

Chapter 4

Acids and Bases

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As stated in Chapter 1, the structure of a molecule determines its reactivity. In the first three chapters the structures of organic molecules were carefully examined. A deep understanding of their wonderful complexity developed through the ideas of bonding, charges, resonance, orbital hybridization, bond angles and lengths, polarity, conformations, and stereochemistry. Knowing the structural possibilities of organic molecules, we can now pursue the second half of the dual nature of molecules: reactivity. Indeed, the reactions of organic molecules compose most of the remaining agenda of this book. When dealing with reactions, however, we will whenever possible base the reactivity of a molecule on its structure.

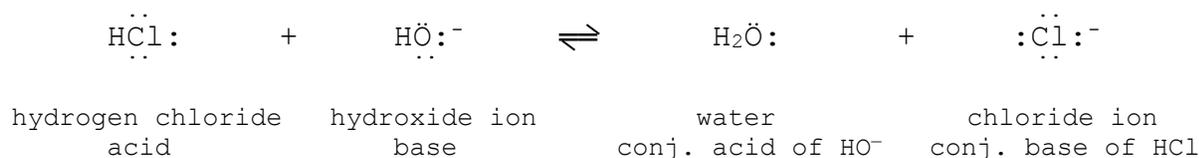
Our first exploration of reactions treats a subject already encountered in general chemistry. Acids and bases are fundamentally important to both general and organic chemistry. They have been defined in various ways as chemistry has developed over the last hundred years. For organic chemistry we must master the two theories of acids and bases presented in this chapter. In fact, one of these theories provides the key concept for our whole study of organic chemical reactions.

4.1 Brønsted-Lowry Theory of Acids and Bases

No doubt, you already learned the **Brønsted-Lowry** (or simply **Brønsted**) theory of acids and bases in general chemistry (Johannes N. Brønsted, Denmark, 1879-1947; Thomas M. Lowry, England, 1874-1936). Indeed, organic chemists usually consider acids and bases in light of this theory.

4.1A Definitions of Brønsted Acids and Bases

What is an acid or a base? By the Brønsted theory the acid and base exchange a proton, that is, a hydrogen cation, H^+ . *An acid donates a proton to a base; a base takes the proton.* Here is a familiar example:



Hydrogen chloride is the acid because it donates a proton to hydroxide ion. Hydroxide reacts as the base by bonding to the proton. The Brønsted theory also involves the products. Water is the **conjugate acid** of hydroxide ion because it can revert to hydroxide ion by donating a proton to a base. Similarly, chloride ion is the **conjugate base** of hydrogen chloride because it can become hydrogen chloride by accepting a proton from an acid.

Reversing this analysis, we see that hydroxide ion is the conjugate base of water and that hydrogen chloride is the conjugate acid of chloride ion. In a sense, the two bases, one on each side of the equilibrium, compete for one proton. Hydroxide ion and chloride ion try to take a proton from each other's conjugate acid. So, in theory the above reaction, like any acid-base reaction, is reversible. In most actual acid-base reactions, however, either the forward or the backward reaction predominates.

Puzzle 4.1

For each of the following acid-base reactions, identify the acid and the base on each side of the equilibrium.

- (a) $H_2O + NH_3 \rightleftharpoons HO^- + {}^+NH_4$
 (b) $H_2O + H_2SO_4 \rightleftharpoons H_3O^+ + HSO_4^-$
 (c) $H_2S + HNO_3 \rightleftharpoons H_3S^+ + NO_3^-$
 (d) $H_2S + HO^- \rightleftharpoons HS^- + H_2O$
 (e) $NH_3 + H^- \rightleftharpoons {}^-NH_2 + H_2$

Puzzle 4.2

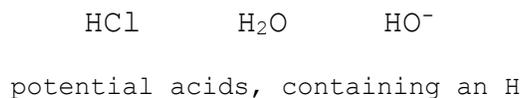
Draw the products of each reaction and identify the acid and base among the products. Assume the first reactant is the base in each case.

- (a) $CH_3NH_2 + HF \rightleftharpoons$ (b) $N\equiv C^- + CH_3NH_3^+ \rightleftharpoons$
 (c) $CH_3O^- + CH_3OH \rightleftharpoons$ (d) $CH_3NH^- + HC\equiv CH \rightleftharpoons$

4.1B Structures of Brønsted Acids and Bases

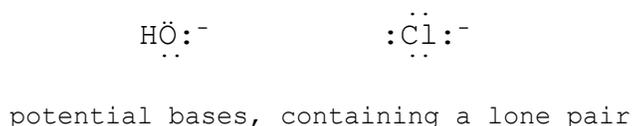
What distinguishes the structure of a Brønsted acid? To be able to donate a proton, a molecule must contain a hydrogen atom. Thus, of the molecules in the above reaction, hydrogen

chloride, water and even hydroxide ion (under extreme conditions) are potential acids.

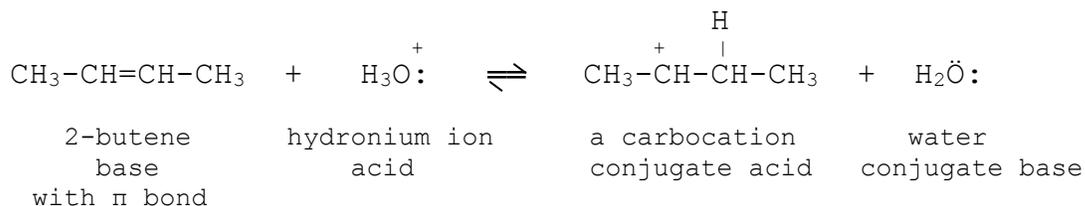


The extent to which a potential acid actually donates a proton depends on its strength and the strength of the base present, as discussed in Section 4.4.

What distinguishes the structure of a Brønsted base? Consider the bases on either side of the reaction of Section 4.1A. What structural feature enables the hydroxide and chloride ions to accept a hydrogen cation? It is not a negative charge. Not every base has a negative charge, although that feature does increase base strength. A more essential factor operates here: a lone electron pair.



By forming the bond between the base and the donated proton, a lone pair makes each of the above two ions a base. In a second, less common type of base, a π electron pair from a carbon-carbon double or triple bond can bond to the donated proton:



Can a molecule be an acid in one reaction but a base in another? Consider water. In the reverse of the earlier reaction between hydrogen chloride and hydroxide ion, water reacts as an acid with the base, chloride ion. But could it also react as a base in the presence of an acid? Yes, because it has lone pairs, either of which can take a proton from a strong enough acid. Thus, in the reverse of the last reaction above, water picks a proton from a carbocation to become hydronium ion. The nature of the other reactant determines whether a "two-faced" molecule such as water, which contains both a hydrogen atom and a lone pair, reacts as an acid or base.

Puzzle 4.3

Draw the conjugate acid and the conjugate base of each of the following molecules. If either conjugate form does not exist, say so.

- (a) NH_3 (b) $^+\text{NH}_4$ (c) $^-\text{NH}_2$ (d) CH_3OH (e) HO^- (f) H_3O^+ (g) CH_4 (h) $^-\text{CH}_3$
 (i) $^+\text{CH}_3$ (j) HCl (k) Br_2 (l) $\text{CH}_2=\text{CH}_2$

4.2 Acidities

What does **acidity** (i.e., acid strength) mean and how can we quantify it? Acidity is the tendency to donate a proton. The stronger this tendency is, the stronger the acid. Sulfuric acid, H_2SO_4 , is a strong acid because it readily donates a proton even to weak bases, such as water. This tendency can be quantified by an equilibrium constant. Consider the following equilibrium, which depicts donation of a proton to water to form hydronium ion (i.e., a hydrated proton,

$\text{H}_2\text{O}-\text{H}^+$):



The equilibrium constant for this acid dissociation in water is called the acidity constant, K_a . Like other equilibrium constants it is expressed in terms of product and reactant concentrations at equilibrium:

$$K_a = \frac{[\text{HSO}_4^-][\text{H}_3\text{O}^+]}{[\text{H}_2\text{SO}_4]}$$

(Being approximately constant, the concentration of water solvent is omitted from the equilibrium constant.) Among various acids, as the tendency to dissociate and donate a proton to water increases, so does K_a . Thus K_a values allow quantitative comparisons of acidity.

Sometimes $\text{p}K_a$ values replace K_a values. Similar to the equation relating proton concentration to pH, an equation transforms K_a into $\text{p}K_a$:

$$\text{p}K_a = -\log K_a$$

For example, the K_a of sulfuric acid is 10^9 , while its $\text{p}K_a$ is -9. We will use K_a , not $\text{p}K_a$, values because they directly reflect acidity, whereas $\text{p}K_a$ values vary inversely with acidity:

as $K_a \uparrow$, acidity \uparrow but $\text{p}K_a \downarrow$

Table 4.1 presents K_a and $\text{p}K_a$ values for a wide variety of inorganic and organic molecules. With this table we may compare acidities of any two acids listed. For example, the strong acid sulfuric acid is found to be $10^9/10^7 = 100$ times more acidic than the strong acid hydrogen chloride, according to K_a values of the two acids.

Table 4.1 K_a and pK_a Values for Various Acids

Acid	K_a	pK_a	Acid	K_a	pK_a
${}^+\text{PH}_4$	10^{14}	-14	H_2S	1×10^{-7}	7.0
HI	10^{10}	-10	$\begin{array}{c} \text{O} \\ \parallel \\ \text{HO}-\text{P}-\text{O}^- \\ \\ \text{OH} \end{array}$	6×10^{-8}	7.2
$\begin{array}{c} \text{O} \\ \parallel \\ \text{HO}-\text{S}-\text{OH} \\ \parallel \\ \text{O} \end{array}$	10^9	-9	$\begin{array}{c} \text{O} \quad \text{O} \\ \parallel \quad \parallel \\ \text{H}_3\text{CC}-\text{CH}_2-\text{CCH}_3 \end{array}$	1×10^{-9}	9.0
HBr	10^9	-9	$\text{HC}\equiv\text{N}$	6×10^{-10}	9.2
$\begin{array}{c} {}^+\text{OH} \\ \parallel \\ \text{H}_3\text{C}-\text{C}-\text{CH}_3 \end{array}$	10^7	-7	${}^+\text{NH}_4$	5×10^{-10}	9.3
HCl	10^7	-7	$\text{Ph}-\text{OH}$	1×10^{-10}	10.0
$\begin{array}{c} {}^+ \\ \text{H}_3\text{C}-\text{OH}_2 \end{array}$	10^2	-2	$\begin{array}{c} \text{O} \\ \parallel \\ \text{HO}-\text{C}-\text{O}^- \end{array}$	6×10^{-11}	10.2
H_3O^+	5×10	-1.7	$\begin{array}{c} \text{O} \\ \parallel \\ \text{H}_3\text{C}-\text{N}-\text{O}^- \\ + \end{array}$	6×10^{-11}	10.2
$\begin{array}{c} \text{O} \\ \parallel \\ \text{HO}-\text{N}-\text{O}^- \\ + \end{array}$	2×10	-1.3	$\begin{array}{c} \text{O} \\ \parallel \\ \text{H}_3\text{C}-\text{NH}_3 \\ + \end{array}$	2×10^{-11}	10.7
$\begin{array}{c} \text{O} \\ \parallel \\ \text{Ph}-\text{S}-\text{OH} \\ \parallel \\ \text{O} \end{array}$	4	-0.6	HSe^-	1×10^{-11}	11.0
$\begin{array}{c} \text{O} \\ \parallel \\ \text{HO}-\text{P}-\text{OH} \\ \\ \text{OH} \end{array}$	8×10^{-3}	2.1	HS^-	1×10^{-13}	13.0
HF	6×10^{-4}	3.2	$\text{H}-\text{Cyclopentadiene}$	3×10^{-16}	15.5
$\text{HO}-\text{N}=\text{O}$	5×10^{-4}	3.3	$\text{H}_3\text{C}-\text{OH}$	3×10^{-16}	15.5
H_2Se	1×10^{-4}	4.0	H_2O	2×10^{-16}	15.7
$\begin{array}{c} {}^+ \\ \text{Ph}-\text{NH}_3 \end{array}$	3×10^{-5}	4.5	$\begin{array}{c} \text{O} \\ \parallel \\ \text{H}_3\text{C}-\text{C}-\text{CH}_3 \end{array}$	10^{-20}	20
$\begin{array}{c} \text{O} \\ \parallel \\ \text{H}_3\text{C}-\text{C}-\text{OH} \end{array}$	2×10^{-5}	4.7	$\text{H}_3\text{C}-\text{C}\equiv\text{N}$	10^{-25}	25
$\text{C}_6\text{H}_5\text{NH}^+$	6×10^{-6}	5.2	$\text{HC}\equiv\text{CH}$	10^{-25}	25
$\begin{array}{c} \text{O} \\ \parallel \\ \text{HO}-\text{C}-\text{OH} \end{array}$	4×10^{-7}	6.4	NH_3	10^{-34}	34
			H_2	10^{-35}	35
			$\text{Ph}-\text{CH}_3$	10^{-41}	41
			$\text{H}_2\text{C}=\text{CH}_2$	10^{-44}	44
			CH_4	10^{-50}	50

The K_a scale is based on the tendency of an acid to donate a proton to water when water is the solvent. This is indeed the standard and a very useful scale. Of course, acids can also donate protons to bases in solvents other than water. In other solvents the acidity constants change, sometimes dramatically. Yet, because water is such a common solvent and because the K_a scale based on aqueous solvent is so well established, we will use this scale and assume that acid-base reactions occur in water.

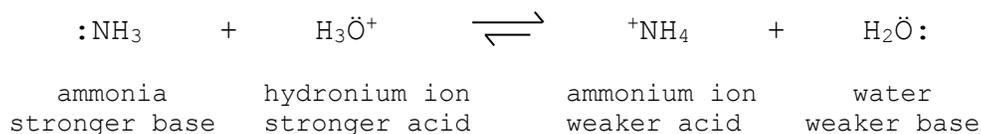
Puzzle 4.4

Decide which acid in each pair is stronger. Use Table 4.1.

(a) $\text{HNO}_3, \text{HNO}_2$ (b) $\text{H}_2\text{O}, \text{H}_3\text{O}^+$ (c) NH_3, CH_4 (d) $\text{H}_2\text{O}, \text{H}_2\text{S}$

4.3 Basicities

Now that we know how to assess relative strengths of acids, let us do the same with bases. **Basicity** (i.e., base strength) is the tendency to acquire a proton. The stronger this tendency is, the stronger the base. How can we compare basicities? Although a basicity scale (i.e., K_b) analogous to the K_a acidity scale does exist, we shall instead use the K_a scale to quantitatively compare basicities. Consider ammonia reacting as a base by taking a proton from hydronium ion:

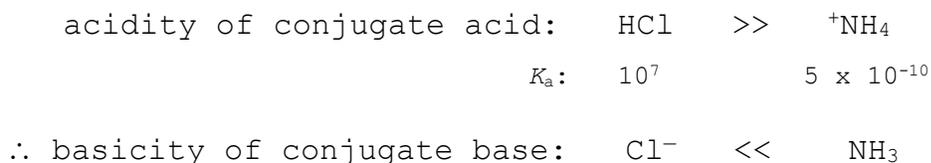


Ammonia is known to be a stronger base than water, the base on the product side of the equilibrium. Because ammonia more readily accepts a proton to become ammonium ion, ammonium ion must release a proton more reluctantly than does hydronium ion, the conjugate acid of water. In Table 4.1 note that its K_a of 5×10^{-10} makes ammonium ion a weaker acid than hydronium ion with its K_a of 50. Thus, the stronger basicity of ammonia directly reflects the weaker acidity of its conjugate acid. This relationship between a base and its conjugate acid is entirely general:

as conjugate acid's acidity ↓, base's basicity ↑

Therefore, we can use Table 4.1, not only to gauge the acidity of acids, but also to quantify the basicity of conjugate bases of those acids.

Suppose that we want to know if chloride ion is a weaker or stronger base than ammonia. By Table 4.1 the *conjugate acid* of chloride ion, hydrogen chloride, has a K_a value of 10^7 . Clearly, hydrogen chloride is a much stronger acid than ammonium ion. Therefore, chloride ion must be a much weaker base than ammonia.



This inversion of strengths for acids and bases applies to *conjugate* forms only. This principle must be carefully applied to an amphoteric molecule, which can serve as an acid and a base. If compounds A and B are amphoteric and A is a stronger acid than B, we *cannot* conclude that A is a weaker base than B.

**as a molecule's acidity ↓, its *conjugate base's* basicity ↑
but the *original molecule's* basicity ?**

Likewise, if amphoteric C is more basic than amphoteric D, we know nothing about their relative acidities.

as a molecule's basicity ↓, its *conjugate acid's* acidity ↑ but the *original molecule's* acidity ?

For example, Table 4.1 indicates that hydrogen carbonate ion, HOCO_2^- , with a K_a of 6×10^{-11} is a stronger acid than water with a K_a of 2×10^{-16} . Accordingly, carbonate anion, CO_3^{2-} is a weaker base than hydroxide anion, HO^- . Yet, we can deduce nothing about the relative basicities of the acids themselves, hydrogen carbonate ion and water.

acidity of molecule:	HOCO_2^-	>	H_2O
K_a :	6×10^{-11}		2×10^{-16}
\therefore basicity of conjugate base:			
	CO_3^{2-}	<	HO^-
\therefore basicity of original molecule:			
	HOCO_2^-	?	H_2O

As a matter of fact, HOCO_2^- is a stronger base than H_2O , as the K_a values of their conjugate acids indicate: 4×10^{-7} for HOCO_2H , 5×10 for H_3O^+ . Remarkably, hydrogen carbonate ion is both a stronger acid and a stronger base than water! If carefully used, Table 4.1 can also serve as a table of basicities of conjugate bases.

Puzzle 4.5

Decide which base in each pair is stronger. Use Table 4.1.

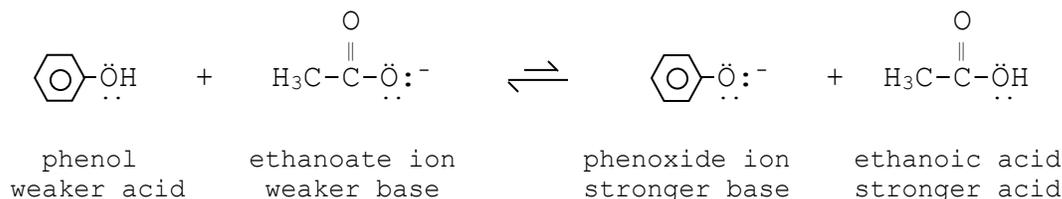
(a) CH_3OH , CH_3O^- (b) $\text{C}_6\text{H}_5\text{NH}_2$, CH_3NH_2 (c) F^- , Cl^- (d) HO^- , H_2N^-

4.4 Acid-Base Equilibria

We already know that every acid-base reaction is reversible in theory, so that an equilibrium is eventually reached. How can we predict whether a given acid-base reaction or its reverse occurs to the greater extent? An important thermodynamic principle provides the answer. Stable molecules are low in energy and react poorly. On the other hand, stable, low-energy molecules are easy to produce. Therefore:

as stability ↑, energy ↓ and reactivity ↓ but product yield ↑

Let us decide the favorable direction for the following acid-base equilibrium:

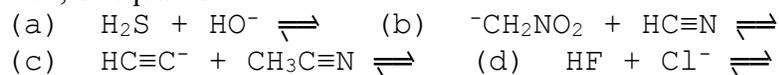


Of the two acids reacting in this equilibrium, phenol and ethanoic (i.e., acetic) acid, the stronger will react to a greater extent because of its greater energy and lower stability. According to Table 4.1, ethanoic acid has the larger K_a (2×10^{-5} vs. 1×10^{-10}) and so reacts to a greater extent. The base, phenoxide ion that reacts with the stronger acid is also stronger than the opposing base, ethanoate ion, on the other side of the equilibrium. Finding the stronger acid and stronger base on the same side of the equilibrium is not a coincidence, but results from the reciprocity of acid-base relationships. The stronger of the two acids necessarily reacts with the stronger of the two bases on one side or other of any acid-base equilibrium. Consequently, we need only identify either the stronger acid or the stronger base to determine the favored direction of equilibrium. In our present example the reverse reaction involving the stronger acid (ethanoic acid) and stronger base (phenoxide ion) proceeds farther than the forward reaction until equilibrium is reached. The equilibrium constant, K , is less than 1. In other words, at equilibrium the more stable molecules, phenol and ethanoate ion, have greater concentrations than do the less stable molecules on the other side of the equilibrium.

We might call this the principle of "survival of the weakest," in contrast to evolution's "survival of the fittest." In chemistry it is the weaker, more stable, less energetic molecules that predominate at equilibrium because they react less, whereas the stronger, less stable, more energetic molecules diminish themselves by reacting more.

Puzzle 4.6

Draw the products of each reaction. Then using Table 4.1, determine if the K is greater than, less than, or equal to 1.

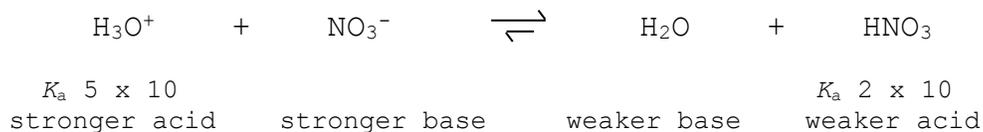


4.5 Successful Acid-Base Reactions

How strong must acids and bases be to react to a favorable extent? From the discussion in the preceding section, we know that an acid-base equilibrium favors the forward reaction if the acid and base reactants are stronger than the products. How strong of a base is needed for a favorable reaction (i.e., $K > 1$) with a given acid? For example, what basicity would allow favorable reaction with ammonium ion, $^+\text{NH}_4$? Ammonium ion has a K_a of 5×10^{-10} . If the acid produced in an acid-base reaction is to be weaker than ammonium ion, it must have a K_a less than 5×10^{-10} . Accordingly, the base reactant must be the conjugate base of this weaker acid product. For example phenoxide ion, $\text{C}_6\text{H}_5\text{O}^-$, is a strong enough base:



Now let us consider a strong acid, such as hydronium ion, H_3O^+ . What basicity is needed for a favorable reaction with hydronium ion? Hydronium ion has a K_a of 5×10^{-10} in Table 4.1. Therefore, a weaker acid product must have a K_a less than 5×10^{-10} . An appropriate base reactant would have this weaker acid as a conjugate acid. The weakest base in Table 4.1 that qualifies is nitrate ion, the conjugate base of nitric acid, HNO_3 . Thus, this reaction would be favorable:



Let us find a suitable acid for hydrogen carbonate ion base, HCO_3^- . Its conjugate acid, carbonic acid (H_2CO_3), would be the acid produced in the reaction. An appropriate acid reactant must be stronger than this conjugate acid, which has a K_a of 4×10^{-7} . The weakest acid in Table 4.1 that would react favorably is pyridinium ion, $\text{C}_5\text{H}_5\text{NH}^+$:



Puzzle 4.7

Find the weakest base in Table 4.1 that would favorably react with each of these acids.
 (a) HCl (b) $\text{CH}_3\text{CO}_2\text{H}$ (c) H_2O (d) NH_3

Puzzle 4.8

Find the weakest acid in Table 4.1 that would favorably react with each of the following bases.
 (a) Cl^- (b) CH_3CO_2^- (c) HO^- (d) NH_3

4.6 Absolute Acid and Base Strengths

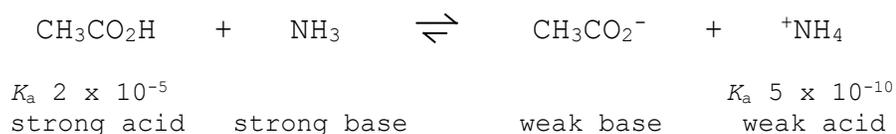
Having established the K_a scale for determining *relative* acidities and basicities, can we establish a reasonable, absolute standard for distinguishing strong from weak acids and strong from weak bases? Such a standard would ideally satisfy these five criteria:

1. Any strong acid has a weak conjugate base and any weak acid has a strong conjugate base.
2. Any strong acid reacts with any strong base in a favorable equilibrium with $K > 1$.
3. Any weak acid reacts with any weak base in an unfavorable equilibrium with $K < 1$.
4. Combining an equal number of moles of any weak acid and any strong base yields a basic solution with $\text{pH} > 7$.

5. Combining an equal number of moles of any strong acid and any weak base yields an acidic solution with $\text{pH} < 7$.

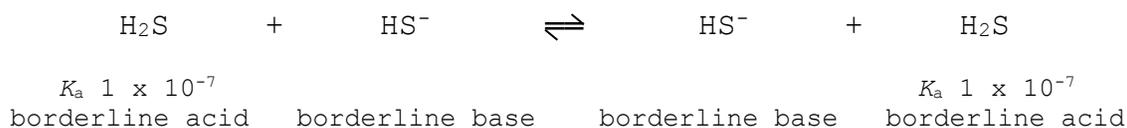
The above criteria seem reasonable and intuitive. Yet, general chemistry texts fail to meet them when they state that strong acids dissociate completely in water. It turns out that the only standard that satisfies all five of the above criteria is much different: *an acid is strong if and only if it has a $K_a > 10^{-7}$; an acid is weak if and only if it has a $K_a < 10^{-7}$. A strong base has a weak conjugate acid, and a weak base has a strong conjugate acid.* We will use this standard throughout this text to make the chemistry more rational and intuitive.

Clearly, this standard observes the first criterion above. Proving that it also satisfies the other four criteria lies beyond the scope of this text. Yet, we can illustrate the value of this standard with a couple of examples.



Because $\text{CH}_3\text{CO}_2\text{H}$ has a $K_a > 10^{-7}$, it is a strong acid. NH_3 is a strong base because its conjugate acid, $^+\text{NH}_4$, has a K_a of 5×10^{-10} , less than 10^{-7} . The equilibrium constant for this reaction is 4×10^4 , consistent with expectations for the reaction between two strong reactants and with criterion 2 above. Yet, general chemistry texts call these two reactants weak!

A borderline case also shows the value of the $K_a = 10^{-7}$ dividing line.



Because the products match the reactants, this may seem a trivial example, but actually it shows the value of our standard. An equal number of moles of the two reactants of borderline strength make a buffer solution of $\text{pH} 7$, consistent with the reactants' equal strength. Any K_a dividing line other than 10^{-7} would make one reactant strong and the other one weak in violation of criterion 4 or 5.

According to this standard, a less reactive, weak acid reacts successfully only with a very reactive, strong base. In contrast, a more reactive, strong acid can react with either a strong or a weak (but not too weak) base. The same pattern applies to acids suitable for a given kind of base. *In general, if one reactant is very reactive, the other reactant can be less reactive. For a successful acid-base reaction with $K > 1$, either the acid or the base reactant or both must be strong.* Otherwise, if both reactants are weak, the acid and base products will be strong, ensuring a poor reaction.

Puzzle 4.9

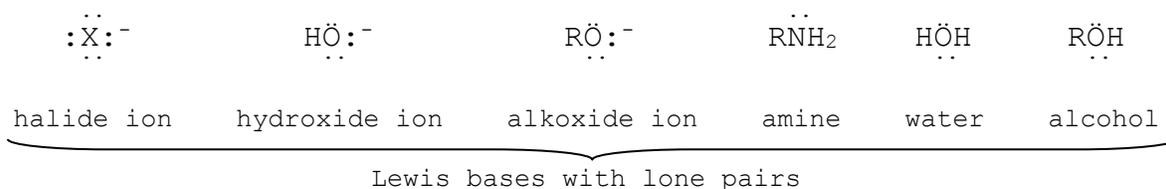
- (a) Which acid reactants in Puzzle 4.4 are strong?
 (b) Which base reactants in Puzzle 4.5 are strong?

Puzzle 4.10

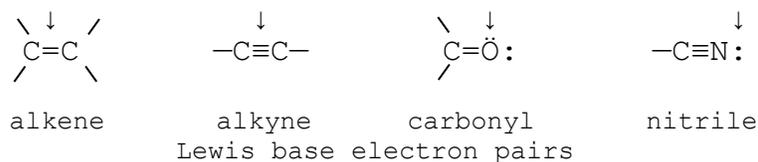
(a) Is methane a strong acid? Explain. (b) Is methane a strong base? Explain.

4.7 Lewis Theory of Acids and Bases

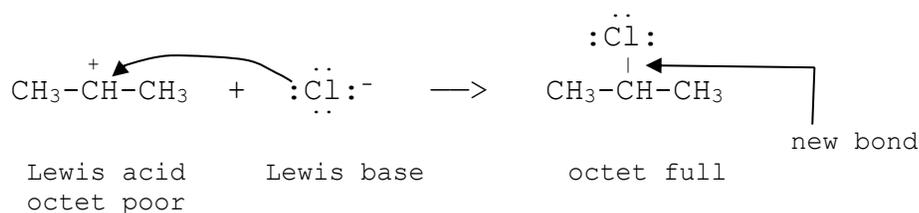
We next turn to our second theory of acids and bases: the Lewis theory (Gilbert N. Lewis, USA, 1875-1946). As an electron pair donor, a Lewis base brings an electron pair to a Lewis acid to form a bond. Lewis bases must be electron-rich in order to offer an electron pair for bonding. The first type of Lewis base carries a lone pair. Because it is exposed and not constrained in a bond, a lone pair provides the more common kind of Lewis base. Here are examples of this type of Lewis base:



The electron pair in a carbon-carbon π bond provides a second, less common type of Lewis base. Compared to a σ bond, a π bond is relatively weak and exposed in an electron-rich region with at least four electrons. So, it can break and its electron pair can bond to a Lewis acid. Alkenes and alkynes compose this class of Lewis base. In contrast, carbon-oxygen and carbon-nitrogen π bonds rarely donate their π electron pairs because the lone pairs on the oxygen or nitrogen atom are more exposed and reactive. Arrows mark the Lewis base electron pairs in these molecules:



A Lewis acid is the other half of the story. By accepting the electron pair with the Lewis base, it bonds to the base. In contrast to electron-rich Lewis bases, Lewis acids are generally electron-poor. So these opposites naturally attract and react. Some Lewis acids have an empty orbital, which bonds with the incoming electron pair. For example, a **carbocation** has a carbon with a positive charge and an empty $2p$ orbital and can react with a Lewis base, such as chloride ion:



Without a full octet, the carbocation simply forms a σ bond with the Lewis base to complete its

electrophile and nucleophile, inherited from the Lewis theory, are not only general, but also powerful. In fact, *they are the single most important concept for organic chemical reactions*. Almost every reaction in this book can and will be viewed as a reaction between a nucleophile and an electrophile.

Puzzle 4.13

Label each reactant in Puzzles 4.11 and 4.12 as a nucleophile or electrophile. For each nucleophile identify the electron pair that is the nucleophilic agent. For each electrophile identify the atom that bonds to the nucleophile.

4.9 Hard and Soft Electrophiles and Nucleophiles

As we know, the strengths of acids and bases can be evaluated by K_a values. Yet, no numerical scale measures the strengths of nucleophiles and electrophiles. Whereas a base bonds only to a proton from an acid, a nucleophile can bond to a wide variety of atoms in various electrophiles. No single scale of nucleophilicity (i.e., nucleophilic strength) can suit so many kinds of electrophiles.

One theory does account for different kinds of electrophiles by distinguishing between so-called **hard** and **soft** electrophiles and nucleophiles. A harder electrophile has an electrophilic atom that has more positive charge density. Charge density is the ratio of atomic charge to atomic volume.

charge density \uparrow as atomic charge \uparrow and as atomic volume \downarrow

For example, the more highly charged Fe^{3+} ion is a harder electrophile with a greater charge density than Fe^{2+} ion. Also the smaller Li^+ ion has larger charge density and hardness than Na^+ ion.

A softer electrophile has an electrophilic atom that has less positive charge density. A harder nucleophile has its nucleophilic electron pair on an atom that has more negative charge density. A softer nucleophile has its nucleophilic electron pair on an atom that has less negative charge density. Note that we examine the reacting *atom*, not the whole reactant molecule. Table 4.2 displays the characteristics of harder and softer reactants.

Table 4.2 Properties of Harder and Softer Reactants

Reactant	Harder	Softer
Electrophilic atom:	More + charge density	Less + charge density
- - - - -		
Nucleophilic atom:	More - charge density	Less - charge density

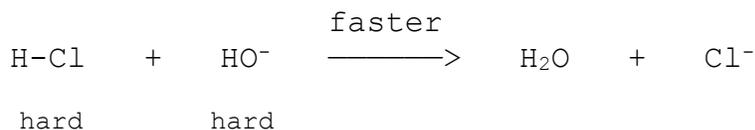
For example, hydrogen sulfide ion, HS^- , is a softer nucleophile than hydroxide ion, HO^- ,

because sulfur is larger than oxygen. For the same reason, chloride ion is a softer nucleophile than fluoride ion. Among electrophiles hydrogen chloride is harder than chloromethane because hydrogen is a smaller electrophilic atom than is carbon.

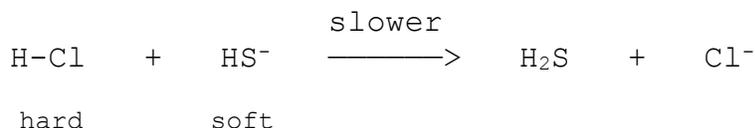
Hard nucleophiles and hard electrophiles share the attributes of densely charged reaction sites. Soft nucleophiles and soft electrophiles feature sparsely charged reaction sites:

as charge density ↑, hardness ↑

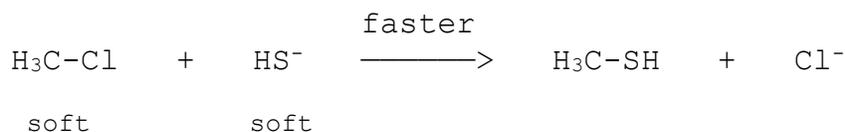
These pairs of reactants also share reactivity: *soft nucleophiles react better with soft electrophiles; hard nucleophiles react better with hard electrophiles*. Acids (Brønsted) are generally hard electrophiles because of their tiny reaction site, a hydrogen. Thus, an acid tends to react faster with a hard base nucleophile:



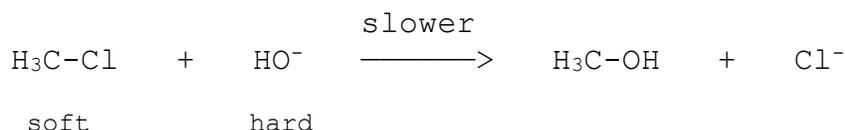
than with a soft base nucleophile:



Likewise two soft reactants tend to react faster:



than reactants of different hardness:



Puzzle 4.14

In each pair of electrophiles, determine which is harder.

- (a) Be^{2+} , Mg^{2+} (b) Na^+ , Mg^{2+} (c) BH_3 , BF_3 (d) CH_3Cl , CH_3F
 (e) $\text{CH}_3\text{CH}_2\text{Cl}$, $\text{CH}_3\text{C}(=\text{O})\text{Cl}$

Puzzle 4.15

In each pair of nucleophiles, determine which is harder.

(a) Cl^- , Br^- (b) $\text{N}(\text{CH}_3)_3$, $\text{P}(\text{CH}_3)_3$ (c) H_2O , HO^- (d) NH_3 , H_2O

4.10 Structural Influences on Acid and Base Strengths

Sometimes we wish to compare acidities or basicities when appropriate K_a values are not available, or we want to understand why one K_a value surpasses another. Then we must return to the axiom: *structure determines reactivity*. Let us apply this axiom to several acid or base comparisons, without using K_a values. Because structural factors operate more clearly in bases than in acids and because basicities of bases reflect acidities of conjugate acids (Section 4.3), *we will normally compare bases instead of acids*, even when the puzzle involves acids.

4.10A Influence of Base Atom's Hardness

Suppose that we wish to rank the acidities of the hydrogen halides: hydrogen fluoride, hydrogen chloride, hydrogen bromide and hydrogen iodide. This is easy to do with Table 4.1, but now we want to solve the puzzle by structure, not by K_a value. The first step is to convert these acids to their more easily analyzed conjugate bases:



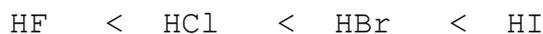
The atoms holding the base lone pairs are all from the same column of the periodic table. What factor affects the base electrons of the lone pairs differently? The size of an atom with the lone pairs increases dramatically with distance down the column. As the size increases, charge density and hardness decrease, and ability of the base electrons to react with an acid, which is a hard electrophile, decreases:

as hardness of base atom ↓, ability of base e's to pluck H^+ ↓ & basicity ↓

Thus:



relative basicity of conjugate bases based on hardness



relative acidity of acids

This ranking is verified by K_a values of 6×10^{-4} , 10^7 , 10^9 , and 10^{10} , respectively.

Electronegativity is another factor that affects the base lone pairs differently. But in a single column of the periodic table electronegativity changes less dramatically and so influences basicity less than hardness does. In general, *we consider hardness when comparing different base*

atoms in one column of the periodic table. On the other hand, the hardness of a *non-base* atom in the base molecule does not affect basicity. For example, the hardness of the halogens in the following series of molecules does not affect basicity because the oxygens, not the halogens, are the base atoms:



oxygens, not halogens, as base atoms

We will learn how to treat this series in Section 4.10D.

Puzzle 4.16

Rank the acidities of the following molecules: H_2O , H_2S , H_2Se . Explain in terms of structures, not by K_a values.

4.10B Influence of Base Atom's Electronegativity

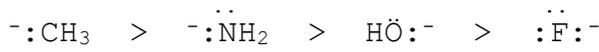
Next let us rank the acidities of methane, ammonia, water and hydrogen fluoride. Consider the more easily analyzed conjugate bases:



The atoms with the base lone pairs are all second-row atoms. What factor affects the base electrons of the lone pairs differently? Electronegativity increases greatly toward the right in one periodic row. Because electronegativity reflects the attraction of an atom for an electron pair in a bond, it correlates with the stability of a nonbonding electron pair on the atom, i.e., the stability of base electrons.

as electronegativity of base atom \uparrow , stability of base e's \uparrow & basicity \downarrow

Thus:



relative basicity of conjugate bases based on electronegativity



relative acidity of acids

K_a values of 10^{-50} , 10^{-34} , 2×10^{-16} , and 6×10^{-4} , respectively, confirm this ranking. Note that the *number* of lone pairs on the base atom does not greatly influence basicity. In this particular series the strongest base actually has the fewest lone pairs. In general, we consider electronegativity

when comparing different base atoms from one periodic row.

Puzzle 4.17

Rank the acidities of the following molecules: SiH_4 , PH_3 , H_2S , HCl . Explain in terms of structures, not by K_a values.

Puzzle 4.18

Which hydrogen in 2-aminoethanol, $\text{H}_2\text{NCH}_2\text{CH}_2\text{OH}$, is most acidic? Explain in terms of structure.

4.10C Influence of Formal Charge

Which is more acidic, ammonia or its conjugate acid, ammonium ion? As usual we consider the basicities of the conjugate bases:



This time the base atoms are both nitrogens. What factor affects their base electrons differently? Clearly formal charge differs for the two bases. The negative charge repels and destabilizes the negatively charged base electrons of the first base. Therefore:



relative basicity of conjugate bases based on formal charge

Note that the negative charge, not the number of base electrons, affects the basicity. So:



relative acidity of acids

consistent with K_a values of 10^{-35} and 5×10^{-10} , respectively. Because of differing formal charges, an acid is always more acidic than its conjugate base, and a base is always more basic than its conjugate acid.

Another example illustrates how a charge remote from the base atom can also affect basicity. Which is more acidic, propanoic acid ($\text{CH}_3\text{CH}_2\text{CO}_2\text{H}$) or the amino acid, glycine ($^+\text{NH}_3\text{CH}_2\text{CO}_2\text{H}$), a component of proteins? Compare the conjugate bases:



Because the base atoms are both oxygens with negative charges, what other factor might affect their base electrons differently? The formal positive charge on the nitrogen attracts and stabilizes

the negatively charged base electrons of glycine's conjugate base. Consequently:



relative basicity of conjugate bases based on formal charge



relative acidity of acids

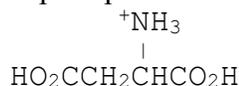
K_a values of 1×10^{-5} and 5×10^{-3} , respectively, confirm this structural assessment. Because the positive charge is farther from the base electrons, it affects basicity less ($5 \times 10^{-3}/(1 \times 10^{-5}) = 5 \times 10^2$) than the negative charge in the previous example ($5 \times 10^{-10}/10^{-35} = 10^{25}$). Yet, *positive or negative charge affects basicity, even if the charge is not on the base atom itself.*

Puzzle 4.19

Which is more acidic, $\text{HO}_2\text{C-CO}_2\text{H}$ or $\text{HO}_2\text{C-CO}_2^-$? Explain in terms of structures.

Puzzle 4.20

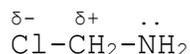
Aspartic acid is one of the amino acids that compose proteins. In water at pH 1 it has the structure:



As the pH increases, which carboxylic acid $-\text{CO}_2\text{H}$ hydrogen is abstracted first? Explain.

4.10D Influence of Partial Charge

Which is more basic, CH_3NH_2 or ClCH_2NH_2 ? *We are already dealing with these as bases, so we need not consider their conjugate bases (or acids).* What factor affects the base electrons differently? The base atoms are both nitrogens with no charge, so we must look further. The second base is substituted with a chlorine instead of a hydrogen. Because chlorine has a greater electronegativity than carbon, partial charges result:



Both partial charges affect the base electrons, but the partial positive charge has greater effect because it is closer. Because the partial positive charge attracts and stabilizes the base electrons, ClCH_2NH_2 is the weaker base.



relative basicity based on partial charge

Thus *both partial and formal charges can affect basicities*:

as positive charge ↑, stability of base e's ↑ and basicity ↓

as negative charge ↑, stability of base e's ↓ and basicity ↑

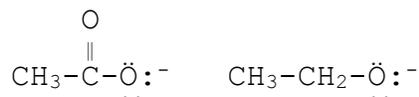
These charge effects diminish quickly as the number of intervening bonds increases.

Puzzle 4.21

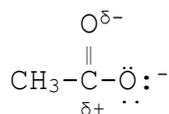
- (a) Rank the acidities of the following molecules: HOF, HOCl, HOBr, HOI. Explain in terms of structures.
- (b) Rank the acidities of the following molecules: HF, HCl, HBr, HI. Explain in terms of structures.

4.10E Influence of Resonance

Let us next rank the acidities of ethanoic (i.e., acetic) acid ($\text{CH}_3\text{CO}_2\text{H}$) and ethanol. Once again we consider the conjugate bases:



What factor affects the base electrons differently? The base atoms are both oxygens with negative charges, so again we must look further. The first base has an extra electronegative atom, a second oxygen, which the second base does not have. Thus, the first base has partial charges, which affect basicity:



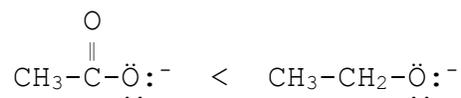
The partial positive charge on the nearby carbon attracts and stabilizes the base electrons on the negatively charged oxygen.

A second factor that distinguishes the first base is resonance:



Resonance disperses and stabilizes the base electrons. So, both resonance and the partial charge

effect stabilize the first base.



relative basicity of conjugate bases based on resonance & charge effect



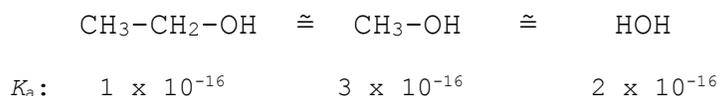
relative acidity of acids

as their respective K_a values of 2×10^{-5} and 1×10^{-16} verify. Thus carboxylic acids, such as ethanoic acid, are strong acids. *Resonance often strongly influences the chemistry of organic molecules by stabilizing them*, and often a resonance effect exceeds a partial charge effect.

The K_a given here for ethanol (1×10^{-16}) approximates the K_a for methanol in Table 4.1 (3×10^{-16}). This is not a coincidence. Because carbon and hydrogen have similar electronegativities, little partial charge effect is found in the conjugate bases:



relative basicity of conjugate bases



acidity of acids

Consequently, the additional carbon in ethanol does not greatly affect the K_a . Indeed most simple alcohols have K_a values of about 10^{-16} . By the same structural analysis, we are not surprised to find water with a similar K_a of 2×10^{-16} in Table 4.1. Once again, as for nucleophiles and electrophiles in Section 4.7, substitution of a carbon group for hydrogen often does not alter the chemistry of a molecule very much. (Carbon groups, however, do affect so-called steric factors and hyperconjugation, considered in later chapters.)

Puzzle 4.22 _____

Which is more basic, HO_3SO^- or HO_2SO^- ? Explain in terms of structures.

Puzzle 4.23 _____

Fats are made from fatty acids, that is, long chain carboxylic acids. For example, octadecanoic acid (i.e., stearic acid) is a fatty acid: $\text{CH}_3(\text{CH}_2)_{16}\text{CO}_2\text{H}$. Using Table 4.1, estimate the K_a of octadecanoic acid.

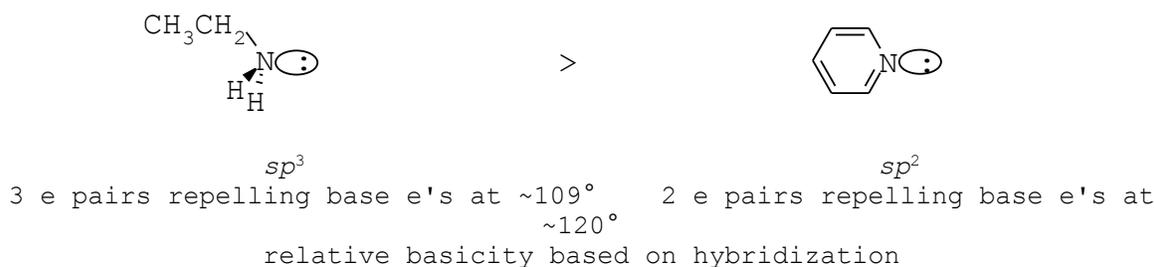
4.10F Influence of Base Atom's Hybridization

Finally, consider the basicities of ethylamine and pyridine.



Because the bases themselves are under consideration, we should not analyze the structures of their conjugate acids or bases. What factor affects the base electrons differently? An uncharged nitrogen is the base atom in each case, so we must examine other structural factors. Yet, neither base has an extra formal or partial charge. Although resonance does stabilize pyridine's π electrons, it does not affect its base electrons.

The structural factor that distinguishes base strength here is hybridization of the base atom. The sp^3 hybridization of ethylamine's nitrogen means that three repelling electron pairs repel its base lone pair (four repelling electron pairs altogether, Section 1.6D). Furthermore, these electron pairs are at a relatively close angle of about 109° .



In pyridine the base atom is hybridized sp^2 and only two repelling electron pairs at a more distant angle of about 120° repel the base electrons. Recall that π electron pairs don't count as repelling electron pairs (Section 1.6C). This diminished repulsion destabilizes the base electrons less, so pyridine is less basic.

as # of repelling e pairs \uparrow , stability of base e's \downarrow and basicity \uparrow

The K_a values of pyridine's and ethylamine's conjugate acids are 6×10^{-6} and 2×10^{-11} , respectively, and confirm the order of basicity. (An alternative rationalization in terms of electronegativity and orbital size contradicts the relative basicities of halide ions among others.)

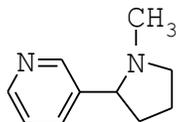
In the subsections of Section 4.10, we have observed that *in an acid a more electronegative atom, or a softer atom, or an atom with more s character is more able to donate a proton*. We have also seen for the first time how a careful examination of molecular structure can give keen insights into the reactivity of molecules.

Puzzle 4.24

- (a) According to Table 4.1, which is more acidic, ethyne ($\text{HC}\equiv\text{CH}$) or methane? Explain in terms of structure.
- (b) According to Table 4.1, which is more acidic, hydrocyanic acid ($\text{HC}\equiv\text{N}$) or ethyne? Explain in terms of structure.

Puzzle 4.25

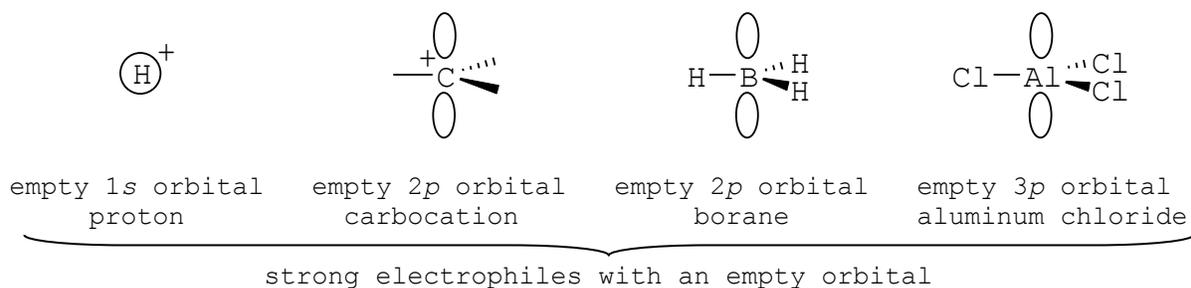
Nicotine, a drug found in tobacco and an insecticide, has two nitrogens:



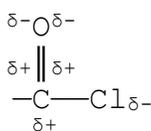
Draw its predominant structure after single protonation.

4.11 Strengths of Electrophiles and Nucleophiles

Now let us roughly gauge the strengths of electrophiles and nucleophiles. Strong electrophiles are especially electron-poor thanks to either an empty orbital or a large positive charge, or both. For example:



An acid chloride is a strong electrophile, in part, because one of its atoms has a large positive charge, despite having a full octet:



The three partial positive charges on the carbon form a large positive charge, which strongly attracts a nucleophile.

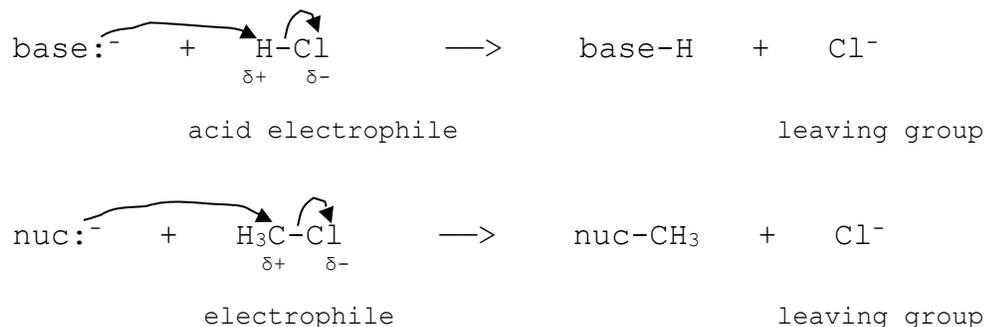
Weak electrophiles have no empty orbital or a large positive charge, but accommodate a new bond by breaking an existing bond and releasing the bonding electrons onto a stable leaving group. Here are examples of weak electrophiles with halide ion leaving groups:



weak electrophiles

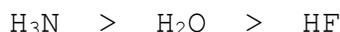
Note that electrophilicity (i.e., electrophilic strength) does not correspond to electrophilic hardness or softness. Whereas H^+ , R^+ and $AlCl_3$ are hard, strong electrophiles, BH_3 is a soft, strong electrophile lacking even a partial positive charge.

Nucleophilicity, affected by various factors, is more difficult to estimate. The most important factor is basicity. Strong bases are generally strong nucleophiles. Two very similar reactions illustrate the connection:



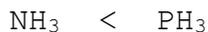
Both the base and the nucleophile use an electron pair to bond to an electrophilic atom with a partial positive charge. Simultaneously this electrophilic atom breaks a bond to an atom able to receive the bonding electrons. This comparison highlights a recurring theme in organic chemistry. *The chemistry of carbon compounds often resembles the chemistry of hydrogen analogs.* Hydrogen halides (HX) and alkyl halides (RX) can react similarly as electrophiles. Both a proton (H^+) and a carbocation (R^+) are strong electrophiles with empty orbitals.

The correlation between strong bases and strong nucleophiles holds best when the nucleophilic atoms are in the same row of the periodic table. Thus, these rankings hold for both basicity and nucleophilicity:



relative basicity and nucleophilicity for second-row atoms

A second, auxiliary factor that can sometimes increase nucleophilicity is softness. This factor can be important to a soft electrophile, which prefers to react with a soft nucleophile (Section 4.9). Consider the related nucleophiles NH_3 and PH_3 :



relative softness and reactivity with soft H_3CCl

Because phosphorus is softer than nitrogen, PH_3 reacts better with the soft electrophile, H_3CCl .

On the other hand, if the electrophile is hard, a soft nucleophile has no advantage, and basicity alone determines nucleophilicity. For example, in ability to take a proton from any acid (inevitably a hard electrophile), basicity alone applies:



relative basicity and reactivity with acids

As with acids and bases (Section 4.6), a strong electrophile is not selective and can react well not only with a strong nucleophile, but also with some weak nucleophiles. In contrast, a weak electrophile is selective and needs a strong nucleophile to compensate for its low reactivity. Table 4.3 indicates the kinds of nucleophiles reactive with a given kind of electrophile.

Table 4.3 Suitable Nucleophiles for a Kind of Electrophile

Kind of electrophile	Suitable kind of nucleophile
strong & soft e.g., BH_3	strong or weak base, soft or hard
strong & hard e.g., R^+	strong or weak base, soft or hard
weak & soft e.g., RX	strong: strong base (e.g., O^-) or soft (e.g., Br^-)
weak & hard e.g., weak acid	strong: strong base (e.g., N^-)

In Section 4.6 we concluded that a successful acid-base reaction requires at least one reactant to be strong. Now we can generalize that a successful electrophile-nucleophile reaction demands that either the electrophile or the nucleophile, if not both, be strong.

Puzzle 4.26

Determine whether HO^- or HS^- would react more readily with each of the following electrophiles. (a) $^+\text{NH}_4$ (b) $\text{H}_3\text{C-Br}$

Puzzle 4.27

Carbon monoxide, CO , can kill by binding to hemoglobin in the blood in place of molecular oxygen. If carbon monoxide is almost nonpolar (see Puzzle 1.55), why does its carbon, not its oxygen, bind to the iron of hemoglobin?

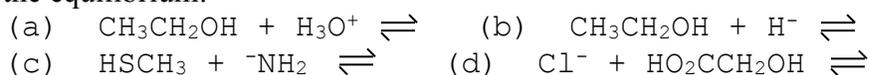
Chapter Summary

1. By the Brønsted theory, an acid donates a proton to a base. The resulting conjugate acid and conjugate base can reverse the process.
2. A Brønsted acid must have a hydrogen. A Brønsted base must have a lone pair or a π electron pair. A molecule with both acid and base features can react as an acid in one reaction and a base in another reaction.

3. Acidity, the tendency to donate a proton, is quantified by K_a , the equilibrium constant for the donation of a proton to water. The greater K_a is, the stronger the acid.
4. Basicity, the tendency to accept a proton, is assessed by the K_a of the conjugate acid. The greater the K_a of the conjugate acid is, the weaker the base.
5. Found on one side of an acid-base equilibrium, the stronger acid and stronger base react to a greater extent.
6. An acid is strong if and only if its K_a exceeds 10^{-7} . A base is strong if and only if its conjugate acid has a K_a below 10^{-7} .
7. Weak acids need strong bases to react extensively, whereas weak bases need strong acids.
8. A nucleophile (i.e., Lewis base) is an electron-rich molecule that provides an electron pair for a σ bond with an electron-poor electrophile (i.e., Lewis acid).
9. Hard nucleophiles and electrophiles generally have a densely charged reaction site. Soft nucleophiles and electrophiles generally have a sparsely charged reaction site. Nucleophiles and electrophiles with similar hardness tend to react well together.
10. Analysis of the molecular structures of bases allows a qualitative comparison of acidities or basicities. Increasing softness or electronegativity of the base atom, positive charge (formal or partial), or resonance with base lone pairs weakens the base. A formal or partial negative charge strengthens the base.
11. Strong electrophiles have an empty orbital or a large positive charge. A weak electrophile has neither an empty orbital nor a large positive charge.
12. A strong nucleophile is generally a strong base, but may also be a soft, weak base if the electrophile is soft.
13. The chemistry of carbon compounds often resembles the chemistry of their hydrogen analogs.

Additional Puzzles

4.28 Show the products of each acid-base reaction and identify the acid and base on each side of the equilibrium:



4.29 (a) Identify a chemical that cannot be an (Brønsted) acid.

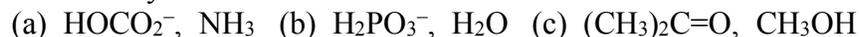
(b) Identify a chemical that cannot be a (Brønsted) base.

(c) Identify a chemical that cannot be either an acid or a base.

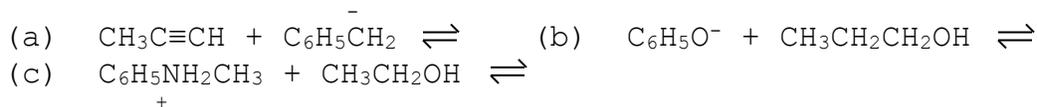
4.30 Decide which acid in each pair is stronger. Also decide which acids are strong. Use Table 4.1 if necessary.



4.31 Decide which is the stronger base and which is the stronger acid in each pair. Use Table 4.1 if necessary.

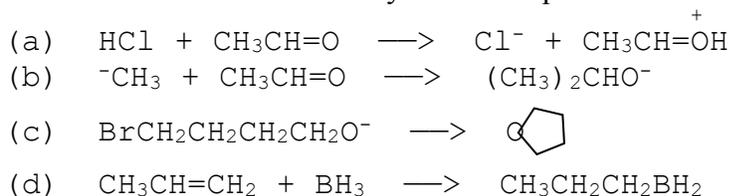


4.32 Show the products of each acid-base reaction. Then using Table 4.1, determine if reactants or products predominate at equilibrium.

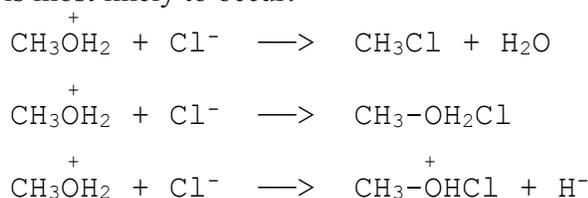


4.33 (a) Does hydroxide ion efficiently convert methanol to its conjugate base? Explain.
 (b) Identify a more efficient reagent for the conversion.

4.34 For each reaction identify the nucleophilic and electrophilic atoms in the reactants:

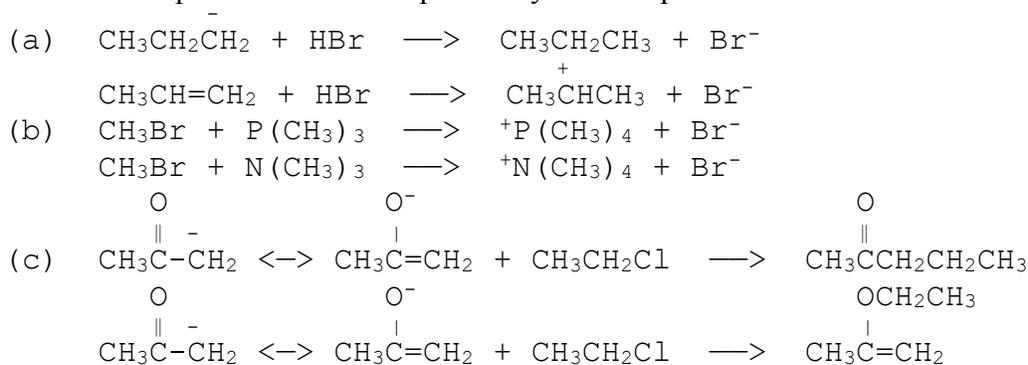


4.35 Which of these reactions is most likely to occur:

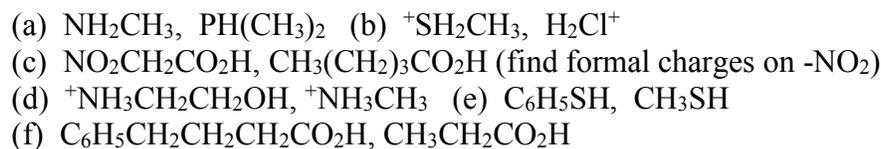


Explain.

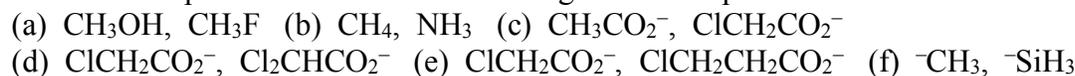
4.36 In each pair of reactions explain why the first proceeds faster than the second.



4.37 In each pair decide which is the stronger acid. If there is no clear choice, say so. Explain in structural terms.



4.38 In each pair decide which is the stronger base. Explain in structural terms.



4.39 Using Table 4.1, estimate the K_a for each molecule:



4.48 The main component of air is N_2 , which is obviously safe to breathe. In contrast, ammonia is much more toxic, in part because it is a strong base. Why isn't N_2 a strong base?

4.49 (a) Can a weak acid be a weak base? If so, give an example.

(b) Can a weak acid be a strong base? If so, give an example.

(c) Can a strong acid be a weak base? If so, give an example.

(d) Prove that a strong acid cannot be a strong base. Hint: assume that $H-Z$ is a strong acid and a strong base, and then find a contradiction.