# Molecular Representations

# DID YOU EVER WONDER...

how new drugs are designed?

Scientists employ many techniques in the design of new drugs. One such technique, called lead modification, enables scientists to identify the portion of a compound responsible for its medicinal properties and then to design similar compounds with better properties. We will see an example of this technique, specifically, where the discovery of morphine led to the development of a whole family of potent analgesics (codeine, heroin, methadone, and many others).

In order to compare the structures of the compounds being discussed, we will need a more efficient way to draw the structures of organic compounds. Lewis structures are only efficient for small molecules, such as those we considered in the previous chapter. The goal of this chapter is to master the skills necessary to use and interpret the drawing method most often utilized by organic chemists and biochemists. These drawings, called bond-line structures, are fast to draw and easy to read, and they focus our attention on the reactive centers in a compound. In the second half of this chapter, we will see that bond-line structures are inadequate in some circumstances, and we will explore the technique that chemists employ to deal with the inadequacy of bond-line structures.

### 2.1 Molecular Representations

- 2.2 Bond-Line Structures
- 2.3 Identifying Functional Groups
- 2.4 Carbon Atoms with Formal Charges
- 2.5 Identifying Lone Pairs
- 2.6 Three-Dimensional Bond-Line Structures
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NOH

- 2.9 Formal Charges in Resonance Structures
- 2.10 Drawing Resonance Structures via Pattern Recognition
- 2.11 Assessing Relative Importance of Resonance Structures
- 2.12 Delocalized and Localized Lone Pairs

### DO YOU REMEMBER?

Before you go on, be sure you understand the following topics. If necessary, review the suggested sections to prepare for this chapter:

- Electrons, Bonds, and Lewis Structures (Section 1.3)
  - Identifying Formal Charges (Section 1.4)

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# 2.1 Molecular Representations

Chemists use many different styles to draw molecules. Let's consider the structure of isopropanol, also called isopropyl rubbing alcohol, which is used as a disinfectant in sterilizing pads. The structure of this compound is shown below in a variety of drawing styles:

• Molecular Orbital Theory (Section 1.8)



Lewis structures were discussed in the previous chapter. The advantage of Lewis structures is that all atoms and bonds are explicitly drawn. However, Lewis structures are only practical for very small molecules. For larger molecules, it becomes extremely burdensome to draw out every bond and every atom.

In partially condensed structures, the C—H bonds are not all drawn explicitly. For example, in the drawing above, CH<sub>3</sub> refers to a carbon atom with bonds to three hydrogen atoms. Once again, this drawing style is only practical for small molecules.

In condensed structures, none of the bonds are drawn. Groups of atoms are clustered together, when possible. For example, isopropanol has two CH<sub>3</sub> groups, both of which are connected to the central carbon atom, shown like this: (CH<sub>3</sub>)<sub>2</sub>CHOH. Once again, this drawing style is only practical for small molecules with simple structures.

The molecular formula of a compound simply shows the number of each type of atom in the compound  $(C_3H_8O)$ . No structural information is provided. There are actually three constitutional isomers with molecular formula C<sub>3</sub>H<sub>8</sub>O:



In reviewing some of the different styles for drawing molecules, we see that none are convenient for larger molecules. Molecular formulas do not provide enough information, Lewis structures take too long to draw, and partially condensed and condensed drawings are only suitable for relatively simple molecules. In upcoming sections, we will learn the rules for drawing bond-line structures, which are most commonly used by organic chemists. For now, let's practice the drawing styles above, which will be used for small molecules throughout the course.

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need more **PRACTICE?** Try Problems 2.49, 2.50

## 2.2 Bond-Line Structures

It is not practical to draw Lewis structures for all compounds, especially large ones. As an example, consider the structure of amoxicillin, one of the most commonly used antibiotics in the penicillin family:



Previously fatal infections have been rendered harmless by antibiotics such as the one above. Amoxicillin is not a large compound, yet drawing this compound is time consuming. To deal with this problem, organic chemists have developed an efficient drawing style that can be used to draw molecules very quickly. **Bond-line structures** not only simplify the drawing process but also are easier to read. The bond-line structure for amoxicillin is



Most of the atoms are not drawn, but with practice, these drawings will become very userfriendly. Throughout the rest of this textbook, most compounds will be drawn in bond-line format, and therefore, it is absolutely critical to master this drawing technique. The following sections are designed to develop this mastery.

#### How to Read Bond-Line Structures

Bond-line structures are drawn in a zigzag format ( ), where each corner or endpoint represents a carbon atom. For example, each of the following compounds has six carbon atoms (count them!):



Double bonds are shown with two lines, and triple bonds are shown with three lines:



Notice that triple bonds are drawn in a linear fashion rather than in a zigzag format, because triple bonds involve *sp*-hybridized carbon atoms, which have linear geometry (Section 1.9). The two carbon atoms of a triple bond and the two carbon atoms connected to them are drawn in a straight line. All other bonds are drawn in a zigzag format; for example, the following compound has eight carbon atoms.



#### **BY THE WAY**

You may find it worthwhile to purchase or borrow a molecular model set. There are several different kinds of molecular model sets on the market, and most of them are comprised of plastic pieces that can be connected to generate models of small molecules. Any one of these model sets will help you to visualize the relationship between molecular structures and the drawings used to represent them.

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Hydrogen atoms bonded to carbon are also not shown in bond-line structures, because it is assumed that each carbon atom will possess enough hydrogen atoms so as to achieve a total of four bonds. For example, the highlighted carbon atom below appears to have only two bonds:



Therefore, we can infer that there must be two more bonds to hydrogen atoms that have not been drawn (to give a total of four bonds). In this way, all hydrogen atoms are inferred by the drawing:



With a bit of practice, it will no longer be necessary to count bonds. Familiarity with bondline structures will allow you to "see" all of the hydrogen atoms even though they are not drawn. This level of familiarity is absolutely essential, so let's get some practice.

# SKILLBUILDER



LEARN the skill

Consider the structure of diazepam, first marketed by the Hoffmann-La Roche Company under the trade name Valium:



Valium is a sedative and muscle relaxant used in the treatment of anxiety, insomnia, and seizures. Identify the number of carbon atoms in diazepam, then fill in all the missing hydrogen atoms that are inferred by the drawing.



#### SOLUTION

Remember each corner and each endpoint represents a carbon atom. This compound therefore has 16 carbon atoms, highlighted below:

STEP 1 Count the carbon atoms, which are represented by corners or endpoints.





**STEP 2** 

four bonds.

Count the hydrogen atoms. Each carbon atom will have enough hydrogen atoms to have exactly Each carbon atom should have four bonds. We therefore draw enough hydrogen atoms in order to give each carbon atom a total of four bonds. Any carbon atoms that already have four bonds will not have any hydrogen atoms:



**PRACTICE** the skill **2.5** For each of the following molecules, determine the number of carbon atoms present, and then determine the number of hydrogen atoms connected to each carbon atom:



#### APPLY the skill

**2.6** Each transformation below shows a starting material being converted into a product (the reagents necessary to achieve the transformation have not been shown). For each transformation, determine whether the product has more carbon atoms, fewer carbon atoms, or the same number of carbon atoms as the starting material. In other words, determine whether each transformation involves an increase, decrease, or no change in the number of carbon atoms.



**2.7** Identify whether each transformation below involves an increase, a decrease, or no change in the number of hydrogen atoms:





-----> need more **PRACTICE?** Try Problems 2.39, 2.49, 2.52



### How to Draw Bond-Line Structures

It is certainly important to be able to read bond-line structures fluently, but it is equally important to be able to draw them proficiently. When drawing bond-line structures, the following rules should be observed:

1. Carbon atoms in a straight chain should be drawn in a zigzag format:



- 2. When drawing double bonds, draw all bonds as far apart as possible:



3. When drawing single bonds, the direction in which the bonds are drawn is irrelevant:



These two drawings do not represent constitutional isomers—they are just two drawings of the same compound. Both are perfectly acceptable.

**4.** All *heteroatoms* (atoms other than carbon and hydrogen) must be drawn, and any hydrogen atoms attached to a heteroatom must also be drawn. For example:



5. Never draw a carbon atom with more than four bonds. Carbon only has four orbitals in its valence shell, and therefore carbon atoms can only form four bonds.



#### **2.3** DRAWING BOND-LINE STRUCTURES

LEARN the skill

Draw a bond-line structure for the following compound:



Drawing a bond-line structure requires just a few conceptual steps. First, delete all hydrogen atoms except for those connected to heteroatoms: **STEP 1** -c-c≡c-c´'' H H H C-C-H H C-C-Delete hydrogen ----> atoms, except for those connected to heteroatoms. Then, place the carbon skeleton in a zigzag arrangement, making sure that any triple bonds are drawn as linear: **STEP 2** :OH Draw in zigzag format,



c−c−ö−c−c≡c

2.10 In each of the following compounds, identify all carbon atoms that you expect will be deficient in electron density ( $\delta$ +). If you need help, refer to Section 1.5.

CI



------> need more PRACTICE? Try Problems 2.40, 2.41, 2.54, 2.58



# 2.3 Identifying Functional Groups

Bond-line drawings are the preferred drawing style used by practicing organic chemists. In addition to being more efficient, bond-line drawings are also easier to read. As an example, consider the following reaction:

$$(CH_3)_2CHCHC(CH_3)_2 \xrightarrow{H_2} (CH_3)_2CHCH_2CH(CH_3)_2$$

When the reaction is presented in this way, it is somewhat difficult to see what is happening. It takes time to digest the information being presented. However, when we redraw the same reaction using bond-line structures, it becomes very easy to identify the transformation taking place:



It is immediately apparent that a double bond is being converted into a single bond. With bondline drawings, it is easier to identify the functional group. A **functional group** is a characteristic group of atoms/bonds that possess a predictable chemical behavior. In the reactions below, the starting material has a carbon-carbon double bond, which is a functional group. Compounds with carbon-carbon double bonds typically react with molecular hydrogen ( $H_2$ ) in the presence of a catalyst (such as Pt). Both of the starting materials below have a carbon-carbon double bond, and consequently, they exhibit similar chemical behavior.



The chemistry of every organic compound is determined by the functional groups present in the compound. Therefore, the classification of organic compounds is based on their functional groups. For example, compounds with carbon-carbon double bonds are classified as *alkenes*, while compounds possessing an OH group are classified as *alcohols*. Many of the chapters in this book are organized by functional group. Table 2.1 provides a list of common functional groups and the corresponding chapters in which they appear.

### CONCEPTUAL CHECKPOINT

**2.11** Atenolol and enalapril are drugs used in the treatment of heart disease. Both of these drugs lower blood pressure (albeit in different ways) and reduce the risk of heart attack. Using Table 2.1, identify and label all functional groups in these two compounds:





# 2.4 Carbon Atoms with Formal Charges

In Section 1.4 we saw that a formal charge is associated with any atom that does not exhibit the appropriate number of valence electrons. Formal charges are extremely important, and they must be shown in bond-line structures. A missing formal charge renders a bond-line structure incorrect and therefore useless. Accordingly, let's quickly practice identifying formal charges in bond-line structures.

any of the oxygen atoms bear a formal charge:

2.13 For each of the compounds below determine whether



### CONCEPTUAL CHECKPOINT

**2.12** For each of the compounds below determine whether any of the nitrogen atoms bear a formal charge:



Now let's consider formal charges on carbon atoms. We have seen that carbon generally has four bonds, which allows us to "see" all of the hydrogen atoms even though they are not explicitly shown in bond-line structures. Now we must modify that rule: A carbon atom will generally have four bonds only when it does not have a formal charge. When a carbon atom bears a formal charge, either positive or negative, it will have three bonds rather than four. To understand why, let's first consider  $C^+$ , and then we will consider  $C^-$ .

Recall that the appropriate number of valence electrons for a carbon atom is four. In order to have a positive formal charge, a carbon atom must be missing an electron. In other words, it must have only three valence electrons. Such a carbon atom can only form three bonds. This must be taken into account when counting hydrogen atoms:



Now let's focus on negatively charged carbon atoms. In order to have a negative formal charge, a carbon atom must have one extra electron. In other words, it must have five valence electrons. Two of those electrons will form a lone pair, and the other three electrons will be used to form bonds:



In summary, both  $C^+$  and  $C^-$  will have only three bonds. The difference between them is the nature of the fourth orbital. In the case of  $C^+$ , the fourth orbital is empty. In the case of  $C^-$ , the fourth orbital holds a lone pair of electrons.

# 2.5 Identifying Lone Pairs

In order to determine the formal charge on an atom, we must know how many lone pairs it has. On the flip side, we must know the formal charge in order to determine the number of lone pairs on an atom. To understand this, let's examine a case where neither the lone pairs nor the formal charges are drawn:



#### WATCH OUT

Formal charges must always be drawn and can never be omitted, unlike lone pairs, which may be omitted from a bond-line structure. If the lone pairs were shown, then we could determine the charge (two lone pairs would mean a negative charge, and one lone pair would mean a positive charge). Alternatively, if the formal charge were shown, then we could determine the number of lone pairs (a negative charge would mean two lone pairs, and a positive charge would mean one lone pair).

Therefore, a bond-line structure will only be clear if it contains either all of the lone pairs or all of the formal charges. Since there are typically many more lone pairs than formal charges in any one particular structure, chemists have adopted the convention of always drawing formal charges, which allows us to leave out the lone pairs.

Now let's get some practice identifying lone pairs when they are not drawn. The following example will demonstrate the thought process:

∽₀⊖

In order to determine the number of lone pairs on the oxygen atom, we simply use the same two-step process described in Section 1.4 for calculating formal charges:

- 1. *Determine the appropriate number of valence electrons for the atom.* Oxygen is in column 6A of the periodic table, and therefore, it should have six valence electrons.
- 2. Determine if the atom actually exhibits the appropriate number of electrons. This oxygen atom has a negative formal charge, which means it must have one extra electron. Therefore, this oxygen atom must have 6 + 1 = 7 valence electrons. One of those electrons is being used to form the C—O bond, which leaves six electrons to be housed as lone pairs. This oxygen atom must therefore have three lone pairs:



The process above represents an important skill; however, it is even more important to become familiar enough with atoms that the process becomes unnecessary. There are just a handful of patterns to recognize. Let's go through them methodically, starting with oxygen. Table 2.2 summarizes the important patterns that you will encounter for oxygen atoms.

### TABLE 2.2 FORMAL CHARGE ON AN OXYGEN ATOM ASSOCIATED WITH A PARTICULAR NUMBER OF BONDS AND LONE PAIRS No $\Theta$ $\oplus$ Charge 1 bond + 3 lone pairs 2 bonds + 2 lone pairs 3 bonds + 1 lone pair Examples: Examples: Examples: ;0: .|⊕ Н ⊕ Æ `0.<sup>⊖</sup>



- A negative charge corresponds with one bond and three lone pairs.
- The absence of charge corresponds with two bonds and two lone pairs.
- A positive charge corresponds with three bonds and one lone pair.

# SKILLBUILDER

### 2.4 IDENTIFYING LONE PAIRS ON OXYGEN ATOMS

**LEARN** the skill

Draw all of the lone pairs in the following structure:

#### SOLUTION

has just one lone pair:

STEP 1 Determine the appropriate number of valence electrons.

#### **STEP 2**

Analyze the formal charge, and determine the actual number of valence electrons.

#### **STEP 3**

Count the number of bonds, and determine how many of the actual valence electrons must be lone pairs.

**PRACTICE** the skill **2.14** Draw all lone pairs on each of the oxygen atoms in the compounds below. Before doing this, review Table 2.2, and then come back to these problems. Try to identify all lone pairs without having to count. Then, count to see if you were right.



APPLY the skill

**2.15** A carbene is a highly reactive intermediate in which a carbon atom bears a lone pair and no formal charge:



How many hydrogen atoms are attached to the central carbon atom above?



for the atom. Oxygen is in column 6A of the periodic table, and therefore, it should have

six valence electrons. Then, determine if the atom actually exhibits the appropriate number

of electrons. This oxygen atom has a positive charge, which means it is missing an electron:

6 - 1 = 5 valence electrons. Three of these five electrons are being used to form bonds,

which leaves just two electrons for a lone pair. This oxygen atom has only one lone pair.

Alternatively, and less preferably, it is possible to calculate the number of lone pairs using the following two steps. First, determine the appropriate number of valence electrons

The oxygen atom above has a positive formal charge and three bonds. It is preferable to

recognize the pattern—that a positive charge and three bonds must mean that the oxygen

⊕⁄H  $\cap$ 



TABLE 2.3 FORMAL CHARGE ON A NITROGEN ATOM ASSOCIATED WITH A PARTICULAR NUMBER OF BONDS

Now let's look at the common patterns for nitrogen atoms. Table 2.3 shows the important patterns that you will encounter with nitrogen atoms. In summary:

- A negative charge corresponds with two bonds and two lone pairs.
- The absence of charge corresponds with three bonds and one lone pair.
- A positive charge corresponds with four bonds and no lone pairs.



2.5 IDENTIFYING LONE PAIRS ON NITROGEN ATOMS

#### EARN the skill

**SKILLBUILDER** 

**STEP 1** Determine the appropriate number of valence electrons.

#### **STEP 2**

Analyze the formal charge and determine the actual number of valence electrons.

#### **STEP 3**

Count the number of bonds, and determine how many of the actual valence electrons must be lone pairs.

Draw any lone pairs associated with the nitrogen atoms in the following structure:



SOLUTION

The top nitrogen atom has a positive formal charge and four bonds. The bottom nitrogen has three bonds and no formal charge. It is preferable to simply recognize that the top nitrogen atom must have no lone pairs and the bottom nitrogen atom must have one lone pair:

Alternatively, and less preferably, it is possible to calculate the number of lone pairs using the following two steps. First, determine the appropriate number of valence electrons for the atom. Each nitrogen atom should have five valence electrons. Next, determine if each atom actually exhibits the appropriate number of electrons. The top nitrogen atom has a positive charge, which means it is missing an electron. This nitrogen atom actually has only four valence electrons. Since the nitrogen atom has four bonds, it is using each of its four electrons to form a bond. This nitrogen atom does not possess a lone pair. The bottom nitrogen atom has no formal charge, so this nitrogen atom must be using five valence electrons. It has three bonds, which means that there are two electrons left over, forming one lone pair.



**PRACTICE** the skill **2.16** Draw all lone pairs on each of the nitrogen atoms in the compounds below. First, review Table 2.3, and then come back to these problems. Try to identify all lone pairs without having to count. Then, count to see if you were right.



PLY the skill

**2.17** Each of the following compounds contains both oxygen and nitrogen atoms. Identify all lone pairs in each of the following compounds:



2.18 Identify the number of lone pairs in each of the following compounds:



2.19 Amino acids are biological compounds with the following structure, where the R group can vary. The structure and biological function of amino acids will be discussed in Chapter 25. Identify the total number of lone pairs present in an amino acid, assuming that the R group does not contain any atoms with lone pairs.



An amino acid

------> need more **PRACTICE?** Try Problem 2.39

# 2.6 Three-Dimensional Bond-Line Structures

Throughout this book, we will use many different kinds of drawings to represent the threedimensional geometry of atoms. The most common method is a bond-line structure that includes wedges and dashes to indicate three dimensionality. These structures are used for all types of compounds, including acyclic, cyclic, and bicyclic compounds (Figure 2.1). In the drawings in Figure 2.1, a wedge represents a group coming out of the page, and a dash represents a group going behind the page. We will use wedges and dashes extensively in Chapter 5 and thereafter.

**FIGURE 2.1** Bond-line structures with wedges and dashes to indicate three dimensionality.



(No ring)



(One ring)



**Bicyclic** (Two rings)

In certain circumstances, there are other types of drawings that can be used, all of which also indicate three-dimensional geometry (Figure 2.2).



**Fischer projections** are used for acyclic compounds while **Haworth projections** are used exclusively for cyclic compounds. Each of these drawing styles will be used several times throughout this book, particularly in Chapters 5, 9, and 24.

# **MEDICALLY**SPEAKING ))

### Identifying the Pharmacophore

As mentioned in the chapter opener, there are many techniques that scientists employ in the design of new drugs. One such technique is called *lead modification*, which involves modifying the structure of a compound known to exhibit desirable medicinal properties. The known compound "leads" the way to the development of other similar compounds and is therefore called the *lead compound*. The story of morphine provides a good example of this process.

Morphine is a very potent analgesic (pain reliever) that is known to act on the central nervous system as a depressant (causing sedation and slower respiratory function) and as a stimulant (relieving symptoms of anxiety and causing an overall state of euphoria). Because morphine is addictive, it is primarily used for the short-term treatment of acute pain and for terminally ill patients suffering from extreme pain. The analgesic properties of morphine have been exploited for over a millennium. It is the major component of opium, obtained from the unripe seed pods of the poppy plant, *Papaver somniferum*. Morphine was first isolated from opium in 1803, and by the mid-1800s, it was used heavily to control pain during and after surgical procedures. By the end of the 1800s, the addictive properties of morphine became apparent, which fueled the search for nonaddictive analgesics.

In 1925, the structure of morphine was correctly determined. This structure functioned as a lead compound and was modified to produce other compounds with analgesic properties. Early modifications focused on replacing the hydroxyl (OH) groups with other functional groups. Examples include heroin and codeine. Heroin exhibits stronger activity than morphine and is extremely addictive. Codeine shows less activity than morphine and is less addictive. Codeine is currently used as an analgesic and cough suppressant.



Codeine

In 1938, the analgesic properties of meperidine, also known as Demerol, were fortuitously discovered. As the story goes, meperidine was originally prepared to function as an antispasmodic agent (to suppress muscle spasms). When administered to mice, it curiously caused the tails of the mice to become erect. It was already known that morphine and related compounds produced a similar effect in mice, so meperidine was further tested and found to exhibit analgesic properties. This discovery generated much interest by providing new insights in the search for other analgesics. By comparing the structures of morphine, meperidine, and their derivatives, scientists were able to determine which structural features are essential for analgesic activity, shown in red on the next page:

**FIGURE 2.2** Common drawing styles that show three dimensionality for acylic, cyclic, and bicyclic compounds.





When morphine is drawn in this way, its structural similarity to meperidine becomes more apparent. Specifically, the bonds indicated in red represent the portion of each compound responsible for the analgesic activity. This part of the compound is called the *pharmacophore*. If any part of the pharmacophore is removed or changed, the resulting compound will not be capable of binding to the appropriate biological receptor, and the compound will not exhibit analgesic properties. The term *auxophore* refers to the rest of the compound (the bonds shown in black above). Removing any of these bonds may or may not affect the strength with which the pharmacophore binds to the receptor, thereby affecting the compound's analgesic potency. When modifying a lead compound, the auxophoric regions are the portions targeted for modification. For example, the auxophoric regions of morphine were modified to develop methadone and etorphine.



Methadone, developed in Germany during World War II, is used to treat heroin addicts suffering from withdrawal symptoms. Methadone binds to the same receptor as heroin, but it has a longer retention time in the body, thereby enabling the body to cope with the decreasing levels of drug that normally cause withdrawal symptoms. Etorphine is over 3000 times more potent than morphine and is used exclusively in veterinary medicine to immobilize elephants and other large mammals.

Scientists are constantly searching for new lead compounds.

In 1992, researchers at NIH (National Institutes of Health) in Bethesda, Maryland, isolated epibatidine from the skin of the Ecuadorian frog, *Epipedobates tricolor.* Epibatidine was found to be an analgesic that is



Epibatidine

200 times more potent than morphine. Further studies indicated that epibatidine and morphine bind to different receptors. This discovery is very exciting, because it means that epibatidine can serve as a new lead compound. Although this compound is too toxic for clinical use, a significant number of researchers are currently working to identify the pharmacophore of epibatidine and to develop nontoxic derivatives. This area of research indeed looks promising.

#### CONCEPTUAL CHECKPOINT

**2.20** Troglitazone, rosiglitazone, and pioglitazone, all antidiabetic drugs introduced to the market in the late 1990s, are believed to act on the same receptor:



- (a) Based on these structures, try to identify the likely pharmacophore that is responsible for the antidiabetic activity of these drugs.
- (b) Consider the structure of rivoglitazone (below). This compound is currently being studied for potential antidiabetic activity. Based on your analysis of the likely pharmacophore, do you believe that rivoglitazone will exhibit antidiabetic properties?

# 2.7 Introduction to Resonance

#### The Inadequacy of Bond-Line Structures

We have seen that bond-line structures are generally the most efficient and preferred way to draw the structure of an organic compound. Nevertheless, bond-line structures suffer from one major defect. Specifically, a pair of bonding electrons is always represented as a line that is drawn between two atoms, which implies that the bonding electrons are confined to a region of space directly in between two atoms. In some cases, this assertion is acceptable, as in the following structure:



In this case, the  $\pi$  electrons are in fact located where they are drawn, in between the two central carbon atoms. But in other cases, the electron density is spread out over a larger region of the molecule. For example, consider the following ion, called an *allyl carbocation*:

It might seem from the drawing above that there are two  $\pi$  electrons on the left side and a positive charge on the right side. But this is not the entire picture, and the drawing above is inadequate. Let's take a closer look and first analyze the hybridization states. Each of the three carbon atoms above is  $sp^2$  hybridized. Why? The two carbon atoms on the left side are each  $sp^2$  hybridized because each of those carbon atoms is utilizing a p orbital to form the  $\pi$ bond (Section 1.9). The third carbon atom, bearing the positive charge, is also  $sp^2$  hybridized because it has an empty *p* orbital. Now let's draw all of the *p* orbitals (Figure 2.3).



Non-bonding MO



Bonding MO

FIGURE 2.4 The molecular orbitals associated with the  $\pi$  electrons of an allylic system.

This image focuses our attention on the continuous system of p orbitals, which functions as a "conduit," allowing the two  $\pi$  electrons to be associated with all three carbon atoms. Valence bond theory is inadequate for analysis of this system because it treats the electrons as if they were confined between only two atoms. A more appropriate analysis of the allyl cation requires the use of molecular orbital (MO) theory (Section 1.8), in which electrons are associated with the molecule as a whole, rather than individual atoms. Specifically, in MO theory, the entire molecule is treated as one entity, and all of the electrons in the entire molecule occupy regions of space called molecular orbitals. Two electrons are placed in each orbital, starting with the lowest energy orbital, until all electrons occupy orbitals.

According to MO theory, the three p orbitals shown in Figure 2.3 no longer exist. Instead, they have been replaced by three MOs, illustrated in Figure 2.4 in order of increasing energy. Notice that the lowest energy MO, called the *bonding molecular orbital*, has no nodes. The next higher energy MO, called the nonbonding molecular orbital, has one node. The highest energy MO, called the *antibonding molecular orbital*, has two nodes. The  $\pi$  electrons of the



allyl system will fill these MOs, starting with the lowest energy MO. How many  $\pi$  electrons will occupy these MOs? The allyl carbocation has only two  $\pi$  electrons, rather than three, because one of the carbon atoms bears a positive formal charge indicating that one electron is missing. The two  $\pi$  electrons of the allyl system will occupy the lowest energy MO (the bonding MO). If the missing electron were to return, it would occupy the next higher energy MO, which is the nonbonding MO. Focus your attention on the nonbonding MO.

The nonbonding molecular orbital (from Figure 2.4) ssociated with the  $\pi$  electrons of an allylic system.



There should be an electron occupying this nonbonding MO, but the electron is missing. Therefore, the colored lobes are empty and represent regions of space that are electron deficient. In conclusion, MO theory suggests that the positive charge of the allyl carbocation is associated with the two ends of the system, rather than just one end.

In a situation like this, any single bond-line structure that we draw will be inadequate. How can we draw a positive charge that is spread out over two locations, and how can we draw two  $\pi$  electrons that are associated with three carbon atoms?

#### Resonance

The approach that chemists use to deal with the inadequacy of bond-line structures is called **resonance**. According to this approach, we draw more than one bond-line structure and then mentally meld them together:



These drawings are called **resonance structures**, and they show that the positive charge is spread over two locations. Notice that we separate resonance structures with a straight, two-headed arrow, and we place brackets around the structures. The arrow and brackets indicate that the drawings are resonance structures *of one entity*. This one entity, called a **resonance hybrid**, is *not* flipping back and forth between the different resonance structures. To better understand this, consider the following analogy: A person who has never before seen a nectarine asks a farmer to describe a nectarine. The farmer answers:

Picture a *peach* in your mind, and now picture a *plum* in your mind. Well, a *nectarine* has features of both fruits: the inside tastes like a peach, the outside is smooth like a plum, and the color is somewhere in between the color of a peach and the color of a plum. So take your image of a peach together with your image of a plum and *meld them together* in your mind into one image. That's a nectarine.

Here is the important feature of the analogy: the nectarine does not vibrate back and forth every second between being a peach and being a plum. A nectarine is a nectarine all of the time. The image of a peach by itself is not adequate to describe a nectarine. Neither is the image of a plum. But by combining certain characteristics of a peach with certain characteristics of a plum, it is possible to imagine the features of the hybrid fruit. Similarly, with resonance structures, no single drawing adequately describes the nature of the electron density spread out over the molecule. To deal with this problem, we draw several drawings and then meld them together in our minds to obtain one image, or hybrid, just like the nectarine.

Don't be confused by this important point: The term "resonance" does not describe something that is happening. Rather, it is a term that describes the way we deal with the inadequacy of our bond-line drawings.

#### **Resonance Stabilization**

We developed the concept of resonance using the allyl cation as an example, and we saw that the positive charge of an allyl cation is spread out over two locations. This spreading of charge, called **delocalization**, is a stabilizing factor. That is, *the delocalization of either a positive charge or a negative charge stabilizes a molecule*. This stabilization is often referred to as **resonance stabilization**, and the allyl cation is said to be *resonance stabilized*. Resonance stabilization plays a major role in the outcome of many reactions, and we will invoke the concept of resonance in almost every chapter of this textbook. The study of organic chemistry therefore requires a thorough mastery of drawing resonance structures, and the following sections are designed to foster the necessary skills.

# 2.8 Curved Arrows

In this section, we will focus on **curved arrows**, which are the tools necessary to draw resonance structures properly. Every curved arrow has a *tail* and *head*:



Curved arrows used for drawing resonance structures do not represent the motion of electrons they are simply tools that allow us to draw resonance structures with ease. These tools treat the electrons *as if* they were moving, even though the electrons are actually not moving at all. In Chapter 3, we will encounter curved arrows that actually do represent the flow of electrons. For now, keep in mind that all curved arrows in this chapter are just tools and do not represent a flow of electrons.

It is essential that the tail and head of every arrow be drawn in precisely the proper location. The tail shows where the electrons are coming from, and the head shows where the electrons are going (remember, the electrons aren't really going anywhere, but we treat them as if they were for the purpose of drawing the resonance structures). We will soon learn patterns for drawing proper curved arrows. But, first, we must learn where not to draw curved arrows. There are two rules that must be followed when drawing curved arrows for resonance structures:

- 1. Avoid breaking a single bond.
- 2. Never exceed an octet for second-row elements.

Let's explore each of these rules:

1. Avoid breaking a single bond when drawing resonance structures. By definition, resonance structures must have all the same atoms connected in the same order. Breaking a single bond would change this—hence the first rule:



There are very few exceptions to this rule, and we will only violate it two times in this textbook (both in Chapter 9). Each time, we will explain why it is permissible in that case. In all other cases, the tail of an arrow should never be placed on a single bond.

2. Never exceed an octet for second-row elements. Elements in the second row (C, N, O, F) have only four orbitals in their valence shell. Each orbital can either form a bond or hold a lone pair. Therefore, for second-row elements the total of the number of bonds plus the number of lone pairs can never be more than four. They can never have five or six bonds; the most is four. Similarly, they can never have four bonds and a lone pair, because this would also require five orbitals. For the same reason, they can never have three bonds and two lone pairs. Let's see some



examples of curved arrows that violate this second rule. In each of these drawings, the central atom cannot form another bond because it does not have a fifth orbital that can be used.



The violation in each example above is clear, but with bond-line structures, it can be more difficult to see the violation because the hydrogen atoms are not drawn (and, very often, neither are the lone pairs). Care must be taken to "see" the hydrogen atoms even when they are not drawn:



At first it is difficult to see that the curved arrow on the left structure is violating the second rule. But when we count the hydrogen atoms, it becomes clear that the curved arrow above would create a carbon atom with five bonds.

From now on, we will refer to the second rule as the *octet rule*. But be careful—for purposes of drawing resonance structures, it is only considered a violation if a second-row element has *more* than an octet of electrons. However, it is not a violation if a second-row element has *less* than an octet of electrons. For example:



This second drawing above is perfectly acceptable, even though the central carbon atom has only six electrons surrounding it. For our purposes, we will only consider the octet rule to be violated if we exceed an octet.

Our two rules (avoid breaking a single bond and never exceed an octet for a second-row element) reflect the two features of a curved arrow: the tail and the head. A poorly placed arrow tail violates the first rule, and a poorly directed arrow head violates the second rule.



SKILLBUILDER

**2.6** IDENTIFYING VALID RESONANCE ARROWS

LEARN the skill

For the compound below, look at the arrow drawn on the structure and determine whether it violates either of the two rules for drawing curved arrows:



### SOLUTION

In order to determine if either rule has been broken, we must look carefully at the tail and the head of the curved arrow. The tail is placed on a double bond, and therefore, this curved arrow does not break a single bond. So the first rule is not violated.

#### **STEP 1**

Make sure that the tail of the curved arrow is not located on a single bond.

#### **STEP 2**

Make sure that the head of the curved arrow does not violate the octet rule.

Next, we look at the head of the arrow: Has the octet rule been violated? Is there a fifth bond being formed here? Remember that a carbocation ( $C^+$ ) only has three bonds, not four. Two of the bonds are shown, which means that the  $C^+$  has only one bond to a hydrogen atom:



Therefore, the curved arrow will give the carbon atom a fourth bond, which does not violate the octet rule.

The curved arrow is valid, because the two rules were not violated. Both the tail and head of the arrow are acceptable.

RACTICE the skill 2.21 For each of the problems below, determine whether each curved arrow violates either of the two rules, and describe the violation, if any. (Don't forget to count all hydrogen atoms and all lone pairs.)



**APPLY** the skill

2.22 Drawing the resonance structure of the following compound requires one curved arrow. The head of this curved arrow is placed on the oxygen atom, and the tail of the curved arrow can only be placed in one location without violating the rules for drawing curved arrows. Draw this curved arrow.



need more **PRACTICE?** Try Problem 2.51

Whenever more than one curved arrow is used, all curved arrows must be taken into account in order to determine if any of the rules have been violated. For example, the following arrow violates the octet rule:



However, by adding another curved arrow, we remove the violation:



The second curved arrow removes the violation of the first curved arrow. In this example, both arrows are acceptable, because taken together, they do not violate our rules.

Arrow pushing is much like bike riding. The skill of bike riding cannot be learned by watching someone else ride. Learning to ride a bike requires practice. Falling occasionally is a



necessary part of the learning process. The same is true with arrow pushing. The only way to learn is with practice. This chapter is designed to provide ample opportunity for practicing and mastering resonance structures.

# 2.9 Formal Charges in Resonance Structures

In Section 1.4, we learned how to calculate formal charges. Resonance structures very often contain formal charges, and it is absolutely critical to draw them properly. Consider the following example:



In this example, there are two curved arrows. The first arrow pushes one of oxygen's lone pairs to form a bond, and the second arrow pushes the  $\pi$  bond to form a lone pair on a carbon atom. When both arrows are pushed at the same time, neither of the rules is violated. So, let's focus on how to draw the resonance structure by following the instructions provided by the curved arrows. We delete one lone pair from the oxygen and place a  $\pi$  bond between the carbon and oxygen. Then we must delete the C—C  $\pi$  bond and place a lone pair on the carbon:



The arrows are really a language, and they tell us what to do. However, the structure is not complete without drawing formal charges. If we apply the rules of assigning formal charges, the oxygen acquires a positive charge and the carbon acquires a negative charge:



Another way to assign formal charges is to think about what the arrows are indicating. In this case, the curved arrows indicate that the oxygen atom is losing a lone pair and gaining a bond. In other words, it is losing two electrons and only gaining one back. The net result is the loss of one electron, indicating that oxygen must incur a positive charge in the resonance structure. A similar analysis for the carbon atom on the bottom right shows that it must incur a negative charge. Let's practice assigning formal charges in resonance structures.

# **SKILLBUILDER**



2.7 ASSIGNING FORMAL CHARGES IN RESONANCE STRUCTURES

LEARN the skill

Draw the resonance structure below. Be sure to include formal charges.



#### WATCH OUT

The electrons are not really moving. We are just treating them as if they were.



The arrows indicate that one of the lone pairs on the oxygen is coming down to form a bond, and the C=C double bond is being pushed to form a lone pair on a carbon atom. This is very similar to the previous example. The arrows indicate that we must delete one lone pair on the oxygen, place a double bond between the carbon and oxygen, delete the carbon-carbon double bond, and place a lone pair on the carbon:





Finally, we must assign formal charges. In this case, the oxygen started with a negative charge, and this charge has now been pushed down (as the arrows indicate) onto the carbon. Therefore, the carbon must now bear the negative charge:

**STEP 2** Assign formal charges.



Earlier in this chapter, we said that it is not necessary to draw lone pairs, because they are implied by bond-line structures. In the example above, the lone pairs are shown for clarity. This raises an obvious question. Look at the first curved arrow above: the tail is drawn on a lone pair. If the lone pairs had not been drawn, how would the curved arrow be drawn? In situations like this, organic chemists will sometimes draw the curved arrow coming from the negative charge:



Nevertheless, you should avoid this practice, because it can easily lead to mistakes in certain situations. It is highly preferable to draw the lone pairs and then place the tail of the curved arrow on a lone pair, rather than placing it on a negative charge.

After drawing a resonance structure and assigning formal charges, it is always a good idea to count the total charge on the resonance structure. This total charge MUST be the same as on the original structure (conservation of charge). If the first structure had a negative charge, then the resonance structure must also have a net negative charge. If it doesn't, then the resonance structure cannot possibly be correct. The total charge on a compound must be the same for all resonance structures, and there are no exceptions to this rule.

PRACTICE the skill

**2.23** For each of the structures below, draw the resonance structure that is indicated by the curved arrows. Be sure to include formal charges.



2.10 Drawing Resonance Structures via Pattern Recognition



**APPLY** the skill

**2.24** In each case below, draw the curved arrow(s) required in order to convert the first resonance structure into the second resonance structure. In each case, begin by drawing all lone pairs, and then use the formal charges to guide you.



need more **PRACTICE?** Try Problems 2.44, 2.53

### 2.10 Drawing Resonance Structures via Pattern Recognition

In order to become truly proficient at drawing resonance structures, we must learn to recognize the following five patterns: (1) an allylic lone pair, (2) an allylic positive charge, (3) a lone pair adjacent to a positive charge, (4) a  $\pi$  bond between two atoms of differing electronegativity, and (5) conjugated  $\pi$  bonds in a ring.

We will now explore each of these five patterns, with examples and practice problems.

1. An allylic lone pair. Let's begin with some important terminology that we will use frequently throughout the remainder of the text. When a compound contains a carboncarbon double bond, the two carbon atoms bearing the double bonds are called **vinylic** positions, while the atoms connected directly to the vinylic positions are called **allylic** positions:



Vinylic positions

Allylic positions

We are specifically looking for lone pairs in an allylic position. As an example, consider the following compound, which has two lone pairs:



We must learn to identify lone pairs in allylic positions. Here are several examples:



In the last three cases above, the lone pairs are not next to a *carbon-carbon* double bond and are technically not allylic lone pairs (an allylic position is the position next to a

carbon-carbon double bond and not any other type of double bond). Nevertheless, for purposes of drawing resonance structures, we will treat these lone pairs in the same way that we treat allylic lone pairs. Specifically, all of the examples above exhibit at least one lone pair next to a  $\pi$  bond.

For each of the examples above, there will be a resonance structure that can be obtained by drawing exactly two curved arrows. The first curved arrow goes from the lone pair to form a  $\pi$  bond, while the second curved arrow goes from the  $\pi$  bond to form a lone pair:



Let's carefully consider the formal charges produced in each of the cases above. When the atom with the lone pair has a negative charge, then it transfers its negative charge to the atom that ultimately receives a lone pair:



When the atom with the lone pair does not have a negative charge, then it will incur a positive charge, while the atom receiving the lone pair will incur a negative charge:



Recognizing this pattern (a lone pair next to a  $\pi$  bond) will save time in calculating formal charges and determining if the octet rule is being violated.



### CONCEPTUAL CHECKPOINT

**2.25** For each of the compounds below, locate the pattern we just learned (lone pair next to a  $\pi$  bond) and draw the appropriate resonance structure:



**2.** *An allylic positive charge.* Again we are focusing on allylic positions, but this time, we are looking for a positive charge located in an allylic position:



Allylic positive charge

When there is an allylic positive charge, only one curved arrow will be required; this arrow goes from the  $\pi$  bond to form a new  $\pi$  bond:



Notice what happens to the formal charge in the process. The positive charge is moved to the other end of the system.

In Chapter 17, we will explore **conjugated**  $\pi$  **bonds**, which are systems comprised of alternating double and single bonds. In some cases, we will encounter a positive charge next to a conjugated system.



When this happens, we push each of the double bonds over one at a time:



It is not necessary to waste time recalculating formal charges for each resonance structure, because the arrows indicate what is happening. Think of a positive charge as a hole of electron density—a place that is missing an electron. When we push  $\pi$  electrons to plug up the hole, a new hole is created nearby. In this way, the hole is simply moved from one location

to another. Notice that in the above structures the tails of the curved arrows are placed on the  $\pi$  bonds, not on the positive charge. *Never place the tail of a curved arrow on a positive charge* (that is a common mistake).

# CONCEPTUAL CHECKPOINT

**2.26** Draw the resonance structure(s) for each of the compounds below:



3. A lone pair adjacent to a positive charge. Consider the following example:



The oxygen atom exhibits three lone pairs, all of which are adjacent to the positive charge. This pattern requires only one curved arrow. The tail of the curved arrow is placed on a lone pair, and the head of the arrow is placed to form a  $\pi$  bond between the lone pair and the positive charge:



Notice what happens with the formal charges above. The atom with the lone pair has a negative charge in this case, and therefore the charges end up canceling each other. Let's consider what happens with formal charges when the atom with the lone pair does not bear a negative charge. For example, consider the following:



Once again, there is a lone pair adjacent to a positive charge. Therefore, we draw only one curved arrow: the tail goes on the lone pair, and the head is placed to form a  $\pi$  bond. In this case, the oxygen atom did not start out with a negative charge. Therefore, it will incur a positive charge in the resonance structure (remember conservation of charge).

### CONCEPTUAL CHECKPOINT





#### 2.10 Drawing Resonance Structures via Pattern Recognition



In one of the problems above, a negative charge and a positive charge are seen canceling each other to become a double bond. However, there is one situation where it is not possible to combine charges to form a double bond—this occurs with the nitro group. The structure of the nitro group looks like this:

In this case, there is a lone pair adjacent to a positive charge, yet we cannot draw a single curved arrow to cancel out the charges:



Why not? The curved arrow shown above violates the octet rule, because it would give the nitrogen atom five bonds. Remember that second-row elements can never have more than four bonds. There is only one way to draw the curved arrow above without violating the octet rule—we must draw a second curved arrow, like this:



Look carefully. These two curved arrows are simply our first pattern (a lone pair next to a  $\pi$  bond). Notice that the charges have not been canceled. Rather, the location of the negative charge has moved from one oxygen atom to the other. The two resonance structures above are the only two valid resonance structures for a nitro group. In other words, the nitro group must be drawn with charge separation, even though the nitro group is overall neutral. The structure of the nitro group cannot be drawn without the charges.

4. A π bond between two atoms of differing electronegativity. Recall that electronegativity measures the ability of an atom to attract electrons. A chart of electronegativity values can be found in Section 1.11. For purposes of recognizing this pattern, we will focus on C=O and C=N double bonds.



In these situations, we move the  $\pi$  bond up onto the electronegative atom to become a lone pair:



Notice what happens with the formal charges. A double bond is being separated into a positive and negative charge (this is the opposite of our second pattern, where the charges came together to form a double bond).



#### CONCEPTUAL CHECKPOINT

**2.28** Draw a resonance structure for each of the compounds below.



**2.29** Draw a resonance structure of the compound below, which was isolated from the fruits of *Ocotea corymbosa*, a native plant of the Brazilian Cerrado.



**2.30** Draw a resonance structure of the compound shown below, called 2-heptanone, which is found in some kinds of cheese.



5. Conjugated  $\pi$  bonds enclosed in a ring. In one of the previous patterns, we introduced the term *conjugation* to refer to a system of alternating double and single bonds.

When conjugated  $\pi$  bonds are enclosed in a ring, we push all of the  $\pi$  bonds over by one position:



When drawing the resonance structure above, all of the  $\pi$  bonds can be pushed clockwise or they can all be pushed counterclockwise. Either way achieves the same result.

### CONCEPTUAL CHECKPOINT

**2.31** Fingolimod is a novel drug that has recently been developed for the treatment of multiple sclerosis. In April of 2008, researchers reported the results of phase III clinical trials of fingolimod, in which 70% of patients who took the drug daily for three years were relapse free. This is a tremendous improvement over previous drugs that only prevented relapse in 30% of patients. Draw a resonance structure of fingolimod:



Figure 2.5 summarizes the five patterns for drawing resonance structures. Take special notice of the number of curved arrows used for each pattern. When drawing resonance structures, always begin by looking for the patterns that utilize only one curved arrow. Otherwise, it is possible to miss a resonance structure. For example, consider the resonance structures of the following compound:



In this molecule, called benzene, the electrons are

LOOKING AHEAD

delocalized. As a result, benzene exhibits significant resonance stabilization. We will explore the pronounced stability of benzene in Chapter 18.

2.11 Assessing Relative Importance of Resonance Structures



Notice that each pattern used in this example involves only one curved arrow. If we had started by recognizing a lone pair next to a  $\pi$  bond (which utilizes two curved arrows), then we might have missed the middle resonance structure above:



CONCEPTUAL CHECKPOINT





# 2.11 Assessing Relative Importance of Resonance Structures

Not all resonance structures are equally significant. A compound might have many valid resonance structures (structures that do not violate the two rules), but it is possible that one or more of the structures is insignificant. To understand what we mean by "insignificant," let's revisit the analogy used at the beginning of the chapter.

Recall the nectarine analogy (being a hybrid between a peach and plum) to explain the concept of resonance. Now, imagine that we create a new type of fruit that is a hybrid between *three* fruits: a peach, a plum, and a kiwi. Suppose that the hybrid fruit has the following character: 65% peach character, 34% plum character, and 1% kiwi character. This hybrid fruit will look almost exactly like a nectarine, because the amount of kiwi character is too small to affect the nature of the resulting hybrid. Even though the new fruit is actually a hybrid of all three fruits, it will look like a hybrid of only two fruits—because the kiwi character is *insignificant*.

A similar concept exists when comparing resonance structures. For example, a compound could have three resonance structures, but the three structures might not contribute equally to the overall resonance hybrid. One resonance structure might be the major contributor (like the peach), while another might be insignificant (like the kiwi). In order to understand the true nature of the compound, we must be able to compare resonance structures and determine which structures are major contributors and which structures are not significant. Three rules will guide us in determining the significance of resonance structures:

1. *Minimize charges.* The best kind of structure is one without any charges. It is acceptable to have one or two charges, but structures with more than two charges should be avoided, if possible. Compare the following two cases:



Both compounds have a lone pair next to a C=O double bond. So we might expect these compounds to have the same number of significant resonance structures. But they do not. Let's see why. Consider the resonance structures of the first compound:



The first resonance structure is the major contributor to the overall resonance hybrid, because it has no charge separation. The other two drawings have charge separation, but there are only two charges in each drawing, so they are both significant resonance structures. They might not contribute as much character as the first resonance structure does, but they are still significant. Therefore, this compound has three significant resonance structures.

Now, let's try the same approach for the other compound:



The first and last structures are acceptable (each has only one charge), but the middle resonance structure has too many charges. This resonance structure is not significant, and therefore, it will not contribute much character to the overall resonance hybrid. It is like the kiwi in our analogy above. This compound has only two significant resonance structures.

One notable exception to this rule involves compounds containing the nitro group  $(-NO_2)$ , which have resonance structures with more than two charges. Why? We saw earlier that the structure of the nitro group must be drawn with charge separation in order to avoid violating the octet rule:



Therefore, the two charges of a nitro group don't really count when we are counting charges. Consider the following case as an example:



If we apply the rule about limiting charge separation to no more than two charges, then we might say that the second resonance structure above appears to have too many charges to be significant. But it actually is significant, because the two charges associated with the nitro group are not included in the count. We would consider the resonance structure above as if it only had two charges, and therefore it is significant.



2. Electronegative atoms, such as N, O, and Cl, can bear a positive charge, but only if they possess an octet of electrons. Consider the following as an example:

The second resonance structure is significant, even though it has a positive charge on oxygen. Why? Because the positively charged oxygen has an octet of electrons (three bonds plus one lone pair = 6 + 2 = 8 electrons). In fact, the second resonance structure above is even



more significant than the first resonance structure. We might have thought otherwise, because the first resonance structure has a positive charge on carbon, which is generally much better than having a positive charge on an electronegative atom.

Nevertheless, the second resonance structure is more significant because all of its atoms achieve an octet. In the first structure, the oxygen has its octet, but the carbon only has six electrons. In the second resonance structure, both oxygen and carbon have an octet, which makes that structure more significant, even though the positive charge is on oxygen.

Here is another example, this time with the positive charge on nitrogen:



Once again, the second structure is significant, in fact, even more significant than the first. *In summary, the most significant resonance structures are generally those in which all atoms have an octet.* 

**3.** Avoid drawing a resonance structure in which two carbon atoms bear opposite charges. Such resonance structures are generally insignificant, for example:



In this case, the third resonance structure is insignificant because it has both a C+ and a C-. The presence of carbon atoms with opposite charges, whether close to each other (as in the example above) or far apart, renders the structure insignificant. Throughout this text, we will see only one exception to this rule (in problem 18.54).

# **SKILLBUILDER**



**2.8** DRAWING SIGNIFICANT RESONANCE STRUCTURES



Using the five patterns, identify a resonance structure.

#### Draw all significant resonance structures of the following compound:

#### SOLUTION

We begin by looking for any of the five patterns. This compound contains a C=O bond (a  $\pi$  bond between two atoms of differing electronegativity), and we can therefore draw the following resonance structure:



. Ю—н

This resonance structure is valid, because it was generated using one of the five patterns. However, it has too many charges, and it is therefore not significant. In general, try to avoid drawing resonance structures with three or more charges. STEP 2 Identify if the resonance structure is significant by inspecting the number of charges and the number

of electrons on heteroatoms.

Next, we look at the other C=O bond, and we try the same pattern:



To determine if this resonance structure is significant, we ask three questions:

**1.** Does this structure have an acceptable number of charges? Yes, it has only one charge (on the carbon atom), which is perfectly acceptable.

**2.** Do all electronegative atoms have an octet? Yes, both oxygen atoms have an octet of electrons.

3. Does the structure avoid having carbon atoms with opposite charges? Yes.

This resonance structure passes the test, and therefore it is a significant resonance structure.

Now that we have found a significant resonance structure, we analyze it to see if any of the five patterns will allow us to draw another resonance structure. In this case, there is a positive charge next to a  $\pi$  bond. So we draw one curved arrow, generating the following resonance structure:





To determine whether the structure is significant, we first check to see whether it has an acceptable number of charges. It has only one charge, which is perfectly acceptable. Next we check whether all electronegative atoms have an octet. The oxygen atom bearing the positive charge does not have an octet of electrons, which is not acceptable and means that this resonance structure is not significant. In summary, this compound has the following significant resonance structure:



**RACTICE** the skill 2.33 Draw all significant resonance structures for each of the following compounds:



**PPLY** the skill

**2.34** Use resonance structures to help you identify all sites of low electron density  $(\delta+)$  in the following compound:



**2.35** Use resonance structures to help you identify all sites of high electron density  $(\delta -)$  in the following compound:





## 2.12 Delocalized and Localized Lone Pairs

In this section, we will explore some important differences between lone pairs that participate in resonance and lone pairs that do not participate in resonance.

#### **Delocalized Lone Pairs**

Recall that one of our five patterns was a lone pair that is allylic to a  $\pi$  bond. Such a lone pair will participate in resonance and is said to be **delocalized**. When an atom possesses a delocalized lone pair, the geometry of that atom is affected by the presence of the lone pair. As an example, consider the structure of an amide:



The rules we learned in Section 1.10 would suggest that the nitrogen atom should be  $sp^3$  hybridized and trigonal pyramidal, but this is not correct. Instead, the nitrogen atom is actually  $sp^2$  hybridized and trigonal planar. Why? The lone pair is participating in resonance and is therefore delocalized:



An illustration of the overlapping atomic p orbitals of an amide.



In the second resonance structure above, the nitrogen atom does not bear a lone pair. Rather, the nitrogen atom bears a p orbital being used to form a  $\pi$  bond. In that resonance structure, the nitrogen atom is clearly  $sp^2$  hybridized. This creates a conflict: How can the nitrogen atom be  $sp^3$  hybridized in one resonance structure and  $sp^2$  hybridized in the other structure? That would imply that the geometry of the nitrogen atom is flipping back and forth between trigonal pyramidal and trigonal planar. This cannot be the case, because resonance is not a physical process. The nitrogen atom is actually  $sp^2$  hybridized and trigonal planar in both resonance structures. How? The nitrogen atom has a delocalized lone pair, and it therefore occupies a p orbital (rather than a hybridized orbital), so that it can overlap with the p orbitals of the  $\pi$  bond (Figure 2.6).

Whenever a lone pair participates in resonance, it will occupy a p orbital rather than a hybridized orbital, and this must be taken into account when predicting geometry. This will be extremely important in Chapter 25 when we discuss the three-dimensional shape of proteins.

#### Localized Lone Pairs

A localized lone pair, by definition, is a lone pair that does not participate in resonance. In other words, the lone pair is not allylic to a  $\pi$  bond:



Localized



Delocalized

In some cases, a lone pair might appear to be delocalized even though it is actually localized. For example, consider the structure of pyridine:



The lone pair in pyridine appears to be allylic to a  $\pi$  bond, and it is tempting to use our pattern to draw the following resonance structure:



However, this resonance structure is not valid. Why not? In this case, the lone pair on the nitrogen atom is actually not participating in resonance, even though it is next to a  $\pi$  bond. Recall, that in order for a lone pair to participate in resonance, it must occupy a *p* orbital that can overlap with the neighboring *p* orbitals, forming a "conduit" (Figure 2.7). In the case of pyridine, the nitrogen atom is already using a *p* orbital for the  $\pi$  bond (Figure 2.8). The nitrogen atom can only use one *p* orbital to join in the conduit shown in Figure 2.8, and that *p* orbital is already being utilized by the  $\pi$  bond. As a result, the lone pair cannot join in the conduit, and therefore it cannot participate in resonance. In this case, the lone pair occupies an *sp*<sup>2</sup>-hybridized orbital, which is in the plane of the ring.



**FIGURE 2.8** The overlapping *p* orbitals of pyridine.

Here is the bottom line: Whenever an atom possesses both a  $\pi$  bond and a lone pair, they will not both participate in resonance. In general, only the  $\pi$  bond will participate in resonance, and the lone pair will not.

Let's get some practice identifying localized and delocalized lone pairs and using that information to determine geometry.



#### FIGURE 2.7

Resonance applies to systems that involve overlapping p orbitals that form a "conduit."



# **SKILLBUILDER**



#### **2.9** IDENTIFYING LOCALIZED AND DELOCALIZED LONE PAIRS

LEARN the skill

Histamine is a compound that plays a key role in many biological functions. Most notably, it is involved in immune responses, where it triggers the symptoms of allergic reactions:





Each nitrogen atom exhibits a lone pair. In each case, identify whether the lone pair is localized or delocalized, and then use that information to determine the hybridization state and geometry for each nitrogen atom in histamine.



Let's begin with the nitrogen on the right side of the compound. This lone pair is localized, and therefore we can use the method outlined in Section 1.10 to determine the hybridization state and geometry:



There are 3 bonds and 1 lone pair, and therefore: 1) Steric number = 3 + 1 = 42)  $4 = sp^3$  = electronically tetrahedral 3) Arrangement of atoms = trigonal pyramidal

This lone pair is not participating in resonance, so our method accurately predicts the geometry to be trigonal pyramidal.

Now, let's consider the nitrogen atom on the left side of the compound. The lone pair on that nitrogen atom is delocalized by resonance:



Therefore, this lone pair is actually occupying a p orbital, rendering the nitrogen atom  $sp^2$  hybridized, rather than  $sp^3$  hybridized. As a result, the geometry is trigonal planar.

Now let's consider the remaining nitrogen atom:



This nitrogen atom already has a  $\pi$  bond participating in resonance. Therefore, the lone pair cannot also participate in resonance. In this case, the lone pair must be localized. The nitrogen atom is in fact  $sp^2$  hybridized and exhibits bent geometry.

To summarize, each of the nitrogen atoms in histamine has a different geometry:



**PRACTICE the skill** 2.36 For each compound below, identify all lone pairs and indicate whether each lone pair is localized or delocalized. Then, use that information to determine the hybridization state and geometry for each atom that exhibits a lone pair.



APPLY the skill

2.37 Nicotine is a toxic substance present in tobacco leaves.



There are two lone pairs in the structure of nicotine. In general, localized lone pairs are much more reactive than delocalized lone pairs. With this information in mind, do you expect both lone pairs in nicotine to be reactive? Justify your answer.

**2.38** Isoniazid is used in the treatment of tuberculosis and multiple sclerosis. Identify each lone pair as either localized or delocalized. Justify your answer in each case.



Isoniazid

need more **PRACTICE?** Try Problems 2.47, 2.61



#### **SECTION 2.1**

- Chemists use many different drawing styles to communicate structural information, including Lewis structures, **partially** condensed structures, and condensed structures.
- The molecular formula does not provide structural information.

#### **SECTION 2.2**

- In **bond-line structures**, carbon atoms and most hydrogen atoms are not drawn.
- Bond-line structures are faster to draw and easier to interpret than other drawing styles.

#### **SECTION 2.3**

- A **functional group** is a characteristic group of atoms/bonds that show a predictable chemical behavior.
- The chemistry of every organic compound is determined by the functional groups present in the compound.

#### **SECTION 2.4**

- A formal charge is associated with any atom that does not exhibit the appropriate number of valence electrons.
- When a carbon atom bears either a positive or negative charge, it will have only three, rather than four, bonds.

#### **SECTION 2.5**

• Lone pairs are often not drawn in bond-line structures. It is important to recognize that these lone pairs are present.

#### **SECTION 2.6**

- In bond-line structures, a **wedge** represents a group coming out of the page, and a **dash** represents a group behind the page.
- Other drawings used to show three dimensionality include **Fischer projections** and **Haworth projections**.

#### **SECTION 2.7**

- Bond-line structures are inadequate in some situations, and an approach called **resonance** is required.
- **Resonance structures** are separated by double-headed arrows and surrounded by brackets:



# KEY TERMINOLOGY

#### allylic 73

dash 63 delocalization 68 delocalized lone pair 83 Fischer projections 64 functional group 57 Haworth projections 64 localized lone pair 83 partially condensed structures 50 resonance 67 resonance hybrid 67 resonance stabilization 68 resonance structures 67 vinylic 73 wedge 63

• **Resonance stabilization** refers to the **delocalization** of either a positive charge or a negative charge via resonance.

#### **SECTION 2.8**

- Curved arrows are tools for drawing resonance structures.
- When drawing curved arrows for resonance structures, avoid breaking a single bond and never exceed an octet for second-row elements.

#### **SECTION 2.9**

 All formal charges must be shown when drawing resonance structures.

#### **SECTION 2.10**

- Resonance structures are most easily drawn by looking for the following five patterns:
- 1. An **allylic** lone pair
- 2. An allylic positive charge
- 3. A lone pair adjacent to a positive charge
- 4. A  $\pi$  bond between two atoms of differing electronegativity
- 5. Conjugated  $\pi$  bonds enclosed in a ring.
- When drawing resonance structures, always begin by looking for the patterns that utilize only one curved arrow.

#### **SECTION 2.11**

- There are three rules for identifying significant **resonance structures**:
  - 1. Minimize charge.
  - 2. Electronegative atoms (N, O, Cl, etc.) can bear a positive charge, but only if they possess an octet of electrons.
  - 3. Avoid drawing a resonance structure in which two carbon atoms bear opposite charges.

#### **SECTION 2.12**

- A **delocalized lone pair** participates in resonance and occupies a *p* orbital.
- A localized lone pair does not participate in resonance.

# **SKILLBUILDER** REVIEW

#### 2.1 CONVERTING BETWEEN DIFFERENT DRAWING STYLES



<sup>-----&</sup>gt; Try Problems 2.1–2.4, 2.49, 2.50

#### **2.2** READING BOND-LINE STRUCTURES



#### 2.3 DRAWING BOND-LINE STRUCTURES



#### 2.4 IDENTIFYING LONE PAIRS ON OXYGEN ATOMS

Oxygen with a negative charge...

A neutral oxygen atom...



Oxygen with a positive charge...

Æ

...has three lone pairs.

...has two lone pairs.

...has one lone pair.



#### 2.5 IDENTIFYING LONE PAIRS ON NITROGEN ATOMS



#### 2.6 IDENTIFYING VALID RESONANCE ARROWS



#### 2.7 ASSIGNING FORMAL CHARGES IN RESONANCE STRUCTURES



#### **2.8** DRAWING SIGNIFICANT RESONANCE STRUCTURES



#### 2.9 IDENTIFYING LOCALIZED AND DELOCALIZED LONE PAIRS



# **PRACTICE** PROBLEMS

**2.39** Draw all carbon atoms, hydrogen atoms, and lone pairs for the following compounds:



2.40 Draw bond-line structures for all constitutional isomers of C<sub>4</sub>H<sub>10</sub>.

2.41 Draw bond-line structures for all constitutional isomers of  $C_5H_{12}$ .

**2.42** Draw bond-line structures for vitamin A and vitamin C:



Vitamin A



2.43 How many lone pairs are found in the structure of vitamin C?

2.44 Identify the formal charge in each case below:





PLUS WileyPLUS, an online teaching and learning solution.

**2.45** Draw significant resonance structures for the following compound:



- **2.46** Learning to extract structural information from molecular formulas:
- (a) Write out the molecular formula for each of the following compounds:



Compare the molecular formulas for the above compounds and fill in the blanks in the following sentence: The number of hydrogen atoms is equal to \_\_\_\_\_\_ times the number of carbon atoms, plus

(b) Now write out the molecular formula for each of these compounds:



Each of the compounds above has either a double bond or a ring. Compare the molecular formulas for each of these compounds. In each case, the number of hydrogen atoms \_\_\_\_ times the number of carbon atoms. Fill in the is blank.

(c) Now write out the molecular formula for each of these compounds:



Each of the compounds above has either a triple bond or two double bonds or two rings or a ring and a double bond. Compare the molecular formulas for each of these compounds. In each case, the number of hydrogen atoms is \_\_\_\_\_ \_ times the number of carbon atoms minus \_. Fill in the blanks.

(d) Based on the trends above, answer the following questions about the structure of a compound with molecular formula



 $C_{24}H_{48}$ . Is it possible for this compound to have a triple bond? Is it possible for this compound to have a double bond?

(e) Draw all constitutional isomers that have the molecular formula  $\mbox{C}_4\mbox{H}_8.$ 

**2.47** Each compound below exhibits one lone pair. In each case, identify the type of atomic orbital in which the lone pair is contained.



**2.48** Draw all significant resonance structures for each of the following compounds:



**2.49** Write a condensed structural formula for each of the following compounds:



**2.50** What is the molecular formula for each compound in the previous problem?

**2.51** Which of the following drawings is not a resonance structure for 1-nitrocyclohexene? Explain why it cannot be a valid resonance structure.



**2.52** Identify the number of carbon atoms and hydrogen atoms in the compound below:



**2.53** Identify any formal charges in the following structures:



**2.55** Draw resonance structures for each of the following compounds:



**2.56** Determine the relationship between the two structures below. Are they resonance structures or are they constitutional isomers?



**2.57** Consider each pair of compounds below, and determine whether the pair represent the same compound, constitutional isomers, or different compounds that are not isomeric at all:



**2.58** Draw a bond-line structure for each of the following compounds:

(a)  $CH_2 = CHCH_2C(CH_3)_3$ (b) (CH<sub>3</sub>CH<sub>2</sub>)<sub>2</sub>CHCH<sub>2</sub>CH<sub>2</sub>OH (c)  $CH \equiv COCH_2CH(CH_3)_2$ (d) CH<sub>3</sub>CH<sub>2</sub>OCH<sub>2</sub>CH<sub>2</sub>OCH<sub>2</sub>CH<sub>3</sub> (e) (CH<sub>3</sub>CH<sub>2</sub>)<sub>3</sub>CBr (f) (CH<sub>3</sub>)<sub>2</sub>C=CHCH<sub>3</sub>

**2.59** A mixture of sulfuric acid and nitric acid will produce small quantities of the nitronium ion  $(NO_2^+)$ :

Does the nitronium ion have any significant resonance structures? Why or why not?

**2.60** Consider the structure of ozone:

Ozone is formed in the upper atmosphere, where it absorbs short-wavelength UV radiation emitted by the sun, thereby protecting us from harmful radiation. Draw all significant resonance structures for ozone (Hint: Begin by drawing all lone pairs).

**2.61** Melatonin is an animal hormone believed to have a role in regulating the sleep cycle:



The structure of melatonin incorporates two nitrogen atoms. What are the hybridization state and geometry of each nitrogen atom? Explain your answer.

2.62 Draw all significant resonance structures for each of the following compounds:



(Female sex hormone)

(Male sex hormone)

# **INTEGRATED** PROBLEMS

**2.63** Cycloserine is an antibiotic isolated from the microbe Streptomyces orchidaceous. It is used in conjunction with other drugs for the treatment of tuberculosis.



Cycloserine

- (a) What is the molecular formula of this compound?
- (b) How many sp<sup>3</sup>-hybridized carbon atoms are present in this structure?
- (c) How many  $sp^2$ -hybridized carbon atoms are present in this structure?
- (d) How many sp-hybridized carbon atoms are present in this structure?
- (e) How many lone pairs are present in this structure?
- (f) Identify each lone pair as localized or delocalized.
- (g) Identify the geometry of each atom (except for hydrogen atoms).
- (h) Draw all significant resonance structures of cycloserine.

2.64 Ramelteon is a hypnotic agent used in the treatment of insomnia:



Ramelteon

- (a) What is the molecular formula of this compound?
- (b) How many  $sp^3$ -hybridized carbon atoms are present in this structure?
- (c) How many  $sp^2$ -hybridized carbon atoms are present in this structure?
- (d) How many sp-hybridized carbon atoms are present in this structure?
- (e) How many lone pairs are present in this structure?
- (f) Identify each lone pair as localized or delocalized.
- (g) Identify the geometry of each atom (except for hydrogen atoms).



# **CHALLENGE** PROBLEMS

**2.65** In the compound below, identify all carbon atoms that are electron deficient ( $\delta$ +) and all carbon atoms that are electron rich ( $\delta$ -). Justify your answer with resonance structures.



**2.66** Consider the following two compounds:



- (a) Identify which of these two compounds has greater resonance stabilization.
- (b) Would you expect compound C (below) to have a resonance stabilization that is more similar to compound A or to compound B?



Compound C

**2.67** Single bonds generally experience free rotation at room temperature (as will be discussed in more detail in Chapter 4):



Nevertheless, the "single bond" shown below exhibits a large barrier to rotation. In other words, the energy of the system is greatly increased if that bond is rotated. Explain the source of this energy barrier. (*Hint:* Think about the atomic orbitals being used to form the "conduit.")

