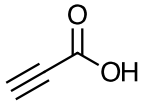
Objective 11. Apply acid-base principles to organic acids.

Organic acids are weak acids.
Remember:

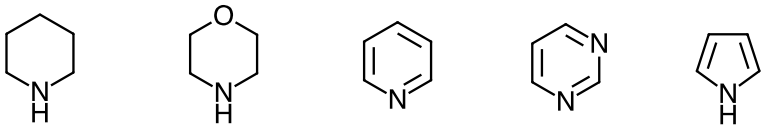
- An acid is a H^+ donor and a base is a H^+ acceptor.
- Every acid has a conjugate (partner) base.
- The acid has a higher charge than its conjugate base, e.g., H_2O acid has a charge of 0 and OH^-, its conjugate base, has a charge of -1.
- K_a (or pK_a) determines acid strength: higher K_a (or lower pK_a) means stronger acid.
- A strong acid has a weak conjugate base and a weak acid has a strong conjugate base.
- A weak base is more stable and less reactive (does not want to donate its H^+) than a strong base.
- A strong acid forms a stable (weak) conjugate base. (In other words, you can explain acid strength by looking at the stability of the conjugate base.)
- A weak (stable) base spreads out its charge (inductive or resonance effect) on the basic atom whereas a strong (unstable) base concentrates its charge on the basic atom.

1. a. (i) Draw the structures of acetic acid (pK_a = 4.8) and ethanol (pK_a = 16) and their conjugate bases.
(ii) Acetate ion is more stable than ethoxide ion because the negative charge on the O is delocalized over three atoms due to ___.
b. (i) Draw the structures of acetic acid and chloroacetic acid (pK_a = 2.8) and their conjugate bases.
(ii) How does Cl stabilize the negative charge on chloroacetate better than the H on acetate?
(iii) Compare chloroacetic acid to dichloroacetic acid. Which acid is stronger? Why?
c. (i) Draw the structures of acetic acid and benzoic acid (pK_a = 4.2) and their conjugate bases.
(ii) How does the phenyl group stabilize the negative charge on benzoate better than the H on acetate?
d. Compare chloroacetic acid to benzoic acid. How does Cl stabilize the negative charge on chloroacetate better than the phenyl group on benzoate?
e. The acid shown below has a pK_a of approximately 2.



(i) Explain why this acid is a stronger acid than acetic acid. (Hint: see inductive effect of HCC group.)
(ii) You can draw a resonance structure of the conjugate base that involves the pi bond from the triple bond. Draw this resonance structure (hint: more than one atom will have a charge). Is the resonance effect stronger or weaker than the inductive effect?

2. The five bases below are ranked from strongest (left) to weakest (right).

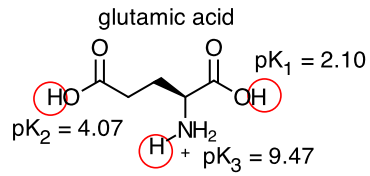


a. Explain the ranking. Do you expect the strongest base to have a localized lone pair or not?
b. Which base has the strongest conjugate acid? Draw the structure of this conjugate acid.

A titration curve is a graph of pH vs. volume. It gives us information about:

- the relative concentrations of acid and conjugate base at different pH's.
- The charge at different pH's.
- The pH at which a buffer can be made.

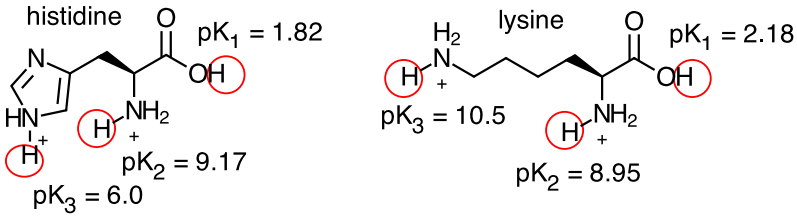
For the buffer region: Henderson-Hasselbach equation, $pH = pK_a + \log [base]/[acid]$
At half-way point $pH = pK_a$ because [base] = [acid].
For a polyprotic acid, such as an amino acid or protein, use $pH = 0.5(pK_{ai} + pK_{a(i+1)})$.
The isoelectric point (pI) is the pH at which an amino acid or protein has a neutral charge (charge = 0).
3. Glutamic acid is used to make the food flavor enhancer, MSG (monosodium glutamate).



a. (i) Draw a titration curve of glutamic acid if titrated with 0.1 M NaOH. Calculate the pH at each half-way point and the first and second end points. (Answer: at 1st end point, $pH = 0.5(pK_1 + pK_2) = 0.5(2.10 + 4.07) = 3.08$)

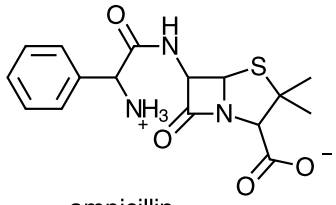
(ii) Show the charge of the amino acid at each half-way point and each end point. (Answer: at 1st half-way point, pH = 2.10 and charge is 50% +1 charge and 50% 0 charge; at 2nd end point, pH = 0.5(pK_2 + pK_3) = 0.5(4.07 + 9.47) = 6.77 and charge is -1.)
b. MSG: What is the charge on the glutamate ion? At what pH is glutamic acid in the form of glutamate so you can make MSG? Give reasons.
c. What is the isoelectric point of glutamic acid?

4. You are given a 0.1 M mixture of two amino acids, histidine and lysine, and want to separate the amino acids by electrophoresis. The Lewis structures of each amino acid, the acidic protons, and pKa's are shown.



a. (i) Draw a titration curve of each amino acid if titrated with 0.1 M NaOH. Calculate the pH at each half-way point and the first and second end points.
(ii) Show the charge of each amino acid at each half-way point and each end point.
b. What is the isoelectric point of histidine? Lysine?
c. What pH would you use in an electrophoresis experiment to separate these two amino acids? Give reasons. (Hint: Choose a pH at which the charge of one amino acid is different than the other amino acid.)
d. Identify the amino acid and salt (conjugate base) combination you would use to make a pH 5 buffer. Describe how you would make this buffer.

5. Ampicillin is a beta-lactam (a beta-lactam is an amide group in a four sided ring) antibiotic. The structure of ampicillin at physiological pH is shown below.



ampicillin

a. Ampicillin is a diprotic acid. The structure above shows one acidic proton and the conjugate base of the other acidic proton. Circle the acidic proton and the conjugate base of the other acidic proton.
b. Which acidic proton has a pK_a below 7? Give reasons.
c. Beta-lactam antibiotics are typically effective at treating bacterial meningitis infections but may have some problems crossing the blood brain barrier, which allows small, lipophilic molecules to cross. Explain why ampicillin has trouble crossing the blood brain barrier.