

## 2.1 Brønsted–Lowry Acids and Bases

The general words “acid” and “base” usually mean a *Brønsted–Lowry acid* and *Brønsted–Lowry base*.

$\text{H}^+$  = proton

$\text{H}-\text{A}$  = general Brønsted–Lowry acid.  
 $\text{B}:$  = general Brønsted–Lowry base.

The Brønsted–Lowry definition describes acidity in terms of protons: positively charged **hydrogen ions,  $\text{H}^+$** .

- A Brønsted–Lowry acid is a *proton donor*.
- A Brønsted–Lowry base is a *proton acceptor*.

**A Brønsted–Lowry acid must contain a *hydrogen atom*.** This definition of an acid is often familiar to students, because many inorganic acids in general chemistry are Brønsted–Lowry acids. The symbol  $\text{H}-\text{A}$  is used for a general Brønsted–Lowry acid.

**A Brønsted–Lowry base must be able to form a bond to a proton.** Because a proton has no electrons, **a base must contain an “available” electron pair** that can be easily donated to form a new bond. These include **lone pairs** or electron pairs in  $\pi$  **bonds**. The symbol  $\text{B}:$  is used for a general Brønsted–Lowry base.

**Figure 2.1**

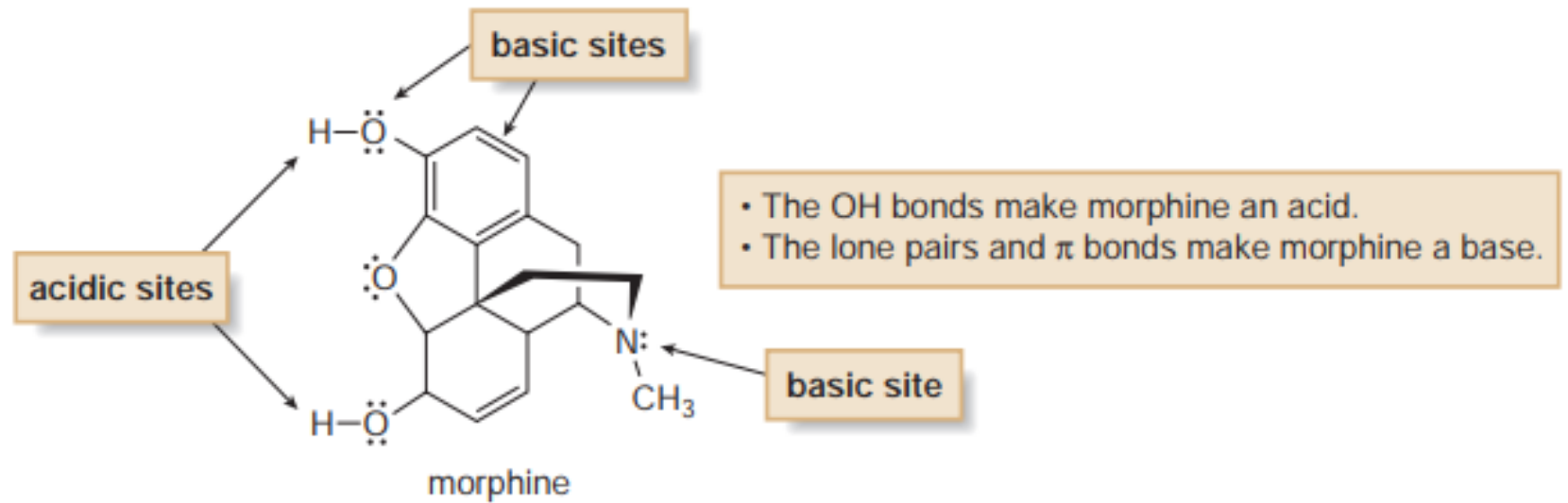
Examples of Brønsted–Lowry acids and bases

Brønsted–Lowry acids [H – A]		Brønsted–Lowry bases [B:]	
Inorganic	Organic	Inorganic	Organic
HCl	CH <sub>3</sub> CO <sub>2</sub> H		CH <sub>3</sub> $\ddot{\text{N}}\text{H}_2$
H <sub>2</sub> SO <sub>4</sub>	acetic acid	H <sub>2</sub> $\ddot{\text{O}}:$	methylamine
HSO <sub>4</sub> <sup>–</sup>		:NH <sub>3</sub>	CH <sub>3</sub> $\ddot{\text{O}}:$ <sup>–</sup>
H <sub>2</sub> O			methoxide
H <sub>3</sub> O <sup>+</sup>	$\text{HO}_2\text{CCH}_2-\overset{\text{OH}}{\underset{\text{COOH}}{\text{C}}}-\text{CH}_2\text{CO}_2\text{H}$ citric acid	$\ddot{\text{O}}\text{H}^-$	$\begin{array}{c} \text{CH}_3 \\ \diagdown \\ \text{C}=\ddot{\text{O}} \\ \diagup \\ \text{CH}_3 \end{array}$ acetone
		$\ddot{\text{N}}\text{H}_2^-$	CH <sub>2</sub> =CH <sub>2</sub>
			ethylene
<ul style="list-style-type: none"> <li>All Brønsted–Lowry acids contain a proton.</li> <li>The net charge may be zero, (+), or (–).</li> </ul>		<ul style="list-style-type: none"> <li>All Brønsted–Lowry bases contain a lone pair of electrons or a π bond.</li> <li>The net charge may be zero or (–).</li> </ul>	

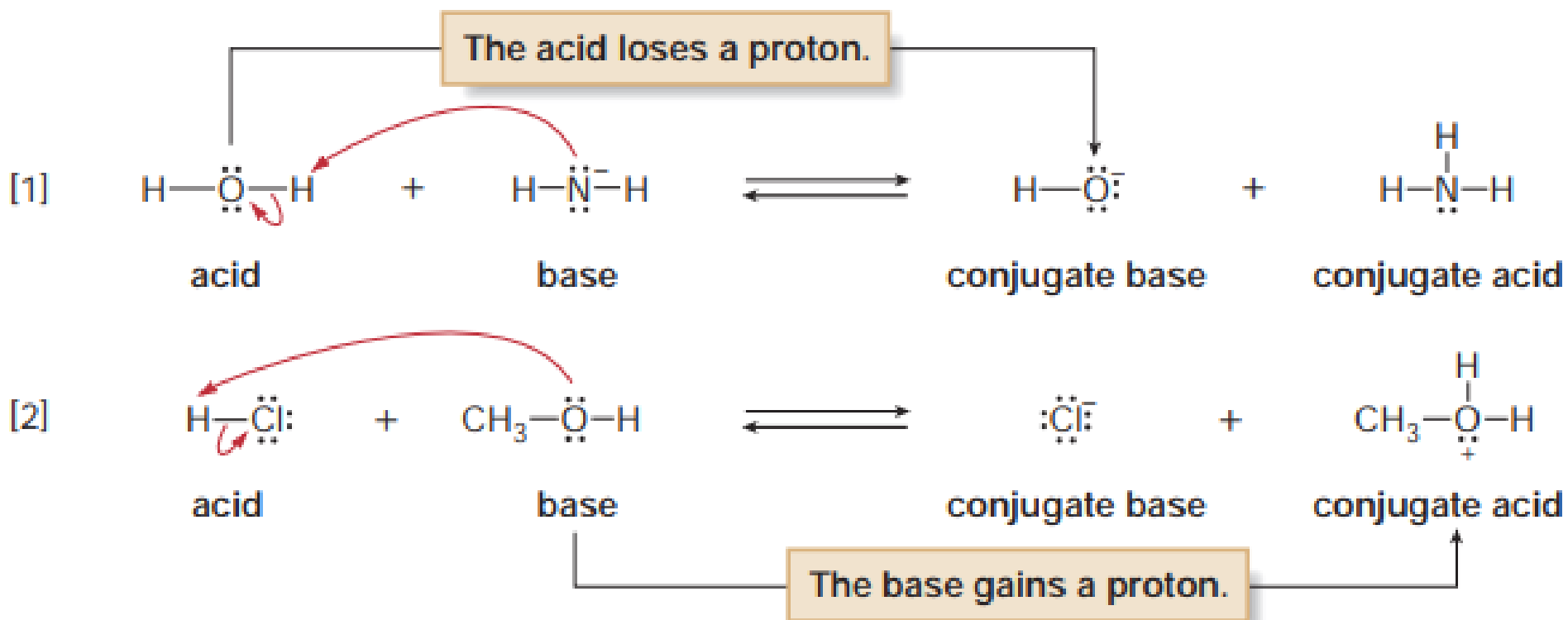
Morphine is obtained from the opium poppy.



**morphine** is a Brønsted–Lowry acid because it contains many hydrogen atoms. It is also a Brønsted–Lowry base because it has lone pairs on O and N, and four  $\pi$  bonds.



Two examples of proton transfer reactions are drawn here with curved arrow notation.

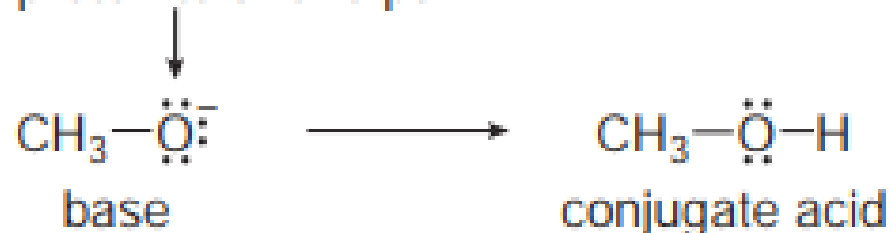


- a. What is the conjugate acid of  $\text{CH}_3\text{O}^-$ ?  
 b. What is the conjugate base of  $\text{NH}_3$ ?

## Solution

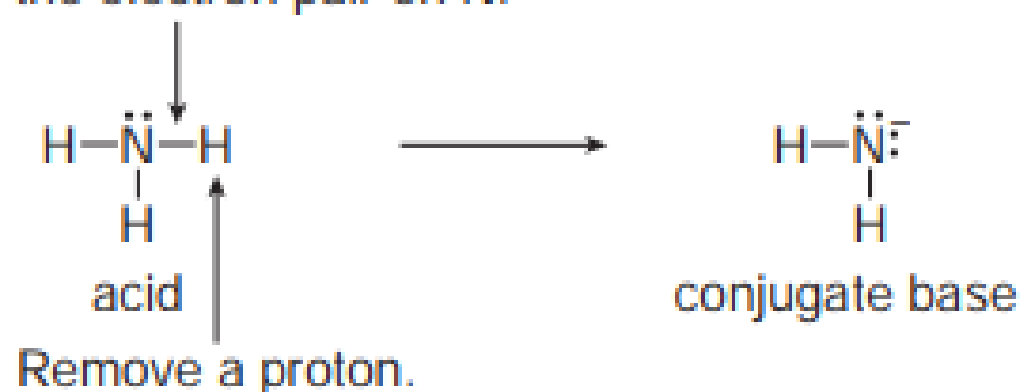
- a. Add  $\text{H}^+$  to  $\text{CH}_3\text{O}^-$  to form its conjugate acid.

Add a proton to a lone pair.



- b. Remove  $\text{H}^+$  from  $\text{NH}_3$  to form its conjugate base.

Leave the electron pair on N.

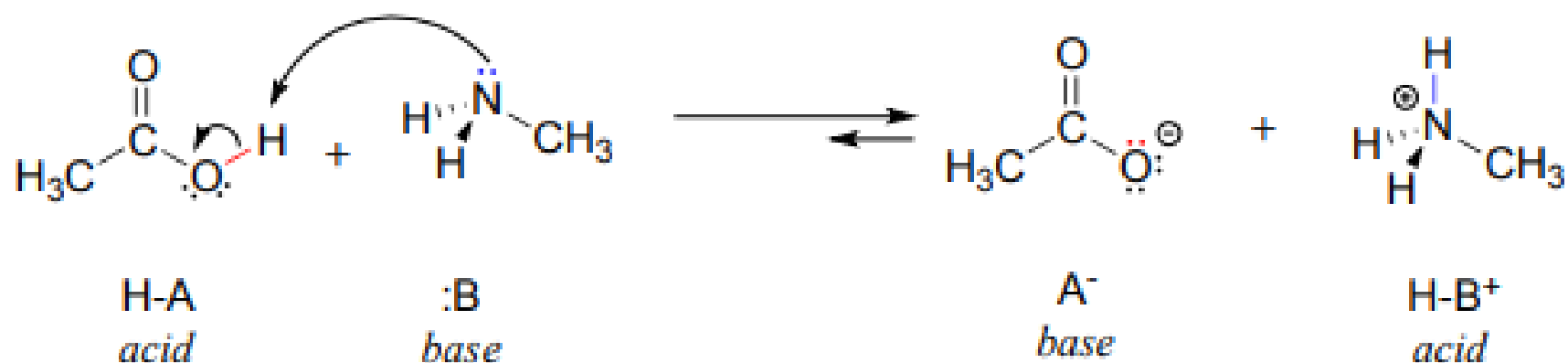


## Problem 2.6

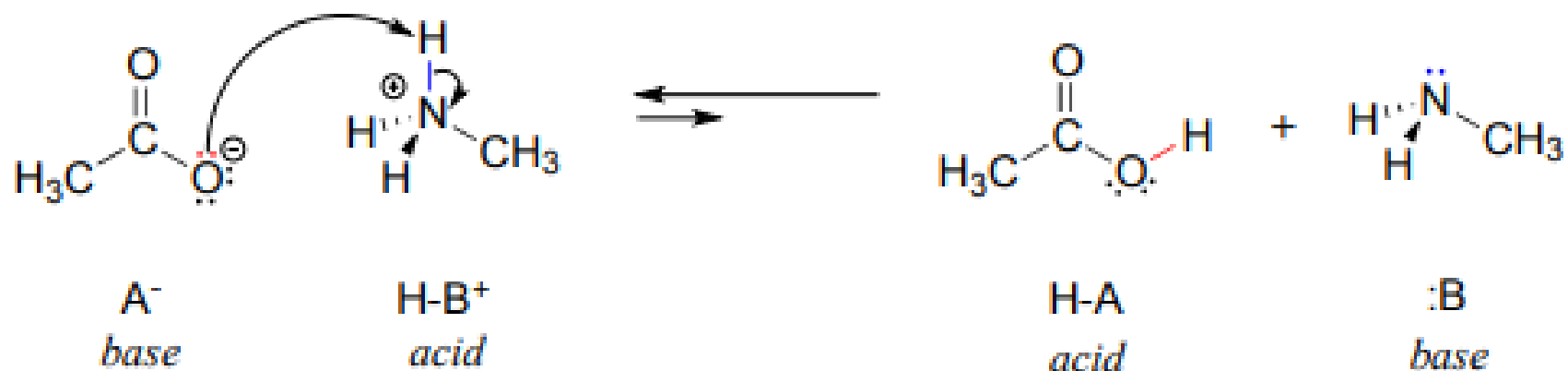
Draw the products of each proton transfer reaction.



Here is an organic acid-base reaction, between acetic acid and methylamine:



In the reverse of this reaction, acetate ion is the base and methylammonium ion (protonated methylamine) is the acid.

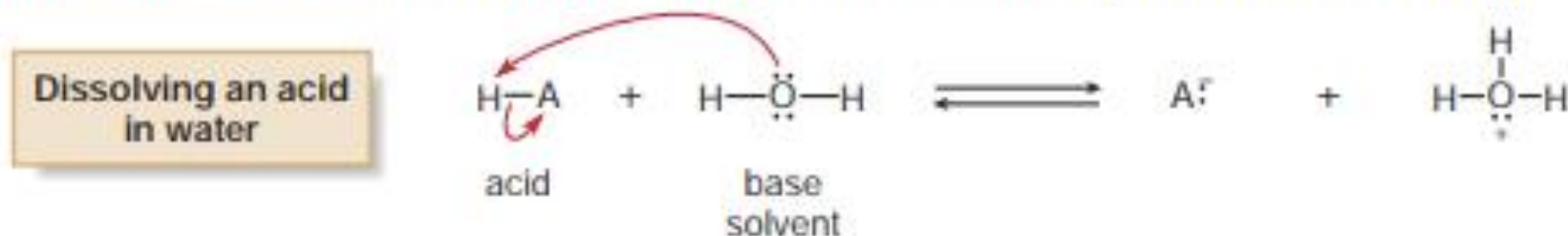


## 2.3 Acid Strength and $pK_a$

**Acid strength is the tendency of an acid to donate a proton.**

- The more readily a compound donates a proton, the stronger the acid.

Acidity is measured by an equilibrium constant. When a Brønsted–Lowry acid  $H-A$  is dissolved in water, an acid–base reaction occurs, and an equilibrium constant  $K_{eq}$  can be written for the reaction.



Equilibrium constant

$$K_{eq} = \frac{[\text{products}]}{[\text{starting materials}]} = \frac{[H_3O^+][A^-]}{[H-A][H_2O]}$$

Because the concentration of the solvent  $H_2O$  is essentially constant, the equation can be rearranged and a new equilibrium constant, called the **acidity constant**,  $K_a$ , can be defined.

$$\text{Acidity constant} = K_a = [H_2O]K_{eq} = \frac{[H_3O^+][A^-]}{[H-A]}$$

How is the magnitude of  $K_a$  related to acid strength?

- The *stronger the acid*, the further the equilibrium lies to the right, and the *larger the  $K_a$* .

For most organic compounds,  $K_a$  is small, typically  $10^{-5}$  to  $10^{-50}$ . This contrasts with the  $K_a$  values for many inorganic acids, which range from  $10^0$  to  $10^{10}$ . Because dealing with exponents can be cumbersome, it is often more convenient to use  $pK_a$  values instead of  $K_a$  values.

Definition:  $pK_a = -\log K_a$

How does  $pK_a$  relate to acid strength?



$K_a$	$pK_a = -\log K_a$
$K_a$ values of typical organic acids $10^{-5}$ to $10^{-50}$ larger number stronger acid      smaller number weaker acid	$pK_a$ values of typical organic acids +5 to +50 smaller number stronger acid      larger number weaker acid

Recall that a **log** is an **exponent**; for example,  $\log 10^{-5} = -5$ .

- The *smaller the  $pK_a$* , the *stronger the acid*.



**Table 2.1****Selected  $pK_a$  Values**

	<b>Acid</b>	<b><math>pK_a</math></b>	<b>Conjugate base</b>	
 Increasing acidity of the acid	H-Cl	-7	Cl <sup>-</sup>	 Increasing basicity of the conjugate base
	CH <sub>3</sub> COO-H	4.8	CH <sub>3</sub> COO <sup>-</sup>	
	HO-H	15.7	HO <sup>-</sup>	
	CH <sub>3</sub> CH <sub>2</sub> O-H	16	CH <sub>3</sub> CH <sub>2</sub> O <sup>-</sup>	
	HC≡CH	25	HC≡C <sup>-</sup>	
	H-H	35	H <sup>-</sup>	
	H <sub>2</sub> N-H	38	H <sub>2</sub> N <sup>-</sup>	
	CH <sub>2</sub> =CH <sub>2</sub>	44	CH <sub>2</sub> =C <sup>-</sup> H	
	CH <sub>3</sub> -H	50	CH <sub>3</sub> <sup>-</sup>	

The  $pK_a$  values in Table 2.1 span a large range (-7 to 50). The  **$pK_a$  scale is logarithmic**, so a small difference in  $pK_a$  translates into a large numerical difference. For example, the difference between the  $pK_a$  of NH<sub>3</sub> (38) and CH<sub>2</sub>=CH<sub>2</sub> (44) is six  $pK_a$  units. This means that NH<sub>3</sub> is 10<sup>6</sup> or **one million times more acidic** than CH<sub>2</sub>=CH<sub>2</sub>.

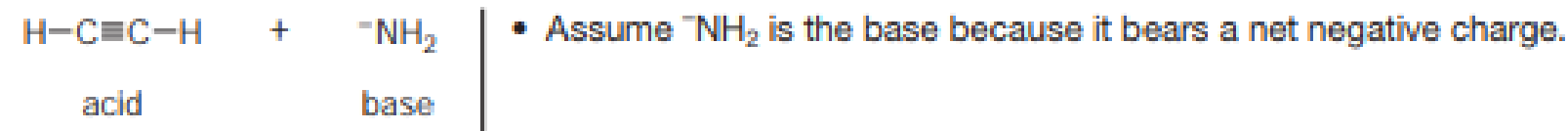
Determine the direction of equilibrium in the following proton transfer reaction.



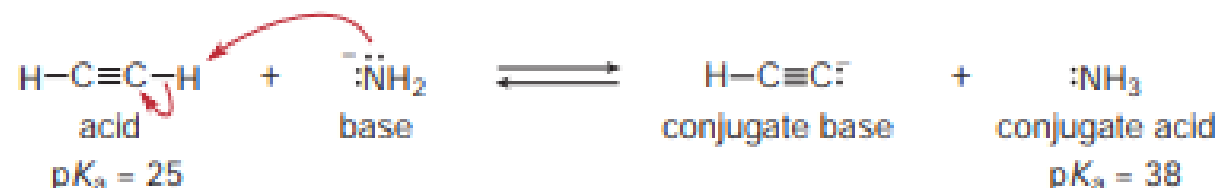
### Solution

Follow three steps to determine the position of equilibrium:

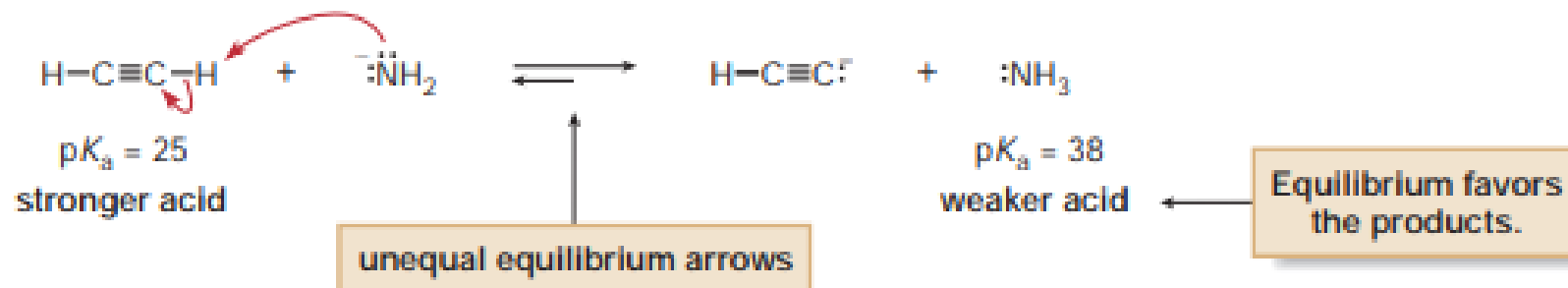
**Step [1]** Identify the acid and base in the starting materials.



**Step [2]** Draw the products of proton transfer and identify the conjugate acid and base in the products.



**Step [3]** Compare the  $pK_a$  values of the acid and the conjugate acid. Equilibrium favors formation of the weaker acid with the higher  $pK_a$ .



- Because the  $pK_a$  of the starting acid (25) is **lower** than the  $pK_a$  of the conjugate acid (38),  $\text{HC}\equiv\text{CH}$  is a **stronger** acid and equilibrium favors the products.

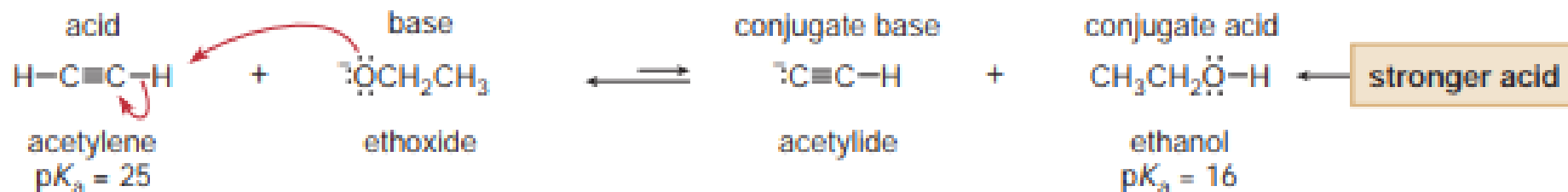
Compare any two entries in Table 2.1, such as ethanol ( $\text{CH}_3\text{CH}_2\text{OH}$ ;  $\text{p}K_a = 16$ ) and acetylene ( $\text{HC}\equiv\text{CH}$ ;  $\text{p}K_a = 25$ ), and their conjugate bases, ethoxide ( $\text{CH}_3\text{CH}_2\text{O}^-$ ) and acetylide ( $\text{HC}\equiv\text{C}^-$ ). Ethanol is a stronger acid than acetylene, so acetylide is a stronger base than ethoxide.

	acid	$\text{p}K_a$	conjugate base
stronger acid	$\text{CH}_3\text{CH}_2\ddot{\text{O}}\text{H}$ ethanol	16	$\text{CH}_3\text{CH}_2\ddot{\text{O}}^-$ ethoxide
	$\text{H}-\text{C}\equiv\text{C}-\text{H}$ acetylene	25	$\text{H}-\text{C}\equiv\text{C}^-$ ← stronger base acetylide

Because Table 2.1 is arranged from low to high  $\text{p}K_a$ , an acid can be deprotonated by the conjugate base of any acid below it in the table.

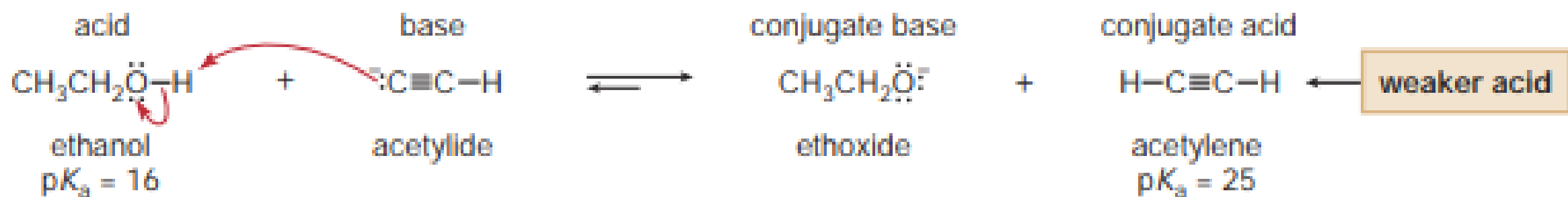
Two proton transfer reactions are possible.

- [1] Reaction of acetylene with ethoxide forms acetylide and ethanol. Because the stronger acid is the product of the reaction, *equilibrium favors the starting materials*. The base ethoxide is *not strong enough to deprotonate acetylene*.



Equilibrium favors the starting materials.

[2] Reaction of ethanol with acetylide forms ethoxide and acetylene. Because the weaker acid is the product of the reaction, *equilibrium favors the products*. Thus, **the base acetylide is strong enough to deprotonate ethanol**.



Equilibrium favors the products.

In the second reaction, **ethanol is deprotonated by acetylide, the conjugate base of an acid weaker than itself**. This is a specific example of a general fact.

- An acid can be deprotonated by the conjugate base of any acid having a *higher*  $pK_a$ .

# Factors That Determine Acid Strength

We have already learned in Section 2.3 that a tremendous difference in acidity exists among compounds. HCl ( $pK_a < 0$ ) is an extremely strong acid. Water ( $pK_a = 15.7$ ) is moderate in acidity, and  $\text{CH}_4$  ( $pK_a = 50$ ) is an extremely weak acid. How are these differences explained? There is one general rule.

- Anything that stabilizes a conjugate base  $\text{A}^-$  makes the starting acid  $\text{H}-\text{A}$  more acidic.

Four factors affect the acidity of  $\text{H}-\text{A}$ :

- [1] **Element effects**
- [2] **Inductive effects**
- [3] **Resonance effects**
- [4] **Hybridization effects**

No matter which factor is discussed, the same procedure is always followed. To compare the acidity of any two acids:

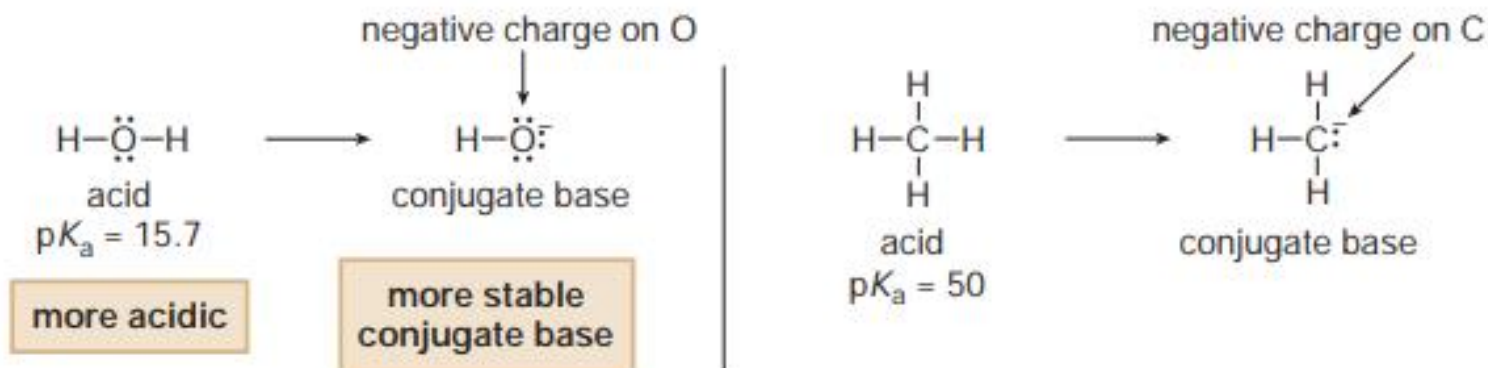
- **Always draw the conjugate bases.**
- **Determine which conjugate base is more stable.**
- **The *more stable* the conjugate base, the *more acidic* the acid.**

## Element Effects—Trends in the Periodic Table

The most important factor determining the acidity of H–A is the location of A in the periodic table.

### Comparing Elements in the Same Row of the Periodic Table

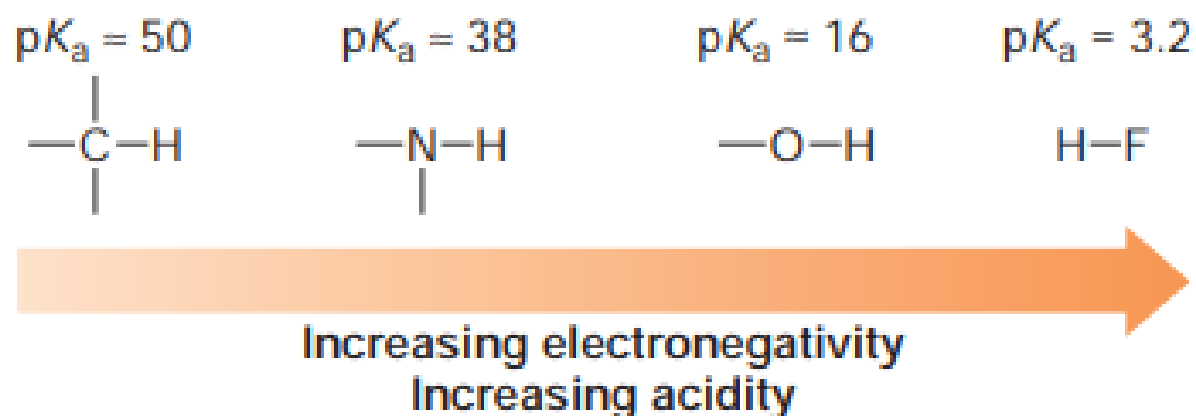
Examine acidity trends **across a row** of the periodic table by comparing CH<sub>4</sub> and H<sub>2</sub>O, two compounds having H atoms bonded to a second-row element. We know from Table 2.1 that **H<sub>2</sub>O has a much lower pK<sub>a</sub> and therefore is much more acidic than CH<sub>4</sub>**, but why is this the case?



Because the oxygen atom is much **more electronegative** than carbon, oxygen more readily accepts a negative charge, making <sup>-</sup>OH much more stable than CH<sub>3</sub><sup>-</sup>. **H<sub>2</sub>O is a stronger acid than CH<sub>4</sub> because <sup>-</sup>OH is a more stable conjugate base than CH<sub>3</sub><sup>-</sup>.** This is a specific example of a general trend.

- Across a row of the periodic table, the acidity of H–A increases as the electronegativity of A increases.

- Across a row of the periodic table, the acidity of H – A increases as the electronegativity of A increases.



The enormity of this effect is evident by noting the approximate  $pK_a$  values for these bonds. **A C – H bond is approximately  $10^{47}$  times *less acidic* than H – F.**

## Comparing Elements Down a Column of the Periodic Table

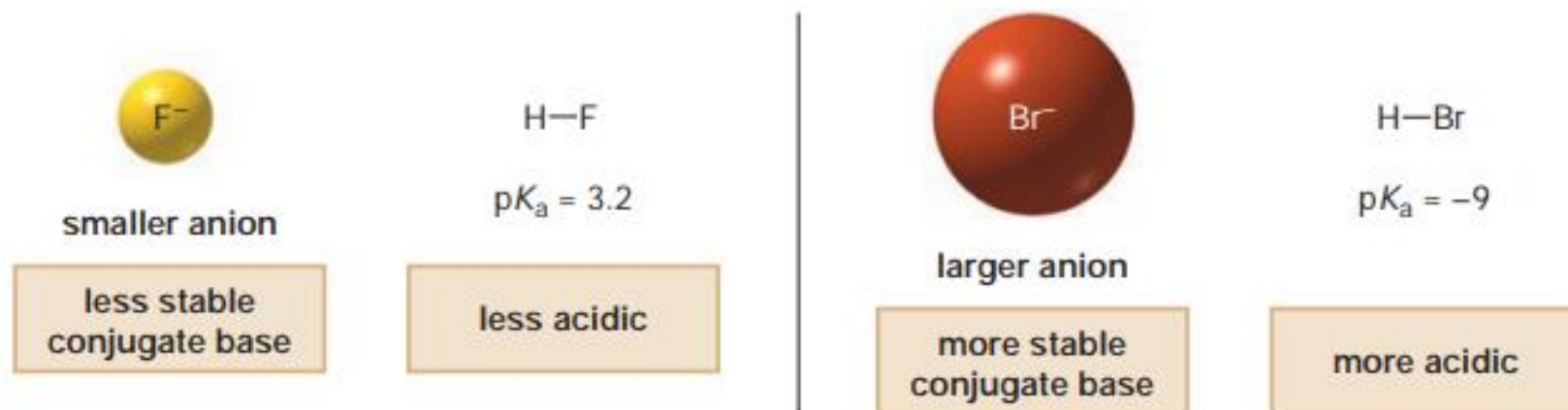
Now examine acidity trends down a column of the periodic table by comparing H-F and H-Br. Once again, first draw both conjugate bases and then determine which is more stable. In this case, removal of a proton forms  $F^-$  and  $Br^-$ .



There are two important differences between  $F^-$  and  $Br^-$ —electronegativity and size. In this case, **size is more important than electronegativity**. The size of an atom or ion increases down a column of the periodic table, so  $Br^-$  is much larger than  $F^-$ , and this stabilizes the negative charge.

- Positive or negative charge is stabilized when it is spread over a larger volume.

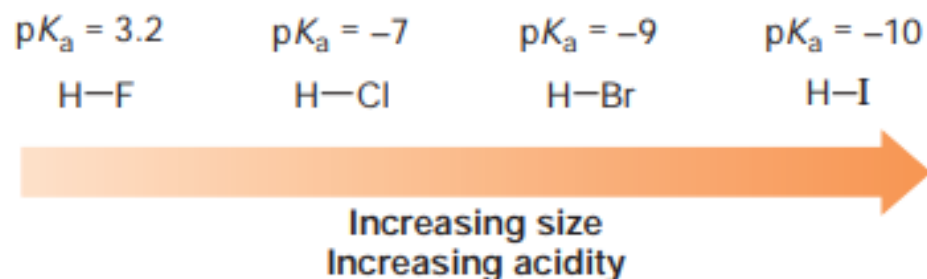
**Because  $Br^-$  is larger than  $F^-$ ,  $Br^-$  is more stable than  $F^-$ , and H-Br is a stronger acid than H-F.**





This again is a specific example of a general trend.

- Down a column of the periodic table, the acidity of H–A increases as the size of A increases.



Because of carbon's position in the periodic table (in the second row and to the left of O, N, and the halogens), **C–H bonds are usually the *least acidic* bonds in a molecule.**

This is *opposite* to what would be expected on the basis of electronegativity differences between F and Br, because F is more electronegative than Br. **Size and *not* electronegativity determines acidity down a column.** Combining both trends together:

- The acidity of H–A increases both left-to-right across a row and down a column of the periodic table.

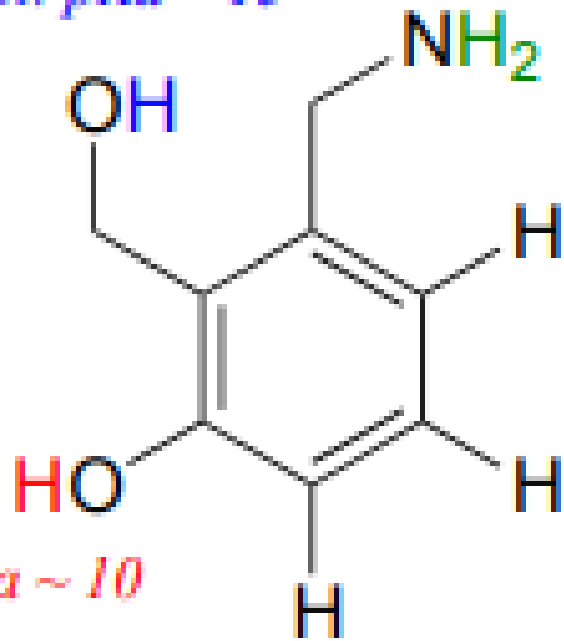
## Typical pKa values

<b>group</b>	<i>approximate pKa</i>
hydronium ion ( $\text{H}_3\text{O}^+$ )	0
protonated alcohol	0
protonated carbonyl	0
carboxylic acids	5
protonated imines	7
protonated amines	10
phenols	10
thiols	10
alcohols, water	15
$\alpha$ -carbon acids*	20

*\* $\alpha$ -carbon acids will be explained in section 7.6A*

*alcohol: pKa ~ 15*

*amine: not acidic (pKa ~ 35)*



*phenol: pKa ~ 10*

*aromatic protons: not acidic (pKa ~ 45)*

We can do the same rough calculation for other common functional groups found in biomolecules.

### At physiological pH:

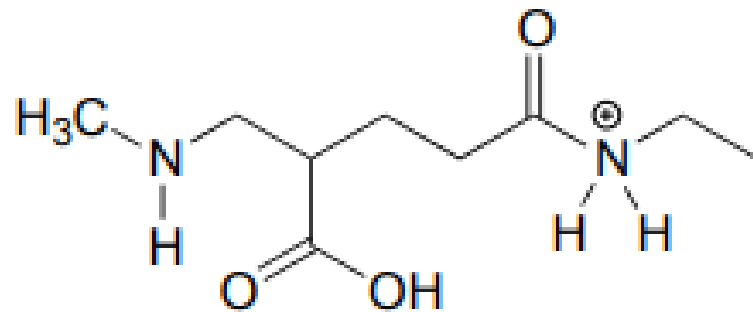
Carboxylic acids are deprotonated (in the carboxylate anion form)

Amines are protonated (in the ammonium cation form)

Thiols, phenols, alcohols, and amides are uncharged

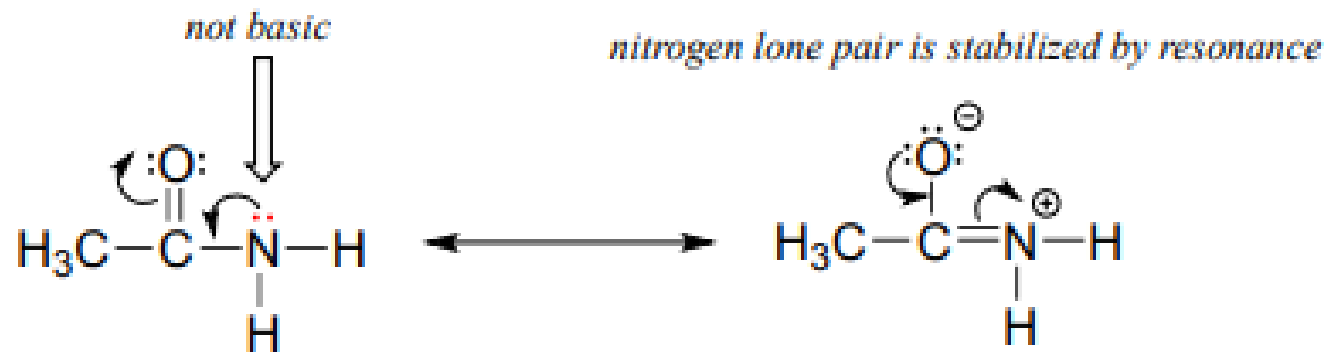
Imines are a mixture of the protonated (cationic) and deprotonated (neutral) states.

We will talk about the physiological protonation state of phosphate groups in chapter 9.

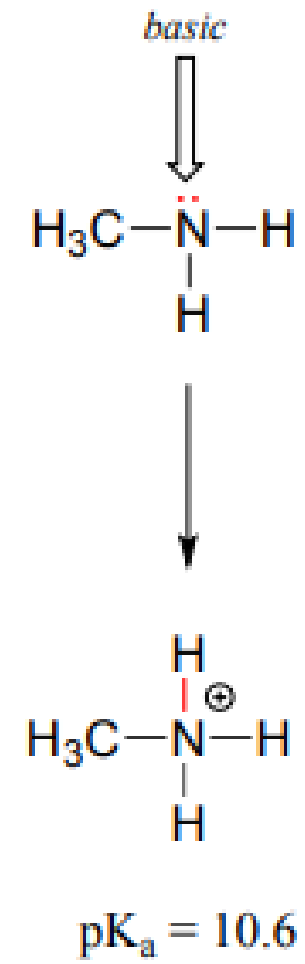


Cuál es la estructura a pH fisiológico??

## amide

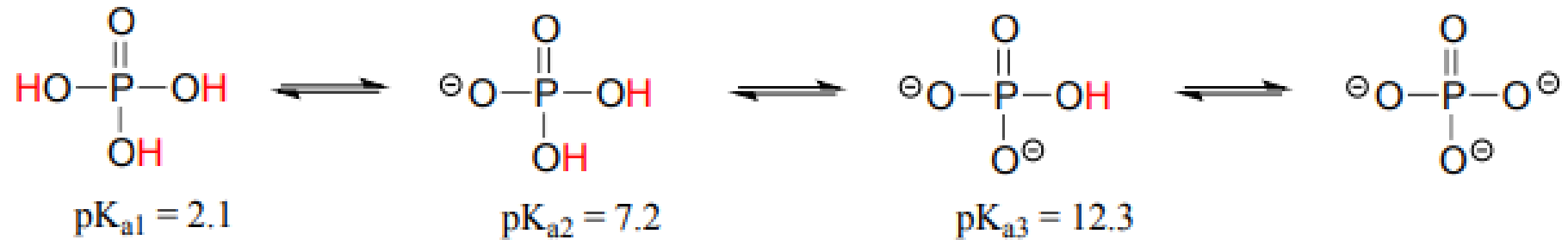


## amine



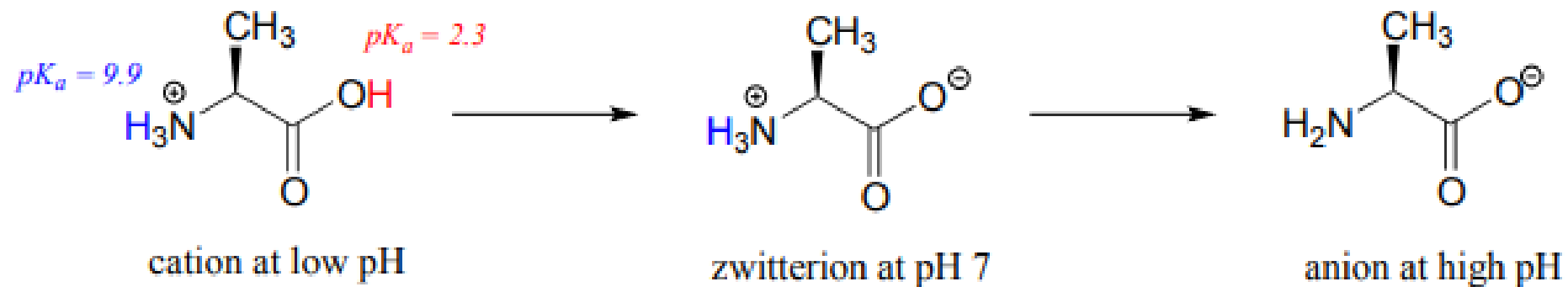
## Section 7.7: Polyprotic acids

Polyprotic acids are capable of donating more than one proton. The most important polyprotic acid group from a biological standpoint is triprotic phosphoric acid. Because phosphoric acid has three acidic protons, it also has three pK<sub>a</sub> values.



The pK<sub>a</sub> values for any polyprotic acid always get progressively higher, because it becomes increasingly difficult to stabilize the additional electron density that results from each successive proton donation. H<sub>3</sub>PO<sub>4</sub> is a strong acid because the (single) negative charge on its conjugate base H<sub>2</sub>PO<sub>4</sub><sup>-</sup> can be delocalized over two oxygen atoms.

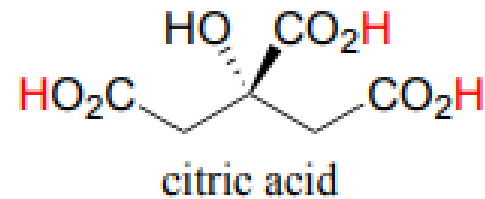
Free amino acids are polyprotic, with pKa values of approximately 2 for the carboxylic acid group and 9-10 for the ammonium group. Alanine, for example, has the acid constants  $pK_{a1} = 2.3$  and  $pK_{a2} = 9.9$ .



The Henderson-Hasselbalch equation tells us that alanine is almost fully protonated and positively charged when dissolved in a solution that is buffered to pH 0.5. At pH 7, alanine has lost one proton from the carboxylic acid group, and thus is a **zwitterion** (it has both a negative and a positive formal charge). At pH levels above 12, the ammonium group is fully deprotonated, and alanine has a negative overall charge.

Many biological organic molecules have several potentially ionizable functional groups and thus can be considered polyprotic acids. Citric acid, found in abundance in oranges, lemons, and other citrus fruits, has three carboxylic acid groups and  $pK_a$  values of 3.1, 4.8, and 6.4.

*three acidic groups*





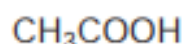
## 2.6 Common Acids and Bases

Many strong or moderately strong acids and bases are used as reagents in organic reactions.

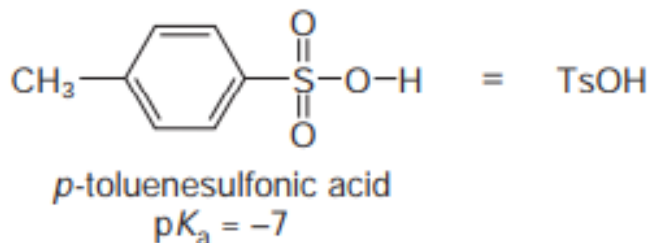
### 2.6A Common Acids

Several organic reactions are carried out in the presence of strong inorganic acids, most commonly **HCl** and **H<sub>2</sub>SO<sub>4</sub>**. These strong acids, with **p*K<sub>a</sub>* values ≤ 0**, should be familiar from previous chemistry courses.

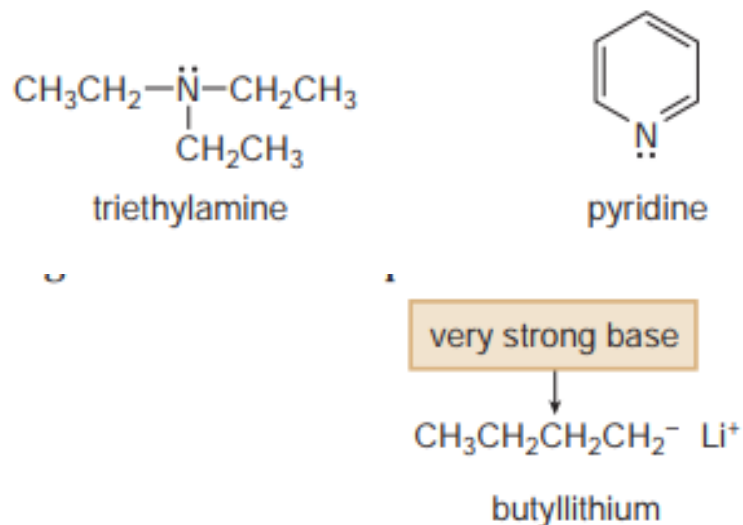
Two organic acids are also commonly used, namely **acetic acid** and ***p*-toluenesulfonic acid** (usually abbreviated as **TsOH**). Although acetic acid has a higher p*K<sub>a</sub>* than the inorganic acids, making it a weaker acid, it is more acidic than most organic compounds. *p*-Toluenesulfonic acid is similar in acidity to the strong inorganic acids. Because it is a solid, small quantities can be easily weighed on a balance and then added to a reaction mixture.



acetic acid  
p*K<sub>a</sub>* = 4.8

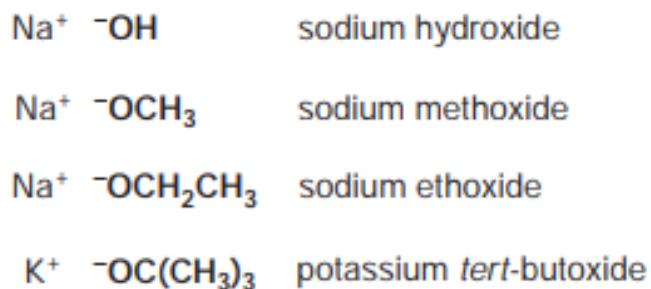


Two other weaker organic bases are **triethylamine** and **pyridine**. These compounds have a lone pair on nitrogen, making them basic, but they are considerably weaker than the amide bases because they are neutral, not negatively charged.

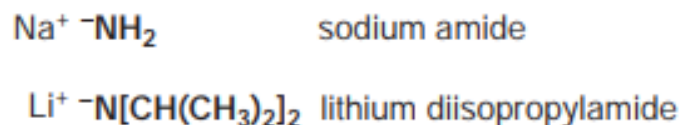


**Figure 2.6**  
Some common negatively charged bases

oxygen bases



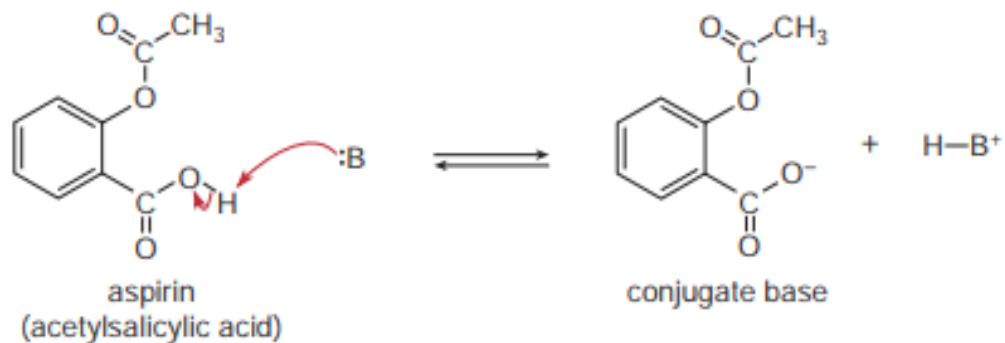
nitrogen bases



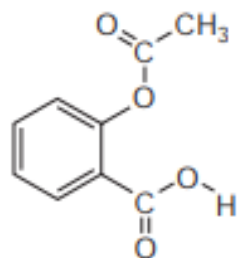
hydride



Like many drugs, aspirin is capable of undergoing a proton transfer reaction. Its most acidic proton is the H bonded to O, and in the presence of base, this H is readily removed.

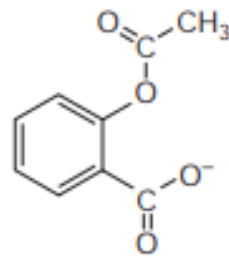


Why is this acid–base reaction important? After ingestion, aspirin first travels into the stomach and then the intestines. In the acidic environment of the stomach, aspirin remains in its neutral form, but in the basic environment of the small intestine, aspirin is deprotonated to form its conjugate base, an ion.



acetylsalicylic acid  
neutral form

This form exists in the **stomach**.

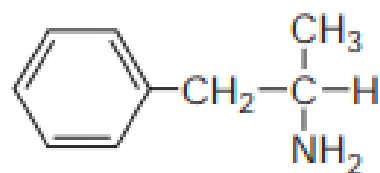


conjugate base  
ionic form

This form exists in the **intestines**.

Whether aspirin is present as its acid or its conjugate base is very important in determining whether it can permeate a cell. **To be active, aspirin must cross a cell membrane, and to do so,**

## Problem 2.22



amphetamine

Compounds like amphetamine that contain nitrogen atoms are protonated by the HCl in the gastric juices of the stomach, and the resulting salt is then deprotonated in the basic environment of the intestines to regenerate the neutral form. Write proton transfer reactions for both of these processes.

Where is amphetamine likely to be absorbed by the body?

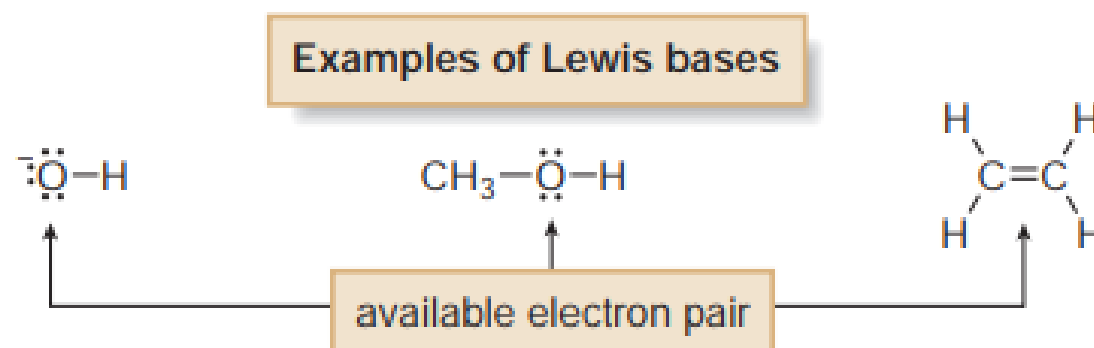
## 2.8 Lewis Acids and Bases

The Lewis definition of acids and bases is more general than the Brønsted–Lowry definition.

- A Lewis acid is an *electron pair acceptor*.
- A Lewis base is an *electron pair donor*.

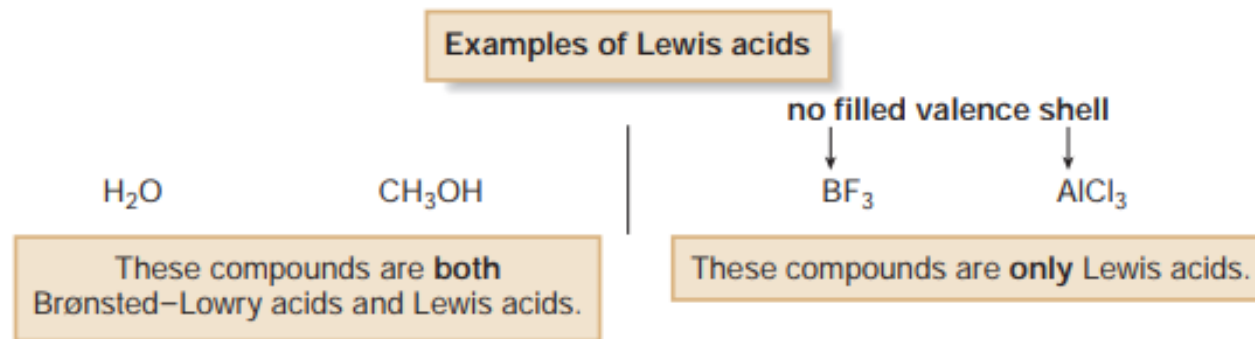
**Lewis bases are structurally the same as Brønsted–Lowry bases.** Both have an **available electron pair**—a lone pair or an electron pair in a  $\pi$  bond. A Brønsted–Lowry base always donates this electron pair to a proton, but a Lewis base donates this electron pair to anything that is electron deficient.

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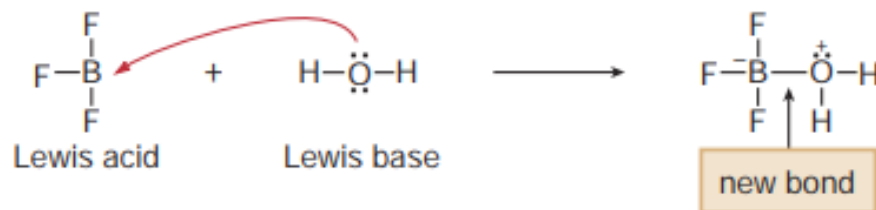


**A Lewis acid must be able to accept an electron pair**, but there are many ways for this to occur. **All Brønsted–Lowry acids are also Lewis acids, but the reverse is not necessarily true.** Any species that is electron deficient and capable of accepting an electron pair is also a Lewis acid.

Common examples of Lewis acids (which are not Brønsted–Lowry acids) include  $\text{BF}_3$  and  $\text{AlCl}_3$ . These compounds contain elements in group 3A of the periodic table that can accept an electron pair because they do not have filled valence shells of electrons.



**In the simplest Lewis acid–base reaction one bond is formed and no bonds are broken.** This is illustrated with the reaction of  $\text{BF}_3$  with  $\text{H}_2\text{O}$ .  $\text{BF}_3$  has only six electrons around B, so it is the electron-deficient Lewis acid.  $\text{H}_2\text{O}$  has two lone pairs on O, so it is the electron-rich Lewis base.



**$\text{H}_2\text{O}$  donates an electron pair to  $\text{BF}_3$  to form one new bond.** The electron pair in the new B–O bond comes from the oxygen atom, and a single product is formed. Both B and O bear formal charges in the product, but the overall product is neutral.

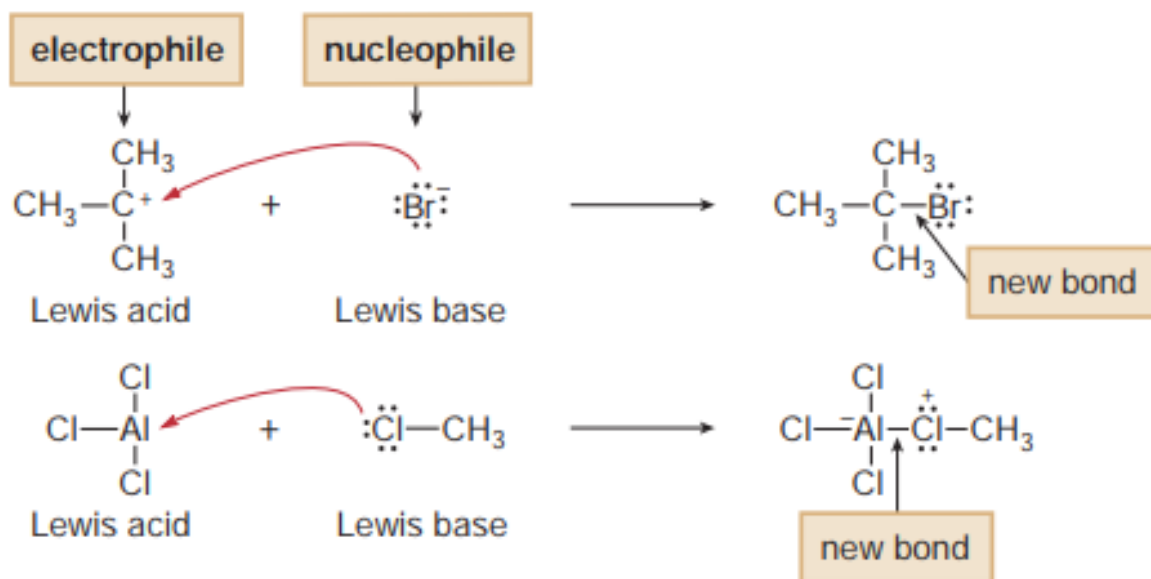
Nucleophile = nucleus loving.

Electrophile = electron loving.

- A Lewis acid is also called an *electrophile*.
- When a Lewis base reacts with an electrophile other than a proton, the Lewis base is also called a *nucleophile*.

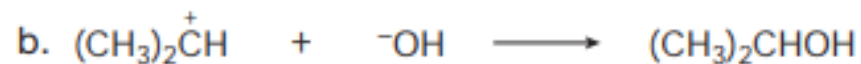
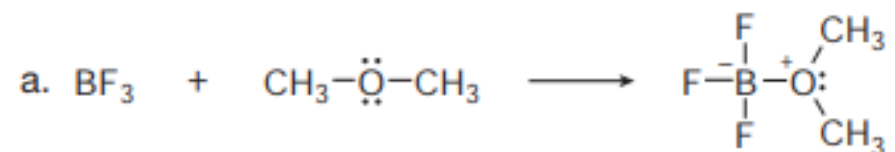
In this Lewis acid–base reaction, **BF<sub>3</sub> is the electrophile** and **H<sub>2</sub>O is the nucleophile**.

Two other examples are drawn. In each reaction the **electron pair is not removed from the Lewis base**; instead, the electron pair is donated to an atom of the Lewis acid, and one new covalent bond is formed.



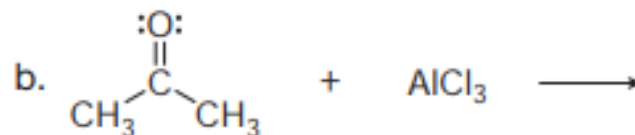
### Problem 2.25

For each reaction, label the Lewis acid and base. Use curved arrow notation to show the movement of electron pairs.



### Problem 2.26

Draw the products of each reaction, and label the nucleophile and electrophile.





## *Key Concepts—Acids and Bases*

### A Comparison of Brønsted–Lowry and Lewis Acids and Bases

Type	Definition	Structural feature	Examples
Brønsted–Lowry acid (2.1)	proton donor	a proton	HCl, H <sub>2</sub> SO <sub>4</sub> , H <sub>2</sub> O, CH <sub>3</sub> COOH, TsOH
Brønsted–Lowry base (2.1)	proton acceptor	a lone pair <i>or</i> a $\pi$ bond	<sup>-</sup> OH, <sup>-</sup> OCH <sub>3</sub> , H <sup>+</sup> , <sup>-</sup> NH <sub>2</sub> , NH <sub>3</sub> , CH <sub>2</sub> =CH <sub>2</sub>
Lewis acid (2.8)	electron pair acceptor	a proton, <i>or</i> an unfilled valence shell, <i>or</i> a partial (+) charge	BF <sub>3</sub> , AlCl <sub>3</sub> , HCl, CH <sub>3</sub> COOH, H <sub>2</sub> O
Lewis base (2.8)	electron pair donor	a lone pair <i>or</i> a $\pi$ bond	<sup>-</sup> OH, <sup>-</sup> OCH <sub>3</sub> , H <sup>+</sup> , <sup>-</sup> NH <sub>2</sub> , NH <sub>3</sub> , CH <sub>2</sub> =CH <sub>2</sub>