MDCM 601 2023 Exam 1 Key

Zarko V. Boskovic

September 6, 2023

Problem 1. Isomerization glucose – 1-phosphate (G_1P) $\rightleftharpoons$ glucose – 6-phosphate (G_6P) proceeds until the equilibrium concentration is reached. At equilibrium, G1P is 1 mM, and G6P is 19 mM. Calculate the equilibrium constant for this isomerization, and the standard Gibbs free energy ΔG°. R = 8.314 J/molK; T = 298 K.
Answer

- Equilibrium constant
  glucose – 1-phosphate (G_1P) $\rightleftharpoons$ glucose – 6-phosphate (G_6P)

$$K_{eq} = \frac{[G6P]_{eq}}{[G1P]_{eq}} = 19$$

- Standard Gibbs free energy

$$\begin{aligned}\Delta G^\circ &= -RT \ln K_{eq} \\ &= -8.314\,\text{J/molK} \times 298\,\text{K} \times \ln 19 \\ &= -7.30\,\text{kJ/mol}\end{aligned}$$

- This isomerization is **spontaneous**.

Problem 2. pH of blood is 7.4. What is the concentration of protons in blood? Your answer should be in nM with 2 significant figures.
Answer

- Concentration of protons in blood.

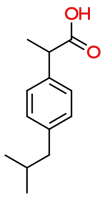
$$\begin{aligned}[H^+] &= 10^{-pH} \times \frac{1 \times 10^9\,\text{nM}}{\text{M}} \\ &= 10^{9-pH} \\ &= 10^{1.6} \\ &= 40\,\text{nM}\end{aligned}$$

- Carbonic acid – bicarbonate buffer is the main buffer in the blood.

Problem 3. What is the pH of acetate buffer that contains 0.25 M acetic acid and 0.15 M sodium acetate. pK_a of acetic acid is 4.75?
Answer

$$\begin{aligned} pH &= pK_a + \log \frac{[A^-]}{[HA]} \\ &= 4.75 + \log \frac{0.15\,\text{M}}{0.25\,\text{M}} \\ &= 4.53 \end{aligned}$$

Problem 4. Ibuprofen (structure shown) has a p$K_a = 4.45$.

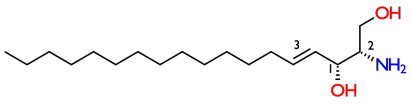


- At what pH will the concentration of protonated ibuprofen be 100 times greater than deprotonated ibuprofen? Answer with three signficant figures.

$$\begin{aligned} pH &= pK_a + \log \frac{[A^-]}{[HA]} \\ &= 4.45 + \log \frac{1}{100} \\ &= 4.45 - 2 \\ &= 2.45 \end{aligned}$$

- In blood (pH =7.4) ibuprofen would be mostly **deprotonated**.
- Ibuprofen has **1** stereocenter(s). (Use numbers for your answer.)
- When it is deprotonated, the two C−O bonds in ibuprofen are of **same** length due to **resonance**.
- Aqueous solubility of ibuprofen is higher at **higher** pH.

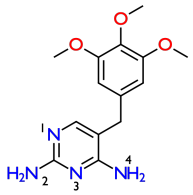
Problem 5. Sphingosine (shown) is an important component of biological lipids.



- Configuration of the stereocenter 1 is: R
- Configuration of the stereocenter 2 is: S

- Configuration of the double bond 3 is: E
- How many carbons does sphingosine consist of? 18
- pKa of sphingosine is 6.7. At a pH lower than that, **amine** (functional group) is positively charged.

Problem 6. Answer the following questions about trimethoprim (shown).



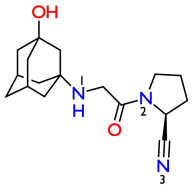
- Which two nitrogens are most likely to be protonated first? Nitrogens **1** and **3** are most likely to be protonated first.
- Metabolism of trimethoprim involves demethylation of one of the methyl ethers. This produces a functional group called **phenol** .
- pKa of this group is 10. If you dissolve this metabolite in a 1 mM NaOH solution, what percentage of metabolite will remain neutral (2 sigfigs)?

$$pH = pK_a + \log \frac{[A^-]}{[HA]}$$

$$\begin{aligned} \text{percent neutral} &= \frac{1}{10^{pH-pK_a}+1} \times 100 \\ &= \frac{1}{10^{14-3-10}+1} \times 100 \\ &= 9.1\% \end{aligned}$$

- Pyrimidine is the heterocycle found in trimethoprim. It has **6** π electrons.

Problem 7. Vildagliptin (shown) is an orally active antihyperglycemic agent.



- Configuration of its stereocenter is: ***S*** item Nitrogen labeled **1** is the most basic nitrogen.
- Nitrogen labeled **3** is the sp-hybridized nitrogen.

- Amide nitrogen is labeled with **2**.
- The alcohol in the structure is **tertiary**.
- There are **2** hydrogen-bond donors.

Problem 8. How many acidic protons does carbonic acid have?
Answer Carbonic acid has **2** acidic protons.

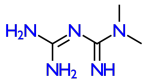
Problem 9. For double-helix formation, ΔG can be measured to be $-10\,\text{kcal/mol}$ at $25\,^\circ\text{C}$ ($298\,\text{K}$). The heat released indicates an enthalpy change of $-120\,\text{kcal/mol}$. For this process, calculate the entropy change for the system. If you know that each base pairing decreases entropy by $25\,\text{cal/molK}$, how many base pairs does this double helix have?
Answer

$$\Delta G = \Delta H - T\Delta S$$

$$\begin{aligned}\Delta S &= \frac{\Delta G - \Delta H}{-T} \\ &= \frac{-10\,\text{kcal/mol} - -120\,\text{kcal/mol}}{-298\,\text{K}} \\ &= -0.369\,\text{kcal/molK}\end{aligned}$$

Number of base pairs: $\frac{369\,\text{cal/molK}}{25\,\text{cal/molK}} \approx 15$

Problem 10. Metformin (shown) is a drug used to treat diabetes mellitus in adults and children over the age of 10. Its pK_a is 12.4. What is the concentration of NaOH that would be required to achieve the pH at which concentrations of protonated and unprotonated forms are equal? Recall that pH +pOH =14



Answer
If concentrations of deprotonated and protonated forms are equal, then pH = pK_a.
$pH = pK_a = 12.4$
$pOH = 14 - 2.4 = 1.6$
$[\text{OH}^-] = 10^{-1.6} M = 0.025\,\text{M}$