chapter 2 Water

1. **Effect of Local Environment on Ionic Bond Strength** If the ATP-binding site of an enzyme is buried in the interior of the enzyme, in a hydrophobic environment, is the ionic interaction between enzyme and substrate stronger or weaker than that same interaction would be on the surface of the enzyme, exposed to water? Why?

Answer The strength, or force (F), of ionic interactions in a solution depends on the magnitude of the charges (Q), the distance between the charged groups (r), and the dielectric constant (ε, which is dimensionless) of the solvent in which the interactions occur, according to the following equation:

$$F = \frac{Q_1 Q_2}{\varepsilon r^2}$$

When comparing the strength of the same ionic bond in water and in the hydrophobic environment inside a protein, we know that Q and r are the same; only ε is different. Water has a large dielectric constant because of the large number of dipoles. A hydrophobic "solvent" such as the inside of a protein has a much smaller dielectric constant. Given that the strength of the ionic interaction (F) varies as the inverse of the dielectric constant (ε), the ionic interaction would be stronger in the protein environment, with the smaller dielectric constant.

2. **Biological Advantage of Weak Interactions** The interactions between biomolecules are often stabilized by weak interactions such as hydrogen bonds. How might this be an advantage to the organism?

Answer Weak interactions are biologically advantageous in many ways. Collectively, many weak interactions can be stronger than one or a few stronger bonds. Biomolecular interactions need to be both specific and reversible. Many weak interactions can allow a high specificity of binding. At the same time, many biomolecular interactions are, of necessity, transient. A small change in conformation or in the environment (pH, ionic strength, or the presence or absence of a divalent cation, for example) can sufficiently alter the strength of weak bonds to allow the interactions between molecules to be reversible.

3. **Solubility of Ethanol in Water** Explain why ethanol (CH_3CH_2OH) is more soluble in water than is ethane (CH_3CH_3).

Answer Ethanol is polar; ethane is not. The ethanol —OH group can hydrogen-bond with water.

4. **Calculation of pH from Hydrogen Ion Concentration** What is the pH of a solution that has an H^+ concentration of **(a)** 1.75×10^{-5} mol/L; **(b)** 6.50×10^{-10} mol/L; **(c)** 1.0×10^{-4} mol/L; **(d)** 1.50×10^{-5} mol/L?

Answer Using $\text{pH} = -\log\,[H^+]$:
(a) $-\log\,(1.75 \times 10^{-5}) = 4.76$; **(b)** $-\log\,(6.50 \times 10^{-10}) = 9.19$; **(c)** $-\log\,(1.0 \times 10^{-4}) = 4.0$;
(d) $-\log\,(1.50 \times 10^{-5}) = 4.82$.

5. Calculation of Hydrogen Ion Concentration from pH What is the H^+ concentration of a solution with pH of **(a)** 3.82; **(b)** 6.52; **(c)** 11.11?

Answer Using $[H^+] = 10^{-pH}$:
(a) $[H^+] = 10^{-3.82} = 1.51 \times 10^{-4}$ M; **(b)** $[H^+] = 10^{-6.52} = 3.02 \times 10^{-7}$ M;
(c) $[H^+] = 10^{-11.11} = 7.76 \times 10^{-12}$ M.

6. Acidity of Gastric HCl In a hospital laboratory, a 10.0 mL sample of gastric juice, obtained several hours after a meal, was titrated with 0.1 M NaOH to neutrality; 7.2 mL of NaOH was required. The patient's stomach contained no ingested food or drink; thus assume that no buffers were present. What was the pH of the gastric juice?

Answer Multiplying volume (L) by molar concentration (mol/L) gives the number of moles in that volume of solution. If x is the concentration of gastric HCl (mol/L),

$$(0.010\ \text{L})x = (0.0072\ \text{L})(0.1\ \text{mol/L})$$

$$x = 0.072\ \text{M gastric HCl}$$

Given that $\text{pH} = -\log [H^+]$ and that HCl is a strong acid,

$$\text{pH} = -\log (7.2 \times 10^{-2}) = 1.1$$

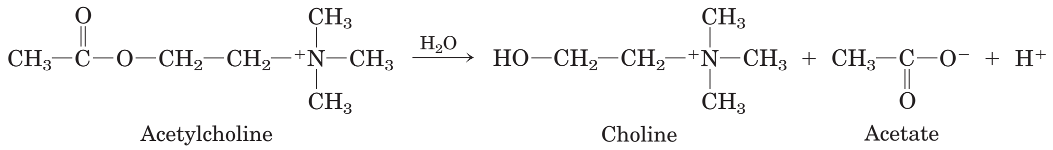
7. Calculation of the pH of a Strong Acid or Base **(a)** Write out the acid dissociation reaction for hydrochloric acid. **(b)** Calculate the pH of a solution of 5.0×10^{-4} M HCl. **(c)** Write out the acid dissociation reaction for sodium hydroxide. **(d)** Calculate the pH of a solution of 7.0×10^{-5} M NaOH.

Answer
(a) $HCl \rightleftharpoons H^+ + Cl^-$
(b) HCl is a strong acid and fully dissociates into H^+ and Cl^-. Thus, $[H^+] = [Cl^-] = [HCl]$.
$\text{pH} = -\log [H^+] = -\log (5.0 \times 10^{-4}\ \text{M}) = 3.3$ (two significant figures)
(c) $NaOH \rightleftharpoons Na^+ + OH^-$
(d) NaOH is a strong base; dissociation in aqueous solution is essentially complete, so $[Na^+] = [OH^-] = [NaOH]$.
$\text{pH} + \text{pOH} = 14$
$\text{pOH} = -\log [OH^-]$
$\text{pH} = 14 + \log [OH^-]$
$= 14 + \log (7.0 \times 10^{-5}) = 9.8$ (two significant figures)

8. Calculation of pH from Concentration of Strong Acid Calculate the pH of a solution prepared by diluting 3.0 mL of 2.5 M HCl to a final volume of 100 mL with H_2O.

Answer Because HCl is a strong acid, it dissociates completely to $H^+ + Cl^-$. Therefore, 3.0 mL × 2.5 M HCl = 7.5 meq of H^+. In 100 mL of solution, this is 0.075 M H^+.
$\text{pH} = -\log [H^+] = -\log (0.075) = -(-1.1) = 1.1$ (two significant figures)

9. Measurement of Acetylcholine Levels by pH Changes The concentration of acetylcholine (a neurotransmitter) in a sample can be determined from the pH changes that accompany its hydrolysis. When the sample is incubated with the enzyme acetylcholinesterase, acetylcholine is converted to choline and acetic acid, which dissociates to yield acetate and a hydrogen ion:



$$CH_3{-}C({=}O){-}O{-}CH_2{-}CH_2{-}{}^+N(CH_3)_2{-}CH_3 \xrightarrow{H_2O} HO{-}CH_2{-}CH_2{-}{}^+N(CH_3)_2{-}CH_3 + CH_3{-}C({=}O){-}O^- + H^+$$

In a typical analysis, 15 mL of an aqueous solution containing an unknown amount of acetylcholine had a pH of 7.65. When incubated with acetylcholinesterase, the pH of the solution decreased to 6.87. Assuming there was no buffer in the assay mixture, determine the number of moles of acetylcholine in the 15 mL sample.

Answer Given that pH $= -\log\,[\text{H}^+]$, we can calculate $[\text{H}^+]$ at the beginning and at the end of the reaction:

$$\text{At pH 7.65, } \log\,[\text{H}^+] = -7.65 \qquad [\text{H}^+] = 10^{-7.65} = 2.24 \times 10^{-8}\ \text{M}$$

$$\text{At pH 6.87, } \log\,[\text{H}^+] = -6.87 \qquad [\text{H}^+] = 10^{-6.87} = 1.35 \times 10^{-7}\ \text{M}$$

The difference in $[\text{H}^+]$ is

$$(1.35 - 0.22) \times 10^{-7}\ \text{M} = 1.13 \times 10^{-7}\ \text{M}$$

For a volume of 15 mL, or 0.015 L, multiplying volume by molarity gives

$$(0.015\ \text{L})(1.13 \times 10^{-7}\ \text{mol/L}) = 1.7 \times 10^{-9}\ \text{mol of acetylcholine}$$

10. Physical Meaning of pK_a Which of the following aqueous solutions has the lowest pH: 0.1 M HCl; 0.1 M acetic acid (pK_a = 4.86); 0.1 M formic acid (pK_a = 3.75)?

Answer A 0.1 M HCl solution has the lowest pH because HCl is a strong acid and dissociates completely to $\text{H}^+ + \text{Cl}^-$, yielding the highest $[\text{H}^+]$.

11. Meanings of K_a and pK_a **(a)** Does a strong acid have a greater or lesser tendency to lose its proton than a weak acid? **(b)** Does the strong acid have a higher or lower K_a than the weak acid? **(c)** Does the strong acid have a higher or lower pK_a than the weak acid?

Answer **(a)** greater; by definition, the stronger acid has the greater tendency to dissociate a proton; **(b)** higher; as $K_a = [\text{H}^+]\,[\text{A}^-]/[\text{HA}]$, whichever acid yields the larger concentration of $[\text{H}^+]$ has the larger K_a; **(c)** lower; p$K_a = -\log K_a$, so if K_a is larger, $-\log K_a$ will be smaller.

12. Simulated Vinegar One way to make vinegar (*not* the preferred way) is to prepare a solution of acetic acid, the sole acid component of vinegar, at the proper pH (see Fig. 2–15) and add appropriate flavoring agents. Acetic acid (M_r 60) is a liquid at 25 °C, with a density of 1.049 g/mL. Calculate the volume that must be added to distilled water to make 1 L of simulated vinegar (see Fig. 2–16).

Answer From Figure 2–16, the pK_a of acetic acid is 4.76. From Figure 2–15, the pH of vinegar is ~3; we will calculate for a solution of pH 3.0. Using the Henderson-Hasselbalch equation

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

and the fact that dissociation of HA gives equimolar $[\text{H}^+]$ and $[\text{A}^-]$ (where HA is CH_3COOH, and A^- is CH_3COO^-), we can write

$$3.0 = 4.76 + \log\,([\text{A}^-]/[\text{HA}])$$

$$-1.76 = \log\,([\text{A}^-]/[\text{HA}]) = -\log\,([\text{HA}]/[\text{A}^-])$$

$$[\text{HA}]/[\text{A}^-] = 10^{1.76} = 58$$

Thus, $[\text{HA}] = 58[\text{A}^-]$. At pH 3.0, $[\text{H}^+] = [\text{A}^-] = 10^{-3}$, so

$$[\text{HA}] = 58 \times 10^{-3}\ \text{M} = 0.058\ \text{mol/L}$$

Dividing density (g/mL) by molecular weight (g/mol) for acetic acid gives

$$\frac{1.049\ \text{g/mL}}{60\ \text{g/mol}} = 0.017\ \text{mol/mL}$$

Dividing this answer into 0.058 mol/L gives the volume of acetic acid needed to prepare 1.0 L of a 0.058 M solution:

$$\frac{0.058\ \text{mol/L}}{0.017\ \text{mol/mL}} = 3.3\ \text{mL/L}$$

13. **Identifying the Conjugate Base** Which is the conjugate base in each of the pairs below?

(a) RCOOH, $RCOO^-$
(b) RNH_2, RNH_3^+
(c) $H_2PO_4^-$, H_3PO_4
(d) H_2CO_3, HCO_3^-

Answer In each pair, the acid is the species that gives up a proton; the conjugate base is the deprotonated species. By inspection, the conjugate base is the species with fewer hydrogen atoms. **(a)** $RCOO^-$ **(b)** RNH_2 **(c)** $H_2PO_4^-$ **(d)** HCO_3^-

14. **Calculation of the pH of a Mixture of a Weak Acid and Its Conjugate Base** Calculate the pH of a dilute solution that contains a molar ratio of potassium acetate to acetic acid ($pK_a = 4.76$) of **(a)** 2:1; **(b)** 1:3; **(c)** 5:1; **(d)** 1:1; **(e)** 1:10.

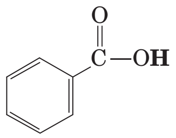
Answer Using the Henderson-Hasselbalch equation,

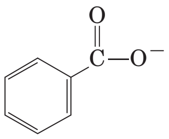
$$\text{pH} = \text{p}K_a + \log \frac{[\text{A}^-]}{[\text{HA}]}$$

pH = 4.76 + log ([acetate]/[acetic acid]), where [acetate]/[acetic acid] is the ratio given for each part of the question.

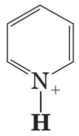
(a) $\log (2/1) = 0.30$; $\text{pH} = 4.76 + 0.30 = 5.06$
(b) $\log (1/3) = -0.48$; $\text{pH} = 4.76 + (-0.48) = 4.28$
(c) $\log (5/1) = 0.70$; $\text{pH} = 4.76 + 0.70 = 5.46$
(d) $\log (1/1) = 0$; $\text{pH} = 4.76$
(e) $\log (1/10) = -1.00$; $\text{pH} = 4.76 + (-1.00) = 3.76$

15. **Effect of pH on Solubility** The strongly polar hydrogen-bonding properties of water make it an excellent solvent for ionic (charged) species. By contrast, nonionized, nonpolar organic molecules, such as benzene, are relatively insoluble in water. In principle, the aqueous solubility of any organic acid or base can be increased by converting the molecules to charged species. For example, the solubility of benzoic acid in water is low. The addition of sodium bicarbonate to a mixture of water and benzoic acid raises the pH and deprotonates the benzoic acid to form benzoate ion, which is quite soluble in water.

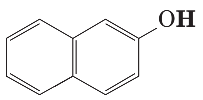

Benzoic acid
$pK_a \approx 5$


Benzoate ion

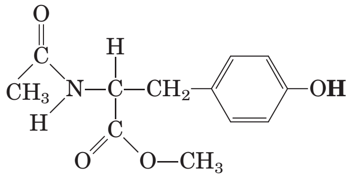
Are the following compounds more soluble in an aqueous solution of 0.1 M NaOH or 0.1 M HCl? (The dissociable proton are shown in bold.)


Pyridine ion
$pK_a \approx 5$

(a)


β-Naphthol
$pK_a \approx 10$

(b)

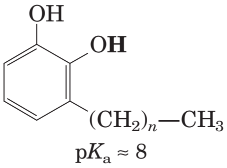

N-Acetyltyrosine methyl ester
$pK_a \approx 10$

(c)

Answer

(a) Pyridine is ionic in its protonated form and therefore more soluble at the lower pH, in 0.1 M HCl.
(b) β-Naphthol is ionic when *de*protonated and thus more soluble at the higher pH, in 0.1 M NaOH.
(c) *N*-Acetyltyrosine methyl ester is ionic when *de*protonated and thus more soluble in 0.1 M NaOH.

16. Treatment of Poison Ivy Rash The components of poison ivy and poison oak that produce the characteristic itchy rash are catechols substituted with long-chain alkyl groups.

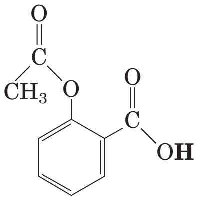


If you were exposed to poison ivy, which of the treatments below would you apply to the affected area? Justify your choice.

(a) Wash the area with cold water.
(b) Wash the area with dilute vinegar or lemon juice.
(c) Wash the area with soap and water.
(d) Wash the area with soap, water, and baking soda (sodium bicarbonate).

Answer The best choice is **(d).** Soap helps to emulsify and dissolve the hydrophobic alkyl group of an alkylcatechol. Given that the pK_a of an alkylcatechol is about 8, in a mildly alkaline solution of bicarbonate ($NaHCO_3$) its —OH group ionizes, making the compound much more water-soluble. A neutral or acidic solution, as in **(a)** or **(b),** would not be effective.

17. pH and Drug Absorption Aspirin is a weak acid with a pK_a of 3.5 (the ionizable H is shown in bold):



It is absorbed into the blood through the cells lining the stomach and the small intestine. Absorption requires passage through the plasma membrane, the rate of which is determined by the polarity of the molecule: charged and highly polar molecules pass slowly, whereas neutral hydrophobic ones pass rapidly. The pH of the stomach contents is about 1.5, and the pH of the contents of the small intestine is about 6. Is more aspirin absorbed into the bloodstream from the stomach or from the small intestine? Clearly justify your choice.

Answer With a pK_a of 3.5, aspirin is in its protonated (neutral) form at pH below 2.5. At higher pH, it becomes increasingly deprotonated (anionic). Thus, aspirin is better absorbed in the more acidic environment of the stomach.

18. Calculation of pH from Molar Concentrations What is the pH of a solution containing 0.12 mol/L of NH_4Cl and 0.03 mol/L of NaOH (pK_a of NH_4^+/NH_3 is 9.25)?

Answer For the equilibrium

$$NH_4^+ \rightleftharpoons NH_3 + H^+$$

$$pH = pK_a + \log([NH_3]/[NH_4^+])$$

we know that $[NH_4^+] + [NH_3] = 0.12$ mol/L, and that NaOH completely dissociates to give $[OH^-] = 0.03$ mol/L. Thus, $[NH_3] = 0.03$ mol/L and $[NH_4^+] = 0.09$ mol/L, and

$$pH = 9.25 + \log(0.03/0.09) = 9.25 - 0.48 = 8.77, \text{ which rounds to 9.}$$

19. Calculation of pH after Titration of Weak Acid A compound has a pK_a of 7.4. To 100 mL of a 1.0 M solution of this compound at pH 8.0 is added 30 mL of 1.0 M hydrochloric acid. What is the pH of the resulting solution?

Answer Begin by calculating the ratio of conjugate base to acid in the starting solution, using the Henderson-Hasselbalch equation:

$$\mathrm{pH} = \mathrm{p}K_a + \log([\mathrm{A}^-]/[\mathrm{HA}])$$

$$8.0 = 7.4 + \log([\mathrm{A}^-]/[\mathrm{HA}])$$

$$\log([\mathrm{A}^-]/[\mathrm{HA}]) = 0.6$$

$$[\mathrm{A}^-]/[\mathrm{HA}] = 10^{0.6} = 4$$

The solution contains 100 meq of the compound (conjugate base plus acid), so 80 meq are in the conjugate base form and 20 meq are in the acid form, for a [base]/[acid] ratio of 4.

Because HCl is a strong acid and dissociates completely, adding 30 mL of 1.0 M HCl adds 30 meq of H^+ to the solution. These 30 meq titrate 30 meq of the conjugate base, so the [base]/[acid] ratio is 1. Solving the Henderson-Hasselbalch equation for pH:

$$\mathrm{pH} = \mathrm{p}K_a + \log([\mathrm{A}^-]/[\mathrm{HA}])$$

$$= 7.4 + \log 1 = 7.4$$

20. Properties of a Buffer The amino acid glycine is often used as the main ingredient of a buffer in biochemical experiments. The amino group of glycine, which has a pK_a of 9.6, can exist either in the protonated form ($—\mathrm{NH}_3^+$) or as the free base ($—\mathrm{NH}_2$), because of the reversible equilibrium

$$\mathrm{R—NH}_3^+ \rightleftharpoons \mathrm{R—NH}_2 + \mathrm{H}^+$$

(a) In what pH range can glycine be used as an effective buffer due to its amino group?

(b) In a 0.1 M solution of glycine at pH 9.0, what fraction of glycine has its amino group in the $—\mathrm{NH}_3^+$ form?

(c) How much 5 M KOH must be added to 1.0 L of 0.1 M glycine at pH 9.0 to bring its pH to exactly 10.0?

(d) When 99% of the glycine is in its $—\mathrm{NH}_3^+$ form, what is the numerical relation between the pH of the solution and the pK_a of the amino group?

Answer

(a) In general, a buffer functions best in the zone from about one pH unit below to one pH unit above its pK_a. Thus, glycine is a good buffer (through ionization of its amino group) between pH 8.6 and pH 10.6.

(b) Using the Henderson-Hasselbalch equation

$$\mathrm{pH} = \mathrm{p}K_a + \log\frac{[\mathrm{A}^-]}{[\mathrm{HA}]}$$

we can write

$$9.0 = 9.6 + \log\frac{[\mathrm{A}^-]}{[\mathrm{HA}]}$$

$$\frac{[\mathrm{A}^-]}{[\mathrm{HA}]} = 10^{-0.6} = 0.25$$

which corresponds to a ratio of 1/4. This indicates that the amino group of glycine is about 1/5 deprotonated and 4/5 protonated at pH 9.0.

(c) From **(b)** we know that the amino group is about 1/5, or 20%, deprotonated at pH 9.0. Thus, in moving from pH 9.0 to pH 9.6 (at which, by definition, the amino group is 50% deprotonated), 30%, or 0.3, of the glycine is titrated. We can now calculate from the Henderson-Hasselbalch equation the percentage protonation at pH 10.0:

$$10.0 = 9.6 + \log \frac{[\mathrm{A}^-]}{[\mathrm{HA}]}$$

$$\frac{[\mathrm{A}^-]}{[\mathrm{HA}]} = 10^{0.4} = 2.5 = 5/2$$

This ratio indicates that glycine is 5/7, or 71%, deprotonated at pH 10.0, an additional 21%, or 0.21, deprotonation above that (50%, or 0.5) at the $\mathrm{p}K_\mathrm{a}$. Thus, the total fractional deprotonation in moving from pH 9.0 to 10.0 is $0.30 + 0.21 = 0.51$, which corresponds to

$$0.51 \times 0.1 \text{ mol} = 0.05 \text{ mol of KOH}$$

Thus, the volume of 5 M KOH solution required is (0.5 mol)/(5 mol/L) = 0.01 L, or 10 mL.

(d) From the Henderson-Hasselbalch equation,

$$\begin{aligned} \mathrm{pH} &= \mathrm{p}K_\mathrm{a} + \log\,([\text{—NH}_2]/[\text{—NH}_3^+]) \\ &= \mathrm{p}K_\mathrm{a} + \log\,(0.01/0.99) \\ &= \mathrm{p}K_\mathrm{a} + (-2) = \mathrm{p}K_\mathrm{a} - 2 \end{aligned}$$

In general, any group with an ionizable hydrogen is almost completely protonated at a pH at least two pH units below its $\mathrm{p}K_\mathrm{a}$ value.

21. Calculation of the pK_a of an Ionizable Group by Titration The $\mathrm{p}K_\mathrm{a}$ values of a compound with two ionizable groups are $\mathrm{p}K_1 = 4.10$ and $\mathrm{p}K_2$ between 7 and 10. A biochemist has 10 mL of a 1.0 M solution of this compound at a pH of 8.00. She adds 10.0 mL of 1.00 M HCl, which changes the PH to 3.20. What is $\mathrm{p}K_2$?

Answer The dibasic acid H_2A has two dissociable protons:

$$\mathrm{H_2A} \xrightarrow[\mathrm{p}K_1]{} \mathrm{HA}^- \xrightarrow[\mathrm{p}K_2]{} \mathrm{A}^{2-}$$

The initial pH (8.00) is so far above $\mathrm{p}K_1$ that we know the first proton is fully dissociated, and some of the HA^- has dissociated to A^{2-}. We can calculate how much of the 10 mmol of HCl (10 mL × 1.0 mmol/mL) was used to convert HA^- to $\mathrm{H_2A}$, using the Henderson-Hasselbalch equation for the group of $\mathrm{p}K_1$:

$$\mathrm{pH} = \mathrm{p}K_1 + \log\,([\mathrm{HA}^-]/[\mathrm{H_2A}])$$

$$\mathrm{pH} - \mathrm{p}K_1 = \log\,([\mathrm{HA}^-]/[\mathrm{H_2A}])$$

$$\mathrm{p}K_1 - \mathrm{pH} = \log\,([\mathrm{H_2A}]/[\mathrm{HA}^-])$$

Substituting the final pH of 3.20 and the $\mathrm{p}K_1$ of 4.10, we get:

$$4.10 - 3.20 = 0.90 = \log\,([\mathrm{H_2A}]/[\mathrm{HA}^-])$$

$$10^{0.90} = [\mathrm{H_2A}]/[\mathrm{HA}^-]$$

$$7.94 = [\mathrm{H_2A}]/[\mathrm{HA}^-]$$

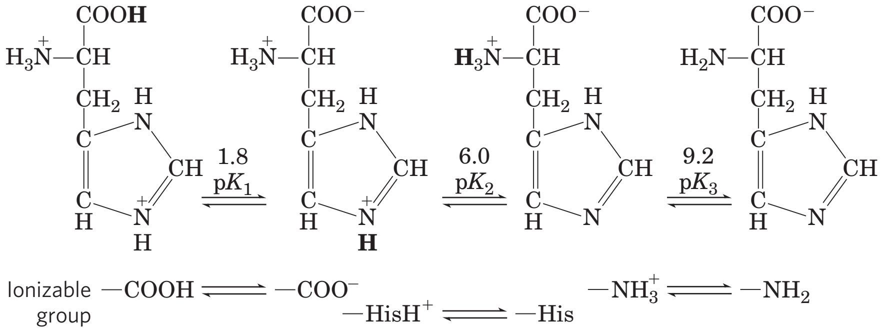
Following titration, we have 7.94 parts $\mathrm{H_2A}$ per part HA^-, and can calculate the percentage of $\mathrm{H_2A}$ in the final solution.

$$\frac{[\mathrm{H_2A}]}{[\mathrm{H_2A}]+[\mathrm{HA}^-]} = \frac{7.94}{1+7.94} = 0.888 = 88.8\%$$

Since we started with 10 mmol of the compound and an equal amount of HCl, then 88.8% of the HCl was used up when 88.8% of the compound was converted to H_2A. The remaining 11.2%, or 1.12 mmol, of the 10 mmol of HCl must have been used in titrating (protonating) the amount of A^{2-} in the initial solution of pH 8.00. Therefore, the initial solution must have contained 1.12 mmol of the compound in the form A^{2-} (the conjugate base), and the remaining 8.88 mmol must have been present initially as HA^- (the acid). Again using the Henderson-Hasselbalch equation, we can calculate pK_2:

$$\begin{aligned} \text{pH} &= pK_2 + \log([A^{2-}]/[HA^-]) \\ pK_2 &= \text{pH} - \log([A^{2-}]/[HA^-]) \\ &= 8.0 - \log \frac{1.12}{8.88} \\ &= 8.0 - (-0.90) \\ &= 8.9 \text{ (2 significant figures)} \end{aligned}$$

22. Calculation of the pH of a Solution of a Polyprotic Acid Histidine has ionizable groups with pK_a values of 1.8, 6.0, and 9.2, as shown below (His = imidazole group). A biochemist makes up 100 mL of a 0.100 M solution of histidine at a pH of 5.40. She then adds 40 mL of 0.10 M HCl. What is the pH of the resulting solution?



Answer The initial pH of 5.40 is so far below pK_3 (that of the amino group of histidine), that we know the group is completely dissociated at the initial pH, so we only need to consider the groups of pK_1 and pK_2 (i.e., the H on the carboxyl group and the H on the imidazole ring).

Initially, the pH was 5.40, from which we can calculate the fraction of the imidazole hydrogen that was dissociated (the ratio of the conjugate base His to the acid $HisH^+$):

$$\text{pH} = pK_2 + \log([\text{His}]/[\text{HisH}^+])$$

Next, substitute the values for pH and pK_2, rearrange, and take the antilog of both sides:

$$\begin{aligned} 5.40 &= 6.00 + \log([\text{His}]/[\text{HisH}^+]) \\ -0.60 &= \log([\text{His}]/[\text{HisH}^+]) \\ 0.60 &= \log([\text{HisH}^+]/[\text{His}]) \\ 10^{0.60} &= ([\text{HisH}^+]/[\text{His}]) = 4.0 \end{aligned}$$

Thus, in the initial solution, the ratio of $[HisH^+]$ to [His] is 4 to 1; 4 out of 5 of the imidazole groups were initially protonated.

The initial solution contains 10.0 mmol of histidine (10.0 mL × 0.100 mmol/mL), 1/5 of which (2.0 mmol) had unprotonated imidazole groups. The amount of HCl added was 4.0 mmol, of which 2.0 mmol was consumed in protonating the remaining imidazole groups. The other 2.0 mmol of HCl protonated a fraction (2.0 of the 10.0 mmol) of the carboxylate groups (with pK_1), leaving 8.0 mmol in the deprotonated form. From these ratios of acid and base after the titration, we can calculate the final pH:

$$\begin{aligned} pH &= pK_1 + \log([-COO^-]/[-COOH]) \\ &= 1.82 + \log\frac{8.0}{2.0} = 1.82 + 0.60 = 2.42 \\ &= 2.4 \text{ (2 significant figures)} \end{aligned}$$

23. Calculation of the Orginal pH from the Final pH after Titration A biochemist has 100 mL of a .10 M solution of a weak acid with a pK_a of 6.3. She adds 6.0 mL of 1.0 M HCl, which changes the pH to 5.7. What was the pH of the original solution?

Answer First calculate the ratio of acid to conjugate base in the final solution:

$$\begin{aligned} pH &= pK_a + \log([\text{base}]/[\text{acid}]) \\ pH - pK_a &= \log([\text{base}]/[\text{acid}]) \\ pK_a - pH &= \log([\text{acid}]/[\text{base}]) \\ 6.3 - 5.7 = 0.6 &= \log([\text{acid}]/[\text{base}]) \\ 10^{0.6} &= [\text{acid}]/[\text{base}] \\ 4 &= [\text{acid}]/[\text{base}] \end{aligned}$$

If the ratio of acid to conjugate base is 4 to 1, then 80% (4/5) of the compound is protonated after the addition of HCl.

The initial amount of the compound is 10 mmol (100 mL × 0.10 mmol/mL). So after HCl addition, 8.0 mmol of the compound are in the protonated form. The amount of HCl added was 6.0 mmol, so before HCl addition, only 2.0 mmol of the compound was protonated (acid), leaving 8.0 mmol unprotonated (conjugated base). Now we can calculate the pH of the initial solution:

$$\begin{aligned} pH &= pK_a + \log([\text{conjugate base}]/[\text{acid}]) \\ &= 6.3 + \log\frac{8.0}{2.0} \\ &= 6.3 + 0.60 = 6.9 \text{ (2 significant figures)} \end{aligned}$$

24. Preparation of a Phosphate Buffer What molar ratio of HPO_4^{2-} to $H_2PO_4^-$ in solution would produce a pH of 7.0? Phosphoric acid (H_3PO_4), a triprotic acid, has 3 pK_a values: 2.14, 6.86, and 12.4. Hint: Only one of the pK_a values is relevant here.

Answer Only the pK_a close to the pH is relevant here, because the concentrations of the other species (H_3PO_4 and PO_4^{3-}) are insignificant compared with the concentrations of HPO_4^{2-} and $H_2PO_4^-$. Begin with the Henderson-Hasselbalch equation:

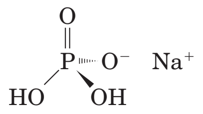
$$pH = pK_a + \log([\text{conjugate base}]/[\text{acid}])$$

$$\log([HPO_4^{2-}]/[H_2PO_4^-]) = pH - pK_a = 7.0 - 6.86 = 0.14$$

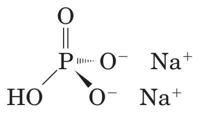
$$[HPO_4^{2-}]/[H_2PO_4^-] = 10^{0.14} = 1.38 = 1.4 \text{ (two significant figures)}$$

25. Preparation of Standard Buffer for Calibration of a pH Meter The glass electrode used in commercial pH meters gives an electrical response proportional to the concentration of hydrogen ion. To convert these responses to a pH reading, the electrode must be calibrated against standard solutions of known H^+ concentration. Determine the weight in grams of sodium dihydrogen phosphate ($NaH_2PO_4 \cdot H_2O$; FW 138) and disodium hydrogen phosphate (Na_2HPO_4; FW 142) needed to prepare 1 L of a standard buffer at pH 7.00 with a total phosphate concentration of 0.100 M (see Fig. 2–16). See Problem 24 for the pK_a values of phosphoric acid.

Answer In solution, the two salts ionize as indicated below.



Sodium dihydrogen phosphate
(sodium phosphate, monobasic)
$NaH_2PO_4 \cdot H_2O$



Disodium hydrogen phosphate
(sodium phosphate, dibasic)
Na_2HPO_4

The buffering capacity of the solution is determined by the concentration ratio of proton acceptor (A^-) to proton donor (HA), or $[HPO_4^{2-}]/[H_2PO_4^-]$. From Figure 2–16, the pK_a for the dissociation of the ionizable hydrogen of dihydrogen phosphate

$$H_2PO_4^- \rightleftharpoons HPO_4^{2-} + H^+$$

is 6.86. Using the Henderson-Hasselbalch equation,

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

we calculate:

$$7.00 - 6.86 = \log \frac{[A^-]}{[HA]}$$

$$\frac{[A^-]}{[HA]} = 10^{0.14} = 1.38$$

This ratio is approximately 7/5; that is, 7 parts Na_2HPO_4 to 5 parts $NaH_2PO_4 \cdot H_2O$. Because $[HPO_4^{2-}] + [H_2PO_4^-] = 0.100$ M, $[H_2PO_4^-] = 0.100\text{ M} - [HPO_4^{2-}]$, and we can now calculate the amount of each salt required for a 0.100 M solution:

$$\frac{[HPO_4^{2-}]}{0.100\text{ M} - [HPO_4^{2-}]} = 1.38$$

Solving for $[HPO_4^{2-}]$,

$$[HPO_4^{2-}] = \frac{0.138}{2.38}\text{ M} = 0.058\text{ M} = 0.058\text{ mol/L}$$

and $[H_2PO_4^-] = 0.100\text{ M} - 0.058\text{ M} = 0.042\text{ M} = 0.042$ mol/L.

The amount needed for 1 L of solution = FW (mol/L).

$$\text{For } NaH_2PO_4 \cdot H_2O\text{: } (138\text{ g/mol})(0.042\text{ mol/L}) = 5.8\text{ g/L}$$

$$\text{For } Na_2HPO_4\text{: } (142\text{ g/mol})(0.058\text{ mol/L}) = 8.2\text{ g/L}$$

26. Calculation of Molar Ratios of Conjugate Base to Weak Acid from pH For a weak acid with a pK_a of 6.0, calculate the ratio of conjugate base to acid at a pH of 5.0.

Answer Using the Henderson-Hasselbalch equation,

$$pH = pK_a + \log ([A^-]/[HA])$$
$$5.0 = 6.0 + \log ([A^-]/[HA])$$
$$\log ([A^-]/[HA]) = -1.0$$
$$[A^-]/[HA] = 10^{-1.0} = 0.10$$

27. Preparation of Buffer of Known pH and Strength Given 0.10 M solutions of acetic acid (pK_a = 4.76) and sodium acetate, describe how you would go about preparing 1.0 L of 0.10 M acetate buffer of pH 4.00.

Answer Use the Henderson-Hasselbalch equation to calculate the ratio $[Ac^-]/[HAc]$ in the final buffer.

$$pH = pK_a + \log ([Ac^-]/[HAc])$$
$$\log ([Ac^-]/[HAc]) = pH - pK_a = 4.00 - 4.76 = -0.76$$
$$[Ac^-]/[HAc] = 10^{-0.76}$$

The fraction of the solution that is $Ac^- = [Ac^-]/[HAc + Ac^-] = 10^{-0.76}/(1 + 10^{-0.76}) = 0.148$, which must be rounded to 0.15 (two significant figures). Therefore, to make 1.0 L of acetate buffer, use 150 mL of sodium acetate and 850 mL of acetic acid.

28. Choice of Weak Acid for a Buffer Which of these compounds would be the best buffer at pH 5.0: formic acid ($pK_a = 3.8$), acetic acid ($pK_a = 4.76$), or ethylamine ($pK_a = 9.0$)? Briefly justify your answer.

Answer Acetic acid; its pK_a is closest to the desired pH.

29. Working with Buffers A buffer contains 0.010 mol of lactic acid ($pK_a = 3.86$) and 0.050 mol of sodium lactate per liter. **(a)** Calculate the pH of the buffer. **(b)** Calculate the change in pH when 5 mL of 0.5 M HCl is added to 1 L of the buffer. **(c)** What pH change would you expect if you added the same quantity of HCl to 1 L of pure water?

Answer Using the Henderson-Hasselbalch equation,

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

(a) $pH = pK_a + \log ([\text{lactate}]/[\text{lactic acid}]) = 3.86 + \log (0.050\ \text{M}/0.010\ \text{M}) = 3.86 + 0.70 = 4.56$. Thus, the pH is 4.6.

(b) Strong acids ionize completely, so 0.005 L × 0.5 mol/L = 0.002 mol of H^+ is added. The added acid will convert some of the salt form to the acid form. Thus, the final pH is

$$pH = 3.86 + \log [(0.050 - 0.0025)/(0.010 - 0.0025)]$$
$$= 3.86 + 0.58 = 4.44$$

The change in pH = 4.56 − 4.44 = 0.12, which rounds to 0.1 pH unit.

(c) HCl completely dissociates. So, when 5 mL of 0.5 M HCl is added to 1 L of water,

$$[H^+] = (0.002\ \text{mol})/(1\ \text{L}) = 0.002\ \text{mol/L} = 0.002\ \text{M}$$
$$pH = -\log 0.002 = 2.7$$

The pH of pure water is 7.0, so the change in pH = 7.0 – 2.7 = 4.3, which rounds to 4 pH units.

30. Use of Molar Concentrations to Calculate pH What is the pH of a solution that contains 0.20 M sodium acetate and 0.60 M acetic acid ($pK_a = 4.76$)?

Answer pH = pK_a + log ([base]/[acid])

= pK_a + log ([acetate]/[acetic acid])

= 4.76 + log (0.20/0.60)

= 4.76 + (−0.48) = 4.3 (two significant figures, based on precision of concentrations)

31. Preparation of an Acetate Buffer Calculate the concentrations of acetic acid ($pK_a = 4.76$) and sodium acetate necessary to prepare a 0.2 M buffer solution at pH 5.0.

Answer First, calculate the required ratio of conjugate base to acid.

$$\text{pH} = pK_a + \log\,([\text{acetate}]/[\text{acetic acid}])$$

$$\log\,([\text{acetate}]/[\text{acetic acid}]) = \text{pH} - pK_a = 5.0 - 4.76 = 0.24$$

$$[\text{acetate}]/[\text{acetic acid}] = 10^{0.24} = 1.7$$

$$[\text{acetate}]/[\text{acetate} + \text{acetic acid}] = 1.7/2.7 = 0.63 \text{ (two significant figures)}$$

Thus, 63% of the 0.2 M buffer is acetate and 27% is acetic acid. So at pH 5.0 the buffer has 0.13 M acetate and 0.07 M acetic acid.

32. pH of Insect Defensive Secretion You have been observing an insect that defends itself from enemies by secreting a caustic liquid. Analysis of the liquid shows it to have a total concentration of formate plus formic acid ($K_a = 1.8 \times 10^{-4}$) of 1.45 M; the concentration of formate ion is 0.015 M. What is the pH of the secretion?

Answer Solve the Henderson-Hasselbalch equation for pH.

$$\text{pH} = pK_a + \log\,([\text{conjugate base}]/[\text{acid}])$$

Given the K_a of formic acid ($K_a = 1.8 \times 10^{-4}$), you can calculate pK_a as $-\log K_a = 3.7$. If the concentration of formate + formic acid = 1.45 M and the concentration of formate is 0.015 M, then the concentration of formic acid is 1.45 M − 0.015 M + 1.435 M.

$$\log\,([\text{formate}]/[\text{formic acid}]) = \log\,(0.015/1.435) = -2.0$$

$$\text{pH} = 3.7 - 2.0 = 1.7 \text{ (two significant figures)}$$

33. Calculation of pK_a An unknown compound, X, is thought to have a carboxyl group with a pK_a of 2.0 and another ionizable group with a pK_a between 5 and 8. When 75 mL of 0.1 M NaOH is added to 100 mL of a 0.1 M solution of X at pH 2.0, the pH increases to 6.72. Calculate the pK_a of the second ionizable group of X.

Answer At the first pH (pH = 2), 50% of the carboxyl group is dissociated (pK_a = pH). Then

$$\text{Amount of NaOH added} = 0.075\text{ L} \times 0.1\text{ mol/L} = 0.0075\text{ mol}$$

$$\text{Amount of X present} = 0.1\text{ L} \times 0.1\text{ mol/L} = 0.01\text{ mol}$$

At the new pH of 6.72, the carboxyl group is completely dissociated (because pH is much greater than the pK_a). The amount of NaOH required to titrate this remaining 50% of the carboxyl group is 0.5 × 0.01 mol = 0.005 mol.

Thus, 0.0075 mol − 0.005 mol = 0.0025 mol of NaOH is available to titrate the other group, and, using the Henderson-Hasselbalch equation,

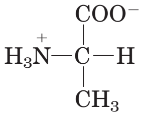
$$\text{pH} = pK_a + \log \frac{[\text{A}^-]}{[\text{HA}]}$$

we can find the pK_a of the second ionizable group of X:

$$6.72 = pK_a + \log\,[0.0025/(0.01 - 0.0025)]$$

$$pK_a = 6.72 - (-0.48) = 7.20\text{, which rounds to 7.}$$

34. Ionic Forms of Alanine Alanine is a diprotic acid that can undergo two dissociation reactions (see Table 3–1 for pK_a values). **(a)** Given the structure of the partially protonated form (or zwitterion; see Fig. 3–9) below, draw the chemical structures of the other two forms of alanine that predominate in aqueous solution: the fully protonated form and the fully deprotonated form.



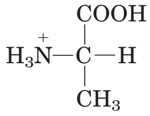
$$H_3\overset{+}{N}-\underset{CH_3}{\overset{COO^-}{C}}-H$$

Alanine

Of the three possible forms of alanine, which would be present at the highest concentration in solutions of the following pH: **(b)** 1.0; **(c)** 6.2; **(d)** 8.02; **(e)** 11.9. Explain your answers in terms of pH relative to the two pK_a values.

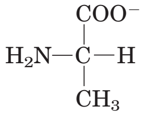
Answer

(a)



$$H_3\overset{+}{N}-\underset{CH_3}{\overset{COOH}{C}}-H$$

Fully protonated



$$H_2N-\underset{CH_3}{\overset{COO^-}{C}}-H$$

Fully deprotonated

(b) At pH 1.0, 1.3 pH units below the pK_a of the carboxyl group, more than 90% of the carboxyl groups are protonated, and protonated amino groups predominate by a factor of more than 107.

(c) At pH 6.2 the zwitterion predominates. This is 4 pH units above the pK_a of the carboxyl group, so the vast majority of carboxyl groups are deprotonated. It is 3.5 pH units below the pK_a of the amino group, so the vast majority of amino groups are protonated.

(d) At pH 8.02 the zwitterion still predominates. The carboxyl groups are deprotonated and, with the pH still 1.6 units below the pK_a of the amino group, the vast majority of amino groups are protonated.

(e) At pH 11.9, 2.2 pH units above the pK_a of the amino group, the vast majority of amino groups are deprotonated; and the carboxyl groups, at 9.6 pH units above their pK_a, remain deprotonated.

35. Control of Blood pH by Respiratory Rate

(a) The partial pressure of CO_2 in the lungs can be varied rapidly by the rate and depth of breathing. For example, a common remedy to alleviate hiccups is to increase the concentration of CO_2 in the lungs. This can be achieved by holding one's breath, by very slow and shallow breathing (hypoventilation), or by breathing in and out of a paper bag. Under such conditions, pCO_2 in the air space of the lungs rises above normal. Qualitatively explain the effect of these procedures on the blood pH.

(b) A common practice of competitive short-distance runners is to breathe rapidly and deeply (hyperventilate) for about half a minute to remove CO_2 from their lungs just before the race begins. Blood pH may rise to 7.60. Explain why the blood pH increases.

(c) During a short-distance run, the muscles produce a large amount of lactic acid ($CH_3CH(OH)COOH$, $K_a = 1.38 \times 10^{-4}$ M) from their glucose stores. In view of this fact, why might hyperventilation before a dash be useful?

Answer

(a) Blood pH is controlled by the carbon dioxide–bicarbonate buffer system, as shown by the net equation

$$CO_2 + H_2O \rightleftharpoons H^+ + HCO_3^-$$

During *hypoventilation*, the concentration of CO_2 in the lungs and arterial blood increases, driving the equilibrium to the right and raising the $[H^+]$; that is, the pH is lowered.

(b) During *hyperventilation*, the concentration of CO_2 in the lungs and arterial blood falls. This drives the equilibrium to the left, which requires the consumption of hydrogen ions, reducing $[H^+]$ and increasing pH.

(c) Lactate is a moderately strong acid (pK_a = 3.86) that completely dissociates under physiological conditions:

$$CH_3CH(OH)COOH \rightleftharpoons CH_3CH(OH)COO^- + H^+$$

This lowers the pH of the blood and muscle tissue. Hyperventilation is useful because it removes hydrogen ions, raising the pH of the blood and tissues in anticipation of the acid buildup.

36. Calculation of Blood pH from CO_2 and Bicarbonate Levels Calculate the pH of a blood plasma sample with a total CO_2 concentration of 26.9 mM and bicarbonate concentration of 25.6 mM. Recall from page 67 that the relevant pK_a of carbonic acid is 6.1.

Answer Use the Henderson-Hasselbalch equation:

$$\text{pH} = \text{p}K_a + \log\ ([\text{bicarbonate}]/[\text{carbonic acid}])$$

If total [CO_2] = 26.9 M and [bicarbonate] = 25.6 M, then the concentration of carbonic acid is 26.9 M − 25.6 M = 1.3 M.

$$\text{pH} = 6.1 + \log\ (25.6/1.3) = 7.4 \text{ (two significant figures)}$$

37. Effect of Holding One's Breath on Blood pH The pH of the extracellular fluid is buffered by the bicarbonate/carbonic acid system. Holding your breath can increase the concentration of $CO_2(g)$ in the blood. What effect might this have on the pH of the extracellular fluid? Explain by showing the relevant equilibrium equation(s) for this buffer system.

Answer Dissolving more CO_2 in the blood increases [H^+] in blood and extracellular fluids, lowering pH: $CO_2(d) + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$

Data Analysis Problem

38. "Switchable" Surfactants Hydrophobic molecules do not dissolve well in water. Given that water is a very commonly used solvent, this makes certain processes very difficult: washing oily food residue off dishes, cleaning up spilled oil, keeping the oil and water phases of salad dressings well mixed, and carrying out chemical reactions that involve both hydrophobic and hydrophilic components.

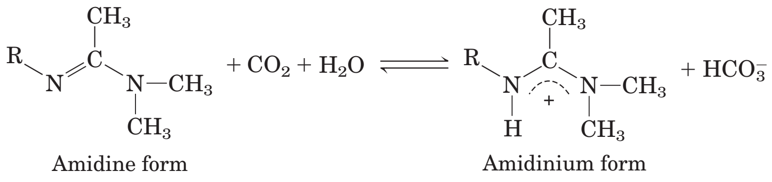
Surfactants are a class of amphipathic compounds that includes soaps, detergents, and emulsifiers. With the use of surfactants, hydrophobic compounds can be suspended in aqueous solution by forming micelles (see Fig. 2–7). A micelle has a hydrophobic core consisting of the hydrophobic compound and the hydrophobic "tails" of the surfactant; the hydrophilic "heads" of the surfactant cover the surface of the micelle. A suspension of micelles is called an emulsion. The more hydrophilic the head group of the surfactant, the more powerful it is—that is, the greater its capacity to emulsify hydrophobic material.

When you use soap to remove grease from dirty dishes, the soap forms an emulsion with the grease that is easily removed by water through interaction with the hydrophilic head of the soap molecules. Likewise, a detergent can be used to emulsify spilled oil for removal by water. And emulsifiers in commercial salad dressings keep the oil suspended evenly throughout the water-based mixture.

There are some situations in which it would be very useful to have a "switchable" surfactant: a molecule that could be reversibly converted between a surfactant and a nonsurfactant.

(a) Imagine such a "switchable" surfactant existed. How would you use it to clean up and then recover the oil from an oil spill?

Liu et al. describe a prototypical switchable surfactant in their 2006 article "Switchable Surfactants." The switching is based on the following reaction:

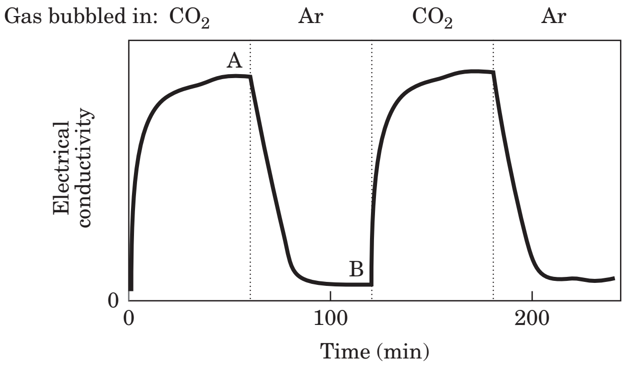


(b) Given that the pK_a of a typical amidinium ion is 12.4, in which direction (left or right) would you expect the equilibrium of the above reaction to lie? (See Fig. 2–16 for relevant pK_a values.) Justify your answer. Hint: Remember the reaction $H_2O + CO_2 \rightleftharpoons H_2CO_3$.

Liu and colleagues produced a switchable surfactant for which R = $C_{16}H_{33}$. They do not name the molecule in their article; for brevity, we'll call it s-surf.

(c) The amidinium form of s-surf is a powerful surfactant; the amidine form is not. Explain this observation.

Liu and colleagues found that they could switch between the two forms of s-surf by changing the gas that they bubbled through a solution of the surfactant. They demonstrated this switch by measuring the electrical conductivity of the s-surf solution; aqueous solutions of ionic compounds have higher conductivity than solutions of nonionic compounds. They started with a solution of the amidine form of s-surf in water. Their results are shown below; dotted lines indicate the switch from one gas to another.



(d) In which form is the majority of s-surf at point A? At point B?
(e) Why does the electrical conductivity rise from time 0 to point A?
(f) Why does the electrical conductivity fall from point A to point B?
(g) Explain how you would use s-surf to clean up and recover the oil from an oil spill.

Answer

(a) Use the substance in its surfactant form to emulsify the spilled oil, collect the emulsified oil, then switch to the nonsurfactant form. The oil and water will separate and the oil can be collected for further use.

(b) The equilibrium lies strongly to the right. The stronger acid (lower pK_a), H_2CO_3, donates a proton to the conjugate base of the weaker acid (higher pK_a), amidine.

(c) The strength of a surfactant depends on the hydrophilicity of its head groups: the more hydrophilic, the more powerful the surfactant. The amidinium form of s-surf is much more hydrophilic than the amidine form, so it is a more powerful surfactant.

(d) *Point A:* amidinium; the CO_2 has had plenty of time to react with the amidine to produce the amidinium form. *Point B:* amidine; Ar has removed CO_2 from the solution, leaving the amidine form.

(e) The conductivity rises as uncharged amidine reacts with CO_2 to produce the charged amidinium form.

(f) The conductivity falls as Ar removes CO_2, shifting the equilibrium to the uncharged amidine form.

(g) Treat s-surf with CO_2 to produce the surfactant amidinium form and use this to emulsify the spill. Treat the emulsion with Ar to remove the CO_2 and produce the nonsurfactant amidine from. The oil will separate from the water and can be recovered.

Reference

Liu, Y., Jessop, P.G., Cunningham, M., Eckert, C.A., & Liotta, C.L. (2006) *Science* **313,** 958–960.