

- **At low pH,**
→ both the ammonium group and the carboxyl group are **protonated**.



- **At high pH,**
→ **neither is protonated.**

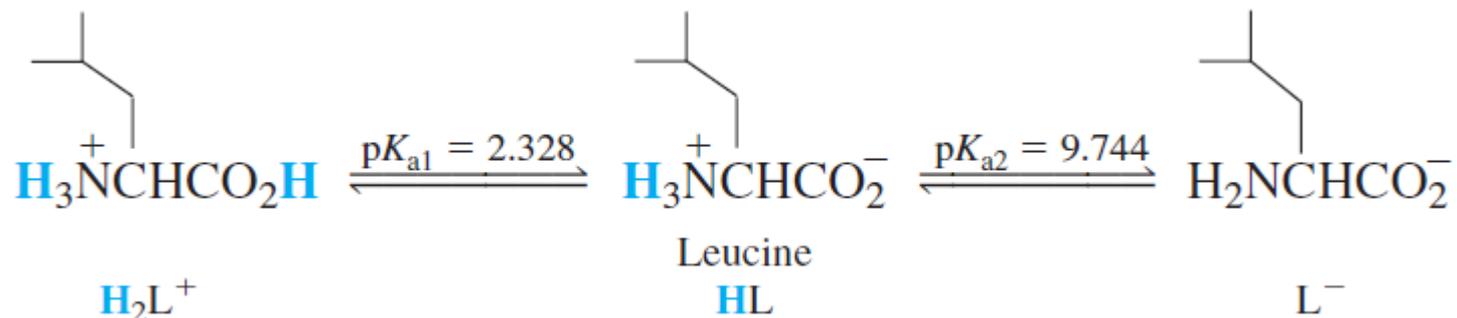


- Acid dissociation constants of amino acids are listed in Table 10-1
→ where each compound is drawn in its fully protonated form.

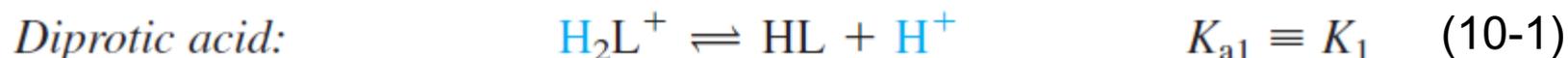
See Table 10-1

- Zwitterions are stabilized in solution
 - by interactions of $-\text{NH}_3^+$ and $-\text{CO}_2^-$ with water.
- In the **solid state**,
 - The zwitterion is also the stable form of the amino acid
 - where hydrogen bonding from $-\text{NH}_3^+$ to $-\text{CO}_2^-$ of neighboring molecules occurs.
- In the **gas phase**,
 - there are no neighbors to stabilize the charges,
 - so the nonionized structure with intramolecular hydrogen bonding from $-\text{NH}_2$ to a carboxyl oxygen, predominates.

- Our discussion will focus on the **amino acid leucine**, designated HL.



- The equilibrium constants refer to the following reactions:



→ We customarily omit the subscript "a" in $K_{\text{a}1}$ and $K_{\text{a}2}$.

→ We will always write the subscript "b" in $K_{\text{b}1}$ and $K_{\text{b}2}$.

- Recall that the relations between the acid and base equilibrium constants are

*Relations between
 K_a and K_b :*

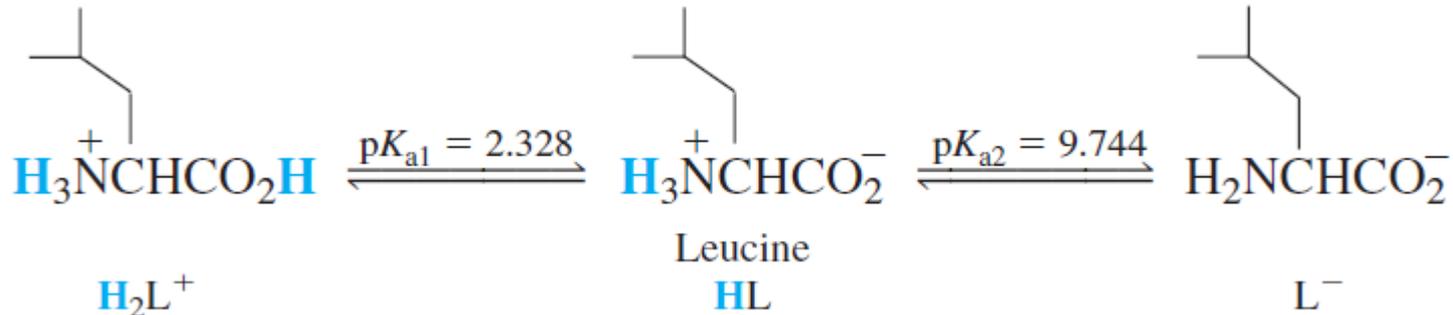
$$K_{a1} \cdot K_{b2} = K_w$$

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

- Calculate the pH and composition of individual solutions of
 - i) 0.050 0 M H_2L^+ ,
 - ii) 0.050 0 M HL,
 - iii) and 0.050 0 M L^- .

The acidic form, H₂L⁺

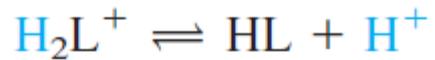
- Leucine hydrochloride contains the protonated species, H₂L⁺,
→ which can **dissociate twice** (Reactions 10-1 and 10-2).



Diprotic acid:



- H₂L⁺ is a weak acid.
→ Because $K_1 = 4.70 \times 10^{-3}$
- HL is an even weaker acid,
→ because $K_2 = 1.80 \times 10^{-10}$.



$$K_{a1} \equiv K_1 = 4.70 \times 10^{-3}$$

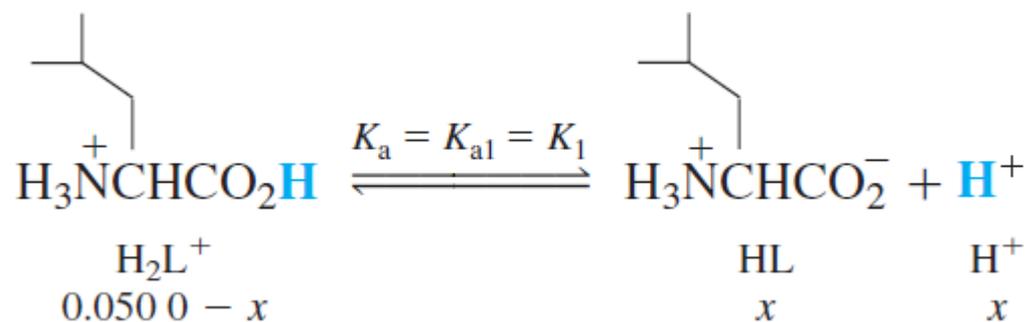


$$K_{a2} \equiv K_2 = 1.80 \times 10^{-10}$$

- The H_2L^+ will dissociate only partly,
- The resulting HL will hardly dissociate at all.

- For this reason,
 - we make the approximation that a solution of H_2L^+ **behaves as a monoprotic acid**, with $K_a = K_1$.

- With this approximation,
 - finding the pH of 0.050 0 M H_2L^+ is easy.



$$K_a = K_1 = 4.70 \times 10^{-3}$$

$$\frac{x^2}{F - x} = K_a \Rightarrow x = 1.32 \times 10^{-2} \text{ M}$$

$$[\text{HL}] = x = 1.32 \times 10^{-2} \text{ M}$$

$$[\text{H}^+] = x = 1.32 \times 10^{-2} \text{ M} \Rightarrow \text{pH} = 1.88$$

$$[\text{H}_2\text{L}^+] = F - x = 3.68 \times 10^{-2} \text{ M}$$

- What is **the concentration of L⁻** in the solution?
 - We have already assumed that it is very small,
 - but it cannot be 0.
- We can calculate [L⁻] from the K₂ equation,
 - with the concentrations of HL⁻ and H⁺ that we just computed.

$$K_2 = \frac{[\text{H}^+][\text{L}^-]}{[\text{HL}]} \Rightarrow [\text{L}^-] = \frac{K_2[\text{HL}]}{[\text{H}^+]}$$

$$[\text{L}^-] = \frac{(1.80 \times 10^{-10})(1.32 \times 10^{-2})}{(1.32 \times 10^{-2})} = 1.80 \times 10^{-10} \text{ M } (= K_2)$$

- Our approximation is confirmed by this last result.

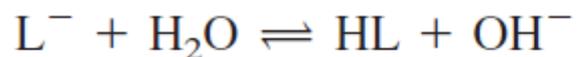
- The concentration of L^- is about eight orders of magnitude smaller than that of HL.
 - The dissociation of HL is indeed negligible relative to the dissociation of H_2L^+ .

- For most diprotic acids,
 - K_1 is sufficiently larger than K_2
 - this approximation is valid.

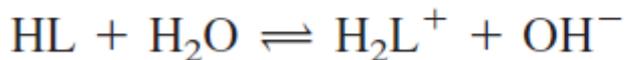
- **In summary,**
 - a solution of a diprotic acid behaves like a solution of a monoprotic acid, with $K_a = K_1$.

The basic form, L⁻

- The species L⁻,
 - found in a salt such as sodium leucinate,
 - can be prepared by treating leucine (HL) with an equimolar quantity of NaOH.
- Dissolving sodium leucinate in water gives a solution of L⁻, the fully basic species.
- K_b values for this dibasic anion are



$$K_{b1} = K_w/K_{a2} = 5.55 \times 10^{-5}$$



$$K_{b2} = K_w/K_{a1} = 2.13 \times 10^{-12}$$



- K_{b1} tells us that
 - L^- will not hydrolyze (react with water) very much to give HL.
- Furthermore, K_{b2} tells us that
 - the resulting HL is such a weak base that hardly any further reaction to make H_2L^+ will occur.
- We therefore **treat L^- as a monobasic species**, with $K_b = K_{b1}$.
 - This approximation simplify the calculations:

- The concentration of H_2L^+ can be found from the K_{b2} (or K_{a1}) equilibrium.

$$K_{b2} = \frac{[\text{H}_2\text{L}^+][\text{OH}^-]}{[\text{HL}]} = \frac{[\text{H}_2\text{L}^+]x}{x} = [\text{H}_2\text{L}^+]$$

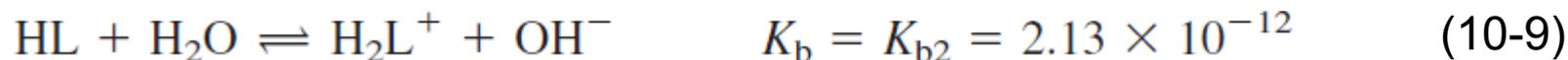
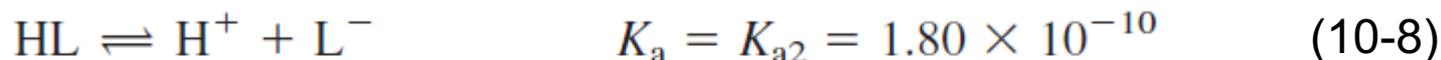
- We find that $[\text{H}_2\text{L}^+] = K_{b2} = 2.13 \times 10^{-12} \text{ M}$
 - The approximation that $[\text{H}_2\text{L}^+]$ is insignificant relative to $[\text{HL}]$ is well justified.

In summary,

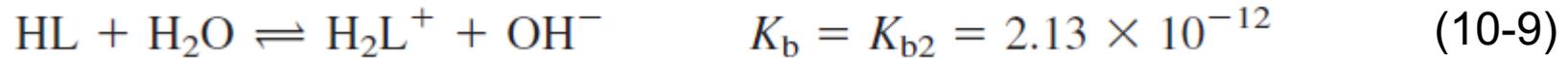
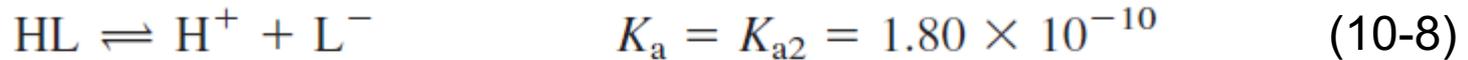
- if there is any reasonable separation between K_{a1} and K_{a2} (and, therefore, between K_{b1} and K_{b2}),
 - the fully basic form of a diprotic acid can be treated as monobasic, with $K_b = K_{b1}$.

The intermediate form, HL

- A solution prepared from leucine, HL, is more **complicated** than one prepared from either H_2L^+ or L^- ,
→ because HL is **both an acid and a base**.

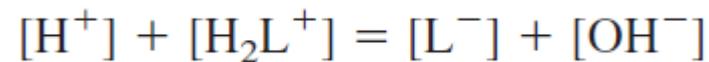


- A molecule that can both donate and accept a proton
→ is said to be **amphiprotic**.
- The acid dissociation reaction (10-8) has **a larger equilibrium constant** than the base hydrolysis reaction (10-9),
→ so we expect that a solution of **leucine will be acidic**.



- However, we **cannot simply ignore Reaction 10-9**,
→ even if K_a and K_b differ by several orders of magnitude.
- **Both reactions proceed to nearly equal extent**,
→ because H^+ produced in Reaction 10-8 **reacts with OH^-** from Reaction 10-9,
→ thereby driving Reaction 10-9 to the right.
- To treat this case,
→ we resort to the **systematic treatment of equilibrium**.

- For Reactions 10-8 and 10-9, the **charge balance** is



$$[\text{H}_2\text{L}^+] - [\text{L}^-] + [\text{H}^+] - [\text{OH}^-] = 0$$

- From the **acid dissociation equilibria**,
 - we replace $[\text{H}_2\text{L}^+]$ with $[\text{HL}][\text{H}^+]/K_1$, and $[\text{L}^-]$ with $[\text{HL}]K_2/[\text{H}^+]$.
 - Also, we can always write $[\text{OH}^-] = K_w/[\text{H}^+]$.
- Putting these expressions into the charge balance gives

$$\frac{[\text{HL}][\text{H}^+]}{K_1} - \frac{[\text{HL}]K_2}{[\text{H}^+]} + [\text{H}^+] - \frac{K_w}{[\text{H}^+]} = 0$$

$$\frac{[\text{HL}][\text{H}^+]}{K_1} - \frac{[\text{HL}]K_2}{[\text{H}^+]} + [\text{H}^+] - \frac{K_w}{[\text{H}^+]} = 0$$

- First, multiply all terms by $[\text{H}^+]$:

$$\frac{[\text{HL}][\text{H}^+]^2}{K_1} - [\text{HL}]K_2 + [\text{H}^+]^2 - K_w = 0$$

- Then rearrange and factor out $[\text{H}^+]^2$:

$$[\text{H}^+]^2 \left(\frac{[\text{HL}]}{K_1} + 1 \right) = K_2[\text{HL}] + K_w$$
$$[\text{H}^+]^2 = \frac{K_2[\text{HL}] + K_w}{\frac{[\text{HL}]}{K_1} + 1}$$

- Now multiply the numerator and denominator by K_1 and take the square root:

$$[\text{H}^+] = \sqrt{\frac{K_1 K_2 [\text{HL}] + K_1 K_w}{K_1 + [\text{HL}]}} \quad (10-10)$$

- Up to this point, we have made **no approximations**, except to neglect activity coefficients.
- We solved for $[\text{H}^+]$ in terms of **known constants** plus the **single unknown**, $[\text{HL}]$.
- Where do we proceed from here?
 - The **major species is HL**, because it is both a **weak acid and a weak base**.
 - Neither Reaction 10-8 nor Reaction 10-9 goes very far.
- **For $[\text{HL}]$** in Equation 10-10,
 - you can **simply substitute the formal concentration**, 0.050 0 M.

- We write Equation 10-10 in its most useful form.

$$[\text{H}^+] = \sqrt{\frac{K_1 K_2 [\text{HL}] + K_1 K_w}{K_1 + [\text{HL}]}}$$

Intermediate form of diprotic acid: $[\text{H}^+] \approx \sqrt{\frac{K_1 K_2 F + K_1 K_w}{K_1 + F}}$ (10-11)

- where F is the formal concentration of HL
 → 0.050 0 M in the present case.
- At long last, we can calculate the pH of 0.050 0 M leucine:

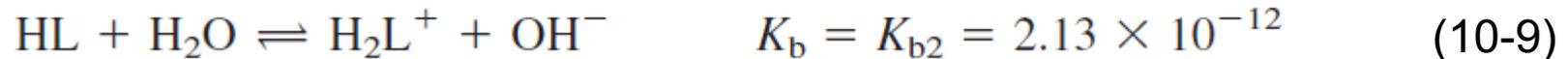
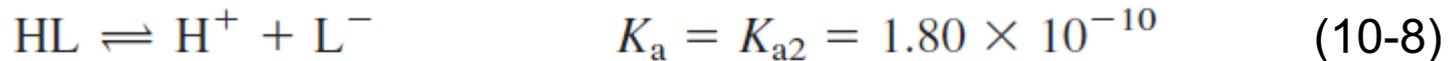
$$\begin{aligned} [\text{H}^+] &= \sqrt{\frac{(4.70 \times 10^{-3})(1.80 \times 10^{-10})(0.0500) + (4.70 \times 10^{-3})(1.0 \times 10^{-14})}{4.70 \times 10^{-3} + 0.0500}} \\ &= 8.80 \times 10^{-7} \text{ M} \Rightarrow \text{pH} = 6.06 \end{aligned}$$

- The concentrations of H_2L^+ and L^-
 - can be found from the K_1 and K_2 equilibria,
 - using $[\text{H}^+] = 8.80 \times 10^{-7} \text{ M}$ and $[\text{HL}] = 0.0500 \text{ M}$.

$$[\text{H}_2\text{L}^+] = \frac{[\text{H}^+][\text{HL}]}{K_1} = \frac{(8.80 \times 10^{-7})(0.0500)}{4.70 \times 10^{-3}} = 9.36 \times 10^{-6} \text{ M}$$

$$[\text{L}^-] = \frac{K_2[\text{HL}]}{[\text{H}^+]} = \frac{(1.80 \times 10^{-10})(0.0500)}{8.80 \times 10^{-7}} = 1.02 \times 10^{-5} \text{ M}$$

- Was the approximation $[\text{HL}] \approx 0.0500 \text{ M}$ a good one?
 - It certainly was, because $[\text{H}_2\text{L}^+]$ ($9.36 \times 10^{-6} \text{ M}$) and $[\text{L}^-]$ ($1.02 \times 10^{-5} \text{ M}$) are small in comparison with $[\text{HL}]$ ($\approx 0.0500 \text{ M}$).
 - Nearly all the leucine remained in the form HL.



$$[\text{H}_2\text{L}^+] = \frac{[\text{H}^+][\text{HL}]}{K_1} = \frac{(8.80 \times 10^{-7})(0.0500)}{4.70 \times 10^{-3}} = 9.36 \times 10^{-6} \text{ M}$$

$$[\text{L}^-] = \frac{K_2[\text{HL}]}{[\text{H}^+]} = \frac{(1.80 \times 10^{-10})(0.0500)}{8.80 \times 10^{-7}} = 1.02 \times 10^{-5} \text{ M}$$

- Note also that $[\text{H}_2\text{L}^+]$ is nearly equal to $[\text{L}^-]$.
- This result confirms that Reactions 10-8 and 10-9 **proceed equally**,
→ even though K_a is 84 times bigger than K_b for leucine.

- A summary of results for leucine is given here.

Solution	pH	$[H^+]$ (M)	$[H_2L^+]$ (M)	$[HL]$ (M)	$[L^-]$ (M)
0.050 0 M H_2A	1.88	1.32×10^{-2}	3.68×10^{-2}	1.32×10^{-2}	1.80×10^{-10}
0.050 0 M HA^-	6.06	8.80×10^{-7}	9.36×10^{-6}	5.00×10^{-2}	1.02×10^{-5}
0.050 0 M HA^{2-}	11.21	6.11×10^{-12}	2.13×10^{-12}	1.64×10^{-3}	4.84×10^{-2}

Simplified Calculation for the Intermediate Form

- Usually Equation 10-11 is a fair-to-excellent approximation.
- An **even simpler form** results from **two conditions** that usually exist.
- First, if $K_2F \gg K_w$
→ the second term in the numerator of Equation 10-11 can be dropped.

$$[H^+] \approx \sqrt{\frac{K_1K_2F + K_1K_w}{K_1 + F}}$$

- Then, if $K_1 \ll F$, the first term in the denominator also can be neglected.

$$[H^+] \approx \sqrt{\frac{K_1K_2F}{K_1 + F}}$$

- Canceling F in the numerator and denominator gives

$$[\text{H}^+] \approx \sqrt{\frac{K_1 K_2 F}{K_1 + F}}$$

$$[\text{H}^+] \approx \sqrt{K_1 K_2}$$

$$\log[\text{H}^+] \approx \frac{1}{2}(\log K_1 + \log K_2)$$

$$-\log[\text{H}^+] \approx -\frac{1}{2}(\log K_1 + \log K_2)$$

$$\log(x^{1/2}) = \frac{1}{2} \log x$$

$$\log(xy) = \log x + \log y$$

$$\log(x/y) = \log x - \log y$$

Intermediate form of diprotic acid:

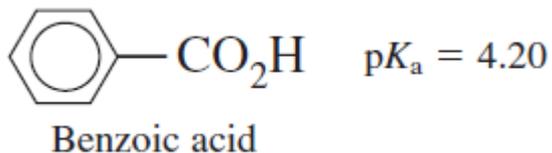
$$\text{pH} \approx \frac{1}{2}(\text{p}K_1 + \text{p}K_2) \quad (10-12)$$

- Equation 10-12 says that

→ the pH of the intermediate form of a diprotic acid is close to midway between $\text{p}K_1$ and $\text{p}K_2$, regardless of the formal concentration.

10.4 Which is the principal species?

- We sometimes must identify **which species of acid, base, or intermediate predominates** under given conditions.
- For example, "What is the **principal form** of benzoic acid **at pH 8**?"



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

- pK_a for benzoic acid is 4.20.
- So, at pH 4.20,
→ there is a 1:1 mixture of benzoic acid (HA) and benzoate ion (A^-).

- At $\text{pH} = \text{pK}_a + 1$ (= 5.20),
→ the quotient $[\text{A}^-]/[\text{HA}]$ is 10:1.

$$\text{pH} = \text{pK}_a + \log \frac{[\text{A}^-]}{[\text{HA}]}$$

- At $\text{pH} = \text{pK}_a + 2$ (= 6.20),
→ the quotient $[\text{A}^-]/[\text{HA}]$ is 100:1.

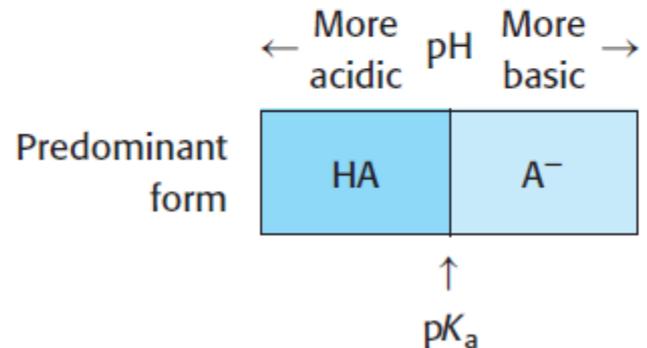
- As **pH increases**,
→ the quotient $[\text{A}^-]/[\text{HA}]$ **increases** still further.

For a monoprotic system,

- When $\text{pH} > \text{pK}_a$
→ the basic species A^- is the predominant form
- When $\text{pH} < \text{pK}_a$
→ the acidic species, HA , is the predominant form.
- The predominant form of benzoic acid at $\text{pH } 8$
→ is the benzoate anion, $\text{C}_6\text{H}_5\text{CO}_2^-$

$$\text{pH} = \text{pK}_a + \log \frac{[\text{A}^-]}{[\text{HA}]}$$

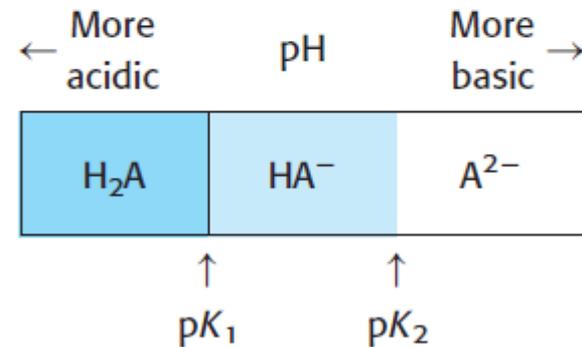
pH	Major species
$< \text{pK}_a$	HA
$> \text{pK}_a$	A^-



For polyprotic systems,

- Our reasoning is similar,
→ but there are several values of pK_a .
- Consider oxalic acid, H_2Ox ,
with $pK_1 = 1.25$ and $pK_2 = 4.27$.
- At $pH = pK_1$,
→ $[H_2Ox] = [HOx^-]$.
- At $pH = pK_2$,
→ $[HOx^-] = [Ox^{2-}]$.

pH	Major species
$pH < pK_1$	H_2A
$pK_1 < pH < pK_2$	HA^-
$pH > pK_2$	A^{2-}



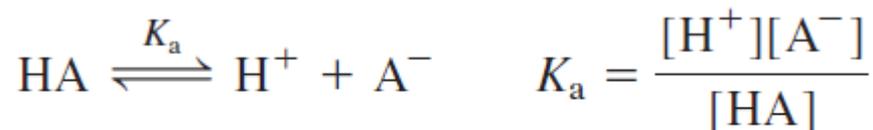
→ The chart in the margin shows the major species in each pH region.

10.5 Fractional Composition Equations

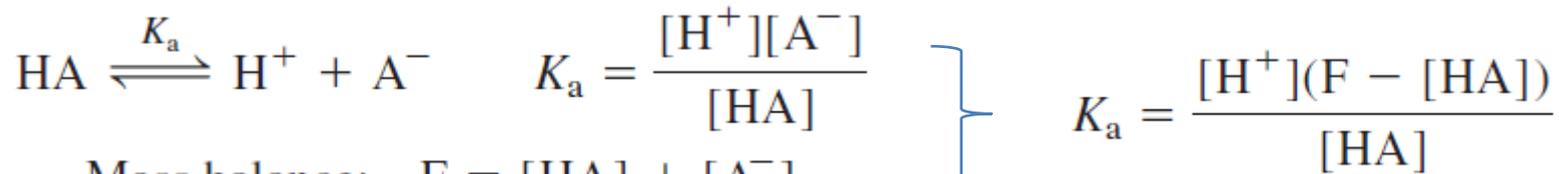
- Derive equations that give the fraction of each species of acid or base at a given pH.

1) Monoprotic Systems

- Our goal is to find an expression for the fraction of an acid in each form (HA and A⁻) as a function of pH.
- We can do this by combining the equilibrium constant with the mass balance.
- Consider an acid with formal concentration F:



$$\text{Mass balance: } F = [\text{HA}] + [\text{A}^-]$$



Mass balance: $F = [\text{HA}] + [\text{A}^-]$

$$K_a = \frac{[\text{H}^+](F - [\text{HA}])}{[\text{HA}]}$$



$$[\text{HA}] = \frac{[\text{H}^+]F}{[\text{H}^+] + K_a}$$

- The fraction of molecules in the form HA is called α_{HA} .

$$\alpha_{\text{HA}} = \frac{[\text{HA}]}{[\text{HA}] + [\text{A}^-]} = \frac{[\text{HA}]}{F}$$

Fraction in the form HA: $\alpha_{\text{HA}} = \frac{[\text{HA}]}{F} = \frac{[\text{H}^+]}{[\text{H}^+] + K_a}$

In a similar manner,

- the fraction in the form A^- , designated α_{A^-} , can be obtained:

Fraction in the form A^- :

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

α_{HA} = fraction of species in the form HA

α_{A^-} = fraction of species in the form A^-

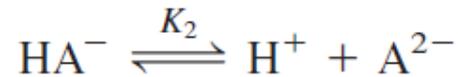
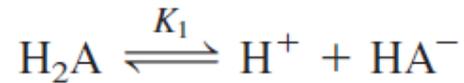
$$\alpha_{HA} + \alpha_{A^-} = 1$$

See Fig 10-3

- Figure 10-3 shows α_{HA} and α_{A^-} for a system with $pK_a = 5.00$.
- At low pH,
→ almost all of the acid is in the form HA.
- At high pH,
→ almost everything is in the form A^- .

2) Diprotic Systems

- The derivation of fractional composition equations for a diprotic system follows the same pattern used for the monoprotic system.



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

$$K_2 = \frac{[\text{H}^+][\text{A}^{2-}]}{[\text{HA}^-]} \Rightarrow \underline{[\text{A}^{2-}]} = [\text{HA}^-] \frac{K_2}{[\text{H}^+]} = [\text{H}_2\text{A}] \frac{K_1 K_2}{[\text{H}^+]^2}$$

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

$$F = [\text{H}_2\text{A}] + \frac{K_1}{[\text{H}^+]} [\text{H}_2\text{A}] + \frac{K_1 K_2}{[\text{H}^+]^2} [\text{H}_2\text{A}]$$

$$F = [\text{H}_2\text{A}] \left(1 + \frac{K_1}{[\text{H}^+]} + \frac{K_1 K_2}{[\text{H}^+]^2} \right) = [\text{H}_2\text{A}] \frac{[\text{H}^+]^2 + [\text{H}^+] K_1 + K_1 K_2}{[\text{H}^+]^2}$$

- For a diprotic system,
 - we designate the fraction in the form H_2A as α_{H_2A} ,
 - the fraction in the form HA^- as α_{HA^-} ,
 - and the fraction in the form A^{2-} as $\alpha_{A^{2-}}$.

- From the definition of α_{H_2A} ,
 - we can write,

$$\text{Fraction in the form } H_2A: \quad \alpha_{H_2A} = \frac{[H_2A]}{F} = \frac{[H^+]^2}{[H^+]^2 + [H^+]K_1 + K_1K_2}$$

- In a similar manner,
→ we can derive the following equations:

$$\textit{Fraction in the form HA}^-: \quad \alpha_{\text{HA}^-} = \frac{[\text{HA}^-]}{F} = \frac{K_1[\text{H}^+]}{[\text{H}^+]^2 + [\text{H}^+]K_1 + K_1K_2}$$

$$\textit{Fraction in the form A}^{2-}: \quad \alpha_{\text{A}^{2-}} = \frac{[\text{A}^{2-}]}{F} = \frac{K_1K_2}{[\text{H}^+]^2 + [\text{H}^+]K_1 + K_1K_2}$$

$$\textit{Fraction in the form H}_2\text{A}: \quad \alpha_{\text{H}_2\text{A}} = \frac{[\text{H}_2\text{A}]}{F} = \frac{[\text{H}^+]^2}{[\text{H}^+]^2 + [\text{H}^+]K_1 + K_1K_2}$$

$\alpha_{\text{H}_2\text{A}}$ = fraction of species in the form H_2A

α_{HA^-} = fraction of species in the form HA^-

$\alpha_{\text{A}^{2-}}$ = fraction of species in the form A^{2-}

$$\alpha_{\text{H}_2\text{A}} + \alpha_{\text{HA}^-} + \alpha_{\text{A}^{2-}} = 1$$