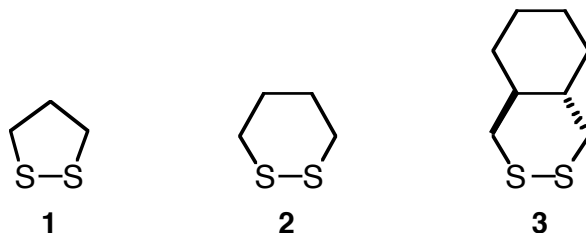


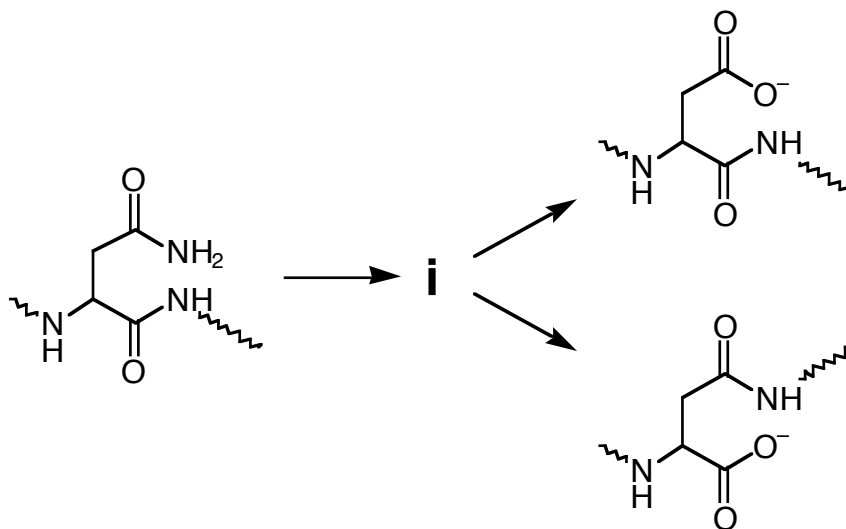
Biochemistry 704
Problem Set 5
Due 03/25/2008

1. Circle the compound below that has the most stable disulfide bond (that is, the one most difficult to reduce).



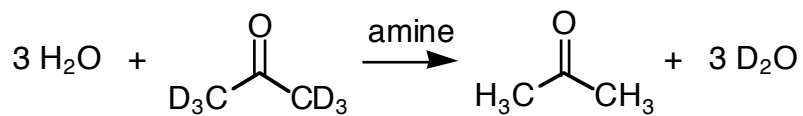
Explain briefly why each of the other two disulfide bonds is less stable.

2. Proteins can suffer irreversible damage at high pH. For example, asparagine residues can degrade spontaneously to form aspartate and “isoaspartate” residues. These two products are formed by the hydrolysis of a common intermediate, **i**.

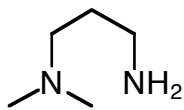
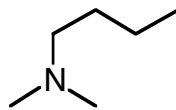


Draw the structure of **i**.

3. The exchange of deuterium between $[D_6]$ acetone and solvent H_2O is catalyzed by amines.

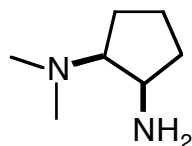


Diamine **4** is a much better catalyst for this reaction than is monoamine **5**.

**4****5**

- a. Propose a mechanism for the exchange reaction as catalyzed by diamine **4**.

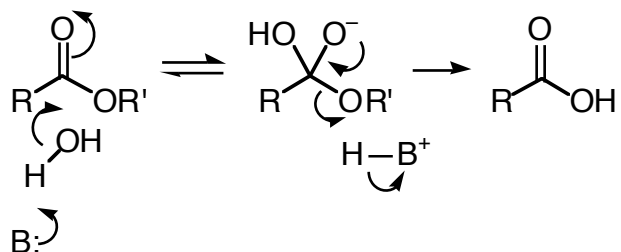
- b. Diamine **6** is an even better catalyst than diamine **4** for the exchange reaction.

**6**

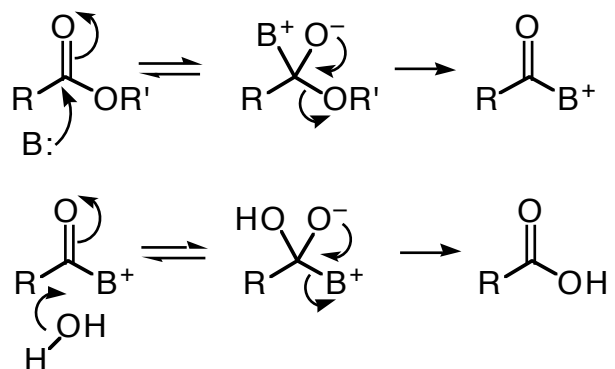
What is the basis for the difference in catalysis by diamines **4** and **6**?

4. The hydrolysis of ester RC(O)OR' is catalyzed by "B:". Two classic mechanisms are postulated:

general base mechanism



nucleophilic mechanism



Propose two experiments that distinguish between these two mechanisms.

- a. The research team synthesizes analogs of **S** and **I** with a variety of R' groups. They then determine both the values of k_{cat}/K_M and K_M for the series of substrates and the values of K_i for the analogous inhibitors. If phosphonamide **I** is a transition state analog, then the change in k_{cat}/K_M for the substrates would be (choose one and explain briefly):
- proportional to the change in K_i for the analogous inhibitors
 - proportional to the change in $1/K_i$ for the analogous inhibitors
 - proportional to the change in K_i/K_M for the **I,S** pairs
 - independent of the change in K_i for the analogous inhibitors
- b. If phosphonamide **I** is a transition state analog, then the change in K_M for the substrates would be (choose one and explain briefly):
- proportional to the change in K_i for the analogous inhibitors
 - proportional to the change in $1/K_i$ for the analogous inhibitors
 - proportional to the change in K_i/K_M for the **I,S** pairs
 - independent of the change in K_i for the analogous inhibitors
- c. The research team uses site-directed mutagenesis to change an active-site residue in the protease. In an assay of the variant protease, the team observes a decrease in the value of k_{cat}/K_M but no change in the value of K_M for substrate **S**. If phosphonamide **I** is a transition state analog, then the value of K_i for phosphonamide **I** would (choose one and explain briefly):
- increase
 - decrease
 - not change