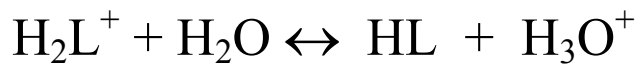
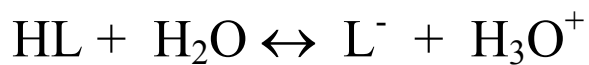
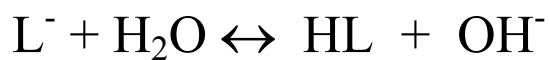
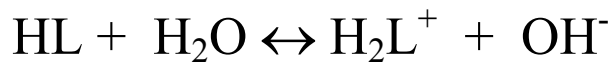


## Chapter 9 (Polyprotic Acids and Bases)

### Chapter 9

### Diprotic Acids

 $K_{a1}$  $K_{a2}$  $K_{b1}$  $K_{b2}$ 

$$K_w = K_{a1} K_{b2}$$

$$K_w = K_{a2} K_{b1}$$

Zwitter ion (amino acids)

Example 1 – (diprotic system, where neutral species is the most acidic form)

Calculate the pH of 0.010 M malonic acid,  $\text{H}_2\text{M}$ , solution.

$$K_{a1} = 1.42 \cdot 10^{-3}$$

$$K_{a2} = 2.01 \cdot 10^{-6}$$



$$K_{a1} = [\text{HM}^-] [\text{H}_3\text{O}^+] / [\text{H}_2\text{M}] \approx x^2 / F_{\text{H}_2\text{M}} \rightarrow x = 3.76 \cdot 10^{-3} \text{ M, approx. 2 invalid!)$$

$$\text{Succ. Approx.} \rightarrow x = 0.006182 \text{ M, pH} = 2.21$$

This assumes that the second equilibrium is unimportant!! Is it?

Succ. Approx.  $\rightarrow x = 0.006182 \text{ M}$ ,  $\text{pH} = 2.21$

This assumes that the second equilibrium is unimportant!! Is it?

$$K_{a2} = [\text{M}^{2-}][\text{H}_3\text{O}^+]/[\text{HM}^-]$$

$$[\text{M}^{2-}] = K_{a2} [\text{HM}^-]/[\text{H}_3\text{O}^+] = (2.01 \cdot 10^{-6})(0.006182)/(0.006182) = 2.01 \cdot 10^{-6} \text{ M}$$

$$\alpha_2 = [\text{M}^{2-}]/[\text{HM}^-] = 2.01 \cdot 10^{-6} / 0.006182 = 0.000325$$

or  $\approx 0.03 \%$

It is unimportant!!!!

Example 2 (diprotic system, where neutral species is the most basic form)

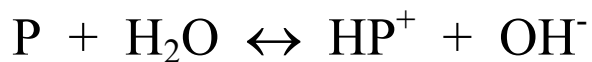
Calculate the pH of a 0.10 M piperazine (P) solution

$$K_{a1} = 4.65 \cdot 10^{-6}$$

$$K_{a2} = 1.86 \cdot 10^{-10}$$

$$K_{b1} = K_w / K_{a2} = 5.43 \cdot 10^{-5}$$

$$K_{b2} = K_w / K_{a1} = 2.79 \cdot 10^{-9}$$



$$K_{b1} = [HP^+][OH^-] / [P] \approx x^2 / F_P \rightarrow x = [OH^-] = 2.33 \cdot 10^{-3} \text{ M approx. 2 is valid!)$$

$$[H_3O^+] = 4.334 \cdot 10^{-12} \text{ M, pH} = 11.36$$

This assumes that the second equilibrium is unimportant!! Is it?

$$[\text{H}_3\text{O}^+] = 4.334 \cdot 10^{-12} \text{ M}, \text{pH} = 11.36$$

This assumes that the second equilibrium is unimportant!! Is it?

$$K_{b2} = [\text{H}_2\text{P}^{2+}][\text{OH}^-]/[\text{HP}^+]$$

$$[\text{H}_2\text{P}^{2+}] = K_{b2} [\text{HP}^+]/[\text{OH}^-] = (2.79 \cdot 10^{-9})(2.33 \cdot 10^{-3}) / (2.33 \cdot 10^{-3}) = 2.79 \cdot 10^{-9} \text{ M}$$

$$\alpha_2 = [\text{M}^{2-}]/[\text{HM}^-] = 2.79 \cdot 10^{-9} / 2.33 \cdot 10^{-3} \approx 1 \cdot 10^{-6}$$

The second equilibrium has a negligible effect on the pH!!!!

This is almost always the case!!!!!!..... Unless  $K_{a1}$  and  $K_{a2}$  are very close, and even then the pH will not be off by much.

For instance,

Calculate the pH of a 0.010 M  $\text{H}_2\text{A}$ , where  $K_{a1}$  and  $K_{a2}$  are  $1.00 \cdot 10^{-4}$  and  $3.00 \cdot 10^{-4}$ , respectively.

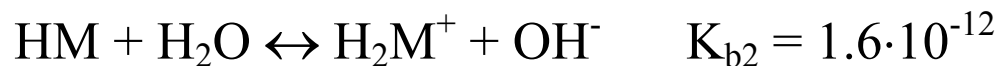
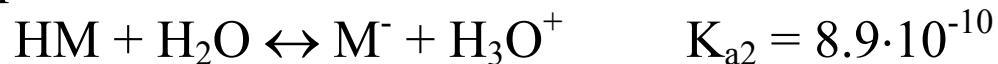
Ignoring the second equilibrium,  $\rightarrow \text{pH} = 3.02$

Solving strictly (we will learn how to do this when we cover chapter 9)  $\rightarrow \text{pH} = 2.93$

Example 3 (diprotic system, where neutral species is the intermediate form)

Calculate the pH of a 0.050 M solution of Methionine (HM).

Methionine is an amino acid. Its neutral form is the intermediate species, HM, of a diprotic system ( $K_{a1} = 6.3 \cdot 10^{-3}$  and  $K_{a2} = 8.9 \cdot 10^{-10}$ ). Two different equilibria are possible with HM in water.



Both will occur, and in fact based on LeChatlier's principle they will drive one another, since  $\text{H}_3\text{O}^+$  reacts rapidly with  $\text{OH}^-$ . How can we deal with this?

Charge balance:

$$[\text{OH}^-] + [\text{M}^-] = [\text{H}_3\text{O}^+] + [\text{H}_2\text{M}^+]$$

make substitutions from  $K_{a2}$  and  $K_{b2}$  expressions!!!

$$K_{a2} = [\text{M}^-] [\text{H}_3\text{O}^+] / [\text{HM}] \rightarrow [\text{M}^-] = K_{a2} [\text{HM}] / [\text{H}_3\text{O}^+]$$

$$K_{b2} = [\text{H}_2\text{M}^+] [\text{OH}^-] / [\text{HM}] \rightarrow [\text{H}_2\text{M}^+] = K_{b2} [\text{HM}] / [\text{OH}^-]$$

$$[\text{OH}^-] = K_w / [\text{H}_3\text{O}^+]$$

$$[\text{OH}^-] + K_{a2} [\text{HM}] / [\text{H}_3\text{O}^+] = [\text{H}_3\text{O}^+] + K_{b2} [\text{HM}] / [\text{OH}^-]$$

$$K_w / [\text{H}_3\text{O}^+] + K_{a2} [\text{HM}] / [\text{H}_3\text{O}^+] = [\text{H}_3\text{O}^+] + K_{b2} [\text{HM}] [\text{H}_3\text{O}^+] / K_w$$

$$K_w + K_{a2} [\text{HM}] = [\text{H}_3\text{O}^+]^2 + K_{b2} [\text{HM}] [\text{H}_3\text{O}^+]^2 / K_w$$

$$(K_w + K_{a2} [\text{HM}]) = [\text{H}_3\text{O}^+]^2 (1 + K_{b2} [\text{HM}] / K_w)$$

$$(K_w + K_{a2} [\text{HM}]) / (1 + K_{b2} [\text{HM}] / K_w) = [\text{H}_3\text{O}^+]^2$$

$$[\text{H}_3\text{O}^+] = [(K_w + K_{a2} [\text{HM}]) / (1 + K_{b2} [\text{HM}] / K_w)]^{1/2}$$

$$[\text{H}_3\text{O}^+] = [(\text{K}_w + \text{K}_{a2} [\text{HM}]) / (1 + \text{K}_{b2} [\text{HM}] / \text{K}_w)]^{1/2}$$

simplify

$$[\text{H}_3\text{O}^+] = [(\text{K}_w + \text{K}_{a2} [\text{HM}]) / (1 + [\text{HM}] / \text{K}_{a1})]^{1/2}$$

$$[\text{H}_3\text{O}^+] = [\text{K}_{a1}(\text{K}_w + \text{K}_{a2} [\text{HM}]) / (\text{K}_{a1} + [\text{HM}])]^{1/2}$$

$$[\text{H}_3\text{O}^+] = [\text{K}_{a1}\text{K}_w + \text{K}_{a1}\text{K}_{a2} [\text{HM}]] / (\text{K}_{a1} + [\text{HM}])^{1/2}$$

---

Now,  $\text{K}_{a2}$  and  $\text{K}_{b2}$  are small, so you can make the following approximation.

$F_{\text{HM}} \approx [\text{HM}]$ , and therefore,

$$[\text{H}_3\text{O}^+] = [\text{K}_{a1}\text{K}_w + \text{K}_{a1}\text{K}_{a2} F_{\text{HM}} / (\text{K}_{a1} + F_{\text{HM}})]^{1/2}$$

So,  $[\text{H}_3\text{O}^+] =$

$$[(6.3 \cdot 10^{-3})(1.01 \cdot 10^{-14}) + (6.3 \cdot 10^{-3})(8.9 \cdot 10^{-10})(.050)] / (6.3 \cdot 10^{-3} + .050)^{1/2}$$

$$2.23 \cdot 10^{-6} \text{ M}$$

$$\text{pH} = 5.65$$

Is the approximation a good one?

$$K_{b2} = [\text{H}_2\text{M}^+] [\text{OH}^-] / [\text{HM}] \rightarrow$$

$$[\text{H}_2\text{M}^+] = K_{b2} [\text{HM}] / [\text{OH}^-] =$$

$$(1.6 \cdot 10^{-12})(0.050) / (4.53 \cdot 10^{-9}) = 1.8 \cdot 10^{-5} \text{ M}$$

$$K_{a2} = [\text{M}^-] [\text{H}_3\text{O}^+] / [\text{HM}] \rightarrow$$

$$[\text{M}^-] = K_{a2} [\text{HM}] / [\text{H}_3\text{O}^+] =$$

$$(8.9 \cdot 10^{-10})(0.050) / (2.23 \cdot 10^{-6}) = 2.0 \cdot 10^{-5} \text{ M}$$

Approximation was valid!! Note that  $[\text{H}_2\text{M}^+] \approx [\text{M}^-]$ . This is the case even though  $K_{a2}$  is greater than  $K_{b2}$  by almost three orders of magnitude!!!

## Polyprotic systems

$\text{H}_3\text{PO}_4$	weak acid equilibrium; using $K_{a1}$ $K_{a1} = x^2/F$ , where $x = [\text{H}_3\text{O}^+]$
$\text{NaH}_2\text{PO}_4$	intermediate; using $K_{a1}$ and $K_{a2}$ $\text{pH} \approx (\text{p}K_{a1} + \text{p}K_{a2})/2$
$\text{Na}_2\text{HPO}_4$	intermediate; using $K_{a2}$ and $K_{a3}$ $\text{pH} \approx (\text{p}K_{a2} + \text{p}K_{a3})/2$
$\text{K}_3\text{PO}_4$	weak base equilibrium; using $K_{b1}$ $K_{b1} = x^2/F$ , where $x = [\text{OH}^-]$

Remember  $K_{b1} = K_w/K_{a3}$

## Polyprotic buffers

A pH 7 phosphate buffer contains approximately equal amounts of



$$K_{a1} = 7.11 \cdot 10^{-3}, \text{p}K_{a1} = 2.148$$



$$K_{a2} = 6.34 \cdot 10^{-8}, \text{p}K_{a2} = 7.198$$



$$K_{a3} = 4.22 \cdot 10^{-13}, \text{p}K_{a3} = 12.375$$



### Problem 9-13

How many grams of  $\text{Na}_2\text{CO}_3$  (FM 105.99) should be mixed with 5.00 g  $\text{NaHCO}_3$  (FM 84.01) to produce 100 mL of a buffer with a pH of 10.00.

Carbonic acid system:



$$\text{pK}_{\text{a}1} = 6.351$$



$$\text{pK}_{\text{a}1} = 10.329$$



$$10.00 =$$

$$10.329 + \log \left\{ \frac{\text{mass Na}_2\text{CO}_3 / 105.99}{5.00 / 84.01} \right\}$$

Solve for mass  $\text{Na}_2\text{CO}_3$

$$\text{mass Na}_2\text{CO}_3 = 2.96 \text{ g}$$

Which is the Principle Species?

Histidine ( $\text{H}_3\text{His}^{2+}$ ,  $\text{H}_2\text{His}^+$ ,  $\text{HHis}$ ,  $\text{His}^-$ )

$$\text{pK}_{\text{a}1} = 1.7$$

$$\text{pK}_{\text{a}2} = 6.02$$

$$\text{pK}_{\text{a}3} = 9.08$$

pH	Principle species
1	
2	
3	
4	
5	
6	
7	
8	
9	
10	
11	
12	
13	
14	

answer

pH	Principle species
1	$\text{H}_3\text{His}^{2+}$
2	$\text{H}_2\text{His}^+$
3	$\text{H}_2\text{His}^+$
4	$\text{H}_2\text{His}^+$
5	$\text{H}_2\text{His}^+$
6	$\text{H}_2\text{His}^+$ , $\text{HHis}$
7	$\text{HHis}$
8	$\text{HHis}$
9	$\text{HHis}$ , $\text{His}^-$
10	$\text{His}^-$
11	$\text{His}$
12	$\text{His}$
13	$\text{His}$
14	$\text{His}$

## Alpha Fractions

### Monoprotic systems (HA or B)

#### Monoprotic acid

$$\alpha_{\text{HA}} = [\text{HA}] / F_{\text{HA}}, \text{ where } F_{\text{HA}} = [\text{HA}] + [\text{A}^-], \text{ or} \\ [\text{HA}] / ([\text{HA}] + [\text{A}^-])$$

$$\alpha_{\text{A}^-} = [\text{A}^-] / F_{\text{HA}}, \text{ where } F_{\text{HA}} = [\text{HA}] + [\text{A}^-], \text{ or} \\ [\text{A}^-] / ([\text{HA}] + [\text{A}^-])$$

#### Monoprotic base

$$\alpha_{\text{B}} = [\text{B}] / F_{\text{B}}, \text{ where } F_{\text{B}} = [\text{B}] + [\text{HB}^+], \text{ or} \\ [\text{B}] / ([\text{B}] + [\text{HB}^+])$$

$$\alpha_{\text{HB}^+} = [\text{HB}^+] / F_{\text{B}}, \text{ where } F_{\text{B}} = [\text{B}] + [\text{HB}^+], \text{ or} \\ [\text{HB}^+] / ([\text{B}] + [\text{HB}^+])$$

Monoprotic acid

$$K_a = [\text{H}_3\text{O}^+][\text{A}^-]/[\text{HA}] = [\text{H}_3\text{O}^+](F_{\text{HA}} - [\text{HA}])/[\text{HA}]$$

A little algebra

$$[\text{HA}] K_a + [\text{H}_3\text{O}^+][\text{HA}] = [\text{H}_3\text{O}^+]F_{\text{HA}}$$

$$[\text{HA}] (K_a + [\text{H}_3\text{O}^+]) = [\text{H}_3\text{O}^+]F_{\text{HA}}$$

$$[\text{HA}] / F_{\text{HA}} = [\text{H}_3\text{O}^+] / (K_a + [\text{H}_3\text{O}^+])$$

$$\alpha_{\text{HA}} = [\text{HA}]/F_{\text{HA}} = [\text{H}_3\text{O}^+] / (K_a + [\text{H}_3\text{O}^+])$$

similarly, you can derive

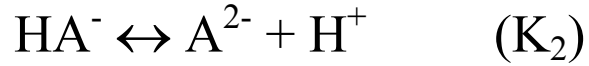
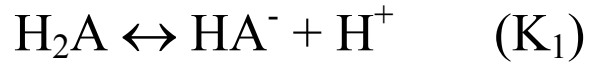
$$\alpha_{A^-} = [A^-]/F_{HA} = K_a / (K_a + [H_3O^+])$$

or for a monoprotic base,

$$\alpha_B = [B]/F_B = K_a / (K_a + [H_3O^+])$$

$$\alpha_{HB^+} = [HB^+]/F_B = [H_3O^+] / (K_a + [H_3O^+])$$

## alpha fractions for a Diprotic System



$$\text{K}_1 = \frac{[\text{H}^+][\text{HA}^-]}{[\text{H}_2\text{A}]} \rightarrow [\text{HA}^-] = [\text{H}_2\text{A}] \left\{ \frac{\text{K}_1}{[\text{H}^+]} \right\} \quad (1)$$

$$\text{K}_2 = \frac{[\text{H}^+][\text{A}^{2-}]}{[\text{HA}^-]} \rightarrow [\text{A}^{2-}] = [\text{HA}^-] \left\{ \frac{\text{K}_2}{[\text{H}^+]} \right\} \quad (2)$$

Mass balance equation

$$F = [\text{H}_2\text{A}] + [\text{HA}^-] + [\text{A}^{2-}]$$

Mass balance equation

$$F = [\text{H}_2\text{A}] + [\text{HA}^-] + [\text{A}^{2-}]$$

First solve for the  $\alpha_{\text{H}_2\text{A}}$ . To do these we need to write expression that puts the three other species in terms of  $\text{H}_2\text{A}$ .

We already have eq 1

$$[\text{HA}^-] = [\text{H}_2\text{A}]\text{K}_1/[\text{H}^+]$$

Now substitute this into eq 2 to get

$$[\text{A}^{2-}] = [\text{H}_2\text{A}]\text{K}_1\text{K}_2/[\text{H}^+]^2$$

Substitute these three new equations into the mass balance equation

$$F = [\text{H}_2\text{A}] + [\text{H}_2\text{A}]\text{K}_1/[\text{H}^+] + [\text{H}_2\text{A}]\text{K}_1\text{K}_2/[\text{H}^+]^2$$

$$F = [\text{H}_2\text{A}] (1 + \text{K}_1/[\text{H}^+] + \text{K}_1\text{K}_2/[\text{H}^+]^2)$$

$$F/[\text{H}_3\text{A}] = 1 + \text{K}_1/[\text{H}^+] + \text{K}_1\text{K}_2/[\text{H}^+]^2$$

Get a common denominator

$$F/[\text{H}_3\text{A}] = ([\text{H}^+]^2 + [\text{H}^+]\text{K}_1 + \text{K}_1\text{K}_2) / [\text{H}^+]^2$$

Flip the numerator and denominator on both sides

$$\alpha_{\text{H}_2\text{A}} = [\text{H}_2\text{A}]/F = [\text{H}^+]^2/([\text{H}^+]^2 + [\text{H}^+]\text{K}_1 + \text{K}_1\text{K}_2)$$

Next I will solve for  $\alpha_{\text{HA}^-}$ . To do these we need to write expression that put the three other species in terms of  $\text{HA}^-$ .

rearranging eq 1 we get

$$[\text{H}_2\text{A}] = [\text{HA}^-][\text{H}^+]/K_1$$

eq 2 gives us the expression for  $\text{A}^{2-}$

$$[\text{A}^{2-}] = [\text{HA}^-]K_2/[\text{H}^+]$$

Substitute these into the mass balance equation

$$F = [\text{HA}^-][\text{H}^+]/K_1 + [\text{HA}^-] + [\text{HA}^-]K_2/[\text{H}^+]$$

$$F = [\text{HA}^-] ([\text{H}^+]/K_1 + 1 + K_2/[\text{H}^+])$$

$$F/[\text{HA}^-] = [\text{H}^+]/K_1 + 1 + K_2/[\text{H}^+]$$

Get a common denominator

$$F/[\text{HA}^-] = ([\text{H}^+]^2 + [\text{H}^+]K_1 + K_1K_2) / K_1[\text{H}^+]$$

Flip the numerator and denominator on both sides

$$\alpha_{\text{HA}^-} = [\text{HA}^-]/F = (K_1[\text{H}^+]) / ([\text{H}^+]^2 + [\text{H}^+]K_1 + K_1K_2 + K_1K_2)$$

Next I will solve for  $\alpha_{A^{2-}}$ . To do these we need to write expression that put the three other species in terms of  $A^{2-}$ .

Eq 2 gives us an expression for  $A^{2-}$

$$[HA^-] = [A^{2-}][H^+]/K_2$$

Rearrange eq 1 to get

$$[H_2A] = [HA^-][H^+]/K_1$$

Rearrange eq 1 and substitute

$$[H_2A] = [A^{2-}][H^+]^2/K_1K_2$$

$$F = [A^{2-}][H^+]^2/K_1K_2 + [A^{2-}][H^+]/K_2 + [A^{2-}]$$

$$F = [A^{2-}] ([H^+]^2/K_1K_2 + [H^+]/K_2 + 1)$$

$$F/[A^{2-}] = [H^+]^2/K_1K_2 + [H^+]/K_2 + 1$$

Get a common denominator

$$F/[A^{2-}] = ([H^+]^2 + [H^+]K_1 + K_1K_2) / K_1K_2$$

Flip the numerator and denominator on both sides

$$\alpha_{A^{2-}} = [A^{2-}]/F = (K_1K_2) / ([H^+]^2 + [H^+]K_1 + K_1K_2)$$

## Isoelectric point and electrophoresis

Isoelectric point =  $\text{pH} = (\text{p}K_{a1} + \text{p}K_{a2})$

isoionic pt;  $[\text{H}_3\text{O}^+] = [\text{K}_{a1}\text{K}_w + \text{K}_{a1}\text{K}_{a2} F_{\text{HM}} / (\text{K}_{a1} + F_{\text{HM}})]^{1/2}$

## Separation of peptides

Ions move in response to an electric field. If we place our peptide mixture in a capillary column and then create a pH gradient across the capillary, the peptides will migrate until they reach a pH where the average charge on the peptide is zero (the isoelectric point)