

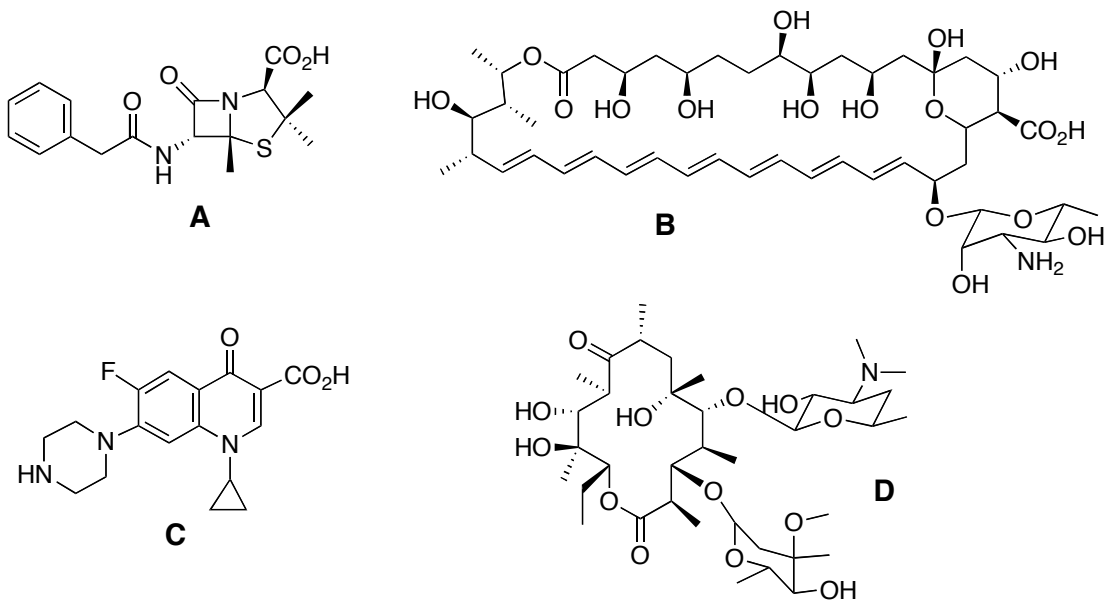
Exercise 3, KJ 5230: Nov. 23th – 2010

Left-overs from last week?

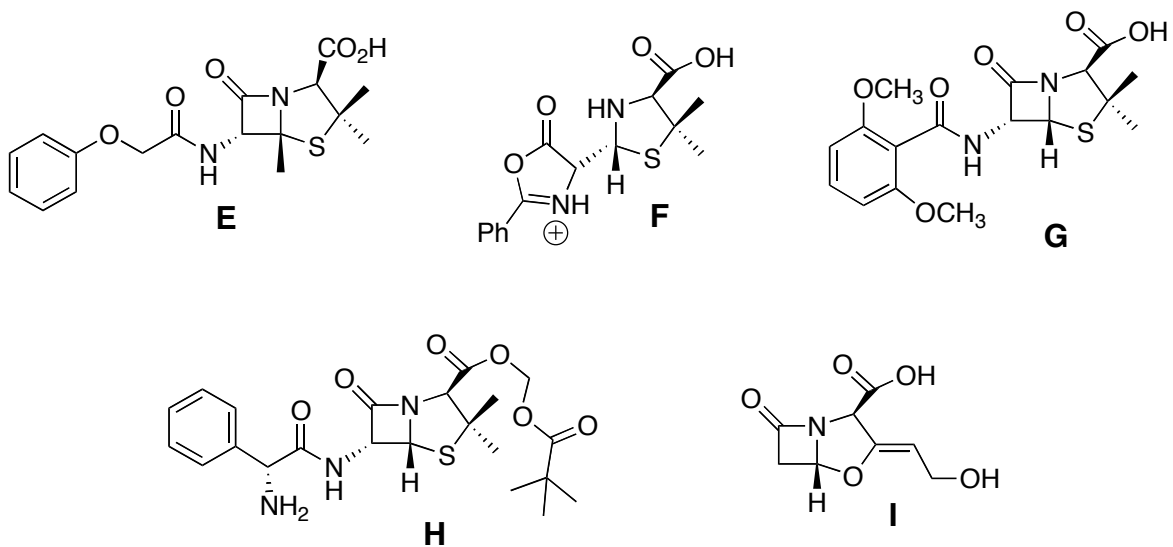
1. Explain how you may determine if a compound is a competitive or non-competitive inhibitor of an enzyme.

2.

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



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



c) **A** is naturally occurring, 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 cephalosporins and compare with penicillins

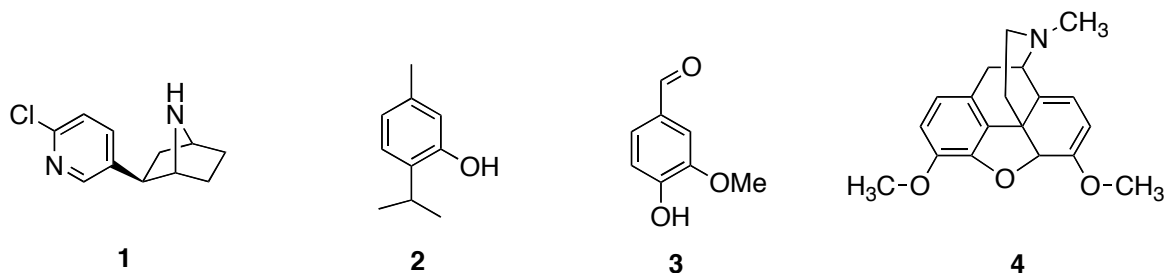
3.

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).

4.

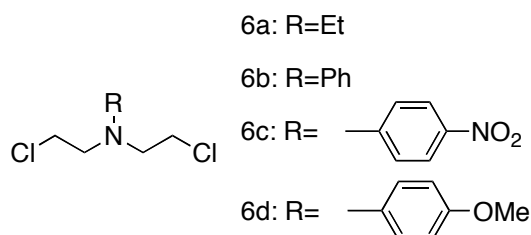
a) Which classes of natural products do the following compounds belong to



b) Show how squalene biosynthetically can be transformed into steroids. Which drugs do you know that interfere with normal steroid biosynthesis? List compounds, drug class and mechanism of action.

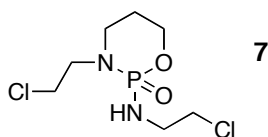
5.

a) Suggest possible drug class for the compounds **6**. Show their mechanism of action.



b) Discuss relative reactivity of compounds **6**.

c) Compound **7** is a pro-drug. Why is not **7** it self active? Show how **7** may be metabolized into active compound(s)



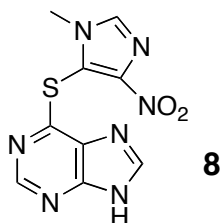
d) Why is compound **7** sometimes administered together with $\text{NaO}_3\text{S}(\text{CH}_2)_3\text{SH}$?

6.

a) Explain the mechanism of action for 5-Fluoruracil. What would be a good drug to be used together with 5-FU in combination therapy?

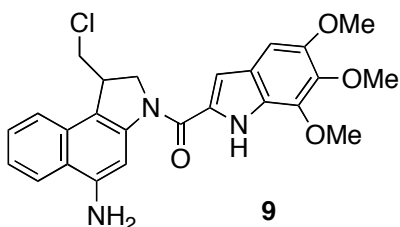
b) 5-Fluorocytosin was used earlier as an antimycoticum. The compound is relatively non-toxic to humans and cannot be used as an anticancer drug. Suggest a mechanism of action as antimycoticum.

c) Azathioprine **8** is metabolized to 6-mercaptopurine. Glutathione is involved. Suggest a mechanism.

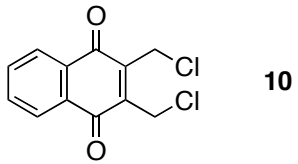


7.

a) Compound **9** alkylates DNA, suggest mechanism.



b) Compound **10** must be activated by NADPH before reacting with DNA, suggest mechanism for activation and reaction.



8

a) Explain the mechanism of action for anthracyclines

b) Dymecicin **11** is a so-called endiyne antitumor antibiotic. It is activated by a reducing agent (NADPH or a thiol). Suggest mechanism of action

