

7.2.1: Biology- Biologically Active Exceptions to the Octet Rule

Lewis' octet theory correctly predicts formulas for nearly all ionic compounds and accounts for most covalent bonding schemes for biologically important molecules. But the ones that are exceptions are among the most biologically interesting compounds.

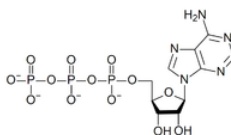
Lewis' theory concentrates on resemblances to noble-gas ns^2np^6 valence octets. Therefore it is most successful in accounting for formulas of compounds of the representative elements (especially in periods 1 and 2), whose distinguishing electrons are also s and p electrons. The octet rule is much less useful in dealing with compounds of the transition elements or inner transition elements, most of which involve some participation of d or f orbitals in bonding.

Even among the representative elements there are some interesting exceptions to the Lewis theory. These fall mainly into three categories:

1. **"Expanded Valence Shell"** compounds formed by elements in the third period and below which can accommodate more than an octet of electrons. Although elements such as Si, P, S, Cl, Br, and I obey the octet rule in many cases, under other circumstances they form more bonds than the rule allows because the third shell has s , p , and d orbitals.
2. **"Free Radicals"** which have unpaired electrons, like the key vertebrate biological messenger nitric oxide, NO, which plays a role in a variety of biological processes. The 1998 Nobel Prize in Medicine was awarded for discoveries concerning nitric oxide as a signalling molecule in the cardiovascular system.
3. **"Electron deficient"** compounds do not have enough electrons to achieve octets around all atoms, but still have stable molecules. They often contain Be, B, or Al.

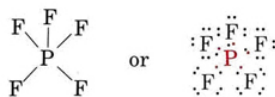
Expansion of Valence Shell

The typical structural formula for ATP (adenosine triphosphate) shows three single bonds and one double bond on the phosphorus atom, for a total of 5 electron pairs. This is possible because P has 3d orbitals as well as 3s and 3p orbitals to accommodate the electrons. The bonding is shown in the simple phosphate ion $[\text{PO}_4]^{3-}$:



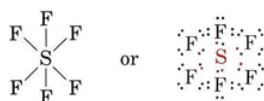
ATP

Other examples of molecules with more than an octet of electrons are phosphorus pentafluoride (PF_5) and sulfur hexafluoride (SF_6). Phosphorus pentafluoride is a gas at room temperature. It consists of PF_5 molecules in which each fluorine atom is bonded to the phosphorus atom. Since each bond corresponds to a shared pair of electrons, the Lewis structure is Expansion of the valence shell is impossible for an atom in the second period because there is no such thing as a $2d$ orbital. The valence ($n = 2$) shell of nitrogen, for example, consists of the $2s$ and $2d$ subshells only. Thus nitrogen can form NF_3 (in which nitrogen has an octet) but not NF_5 . Phosphorus, on the other hand, forms both PF_3 and PF_5 , the latter involving expansion of the valence shell to include part of the $3d$ subshell.



P is connected to two equally spaced F atoms below it and three equally spaced F atoms above it. The dot diagram shows that P has a total of ten electrons on its valence.

Instead of an octet the phosphorus atom has 10 electrons in its valence shell. Sulfur hexafluoride (also a gas) consists of SF_6 molecules. Its structure is



Sulfur bonded to six Fluorine that are equally spaced out from one another. The dot diagram shows that sulfur has 12 electrons in its valence shell.

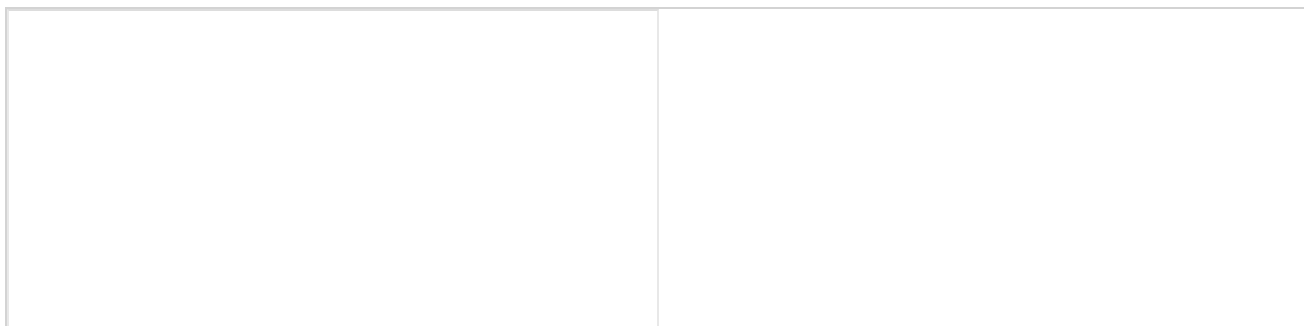
Here the sulfur atom has six electron pairs in its valence shell.

Free Radicals

Another exception to the octet rule occurs in molecules called **free radicals**. These molecules contain at least one unpaired electron, a clear violation of the octet rule. Free radicals play many important roles a wide range of applied chemistry fields, including biology and medicine.

Nitric Oxide

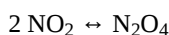
Nitric oxide, known as the 'endothelium-derived relaxing factor', or 'EDRF', is synthesized in the body from arginine and oxygen by various enzymes and by reduction of inorganic nitrate. It is released by the lining of blood vessels, and causes the surrounding muscle to relax, increasing blood flow.



During World War I, soldiers who handled nitroglycerin explosives were found to have low blood pressure. This led to the discovery that nitroglycerine serves as a vasodilator because it is converted to nitric oxide in the body. Sildenafil, popularly known by the trade name Viagra, stimulates erections primarily by enhancing signaling through the nitric oxide pathway in the penis. Nitric oxide therapy may in some cases save the lives of infants at risk for pulmonary vascular disease. As expected for a non-octet compound, nitric oxide is highly reactive (having a lifetime of a few seconds), yet diffuses freely across membranes. Appropriate levels of NO production are important in protecting an organ such as the liver from ischemic (constriction of blood vessels) damage.

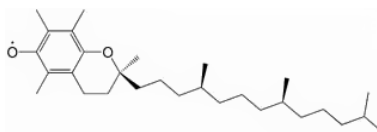
Nitrogen Dioxide

Nitrogen dioxide, NO_2 is another free radical which is the brown, toxic component of smog. It partially dimerizes to attain a Lewis octet:



Vitamin E

Free radical scavengers may be important anti-aging biomolecules. Free radicals are generated by several natural processes in the body, and if they aren't destroyed immediately, they can attack DNA and other critical molecules. It has been claimed that α -tocopherol (Vitamin E) rapidly accepts electrons from free radicals produced by the lipid peroxidation chain reaction, becoming the Vitamin E Free Radical.



Vitamin E Free Radical
and protecting DNA.

Note the similarity to the 7 electron **hydroxide free radical**, one of the damaging (but short lived) free radicals of the body:



Oxygen

The Lewis structure for Oxygen usually hides the fact that it is a "**diradical**", containing two unpaired electrons. This is sometimes cited as a serious flaw in Lewis bond theory, and was a major impetus for development of molecular orbital theory.

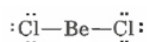
The paramagnetic character of oxygen was mentioned before, and is easily demonstrated by attraction of oxygen to an external magnet.

Electron Deficient Compounds

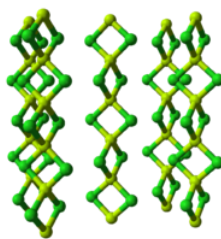
The elements beryllium, boron, and aluminum are notorious for forming "electron deficient" compounds (with fewer than the typical 8 valence electrons). This gives them special properties in synthetic biochemical and organic chemistry, but they almost always react to form species that obey the Lewis octet rule in biochemical systems.

Beryllium

A good example is Beryllium dichloride, BeCl_2 , which melts at 405°C and boils at 520°C . That compares with 714°C and 1412°C for magnesium chloride. Individual BeCl_2 molecules exist only in the gas phase above 750°C :

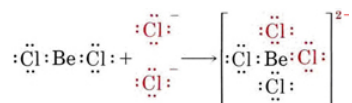


Instead of an octet, the valence shell of Be contains only *two* electron pairs. It is reactive because it does not have the octet, and upon cooling, forms molecules that do, where Cl atoms donate a pair of their non-bonding electrons to a neighboring Be atom so that they bridge two Be atoms, satisfying the valence of both:



But the extremely high toxicity of beryllium is probably due to ionic species, and the [pillsm.com/?a=7539 | Blood Beryllium Lymphocyte Proliferation Test] uses beryllium sulfate, a typical ionic compound of Be^{2+} (aq), or $\text{Be}(\text{H}_2)_4^{2-}$, to mimic the biological form of beryllium.

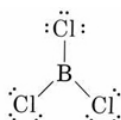
Beryllium may also acquire an octet by formation of "coordinate covalent bonds", accepting both electrons in the bond from another species. Thus BeCl_2 reacts with Cl^- ions or OH^- ions under normal conditions to form BeCl_4^{2-} or $\text{Be}(\text{OH})_4^{2-}$:



A BeCl_2 molecule reacts with two chlorine anions to give BeCl_4^{2-} with a complete octet set. The overall charge of the molecule is negative 2.

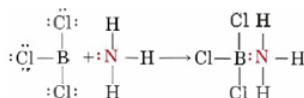
Boron

Similar arguments can be applied to boron trichloride, BCl_3 , which is a stable gas at room temperature. We are forced to write its structure as



A central B atom is single bonded to three chlorine atoms. The three chlorine atoms are 60 degrees from one another and form a triangular shape with boron in the center. The three pairs of unpaired electrons on chlorine are shown as dots.

in which the valence shell of boron has only three pairs of electrons. Molecules such as BeCl_2 and BCl_3 are referred to as **electron deficient** because some atoms do not have complete octets. BCl_3 reacts with NH_3 in the following way:



Again, the most stable boron compounds under normal conditions follow the Lewis rule: Boric acid, H_3BO_3 is traditionally used as an insecticide, notably against ants, fleas, and cockroaches, but it is as innocuous as salt to Humans, as are borates, which contain the BO_4^{2-} ion.

Aluminum

Aluminum Chloride is a low melting covalent compound which exists as AlCl_3 only in the gas phase. Because it has only 6 electrons in its Lewis structure, it reacts with electron pair donors like water:



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