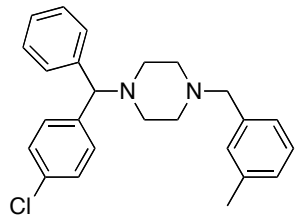
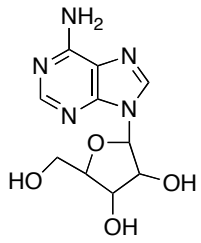
Exercise 2 KJ 5230: Nov. 16, 2010

Left overs from last week?

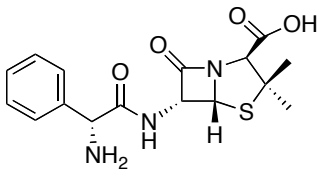
1.
The druglikeness (oral availability) of the compounds shown below was determined based on Lipinsky's rule of 5, last week.



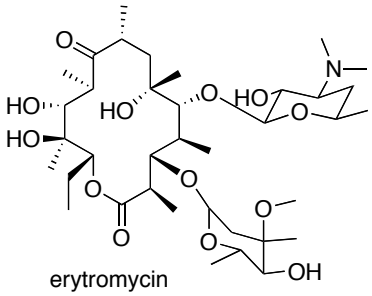
Meklozin



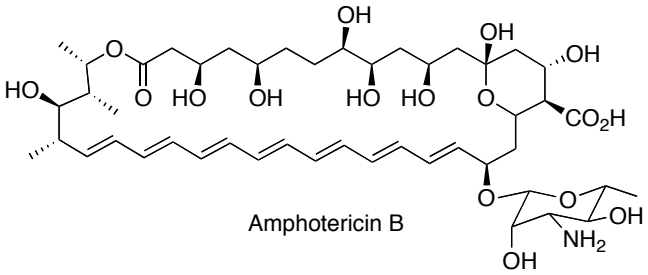
Adenosin



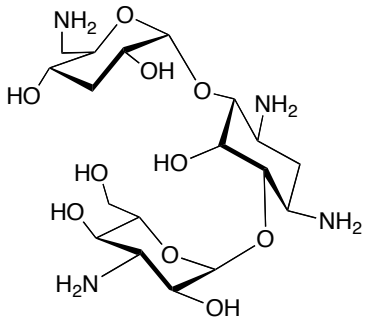
Ampicillin



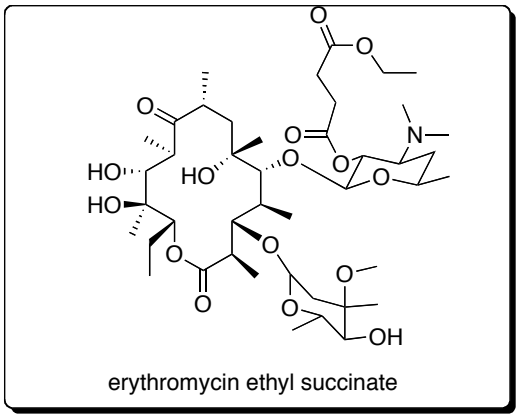
erytromycin



Amphotericin B



kanamycin A



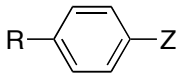
erythromycin ethyl succinate

- Meklozin (antihistamine) is given as tablets
- Adenosine (hart therapy) is given as injections / infusions
- Ampicillin (anibiotic, penicillin) is given as injections / infusions
- Erythromycin (antibiotic, macrolide) is gived as injections / infusions and the succinate shown above as tablets
- Amphothericine B is given as injections / infusions
- Kanamycin A (not in use in Norway) can be given both as tablets and as injections / infusions

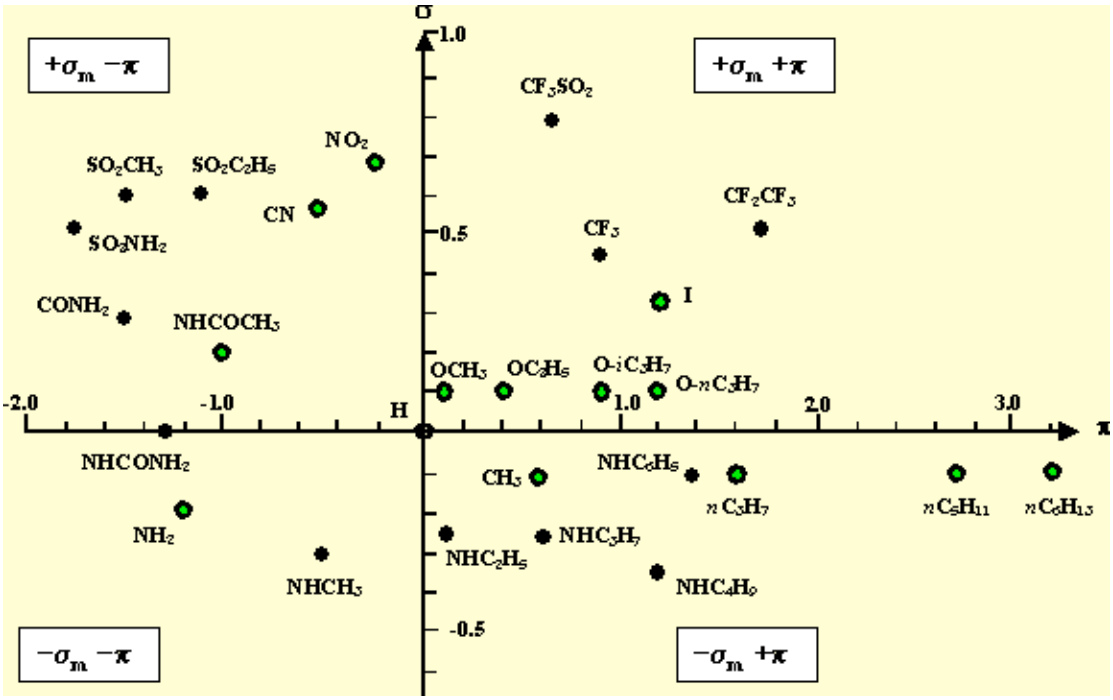
Explain why some of the compounds which should have a good oral availability according to “Lipinsky” are not given as tablets and *vice versa*.

2.

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

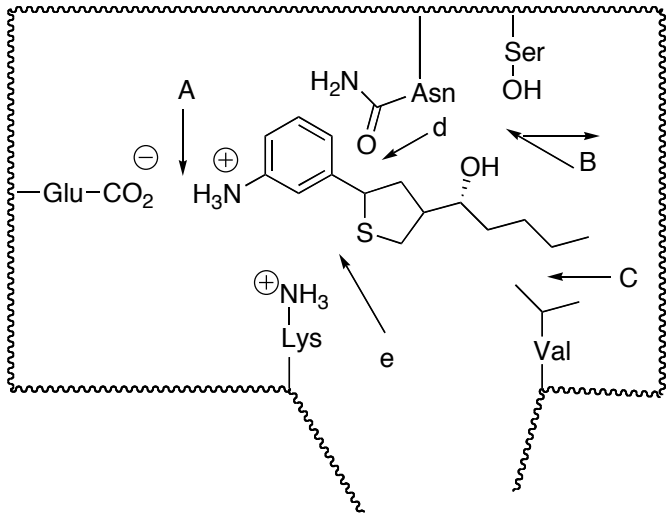


Z	% Antibacterial activity *in vitro*
H	50
Cl	80
CH_3	45
OCH_3	25
OH	10
CF_3	85
NO_2	55



3.

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



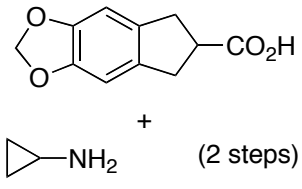
4.

(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.

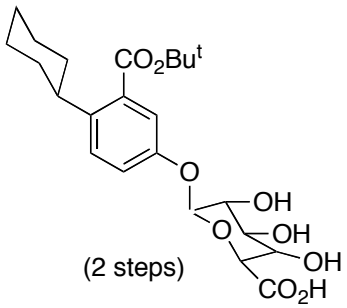
(b) Draw dose-responce curves (in the same plot of i) a full agonist; ii) a mixt of fullagonist and competitive antagonist

5.

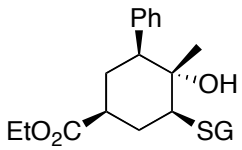
Predict the structures of the compounds that produce the following metabolites (work backwards from metabolite to compound). Show steps (not detailed mech.) and suggest enzymes.



(2 steps)



(2 steps)



(2 steps)

6.

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