

The background of the book cover is a dark teal color with faint, glowing chemical structures. These include a benzene ring in the top right, a vertical chain of three circles connected by horizontal lines in the top center, a square with a central circle in the middle right, a triangle with internal lines in the middle left, and a large ring with two smaller circles attached at the bottom center.

STEVEN FARMER

# STRANGE CHEMISTRY

THE STORIES YOUR CHEMISTRY TEACHER  
WOULDN'T TELL YOU

WILEY



## Strange Chemistry



# **Strange Chemistry**

The Stories Your Chemistry Teacher Wouldn't Tell You

*Steven Farmer*

*Sonoma State University, Rohnert Park, California, USA*

**WILEY**

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## Dedication

**I would like to dedicate this book to my parents James and Margaret.**

Throughout my whole life whenever I looked, you were there; ready to give me love and support, guidance and security, and praise and encouragement. You filled me with your dreams and showed me what it takes to succeed in life. Without you both none of the things I have accomplished would have been possible. I am truly blessed to have such incredible parents, and I love you both.





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## Preface

Growing up in Northern California was much more curious than one might think. Napa, being part of Northern California, was affected by the LSD (lysergic acid diethylamine) counterculture centered in Berkeley and San Francisco. LSD was everywhere and I recall multiple instances in high school where a classmate would admit to attending class under the influence of LSD and try to describe the effects. This seems very rebellious, but in one of the most tragic events of my life, a high school friend jumped in front of a car on the highway after ingesting LSD. He was killed instantly. This event had such a profound effect on me that it eventually drove me toward a career in chemistry – I needed to understand what had happened to my friend. How could the ingestion of a molecule cause such profound effects? Is awareness really just a fragile chemical process that can be so easily tricked?

After the mass closures of the 1980s, Napa State Hospital was one of the few remaining state run mental hospitals in California. If you have seen the movie *One Flew Over the Cuckoo's Nest*, it was filmed at Napa State Hospital. As a child, I would often wonder about the causes of mental illness. I was told that mental illness was the result of a “chemical imbalance” in the brain, but what did that really mean? Could a slight change in a chemical really change our perception of the world?

Similar to many scientists before me, my career in chemistry was driven by a quest to better understand some of the questions that haunted my childhood. Surely, obtaining a degree in chemistry would allow me to understand how hallucinogens work, or what causes mental illnesses. Unfortunately, I was wrong. Chemistry courses seemed to steer clear of any topic of an edgy, dangerous, or unusual nature. In fact, initially learning about these fascinating topics required a course outside the chemistry department. Eventually, a graduate elective course from a psychology department, called “Psychopharmacology,” explained the chemical basis for the effect of hallucinogens and the causes of mental illness (I share what I learned in this book).

Later, when I became a chemistry instructor, I made it a point to share these and other stories. It was delightful to find that almost everyone found these

topics just as interesting as I did. As I collected new stories, I realized how much of this material was never discussed as part of the numerous chemistry courses required for my Ph.D. Roughly 90% of these stories contained in this book were learned after I graduated. This is where the subtitle of this book, “The stories your chemistry teacher wouldn’t tell you” comes from. It seems that there is an overwhelming push to teach the fundamentals of chemistry while neglecting to show the utility of learning the material by connecting it to the real world. Particularly for organic chemistry, there seems to be an aversion of some of these topics, which I feel is because chemists do not want their science associated with anything that poisons you, blows you up, or gets you high. However, these are the topics that many people find exciting (as can be seen by looking at the plot of almost any action movie). Ask a nonchemist where chemicals appear in everyday life and inevitably the answer involves pharmaceuticals, toxins, or illicit drugs.

To share these stories with my students, I usually would take about 5–10 minutes each week to present one of the stories described in this book. For those of you who are teachers or who plan to be, I can say that these stories have been the largest source of positive feedback I have received from my students. Although there is an enormous amount of material that needs to be covered in a typical chemistry course, I say make the time for these extras. It is that important! On multiple occasions, students admitted to me that they only came to class that day so that they could hear the story. Many times, students would speak to me after the lecture to share how that day’s story had touched them in some way. One student had been to the emergency room for an acetaminophen overdose, another had a stepfather who was addicted to opioids, and yet another was prescribed amphetamine to treat their attention deficit hyperactivity disorder (ADHD).

You will note that most of the presented stories are short and involve a question or a defined idea. This is done for two reasons: First, I love presenting these questions to my students and trying to evoke an answer from them. Putting students on the spot drives home how little they actually know about the world and how learning chemistry helps them understand their lives. I admit, few things have made me feel more educated than seeing a single simple question stump a classroom with over 400 students. Try it. You will find that very few people know the answers to the questions posed in this book. In addition, some of the cheeky answers I receive have become the highlights of my teaching. Second, I present the stories in a simple format because they will be easy to remember. Jokingly, I tell students to share these stories with their friends and family members so that they can prove that they are receiving an education at Sonoma State University. I am pleased to say that they do just that. An informal poll of my students showed that 90% of them had shared a story at least once, and 75% said that they shared these stories on a regular basis.



Students, like all human beings, want to understand the world around them – they may just not realize it. Telling stories that help students understand and connect to the world they see inspires them in a primal way, making them want to learn and keep coming back for more. This book contains the best stories I have collected over the last 10 years. If you are a teacher, try some of them out and see the profound effect they have on students. Even if you are not a teacher, read on, better understand the world around you, and see how truly strange chemistry can be.



## Acknowledgments

To my loving wife, Joy: You are still the most beautiful woman I have ever seen. You are my muse, my life, and the air that I breathe. You are the personification of everything that makes me happy in this world. It was only your love that allowed me to face the adversity I have seen. You have been with me since the start of this journey and I cannot wait to see where life takes us.

To my brother, Richard: Thanks for being the oldest friend I have and for being the funniest person I know.

To my first college chemistry professor, Dr Steven Fawl: Thanks for all of those long talks in your office. Thanks for taking time out for someone who had absolutely no idea what he was going to do with his life. Of all my science professors, you seemed the most worldly and grounded. Your knowledge of chemistry seemed to let you understand the world and how it works. It was because of you that I decided to become a chemist.

To the students of Sonoma State University: Thanks for listening to all of my crazy stories and for continually reminding me why I love teaching so much.

To my colleagues in the chemistry department: Thanks for your help in vetting these stories.

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## 1

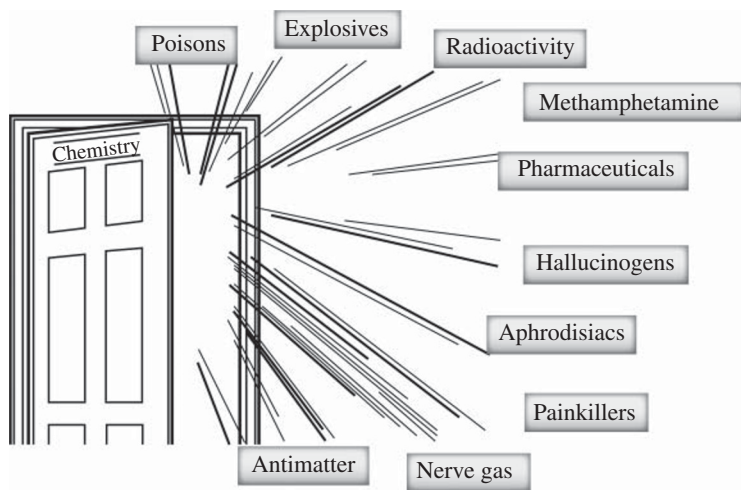
## If You Do Not Know Any Chemistry, This Chapter Is For You

As a professor, I regularly teach college-level chemistry courses. These courses present various materials, which are important for students who wish to continue their careers in chemistry. Although most people reading this book will not need all the information covered in these courses, understanding a few key concepts will allow them to understand various ways in which chemistry shows up in everyday life. In fact, one of the driving forces of compiling these stories is to show that even a basic understanding of chemistry can help us comprehend how the world and society work. In particular, I would like to bring readers up to speed on a few key chemical concepts that are referred to in this book (Figure 1.1).

### Representing Atoms and Molecules in Chemistry

The first concept concerns the representation of atoms and molecules. Often, the structure of molecules can provide insight into its properties or the ways in which it will affect a human being, if ingested. Certain structural features will imbue molecules with particular properties. In addition, molecules with similar structures will often have similar properties. A detailed understanding of chemistry is not required to make this connection, but only the ability to see similarities.

Chemists represent an individual element with a capital letter, such as “C” for carbon, “H” for hydrogen, and “Fe” for iron, as listed in a periodic table. This letter represents all of the protons and neutrons in the atom’s nucleus plus any electrons not involved in bonding. During most chemical reactions, the nucleus of atoms remains unchanged, so this simple representation of elements is helpful to chemists. If an oxygen atom is involved in a chemical reaction, it will remain an oxygen atom. Its structure and bonding may change, but the nucleus will be the same. An important exception is radioactive decay, where a nucleus can be changed and one element can change into another. This will be discussed later.

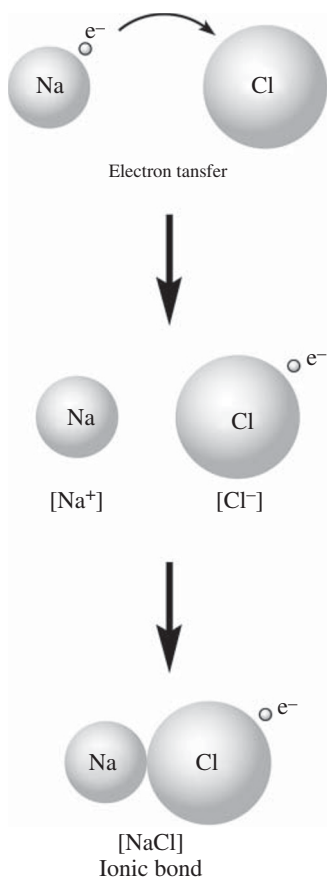


**Figure 1.1** Look at what hides behind the door of understanding chemistry.

In the case of some metals and gases, the atom is not bonded (connected) to any other atoms; hence, the bulk material can be represented with the elemental symbol. A block of iron is made up entirely of iron atoms that can be represented by symbol Fe. Similarly, a balloon filled with helium can be represented with the symbol He.

Although individual elements are important, chemistry truly becomes interesting when atoms start bonding together to form more complex structures. Two major types of bonds are *ionic* and *covalent*. In an ionic bond, one atom gives up one or more electrons, giving it a positive charge, while another atom gains one or more electrons, giving it a negative charge. Electrostatic forces bring the positive and negative ions together. However, when ionic compounds are placed in an appropriate solvent, such as water, the compounds break apart into their ionic species. The classic ionic compound is common table salt sodium chloride (NaCl). In the crystals of table salt, the sodium and chlorine atoms are being held together by the attraction of a positive and negative charge. When placed in water, table salt tends to break apart into its ionic species, in this case  $\text{Na}^+$  and  $\text{Cl}^-$  (Scheme 1.1).

Ionic compounds are generally made with ionic bonds. Ionic bonds are easily identified because they are made by combining a metal (elements on the left-hand side of the periodic table) with a nonmetal (elements found in the upper right-hand corner of the periodic table). Ionic bonds are typically not formally drawn; rather, the ions are drawn together in a molecular formula where the overall compound is neutral. For example,  $\text{FeCl}_3$  means a  $\text{Fe}^{3+}$  ion bonds to three  $\text{Cl}^-$  ions using ionic bonds. This simple discussion will allow for a better understanding of many ionic compounds with which you may be familiar (Table 1.1).

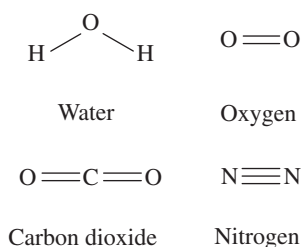


**Scheme 1.1** The formation of an ionic bond in NaCl.

**Table 1.1** Some common ionic compounds.

Compound	Name	Ions involved	Common use
KI	Potassium iodide	K <sup>+</sup> & I <sup>-</sup>	Treatment of hyperthyroidism
PbO <sub>2</sub>	Lead (IV) oxide	Pb <sup>+4</sup> & O <sup>-2</sup>	Found in car batteries
CaCl <sub>2</sub>	Calcium chloride	Ca <sup>+2</sup> & Cl <sup>-</sup>	Road deicing

Covalent bonds differ from ionic bonds in that electrons are shared rather than stolen to form a bond between two atoms. This means that covalent bonds are not easily broken into ionic species and do not break apart when dissolved in water. The sharing of two electrons between two atoms to form a covalent bond is represented with a single line. The water molecule is made up of two H—O single covalent bonds. Similarly, if four electrons are shared between two



**Figure 1.2** The structure of some simple molecules.

atoms, the covalent bond is shown with a double line and is called a double bond. Six shared electrons are depicted by three lines and called a triple bond. Molecular oxygen is made up of a double bond between the two oxygen atoms, and molecular nitrogen is made up of a triple bond between the two nitrogen atoms. Single, double, and triple bonds all have different properties and reactivity that are dependent on the types of atoms involved in the covalent bond. Even now, this basic description of covalent bonds can help you understand the structure of multiple simple molecules (Figure 1.2).

What makes covalent bonds so interesting is their ability to combine to form large molecular structures. Inorganic compounds do not have this ability. Literally, thousands of atoms can be linked together by covalent bonds to create such complex molecules as polymers, proteins, and even deoxyribonucleic acid (DNA).

This book focuses mostly on *organic molecules*, which are typically constructed with covalent bonds. Organic molecules were originally called “organic” because it was believed that these types of compounds could only come from living, organic sources, such as plants or animals. Once it was shown that organic molecules could be made from inorganic materials, the definition was expanded. The current definition states that organic molecules contain the element carbon. *Organic chemistry* is the study of carbon-containing molecules. For the purposes of this book, we will be focusing on the conversion of one organic molecule into another using reactions. Using these reactions, organic chemists create many pharmaceuticals, many plastics, and a multitude of other molecules.

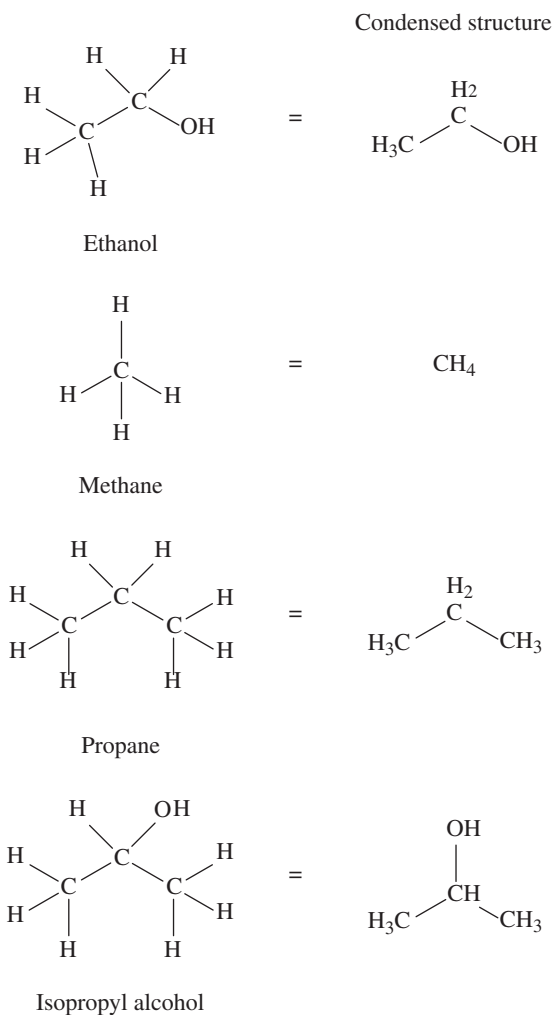
The versatility of covalent bonds creates virtually limitless possible combinations of organic molecules, which is why organic chemistry is such a broad field of study. In college, an entire year of study is devoted to organic chemistry to obtain a typical chemistry degree. At this point, millions of organic compounds are known, with new ones being generated every day. One of the more interesting aspects of organic chemistry is the ability to combine atoms in new ways to make new organic molecules, many of which have never been seen in nature.<sup>1</sup>

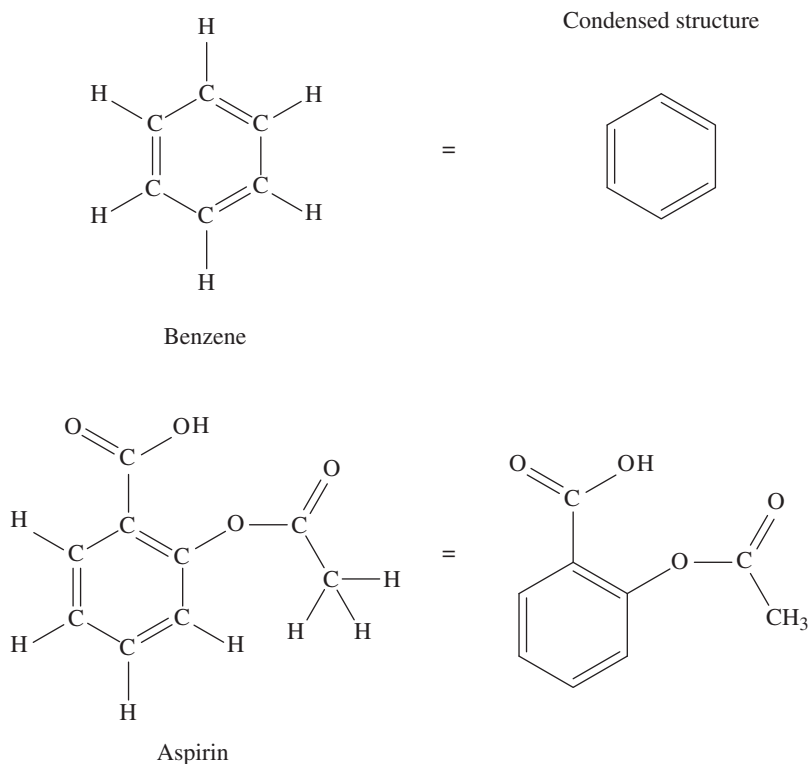
<sup>1</sup> I am formally trained as an organic chemist. During my career, I estimate that I have created roughly 50 novel organic molecules. These include anticancer drugs, novel polymers, linkers for nanoparticles, and supramolecular agents, which allow for the controlled ordering of molecules.



Because of the large numbers of variations, organic molecules are commonly represented by structures as well as their formal names. In addition, due to a large and complex nature of organic molecules, they are often drawn using a condensed form. Because organic molecules typically have a large number of hydrogens in their structures, it is particularly common to represent hydrogens in an abbreviated form. In a condensed structure, the bonds attached to the hydrogens are omitted and the number of H's is represented with a subscript. Examples of these abbreviations are represented below using some simple organic molecules (Figure 1.3).

**Figure 1.3** The condensed structure of some simple organic molecules.

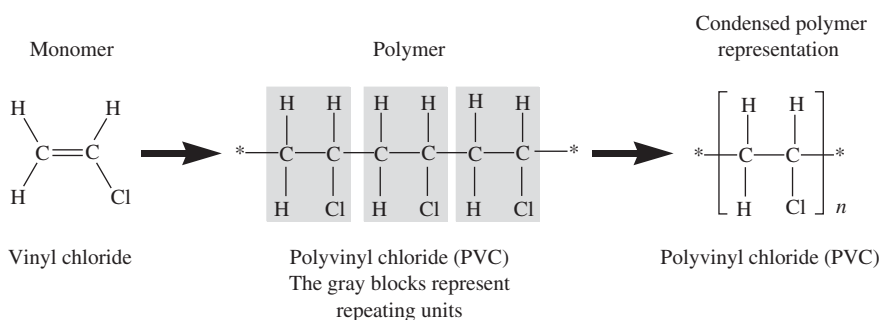




**Figure 1.4** The condensed structure of the benzene ring.

Another important way in which hydrogens are abbreviated involves the *benzene* ring. This ring is immensely important in organic chemistry, and its presence can be seen in many important organic molecules. To simplify the structure, the hydrogens at the points of the benzene ring are commonly omitted. Moreover, the carbon atoms in the benzene ring are represented simply by lines denoting the covalent bonds (Figure 1.4).

Lastly, the structures of polymers are usually represented using a type of abbreviation. Small molecules called *monomers* are connected in large numbers during a polymerization reaction to create large molecules called *polymers*. This process is represented in the name “polymer,” which means many monomers. Because polymers are made up of a repeating monomer subunit, they are represented by the subunit surrounded by brackets. The monomer subunit is repeated a variable number of times, which is represented by the

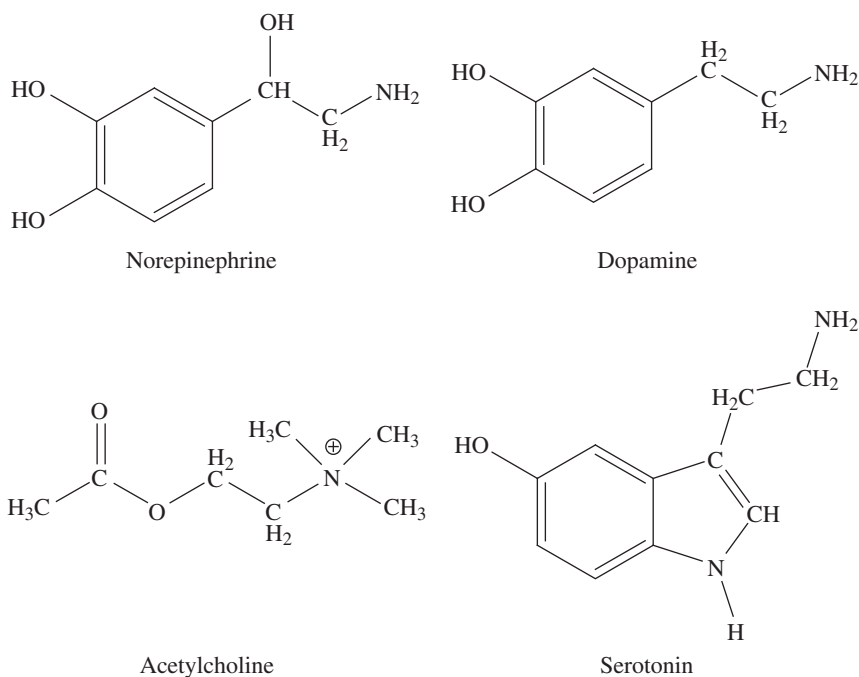


**Figure 1.5** How polymers are represented.

subscript “ $n$ .” The actual number of monomers subunits in a polymer is usually unknown, which is why it is represented by a variable (Figure 1.5).

## Neurotransmitters

In this book, neurotransmitters are the most important molecules used to describe the function of organic molecules in the body. Virtually everything we do involves neurons communicating with one another. Everything from movement, breathing, and even awareness are brought about by electrical impulses moving across our nervous system. Anyone who has seen a Taser in action knows that neurons are affected by electricity; however, certain chemicals also play an important role in how neurons operate. Many neurons are separated by a small gap called the *synaptic cleft*. During a typical nerve impulse, specific molecules called *neurotransmitters* bridge this gap. When an electrical impulse reaches the end of a presynaptic neuron, neurotransmitters are released and subsequently diffused across the synaptic cleft, binding to the receptors on the receiving postsynaptic neuron. *Receptors* are typically proteins on the surface of the neurons, which recognize and bind to specific neurotransmitters. This binding usually brings about a chemical change that creates an electrical impulse in the receiving postsynaptic neuron. In short, neurotransmitters allow for electrical impulses to be transmitted between adjacent neurons despite the presence of a synaptic gap. By repeating this process, electrical nerve impulses can be sent across the body or across the brain. Neurotransmitters that cause a neuron to fire are considered “*excitatory*” and are responsible for motion, mental

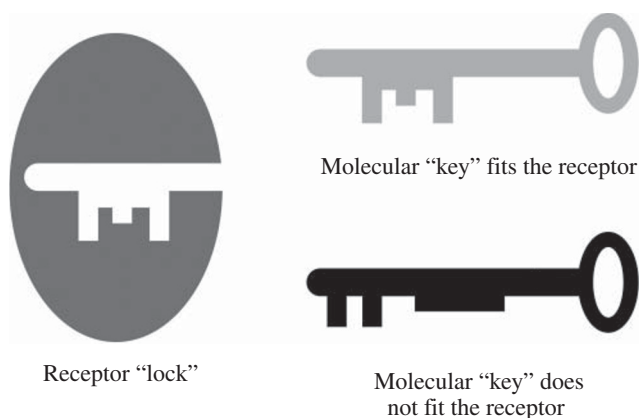


**Figure 1.6** Various neurotransmitters.

cognition, and other activities that require the brain and body to be active (Figure 1.6).

In addition, certain neurotransmitters can also be “*inhibitory*” and actually impede the transmission of impulses in neurons. The effect of inhibitory neurotransmitters in these neurons causes a chemical change within the neuron that opposes the effects of excitatory neurotransmitters. In general, inhibitory neurotransmitters are responsible for inducing sleep and filtering out unnecessary excitatory signals.

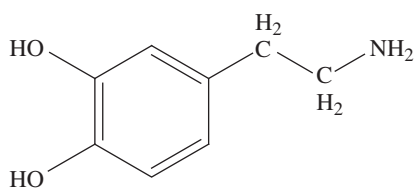
In short, neurotransmitters send chemical messages between neurons and act as the on and off switches of the nervous system. By understanding that chemicals can affect how neurons work, many interesting concepts can be discussed. Many mental illnesses are believed to be caused by a “chemical imbalance” of neurotransmitters in certain areas of the brain. Many medications used to treat mental illnesses, as well as many psychoactive drugs and neurotoxins, obtain their effects by changing the ways in which neurotransmitters are released and absorbed or by simply mimicking the structure



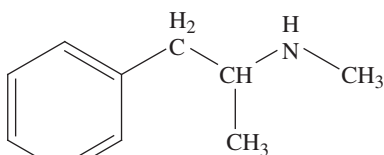
**Figure 1.7** A representation of the lock-and-key model of receptors.

of a neurotransmitter. The key receptors in neurons designed to recognize neurotransmitters look for specific structural features. This is called the lock-and-key model. Receptors proteins are typically wadded into a ball-like structure that has small pockets. Certain structural features of molecules allow them to fit into these pockets, activating the receptors. Because the receptors are looking for specific structural features, molecules that have similar structural features can fool these receptors (Figure 1.7).

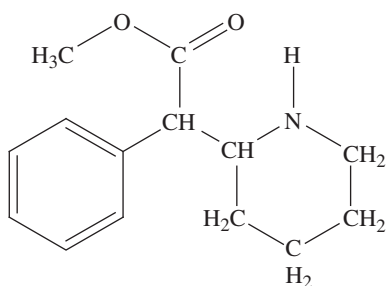
An excellent example is seen with the molecules dopamine and methamphetamine. Dopamine is one of the most important neurotransmitters in the parts of the brain involving motion and alertness. Key receptors in neurons recognize the benzene ring connected to two carbons and a nitrogen found in dopamine. Methamphetamine also has a benzene ring connected to two carbons and nitrogen, so it can also fit into these receptors, which tricks the neurons into thinking that it is dopamine. The presence of methamphetamine causes the areas of the brain, which utilize dopamine to become excited, causing the hyperactivity and insomnia associated with methamphetamine use. Now that we understand the structural features that can allow molecules to mimic dopamine, we can look for them in other molecules. Ritalin<sup>®</sup> has these structural features, and it is used to treat attention deficit hyperactivity disorder (ADHD) by stimulating the parts of the brain associated with attention. In addition, the common decongestant pseudoephedrine has these structural features and has the side effects of causing restlessness and insomnia, which has to be stated on the packaging (Figures 1.8 and 1.9).



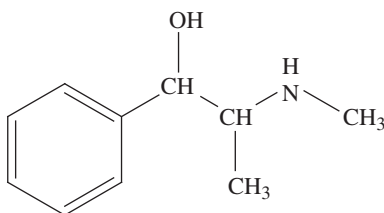
Dopamine



Methamphetamine



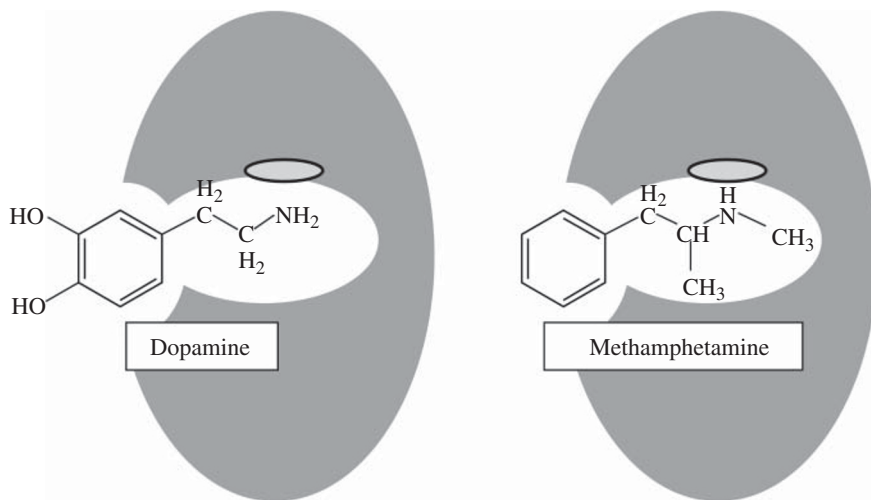
Methylphenidate  
(Ritalin®)



Pseudoephedrine

**Figure 1.8** Molecules with structures similar to dopamine.

Dopamine receptor



**Figure 1.9** A representation of how dopamine and methamphetamine both fit in the dopamine receptor.

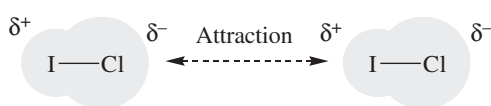
## Intermolecular Forces

Have you ever wondered why some molecules like oxygen are a gas at room temperature and ambient pressure while other molecules like water are liquid and still others like table salt (NaCl) are a solid? This has to do with a concept called *intermolecular forces* (IMF) or the forces between individual molecules. In general, molecules with relatively strong IMFs tend to hold together better and form solids and those with weak IMFs tend not to hold together and form gases. Having a basic understanding of IMFs allows one to have a better understanding of the world. Why a solid is a solid, why does one substance stick to another, and why do some liquids mix while others separate into layer?

To have a basic understanding of IMFs, you just have to remember that positive and negative charges are attracted to each other. The ways in which these positive and negative charges are generated in molecules determine the strength of the IMFs between them.

This book discusses four major IMFs. The strongest is called the *ionic* IMF. As discussed previously, when a compound contains an ionic bond, one or more electrons are shared to form positive and negatively charged species. These charged species are then attracted to each other by the ionic IMF. These compounds, which contain ionic bonds (metals bonded to nonmetals), are typically solids under normal conditions. Salts, such as common table salt (NaCl) or potassium chloride (KCl), as well as most minerals, such as chalk ( $\text{CaCO}_3$ ) and iron pyrite ( $\text{FeS}$ ), all contain ionic bonds and ionic IMFs.

The next strongest IMF is called a *dipole* IMF. Dipole IMFs are typically found when dealing with molecules containing covalent bonds. Although it is possible for organic compounds to have ionic IMFs, most are governed by dipole IMF's. In a covalent bond, electrons are being shared by two atoms, although they are rarely shared equally. *Electronegativity* is a measure of an atom's ability to pull on the electrons in a covalent bond. The elements of the periodic table typically become more electronegative as we travel up and to the right of the table, with fluorine being the most electronegative element. There are many exceptions to this rule, but it is a general trend. In the molecule ICl, the electrons in the I—Cl covalent bond are drawn closer to the chlorine because it is more electronegative than iodine. This gives the chlorine a partial negative charge, which is represented by the symbol  $\delta^-$ . This also gives the iodine a partial positive charge represented by the symbol  $\delta^+$ . The ICl molecule is called *polar* because one side of a molecule has a slight positive charge and the other side has a slight negative charge. A dipole IMF is created when the positive side on one molecule is attracted to the negative side of an adjacent molecule. The molecule ICl has only one covalent bond; however, molecules with multiple covalent bonds can also be polar, depending on the orientations of the bonds and the electronegativity of the atoms involved. Note! The dipole IMF is weaker compared to the ionic IMF because only partial charges are being used (Figure 1.10).



**Figure 1.10** An example of a dipole intermolecular force.

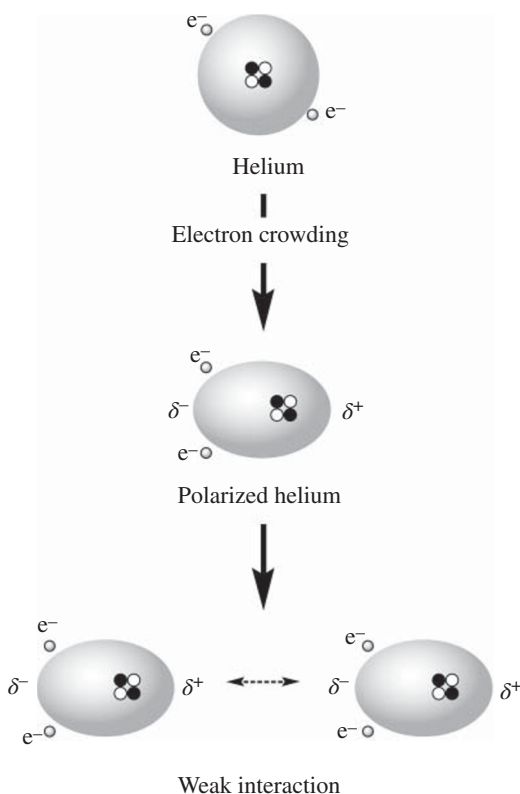
An important subset of dipole IMFs is called *hydrogen bonding*, and it is reserved for some of the most electronegative elements in the periodic table, like nitrogen, oxygen, and fluorine. When these elements are directly bonded to hydrogen in a molecule, this special IMF comes about. In this case, the charge separation caused by these highly electronegative elements is so extreme that dipole interaction is enhanced. The hydrogens are “loose” and do not remain permanent bonded. They freely move around, and they can be shared by other hydrogen-bonding molecules. This causes a hydrogen-bonding interaction, which is stronger compared to a typical dipole interaction. Many common liquids utilize hydrogen-bonding IMFs, including water and alcohol. In addition, DNA strands are held together using hydrogen bonding.

The last IMF is probably the most difficult to conceive, although it is still extremely important. Covalent bonds involve electrons being shared; therefore, they are affected by the electronegativity of the atoms involved. However, what happens when the two atoms are the same? A prime example of this is an oxygen molecule. The two oxygen atoms have exactly the same electronegativity, therefore, exactly the same pull on the electrons in the covalent bond. There is no separation of charge; thus, the molecule is deemed *nonpolar*. This can also come about when dealing with substances that have no bonds, such as helium, or with molecules that orientate their bonds so that there is no charge separation in the molecule, such as methane. All these molecules are also considered nonpolar; however, the fact that they can form liquids when made cold enough shows that there must be some type of IMF in them. This last and weakest IMF has many names, including *instantaneous dipole forces*, *Van der Waals forces*, and *dispersion forces*. I will call them instantaneous dipoles in this book because I feel this name best describes the effect.

Instantaneous dipole IMFs can best be explained by looking at a typical helium atom. It is made up of a nucleus containing two protons and two neutrons surrounded by two electrons. The two negatively charged electrons balance out the two positively charged protons in the nucleus so the overall atom is neutral. Because both electrons are negatively charged, they repel each other and usually stay on the opposite sides of the nucleus. However, these electrons orbit the nucleus at extremely fast speeds, roughly 80% the speed of light; hence, it is possible for these electrons to crowd on one side of the helium atom. When this happens, the nucleus is momentarily exposed, giving the atom a positively charged side ( $\delta^+$ ) while the crowded electrons give the other side of the atom a negative charge ( $\delta^-$ ). This happens only for an instant because the electrons quickly repel each other. This charge separation gives



**Figure 1.11** An example of an instantaneous dipole intermolecular force.



the atom an “instantaneous dipole” and allows two different helium atoms to have an IMF. This idea is also true for molecules that contain multiple atoms, such as methane. Methane is made up of four hydrogen nuclei and a carbon nucleus, which are all surrounded by a cloud of rapidly moving electrons. These electrons can also momentarily crowd to one side of the atom, giving it an instantaneous dipole IMF (Figure 1.11).

One thing to remember about instantaneous dipole IMFs is that in general, larger nonpolar molecules have more electrons; therefore, they can create a stronger IMF. The hydrocarbons (molecules that only contain hydrogen and carbon) are an excellent example of this. Methane ( $\text{CH}_4$ ) and propane ( $\text{C}_3\text{H}_8$ ) are relatively small, and their weak instantaneous dipole IMFs cause them to be gases under normal conditions; however, octane ( $\text{C}_8\text{H}_{18}$ ), the major constituent of gasoline, is large enough to allow for a strong enough instantaneous dipole IMF for it to be a liquid. Eventually, larger hydrocarbons with more than about 20 carbons become solids. The polymer polyethylene is made up essentially of large hydrocarbons and is used to create solid commercial products, such as plastic bags and drinking bottles.



## 2

## The Only True Aphrodisiac and Other Chemical Extremes

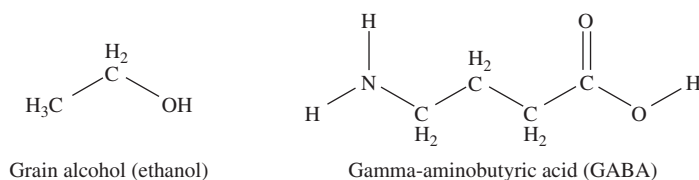
I think that most of us have looked at the “Guinness World Records” at some point, which is one example of our obsession with extremes: the biggest, the fastest, and so on. Believe it or not, even in chemistry, there are extremes. It is my pleasure to present some of the most intriguing to you.

### Death Is Its Withdrawal Symptom!

Though not widely known, alcohol is one of the few drugs for which withdrawal symptoms include death. Most people think drugs such as heroin or methamphetamine would have the worst withdrawal symptoms, since these substances are known to be highly addictive. Dramatic television and movie portrayals of heroin withdrawal symptoms make a great impression on the public as well. Oddly enough, people going through alcohol withdrawal are rarely portrayed in popular media, which is part of the reason most people do not understand the deadly nature of this type of withdrawal.

Why can withdrawal from alcohol be fatal? Consider that alcohol affects virtually all parts of the brain and is involved in a process that activates the nerve cells there. Although the effects of alcohol are complex, its action on *gamma-aminobutyric acid* (GABA) receptors in neurons has long been known to be significant. GABA is the main inhibitory neurotransmitter in the mammalian central nervous system. To put it simply, the presence of GABA prevents the ability of a nerve that contains GABA receptors to fire, thereby deadening it. Alcohol facilitates the inhibitory function of the GABA receptor and keeps the nerves from becoming stimulated, resulting in the euphoric feeling of intoxication (Figure 2.1).

Increased consumption of alcohol causes this numbing of nerve cells to spread, eventually affecting all parts of the brain. Alcohol initially inhibits the most complex brain functions; if consumption continues, it spreads to areas controlling the less complex functions. The first thing to go – the most complex part of the brain – is the cerebral cortex, which controls reasoning.



**Figure 2.1** The structures of ethanol and GABA.

Therefore, judgment is impaired. With more alcohol, the speech centers of the brain are slowed, resulting in a person slurring their words. Next, the brain area controlling movement and coordination is impaired, and the inebriated individual begins to stagger. If one keeps drinking, the neurons involved in controlling involuntary bodily functions such as breathing and heartbeat are affected, and death can occur.

For people who chronically drink large quantities of alcohol, over time the brain will try to compensate for this continual desensitization of neurons. In a process called *homeostasis*, the nerves of the brain become hyperactive to make up for the long-term deadening effect of habitual alcohol consumption. As a result of homeostasis, chronic alcoholics show reduced brain GABA levels and a decrease in GABA receptor sensitivity as an adaptation to the persistent presence of alcohol. If such a person stops drinking, brain GABA levels fall below normal and GABA activity declines during withdrawal. The resulting decrease in inhibitory function may contribute to symptoms of nervous system hyperactivity, which is associated with alcohol withdrawal. This change in brain chemistry takes some time, though, so here, we are talking about chronic alcohol abusers. In fact, it has been estimated that it would take a continual alcohol intake of roughly 100 g (equivalent to about 1 pt of liquor or 96 ounces of beer) per day for this effect to take place.

The abrupt cessation of long-term alcohol consumption produces symptoms associated with having a hyperactive brain, and this is called acute alcohol withdrawal. Mild withdrawal symptoms start as quickly as 6 hours after the initial decline from peak intoxication, and they include feelings of nervousness, anxiety, irritability, and emotional volatility. One to four days of not drinking alcohol can result in severe withdrawal symptoms including hallucinations called *delirium tremens* (DTs). These are horrible hallucinations, surprisingly not often portrayed in television and movies, and are sometimes described as the feeling of having bugs crawling all over one's skin. Those of you who have watched old cartoons may know the common joke where the alcoholic swears off drinking because they have seen something strange, such as a pink elephant. This is all related to the idea that people who are heavily addicted to alcohol tend to have hallucinations when undergoing withdrawals.

In addition to hallucinations, severe withdrawal symptoms can include grand mal seizures. One can literally have the equivalent of an epileptic seizure from

alcohol withdrawal, and it is these seizures that can cause death. The mortality rate among people who are actively having DTs is from 5% to 25%, which means that someone who is having hallucinations from alcohol withdrawal is in serious danger of dying. In addition, clinical data has shown that the likelihood and severity of these seizures increase with the number of past withdrawals.

What circumstances might lead to withdrawal-related death? Typically, death from alcohol withdrawal occurs when alcoholics are arrested or admitted to a hospital and they experience an abrupt removal from alcohol.<sup>1</sup> There are innumerable examples of this reported in the media. In 2009, a county in Montana was ordered to pay \$1.35 million for a case in which an 18-year-old died from alcohol withdrawal after being found shivering and unresponsive in a jail cell after being arrested. In another case, a 37-year-old woman went through severe alcohol withdrawal for 3 days after being incarcerated, and she did not receive treatment until she had already lost consciousness. She later died at a hospital. These cases are representative of the public's general lack of knowledge about the deadly nature of alcohol withdrawal. The uninformed are more likely apathetic toward severe symptoms. What would *you* do with someone who is coming off alcohol?

Besides alcohol, a class of sedatives called *benzodiazepines* (Valium® is a common example) work on GABA receptors in neurons, explaining the similarity of their nerve-numbing effect. In fact, benzodiazepines show cross-tolerance and cross-dependence with alcohol. Recent research suggests that benzodiazepines are likely to be the most effective agent for treating alcohol withdrawal symptoms. However, like alcohol, withdrawal from benzodiazepines can be lethal.

Benzodiazepines are commonly used for alcohol detoxification because the dose given can be easily controlled. Ones that may be utilized include the shorter-acting benzodiazepines, such as Serax® and Ativan®, and the longer-acting benzodiazepines, such as Librium® and Valium®. During a controlled withdrawal process, doctors typically employ a progressive decrease in benzodiazepines dosage over the time span of the entire withdrawal process.

To address the danger of grand mal seizures during alcohol withdrawal, doctors may employ antiseizure medications such as Carbamazepine. Furthermore, physicians may prescribe disulfiram (Antabuse®) or naltrexone (ReViaT®) to help prevent people from returning to drinking. Antabuse® combined with alcohol triggers very unpleasant effects including flushing, nausea, vomiting, and dizziness. Naltrexone reduces the alcoholic's craving for

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1 During the writing of this book, an acquaintance ended up having a seizure during the recovery from a minor surgery, most likely due to alcohol withdrawal. Anyone who regularly abuses alcohol should have a frank discussion with their doctor prior to an extended hospital stay. It could save their life!