MDCM 601 Exam 1 Key

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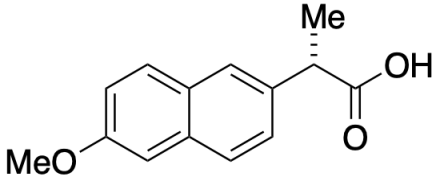
Problem 1. Naproxen (structure shown) has pKa = 4.15.



1. Calculate pH at which concentration of protonated naproxen will be 50 times greater than concentration of deprotonated naproxen.
   Answer:

$$
\begin{aligned}
K_a &= \frac{[H^+][Np^-]}{[HNp]} \\
[H^+] &= \frac{50[Np^-]}{[Np^-]} K_a \\
pH &= -log(50K_a) \\
pH &= -log(50) + pK_a \\
pH &= 2.45
\end{aligned}
$$

2. Calculate pH at which 50% of naproxen will be ionized.
   Answer:
   50% ionization implies $[Np^-] = [HNp]$. Therefore, $pH = pK_a = 4.15$

3. Determine the absolute configuration of the stereocenter in naproxen.
   Answer:
   S

4. How many hydrogen bond donors are there in naproxen?
   Answer:
   1

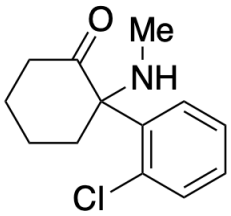
5. How many hydrogen bond acceptors?
   Answer:
   3

6. How many pi electrons make naphthalene in naproxen aromatic?
   Answer:
   10

7. Will the C=O bond be longer or shorter in the carboxylate anion compared to the neutral carboxylic acid?
   Answer:
   Longer due to resonance.

8. True or false? Solubility of naproxen in water would increase at low pH.
   Answer:
   False.

Problem 2. Ketamin (structure shown) conjugate acid has pKa = 7.5.



1. Name the functional group that is protonated in the conjugate acid. *Answer:*
   Amine; Secondary amine.

2. How many stereocenters are there in ketamin?
   Answer:
   1

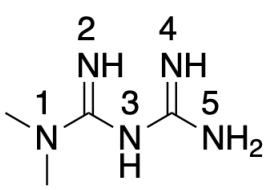
3. How many compounds are represented with the structure below?
   Answer:
   2

4. True or false? Solubility of ketamin in water would increase at low pH.
   Answer:
   True.

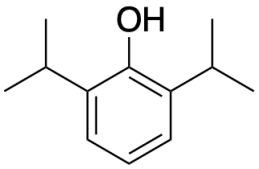
5. Calculate the Gibbs free energy for deprotonation of this conjugate acid. Your answer should be given in kcal/mol with 2 significant figures. (Recall: 1 cal = 4.184 J)
   Answer:

$$\begin{aligned}\Delta G^\circ &= -RT \ln K_{eq} \\ &= -8.314\,\mathrm{J/Kmol} \cdot 298.15\,\mathrm{K} \frac{1\,\mathrm{cal}}{4.184\,\mathrm{J}} \cdot (-7.5) \ln 10 \\ &= 10\,231\,\mathrm{cal/mol} \\ &= 10.2\,\mathrm{kcal/mol}\end{aligned}$$

Problem 3. Metformin (structure shown) conjugate acid has pKa = 12.4.



metformin



propofol

1. Which nitrogen (numbered 1-5 in figure) is most likely to be protonated in the conjugate acid?
   Answer:
   2 or 4.

2. True or false? If propofol (pKa = 11) and metformin were mixed together, propofol would be deprotonated by metformin.
   Answer:
   True.

3. At physiological pH = 7.4 will metformin be neutral or charged?
   Answer:
   Charged.

4. At physiological pH = 7.4 will propofol be neutral or charged?
   Answer:
   Neutral.

5. Extra credit: For the process propofol + metformin -¿ propofol- + metformin-H+, calculate Gibbs free energy.

Problem 4. Calculate the concentration of protons in stomach where pH = 2.
Answer:
$pH = -log_{10}[H^+]$
$[H^+] = 0.01\,\mathrm{M}$

Problem 5. An unknown liquid has enthalpy of freezing $\Delta H^\circ = -1500\,\mathrm{cal/mol}$ and entropy of freezing $\Delta S^\circ = -5\,\mathrm{cal/molK}$ at the freezing point. Calculate the freezing point of this liquid in K. Recall ΔG° for a system at equilibrium.
Answer:
At phase equilibrium $\Delta G^\circ = 0$.

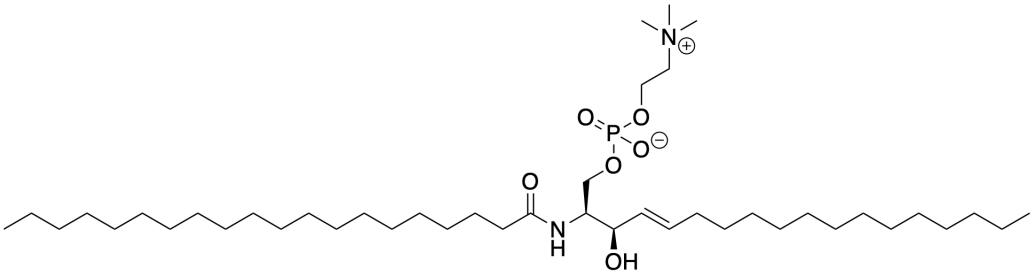
$$\begin{aligned} T &= \frac{\Delta H^\circ}{\Delta S^\circ} \\ &= 300\,\mathrm{K} \end{aligned}$$

Problem 6. What is the pH of acetate buffer that contains 0.2 M acetic acid and 0.05 M sodium acetate. pK_a of acetic acid is 4.7.

Answer:

$$K_a = \frac{[\mathrm{H^+}][\mathrm{OAc^-}]}{[\mathrm{HOAc}]}$$
$$pK_a = pH - \log \frac{[\mathrm{OAc^-}]}{[\mathrm{HOAc}]}$$
$$pH = 4.7 + \log \frac{0.05\,\mathrm{M}}{0.2\,\mathrm{M}}$$
$$pH = 4.1$$

Problem 7. Sphingomyelin is shown below.



1. Is this molecule charged?
   Answer:
   No.

2. Does this molecule contain a phosphodiester group?
   Answer:
   Yes.

3. How many *cis* double bonds does it contain?
   Answer:
   0

4. How many basic nitrogen atoms are there in this molecule (*i.e.* lone electron pairs on N that can readily be protonated)?
   Answer:
   0

5. If the third pK_a of phosphoric acid is 12.7 calculate the ratio of deprotonated to protonated sphingomyelin at physiologic pH = 7.4.

$$K_a = \frac{[H^+][Sp^-]}{[HSp]}$$
$$\frac{[Sp^-]}{[HSp]} = \frac{10^{-12.7}}{10^{-}7.4}$$
$$= 5 \cdot 10^{-6}$$