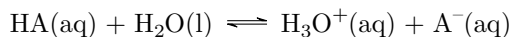


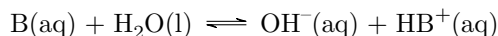
Key for Take-Home Assignment 05

The biopharmaceutical properties of a drug depend on the particular form it takes in the body. This is particularly important for a drug that is a weak acid or a weak base as, depending on the pH, it can exist in a molecular or an ionic form that differ in their ability to diffuse across membranes. For this reason, determining a drug's pK_a value(s) is important.

One method for determining the pK_a of a drug is to prepare a saturated solution of the drug in water and measure the solution's pH when equilibrium is established, as shown here for a drug that is a molecular, monoprotic weak acid, HA



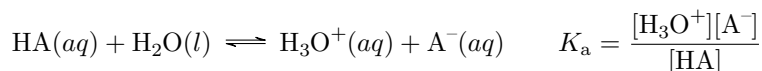
or a molecular, monoprotic weak base, B



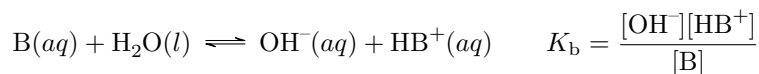
In a typical analysis for the drug pentobarbital, the pH is measured as 5.312. The drug's formula is $\text{C}_{11}\text{H}_{18}\text{N}_2\text{O}_3$ and its mass solubility—the grams of the drug needed to prepare a 1.0 liter saturated solution—is 0.679 g/L. Using this information, determine if pentobarbital is a weak acid or a weak base, and report its pK_a if it is a weak acid and its pK_b if it is a weak base.

This assignment is due in class on Friday.

Answer. The first thing you must do is determine if the drug is a weak acid or a weak base. If the saturated solution is acidic ($\text{pH} < 7$), then the compound is a weak acid; if the saturated solution is basic ($\text{pH} > 7$), then the compound is a weak base. If the compound is a weak acid, then the equilibrium reaction and the equilibrium constant of interest are



and if the compound is a weak base, then the equilibrium reaction and the equilibrium constant of interest are



Once you decide on the correct equilibrium constant expression, you use the pH to determine either the equilibrium concentration of H_3O^+ if the compound is a weak acid or the equilibrium concentration of OH^- if the compound is a weak base; let's call this value x . The equilibrium concentration of the drug is $[\text{drug}]_o - x$, where $[\text{drug}]_o$ is the drug's initial concentration, which is equivalent to

$$[\text{drug}]_o = \frac{\text{solubility in g/L}}{\text{molar mass in g/mol}}$$

Substituting back gives either

$$K_a = \frac{(x)(x)}{[\text{drug}]_o - x} \quad K_b = \frac{(x)(x)}{[\text{drug}]_o - x}$$

which you can now solve to give K_a if your drug is a weak acid, or to give K_b if your drug is a weak base.

Note. You cannot use a compound's K_a or its K_b to determine if it is a weak acid. If a compound is a weak acid, then its K_a value tells you about its strength as an acid; if a compound is a weak base, then its K_b value tells you about its strength as base.