7.10: Carboxylic Acids and Derivatives

Now that we have a fairly solid understanding of the reactions of aldehydes and ketones, we are going to move up one oxidation state to look at the behavior of carboxylic acids and their derivatives (Table $7.0.1$), a group of compounds that includes the acids, esters, amides, acid chlorides, and acid anhydrides. Just as we did with aldehydes and ketones, we will highlight and discuss the reasons for both the similarities and differences observed. The most obvious difference between this group of compounds is that the carboxylic acids are acidic; the other derivatives lack an acidic hydrogen bonded to an O and, therefore, do not participate in simple acid-base reactions[6]. Since we have discussed the reasons for the acidity of carboxylic acids earlier, we will not go over that here at great length, but be sure to check Chapter 1 if you need a refresher. However, we do want to remind you that many organic compounds are acidic (or basic) and can exist as their conjugate base (or acid) in aqueous solutions, and that the relative amounts of conjugate acid or bases change as pH changes. The degree to which a molecule exists in an acidic or basic form (in water) is particularly important for biological systems that (in humans) are buffered at around $7.3–7.4$ Recall that we can relate the pH of a buffered solution to the pK_a of any acid that is participating in the solution using the Henderson-Hasselbalch equation[7]:

$$pH = pK_a + \log \frac{[A^-]}{[HA]} \tag{7.10.1}$$

where HA and A^- are the concentrations of the acid and its conjugate base, respectively. We can rewrite this equation (by taking the anti-log of the terms) so that:

$$\frac{[A^-]}{[HA]} \tag{7.10.2}$$

which allows us to estimate the relative amounts of acid and base.

For example, a typical carboxylic acid has a pK_a of around 4. At physiological pH (~ 7), the ratio of the conjugate base to conjugate acid is $\sim 10^{(7-4)} = 10^3$, that is, there is about 1000 times more of the conjugate base than the conjugate acid for most common carboxylic acids in biological systems.

There are many naturally occurring (that is, biologically relevant) carboxylic acids and most of them exist as the conjugate base at physiological pH. One consequence is that these species are soluble in water because of the favorable ion-dipole interactions that can be formed. Biological molecules that do not contain such polar (ionized) groups ($-COO^-$ or $-NH_3{}^+$) are typically insoluble in water: indeed, the presence of this type of polar (ionic) side chain explains the water solubility of many large biological molecules.