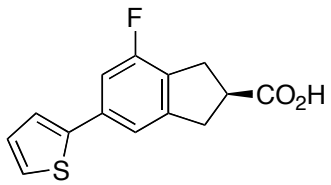
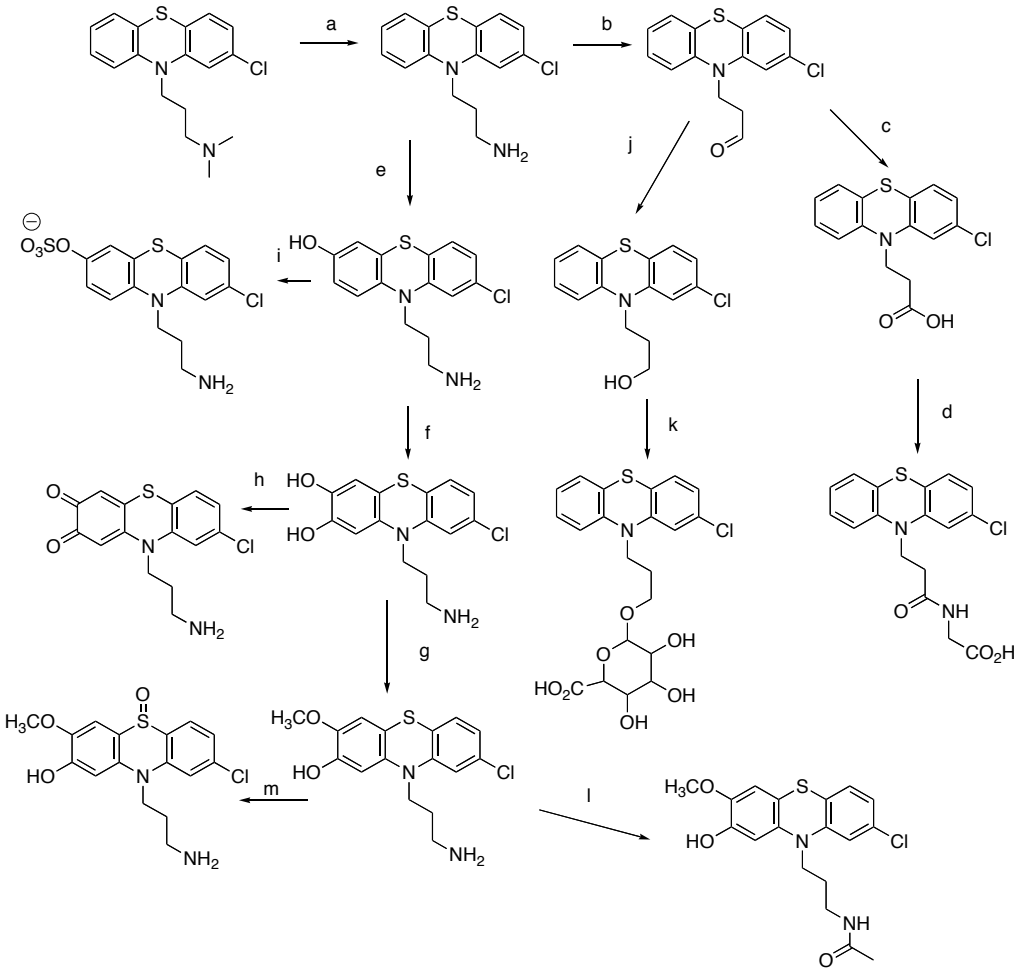
Exercises KJ 5230: Nov. 10th – 2004

1. The compounds shown below has antibacterial activity. Resistance to the compounds was shown to be the result of a single-point mutation of an lysine residue to an aspartate residue in the active site of the target bacterial enzyme. Suggest a structure that may be active against the resistant strain.



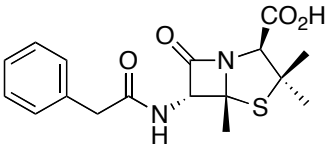
2. Explain how you may determine if a compound is a competitive or non-competitive inhibitor of an enzyme.

3. Which of the hypothetic metabolites are phase I and phase II?. Name reactions and co-actors required. (no mechanisms)

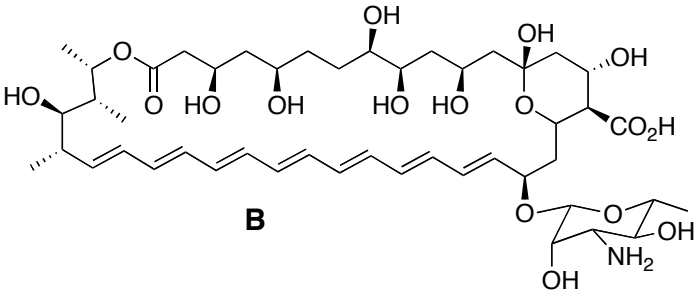


4.

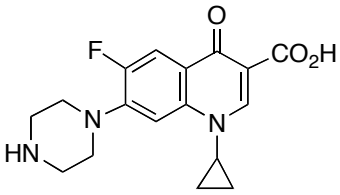
a) Compounds **A**-**D** are used to treat infections. What calsses of drugs do they belong to. Explain how you can distinguish between the drug classes of **B** and **D**.



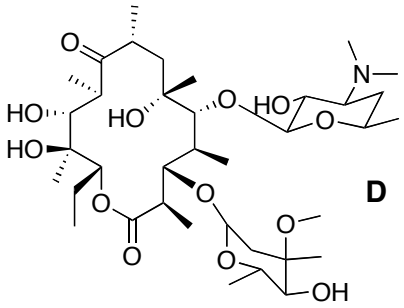
A



B

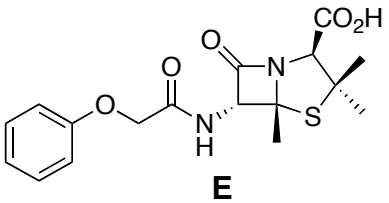


C

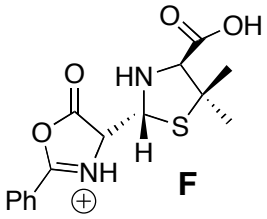


D

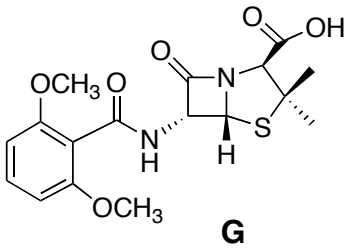
b) **E** is more stable in acidic media than **A**. Show (incl mecanisms) how **A** can be transformed to the intermediate **F** in acidic media and use this mecanism to explain why **E** is more stabile



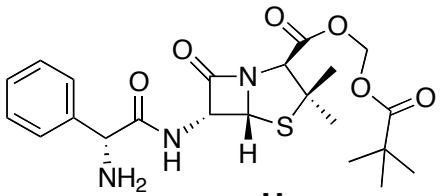
E



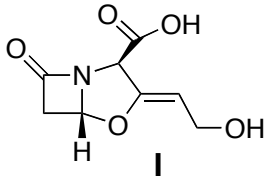
F



G



H



I

c)**A** is naturally occuring, but **G** and **H** are semisynthetic analogs. Explain why these modifications have been done.

d) **I** is used in combination with drugs like **A**. Explain why and show mechanism of action for **I**.

e) **D** has low stability in acidic media. Explain why, and discuss synthetic modifications that would increase stability.

f) Discuss stability (hydrolytic and enzymatic) of cephalosposines and compare with pennicilines

5.

a) Why should not tetracyclines be taken with milk?

b) Compare stability of doxycyclin and oxytetracyclin. (include mechanisms for reactions that may occur in aqueous media at various pH)