Acid/Base Properties of a Pharmaceutical Compound

Many pharmaceutically interesting compounds are weak acids or weak bases, a fact of some importance when preparing them for use by the public. For example, if the active ingredient in a nasal spray is too acidic, then the preparation might include an additional ingredient to neutralize some of the acid; after all, no one wants to spray something as acidic as, say, lemon juice up his or her nose!

Pseudoephedrine is a central nervous system stimulant used in many cold and allergy tablets. In its molecular form it is a weak base (it is an amine), which, for convenience, we may represent as B. In water, the following equilibrium reaction exists

$$B(aq) + H_2O(l) \leftrightarrows OH\text{-}(aq) + HB^+(aq)$$

The Merck Index reports that a 0.030 M solution of pseudoephedrine has an equilibrium pH of 11.44. What is the value of K_b for this compound?

Answer. With a pH of 11.44, the pOH is 2.56 and the equilibrium concentration of OH– is 2.75×10^{-3} M. This value goes in the change column for OH^- and determines the change for B and HB^+

	$B(aq)$	+	H_2O	$\leftrightarrows$	$OH^-(aq)$	+	$HB^+(aq)$
I	0.030 M		—		0		0
C	-2.75×10^{-3} M		—		2.75×10^{-3} M		2.75×10^{-3} M
E	0.02725		—		2.75×10^{-3} M		2.75×10^{-3} M

Now that we have the equilibrium concentrations, we substitute into the K_b expression

$$K_b = \frac{[HB^+][OH^-]}{[B]} = \frac{(2.75\times10^{-3})^2}{0.02725} = 2.77\times10^{-4}$$

Because its base form is only slightly soluble in water, pseudoephedrine typically is dispensed in its weak acid form, HB^+. Pseudoephedrine hydrochloride, therefore, is an ionic compound consisting of protonated pseudoephedrine, HB^+, and Cl^- as a counter ion. The formula for this often is written as B•HCl; don't confuse this with the strong acid HCl. A solution of pseudoephedrine hydrochloride, therefore, is acidic due to the presence of HB^+. Write the K_a reaction responsible for making the solution acidic and report the value for K_a.

Answer. The reaction is $BH^+ + H_2O \leftrightarrows H_3O^+ + B$, for which the equilibrium constant is

$$K_a = K_w/K_b = (1.00\times10^{-14})/(2.77\times10^{-4}) = 3.61\times10^{-11}$$

Suppose you dissolve three tablets of Sudafed®, each containing 30.0 mg of pseudoephedrine hydrochloride, in 200.0 mL of water. What is the pH of the resulting solution? The molar mass for pseudoephedrine hydrochloride is 201.7 g/mol.

Answer. Begin by finding the concentration of pseudoephedrine hydrochloride, which is

$$\frac{3\ \text{tablets} \times \frac{0.030\ \text{g}}{\text{tablet}} \times \frac{1\ \text{mole}}{201.7\ \text{g}}}{0.200\ \text{L}} = 2.23 \times 10^{-3}\ \text{M}$$

Taking this as the initial concentration of HB^+, we solve the problem

	$HB^+(aq)$	+	$H_2O(l)$	$\leftrightarrows$	$H_3O^+(aq)$	+	$B(aq)$
I	2.23×10^{-3} M		—		0		0
C	–X		—		+X		+X
E	2.23×10^{-3} – X		—		X		X

Substituting into the K_a expression and solving gives

$$K_a = \frac{[H_3O^+][B]}{[HB^+]} = \frac{X^2}{2.23 \times 10^{-3} - X} = 3.61 \times 10^{-11}$$

Assuming that $2.23 \times 10^{-3} - X \approx 2.23 \times 10^{-3}$ simplifies this to

$$K_a = \frac{X^2}{2.23 \times 10^{-3}} = 3.61 \times 10^{-11}$$

which gives

$$X = 2.84 \times 10^{-7}$$

Checking our assumption, we find that this produces an error of

$$\%\text{error} = \frac{2.23 \times 10^{-3} - (2.23 \times 10^{-3} - 2.84 \times 10^{-7})}{2.23 \times 10^{-3}} \times 100 = 0.01\%$$

which is acceptable. The concentration of H_3O^+ is X, thus

$$[H_3O^+] = 2.84 \times 10^{-7} \qquad \text{pH} = 6.55$$