3.3: pKa of Organic Acids and Application of pKa to Predict Acid-Base Reaction Outcome

As we mentioned before, all organic compounds could be acids, because they all have hydrogen atoms that could potentially be donated. Most organic acids are weak acids with a small K_a. For example, acetic acid CH_3COOH has a Ka of 1.8×10^{-5}. Lots of other organic acids are even weaker than acetic acid, and it is this weak acidity that makes it difficult to realize that some organic compounds are actually acids.

However, this weak acidity is very important in Organic Chemistry. Since it is not that very convenient to say or to remember K_a values like 1.8×10^{-5}, **pK_a** is used more often in Organic Chemistry to refer to the relative acidity of different acids. The definition of pKa is:

$$pK_a = -\log K_a$$

The smaller the pK_a value, the larger the K_a, and the stronger the acidity is.

The pK_a of most organic acids range between 5~60. While it is impossible to know the pK_a of every organic compound, it is very useful to understand the pK_a (and acidity) based on the functional groups involved, because the same functional groups usually have similar pK_as. The approximate ranges of pK_a values for seven major functional groups are listed in **Table 3.1**, which serves as a very valuable starting point for us to predict and understand the acidity of any organic molecule. The strongest organic acid listed here is carboxylic acid, with a pK_a of about 5; the weakest organic acids are the alkanes with pK_a values of over 50. Since approximate ranges of pK_a values are listed in the table, the exact pK_a value of a group varies for different compounds because of the structural differences. Fortunately however, it is usually not necessary to know the exact pK_a values for most cases in organic chemistry, and the approximate range is good enough.

Acidic Hydrogen in Functional Groups	Approximate Range of pKa	Conjugate Base
Carboxylic acid (R-C(=O)-OH)	~5	(R-C(=O)-O⁻)
Alcohol R—OH	~16 (H_2O: ~16; Phenol: ~10)	R—O⁻
Aldehyde/Ketone (R-C(=O)-H, R-C(=O)-CH₃)	~16 to ~20	(R-C(=O)-C⁻, R-C(=O)-CH₂⁻)
Alkyne R—C≡C—H	~25	R—C≡C⁻
Amine R—NH₂	~35 to 40 (NH_3: ~38)	R—NH⁻
Alkene R—CH=CH₂	~45	R—CH=CH⁻
Alkane R—CH₃	>50	R—CH₂⁻

50)" width="695" height="586"> Table 3.1: Approximate ranges of pKa values for common organic functional groups

- Acidity is the ability of a compound to donate H^+, so when we talk about the acidity (K_a and pK_a) of an organic compound, it must be about a specific **H atom** (highlighted blue in the table). For different H atoms in the same compound, the acidity and pK_a are different. As for the example of methanol:

pKa: ~50   pKa: ~15   The acidity of CH₃OH therefore usually refer to the **H** in **OH** group, the more acidic hydrogen.
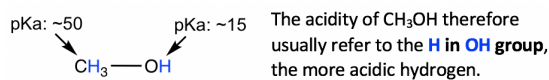
CH₃—OH

Figure 3.3a Methanol

- It is very useful to memorize the approximate ranges of pK_a listed in Table 3.1.
- The acidity of the functional groups in the table *decreases* from top to the bottom, and the basicity of the conjugate bases in the last column *increases* from top to bottom, because **the stronger the acid, the weaker the conjugate base is.**

Predict the Outcome of Organic Acid-Base Reaction — **Use pK_a as Criterion**

With the knowledge of acidity and pK_a, we are now ready to see how to apply this information to the understanding of organic reactions from an acid-base perspective.

The following reaction is an **example** in **Section 3.2.** If you take a closer look at the reactants and products, you will find that the "product" side also contains an acid (ammonia NH_3), and a base (methoxide CH_3O^-). Now the question is, how can we be so sure that the reaction proceeds to the "product" side as written? The question can also be asked in a different way: if equilibrium is established for the reaction mixture, which side will the position of the equilibrium predominantly favour? Left or right?

$$CH_3-\overset{..}{\underset{..}{O}}-H \quad + \quad \overset{\ominus}{:}\overset{..}{N}-H \underset{H}{|} \quad \underset{?}{\rightleftharpoons} \quad CH_3-\overset{..}{\underset{..}{O}}:^{\ominus} \quad + \quad \underset{H}{\overset{\overset{H}{|}}{:N-H}}$$

<div align="center">
<em style="color:red">acid   <em style="color:blue">base   <em style="color:red">conjugate base   <em style="color:blue">conjugate acid
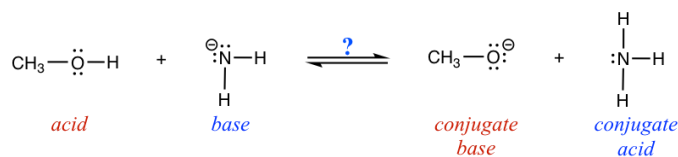</div>

<div align="center">Figure 3.3b Acid-Base Reaction</div>

To answer that question, we will learn about a general rule for acid-base reaction: **Acid-base reactions always favour the formation of the *weaker* acid and the *weaker* base.** This is because the equilibrium always favours the formation of more stable products, and weaker acids and bases are more stable than stronger ones.
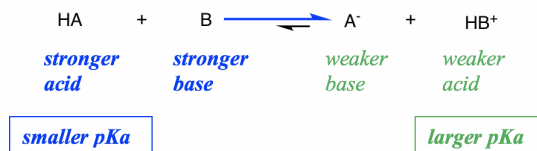
$$HA \quad + \quad B \longrightarrow A^- \quad + \quad HB^+$$

<div align="center">
stronger acid   stronger base   weaker base   weaker acid
</div>

<div align="center">
smaller pKa   larger pKa
</div>

<div align="center">Figure 3.3c Smaller pKa and larger pKa</div>

With pK_a values available at hand, the relative acidity of reactants *vs* products can be compared by comparing their pK_a values, and **the reaction will proceed to the side of the acid with a *larger pK_a*** (larger pK_a means smaller K_a, therefore weaker acid).

So for this reaction, the pK_a check indicates that ammonia NH_3 is a weaker acid than methanol CH_3OH, so the reaction does proceed to the right side with CH_3O^- and NH_3 as the major products.

$$CH_3-\overset{..}{\underset{..}{O}}-H \quad + \quad \overset{\ominus}{:}\overset{..}{N}-H \underset{H}{|} \quad \longrightarrow \quad CH_3-\overset{..}{\underset{..}{O}}:^{\ominus} \quad + \quad \underset{H}{\overset{\overset{H}{|}}{:N-H}}$$

<div align="center">
<em style="color:blue">pKa: ~15 (alcohol)   stronger base   weaker base   <em style="color:blue">pKa: ~35-40 (ammonia)
</div>

<div align="center">
smaller pK_a
stronger acid   larger pK_a
weaker acid
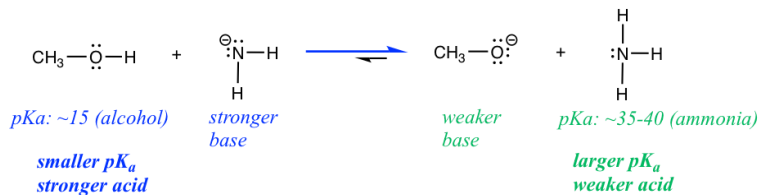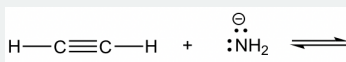</div>

<div align="center">Figure 3.3d Which direction does the reaction go?</div>

Notes: Only comparing between acids is good enough for this purpose, because if CH_3OH is stronger than NH_3, then the conjugate base CH_3O^- must be weaker than the other base NH_2^-.

Examples

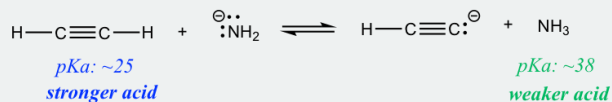Show the products of the following reactions and predict the predominant side of the equilibrium.
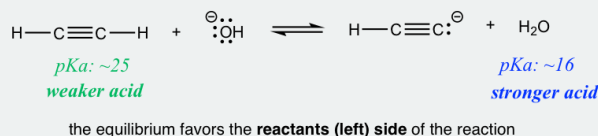
Reaction 1

$$H-C\equiv C-H \quad + \quad \overset{\ominus}{:}NH_2 \quad \rightleftharpoons$$

Reaction 2

$$H-C\equiv C-H \quad + \quad {}^{\ominus}OH \quad \rightleftharpoons$$

Solutions:

Reaction 1

$$H-C\equiv C-H \quad + \quad \overset{\ominus}{:}NH_2 \quad \rightleftharpoons \quad H-C\equiv C:^{\ominus} \quad + \quad NH_3$$

<div align="center">
<em style="color:blue">pKa: ~25   <em style="color:green">pKa: ~38
stronger acid   <em style="color:green">weaker acid
</div>

<div align="center">the equilibrium favors the products (right) side of the reaction</div>

Reaction2

H—C≡C—H + $\overset{\ominus}{:}\underset{\cdot\cdot}{O}H$ ⇌ H—C≡C$\overset{\ominus}{:}$ + H_2O

pKa: ~25
weaker acid

pKa: ~16
stronger acid

the equilibrium favors the **reactants (left) side** of the reaction

Are there any practical applications for such a prediction? Yes! Let's compare the two reactions in the exercises above. Reaction 1 indicates that if ethyne (HC≡CH) and amide (NH_2^-) are mixed together, the reaction **does** proceed to the products side, meaning **HC≡CH could be deprotonated by amide NH_2^-**. However, if HC≡CH and hydroxide OH^- are mixed together as shown in **reaction 2**, no reaction occurs, or we can say that **HC≡CH can not be deprotonated by OH^-** because OH^- is not strong enough! So if you are working in the lab and have the option of choosing between NH_2^- or OH^- to deprotonate HC≡CH, you now know which one to choose.

The idea that OH^- is not a strong enough base may bother you a lot, since it conflicts with the "common knowledge" that we learned in General Chemistry, where OH^- is a strong base. Generally speaking, OH^- is a pretty strong base; however, it is just barely not strong enough to deprotonate HC≡CH, which is a very weak acid, with a pK_a of about ~25. Since HC≡CH is much weaker than the "weak acids" we learned in General Chemistry, a much stronger base, like NH_2^-, is required to deprotonate it.