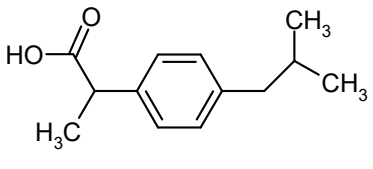
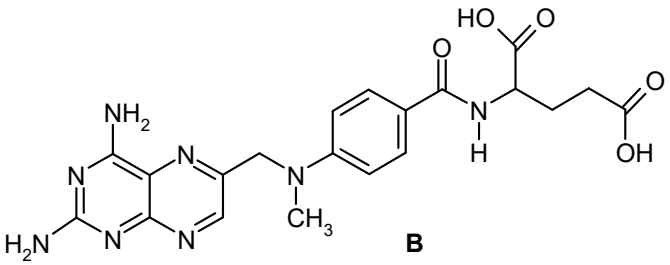
Exercise to the lecture „Modern Methods in Drug Discovery“ WS24/25

4th Assignment

1. In lectures 3 and 4 guidelines 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. Terminating CH_3 and NH_2 groups are not considered as rotatable groups) Judge the following compounds accordingly and complete the table (70 points)

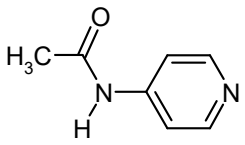


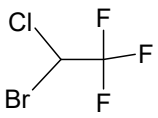
A



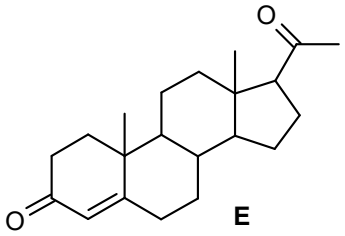
B

C

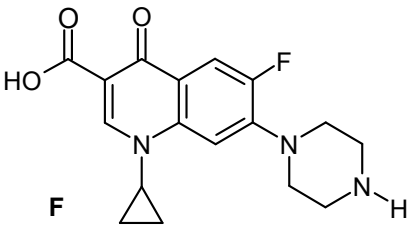




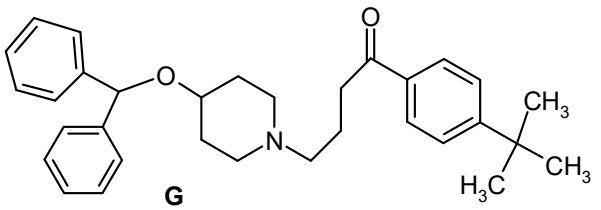
D



E



F

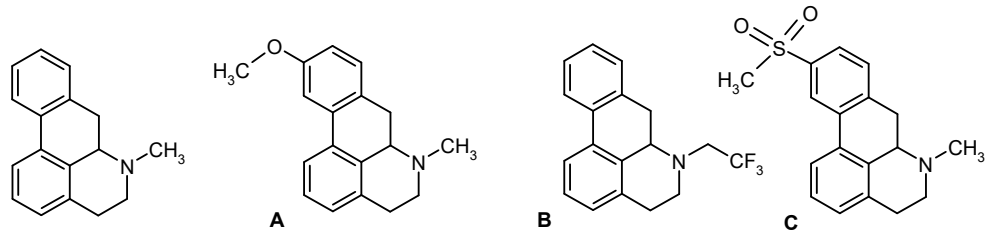


G

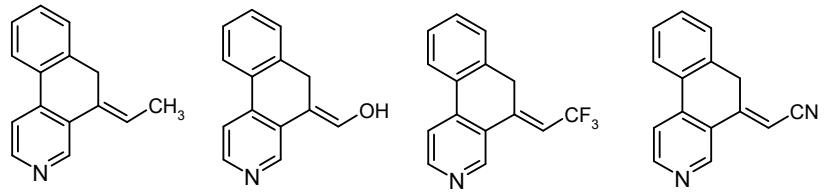
atomic masses: H: 1.0, C: 12.0, N: 14.0, O: 16.0, F: 19.0, Cl: 35.5, Br: 79.9

Compound	logP	MW	H-bond donors	H-bond acceptors	rotatable bonds	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					

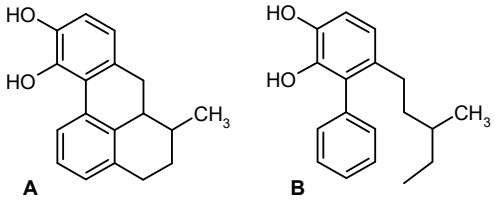
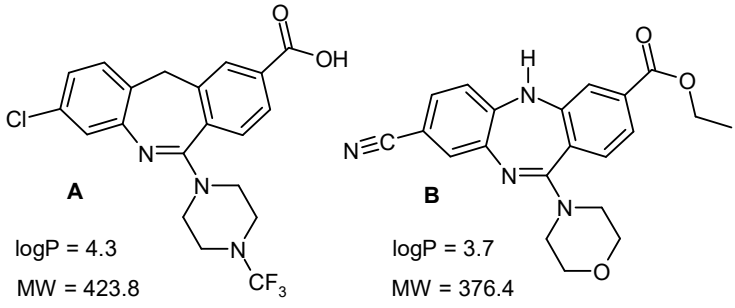
2. Which one of the modifications A, B, or C will make the molecule most hydrophilic?
See also lecture 4 (5 points)



3. Mark the most lipophilic compound in the following series (5 points)



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



5. Which compound is expected to show a better bioavailability? Please indicate your criteria.
Also consider aspects besides Lipinski's rule of five. (10 points)