Estimating pK\textsubscript{a} Values of Organic Structures

MarvinSketch has a very useful tool for estimating pK\textsubscript{a} values of organic molecules. Load MicroMarvinSketch: http://www.widgetbox.com/widget/micromarvin

To determine the pK\textsubscript{a} of an organic structure (e.g., of methylacetamide)

1) draw the structure
2) Call pK\textsubscript{a} from Tools…protonation…
3) Accept default values and click OK

1 is the major species in the pH range 0-14

At low pH, 1 is replaced by 2

• Red values are pK\textsubscript{a} estimates; blue values are estimates of the pK\textsubscript{a} of the conjugate acid.

• Click the structures in windows labeled 1, 2, 3 to see various “microspecies”.

• The plot shows how the microspecies concentrations vary with pH.
Acid-Base Equilibria: Concepts & Definitions

Many protonation and deprotonation steps are reversible. The equilibrium can be expressed in terms of $pK_a$. Let's review the meaning of $pK_a$:

$$
HA + H_2O \rightleftharpoons H_3O^+ + A^-
$$

$$
K_{eq} = \frac{[H_3O^+][A^-]}{[HA][H_2O]}
$$

Assuming the $[H_2O]$ to be constant (55.5 M) i.e., $[H_2O] \gg [H_3O^+]$, we can define a new constant $K_a = K_{eq}[H_2O]$ which allows us to drop water from the above equilibrium expression. This is the basis of the widely used $pK_a$ convention:

$$
HA \rightleftharpoons H^+ + A^-
$$

$$
K_a = \frac{[H^+][A^-]}{[HA]}
$$

Or

$$
log K_a = log [H^+] + \log \frac{[A^-]}{[HA]}
$$

$$
-log K_a = -log [H^+] + \log \frac{[HA]}{[A^-]}
$$

Henderson-Hasselbalch eqn.
Determining the Position of Equilibria

Based on the magnitude of $K_{eq}$, can we conclude that protonated alcohol is a reasonable species?

$K_{eq}$ can be calculated by analyzing this reaction as a sum of two acid / base equilibria

Relevant equilibria

<table>
<thead>
<tr>
<th>Equation</th>
<th>$K_a$</th>
<th>$pK_a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\text{CH}_3\text{O}^+ \rightleftharpoons \text{H}^+ + \text{CH}_3\text{O}^-$</td>
<td>$K_a^{(1)}$</td>
<td>-2.5</td>
</tr>
<tr>
<td>$\text{H}^+ + \text{CH}_3\text{O}^- \rightleftharpoons \text{H}_2\text{O}$</td>
<td>$K_a^{(2)}$</td>
<td>-1.7</td>
</tr>
</tbody>
</table>

$pK_a = -\log K_a$

$K_{eq} = \frac{1}{K_a^{(1)}} \cdot K_a^{(2)}$

$K_{eq} = \frac{10^{-(-1.7)}}{10^{-(-2.5)}} = 0.16$