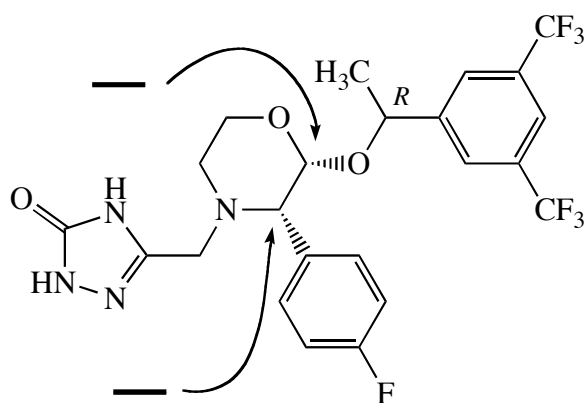




1. (8 pts.) The structure of aprepitant, the active ingredient in Emend, a drug used to treat nausea and vomiting resulting from cancer chemotherapy, is shown. Aprepitant has three stereocenters.

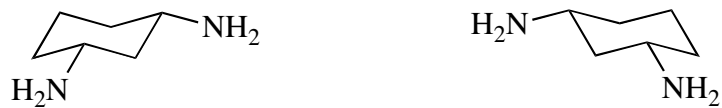


(a) (4 pts.) In the drawing above, arrows point to two of Aprepitant's stereocenters. On the heavy lines next to the arrows, indicate the configurations of these stereocenters.

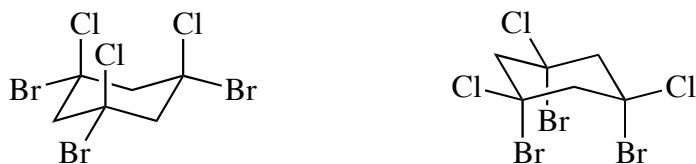
(b) (4 pts.) The third stereocenter in Aprepitant has the R configuration. Draw in the H atom attached to this stereocenter, and use a bold or hashed wedge to indicate an R configuration.

2. (5 pts. each, 30 pts. total.) Describe the relationship of each pair of structures as specifically as possible and in no more than two words.

(a)



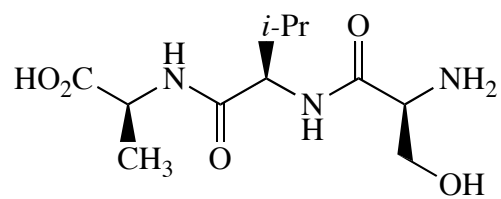
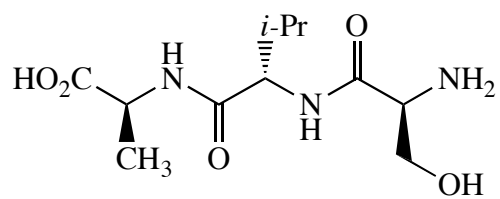
(b)



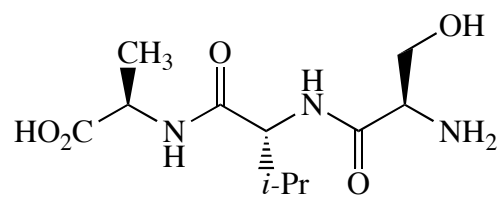
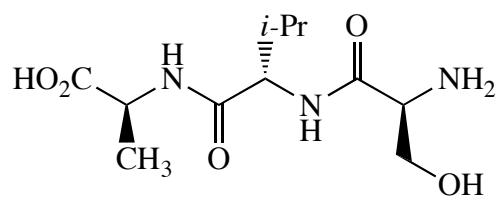
(c)



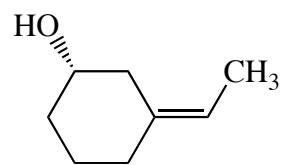
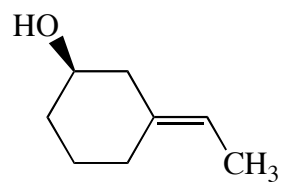
(d)



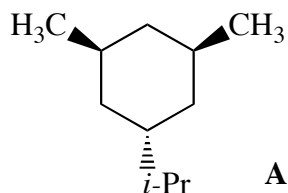
(e)



(f)



3. (24 pts. total.) Consider compound **A** below.



(a) (8 pts.) Draw **A** in *both* of its chair forms.

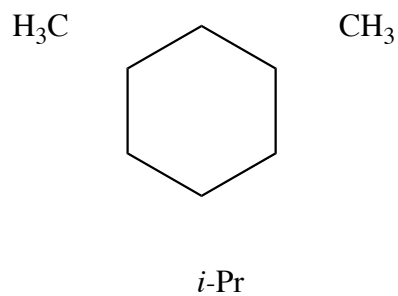
(b) (4 pts.) Using the table below, compute the approximate difference in energy between the structures you drew in (a).

| Interacting axial groups            | Cost of <i>single</i> 1,3-diaxial interaction |
|-------------------------------------|---|
| CH <sub>3</sub> and H               | 0.85 kcal/mol                                 |
| 1° alkyl (e.g., Et) and H           | 0.90 kcal/mol                                 |
| 2° alkyl (e.g., <i>i</i> -Pr) and H | 1.1 kcal/mol                                  |
| 3° alkyl (e.g., <i>t</i> -Bu) and H | 2.7 kcal/mol                                  |
| CH <sub>3</sub> and CH <sub>3</sub> | 3.7 kcal/mol                                  |

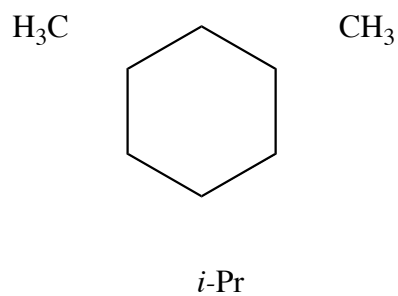
Approximate difference in energy: \_\_\_\_\_

(c) (4 pts.) Circle the structure you drew in (a) that is lower in energy, and explain below what led you to choose that structure.

(d) (4 pts.) By adding wedged bonds (bold or hashed) to the drawing below, draw the compound that is lowest in energy among **A** and its diastereomers.



(e) (4 pts.) By adding wedged bonds (bold or hashed) to the drawing below, draw a chiral diastereomer of **A**. (If **A** is chiral, you may draw **A**.)



4. (4 pts. each, 20 pts. total.) Undergraduate researcher Sally Humdinger prepares a sample of (1*R*,2*R*)-ephedrine. She measures its enantiomeric ratio (er) to be 7:1. For enantiopure (1*S*,2*S*)-ephedrine,  $[\alpha]_{\text{D}}^{25} = +52^{\circ}$ .

(a) What is the ee of Sally's sample of ephedrine?

(b) What  $[\alpha]_{\text{D}}^{25}$  would Sally expect to observe for her sample of ephedrine? Give the *sign* and the *magnitude*.

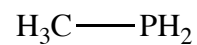
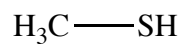
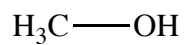
(c) Sally's lab partner gives her a sample of (1*R*,2*S*)-ephedrine. Should Sally expect this sample to be dextrorotatory or levorotatory, or is there no way to tell? Explain your answer.

(d) Sally used chiral chromatography to measure her sample's er. Explain how this method works.

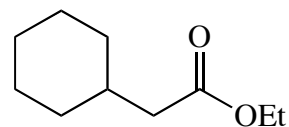
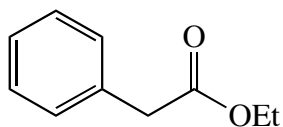
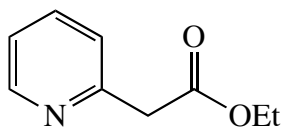
(e) (Extra credit) Sally tells her labmate Will Wurklanghauers that her starting materials for making (1*R*,2*R*)-ephedrine have no stereocenters. Will tells her that's impossible. Who is right, and why?

5. (4 pts. each, 12 pts. total.) Circle the *most acidic* compound in each set, and explain *briefly* (no more than a grammatically correct sentence or two) why you circled that compound. *No credit will be given without a valid explanation.*

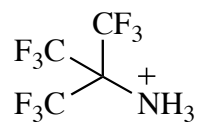
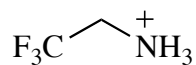
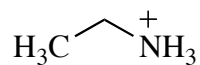
(a)



(b)

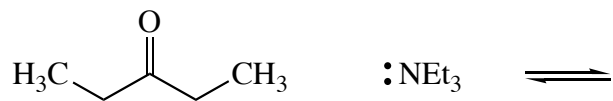


(c)



6. More acid–base chemistry.

(a) (6 pts.) Complete the following acid–base reaction, using curved arrows to show the movement of electrons. You may find it advisable to obey Grossman’s rule before you begin.



(b) (4 pts.) The  $pK_a$  of the acid on the left is 20, and the  $pK_a$  of the acid on the right (if you answered (a) correctly) is 10. Does the equilibrium for this reaction lie to the right or to the left, and what is the equilibrium constant?