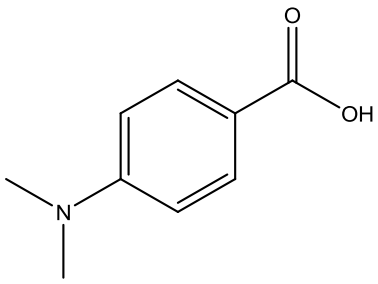
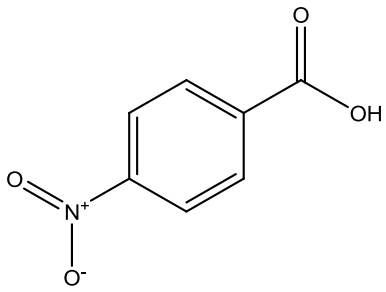
Medchem 562P
Fall 2011
Problem Set #1

Acid/Base Chemistry

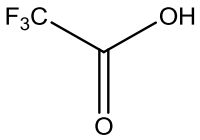
1. Which compound is more acidic? Why?

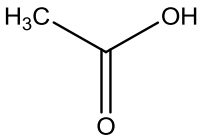
A)





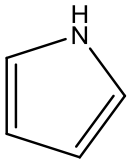
B)

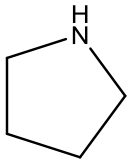




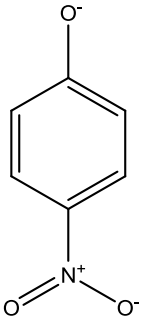
2. Which compound is more basic? Why?

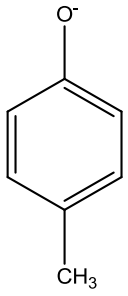
A)



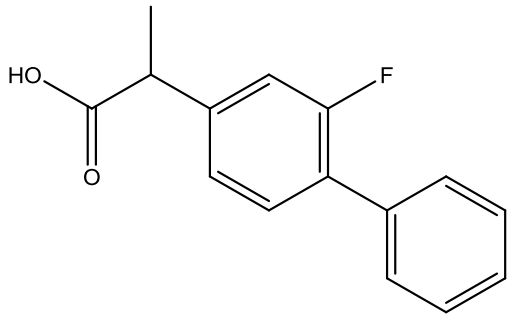


B)





3. Flurbiprofen is a non-steroidal anti-inflammatory drug (NSAID) used to relieve pain, tenderness, swelling, and stiffness caused by osteoarthritis and rheumatoid arthritis. Given its structure below, answer the following questions.



A) What is the approximate pKa of this compound?

B) Draw the structure of the sodium salt of this compound. What are the advantages of administering the salt form of the drug?

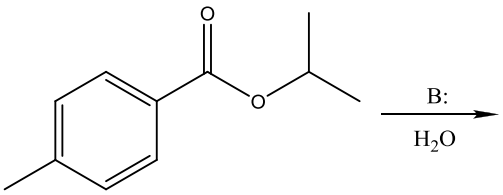
C) Using the Henderson-Hasselbalch equation, calculate the ionized/unionized ratio of the drug at pH 7.

D) If a large fraction of the administered dose of Flurbiprofen is cleared renally in its unprotonated form, would this drug have a longer duration of action at a urinary pH of 4 or 8? Explain your answer.

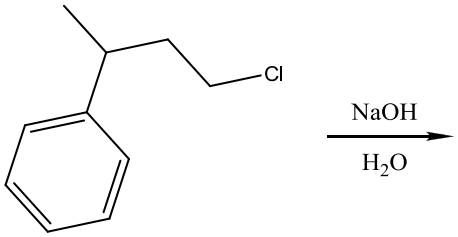
Reaction Mechanisms

Draw the mechanisms for the following reactions and give the structures for the expected products.

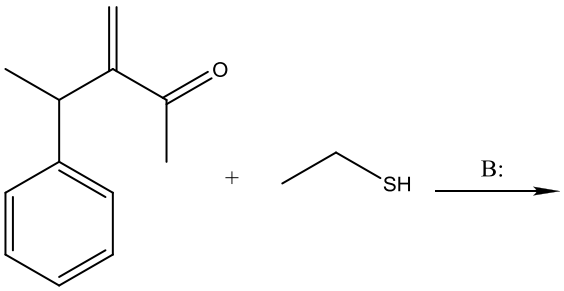
1. General base-catalyzed hydrolysis:



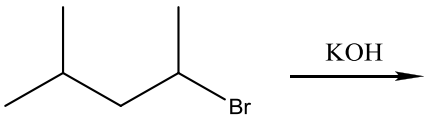
2. Nucleophilic substitution:



3. Special nucleophilic addition (Michael Addition):

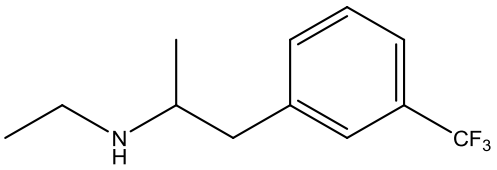


4. Base-catalyzed elimination (For this one only draw the major product):



Stereochemistry

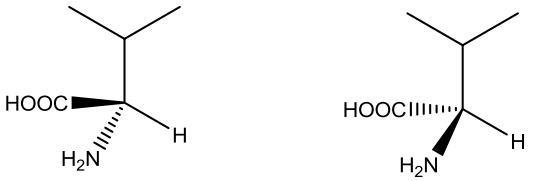
1. Dexfenfluramine (structure below) exists only as the S-isomer. Draw this configuration.



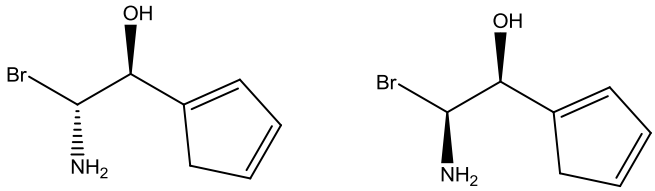
2. For each pair of compounds below, identify whether they are:

a. Geometric Isomers
b. Positional Isomers
c. Enantiomers
d. Diastereomers

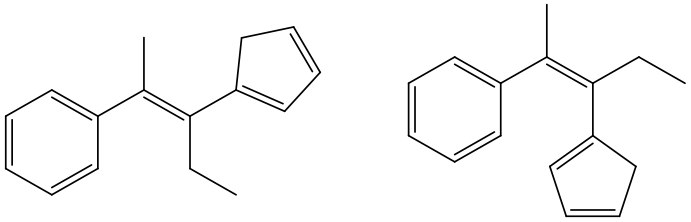
i)



ii)



iii)



iv)