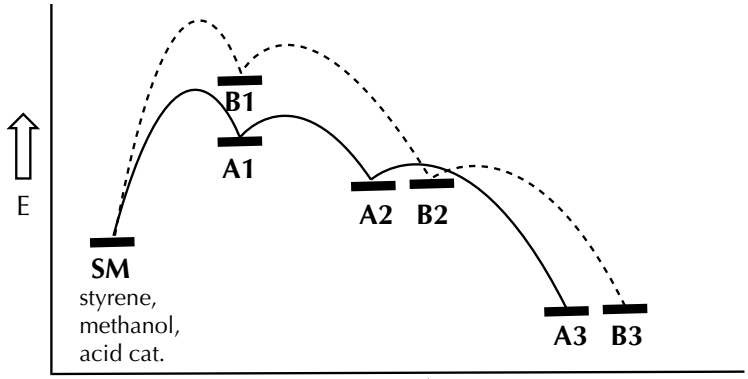
NAME _____

The acid catalyzed electrophilic addition reaction between styrene and methanol is kinetically controlled and results in a pair of products (compounds **P** and **Q**) that are formed with a high degree of regioselectivity (> 98% **P**, < 1% **Q**).



The energy diagram that illustrates the formation of these two products is shown here.

The actual acid catalyst used in the mechanism is the conjugate acid of methanol ($CH_3OH_2^+$).



(a) Answer the following questions about this reaction.

(i) Which of these points corresponds to compound **P**?

(ii) The rate determinating step for the **A3** to **SM** reaction occurs between which two of these points?

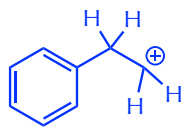
(iii) If the reaction was thermodynamically controlled, the ratio of **P** to **Q** would be what?

circle one: **SM** **A1** **A2** **(A3)** **B1** **B2** **B3**	3	no partial
circle two: **(SM)** **(A1)** **A2** **A3** **B1** **B2** **B3**	3	no partial
circle one: **P > Q** **(P = Q)** **P < Q**	3	no partial

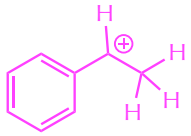
(b) Provide drawings for the following, according to each instruction.

(i) Draw the structure corresponding to **B1**. Include nonbonding electron pairs and any formal charges.

no partial



3/5 for the other regioisomer

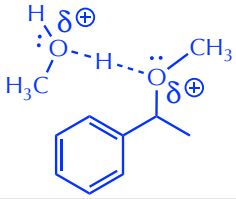


5

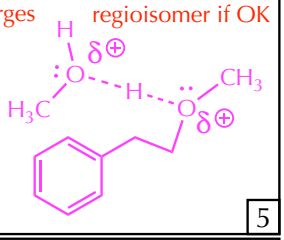
(ii) Draw the transition state structure for the **A2** to **A3** step. Include dotted lines for partial bonds, any partial charges, and nonbonding electron pairs.

be alert: the partial bonds are the electrons, so partial bonds coming from NBE pair is incorrect

3/5 structure (bonds, nbe) if OK, +2 for proper partial charges



3/5 for the other regioisomer if OK



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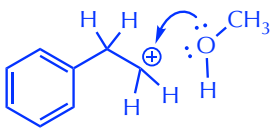
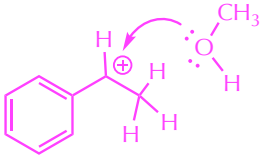
(iii) Draw the curved arrow mechanism for the **B1** to **B2** step. Include nonbonding electron pairs and any formal charges.

Guidance: Draw the **B1** intermediate, any additional reagent(s), and the necessary arrow(s). The **B2** intermediate does not need to be drawn.

no partial; using methoxide is incorrect



3/5 for the other regioisomer



5

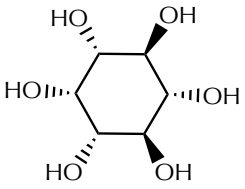
a		/09
b		/15
		/24

Question II (28 points)

NAME _____

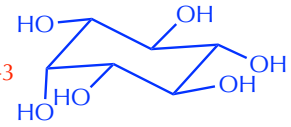
A. Myo-inositol is a naturally occurring sugar found in your body and in foods. One of the "B-complex vitamins," myo-inositol has been used to treat diabetic neuropathy, depression, Alzheimer's disease, panic disorder, and polycystic ovary syndrome.

(a) Draw the most stable chair conformation for myo-inositol. Include only the OH groups shown here in your drawing. Take care to provide completely unambigious directions for the orientation of your bonds. For full credit, clear and consistent drawing matters.

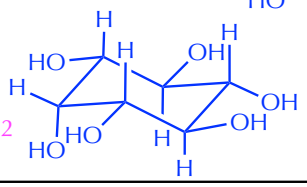


myo-inositol

clear & readable chair form = 3 (if not OK, 0/9)
if chair OK, directionality of 6 bonds OK = +3
(if not OK, 3/9), if the proper set of 6 (1 axial), +3



note: the H's were NOT asked for, but if they are there, they will be graded accordingly: if chair OK, directionality of 12 bonds OK = +3; if proper set of 12 bonds, then +3 for groups



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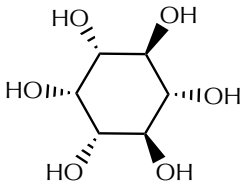
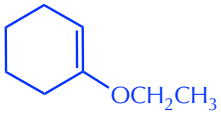
(b) In a 2004 study of myo-inositol, the following transformation was reported (*Org. Lett.* **2004**, *6*, 365). What compound is needed to complete the chemical reaction, which was carried out under acid catalyzed conditions? Of note: the missing reagent will also balance the equation.



myo-inositol

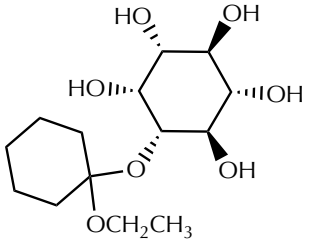
+

no
partial

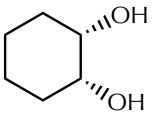


4

acid catalyst



(c) Given that the connectivity (no stereochemical labels) of the following model compound is cyclohexane-1,2-diol, what is the name of the connectivity for myo-inositol?



model compound
connectivity =
cyclohexane-1,2-diol

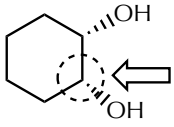
Name for the connectivity (no stereochemical labels) of myo-inositol?

cyclohexane-1,2,3,4,5,6-hexaol or 1,2,3,4,5,6-cyclohexanehexaol

no partial credit (the name is nearly fully modeled in the question) 6

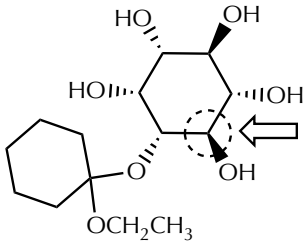
The multiplier term for 6 is hexa (eg, in hexane, and as in the 18 C root name "hexadecane"). We did accept the misspelling "hex" (hexol) but NOT "sex" (sexol). And a note for the future that vowels are not dropped in the multiplier terms (di -> diol, tri -> triol, and so on).

(d) What are the stereochemical configurations for the stereocenters indicated below?



R 3

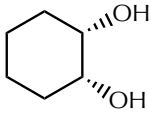
no
partial



R 3

no
partial

(e) What can be said about the structure and optical properties of the stereoisomer of cyclohexane-1,2-diol shown in parts (c) and (d), above? Select one of the options.



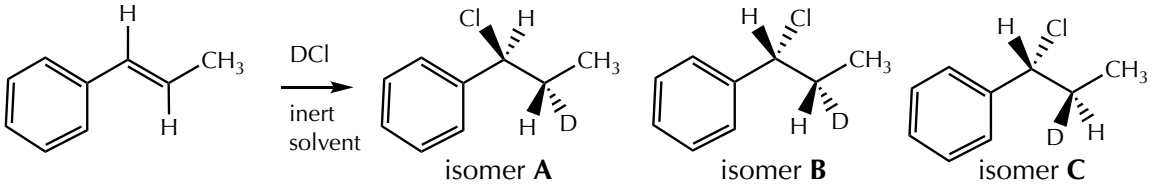
- [ ] the molecule is chiral, and its rotation is dextrorotatory (+)
- [ ] the molecule is chiral, and its rotation is is levorotatory (-)
- [ ] the molecule is chiral, and its rotation is unpredictable
- [X] the molecule is achiral, and it is optically inactive

no partial 3

a		/09
b		/04
c		/06
d		/06
e		/03
		/28

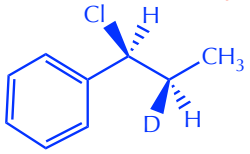
Question III (21 points) NAME _____

The electrophilic addition reaction of DCl (D = deuterium, ^2H, which has the same chemical properties of regular ^1H hydrogen atoms) to the following compound creates a set of four stereoisomeric products. Three of the four stereoisomeric products are shown.



(a) Draw the missing fourth product.

isomer **D**



no
partial

2

(b) What is the stereoisomeric relationship between:

(i) isomers **A** and **B**? diastereomer 2 no partial

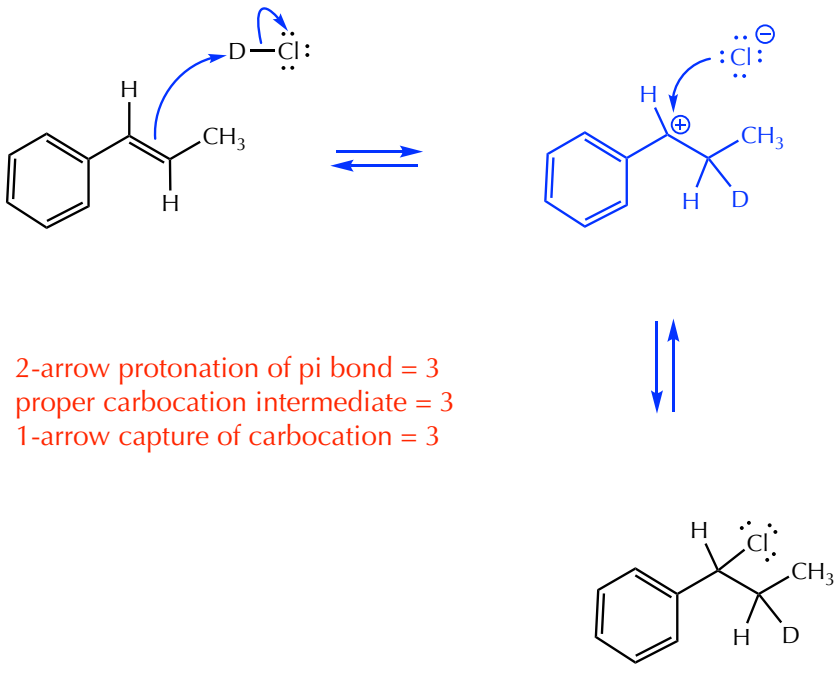
(i) isomers **A** and **C**? enantiomer 2 no partial

(c) Assign the stereochemical configuration to:

(i) the chlorine-bearing center in isomer **B** R 3 no partial

(ii) the deuterium-bearing center in isomer **A** S 3 no partial

(d) Provide the complete curved arrow mechanism for the reaction. In an inert solvent, the DCl is the active reagent. Be sure to provide all nonbonding electron pairs and formal charges. Only the connectivity is necessary for this mechanism; do not include stereochemistry.



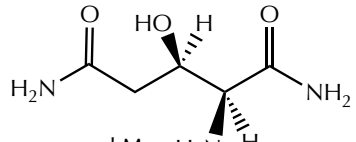
9

a		/02
b		/04
c		/06
d		/09
		/21

Question IV (22 points)

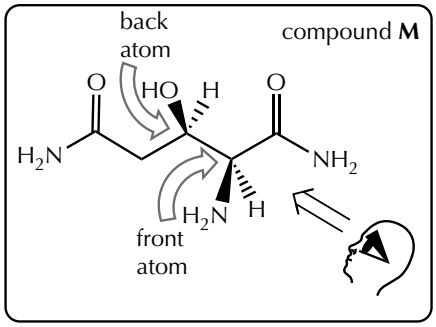
NAME _____

A. Compound **M** is part of a larger secondary metabolite isolated from a fungus that showed bioactivity towards breast cancer cells (*J. Nat. Prod.* doi.org/10.1021/acs.jnatprod.2c00682).

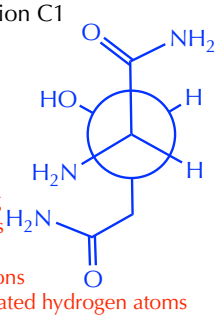


compound **M**

(i) Using the point of view illustrated in the space on the right, draw the Newman projection for this conformation (C1) of compound **M**.



conformation C1

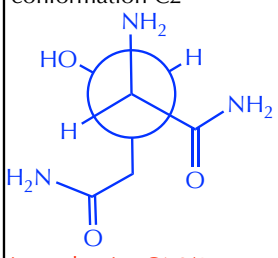


staggered = 2;
if not, 0/6
then, proper set of groups front/back = 2, including correct groups copied,
no extra carbons and all associated hydrogen atoms if not 2/6;
then proper conformation AND connectivity = 2

6

(ii) Rotate the front atom of the Newman projection to create a conformation (C2) that has two gauche interactions.

conformation C2



just redrawing C1 0/4
if new staggered = 2
if correct rotation to 2 gauche= +2
any new drawing error -2

4

(iii) If drawn correctly, there is a single best hydrogen bonding interaction that exists between two of the gauche groups in conformation C1.

(i) Circle the best hydrogen bond donor:

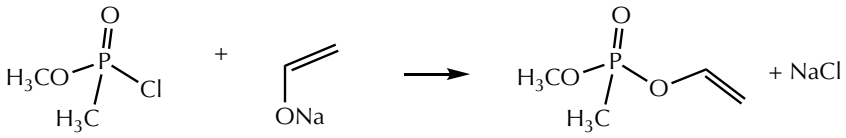
sp^2 NH | **sp^3 OH** | sp^2 O: | sp^2 N: | sp^3 NH | sp^3 N: 2

(ii) Circle the best hydrogen bond acceptor:

sp^2 NH | sp^3 OH | sp^2 O: | sp^2 N: | sp^3 NH | **sp^3 N:** 2

B. Classify the following reactions (Lewis acid-base complexation, addition, substitution, elimination).

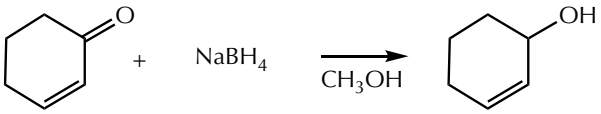
(i)



no partial

substitution 2

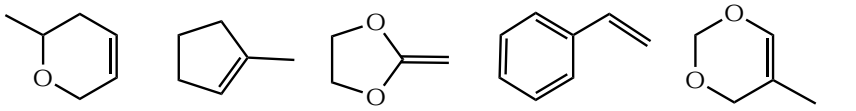
(ii)



no partial

addition 2

C. Assign the relative reaction rates for the electrophilic addition of the following compounds with trifluoroacetic acid (pK_a 0.23; "1" = fastest, "5" = slowest).



5 | 4 | 1 | 3 | 2 | 4

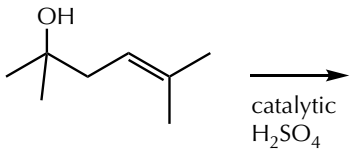
no partial

"1" = fastest, "5" = slowest, for electrophilic addition with trifluoroacetic acid

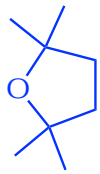
A		/14
B		/04
C		/04
		/22

Question V (25 points) NAME _____

A. When the following compound is treated with a catalytic amount of sulfuric acid, an intramolecular (within the same molecule) electrophilic addition reaction is proposed to take place. The combination of the experimentally-determined information is used to support this conclusion (molecular formula and NMR data). Based upon the summary of these data, what is the structure of the product?



no
partial



4

Data obtained from the product:

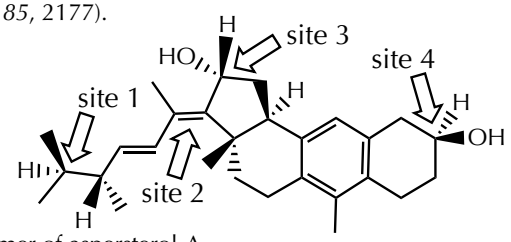
$C_8H_{16}O$

^{13}C-NMR: 3 signals

^{1}H-NMR: 2 signals (12:4 ratio)

B. Aspersterol-A was isolated from a deep sea fungus. Its structure and properties are being studied for potentially useful biological activity (*J. Nat. Prod.* **2022**, *85*, 2177).

aspersterol-A
[α] = -60.7°



(a) Answer the following about this stereoisomer of aspersterol-A

(i) What are the stereochemical configurations for the 4 sites indicated above? If there is none, then write "none."

site 1 [none] site 2 [E] site 3 [R] site 4 [S] 2 pts each 8

(ii) How many enantiomers does this stereoisomer of aspersterol-A have? [1] 2 no partial

(iii) How many achiral diastereomers does this stereoisomer of aspersterol-A have? [0] 2 no partial

(iv) How many sources of stereoisomerism does the aspersterol-A connectivity have? [7] 2 no partial

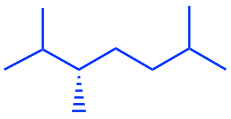
(v) The stereoisomer of Aspersterol-A shown above has an optical rotation of [α] = -60.7°. If you invert the stereocenter at site 4, what do you predict about the optical rotation of the resulting stereoisomer?

- [ ] the [α] is expected to still be -60.7°
- [ ] the [α] is expected to be +60.7°
- [ ] the [α] is expected to be positive, but not 60.7°
- [ ] the [α] is expected to be negative, but not 60.7°
- [X] the [α] cannot be anticipated in either sign or magnitude

2

(b) In an associated study of aspersterol-A, the following compound was prepared: (*S*)-2,3,6-trimethylheptane. Draw this compound:

connectivity = 3, if OK, then check for (S) stereocenter (+2); if connectivity incorrect, 0/5



5

A		/04
Ba		/16
Bb		/05
		/25