Exercises KJ 5230: November 9, 2006

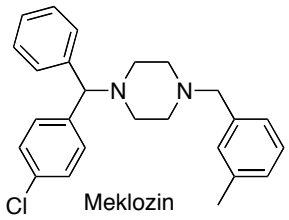
1.

(a) Lipinski has formulated :

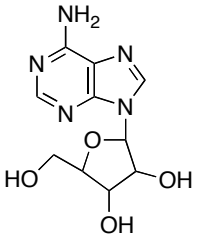
A drug canditate is more likely to have poor absorbtion or permeability if:

1. Mw>500
2. logP>5
3. Σ H-bond donors (NH, OH) >5
4. Σ H-bond acceptors (N, O) >10

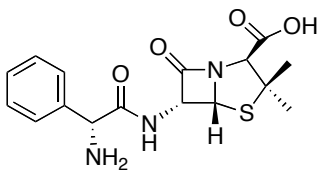
How does the compounds below apply with "Lipinski rule of five"? (Hint: You can find logP from SciFinder)



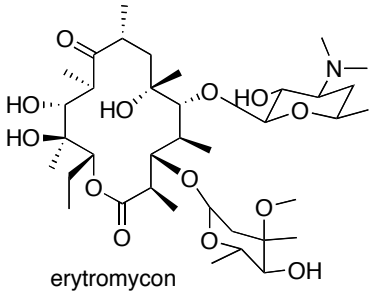
Meklozin



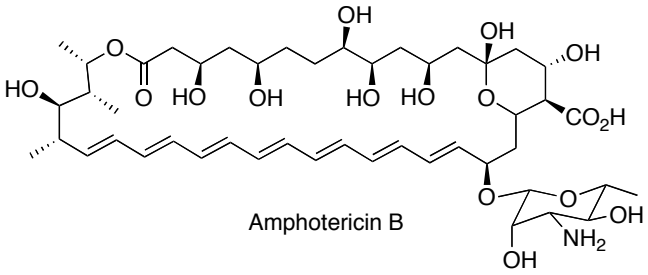
Adenosin



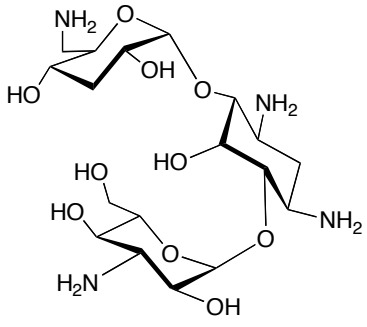
Ampicillin



erytromycon



Amphotericin B

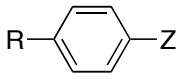


kanamycin A

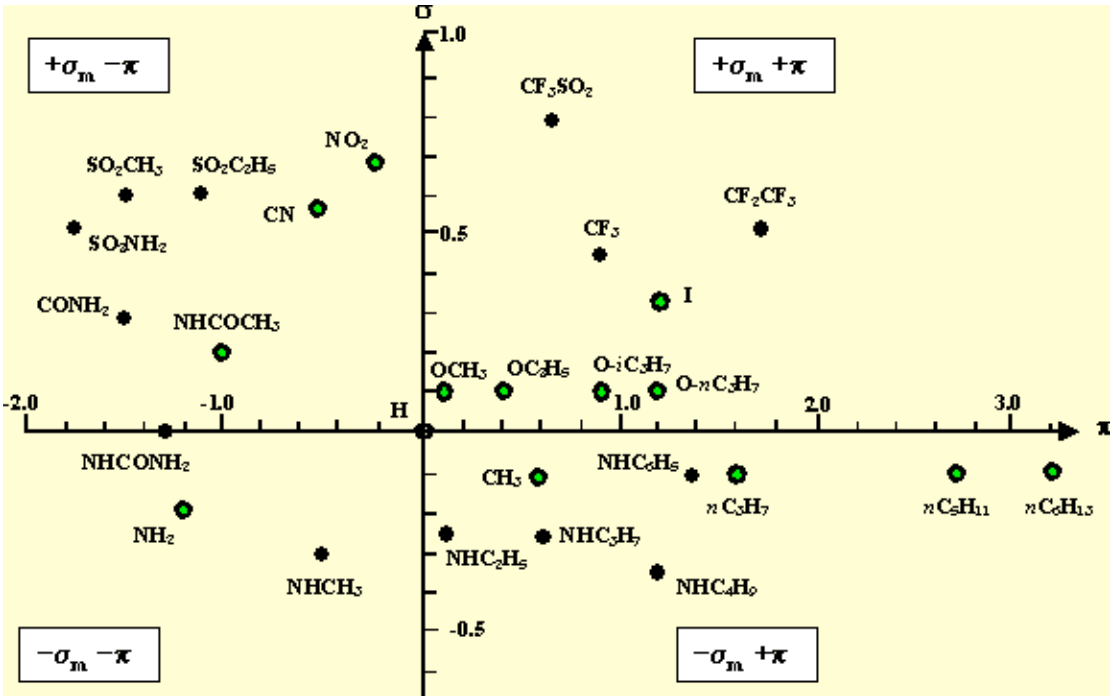
(b) Meklozin ampucillin and etrythromycin can be given orally and adenosine, amphotericin B, kanmycin are given as injection, Explain.

2.

Using the the results in the table as well as the **Craig plot** below, suggest additional compounds to make

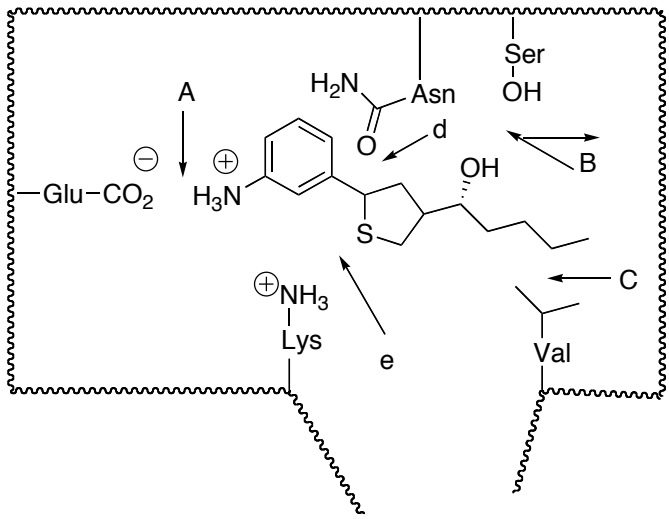


Z	% Antibacterial activity *in vitro*
H	50
Cl	80
CH_3	45
OCH_3	25
OH	10
CF_3	85
NO_2	55



3.

Indicate what drug-receptor interactions are involved at every arrow shown (more than one kind of interact. may be possible fir each letter)



4.

(a) Draw dose-responce curves (in the same plot of 3 diff. drugs. A is more potent and efficient than B and C. B and C are equally efficaciuos but C is more potent.

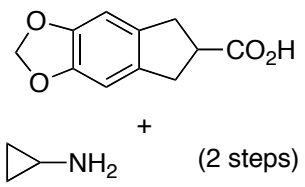
(b) Draw dose-responce curves (in the same plot of i) a full agonist; ii) a mixt of fullagonist and competitive antagonist

5.

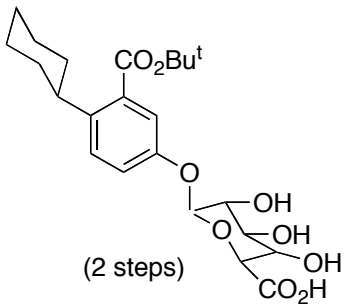
The compounds shown below has antibacterial activity. Resistance to the compounds was shown to be the result of a single-point mutation of an lysine residue to an aspartate residue in the active site of the target bacterial enzyme. Suggest a structure that may be active against the resistant strain.

6.

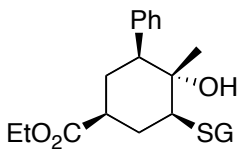
Predict the structures of the compounds that produce the following metabolites (work backwards from metabolite to compound). Show steps (not detailed mech.) and suggest enzymes.



(2 steps)



(2 steps)



(2 steps)