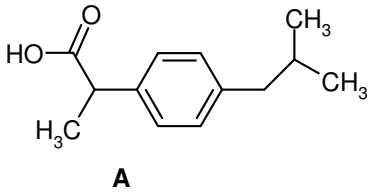
Exercise to the lecture „Modern Methods in Drug Discovery“ WS13/14

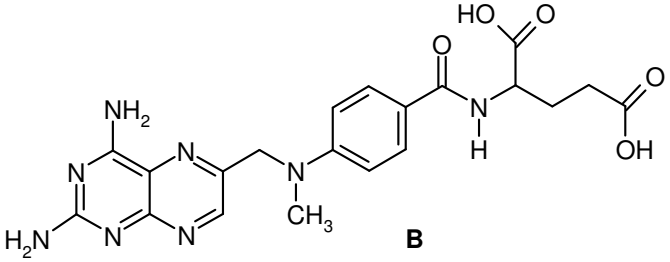
4th Assignment to be handed in until 16.12.2013

your name:

1. In lectures 3 and 4 a number of requirements and criteria have been presented, which a chemical compound should possess for good oral bioavailability (molecular weight (MW), number of hydrogen-bond donors, etc. Hint: A hydrogen-bond donor is an acceptor as well; halogens do not count as H-bond acceptors) Judge the following compounds accordingly and complete the table (56 points)

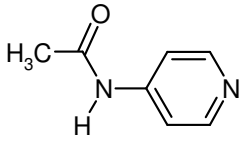


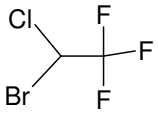
A



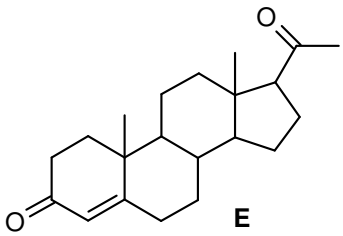
B

C

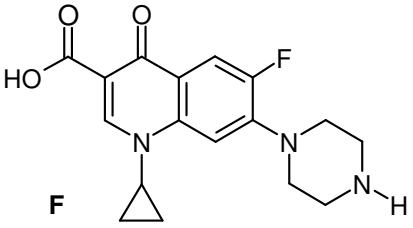




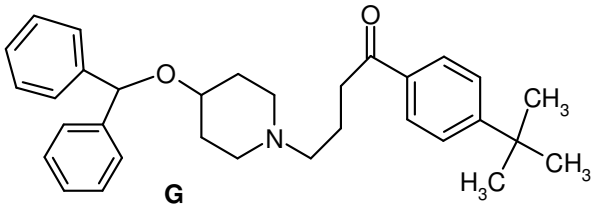
D



E



F

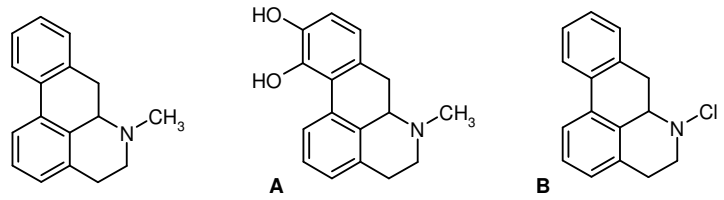


G

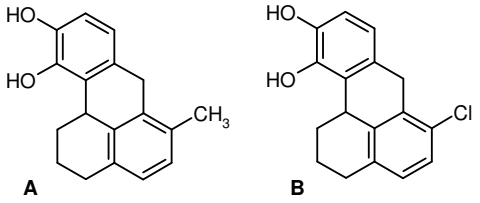
atomic masses: H: 1.0, C: 12.0, N: 14.0, O: 16.0, F: 19.0, Cl: 35.5, Br: 79.9

Compound	logP	MW	H-bond donors	H-bond acceptors	bioavailability (good/bad/so-so)
A	3.5				
B	-1.4				
C	0.4				
D	2.3				
E	3.9				
F	1.3				
G	8.3				

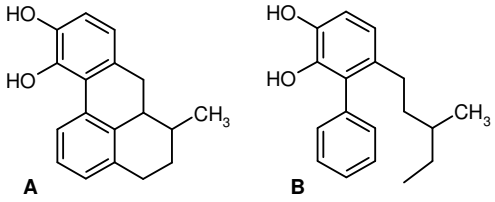
2. Which one of the modifications A or B will make the molecule more hydrophilic?
See also lecture 4 (7 points)



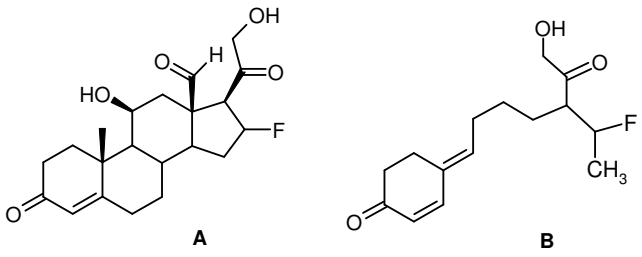
3. Which one of the compounds A or B will be metabolically more stable?
(7 points)



4. Which compound will loose more degrees of freedom upon binding to its target?
Mark the rotatable bonds. (10 points)



5. Which of the compounds A or B should bind more selectively to a given target? Please give a short explanation why! (10 points)



6. Which compound is expected to show a better bioavailability? Please indicate your criteria
(10 points)